Levator ani muscle avulsion following childbirth

Assessment and impact on pelvic floor dysfunction

Kim Wilhelmina Martina van Delft

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Contents

1

Introduction and aims

Introduction and aims

Pelvic floor dysfunction (PFD) includes pelvic organ prolapse (POP), bladder, bowel and sexual dysfunction. PFD is a major health care problem, and is seen in 40% of women attending gynaecology clinics[1]. Although it is not a life-threatening condition, it affects women's quality of life. Treatment for these women can either be conservative or surgical. The necessity of treatment varies among women and is guided by the bothersomeness of their symptoms. As our population is ageing, an increase in the number of women suffering from PFD can be expected. It has been estimated that over the next 30 years, the demand for treatment of PFD will increase with 45%[2]. However, PFD is still underestimated, because women believe that it is part of the ageing process. Furthermore, there seems to be a great taboo, as signs and symptoms of PFD are often embarrassing. There is evidence that younger women are more bothered by symptoms of PFD than older women[1], suggesting that postnatal women are more likely to complain of PFD.

Vaginal childbirth is the most common underlying aetiological factor in the development of PFD. However, there are many other unexpected post-childbirth issues which women have to deal with. As most attention and care is focused on the newborn baby, women with PFD can be neglected. A Cochrane review has suggested the implementation of pelvic floor muscle training during and after pregnancy to prevent urinary and faecal incontinence[3], followed by national and international guidelines. Subsequently, it has been recommended to target women at higher risk of postnatal PFD and to refer them for supervised pelvic floor muscle training[3]. The main muscle being responsible for pelvic organ support and prevention of PFD is the levator ani muscle (LAM), which is trained when performing pelvic floor muscle exercises.

This thesis describes a prospective longitudinal cohort study on the pelvic floor of primiparous women, carried out in urban London (United Kingdom). The thesis aims at increasing the understanding of PFD in relation to childbirth. The focus will be on LAM avulsion sustained during parturition, which may lead to signs and symptoms of PFD. Furthermore, different assessment techniques of LAM avulsion will be evaluated.

The levator ani muscle

The pelvic floor is a musculotendineous sheet that spans the pelvic outlet. The pelvic floor provides support for the urogenital organs and the anorectum, exiting the pelvis through their respective foramens. It mainly consists of the symmetrically paired LAM. The LAM is a broad muscular sheet of variable thickness attached to the internal surface of the true pelvis. It is broadly accepted that the LAM is subdivided into parts according to their attachments. The pubococcygeus muscle is the most

medial part of the LAM[4,5]. The puborectalis muscle is a subdivision of the pubococcygeus muscle and is the most caudal component of the LAM. It is situated cephalad to the deep level of the external anal sphincter, from which it is inseparable posteriorly[6]. The LAM has the ability to maintain constant tone, except during voiding and defaecation. The LAM can contract quickly, for example during a sneeze to maintain continence[7]. However, the LAM has to distend considerably during parturition to give birth[8] and then regress to resume normal functioning.

The LAM and childbirth

Obstetric trauma is the main aetiological factor in the development of LAM avulsion[8,9,10]. Trauma can occur by stretching of the pubococcygeus muscle and by disconnection of its insertion from the inferior pubic ramus and the pelvic side wall[8]. A recent review found a 13-36% incidence of LAM avulsion following the first vaginal delivery[11]. The highest incidence of LAM avulsion (39.5%) was found in women scanned in the early postpartum period[12]. The authors attributed this to the difficulty in differentiating fluid collections from LAM avulsion[12]. Acute LAM avulsion can be diagnosed in the labour ward when it is associated with a large vaginal tear[13].

Previously described risk factors for LAM avulsion are operative vaginal delivery[14], forceps delivery[10,15,16], obstetric anal sphincter injuries[10], episiotomy[10], prolonged second stage of labour[10,16,17], increased fetal head circumference[17] and increased maternal age[10]. On the other hand, epidural analgesia is thought to be a protective factor[16]. Shek et al tried to predict LAM avulsion antepartum, without successful results[18]. Two prediction models for LAM avulsion have been developed in relation to symptomatic PFD in older women presenting to a urogynaecology clinic[19,20], but no prediction model exists for LAM avulsion in relation to childbirth.

LAM avulsion and pelvic floor dysfunction

As previously stated, PFD can affect many women during their life and the main contributor is vaginal delivery. Furthermore, vaginal delivery is the main contributor to damage to the LAM, in the form of LAM avulsion or ballooning of the hiatus[21,22,23,24,25]. Ballooning is excessive distensibility of the levator hiatus, which is often irreversible and can be secondary to LAM avulsion[23].

A community based survey using validated questionnaires on POP in The Netherlands revealed that 12.1% of women aged 45-85 years reported feeling and/or seeing vaginal bulging[26]. However, 40% of the whole population was found to have at least POP stage II prolapse using the validated POP-Q system as suggested by the International Continence Society[26,27], implying that not all anatomical prolapse lead to symptoms. The life time risk for a woman to undergo POP surgery is 11-20%[28,29,30]. Anatomical POP recurrence in the operated compartment occurs in 40% of women, with a 9.7% re-operation rate due to symptomatic recurrence[31]. As most recurrences

occur in the anterior compartment[31], the association between cystocele recurrence and LAM avulsion has been evaluated. Dietz et al and Weemhoff et al found anatomical cystocele recurrence in 40% and 50% of women respectively, which was strongly associated with complete LAM avulsion, revealing a relative risk of 2.9 and 2.4 respectively[32,33]. However, both retrospective studies confirmed that not all women with anatomical recurrence were symptomatic[32,33], again emphasising the importance of validated subjective assessment. In addition to POP[21,22], LAM avulsion has been associated with a reduction in pelvic floor muscle strength (PFMS)[34,35,36] and an increased vaginal hiatus[24,37,38].

Although the literature is ambiguous, these anatomical changes could possibly lead to symptoms of PFD. Increased postpartum faecal incontinence has been found in women with LAM avulsion[39]. Furthermore, the association between faecal incontinence and LAM avulsion has been shown in older women[40,41], however no association was found by others[42]. Postpartum urinary incontinence has been associated with LAM avulsion[9,43]. However, no association between urinary incontinence and LAM avulsion was found in patients with symptomatic prolapse[19,44,45]. Although sexual function is known to deteriorate following childbirth[46], it has not been related to LAM avulsion. However, to date, none of the studies have utilised validated questionnaires to evaluate PFD related to LAM avulsion before and after childbirth.

Diagnosis of LAM avulsion using digital assessment

In 1943, Howard Gainey performed a large study in postpartum women and he was the first one to describe palpable defects in the pelvic floor muscles after childbirth[47]. Shortly thereafter, Arnold Kegel introduced pelvic floor muscle exercises ('Kegel-exercises') to improve PFMS[48]. Assessment of the LAM is still carried out by performing digital vaginal examination. PFMS can be palpated during voluntary contraction[49]. The Modified Oxford Scale is used to evaluate PFMS, which is found to have poor inter-rater reliability[50,51]. Furthermore, digital vaginal examination can be used to evaluate the site of LAM attachment to the pubic bone[52,53]. This is a reliable technique, with a substantial learning curve[52,53]. When comparing digital assessment of the LAM with magnetic resonance imaging (MRI)[52] and transperineal ultrasound (TPUS)[53], poor positive agreement was found, suggesting that digital assessment underestimates LAM avulsion.

Diagnosis of LAM avulsion using imaging techniques

In recent years with advances in imaging techniques, the pelvic floor has become a focus of considerable research. Imaging in the field of urogynaecology has gained a lot of interest and clinicians started to use it in their outpatient clinics. Currently, three imaging techniques are used to assess the LAM, namely MRI[52], transperineal ultrasound (TPUS)[54] and endovaginal ultrasound (EVUS)[5].

MRI was the first method to evaluate the LAM[55] and was therefore perceived to be the gold standard in the diagnosis of LAM avulsion. However, MRI has a number of shortcomings such as costs, accessibility and inability to use it in women with claustrophobia or women with metallic implants. The disadvantages of MRI can be avoided by using ultrasound imaging of the pelvic floor to assess the LAM. The advantage over MRI is that TPUS is easy to use in outpatient settings, and it is at no additional costs after the ultrasound machine is obtained. Since then TPUS has been used throughout the world and various studies have been published including reliability analyses[11].

Using TPUS, volume acquisition is performed at rest, at maximum pelvic floor muscle contraction and at maximum Valsalva manoeuvre. During post processing, all acquired scans can be manipulated to evaluate the LAM in the plane of the minimal hiatal dimensions[56]. Detection of LAM avulsion is possible using 2D TPUS[57]. However, most researchers and clinicians use 3D and 4D TPUS, because reliability and repeatability seem to be better[11]. Hiatus measurements can be performed to determine the size of the levator hiatus in the rendered image[56]. In this image, LAM avulsion can be diagnosed and the unilateral gap between the levator and the urethra (levator urethra gap) can be used to identify LAM avulsion for which cut-off points have been suggested[58]. However, to diagnose LAM avulsion it has been advised to use maximum pelvic floor contraction on tomographic ultrasound imaging[54,59]. Maximum valsalva manoeuvre can be used to identify an enlarged hiatus, and cut-off points for the association with symptoms and signs of POP have been suggested[23].

High resolution 3D endovaginal ultrasound (EVUS) is a relatively new ultrasound technique to image the LAM, which is easy to use in outpatient settings, and again at no additional costs besides machine acquisition costs. The downside is that dynamic studies are not possible because the acquisition of an image takes a minute and it is not possible to maintain a contraction at the same intensity during one minute. Therefore, images are acquired at rest. EVUS provides detailed information on pelvic floor structures, and images have good to very good correlation in cadaveric sections for pelvic floor muscle subdivisions[4,5]. These subdivisions can reliably be evaluated by different raters[4]. Post processing of the images acquired on EVUS can be performed by tilting the 3D volume. This facilitates the visualisation of the different structures and allows the evaluation of the LAM in the plane of the minimal hiatal dimensions[60]. Standardisation of assessment and measurements of the LAM in nulligravid women have been studied[60]. Good to excellent correlation was found for the hiatus measurements[60,61]. However, correlation of measurements does not prove whether the measurements actually agree, so limits of agreement are lacking[62]. Recently, the association between LAM avulsion and POP has been made using EVUS[25]. However, EVUS has not been used to evaluate the LAM in relation to childbirth.

Schwertner-Tiepelmann et al suggested that further comparative studies between TPUS and other imaging techniques are needed[11]. To be able to compare ultrasound techniques, it is important to standardise techniques. Comparisons have been made between TPUS and MRI[63,64,65]. Hiatus measurements revealed good correlation[63,64,65] and acceptable limits of agreement[62,63,64]. The only paper evaluating detection rates of LAM avulsion on MRI and TPUS concluded substantial agreement[65]. Because there seemed to be a significant difference regarding the extent of LAM avulsion, their results were questioned in a letter[65,66]. TPUS has never been compared to EVUS. And furthermore, EVUS has never been compared to digital assessment of LAM avulsion.

The aims of this thesis are:

To identify factors that could influence recruitment in a prospective longitudinal study involving pregnant women (Chapter 2).

- To evaluate inter-rater reliability of digital assessment of levator ani muscle strength and attachment to the pubic bone (Chapter 3).
- To assess intra- and inter-rater reliability of levator ani muscle biometry and avulsion using 3D high frequency endovaginal ultrasound (Chapter 4).
- To estimate diagnostic accuracy between transperineal and endovaginal ultrasound in assessing levator ani muscle biometry and avulsion (Chapter 5).
- To determine agreement of digital assessment of the levator ani muscle with transperineal and endovaginal ultrasound (Chapter 3, 5, 6).
- To evaluate the relationship between haematomas and levator ani muscle avulsion using endovaginal ultrasound and palpation early and late postpartum (Chapter 6).
- To establish the true incidence of levator ani muscle avulsion in primipara and to develop a clinically applicable risk prediction model (Chapter 7).
- To establish the relationship between postpartum levator ani muscle avulsion and signs and/or symptoms of pelvic floor dysfunction three months postpartum (Chapter 8,9).
- To establish the natural history of levator avulsion within one year following childbirth and the relation with signs and symptoms of pelvic floor dysfunction (Chapter 9).
- To provide recommendations for the assessment of the levator ani muscle and the management of levator ani muscle avulsion and pelvic floor dysfunction in relation to childbirth (Chapter 10).

References

1. Dua A, Radley S, Jones G, Farkas A. The personal impact of pelvic floor symptoms and their relationship to age. Int Urogynecol J 2013. doi 10.1007/s00192-013-2167-y
2. Luber KM, Boero S, Choe JY. The demographics of pelvic floor disorders: current observations and future projections. Am J Obstet Gynecol 2001;184:1496-501
3. Boyle R, Hay-Smith EJ, Cody JD, Mørkved S. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database Syst Rev 2012;10:CD007471. doi: 10.1002/14651858.CD007471.pub2
4. Shobeiri SA, Leclaire E, Nihira MA, Quiroz LH, O'Donoghue D. Appearance of the levator ani muscle subdivisions in endovaginal three-dimensional ultrasonography. Obstet Gynecol 2009;114:66-72
5. Shobeiri SA, Rostaminia G, White D, Quiroz LH. The determinants of minimal levator hiatus and their relationship to the puborectalis muscle and the levator plate. BJOG 2013;120:205-211
6. Thakar R, Sultan AH. Anal endosonography and its role in assessing the incontinent patient. Best Pract Res Clin Obstet Gynaecol 2004;18:157-73
7. Ashton-Miller JA, DeLancey JO. Functional anatomy of the female pelvic floor. Ann N Y Acad Sci 2007;1101:266–96
8. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
9. Dietz HP, Lanzarone V. Levator trauma after vaginal delivery. Obstet Gynecol 2005;106:707–712
10. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
11. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
12. Albrich SB, Laterza RM, Skala C, Salvatore S, Koelbl H, Naumann G. Impact of mode of delivery on levator morphology: a prospective observational study with three-dimensional ultrasound early in the postpartum period. BJOG 2012;119:51-60
13. Dietz HP, Gillespie AV, Phadke P. Avulsion of the pubovisceral muscle associated with large vaginal tear after normal vaginal delivery at term. Aust N Z J Obstet Gynaecol 2007;47:341-4
14. Chan SS, Cheung RY, Yiu AK, Lee LL, Pang AW, Choy KW, et al. Prevalence of levator ani muscle injury in Chinese women after first delivery. Ultrasound Obstet Gynecol 2012;39:704-9
15. Krofta L, Otcenasek M, Kasikova E, Feyereisl J. Pubococcygeus–puborectalis trauma after forceps delivery: evaluation of the levator ani muscle with 3D/4D ultrasound. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1175-81
16. Shek K, Dietz HP. Intrapartum risk factors for levator trauma. BJOG 2010;117:1485-92
17. Valsky DV, Lipschuetz M, Bord A, Eldar I, Messing B, Hochner-Celnikier D, et al. Fetal head circumference and length of second stage of labor are risk factors for levator ani muscle injury, diagnosed by 3-dimensional transperineal ultrasound in primiparous women. Am J Obstet Gynecol 2009;201:91.e1–7
18. Shek KL, Dietz HP. Can levator avulsion be predicted antenatally? Am J Obstet Gynecol 2010;202:586.e1–6
19. Dietz HP, Kirby A. Modelling the likelihood of levator avulsion in a urogynaecological population. Aust N Z J Obstet Gynaecol 2010;50:268-72
20. Lammers K, Fütterer JJ, Inthout J, Prokop M, Vierhout ME, Kluivers KB. Correlating signs and symptoms with pubovisceral muscle avulsions on magnetic resonance imaging. Am J Obstet Gynecol 2013;208:148.e1-7
21. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, Hussain H, Umek W, Hsu Y, Ashton-Miller JA. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
22. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
23. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80
24. Dietz HP, Franco AVM, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand 2012;91:211-4

25. Rostaminia G, White D, Hegde A, Quiroz LH, Davila GW, Shobeiri SA. Levator ani deficiency and pelvic organ prolapse severity. Obstet Gynecol 2013;121:1017-24
26. Slieker-ten Hove MC, Pool-Goudzwaard AL, Eijkemans MJ, Steegers-Theunissen RP, Burger CW, Vierhout ME. The prevalence of pelvic organ prolapse symptoms and signs and their relation with bladder and bowel disorders in a general female population. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1037-45
27. Bump RC, Mattiasson A, Bø K, Brubaker LP, DeLancey JO, Klarskov P, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 1996;175:10-7
28. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-6
29. Smith FJ, Holman CD, Moorin RE, Tsokos N. Lifetime risk of undergoing surgery for pelvic organ prolapse. Obstet Gynecol 2010;116:1096-100
30. de Boer TA, Slieker-Ten Hove MC, Burger CW, Kluivers KB, Vierhout ME. The prevalence and factors associated with previous surgery for pelvic organ prolapse and/or urinary incontinence in a cross-sectional study in The Netherlands. Eur J Obstet Gynecol Reprod Biol 2011;158:343-9
31. Miedel A, Tegerstedt G, Mörlin B, Hammerström M. A 5-year prospective follow-up study of vaginal surgery for pelvic organ prolapse. Int Urogynecol J 2008;19:1593-601
32. Dietz HP, Chantarasorn V, Shek KL. Levator avulsion is a risk factor for cystocele recurrence. Ultrasound Obstet Gynecol 2010;36:76-80
33. Weemhoff M, Vergeldt TFM, Notten K, Serroyen J, Kampschoer PHNM, Roumen FJME. Avulsion of puborectalis muscle and other risk factors for cystocele recurrence: a 2-year follow-up study. Int Urogynecol J 2012;23:65-71
34. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-6
35. Steensma AB, Konstantinovic ML, Burger CW, de Ridder D, Timmerman D, Deprest J. Prevalence of major levator abnormalities in symptomatic patients with an underactive pelvic floor contraction. Int Urogynecol J 2010;21:861-7
36. Dietz HP, Shek KL, Chantarasorn V, Langer SE. Do women notice the effect of childbirth-related pelvic floor trauma? Aust N Z J Obstet Gynaecol 2012;52:277-81
37. Abdool Z, Shek KL, Dietz HP. The effect of levator avulsion on hiatal dimension and function. Am J Obstet Gynecol 2009;201:89.e1-5
38. Shek KL, Dietz HP. The effect of childbirth on hiatal dimensions. Obstet Gynecol 2009;113:1272-8
39. Heilbrun ME, Nygaard IE, Lockhart ME, Richter HE, Brown MB, Kenton KS, et al. Correlation between levator ani muscle injuries on magnetic resonance imaging and fecal incontinence, pelvic organ prolapse, and urinary incontinence in primiparous women. Am J Obstet Gynecol 2010;202:488.e1-e6
40. Weinstein MM, Pretorius DH, Jung SA, Nager CW, Mittal RK. Transperineal 3-dimensional ultrasound imaging for detection of anatomical defects in the anal sphincter complex muscles. Clin Gastroenterol Hepatol 2009;7:205-11
41. Lewicky-Gaupp C, Brincat C, Yousuf A, Patel AD, Delancey JO, Fenner DE. Fecal incontinence in older women: are levator ani defects a factor? Am J Obstet Gynecol 2010;202:491.e1-e6
42. Chantarasorn V, Shek KL, Dietz HP. Sonographic detection of puborectalis muscle avulsion is not associated with anal incontinence. Aust N Z J Obstet Gynaecol 2011;51:130-5
43. DeLancey JO, Kearney R, Chou Q, Speights S, Binno S. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. Obstet Gynecol 2003;101:46-53
44. Dietz HP, Kirby A, Shek LK, Bedwell PJ. Does avulsion of the puborectalis muscle affect bladder function? Int Urogynecol J 2009;20:967-72
45. Morgan DM, Cardoza P, Guire K, Fenner DE, DeLancey JOL. Levator ani defect status and lower urinary tract symptoms in women with pelvic organ prolapse. Int Urogynecol J 2010;21:47-52
46. Leeman LM, Rogers RG. Sex after childbirth: postpartum sexual function. Obstet Gynecol 2012;119:647-55
47. Gainey HL. Post-partum observation of pelvic tissue damage. Am J Obstet Gynecol 1943;46:457-66
48. Kegel AH. Prospective resistance exercise in the functional restoration of the perineal muscles. Am J Obstet Gynecol 1948;56:238-48

49. Laycock J. Clinical evaluation of the pelvic floor. In Pelvic floor re-education, Principles and practice, Schüssler B, Laycock J, Norton PA, Stanton SL, eds. Springer-Verlag: London, 1994;42–48
50. Bø K, Finckenhagen HB. Vaginal palpation of pelvic floor muscle strength: inter-test reproducibility and comparison between palpation and vaginal squeeze pressure. Acta Obstet Gynecol Scand 2001;80:883-7
51. Ferreira CH, Barbosa PB, de Oliveira Souza F, Antônio FI, Franco MM, Bø K. Inter-rater reliability study of the modified Oxford Grading Scale and the Peritron manometer. Physiotherapy 2011;97:132-8
52. Kearney R, Miller JM, DeLancey JO. (in plaats van Kearney R, Miller JM, and DeLancey JO. Interrater reliability and physical examination of the pubovisceral portion of the levator ani muscle, validity comparisons using MR imaging. Neurourol Urodyn 2006;25:50-4
53. Dietz HP, Shek C. Validity and reproducibility of the digital detection of levator trauma. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1097-101
54. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
55. Strohbehn K, Ellis JH, Strohbehn JA, DeLancey JO. Magnetic resonance imaging of the levatorani with anatomic correlation. Obstet Gynecol 1996;87:277-85
56. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-5
57. Dietz HP, Shek KL. Levator defects can be detected by 2D translabial ultrasound. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:807-11
58. Dietz HP, Abbu A, Shek KL. The levator-urethra gap measurement: a more objective means of determining levator avulsion? Ultrasound Obstet Gynecol 2008;32:941-5
59. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30
60. Santoro GA, Wieczorek AP, Stankiewicz A, Woźniak MM, Bogusiewicz M, Rechberger T. High-resolution three-dimensional endovaginal ultrasonography in the assessment of pelvic floor anatomy: a preliminary study. Int Urogynecol J 2009;20:1213-22
61. Santoro GA, Wieczorek AP, Shobeiri SA, Mueller ER, Pilat J, Stankiewicz A, et al. Interobserver and interdisciplinary reproducibility of 3D endovaginal ultrasound assessment of pelvic floor anatomy. Int Urogynecol J 2011;22:53-9
62. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 2003;22:85-93
63. Kruger JA, Heap SW, Murphy BA, Dietz HP. Pelvic floor function in nulliparous women using three-dimensional ultrasound and magnetic resonance imaging. Obstet Gynecol 2008;111:631-8
64. Majida M, Braekken IH, Bø K, Benth JS, Engh ME. Validation of three-dimensional perineal ultrasound and magnetic resonance imaging measurements of the pubovisceral muscle at rest. Ultrasound Obstet Gynecol 2010;35:715-22
65. Zhuang RR, Song YF, Chen ZQ, Ma M, Huang HJ, Chen JH, et al. Levator avulsion using a tomographic ultrasound and magnetic resonance-based model. Am J Obstet Gynecol 2011;205:232.e1-8
66. Van Delft KW, Thakar R, Sultan AH. Levator avulsion using a tomographic ultrasound and magnetic resonance-based model. Am J Obstet Gynecol 2012;206:e7

2

Recruitment of pregnant women in research: Experience from a prospective study

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Summary

The aim was to identify factors that could influence recruitment in a prospective longitudinal study involving pregnant women.

269 nulliparous women were required for a prospective longitudinal study to establish the prevalence of levator ani muscle defects during childbirth. The project was explained verbally and potential participants were given an information leaflet. When eligible and interested, they provided their contact details to enquire if they were willing to participate.

Out of 1473 women approached, 269 (18.3%) agreed to participate and 1043 (70.8%) declined. 420 women (40.3%) did not provide a reason for non-participation. Most often mentioned reasons were 'being too busy', 'other pregnancy problems', 'no additional (internal) examination', 'moving (abroad)', and 'husband'.

Women from different ethnicities and age groups gave a wide variety of reasons for non-participation. This information can now be used by researchers recruiting women for comparable studies, to enhance recruitment and participation of eligible patients.

Introduction

Recruitment and retention in longitudinal studies poses a challenge to successful completion of trials. Trials frequently fail to recruit the number of participants required or require extensions of the recruitment period[1,2]. Consequently, this places financial constraints and delays completion and implementation in clinical practice[2]. Furthermore, if in a clinical trial the target sample size is not achieved, it will have less statistical power to convincingly demonstrate potentially important differences, which might make the results less useful or not at all applicable in clinical practice[2]. In addition, it will not improve practice and wastes the contribution of participants who already participated[2]. Researchers have an ethical obligation especially when invasive tests are performed to ensure completion of the study. Failure to do so would imply that subjects have been unnecessarily exposed to futile investigations. Nevertheless, difficulty in obtaining a sample is not justification for failure to study a hard-to-enrol population[3].

Studies comparing different recruitment strategies are largely missing[1]. Despite this, many trials are conducted. But, do researchers themselves think of a best way to recruit in each individual study? The focus group discussions used by Brown et al have elucidated different approaches and experiences of recruiters actively working in health research[4].

Many prospective longitudinal studies are conducted in pregnant women, who are potentially vulnerable because of possible effects on the pregnancy and baby[5].

The aim of this study was to identify factors that could influence recruitment in a prospective longitudinal study involving pregnant women.

Methods

Between January 2011 and May 2012 nulliparous women were approached to participate in a prospective longitudinal study in Croydon University Hospital, London, United Kingdom. The aim of the parent study was to establish the prevalence of levator ani muscle defects during childbirth and to correlate these with pelvic floor symptoms and pelvic floor muscle strength. The protocol involved four different visits: at 36 weeks of gestation, within 3 days after delivery, three months and one year following delivery. The inclusion criteria included a singleton pregnancy, maternal age $>$ 18 years, no previous history of pregnancy of more than 20 weeks gestation, and being able to read and understand English.

Women were approached by a dedicated researcher, in the waiting area of the antenatal clinics, parent craft classes, breastfeeding classes, and the antenatal ward. During the initial contact, women were informed about the project and invited

to participate. They were informed that they would continue to receive routine care if they decided not to participate. Recruited subjects did not receive financial compensation for their participation, apart from reasonable travel expenses. When eligible women showed an interest in the primary study, they were given an information leaflet describing the study, and their contact details were collected. Subsequently, these women were contacted by telephone to enquire whether they were interested in the primary study. If women met the inclusion criteria and were interested in participating, a convenient appointment was scheduled in the ante natal clinics of the hospital. In the majority of cases, a letter was sent out to confirm the appointment, and a phone call was made the day before to remind them of their appointment. If they did not wish to participate, they were asked to state the reasons. During the first visit at 36 weeks of gestation, the consent form to participate in the primary study was signed and they were asked to complete questionnaires relating to bowel, bladder and vaginal symptoms. Subsequently, the participant underwent endovaginal and transperineal ultrasonography. Ethnicity of all approached women was obtained from the electronic database (Protos Evolution 3.5), which contains pregnancy and childbirth related information of all pregnant women registered in Croydon University Hospital.

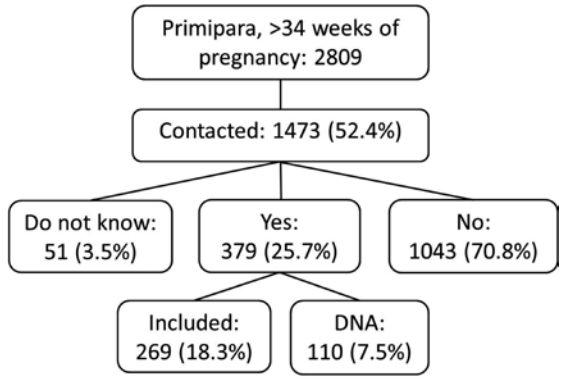
In this study we describe the recruitment process of the primary study of levator ani defects, for which a power calculation revealed that 265 primiparous women were required. The primary study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87).

Results

During the recruitment period, 2809 women over 18 years of age delivered their first baby over 34 weeks of gestation in Croydon University Hospital (Figure 1). Their median age was 29 (range 18-46) years. 1473 of 2809 women (52.4%) provided contact details to the researcher. When recruitment was completed, 3.5% of the women (n=51/1473) were undecided or were less than 34 weeks of gestation (when participation was confirmed). 25.7% (n=379/1473) stated they wished to participate, of whom 110 (110/1473=7.5%) did not attend their first appointment. Their median age was 31 years (range 18-45). The median age of 18.3% of women who attended their first appointment and were consented was 28 years (range 18-40), while the median age of 70.8% of women who did not wish to participate was 28 years (range 15-49).

Table 1 provides a distribution of the different ethnicities of the whole group of women as recorded in Protos Evolution 3.5. The ethnicities of the women that delivered in the recruitment period were similar to the ethnicities of the participating and non-participating women (Table 1).

Figure 1 Flowchart recruitment



DNA = did not attend appointment

Table 1 Breakdown of ethnicity of participants and non-participants

Ethnicity	Primigravid, delivered > 34 weeks (n = 2809)	Declined, all ethnic groups (n = 1043)	DNA, all ethnic groups (n = 110)	Inclusions, all ethnic groups (n = 269)
White	1282 (45.6%)	458 (43.9%)	50 (45.4%)	140 (52%)
Asian	533 (19.0%)	207 (19.8%)	13 (11.8%)	40 (14.9%)
Mixed	88 (3.1%)	28 (2.7%)	6 (5.5%)	17 (6.3%)
Black	680 (24.2%)	218 (20.9%)	37 (33.6%)	63 (23.4%)
Other	226 (8.0%)	132 (12.7%)	4 (3.6%)	9 (3.3%)

Table 2 demonstrates the reasons stated by approached women who declined participation. 11.4% (n=119) of the approached women did not meet the inclusion criteria when confirming interest in participating in the trial. 6.7% (n=70) were not eligible in the first place, because they were under 18 (n=27, 2.6%), they could not speak or read English (n=22, 2.1%), or they were not in their first pregnancy (n=21, 2.0%). 4.7% (n=49) were eligible in the initial discussion in the antenatal clinics, but when having the telephone conversation to investigate if they wanted to take part, they were not eligible anymore. This mainly occurred in women approached while waiting for their first trimester scan: miscarriage (n=39, 3.7%), expecting twins (n=4, 0.4%), not pregnant (n=3, 0.3%), and termination of pregnancy (n=3, 0.3%).

Table 2 Reasons for non-participation

Reason non-participation	Declined (n = 1043)
No reason provided	420 (40.3%)
Delivered before participation	145 (13.9%)
Did not meet inclusion criteria	119 (11.4%)
Too busy	80 (7.7%)
Other pregnancy problems	64 (6.2%)
Incorrect contact details	55 (5.3%)
No additional (internal) examination	49 (4.7%)
Moving (abroad)	44 (4.2%)
Husband	29 (2.8%)
Not delivering in Croydon University Hospital	27 (2.6%)
No research	9 (0.9%)
Midwife does not appreciate participation	1 (0.1%)
No long-term follow-up	1 (0.1%)

To analyse reasons for non-participation and age, patients were divided into different age groups. Table 3 shows reasons for non-participation related to age-groups. Women between 31 and 35 years of age mentioned "being too busy" more often (n=25, 31%) than younger women. Women under 25 years of age acknowledged pregnancy problems less often in their consideration to participate (n=12, 19%). Incorrect contact details were more common among women under the age of 25 (n=26, 47%). Internal examinations were more often seen as a deterrent by women between 31 and 35 years of age (n=12, 31%). Women between 31 and 35 years of age were more likely to move (abroad) (n=16, 36%). The husband's opinion was an important reason for women between 18 and 30 years of age (n=24, 82%). Women between 26 and 30 years of age were more likely to have antenatal appointments and their delivery in a different hospital (n=13, 48%).

Table 4 provides an overview of reasons for non-participation related to different ethnic backgrounds. White women mentioned "being too busy" more often (n=42, 53%), as compared to Asian (n=12, 15%) and other women (n=7, 9%). Compared to Black women (n=6, 9%), more White (n=31, 48%) and Asian women (n=15, 27%) acknowledged other pregnancy problems in their consideration to participate. Incorrect contact details were more common among women from other ethnicities (n=15, 27%). Internal examinations were more often seen as a deterrent by Asian,

Table 3 Reasons non-participation related to age

Reason non-participation	All age groups n=1043	Age < 18 (n=27, 2.6%)	Age Unknown (n=16, 1.5%)	Age 18-25 (n=335,32.1%)	Age 26-30 (n=355,34.0%)	Age 31-35 (n=206,19.8%)	Age > 36 (n=104,10.0%)
No reason provided	420 (40.3%)		8 (1.9%)	150 (35.7%)	148 (35.2%)	82 (19.5%)	32 (7.6%)
Delivered before participation	145 (13.9%)		3 (2.1%)	52 (35.9%)	46 (31.7%)	25 (17.2%)	19 (13.1%)
Did not meet inclusion criteria	119 (11.4%)	27 (22.7%)	1 (0.8%)	26 (21.8%)	30 (25.2%)	15 (12.6%)	20 (16.8%)
Too busy	80 (7.7%)		1 (1.3%)	21 (26.3%)	23 (28.8%)	25 (31.3%)	6 (12.5%)
Other pregnancy problems	64 (6.2%)		0	12 (18.8%)	29 (45.3%)	13 (20.3%)	10 (15.6%)
Incorrect contact details	55 (5.3%)		0	26 (47.3%)	19 (34.5%)	6 (10.9%)	4 (7.3%)
No additional (internal) examination	49 (4.7%)		1 (2.0%)	13 (26.5%)	16 (32.7%)	15 (30.6%)	4 (8.2%)
Moving (abroad)	44 (4.2%)		0	8 (18.2%)	16 (36.4%)	16 (36.4%)	4(9.1%)
Husband	29 (2.8%)		1 (3.4%)	10 (34.5%)	14 (48.3%)	4 (13.8%)	0
Not delivering in Croydon University Hospital	27 (2.6%)		0	9 (33.3%)	13 (48.1%)	4 (14.8%)	1 (3.7%)
No research	9 (0.9%)		1 (11.1%)	6 (66.7%)	1 (11.1%)	1 (11.1%)	0
Midwife does not appreciate it	1 (0.1%)		0	1 (100%)	0	0	0
No long-term follow-up	1 (0.1%)		0	1 (100%)	0	0	0

Table 4 Reasons non-participation related to ethnicity

Reason non-participation	All ethnic groups (n=1043)	White (n=458, 43.9%)	Asian (n=207, 19.8%)	Mixed (n=28, 2.7%)	Black (n=218, 20.9%)	Other (n=132, 12.7%)
No reason provided	420 (40.3%)	215 (51.2%)	80 (19.0%)	11 (2.6%)	80 (19.0%)	34 (8.1%)
Delivered before participation	145 (13.9%)	55 (37.9%)	26 (17.9%)	4 (2.8%)	39 (26.9%)	21 (14.5%)
Did not meet inclusion criteria	119 (11.4%)	43 (36.1%)	16 (13.4%)	3 (2.5%)	37 (31.1%)	20 (16.8%)
Too busy	80 (7.7%)	42 (52.5%)	12 (15.0%)	3 (3.8%)	16 (20.0%)	7 (8.8%)
Other pregnancy problems	64 (6.2%)	31 (48.4%)	17 (26.6%)	4 (6.3%)	6 (9.4%)	6 (9.4%)
Incorrect contact details	55 (5.3%)	22 (40.0%)	5 (9.1%)	1 (1.8%)	12 (21.8%)	15 (27.3%)
No additional (internal) examination	49 (4.7%)	16 (32.7%)	12 (24.5%)	1 (2.0%)	12 (24.5%)	8 (16.3%)
Moving (abroad)	44 (4.2%)	17 (38.6%)	9 (20.5%)	0	4 (9.1%)	14 (31.8%)
Husband	29 (2.8%)	3 (10.3%)	22 (75.9%)	0	2 (6.9%)	2 (6.9%)
Not delivering in Croydon University Hospital	27 (2.6%)	10 (37.0%)	7 (25.9%)	0	6 (22.2%)	4 (14.8%)
No research	9 (0.9%)	3 (33.3%)	1 (11.1%)	0	4 (44.4%)	1 (11.1%)
Midwife does not appreciate it	1 (0.1%)	0	0	1 (100%)	0	0
No long-term follow-up	1 (0.1%)	1 (100%)	0	0	0	0

Black and other women (n=30, 65%). Black women were less likely to move (n=4, 9%). 76% (n=22) of Asian women stated that their husbands did not wish for them to participate. Asian women were more likely to have antenatal appointments and delivery in a different hospital (n=7, 26%).

Discussion

This prospective longitudinal study during pregnancy provides insight into the thought process of women when making a decision to accept or decline participation in a prospective longitudinal study during pregnancy. We identified a wide variety of reasons based on age and ethnicity for non-participation.

Over 10% of approached women did not meet the inclusion criteria when confirming interest in participating in the trial; for example twin-gestation, miscarriage and younger than 18 years. Frequently, the latter ones were given leaflets by different people than the dedicated research fellow (midwives and in parent craft classes). This emphasises that women must be screened for eligibility prior to definite enrolment.

The reasons stated by the non-participants, can help us in future research and recruitment (during pregnancy) in an area similar to urban London, United Kingdom. In order to improve recruitment of women who are busy, the researcher needs to have flexible appointment times to accommodate their preferences. Their willingness to take part will also depend on how demanding the protocol is. Patient burden can be reduced by limiting the number of hospital visits, duration of each clinic visit, and avoiding excessive numbers of questionnaires[6,7]. Our clinic visits were limited to 30-45 minutes. It is generally accepted that pregnant women are a potentially vulnerable population, especially during their first pregnancy. Therefore if complications develop during the pregnancy, women should be given the option of withdrawing from the study. Almost 5% stated that they did not want to have an additional vaginal examination. The examinations (endovaginal and transperineal ultrasonography) performed in the parent study are intrusive and involve exposure of an intimate part of the body. It has been previously shown that studies that involve procedures that may be construed as embarrassing, painful or uncomfortable could deter participants from enrolling[8]. Discomfort during the gynaecological examination has also been shown to be strongly associated with a negative emotional contact with the examiner, young age and nulliparity[8]. This highlights the importance of showing empathy, being gentle and maintaining communication at all times. Researchers need to be aware that women on temporary accommodation and those who plan to relocate may not be available for longer term follow-up. Asian women tend to involve their husbands to a greater degree in decision making and therefore

consideration should be given to their involvement at the initial discussion for participation in research.

The strengths of this study are that women were approached to consider participating in an existing study, rather than opinions acquired from a phantom study[9]. Unlike other retrospective studies[10,11,12], our participants provided the reason for non-participation immediately after the decision was made and hence our results are not biased by recall.

A limitation of the project is that we did not explore the reasons for non-participation further, like other studies have done with in-depth interviews[10,11,12]. Within this project we wanted to use the large numbers we have acquired, to give an overview and to see whether the results can be generalised. Furthermore, we analysed the reason for non-participation only in relation to age and ethnicity and did not comment on education, work experience, household, or salary. This was not done as the patients were initially approached in clinic areas where privacy is lacking. Not respecting this may have offended some women, which could harm the relationship between the researcher and the potential participant. Moreover, if women are not sure whether they want to participate, they would prefer to give the least possible information.

Recruitment to the primary study could also have been influenced by the use of endovaginal ultrasound, which some women may consider invasive. Another limitation is that the results are applicable to women in urban London, United Kingdom and comparable populations globally.

Most often the potential participant was first approach in the waiting area of the antenatal clinics, initially by two dedicated researchers (KvD-NST). After 6 months one of the researchers (KvD) continued the project. Both researchers were females, from a White background, aged 26 and 31 years. Although racial/ethnic matching of project staff and participants is invoked to be useful to recruitment[13], not all approached women in our project could identify themselves with the researcher (Table 1). This is perceived to be of higher importance to 'coloured' researchers, when they were asked for their recruiting experiences in focus groups[4]. It is possible that the responses may have been different if the recruiters were of a different gender or ethnicity.

The researcher approached the women to verbally explain the study, the benefits and commitment, and to provide an information leaflet. This has been shown to be an effective combination to also support the relationship between the recruiter and the participant[4,10,11]. Face to face recruitment produced the highest yield of eligible and willing participants among Africans and Whites[13]. The benefits in the parent study were to get taught how to perform pelvic floor muscle exercises, an additional person looking after them in the peripartum period and provided baseline information regarding the pelvic floor. Clarification of the direct possible benefits for healthy subjects can help in recruitment and retention[13].

It has previously been described that having consistent, personable, and enthusiastic study staff helps both in recruitment and retention[7,14,15]. The attitudes of the staff, feedback to subjects, the staff's handling of questions and problems, respect for participant's time, flexibility in scheduling study appointments, the assurance that their participation is appreciated, and the association with the study emerged as the most important factors influencing continued participation in the study[3,12,13,14]. Developing a personal relationship with the study participant and individualising the recruitment approach for each woman may facilitate recruitment and on-going involvement in research[4,11,13].

One of the participants in the parent study wrote a statement, which illustrates her perception of the project: *"This study was very helpful for me. The first scan gave me an idea of what it was like before giving birth in terms of someone looking at my vagina. Secondly, it helped to know someone was going to be checking me after birth. The research doctor was very gentle and explained everything very well."*

A qualitative study retrospectively explored the reasons for participation in a randomised controlled trial for antibiotics in preterm labour[12]. For most women the decision to participate was primarily based on their exchanges with the healthcare professionals who made the recruitment approach, and appeared to involve a response to socio-emotional aspects of those exchanges rather than their informational consent[11,12]. Kenyon revealed two motivations for taking part: the first was to help other women and their babies in a similar position and the second was the possibility of an improved outcome of their pregnancy[12]. However, a pregnant woman may feel the pressure of conflicting duties: a protective duty to the baby and to be a 'good citizen' when asked to participate in research[10]. Typically, risks to the baby dominate over risks to the mother in decisions to participate in trials[9]. Furthermore, recruiting and retaining participants will improve when the subjects believe the medical research to be important[14]. Also, for some people who take part in research, it is important to receive feedback about the results[10].

One participant in the study made this comment about recruiting pregnant women for this trial: "*Tell possible participants you are there to help them and their pelvic floor muscles, by providing antenatal advice and training for pelvic floor muscle exercises, and a check-up three months after delivery including advice for the future. Basically, all women question themselves: What is happening down there at delivery".*

In conclusion, women from different ethnicities and age groups have given a wide variety of reasons for non-participation. It is important to be clear about the reasons for the study, the commitment and to explain possible benefits if any for the participant. The information from this study can now be used by researchers recruiting women for comparable studies in comparable settings, to enhance recruitment and participation of eligible patients.

References

1. Tooher RL, Middleton PF, Crowther CA. A thematic analysis of factors influencing recruitment to maternal and perinatal trials. Review. BMC Pregnancy Childbirth 2008;8:36
2. Oude Rengerink K, Opmeer BC, Logtenberg SL, Hooft L, Bloemenkamp KWM, Haak MC, et al. IMproving PArticipation of patients in Clinical Trials – rationale and design of IMPACT. BMC Med Res Methodol 2010;10:85
3. Kaiser MM, Hays BJ. Recruiting and enrolling pregnant adolescents for research. Issues Compr Pediatr Nurs 2006;29:45-52
4. Brown BA, Long HL, Milliken N. What's to know about study recruitment? We asked recruiters. Womens Health Issues 2002;12:116-21
5. Sultan AH, Kamm MA, Hudson CN, Thomas JM, Bartram CI. Anal-sphincter disruption during vaginal delivery. N Engl J Med 1993;329:1905-11
6. Vickers AJ. How to improve accrual to clinical trials of symptom control 1: design issues. J Soc Integr Oncol 2007;5:61-4
7. Zielinski R, Ackerson K, Misiunas RB, Miller JM. Feasibility of a longitudinal study of women anticipating first pregnancy and assessed by multiple pelvic exams: recruitment and retention challenges. Contemp Clin Trials 2010;31:544-8
8. Hilden M, Sidenius K, Langhoff-Roos J, Wijma B, Schei B. Women's experiences of the gynecologic examination: factors associated with discomfort. Acta Obstet Gynecol Scand 2003;82:1030-6
9. Rodger MA, Makropoulos D, Walker M, Keely E, Karovitch A, Wells PS. Participation of pregnant women in clinical trials: will they participate and why? Am J Perinatol 2003;20:69-76
10. Mohanna K, Tunna K. Withholding consent to participate in clinical trials: decisions of pregnant women. BJOG 1999;106:892-7
11. Baker L, Lavender T, Tincello D. Factors that influence women's decisions about whether to participate in research: an exploratory study. Birth 2005;32:60-6
12. Kenyon S, Dixon-Woods M, Jackson CJ, Windridge K, Pitchforth E. Participating in a trial in a critical situation: a qualitative study in pregnancy. Qual Saf Health Care 2006;15:98-101
13. Gilliss CL, Lee KA, Gutierrez Y, Taylor DT, Beyene Y, Neuhaus J, et al. Recruitment and retention of healthy minority women into community-based longitudinal research. J Womens Health Gend Based Med 2001;10:77-85
14. Marmor JK, Oliveria SA, Donahue RP, Garrahie EJ, White MJ, Moore LL, et al. Factors encouraging cohort maintenance in a longitudinal study. J Clin Epidemiol 1991;44:531-5
15. Yancey AK, Ortega AN, Kumanyika SK. Effective recruitment and retention of minority research participants. Annu Rev Public Health 2006;27:1-28

3

Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women

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Abstract

Objectives: The modified Oxford scale (MOS) has previously been found to have poor inter-rater reliability, whereas digital assessment of levator ani muscle (LAM) attachment to the pubic bone has been shown to have acceptable reliability. Our aim was to evaluate the inter-rater reliability of the validated MOS and to develop a reliable classification system for digital assessment of LAM attachment, correlating this to findings on transperineal ultrasound (TPUS).

Methods: Evaluation of the MOS by palpation was performed in nulliparous women by two investigators. LAM attachment was evaluated using digital palpation, for which a novel classification system was developed with four grades based on the position of the attachment and presence of discernible muscle. Findings were compared with those on TPUS. Inter-rater reliability was assessed using Cohen's kappa statistic.

Results: Twenty-five nulliparous women were examined. There was agreement in MOS between the investigators in 64% of women (n=16), with a kappa of 0.66 (indicating substantial agreement). There was agreement in palpation of LAM attachment using the new grading system in 96% of women (n=24), with a kappa of 0.90 (indicating almost perfect agreement). TPUS did not show LAM avulsion in any woman, except for one patient with a partial avulsion.

Conclusion: In this group of nulliparous patients, there was substantial agreement between the two investigators in evaluation of the MOS and there was good agreement between grades of LAM attachment using the new classification system, which correlated with findings on TPUS. It therefore appears that these results are reproducible in nulliparous women, and the techniques can be readily learned and reliably incorporated into clinical practice and research after appropriate training. Further research to establish the clinical utility of the grading system for LAM attachment in postpartum women and in women with symptomatic pelvic organ prolapse is required.

Introduction

The palpation of major defects in the pelvic floor muscles after childbirth was first described by Howard Gainey[1]. Shortly thereafter, pelvic floor muscle exercises ('Kegel exercises') were introduced by Arnold Kegel[2]. In recent years, with advances in magnetic resonance imaging and three/four-dimensional imaging techniques, the pelvic floor has become a focus of considerable research. Levator ani muscle (LAM) avulsion during vaginal delivery has been shown to have a strong relationship with pelvic organ prolapse[3,4].

The LAM is clinically palpable during digital vaginal examination. Pelvic floor muscle strength can be quantified by palpation during voluntary contraction using the validated modified Oxford scale (MOS)[5]. In addition, the site of LAM attachment to the pubic bone can be palpated. The MOS has previously been shown to have poor inter-rater reliability[6,7], while digital assessment of LAM attachment has been shown to have acceptable reliability, albeit with a substantial learning curve[8,9]. The presence of LAM avulsion is associated with a significant reduction in pelvic floor muscle strength (PFMS), including side differences due to avulsion[10]. Recently, Dietz et al showed that palpation of LAM attachment can be used interchangeably with evaluation by transperineal ultrasound (TPUS)[11]. However, as the technique of palpating LAM attachment to the pubic bone has not been standardized, comparison of published studies is difficult. Furthermore, the normal range of findings and the reliability of assessment of LAM attachment to the pubic bone in nulliparous women remain to be established.

Our aim was to evaluate the inter-rater reliability of the validated MOS and to develop a reliable classification system for digital assessment of LAM attachment to the pubic bone and to correlate this to ultrasound findings.

Methods

All patients were recruited as part of the ELITE-study (Evaluation of Levator Injuries using Transvaginal Endosonography), a prospective longitudinal study. The aim of the ELITE study was to establish the prevalence of LAM defects sustained during childbirth and to correlate these with pelvic floor symptoms and pelvic floor muscle strength. Women were recruited from the antenatal clinics of Croydon University Hospital, United Kingdom. All women gave written informed consent. The parent study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87).

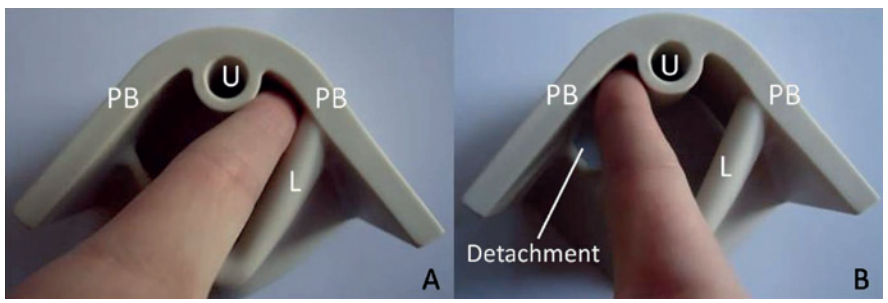
Between January 2011 and May 2011, 25 nulliparous women were included. Patients were examined between 35 and 40 weeks of gestation. They were asked to

empty their bladder prior to the examination. Measurements were carried out in the supine position with the knees semi-flexed. All clinical examinations were performed by two research fellows (KvD and NST) during the same visit, in the same order, prior to the ultrasound assessment. Each examiner was blinded to the other's findings and to the ultrasound findings. We minimised the measurement and technique variability by rigorous investigator training and observation by the principal investigator (RT).

Pelvic floor muscle function was assessed subjectively by digital palpation while inserting a lubricated gloved index finger approximately 4 cm into the vagina[5]. All women were instructed on the 'squeeze' and 'lift inward' techniques of the pelvic floor muscles without activation of other groups of muscles. The investigator observed and rectified any contraction of abdominal, gluteal and adductor muscles. Muscle strength was graded using the six-point MOS: 0 = no contraction, 1 = minor muscle 'flicker', 2 = weak muscle contraction without a circular contraction, 3 = moderate muscle contraction, 4 = good and 5 = strong muscle contraction against resistance by the examining finger[5]**.** A score was given for both the left and right side, and the lower score was used for analysis.

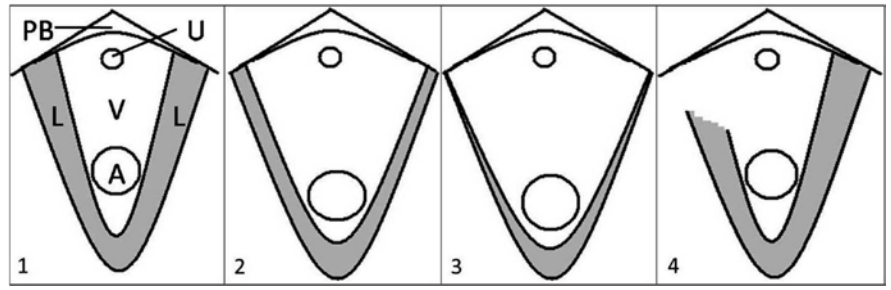
During palpation for LAM attachment to the pubic bone, the index finger is placed immediately lateral to the urethra[8], pressing against the pubic bone. For example, when the patient's right side is palpated, the urethra will be felt to the right of the index finger and the LAM on the left side of the index finger. If the LAM is deficient on the left side, the index finger will slide laterally along the pubic ramus (Figure 1 and Figure 2). The part of the finger that palpates the LAM attachment is the middle of the first phalanx of the index finger; we have measured this in a random group of males and females and it varies between 15 and 20mm in width.

Figure 1 Levator ani muscle palpation demonstrated using a model (supplied courtesy of Professor Hans Peter Dietz, Sydney)



(A) Left side normal levator ani muscle (L) attachment and (B) right side avulsion.
PB, pubic bone; U, urethra.

Figure 2 Diagrammatic representation of the classification system for palpation of levator ani muscle (LAM) avulsion



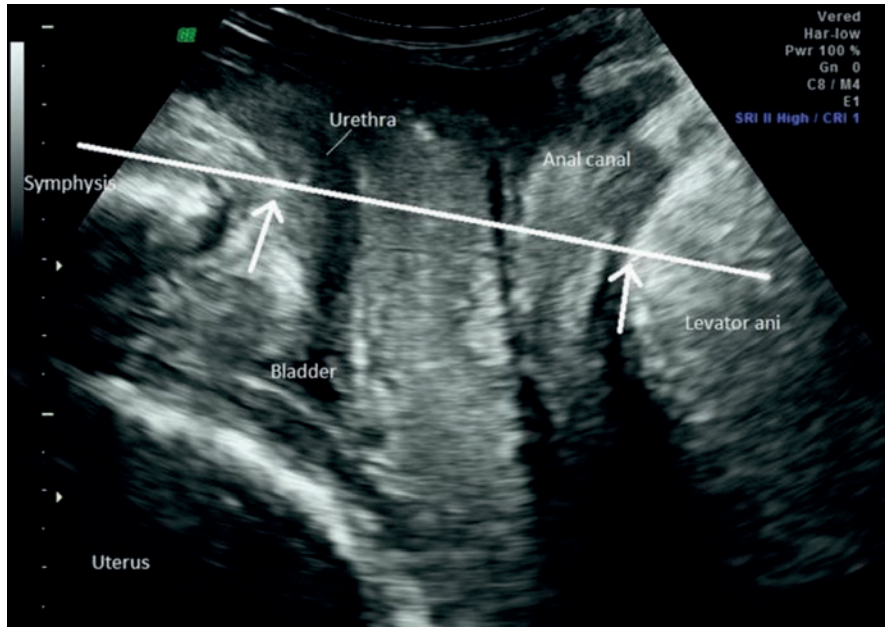
(1) Grade 1, ≤ one finger space between the lateral side of the urethra and the LAM; (2) Grade 2, > one finger space between the lateral side of the urethra and the LAM, with the muscle clearly palpable at rest and on contraction; (3) Grade 3, > one finger space from the lateral side of the urethra laterally along the pubic bone, without any discernible muscle at rest or on contraction; (4) Grade 4, no attachment of the muscle to the pubic bone (right side).
PB, pubic bone; U,urethra; L, levator ani muscle; A, anus; V, vagina.

Palpation assesses presence or absence of muscle bulk at rest and during contraction, with contraction assisting in the identification of the presence of small amounts of muscle[8]. Avulsion was found when there was no LAM insertion felt to the inferior pubic ramus[9]. Both the left and right side were evaluated. The following classification was devised to describe LAM attachment (Grades 1 – 4, Figure 2): Grade 1, ≤ one finger space between the lateral side of the urethra and the LAM; Grade 2, > one finger space between the lateral side of the urethra and the LAM, with the muscle clearly palpable at rest, and on contraction; Grade 3, > one finger space from the lateral side of the urethra laterally along the pubic bone, without any discernible muscle at rest or on contraction; Grade 4 no attachment of the muscle to the pubic bone. The proposed classification system was agreed upon after reviewing the literature[8,9] and the clinical experience of the senior investigators. There is an unmet need to develop a standardized classification system for palpation of the LAM in nulliparous women for clinical and research purposes.

TPUS was performed using a GE Voluson 730 system (GE Medical Systems, Zipf, Austria) with a 4–8 MHz transabdominal curved array volume transducer, with an acquisition angle of 85 degrees. The transducer was positioned on the perineum between the mons pubis and the anal margin, with slight pressure and good tissue contact[12]. Imaging was performed at rest, on maximum pelvic floor muscle contraction and on maximum Valsalva maneuver. In the mid-sagittal plane, all anatomical structures (bladder, urethra, vaginal walls, anal canal and rectum) between the posterior surface of the symphysis pubis and the posterior part of the LAM were

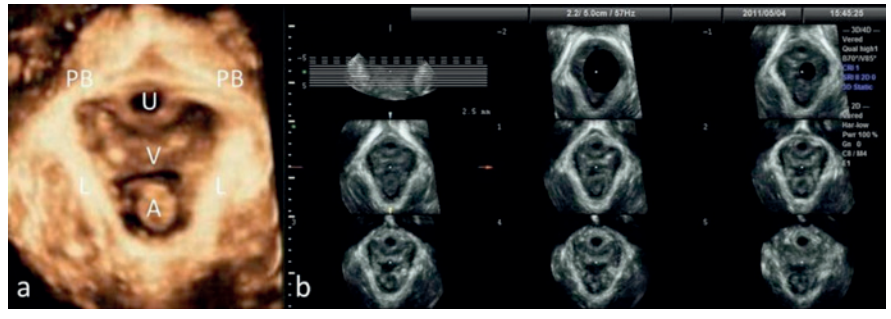
visualized[12]. This view was used to identify the minimal antero-posterior diameter of the levator hiatus, from the posterior margin of the symphysis pubis to the anterior margin of LAM where it defines the anorectal angle (Figure 3)[13]. To analyse the images we used a symmetric rendered volume, of about 1.5–2.5 cm in thickness, rendered caudal to cranial[11]. The visualised landmarks were: pubic bone on both sides, urethra at 12 o'clock position, vagina in the middle, anal canal at 6 o'clock position, and LAM on the left and right side of the vagina, surrounding the anal canal (Figure 4a). An avulsion was diagnosed if a clearly abnormal insertion of the LAM on the inferior pubic ramus was found[11]. Secondly, we used tomographic ultrasound imaging (TUI) to assess the entire LAM and its attachment to the inferior pubic ramus[14]. TUI was performed in the axial plane at 2.5 mm slice intervals, from 5 mm below the plane of minimal hiatal dimensions to 12.5 mm above, producing eight slices per patient (Figure 4b)[14]. Slices were scored as positive or negative for LAM avulsion, using direct visualization of the insertion of LAM on the pelvic sidewall. When all three central slices were abnormal, complete avulsion was diagnosed[15]. Partial avulsion was diagnosed when any of the three central slices was abnormal[15]. Offline analysis

Figure 3 Normal anatomy of the midsagittal plane on transperineal ultrasound.



Arrows indicate plane of the minimal hiatal dimensions, from the posterior margin of the symphysis pubis to the anterior margin of levator ani muscle where it defines the anorectal angle[13]

Figure 4 (a) Normal levator ani muscle (LAM) attachment on three-dimensional rendered ultrasound imaging. (b) Normal LAM attachment on tomographic ultrasound imaging



PB, pubic bone; U, urethra; V, vagina; A, anus; L, levator ani muscle.

was performed using 4D View version 10.2 (GE Medical Systems) with the operator blinded to clinical findings.

A power calculation was not performed, because the grading system for LAM attachment had not been described or used before. We decided to include 25 patients, based on the numbers that have been used in previous publications for the description of a new test and performance of inter-rater reliability analyses[6,7,8,16].

Statistical analysis

Data were analysed using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Agreement between investigators is reported using overall proportion of agreement and agreement corrected for chance (Cohen's kappa). The kappa coefficient gives an indication of the difference between observed and expected agreement[17]. A kappa value of <0 indicates less than chance agreement, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, 0.81–0.99 almost perfect agreement and 1 indicates perfect agreement[17].

Results

Twenty-five nulliparous women with a median age of 31 (range 20 – 42) years were examined at a median of 37 (range 35 – 40) weeks of gestation. Median body mass index was 24 (range 15 – 40) kg/m^2.

Median maximal pelvic floor muscle strength assessed by the MOS was 4 (range 0 – 5). There was agreement between the research fellows in the MOS for the weaker side in 64% of cases (n = 16) (Table 1). In six cases the disagreement was by one category on the MOS and in three cases it was by two categories on the MOS. Cohen's kappa was 0.66, indicating substantial agreement. We found side differences in 16% of nulliparous women (n = 4), without LAM avulsion on TPUS. The range of MOS difference between sides in these women was 1 to 4.

Table 1 Inter-rater reproducibility of the modified Oxford scale (MOS) and of a new classification system for clinical palpation of levator ani muscle (LAM) attachment to the pubic bone in 25 nulliparous pregnant women

Parameter	Weighted kappa	Concordance
MOS		
Left	0.66	0.64
Right	0.65	0.60
Weakest side	0.66	0.64
LAM attachment grade		
Left	0.90	0.96
Right	0.90	0.96

There was agreement between the research fellows in the grading of LAM attachment by palpation in 96% of the cases for both left and right sides (n = 24) (Table 1). Discrepancies between the two observers are demonstrated in Table 2. On the left side there was a discrepancy in one patient (Examiner 1 scored Grade 2 and Examiner 2 scored Grade 1). On the right side there was also one discrepancy (Examiner 1 scored Grade 2 and Examiner 2 scored Grade 3). There was no clear avulsion felt in any of the patients (i.e. no Grade 4). Cohen's kappa was 0.90 for both sides, indicating almost perfect agreement.

In about 20% of our nulliparous women, the space between the urethra and the LAM attachment to the pubic bone was more than one finger (Grade 2). None of these nulliparous women had symptoms of anal incontinence, urinary incontinence

Table 2 Frequencies of reported grades in the classification of palpation of levator ani muscle (LAM) attachment to the pubic bone by two examiners

	LAM attachment			
	Grade 1	Grade 2	Grade 3	Grade 4
Examiner 1: left	18	7	0	0
Examiner 2: left	19	6	0	0
Examiner 1: right	20	5	0	0
Examiner 2: right	20	4	1	0

or pelvic organ prolapse. On clinical examination one of these women had a Grade 2 prolapse of the anterior compartment, which was not bothersome. All women in this subgroup performed pelvic floor muscle contractions correctly and were found to have a good–strong squeeze (MOS 4 and 5); only one patient had a MOS of 2. None of these patients were found to have LAM avulsion on TPUS.

On TPUS, all women had intact LAM on rendered volume imaging. We found one case of left-sided partial avulsion, in which the LAM appeared not to be intact on the third slide of TUI, although the LAM attachment was intact on clinical examination (Grade 1).

Discussion

In this study we demonstrated substantial agreement between two trained research fellows in the clinical assessment of MOS. In addition, we devised a novel classification system for digital palpation of LAM attachment to the pubic bone, with good agreement between two research fellows in this small group of nulliparous patients without symptoms of pelvic organ prolapse or any other relevant symptoms. This standardised classification can be readily learned and reliably used in clinical assessment and research involving multiple assessors. However, this method needs to be tested on parous women and women with (symptomatic) pelvic organ prolapse in order to evaluate the use of the grading system.

Bø et al in 2001 examined 20 non-pregnant women to assess pelvic floor muscle strength subjectively (MOS) and objectively (perineometer)[6]. Their participants were in supine position, and received thorough instruction on the technique of contraction[6]. In their subjective assessment, they found agreement between the physiotherapists

in 45% of cases, with a Cohen's kappa value of 0.37[6]. They concluded that MOS is not reproducible, sensitive or valid to measure pelvic floor muscle strength for scientific purposes[6]. These findings were confirmed by Ferreira et al in 2011, in a comparable group of patients[7]. In contrast, we found better inter-rater agreement in nulliparous women (kappa = 0.64), which we can perhaps attribute to the fact that our subjects were pregnant. Pelvic floor muscle strength seems to increase during pregnancy, as confirmed by subjective and objective findings[18]. It has been hypothesized that this could be explained by the increased load of the gravid uterus on the pelvic floor muscles[18]. Moreover, the majority of pregnant women are advised to perform pelvic floor muscle exercises, which increases muscle strength. It is therefore possible that nulliparous women who do not suffer from prolapse and incontinence will have better pelvic floor muscle strength and that this may improve the inter-rater reliability. Assessment of the pelvic floor muscles depends on the co-operation and position of the woman as well as the experience of the investigators[6]. Digital muscle testing scores have been found to be highest in the supine position, which is patients' preferred position for internal examinations[16]. We controlled for these factors by clearly instructing the women, using the supine position for examinations and implementing rigorous investigator training.

Previous studies have found substantial agreement between MOS and perineometry[19,20]. MOS is widely used in clinical practice as it is easy to perform, inexpensive and no special equipment is required. Furthermore, vaginal palpation is an effective aid to provide feedback to patients when they perform a pelvic floor muscle contraction[6].

By using the new classification system for palpation of LAM attachment to the pubic bone we have demonstrated a higher reliability (kappa = 0.90), than that previously reported[8,9]. A clear limitation of our study is that all participants were nulliparous and we would therefore not expect the occurrence of LAM avulsion. However, our aim was to validate the novel classification system in the nulliparous population. We were surprised to find that in 20% of nulliparous women there was more than one finger space between the lateral side of the urethra and the LAM, although LAM was intact on TPUS. A previous study has shown that an increase in the gap between the muscle's insertion on the inferior pubic ramus and the urethra on palpation is highly suggestive of LAM avulsion[21]. However, the study sample consisted of mainly parous women. We agree that nulliparous women are unlikely to have an avulsion. Using the classification system, we can be sure that the finding of Grade 1 or Grade 2 suggests intact muscles. Although other authors have described the clinical findings of grades 1 and 2, they have not incorporated this into a classification system[8,9]. There is now an opportunity to explore this classification system in parous women and in women with prolapse.

Kearney et al found an overall proportion of inter-rater agreement in clinical detection of LAM avulsion of 79.3%, with Cohen's of kappa 0.57 (acceptable reliability)[8]. Comparison with magnetic resonance imaging (MRI) revealed no false-positive findings on clinical examination, suggesting a minimal risk of overestimating avulsion on physical examination[8]. Dietz et al found agreement between assessors in 81%, with Cohen's kappa of 0.41 (moderate agreement), using digital palpation for the diagnosis of LAM avulsion[9]. They perceived that problems with classification arise in cases with incomplete injuries[9]. Even intact muscle may be difficult to palpate if the woman cannot contract it voluntarily and/or the muscle has undergone a distension injury (microtrauma)[9]. However, caution is required because of the poor positive agreement on LAM avulsion between physical examination and imaging modalities such as MRI and four-dimensional TPUS[8,9]. This suggests that physical examination may grossly underestimate the prevalence of LAM avulsion[8,9]. Furthermore, substantial training for the detection of major LAM trauma by vaginal digital examination is of utmost importance[8,9].

Dietz et al. have suggested the possibility that side differences in pelvic floor muscle strength, as assessed using MOS, are related to LAM avulsion[10]. However, we found side differences in pelvic floor muscle strength in women without LAM avulsion. This suggests that a side difference in pelvic floor muscle strength does not necessarily correlate with LAM avulsion.

Although intact on clinical examination, one patient had a partial LAM avulsion on TUI according to the classification of Dietz, which corresponds with previous reports in the literature[15,22]. However, the observation of LAM avulsion in fewer than three abnormal central slices is much less likely to be associated with symptoms and signs of prolapse and is probably an artefact[15].

To conclude, we found normal variations in the insertion of the LAM to the pubic bone in nulliparous women. There was substantial agreement between the two trained research fellows in the clinical assessment of the MOS and there was good agreement between grades 1 and 2 of LAM attachment to the pubic bone, which correlated with findings on TPUS. It therefore appears that these results are reproducible in nulliparous women. The techniques can be readily learned and reliably incorporated into clinical practice and research after appropriate training. The novel classification to assess LAM attachment to the pubic bone now needs to be evaluated in parous women, who are much more likely to have LAM avulsion. Further evaluation to establish its clinical utility in women postpartum and women with (symptomatic) pelvic organ prolapse is awaited.

References

1. Gainey HL. Post-partum observation of pelvic tissue damage. Am J Obstet Gynecol 1943;46:457-66
2. Kegel AH. Prospective resistance exercise in the functional restoration of the perineal muscles. Am J Obstet Gynecol 1948;56:238-48
3. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
4. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
5. Laycock J. Clinical evaluation of the pelvic floor. In Pelvic floor re-education, Principles and practice, Schüssler B, Laycock J, Norton PA, Stanton SL, eds. Springer-Verlag: London, 1994;42-8
6. Bø K, Finckenhagen HB. Vaginal palpation of pelvic floor muscle strength: inter-test reproducibility and comparison between palpation and vaginal squeeze pressure. Acta Obstet Gynecol Scand 2001;80:883-7
7. Ferreira CH, Barbosa PB, de Oliveira Souza F, Antônio FI, Franco MM, Bø K. Inter-rater reliability study of the modified Oxford Grading Scale and the Peritron manometer. Physiotherapy 2011;97:132-8
8. Kearney R, Miller JM, DeLancey JO. Interrater reliability and physical examination of the pubovisceral portion of the levator ani muscle, validity comparisons using MR imaging. Neurourol Urodyn 2006;25:50-4
9. Dietz HP, Shek C. Validity and reproducibility of the digital detection of levator trauma. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1097-101
10. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-6
11. Dietz HP, Moegni F, Shek KL. Diagnosis of levator avulsion injury: a comparison of three methods. Ultrasound Obstet Gynecol 2012;40:693-8
12. Dietz HP. Pelvic Floor ultrasound: a review. Am J Obstet Gynecol 2010;202:321-34
13. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-5
14. Dietz HP. Quantification of major morphological abnormalities of the levator ani. Ultrasound Obstet Gynecol 2007;29:329-34
15. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
16. Frawley HC, Galea MP, Philips BA, Sherburn M, Bø K. Effect of test position on pelvic floor muscle assessment. Int Urogynecol J Pelvic Floor Dysfunct 2006;17:365-71
17. Viera AJ, Garrett JM. Understanding Interobserver Agreement: the Kappa Statistic. Family Medicine 2005;37:360-3
18. Elenskaia K, Thakar R, Sultan AH, Scheer I, Beggs A. The effect of pregnancy and childbirth on pelvic floor muscle function. Int Urogynecol J 2011;22:1421-7
19. Isherwood PJ, Rane A. Comparative assessment of pelvic floor strength using a perineometer and digital examination. Br J Obstet Gynaecol 2000;107:1007-11
20. Riesco ML, Caroci Ade S, de Oliveira SM, Lopes MH. Perineal muscle strength during pregnancy and postpartum: the correlation between perineometry and digital vaginal palpation. Rev. Latino-Am. Enfermagem 2010;18:1138-44
21. Dietz HP, Abbu A, Shek KL. The levator-urethra gap measurement: a more objective means of determining levator avulsion? Ultrasound Obstet Gynecol 2008;32:941-5
22. Adisuroso T, Shek KL, Dietz HP. Tomographic ultrasound imaging of the pelvic floor in nulliparous pregnant women: limits of normality. Ultrasound Obstet Gynecol 2012;39:698-703

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Intra- and inter-rater reliability of levator ani muscle biometry and avulsion using three dimensional endovaginal ultrasonography

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Abstract

Objectives: Our aims were to test intra- and inter-rater reliability of levator ani muscle (LAM) biometry and avulsion using antenatal and postnatal 3D endovaginal ultrasonography (EVUS), and to determine levator urethra gap (LUG) values on EVUS.
Methods: EVUS was performed at rest using a standardised protocol. During post processing measurements were taken in the plane of minimal hiatal dimensions by two blinded independent investigators. LAM attachment to the pubic bone was assessed at the pubococcygeus and puborectalis level: 1= intact, 2= partial avulsion<50%, 3= partial avulsion≥50%, 4=complete avulsion. Intraclass correlation (ICC) and limits of agreement (LOA) were calculated for each time point.
Results: 169 antenatal scans were performed, 83 early postpartum and 75 three months postpartum. ICC on intra- and inter-rater analysis are presented respectively: hiatus area 0.95 and 0.86-0.88, hiatus transverse 0.90 and 0.16-0.74, hiatus antero-posterior 0.91 and 0.73-0.80, LAM thickness 9 o clock 0.50 and 0.32-0.52, and 3 o clock 0.55 and 0.33-0.45. Both intra- and inter-rater analysis revealed acceptable LOA for hiatus measurements, but too wide for thickness. The correlation of specific LAM avulsion was excellent on intra- and inter-rater analysis. Antenatal mean (±SD) LUG were 18.8mm (±2.4) and 19.2mm (±2.3) on right and left respectively: intra-rater ICC was 0.82-0.91 (acceptable LOA), inter-rater ICC was 0.13-0.68 (wide LOA).
Conclusions: 3D EVUS is a reliable tool in the assessment of hiatus measurements and LAM avulsion in parous women, but less so for thickness and LUG. EVUS can therefore be used in research studies involving childbirth and recurrent prolapse.

Introduction

Obstetric trauma is known to be a cause of levator ani muscle (LAM) avulsion from the pubic bone. Trauma can occur by stretching of the most medial muscle, pubococcygeus, of the pelvic floor hiatus and by disconnection of the muscle from its insertion from the inferior pubic ramus and the pelvic side wall[1,2,3]. LAM avulsion occurs in 13-36% of women usually during their first vaginal delivery[4,5,6] and is associated with female pelvic organ prolapse later in life[7]. LAM avulsion has a relative risk of three for cystocele recurrence[8]. Although obstetric trauma to the pelvic floor has been shown using magnetic resonance imaging (MRI)[9] and transperineal ultrasonography (TPUS)[6], 3 dimensional endovaginal ultrasonography (EVUS) of LAM in the antenatal and postnatal period has not been utilised previously.

Images obtained on EVUS of pelvic floor muscle subdivisions have good to very good cadaveric anatomical correlation[2,3]. Subdivisions of the muscle parts can reliably be visualised by different raters[2]. While the disadvantage of EVUS is that it is an invasive technique and dynamic studies are not possible, the advantage of this technique is that it places the probe next to structures of interest to provide vivid images. The EVUS examination to address LAM biometry has been standardised in nulligravid women[10] and has shown good to excellent reproducibility for measurements of hiatus dimensions with proven interdisciplinary reliability[11]. However, the inter-rater analysis of this technique has not been assessed in parous women and limits of agreement (LOA) have not previously been constructed. Diagnosis of LAM avulsion can be made using EVUS, and this has been associated with clinically significant prolapse[12]. Levator urethra gap (LUG) measurements have been used in parous women using TPUS[13] and MRI[14], and found to be useful in identifying LAM avulsion in doubtful cases[13]. However, these measurements have not been analysed using EVUS.

The aims of this study were to test intra- and inter-rater reliability of LAM biometry and avulsion in the antenatal and postnatal period using 3D EVUS, and to determine LUG values.

Methods

Women were recruited as part of the prospective longitudinal ELITE-study (Evaluation of Levator Injuries using Transvaginal Endosonography). The primary study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87). The aim of the ELITE-study was to establish the prevalence of LAM defects during childbirth and to correlate these with pelvic floor symptoms and pelvic floor muscle strength. Women were recruited from the antenatal clinics of Croydon University Hospital, United Kingdom.

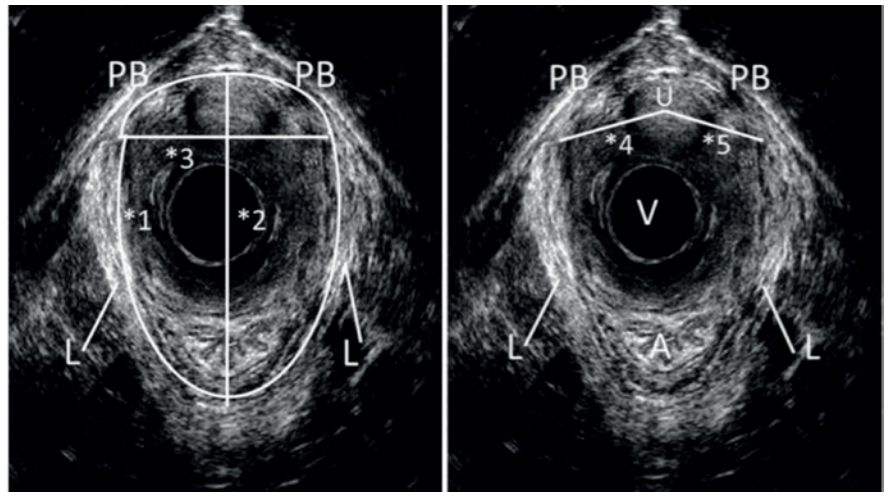
All women have given written informed consent during the first visit. Two research fellows (KvD and NS-T) performed the ultrasound examinations at 36 weeks of gestation, early postpartum, and three months following delivery. We minimised technique variability by rigorous investigator training and observation by the principal investigator (RT). Women were asked to empty their bladder prior to the examination. Examination was carried out in the supine position with knees semi-flexed. All women underwent high frequency 3D EVUS (B-K Medical, Herlev, Denmark, 2050 probe, 9-16 MHz 360° rotational scanner), performed following a previously described approach and images were acquired at rest[2,10]. Detailed descriptions of the volumes have previously been provided[2,3,10,11,12]. Offline analysis for all recorded volumes was conducted by two independent investigators (KvD and SAS), using B-K Medical Viewer version 7.0.0.519. Intra-rater analysis was performed by one investigator (KvD) by re-analysing a random sample of 20 scans acquired three months following delivery, more than 6 months after the initial analysis. The investigators were blinded for delivery details, clinical examination and each other's results. Both investigators used the same standardised protocol to define the plane of the minimal hiatal dimensions. The midsagittal plane was used to identify the minimal distance between the hyperechogenic posterior aspect of the symphysis pubis and the hyperechogenic anterior border of the levator plate just posterior to the anorectal angle[3,15]. After tilting the 3D volume accordingly, the pubic bone ("gothic arch"), the midurethra, the anal canal, and on either sides the pubococcygeus part of LAM should be visualised in the axial plane. Measurements were taken in this plane: hiatus area, hiatus transverse diameter, hiatus antero-posterior diameter, thickness at 9 o'clock and 3 o'clock, and levator urethra gap, as indicated in Figure 1[13,15].

The plane of the minimal levator hiatal dimensions was used to assess LAM attachment to the pubic bone (pubococcygeus level). The following scoring system was used (score 1– 4) as previously used in MRI[16,17] and EVUS studies[12]: 1 = complete attachment of the muscle to the pubic bone, without any injury (intact), 2 = <50% muscle injury (partial avulsion <50%), 3 = ≥50% muscle injury (partial avulsion ≥50%), 4 = complete muscle avulsion and entirely detached from the pubic bone (muscle not intact) (Fig 2). In case of an avulsion, the levator pubic bone gap (LPG) was measured as the distance between the remnants of the pubococcygeus muscle to the original insertion on the pubic bone (Fig 3). Moving the cube slightly more distal in the axial plane, the puborectalis (PR) part of LAM was evaluated applying the same scoring system.

Statistical analysis

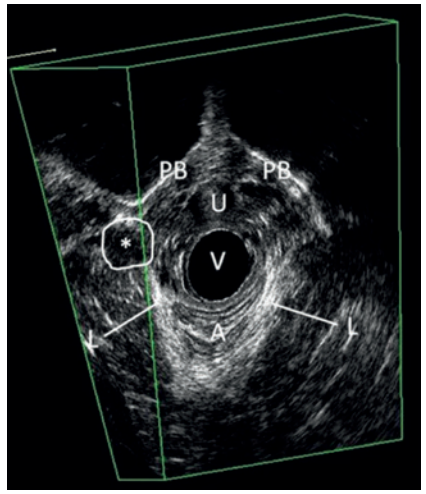
Data were analysed using SPSS 20.0 (SPSS Inc., Chicago, IL). A separate power calculation was not performed. As results of reliability analysis are more reliable when more cases are included[18], we included large numbers as part of our primary study.

Figure 1 Normal levator hiatus measurements



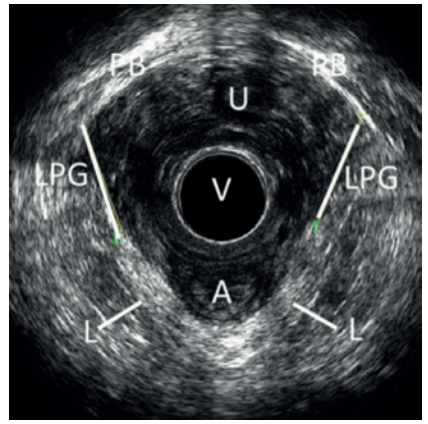
PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; LAM, levator ani muscle
*1, Hiatus area; *2, hiatus antero-posterior diameter; *3, hiatus transverse diameter, *4 and *5 levator urethra gap.

Figure 2 Right sided unilateral pubococcygeus avulsion



PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; L, levator ani muscle; *, avulsion.

Figure 3 Levator pubic bone gap in a bilateral avulsion



PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; L, levator ani muscle; LPG, levator pubic bone gap.

This is expected to result in more accurate reliability as shown by a smaller confidence interval[18]. Statistical analysis of the measurements was carried out for each visit separately. The results are given as mean values with standard deviation (±SD). ICC was calculated for intra- and inter-rater analyses of the measurements and the scoring system (<0.00 no repeatability, 0.0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good, 0.81-1.00 excellent repeatability)[19]. We used the two-way random model, with absolute agreement and single measure as the outcome. Subsequently, Bland Altman analysis was used to construct LOA to control for close agreement of the performed measurements and to detect systemic bias between the two investigators[20]. This approach helps in detecting agreement between two investigators, rather than correlation only[20]. Mean difference (δ) and standard deviation of this difference (SDd) were calculated. LOA was constructed: δ - (1.96 x SDd) = lower limit, andδ + (1.96 x SDd) = upper limit of agreement[20]. Ideally, acceptability of LOA should be determined before the analysis[20]. Because of the lack of data regarding this subject, we could not define a priori maximum widths for LOA and Bland et al suggested that interpretation of LOA should be a clinical decision[20].

Results

A total of 327 EVUS were performed between January 2011 and December 2011. This was a longitudinal cohort including 169/327 (52%) antenatal scans in primigravid women at a median of 36 weeks gestation (range 34 – 41), 83/327 (25%) scans performed following first delivery at a median of 20 hours (range 1 – 92), and 75/327 (23%) scans performed at a median of 13 weeks following delivery (range 10 – 23). The median age of all women was 31 years (range 18 – 45) and median Body Mass Index was 24 kg/m^2 (range 15 – 46).

Although landmarks were visible in all scans, measurements were not possible in some women, as indicated in Tables 1, 2, 3, and 4. Results of the intra-rater analysis measurements acquired in a random sample of postnatal women are shown in Table 1 (n = 20). Inter-rater analysis for antenatal women (n = 169), early postpartum (n = 85) and three months postpartum (n = 75) are represented in Tables 2, 3 and 4 respectively. The distribution of parameters in the random sample chosen for the intra-rater analysis was similar to that in the total set of data. This implies that the chosen sample was representative.

Reliability of hiatus measurements

Intra-rater reliability was excellent for hiatus measurements and moderate for thickness measurements (Table 1). Inter-rater reliability for the subset of nulliparous women revealed excellent reliability for hiatus area (0.86) and hiatus antero-posterior

Table 1 Intra-rater analysis of levator ani muscle biometry measurements

Parameter (cm)	n	Analysis 1 Mean (±SD)	Analysis 2 Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	Standard error	Lower LOA (CI)	Upper LOA (CI)
Hiatus area	20	14.12 (2.97)	13.64 (2.90)	13.88 (2.91)	0.95	0.84, 0.98	-0.48	0.79	0.31	-2.04 (-2.64, 1.44)	1.07 (0.47, 1.67)
Hiatus TV	20	3.61 (0.55)	3.59 (0.55)	3.60 (0.53)	0.90	0.76, 0.96	-0.02	0.26	0.10	-0.53 (-0.72, -0.33)	0.48 (0.29, 0.67)
Hiatus AP	20	5.24 (0.64)	5.14 (0.55)	5.19 (0.58)	0.91	0.78, 0.97	-0.11	0.23	0.09	-0.56 (-0.74, -0.38)	0.35 (0.17, 0.53)
Thickness 9	20	0.39 (0.14)	0.52 (0.19)	0.45 (0.15)	0.50	-0.03, 0.79	0.14	0.14	0.06	-0.14 (-0.25, -0.04)	0.41(0.31, 0.52)
Thickness 3	20	0.39 (0.21)	0.47 (0.17)	0.43 (0.17)	0.55	0.17, 0.79	0.08	0.18	0.07	-0.26 (-0.40, -0.13)	0.42(0.29, 0.56)
LUG right	20	1.98 (0.40)	1.85 (0.44)	1.92 (0.40)	0.82	0.55, 0.93	-0.14	0.23	0.07	-0.58(-0.71, -0.46)	0.34 (0.21, 0.46)
LUG left	20	1.84 (0.26)	1.84 (0.29)	1.84 (0.27)	0.91	0.79, 0.96	-0.00	0.12	0.05	-0.24(-0.33, -0.15)	0.23(0.14, 0.33)

n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; LOA, limits of agreement; Hiatus TV, hiatus transverse diameter; Hiatus AP, hiatus antero-posterior diameter; LPG, levator pubic bone gap; LUG, levator urethra gap

diameter (0.80). In these nulliparous women, fair-moderate reliability was found for thickness (0.32-0.45) and slight for hiatus transverse diameter (0.17) (Table 2). Similar findings were found in the scans analysed early and three months postpartum, with the exception of a much higher ICC for hiatus transverse diameter (0.46-0.74) (Tables 3, 4). In these analyses, the intra- and inter-observer standard deviations of the measurements of hiatus area and hiatus antero-posterior diameter are half of the standard deviations between measurements in women. This implies that there is more accuracy between the observers. This is reflected in narrower LOA, and therefore we feel that LOA of these two measurements are acceptable. Scatter plots can represent this graphically, revealing that LAM avulsion does not appear to influence reliability (Fig 4, 5). LOA of hiatus transverse diameter is acceptable on intra-rater analysis, but too wide on inter-rater analysis. In all analyses, LOA for LAM thickness is very wide, which implies that the measurements are not reliable.

Reliability of LAM avulsion (score 3 or 4)

The early postpartum visit revealed 15 puboccoccygeus avulsions (8 on the right and 7 on the left side) and 13 puborectalis avulsions (8 on the right and 5 on the left side). The three months postpartum visit revealed 14 puboccoccygeus avulsions (7 on either side) and 10 puborectalis avulsions (6 on the right and 4 on the left side). ICC on intra-rater analysis for avulsion of the puboccoccygeus part of LAM was 1.00, and for the puborectalis part 0.79-1.00. ICC on inter-rater analysis for avulsion of the puboccoccygeus part of LAM was 0.97-1.00 and for the puborectalis part 1.00.

Mean LPG on the right side was 1.25cm (±0.51) and 1.25cm (±0.44) on the left side. Although the numbers are small, measurements of LPG demonstrate good to excellent correlation, and LOA is not too wide (Tables 3, 4).

Reliability of LUG measurements

None of the nulliparous women had antenatal LAM avulsions, and LUG values in late pregnancy were determined. Mean LUG on the right side was 1.88cm (±0.24), and 1.92cm (±0.23) on the left side. Intra-rater analysis revealed excellent correlation for LUG, with quite inaccurate LOA. ICC on inter-rater analysis revealed fair correlation for antenatal measurements (0.13-0.21) and moderate to good correlation for both postnatal visits 0.50-0.68. For the inter-rater analysis at the three different time points, the standard deviation between women and the standard deviation between the two investigators were both around 4. This means that it almost does not matter which woman was measured, or which investigator performed the measurement, and therefore the measurements seemed to be quite random. Therefore, wide LOA were found for all time points, different from intra-rater analysis. As these measurements do not appear to be measured reliably between two investigators, we did not suggest cut-off points to diagnose LAM avulsion.

Table 2 Inter-rater analysis of antenatal levator ani muscle biometry measurements

Parameter (cm)	n	Examiner 1 Mean (±SD)	Examiner 2 Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	Standard error	Lower LOA (CI)	Upper LOA (CI)
Hiatus area	n=165	14.95 (3.29)	15.0 (2.86)	14.98 (2.97)	0.86	0.81, 0.89	-.05	1.64	0.22	-3.27 (-3.70, -2.84)	3.17 (2.74, 3.61)
Hiatus TV	n=168	3.76 (0.58)	3.60 (0.41)	3.68 (0.38)	0.16	0.02, 0.30	0.16	0.65	00.9	-1.11 (-1.28, -0.94)	1.43 (1.26, 1.60)
Hiatus AP	n=165	5.21 (0.70)	5.33 (0.63)	5.27 (0.63)	0.80	0.72, 0.85	-0.12	0.41	0.06	-0.93 (-1.04, -0.82)	0.69 (0.58, 0.80)
Thickness 9	n=164	0.42 (0.13)	0.46 (0.14)	0.44 (0.11)	0.32	0.18, 0.45	-0.05	0.16	0.02	-0.35 (-0.39, -0.31)	0.26 (0.22, 0.30)
Thickness 3	n=165	0.46 (0.14)	0.47 (0.14)	0.46 (0.12)	0.45	0.32, 0.56	-0.02	0.15	0.02	-0.30 (-0.34, -0.26)	0.27 (0.23, 0.31)
LUG right	n=169	1.95 (0.38)	1.82 (0.22)	1.88 (0.24)	0.21	0.06, 0.34	0.14	0.38	0.05	-0.61 (-0.71, -0.51)	0.88 (0.78, 0.98)
LUG left	n=169	2.02 (0.37)	1.82 (0.20)	1.92 (0.23)	0.13	-0.01, 2.62	0.20	0.39	0.05	-0.56 (-0.66, -0.46)	0.96 (0.86, 1.06)

n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; LOA, limits of agreement; Hiatus TV, hiatus transverse diameter; Hiatus AP, hiatus antero-posterior diameter; LPG, levator pubic bone gap; LUG, levator urethra gap

Table 3 Inter-rater analysis of levator ani muscle biometry measurements early postpartum

Parameter (cm)	n	Examiner 1 Mean (±SD)	Examiner 2 Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	Standard error	Lower LOA (CI)	Upper LOA (CI)
Hiatus area	n=83	16.80 (4.63)	16.72 (4.33)	16.76 (4.35)	0.88	0.82, 0.92	0.80	2.22	0.83	-4.27 (-5.10, -3.44)	4.43 (3.60, 5.26)
Hiatus TV	n=83	3.75 (0.77)	3.68 (0.70)	3.72 (0.69)	0.74	0.63, 0.82	0.07	0.53	0.20	-0.97 (-1.13, -0.74)	1.11 (0.91, 1.30)
Hiatus AP	n=83	5.71 (0.9)	5.78 (0.79)	5.75 (0.79)	0.73	0.61, 0.81	-0.08	0.63	0.24	-1.31 (-1.55, -1.08)	1.16 (0.92, 1.39)
Thickness 9	n=79	0.41 (0.16)	0.48 (0.21)	0.45 (0.16)	0.41	0.21, 0.58	-0.07	0.19	0.07	-0.45 (-0.52, -0.37)	0.30 (0.23, 0.37)
Thickness 3	n=81	0.46 (0.17)	0.51 (0.21)	0.49 (0.15)	0.33	0.13, 0.51	-0.05	0.22	0.04	-0.48 (-0.51, -0.44)	0.38 (0.35, 0.42)
LPG right	n=7	1.28 (0.49)	1.14 (0.50)	1.21 (0.43)	0.56	-0.22, 0.91	0.14	0.47	0.58	-0.78 (-1.37, -0.20)	1.06 (0.48, 1.64)
LPG left	n=6	1.29 (0.62)	1.21 (0.53)	1.25 (0.57)	0.96	0.78, 0.995	0.09	0.14	0.19	-0.19 (-0.38, 0.01)	0.36 (-0.17,0.56)
LUG right	n=83	1.92 (0.50)	1.94 (0.41)	1.93 (0.41)	0.68	0.54, 0.78	-0.02	0.37	0.14	-0.75 (-0.88, -0.61)	0.71 (0.57, 0.84)
LUG left	n=83	2.06 (0.45)	1.94 (0.38)	2.00 (0.38)	0.67	0.51, 0.78	0.12	0.33	0.12	-0.53 (-0.65, -0.41)	0.76 (0.64, 0.89)

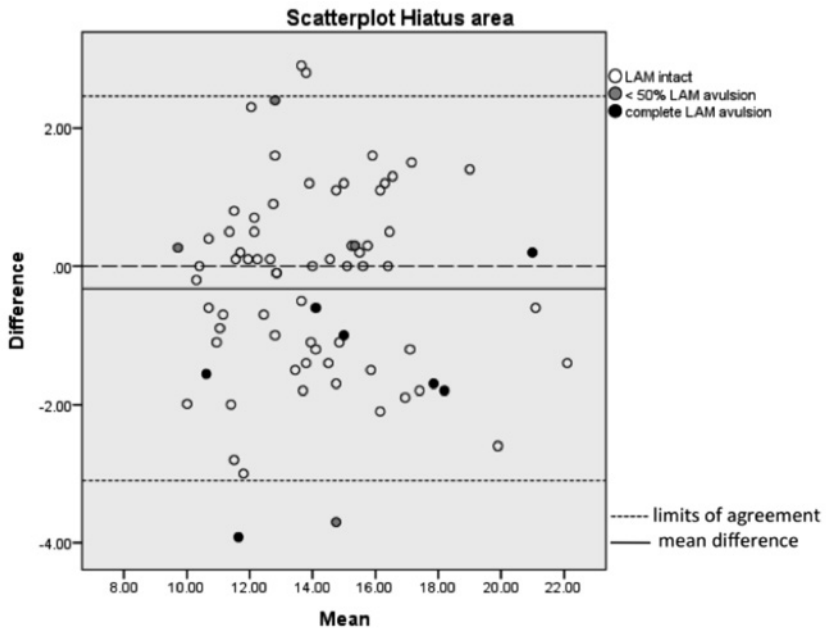
n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; LOA, limits of agreement; Hiatus TV, hiatus transverse diameter; Hiatus AP, hiatus antero-posterior diameter; LPG, levator pubic bone gap; LUG, levator urethra gap

Table 4 Inter-rater analysis of levator ani muscle biometry measurements three months postpartum

Parameter (cm)	n	Examiner 1 Mean (±SD)	Examiner 2 Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	Standard error	Lower LOA (CI)	Upper LOA (CI)
Hiatus area	n=75	13.98 (2.81)	14.31 (2.84)	14.14 (2.73)	0.87	0.80, 0.92	-0.32	1.42	0.28	-3.10 (-3.66, -2.55)	2.46 (1.91, 3.02)
Hiatus TV	n=75	3.74 (0.60)	3.79 (0.54)	3.77 (0.49)	0.46	0.26, 0.62	-0.05	0.60	0.12	-1.23 (-1.46, -0.99)	1.13 (0.89, 1.36)
Hiatus AP	n=75	5.10 (0.58)	5.24 (0.62)	5.17 (0.56)	0.74	0.60, 0.83	-0.14	0.42	0.08	-0.96 (-1.13, -0.80)	0.69 (0.52, 0.85)
Thickness 9	n=73	0.36 (0.14)	0.41 (0.17)	0.39 (0.14)	0.52	0.32, 0.67	-0.05	0.15	0.03	-0.35 (-0.41, -0.29)	0.24 (0.18, 0.30)
Thickness 3	n=71	0.37 (0.15)	0.43 (0.19)	0.40 (0.14)	0.35	0.13, 0.53	-0.06	0.19	0.04	-0.43 (-0.51, -0.35)	0.32 (0.24, 0.39)
LPG right	n=9	1.35 (0.67)	1.22 (0.52)	1.29 (0.59)	0.91	0.64, 0.98	0.13	0.24	0.14	-0.34 (-0.61, -0.07)	0.60 (0.33, 0.87)
LPG left	n=7	1.23 (0.29)	1.27 (0.39)	1.25 (0.32)	0.81	0.23, 0.96	-0.04	0.22	0.14	-0.47 (-0.75, -0.19)	0.39 (0.11, 0.67)
LUG right	n=75	2.04 (0.43)	2.03 (0.33)	2.03 (0.34)	0.52	0.33, 0.67	0.01	0.38	0.08	-0.73 (-0.88, -0.58)	0.76 (0.61, 0.91)
LUG left	n=75	1.93 (0.41)	1.95 (0.29)	1.99 (0.31)	0.50	0.31, 0.65	0.08	0.35	0.07	-0.61 (-0.75, -0.47)	0.76 (0.63,0.90)

n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; LOA, limits of agreement; Hiatus TV, hiatus transverse diameter; Hiatus AP, hiatus antero-posterior diameter; LPG, levator pubic bone gap; LUG, levator urethra gap

Figure 4 Three months follow-up, scatterplot limits of agreement for hiatus area



The x-axis represents the mean hiatus area measurement of the two investigators per subject. The y-axis represents the absolute difference in hiatus area between the two investigators. LOA, Limit of agreement; δ, mean difference between two investigators.

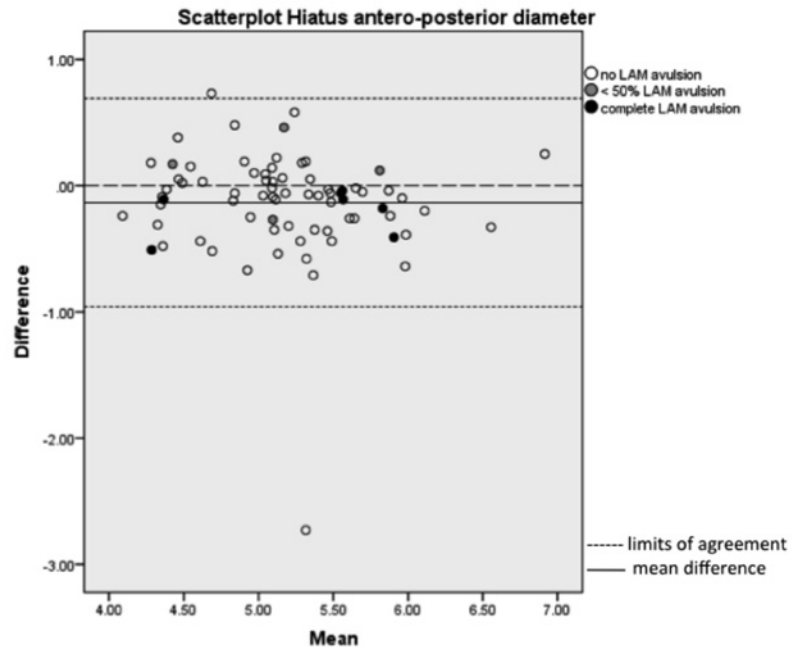
Discussion

Reliability analysis using 3D EVUS in antenatal and postnatal women revealed good correlation with acceptable LOA for levator hiatus area and antero-posterior diameter. The correlation in detection rates of specific LAM avulsions using the proposed scoring system was excellent. In this study we determined LUG values in late pregnancy, however with slight to fair repeatability and wide LOA. 3D EVUS can be reliably used in clinical practice and research to image LAM for hiatus measurements and detection of avulsion.

Technique

EVUS with its high resolution 3D volumes provides useful and reliable details of the female pelvic floor. The acquired 3D volume can easily be manipulated to visualise origin and insertion points of the different parts of LAM to the pubic bone[2]. By tilting the 3D volume, the investigator can be assured that measurements are taken in the

Figure 5 Three months follow-up, scatterplot limits of agreement for hiatus antero-posterior (AP) diameter



Tthe x-axis represents the mean hiatus antero-posterior diameter measurement of the two investigators per subject. The y-axis represents the absolute difference in hiatus antero-posterior diameter between the two investigators. LOA, Limit of agreement; δ, mean difference between two investigators.

true plane of the minimal hiatal dimensions[15]. We minimised bias as the plane in which the measurements were taken was decided upon by each investigator independently. However, 3D EVUS has the main disadvantage that dynamic studies are currently not possible as it is not possible to hold a squeeze or Valsalva manoeuvre for one minute at the same intensity. This could possibly be investigated in future using rapid sequence imaging to see if this changes LAM avulsion detection rate. The strength of our study is that scans of women following childbirth were included, in which LAM avulsion and subsequent anatomical distortions can be expected, which can make visualisation of the landmarks more difficult. In this study, we were able to recognise all anatomical landmarks to analyse the scans. However, we were not able to perform all measurements, mainly due to artefacts. Anatomical identification of the landmarks is of utmost importance in performing reliable and accurate measurements[11,21,22]. Therefore, repeatability of measurements in our study

of parous women with possible anatomical distortion may understandably be slightly lower compared to studies in nulligravida only.

Reliability

Hiatus biometry

LOA for hiatus area and antero-posterior diameter were acceptable, and these measurements are relevant in identifying enlarged hiatus. Enlarged hiatus, or ballooning, as measured by TPUS, is strongly associated with female pelvic organ prolapse[23]. EVUS can help to further understand the pathophysiology of LAM avulsion and enlarged hiatus. The overall repeatability of the hiatus measurements published by Santoro et al using EVUS in nulligravid women was slightly better than our results, although they did not construct LOA[11]. Our hiatus measurements in primigravida are slightly larger than the measurements performed in nulligravida[3,10,11]. This can be explained by an increase in levator hiatus dimensions in primigravida as shown by Elenskaia et al[24]. Measurements of hiatus transverse diameter and LAM thickness were not repeatable. The hiatus transverse diameter was assessed by measuring the width of the hiatus at the inner margin of LAM attachment to the pubic bone[10], unlike measuring the widest transverse diameter used in TPUS[15]. Using this technique, we expected less judgement, leading to higher repeatability than we actually found. Particularly, the poor repeatability of the hiatus transverse diameter found in antenatal ultrasounds was unexpected as least judgement should be necessary in women without anatomical distortions of the LAM. Measurements of LAM thickness were smaller in our analysis[10]. Comparing our nulliparous results on 3D EVUS with others' performing TPUS, our hiatus measurement findings are comparable[25,26,27].

LAM avulsion

The proposed scoring system for avulsion of the pubococcygeus and puborectalis part of LAM has an excellent intra- and inter-observer repeatability. LAM avulsion is known to be a cause of repetitive prolapse surgery due to initial failure[8]. The ability to provide detailed information on LAM structures and avulsion, and the ability to identify women at risk, may help us to understand the pathophysiology further and to optimise surgical decision making and techniques. Follow-up is needed to see whether LPG will increase with time in women with LAM avulsion.

Levator urethra gap

We determined LUG measurements in late pregnancy. However, repeatability was only slight to fair and LOA was too wide. Comparable intra- and inter-rater findings were found in postpartum women. As LUG measurements do not appear reliable between two investigators, cut-off points to diagnose LAM avulsion were not

suggested in this study. Furthermore, the proposed cut-off point of 25 mm on TPUS at maximum pelvic floor muscle contraction[13], does not seem to be applicable here as EVUS images were acquired at rest.

Limitations of the study

Scans were initially interchangeably performed by two investigators (KvD, NS-T). Secondly, scans were not performed twice at the same visit. The technique of acquiring a 3D-volume is standardised and repeatable. We feel that using a stored 3D volume to obtain the required measurements ensures that each investigator follows the protocol to obtain the measurements in the correct plane, unlike 2D ultrasonography where the plane has already been decided upon. Technique variability was minimised by rigorous investigator training and observation by the principal investigator (RT).

Not all scans were analysable due to artefacts or poor quality. This mainly occurred when anatomy was changed and the landmarks were not clearly visible anymore. It was very important to control for that while acquiring the 3D volume. If landmarks were less visible, a new volume was acquired.

We did not perform a separate power calculation but used a larger sample size compared to other reliability studies[11,14], to increase reliability of the results[18]. Furthermore, the study group contained women with and without damage to the pelvic floor following childbirth. It would be interesting to see if our results of diagnosing LAM avulsion also apply to larger cohorts such as those with prolapse, as our cohort had only 29 pubococcygeus and 23 puborectalis avulsions.

Recommendations

3D EVUS can be used reliably to assess levator hiatus area and antero-posterior diameter and LAM attachment to the pubic bone in parous women, but less so for thickness and LUG. This methodology can help identify women at risk of prolapse after childbirth or at risk of recurrent prolapse following initial prolapse surgery. The validity for all measurements needs to be further investigated by comparing measurements with other techniques, such as TPUS and MRI, to establish correlation and agreement. Currently, we are performing both EVUS and TPUS in a large group of women, and comparison of these results is underway.

References

1. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
2. Shobeiri SA, Leclaire E, Nihira MA, Quiroz LH, O'Donoghue D. Appearance of the levator ani muscle subdivisions in endovaginal three-dimensional ultrasonography. Obstet Gynecol 2009;114:66-72
3. Shobeiri SA, Rostaminia G, White D, Quiroz LH. The determinants of minimal levator hiatus and their relationship to the puborectalis muscle and the levator plate. BJOG 2013;120:205-11
4. Dietz HP, Lanzarone V. Levator trauma after vaginal delivery. Obstet Gynecol 2005;106:707-12
5. Valsky VD, Lipschuetz M, Bord A, Eldar I, Messing B, Hochner-Celnikier D, et al. Featal head circumference and length of second stage of labor are risk factors for levator ani muscle injury, diagnosed by 3-dimensional transperineal ultrasound in primiparous women. Am J Obstet Gynecol 2009;201:91.e1-7
6. Shek K, Dietz HP. Intrapartum risk factors for levator trauma. BJOG 2010;117:1485-92
7. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
8. Dietz HP, Chantarasorn V, Shek KL. Levator avulsion is a risk factor for cystocele recurrence. Ultrasound Obstet Gynecol 2010;36:76-80
9. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
10. Santoro GA, Wieczorek AP, Stankiewicz A, Woźniak MM, Bogusiewicz M, Rechberger T. High-resolution three-dimensional endovaginal ultrasonography in the assessment of pelvic floor anatomy: a preliminary study. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1213-22
11. Santoro GA, Wieczorek AP, Shobeiri SA, Mueller ER, Pilat J, Stankiewicz A, et al. Interobserver and inter-disciplinary reproducibility of 3D endovaginal ultrasound assessment of pelvic floor anatomy. Int Urogynecol J 2011;22:53-9
12. Rostaminia G, White D, Hegde A, Quiroz LH, Davila GW, Shobeiri SA. Levator ani deficiency and pelvic organ prolapse severity. Obstet Gynecol. 2013;121:1017-24
13. Dietz HP, Abbu A, Shek KL. The levator-urethra gap measurement: a more objective means of determining levator avulsion? Ultrasound Obstet Gynecol 2008;32:941-5
14. Majida M, Braekken IH, Bø K, Benth JS, Engh ME. Validation of three-dimensional perineal ultrasound and magnetic resonance imaging measurements of the pubovisceral muscle at rest. Ultrasound Obstet Gynecol 2010;35:715-22
15. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-5
16. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
17. DeLancey JO, Trowbridge ER, Miller JM, Morgan DM, Guire K, Fenner DE, et al. Stress urinary incontinence: relative importance of urethral support and urethral closure pressure. J Urol 2008;179:2286-90
18. Walter SD, Eliasziw M, Donner A. Sample size and optimal designs for reliability studies. Statist Med 1998;17:101-10
19. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74
20. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 2003;22:85-93
21. Weinstein MM, Jung S-A, Pretorius DH, Nager CW, den Boer DJ, Mittal RK. The reliability of puborectalis muscle measurements with 3-dimensional ultrasound imaging. Am J Obstet Gynecol 2007;197:68.e1-68.e6
22. Hoyte L, Brubaker L, Fielding JR, Lockhart ME, Heilbrun ME, Salomon CG, et al; Pelvic Floor Disorders Network. Measurements from image-based three dimensional pelvic floor reconstruction: a study of inter- and intraobserver reliability. J Magn Reson Imaging 2009;30:344-50
23. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80

24. Elenskaia K, Thakar R, Sultan AH, Scheer I, Onwude J. Effect of childbirth on pelvic organ support and quality of life: a longitudinal cohort study. Int Urogynecol J 2013;24:927-37
25. Svabík K, Shek KL, Dietz HP. How much does the levator hiatus have to stretch during childbirth? BJOG 2009;116:1657-62
26. Shek KL, Dietz HP. The effect of childbirth on hiatal dimensions. Obstet Gynecol 2009;113:1272-8
27. Shek KL, Kruger J, Dietz HP. The effect of pregnancy on hiatal dimensions and urethral mobility: an observational study. Int Urogynecol J 2012;23:1561-7

5

Diagnostic accuracy of palpation, transperineal and endovaginal ultrasound in levator ani assessment

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Abstract

Objectives: To estimate diagnostic accuracy between transperineal and endovaginal ultrasound in assessing levator ani biometry and avulsion in nullipara and primipara, and to determine agreement between palpation of levator avulsion and both ultrasound modalities.

Methods: This longitudinal cohort study performed in a district general university hospital (United Kingdom) contained 269 nullipara at 36 weeks gestation and 191 primipara 13 weeks postpartum. Women underwent palpation of the levator and avulsion was diagnosed if no attachment to the pubic bone was felt. Subsequently, 3/4D transperineal and 3D endovaginal ultrasound were performed. A standardised protocol was used to perform measurements at rest. Levator avulsion was diagnosed on endovaginal ultrasound at rest if >50% was avulsed and on transperineal ultrasound at maximum contraction if the central three slices were avulsed. Levator avulsion was analysed by two independent blinded investigators. A third investigator resolved discrepancies. Intraclass correlation coefficient and limits of agreement were calculated for each time point.

Results: Intraclass correlation coefficient for levator urethra gap was 0.44-0.54, hiatus area 0.76-0.79, transverse diameter 0.51-0.59, antero-posterior diameter 0.70-0.72. Levator thickness correlated poorly. Endovaginal ultrasound measurements were generally smaller, however limits of agreement were acceptable for hiatus measurements. Overall agreement between both ultrasound techniques in diagnosing levator avulsion was 95%; correlation 0.72 (95%CI 0.67-0.76). Palpation had a high specificity (99%) and a low sensitivity (26-28%).

Conclusions: Transperineal and endovaginal ultrasound can both be used inter-changeably to analyse hiatus area and antero-posterior diameter and to diagnose levator avulsion. Palpation underestimates true avulsion and therefore cannot substitute ultrasound.

Introduction

Obstetric pelvic floor trauma has been implicated in the pathogenesis of pelvic organ prolapse. Levator ani muscle avulsion and hiatal ballooning have been associated with pelvic organ prolapse[1,2,3,4]. Currently, three techniques are used to image the levator: magnetic resonance imaging (MRI)[5], 3/4D transperineal ultrasound (TPUS)[6] and 3D endovaginal ultrasound (EVUS)[7]. Due to the dramatic upsurge in imaging modalities in recent years, it is important to standardise assessment techniques to enable evaluation and comparison.

TPUS is most widely used, with good reliability analyses[8]. Some comparisons have been made between TPUS and MRI, with good correlation for measurements[9,10,11] and substantial agreement for detecting levator avulsion[11], although there seemed to be a significant difference regarding the extent of levator avulsion (letter: Am J Obstet Gynecol. 2012;206:e7).

Unlike TPUS, EVUS is a more recent development and authenticated in cadaveric dissections[7,12]. Good correlation for measurements[13,14,15] and excellent reliability for levator avulsion have been demonstrated[15]. However, there are no published comparative studies between TPUS and EVUS.

Palpation can be useful in detecting levator avulsion[5,16]. Normal variations of insertion have been shown in assessing levator attachment to the pubic bone in nullipara, with excellent inter-rater agreement[17]. Comparisons between palpation, MRI[5] and TPUS[16] indicate that palpation underestimates levator avulsion. No comparison has been made between palpation and EVUS.

The primary aim of this study was to estimate diagnostic accuracy between TPUS and EVUS in assessing levator ani biometry and avulsion in nullipara and primipara. The secondary aim was to determine agreement between palpation of levator avulsion and both ultrasound modalities.

Methods

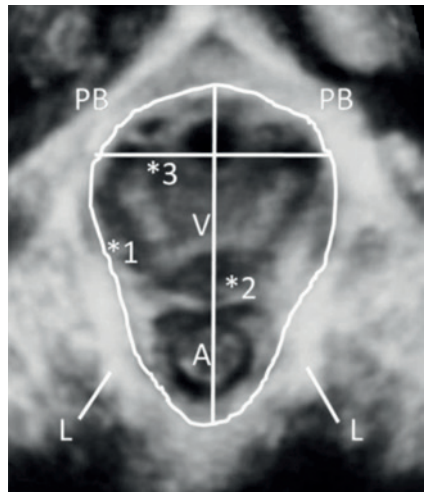
Between January 2011 and May 2012, nulliparous women were invited from the antenatal clinics at Croydon University Hospital to participate in a prospective longitudinal study to establish the prevalence of levator defects sustained during childbirth and to correlate these with pelvic floor symptoms and pelvic floor muscle strength. Information leaflets were provided to women and their interest in the study was subsequently evaluated via telephone. An appointment was booked if women wished to participate. All women gave written informed consent during their first appointment at 36 weeks of gestation and were followed up three months following childbirth. The study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87).

Women were asked to empty their bladder and the examination was performed in supine position, with both knees semi-flexed. Technique variability was minimised by investigator training and observation by the principal investigator (RT) before commencing the study. All examinations were performed by one investigator (KvD) in the same order, during the same visit: palpation, 3/4D TPUS and 3D EVUS. Analysis of the ultrasounds was performed while post-processing the acquired images in an office setting, a few months following examination. The investigators, KvD, RT, SAS and KK have had 0.5, 5, 18 and 5.5 years of experience with pelvic floor ultrasound imaging.

Palpation of levator attachment to the pubic bone was performed by placing the index finger lateral to the urethra, with slight pressure against the pubic bone[5,16,17]. When the index finger is inserted to the woman's right side of the urethra, the levator can be felt on the left side of the index finger[17]. Women were asked to contract their pelvic floor muscles to identify muscle at the point of attachment to the retropubic area[5]. Both sides were evaluated separately using a previously described grading system, for which an inter-rater reliability analysis was carried out by the same investigator (KvD)[17]. If LAM attachment was not palpable, an avulsion was identified[16], corresponding to score 3 or 4 of our previously published scoring system, which had excellent inter-rater reliability in nulliparous women[17]. Previous inter-rater reliability of studies for palpation of levator attachment in women with prolapse revealed a kappa between 0.41[16] and 0.57[5].

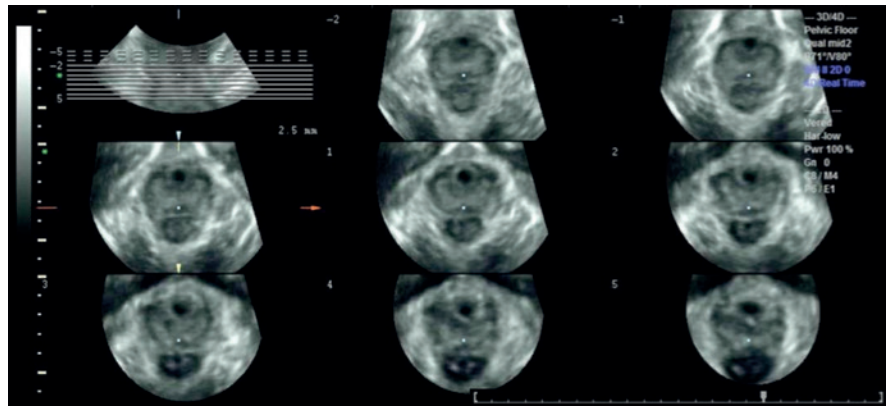
TPUS was then performed using GE Voluson 730, with a 4-8MHz curved array volume transducer with acquisition angle of up to 85 degrees. Imaging was performed at rest and at maximum contraction. We used 4D view version 10.2 for offline analysis of the acquired scans, using a standardised protocol. The image in the two-dimensional midsagittal plane was tilted to the plane of the minimal hiatal dimensions, which is the shortest distance between the posterior margin of the pubic bone and the anterior margin of the levator plate[7,17,18]. The axial plane of the rendered three-dimensional image was used to visualise the pubic bone, urethra, vagina, anal canal and the levator. All hiatus measurements, such as levator urethra gap[19], hiatus area, transverse diameter, antero-posterior diameter[18] and thickness of levator were obtained in the resting sequence following a standardised protocol (Figure 1). We then used tomographic ultrasound imaging on maximum contraction to assess levator attachment to the pubic bone in the axial plane[20]. Eight slices of 2.5 mm interval were produced, from 5 mm below the plane of the minimal hiatal dimensions to 12.5 mm above this plane[20]. Direct visualisation of the levator was used to score the tomographic ultrasound imaging slices, both left and right side separately (Figure 2). Avulsion was diagnosed when the central three slices were abnormal (Figure 3), which is known to be most clinically relevant[6]. All measurements were performed by one investigator (KvD). A test-retest series of 20 postnatal scans on hiatus

Figure 1 Hiatus biometry measurements on TPUS, intact levator ani muscle



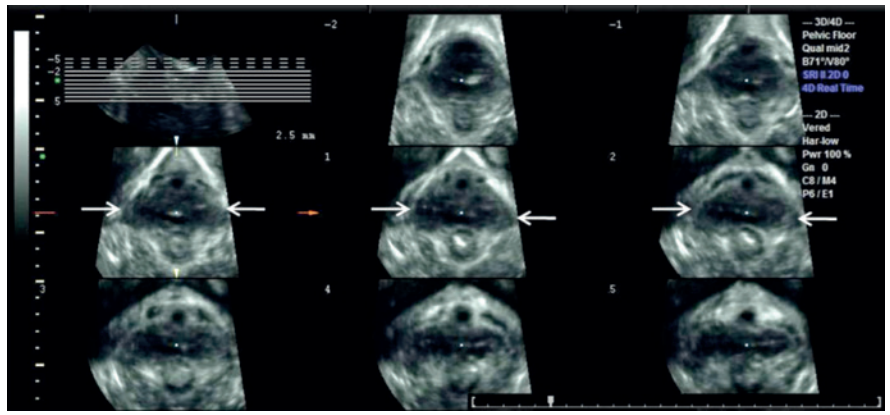
PB, pubic bone; U, urethra; V, vagina; A, anal canal; L, levator ani muscle
*1, Hiatus area; *2, hiatus antero-posterior diameter; *3, hiatus transverse diameter.

Figure 2 Normal levator ani muscle attachment on tomographic ultrasound imaging (TPUS)



measurements was performed by a second investigator (KK). Two independent investigators (KvD and KK) analysed all postnatal TPUS images to diagnose levator avulsion. In presence of discrepancies, consensus was reached by a third investigator (RT). Reliability studies performed by two investigators have previously been

Figure 3 Bilateral levator ani muscle avulsion on tomographic ultrasound imaging on TPUS, three months following a forceps delivery



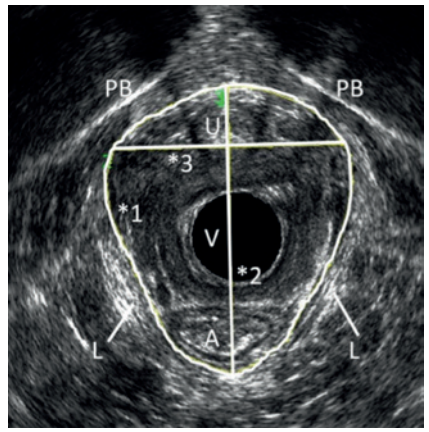
Arrows indicate bilateral LAM avulsion.

published for measurements (intraclass correlation for levator urethra gap 0.71, hiatus area 0.92, transverse diameter 0.96, antero-posterior diameter 0.96)[19,21] and levator avulsion (intraclass correlation 0.83)[22].

TPUS was used as the reference standard when compared with EVUS, as it has been used extensively in levator assessment and diagnosis of avulsion[2,3,4,6,8,9,16,18,19,20,2].

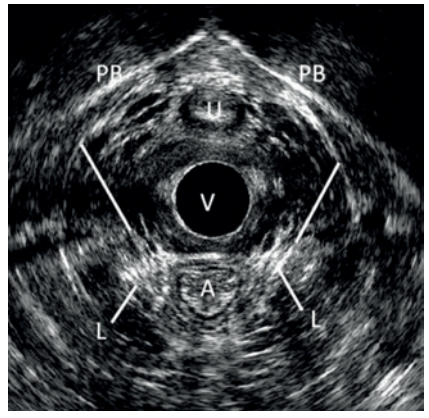
Thirdly, high frequency EVUS was performed (B-K Medical, Herlev, Denmark, Type 2050 (9-16 MHz) 360° rotational probe) at rest. A 3D volume was acquired over a distance of 60mm with intervals of 0.2 mm, providing 300 axial images in one minute[12,13]. For post processing, B-K Medical Viewer version 7.0.0.519 was used to conduct offline analysis of the acquired scans using a standardised protocol, similar to the protocol used to analyse TPUS. In the midsagittal view, the plane of the minimal hiatal dimensions was identified by scrolling through the 3D data volume[7,15,17,18]. The 3D volume was tilted to visualise the pubic bone, urethra, vagina, anal canal and the levator in the axial plane. All hiatus measurements (levator urethra gap, area, transverse diameter, antero-posterior diameter and thickness of LAM) were performed in this plane (Figure 4)[13,15,19]. The levator was scored as intact or avulsed (≥50% avulsion); and left and right side were analysed separately (Figure 5)[15,17,23]. All hiatus measurements were performed by one investigator (KvD). Two independent investigators (KvD and SAS) analysed all postnatal EVUS images to diagnose levator avulsion. In presence of discrepancies, consensus was reached by a third investigator (RT). Reliability studies performed by two independent investigators (KvD and SAS) revealed the following intraclass correlation for measurements (levator urethra gap 0.13-0.68, hiatus area 0.86-0.88, transverse diameter 0.16-0.74, antero-posterior

Figure 4 Hiatus biometry measurements on EVUS, intact levator ani muscle



PB, pubic bone; U, urethra; V, vagina; A, anal canal; L, levator ani muscle
*1, Hiatus area; *2, hiatus antero-posterior diameter; *3, hiatus transverse diameter.

Figure 5 Bilateral levator ani muscle avulsion on EVUS three months following a forceps delivery



PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; L, levator ani muscle
Lines indicate bilateral LAM avulsion.

diameter 0.73-0.80, levator thickness 9 o'clock 0.32-0.52 and 3 o'clock 0.33-0.45) and levator avulsion (0.97-1.00)[15].

While performing the ultrasound analysis, all investigators were blinded to delivery details, findings on palpation and each other's results. After the initial analysis, we found discrepancies in detection of levator avulsion between the two ultrasound techniques. These discrepant scans were reviewed by an independent investigator (RT) to identify clarifications for these discrepancies.

Statistical analysis

Data were analysed using SPSS 20.0 (SPSS Inc., Chicago, IL). Intraclass correlation coefficient was calculated to measure repeatability of levator avulsion diagnosis by TPUS and EVUS using a two way mixed model, with absolute agreement and single measures as the outcome (<0.00 no repeatability, 0.0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good, 0.81-1.00 excellent repeatability)[24]. Bland-Altman analysis was performed to construct limits of agreement to control for close agreement of the measurements acquired by both ultrasound techniques. In this way, systemic bias between the two ultrasound techniques could be detected. The mean difference (δ) and standard deviation of this difference (SDd) were calculated and limits of agreement were constructed: δ - (1.96 x SDd) = lower limit, and δ + (1.96 x SDd) = upper limit of agreement. The standard error of the limits is approximately $\sqrt{3SDd^2/n}$. The 95% confidence interval for the limits of agreement is given by $\pm$ 1.96 standard errors. Interpretation of the limits of agreement is a decision to be made by the clinician. Although acceptability of the limits of agreement should ideally be determined prior to the analysis, we were not able to do so as this is the first time these two ultrasound techniques have been compared[25]. Sensitivity and specificity analyses were performed to evaluate palpation of levator avulsion in relation to TPUS and EVUS.

Results

Between January 2011 and May 2012, 269 nulliparous women were included at a median of 36 weeks gestation (range 34 – 41). The mean age of nulliparous women was 30.2 ($\pm$5.8) and mean BMI was 25.4 ($\pm$5.3). All women underwent palpation, TPUS and EVUS. Levator avulsion was not found in any of these nulliparous women after evaluation of all three modalities. 191/269 women (71%) were seen as primiparous women three months postpartum at a median of 13 weeks (range 10 – 26). One woman declined palpation, and one declined EVUS. There were no adverse events from performing any of the tests in this study.

Moderate to good correlation (intraclass correlation coefficient 0.45-0.84) was found in test-retest analyses by a second investigator for the TPUS measurements in the rendered image.

LAM biometry

TPUS at rest was compared with EVUS at rest for levator biometry. Results of measurement analyses are separated for nulliparous (Table 1) and primiparous women (Table 2). Not all measurements could be taken in all scans (Tables 1 and 2), due to poorer quality as the landmarks could not be identified. For both nulliparous and primiparous women the standard deviation of the differences between the levator urethra gap measurements was larger than the standard deviation of the mean of levator urethra gap measurements on TPUS and EVUS. This implies that there is not much accuracy between TPUS and EVUS for levator urethra gap measurements, resulting in wide limits of agreement, in spite of moderate correlation. Correlation for hiatus measurements was good. The standard deviation of the difference of the hiatus area and antero-posterior measurements was smaller than the standard deviation between measurements in women, resulting in acceptable limits of agreement for nulliparous and primiparous women (Figure 6). Correlation of hiatus transverse diameter was moderate, and limits of agreement were wide. Correlation and limits of agreement for measurements of levator thickness were poor.

Overall, correlation and agreement in nulliparous women was similar to parous women. EVUS measurements were found to be generally smaller than TPUS measurements.

Levator avulsion

To diagnose levator avulsion, we compared TPUS at maximum pelvic floor muscle contraction with EVUS at rest, as these are the optimal assessment techniques for each individual technique[6,7,15,22,23]. 34/380 (8.9%) levator avulsions were found on TPUS and 36/380 (9.5%) on EVUS (Table 3). 26/380 (6.8%) levator avulsions were identified by both TPUS and EVUS, 8 (2.1%) by TPUS only and 10 (2.6%) by EVUS only. Overall agreement was found in 362 levator analyses (95.3%) and the intraclass correlation coefficient was 0.72 (95%CI 0.67-0.76), which implies good correlation. Most discrepancies between the two ultrasound techniques were true disagreements. Four (1%) of the total number of acquired scans were suboptimal due to a poorer quality of the images. A sub analysis was performed to compare TPUS at rest and EVUS at rest and showed a correlation of 0.47, which is only moderate, and considerably less than that obtained when using the optimal modalities for each technique to diagnose levator avulsion.

Palpation

When comparing palpation of levator avulsion with TPUS, a sensitivity of 26% (95% CI 14-45%) was found, specificity 99% (95% CI 96-99%), positive predictive value 64% (95% CI 36-86%) and negative predictive value 93% (95% CI 90-95%). When comparing palpation of levator avulsion with EVUS, a sensitivity of 28% (95% CI

Table 1 Comparison of hiatus measurements on TPUS and EVUS in nulliparous women at 36 weeks of gestation

Parameter cm	n	EVUS Mean (±SD)	TPUS Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	SE	Lower LOA (95% CI)	Upper LOA (95% CI)
LUG right	265	1.82 (0.22)	1.89 (0.26)	1.86 (0.21)	0.45	0.34, 0.55	-0.07	0.25	0.03	-0.56 (-0.61, -0.51)	0.42 (0.37, 0.47)
LUG left	265	1.82 (0.21)	1.91 (0.27)	1.86 (0.21)	0.44	0.30, 0.55	-0.09	0.25	0.03	-0.58 (-0.63, -0.53)	0.40 (0.35, 0.45)
Hiatus area	261	14.80 (2.84)	15.55 (3.46)	15.13 (2.96)	0.79	0.71, 0.84	-6.66	1.95	0.21	-4.49 (-4.90, -4.08)	3.16 (2.75, 3.57)
Hiatus TV	264	3.61 (0.42)	3.73 (0.48)	3.67 (0.39)	0.51	0.40, 0.60	-0.12	0.44	0.05	-0.98 (-1.07, -0.88)	0.75 (0.65, 0.84)
Hiatus AP	261	5.27 (0.64)	5.61 (0.75)	5.43 (0.66)	0.70	0.37, 0.84	-0.33	0.46	0.05	-1.23 (-1.33, -1.14)	0.57 (0.47, 0.67)
Thickness 9	259	0.45 (0.15)	0.54 (0.18)	0.50 (0.13)	0.20	0.07, 0.32	-0.09	0.20	0.02	-0.49 (-0.53, -0.45)	0.31 (0.27, 0.35)
Thickness 3	260	0.48 (0.15)	0.59 (0.18)	0.54 (0.13)	0.22	0.06, 0.35	-0.11	0.20	0.02	-0.51 (-0.55, -0.46)	0.28 (0.24, 0.33)
Thickness 6	230	0.82 (0.25)	0.80 (0.27)	0.81 (0.20)	0.12	-0.01, 0.25	0.02	0.35	0.04	-0.67 (-0.74, -0.59)	0.70 (0.62, 0.78)

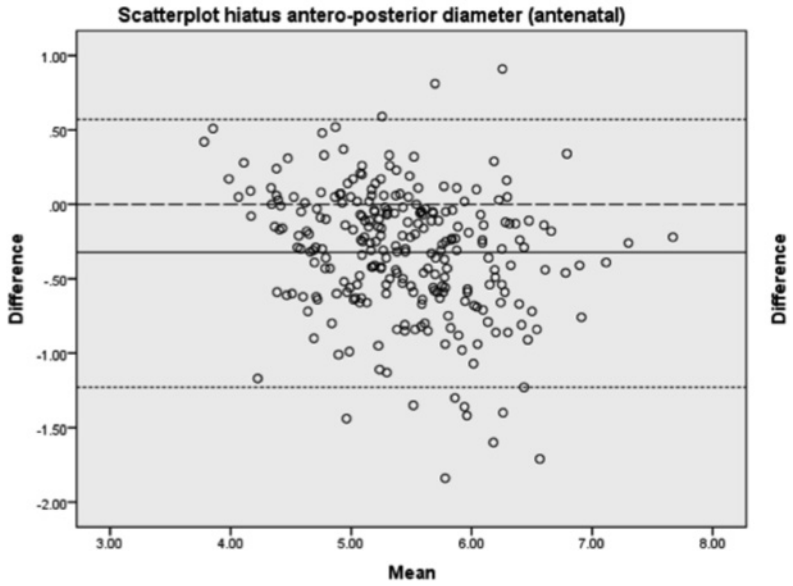
n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; SE, standard error; LOA, limits of agreement; LUG, levator urethra gap; Hiatus TV, hiatus transverse diameter; Hiatus AP, hiatus diameter antero-posterior. Thickness 3, 6, 9 indicates muscle thickness measurements at 3 o'clock, 6 o'clock and 9 o'clock respectively

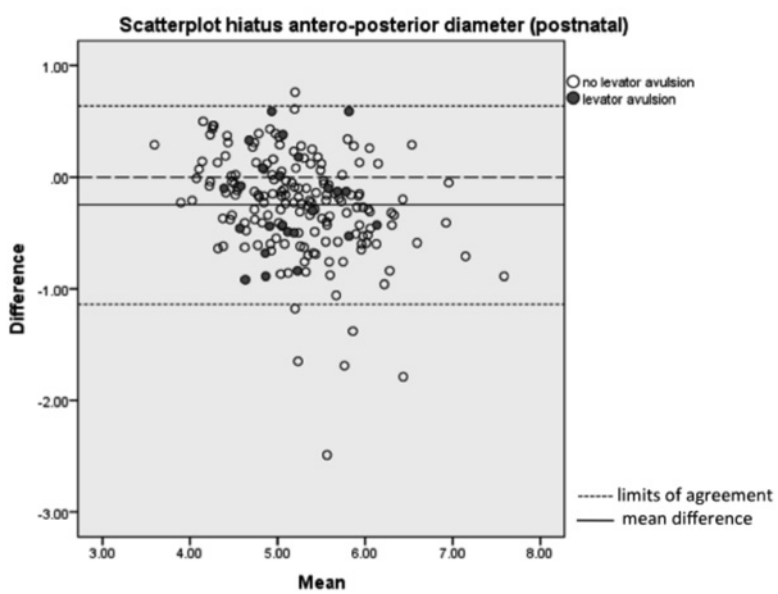
Table 2 Comparison of hiatus measurements on TPUS and EVUS in primiparous women three months following childbirth

Parameter cm	n	EVUS Mean (±SD)	TPUS Mean (±SD)	Overall Mean (±SD)	ICC	95% CI	∂	SDd	SE	Lower LOA (95% CI)	Upper LOA (95% CI)
LUG right	190	1.94 (0.37)	2.07 (0.38)	2.00 (0.33)	0.54	0.46, 0.61	-0.13	0.34	0.04	-0.79 (-0.87, -0.71)	0.53 (0.45, 0.61)
LUG left	190	1.87 (0.30)	2.04 (0.36)	1.96 (0.29)	0.46	0.35, 0.55	-0.17	0.31	0.04	-0.77 (-0.85, -0.70)	0.43 (0.35, 0.50)
Hiatus area	190	13.79 (2.81)	14.82 (3.45)	14.30 (2.97)	0.76	0.66, 0.83	-1.02	2.07	0.26	-5.08 (-5.59, -4.57)	3.03 (2.52, 3.54)
Hiatus TV	190	3.70 (0.61)	3.94 (0.69)	3.82 (6.0)	0.59	0.50, 0.66	-0.24	0.51	0.06	-1.24 (-1.37, -1.11)	0.76 (0.62, 0.89)
Hiatus AP	190	5.12 (0.62)	5.37 (0.76)	5.24 (0.66)	0.72	0.40, 0.84	-0.25	0.45	0.06	-1.14 (-1.25, -1.03)	0.64 (0.53, 0.75)
Thickness 9	190	0.42 (0.18)	0.57 (0.24)	0.50 (0.17)	0.22	0.10, 0.32	-0.15	0.25	0.03	-0.65 (-0.71, -0.58)	0.35 (0.29, 0.41)
Thickness 3	190	0.46 (0.17)	0.60 (0.22)	0.53 (0..6)	0.23	0.09, 0.36	-0.14	0.23	0.03	-0.59 (-0.65, -0.54)	0.31 (0.25, 0.36)
Thickness 6	177	0.73 (0.18)	0.76 (0.20)	0.75 (0.14)	0.12	-0.02, 0.15	-0.03	0.26	0.03	-0.54 (-0.60, -0.47)	0.48 (0.42, 0.55)

n, number; SD, standard deviation; ICC, intraclass correlation coefficient; CI, confidence interval; ∂, mean difference between measurements; SDd, standard deviation of differences; SE, standard error; LOA, limits of agreement; LUG, levator urethra gap; Hiatus TV, hiatus transvers diameter; Hiatus AP, hiatus diameter antero-posterior; Thickness 3, 6, 9 indicates muscle thickness measurements at 3 o'clock, 6 o'clock and 9 o'clock respectively.

Figure 6 Scatter plot limits of agreement for hiatus antero-posterior diameter on antenatal and postnatal assessment





The x-axis represents the mean hiatus antero-posterior diameter of the two ultrasound techniques per subject. The y-axis represents the absolute difference in hiatus antero-posterior diameter between the two ultrasound techniques.

Table 3 LAM avulsion detection by TPUS at maximum pelvic floor contraction vs. EVUS at rest

	TPUS squeeze +	TPUS squeeze –	Predictive Value
EVUS rest +	26	10	Positive= 0.72
EVUS rest –	8	336	Negative=0.98
	Sensitivity=0.76	Specificity=0.97	

+ = LAM avulsion. – = no LAM avulsion
Intraclass correlation coefficient = 0.72 (95%CI 0.67-0.76), overall agreement = 0.95.

15-45%) was found, specificity 99% (95% CI 97-100%), positive predictive value 71% (95% CI 42-90%) and negative predictive value 93% (95% CI 90-95%).

Discussion

This study suggests that TPUS and EVUS can be used interchangeably to analyse levator hiatus area and antero-posterior diameter and to diagnose levator avulsion. Palpation is not a good screening tool as it underestimates true levator avulsion, suggesting that palpation cannot substitute ultrasound.

Strengths and weaknesses

A strength of our study is the inclusion of large numbers of both nullipara and primipara. All examinations were performed in the same order during the same visit as per a standardized protocol. Furthermore we assessed reliability using intraclass correlation coefficient and limits of agreement, to see agreement between measurements rather than only correlation[25]. In addition, for each ultrasound technique, levator avulsion was analysed by two independent investigators and consensus was reached by a third investigator. This implies that there is certainty about the diagnosis, resulting in more valid comparisons between TPUS and EVUS. A limitation of the study is the relatively low incidence of levator avulsion, causing a lower sensitivity and a higher specificity when evaluating a screening tool[26].

MRI was first used to image the levator over a decade ago. Cadaveric studies demonstrated a correlation between detailed levator anatomy seen on MRI and fresh cadavers[27]. Thereafter, as MRI was the only pelvic floor imaging technique available, it was considered to be the gold standard. However, currently, TPUS and EVUS are

accessible, easy to use in outpatient settings, at lower costs, and have the advantage of manipulating acquired images using post-processing software. An advantage of TPUS over EVUS is the possibility of dynamic studies: maximum contraction for levator avulsion[6,22] and maximum valsalva for enlarged hiatus[3] are both associated with signs and symptoms of pelvic organ prolapse[1,2,3,4]. Although EVUS may be considered as intrusive, it has the advantage of placement of the high frequency probe directly next to the tissue of interest negating the need for contraction while providing very detailed information on pelvic floor structures[7,12].

Levator biometry

All measurements were taken in the plane of minimal hiatal dimensions at rest, to reliably compare TPUS and EVUS, similar to comparisons between TPUS and MRI[9,10]. EVUS measurements were slightly smaller than TPUS measurements. A possible explanation is that EVUS measurements were performed in a non-rendered image of 0.2 mm thick slices of the data volume[12] whereas TPUS measurements were taken from a symmetric rendered volume, about 1.5-2.5 cm thick[28]. This is important when comparing the results of the two techniques or when suggesting cut-off points. Although identification of landmarks is crucial in order to perform accurate and reproducible measurements[14,15,29,30], these landmarks can be distorted in presence of levator avulsion. In spite of this hypothesis, correlation and agreement of measurements were not better in nulliparous women compared to primiparous women (Figure 6). The smaller EVUS measurements are interesting and reinforce the notion that given the small size of the probe, the vaginal soft tissue displacement may be regarded inconsequential.

Levator avulsion

TPUS at maximum contraction was used to diagnose levator avulsion[6,22]. As dynamic studies are currently not possible with EVUS, we analysed levator avulsion at rest. For the initial analyses we chose the best modality of diagnosing levator avulsion for each technique, resulting in good correlation. A sub analysis comparing both TPUS and EVUS at rest when diagnosing levator avulsion revealed moderate correlation only. It therefore appears that TPUS at maximum contraction is more reliable than TPUS at rest when diagnosing levator avulsion. The variation in correlation is probably due to differences in the technique: TPUS is diagnosed in the plane of the minimal hiatal dimensions and the two more cranial slices on tomographic ultrasound imaging. EVUS on the other hand is diagnosed in the plane of minimal hiatal dimensions. Although when a distortion is seen on EVUS, the volume can easily be moved backwards and forwards to identify small amounts of muscle and to approach the levator from different angles. Four discrepancies between the two techniques were seen due to poor quality, highlighting the importance of acquiring an optimal image using recognised landmarks while performing the scan.

Palpation

In order to maintain consistency, all examinations were performed by one investigator (KvD) after appropriate training and proven inter-rater reliability analysis[17]. We found good overall agreement between palpation and both ultrasound techniques, which may be biased by the low incidence of levator avulsion. The high specificity indicates that a negative finding is very likely to indicate no levator avulsion[26]. Palpation might therefore be helpful in excluding levator avulsion. On the other hand, the low sensitivity means that we can be less certain about a positive finding indicating levator avulsion[26]. Therefore, palpation cannot be a good screening tool for levator avulsion as many positive findings are actually false positives.

In conclusion, TPUS and EVUS can be used interchangeably to analyse hiatus area, antero-posterior diameter and levator avulsion but less so for the levator urethra gap. Palpation underestimates true avulsion and therefore cannot substitute ultrasound. A topic for future research will be to establish the correlation and agreement of levator biometry and avulsion between MRI and EVUS.

References

1. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
2. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
3. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80
4. Dietz HP, Franco AVM, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand 2012;91:211-14
5. Kearney R, Miller JM, and DeLancey JO. Interrater reliability and physical examination of the pubovisceral portion of the levator ani muscle, validity comparisons using MR imaging. Neurourol Urodyn 2006;25:50-4
6. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
7. Shobeiri SA, Rostaminia G, White D, Quiroz LH. The determinants of minimal levator hiatus and their relationship to the puborectalis muscle and the levator plate. BJOG 2013;120:205-11
8. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
9. Kruger JA, Heap SW, Murphy BA, Dietz HP. Pelvic floor function in nulliparous women using three-dimensional ultrasound and magnetic resonance imaging. Obstet Gynecol 2008;111:631-8
10. Majida M, Braekken IH, Bø K, Benth JS, Engh ME. Validation of three-dimensional perineal ultrasound and magnetic resonance imaging measurements of the pubovisceral muscle at rest. Ultrasound Obstet Gynecol 2010;35:715-22
11. Zhuang RR, Song YF, Chen ZQ, Ma M, Huang HJ, Chen JH, et al. Levator avulsion using a tomographic ultrasound and magnetic resonance-based model. Am J Obstet Gynecol 2011;205:232.e1-8
12. Shobeiri SA, LeClaire E, Nihira MA, Quiroz LH, O`Donoghue D. Appearance of the levator ani muscle subdivisions in endovaginal three-dimensional ultrasonography. Obstet Gynecol 2009;114:66-72
13. Santoro GA, Wieczorek AP, Stankiewicz A, Woźniak MM, Bogusiewicz M, Rechberger T. High-resolution three-dimensional endovaginal ultrasonography in the assessment of pelvic floor anatomy: a preliminary study. Int Urogynecol J 2009;20:1213-22
14. Santoro GA, Wieczorek AP, Shobeiri SA, Mueller ER, Pilat J, Stankiewicz A, et al. Interobserver and interdisciplinary reproducibility of 3D endovaginal ultrasound assessment of pelvic floor anatomy. Int Urogynecol J 2011;22:53-9
15. van Delft K, Shobeiri SA, Thakar R, Schwertner-Tiepelmann N, Sultan AH. Intra- and inter-rater reliability of levator ani muscle biometry and avulsion using three-dimensional endovaginal sonography. Ultrasound Obstet Gynecol 2013. doi: 10.1002/uog.13193
16. Dietz HP, Shek C. Validity and reproducibility of the digital detection of levator trauma. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1097-101
17. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
18. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-5
19. Dietz HP, Abbu A, Shek KL. The levator-urethra gap measurement: a more objective means of determining levator avulsion? Ultrasound Obstet Gynecol 2008;32:941-5
20. Dietz H. Quantification of major morphological abnormalities of the levator ani. Ultrasound Obstet Gynecol 2007;29:329-34
21. Majida M, Braekken IH, Umek W, Bø K, Saltyte Benth J, Ellstrøm Engh M. Interobserver repeatability of three- and four-dimensional transperineal ultrasound assessment of pelvic floor muscle anatomy and function. Ultrasound Obstet Gynecol 2009;33:567-73
22. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30

23. Rostaminia G, White D, Hegde A, Quiroz LH, Davila GW, Shobeiri SA. Levator ani deficiency and pelvic organ prolapse severity. Obstet Gynecol 2013;121:1017-24
24. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-74
25. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 2003;22:85-93
26. Altman DG, Bland MJ. Diagnostic tests 2: predictive values. BMJ 1994;309:102
27. Strohbehn K, Ellis JH, Strohbehn JA, DeLancey JO. Magnetic resonance imaging of the levator ani with anatomic correlation. Obstet Gynecol 1996;87:277-85
28. Dietz HP, Shek KL, Moegni F. Diagnosis of levator avulsion injury: a comparison of three methods. Ultrasound Obstet Gynecol 2012;40:693-8
29. Weinstein MM, Jung S-A, Pretorius DH, Nager CW, den Boer DJ, Mittal RK. The reliability of puborectalis muscle measurements with 3-dimensional ultrasound imaging. Am J Obstet Gynecol 2007;197:68.e1-68.e6
30. Hoyte L, Brubaker L, Fielding JR, Lockhart ME, Heilbrun ME, Salomon CG, et al; Pelvic Floor Disorders Network. Measurements from image-based three dimensional pelvic floor reconstruction: a study of inter- and intraobserver reliability. J Magn Reson Imaging 2009;30:344-50

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Levator haematoma at the attachment zone as an early marker for levator ani muscle avulsion

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Abstract

Objectives: Childbirth causes overstretching of the levator ani muscle (LAM) predisposing to avulsion. LAM has not been evaluated early postpartum using endovaginal ultrasound (EVUS). The aim was to evaluate the relationship between haematomas and LAM avulsion using EVUS and palpation early and late postpartum.
Methods: Nullipara were studied prospectively at 36 weeks gestation, within four days and three months postpartum. Palpation and high frequency 3D EVUS (BK-Medical 9-16MHz, 360° probe) were performed. Two independent investigators reviewed the scans.
Results: No antenatal LAM avulsions were found (n=269). 114/199 (57.3%) women seen early postpartum agreed to examination. 27/114 (24%) had well delineated, hypoechoic areas consistent with haematomas (100% agreement); 26 following vaginal delivery, one following emergency caesarean section. In total, 38 haematomas were found (11 bilateral, 16 unilateral). Haematomas away from the LAM attachment zone to the pubic bone (n=22) resolved. Haematomas at the attachment zone (n=16) manifested as pubococcygeus avulsions three months postpartum. In addition to these 16 avulsions, we found another 20 three months postpartum. 13/20 were not scanned early postpartum and in seven no haematoma but avulsion was seen early postpartum. Overall, LAM avulsion was found in 23/191 (12.0%) women (13 bilateral, 10 unilateral) three months postpartum. Haematomas were significantly associated with episiotomy, instrumental delivery and increased hiatus measurements. Palpation was unreliable early postpartum as only seven avulsions were diagnosed.
Conclusion: Haematomas at the site of LAM attachment to the pubic bone always result in avulsion diagnosed three months postpartum. However, one third of avulsions are not preceded by a haematoma at the site of LAM attachment to the pubic bone.

Introduction

Vaginal delivery is known to be the main aetiological factor for development of levator ani muscle (LAM) avulsions[1,2,3] and these injuries can subsequently lead to pelvic organ prolapse[4]. During vaginal delivery the pubococcygeus muscle, which forms the most medial muscular segment of the levator hiatus, is stretched, and can predispose to disconnection of the muscle from its insertion on the inferior pubic ramus and the pelvic side wall[1,5,6]. In 1943, Howard Gainey performed a large study in postpartum women and identified palpable defects in the pelvic floor muscles[7]. Recently, LAM avulsion has been reported to occur in 13-40% of women usually after the first vaginal delivery using modern imaging techniques, such as magnetic resonance imaging (MRI)[3,8] or 3D transperineal ultrasonography (TPUS)[2,9,10,11,12,13]. Albrich et al found the highest incidence of LAM avulsions in women scanned early postpartum and attributed this to the difficulty in differentiating fluid collections from LAM avulsion[12]. Furthermore, a case report described LAM avulsion diagnosed clinically immediately after delivery in presence of a large vaginal tear[14].

High resolution 3D endovaginal ultrasonography (EVUS) provides detailed information of pelvic floor muscle structures[5,6]. Cadaveric studies have shown that EVUS images of pelvic floor muscle subdivisions have very good anatomical correlation and the subdivisions of muscle can be visualised clearly[5,6]. Although this technique has proven reliability[5,15,16,17], it has not been previously used in a prospective study before and after childbirth.

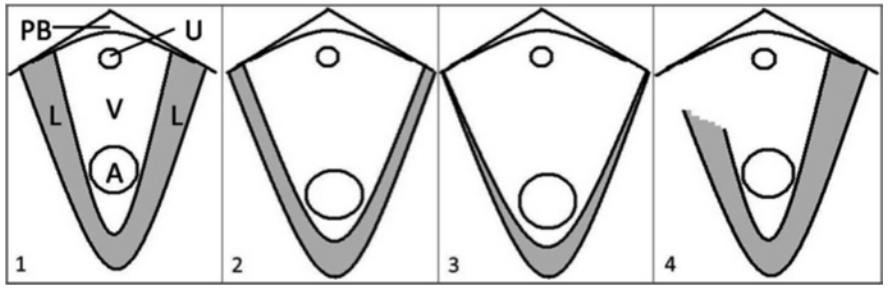
The aim of this study was to evaluate the relationship between haematomas and LAM avulsion using EVUS and palpation during the early and late postpartum period.

Methods

Between January 2011 and May 2012, nulliparous women were invited to participate in the ELITE-study (Evaluation of Levator Injuries using Transvaginal Endosonography), a prospective longitudinal study in Croydon University Hospital, London, United Kingdom. The primary study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87). The inclusion criteria were a singleton pregnancy, maternal age > 18 years, no previous history of pregnancy of more than 20 weeks gestation, and being able to read and understand English. All participants were recruited during pregnancy, and they gave written informed consent at their first visit at 36 weeks of gestation. After childbirth, they were seen early postpartum before they were discharged home from hospital, not more than four days postnatal. The third visit was planned three months following delivery. Delivery details were manually collected from the hospital confidential notes. Not all participants were willing to undergo EVUS immediately after delivery.

Examination was carried out in the dorsal lithotomy position with knees semi-flexed. Women were asked to empty their bladder prior to the examination. LAM attachment was digitally assessed by placing the index finger in the lower third of the vagina immediately lateral to the urethra, pressing against the pubic bone[18,19,20]. This classification has been previously used to assess LAM attachment (Figure 1)[20]. Avulsion was found when there was no LAM insertion felt to the inferior pubic ramus (grade 3 or grade 4)[20]. Although palpation of LAM attachment is known to have a substantial learning curve[18,19], we minimised technique variability by rigorous investigator training and observation by the principal investigator (RT).

Figure 1 Diagrammatic representation of the classification system for palpation of levator ani muscle avulsion



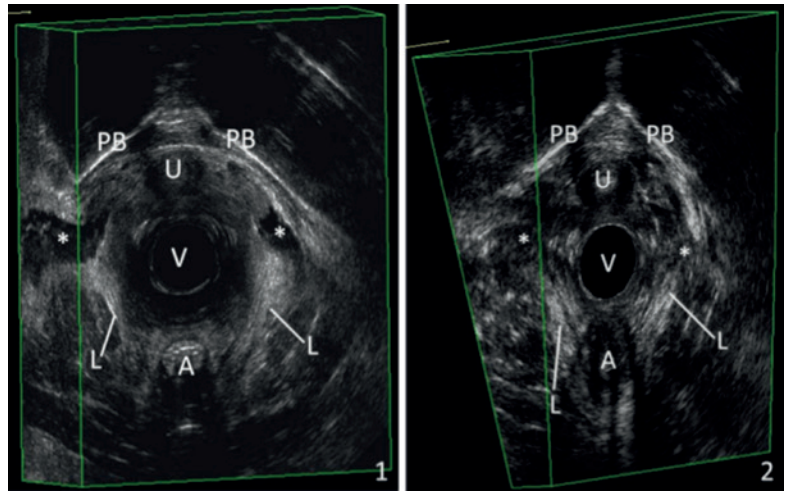
Grade 1, ≤ one finger space between the lateral side of the urethra and the LAM; Grade 2, > one finger space between the lateral side of the urethra and the LAM, with the muscle clearly palpable at rest, and on contraction; Grade 3, > one finger space from the lateral side of the urethra laterally along the pubic bone, without any discernible muscle at rest or on contraction; Grade 4, no attachment of the muscle to the pubic bone (right side).
PB, pubic bone; U, urethra; L, Levator Ani Muscle; A, anus; V, vagina.
(Reproduced by permission of van Delft et al[20]).

Subsequently, all women underwent high frequency EVUS (B-K Medical, Herlev, Denmark, 2050 probe, 9-16 MHZ 360° rotational probe), performed following a previously described approach at rest[5,15] as dynamic studies are currently not possible using EVUS. A 3D volume was created over a 60 mm distance, with 300 axial images taken every 0.2mm, starting at the bladder base[5,15]. Offline analysis was performed by two independent investigators (KvD and SAS) three months after the data volumes were acquired, using B-K Medical Viewer version 7.0.0.51. These investigators were blinded for delivery details, clinical examination details and each other's results. In presence of discrepancies, consensus was reached by a third investigator (RT).

A standardised protocol was used to analyse LAM integrity in the plane of the minimal hiatal dimensions. This is defined as the minimal distance between the

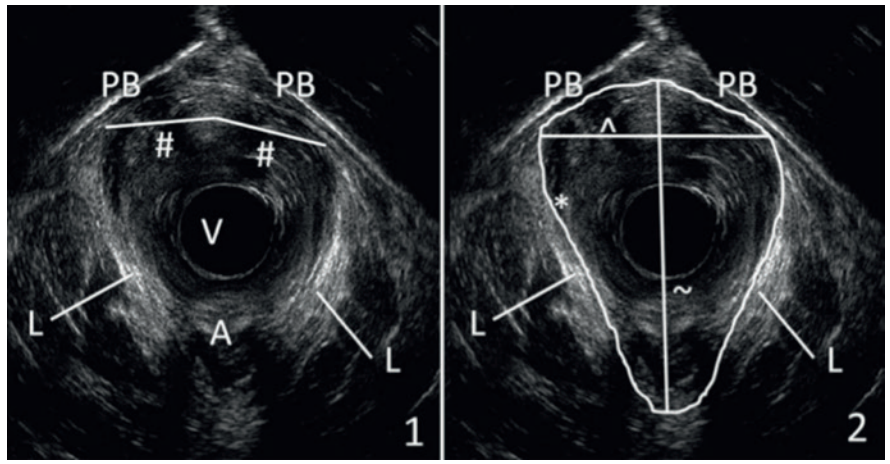
hyperechogenic posterior aspect of the symphysis pubis and the hyperechogenic anterior border of the levator plate just posterior to the anorectal angle[6,21]. The pubic bone ("gothic arch"), the midurethra, the anal canal, and on either sides the pubococcygeus (PC) part of LAM can be visualised in the axial plane. LAM avulsion on EVUS was defined as a discontinuation of the normal attachment to the pubic bone. The previously developed reliable scoring system for LAM was used (score 1 – 4): 1 = complete attachment of the muscle to the pubic bone, without any injury (intact), 2 = < 50% muscle injury (partial avulsion <50%), 3 = ≥ 50% muscle injury (partial avulsion ≥50%), 4 = complete muscle avulsion and entirely detached from the pubic bone (muscle not intact) (Figure 2)[17,22,23,24]. Avulsion was diagnosed when score 3 or 4 were found[17], as major avulsion is most relevant clinically[25]. The pubococcygeus and the puborectalis part of LAM were scored. Previous intra- and inter-rater reliability analysis revealed excellent correlation (ICC 0.79-1.00)[17]. The following measurements were performed in the plane of the minimal hiatal dimensions: levator urethra gap (LUG)[26], hiatus area, hiatus transverse diameter and hiatus antero-posterior diameter (Figure 3)[21].

Figure 2 Endovaginal ultrasound performed 18 hours postpartum (1) and 13 weeks postpartum (2)



PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; L, levator ani muscle;
Image 1 *, bilateral haematoma. Image 2 *, bilateral levator ani muscle avulsion
This woman had a ventouse delivery with the aid of a right-sided mediolateral episiotomy for prolonged second stage of labour.

Figure 3 Hiatus biometry measurements on endovaginal ultrasound



PB, pubic bone; U, urethra; V, vagina (probe inside); A, anal canal; L, levator ani muscle;
1) #, levator urethra gap measurement left and right
2) *, hiatus area measurement; ^ hiatus transverse diameter; ~ hiatus antero-posterior diameter.

Statistical analysis

Statistical analysis was performed using SPSS version 20.0. Chisquare, Mann Whitney U test and Independent samples T-test were performed to analyse differences between groups. A p-value < 0.05 was considered as statistically significant.

Results

269 women were seen during the antenatal visit and no antenatal LAM avulsions were found. 199 of them were seen in the postnatal ward. 114/199 (57.3%) agreed to undergo palpation and EVUS at a median of 21 hours (range 1 – 96). Pain and discomfort were the main reasons to decline the examination. Ethnicity was the only demographic factor that significantly differed between the groups (agreed vs. declined EVUS early postpartum), with Asian women less likely to undergo early postpartum examination (Table 1). 88/114 (77.2%) attended the follow-up visit three month postpartum at a median of 13 weeks (range 10 – 26), and an additional 103 women attended the three months postpartum visit. Of the women who underwent EVUS and palpation following childbirth, 39/114 (34%) had a caesarean section and 75/114 (66%) had a vaginal delivery.

Table 1 Demographic differences between women in EVUS and no EVUS group

Demographics	EVUS performed early postpartum, n=114 Mean (±SD) or *n* (%)	EVUS not performed early postpartum, n=153 Mean (±SD) or *n* (%)	p-value
BMI (kg/m^2)	26 (5.4)	25 (5.2)	0.40
Age (years)	31 (5.3)	30 (6.1)	0.07
Ethnicity	White *68* (60%), Asian *8* (7%), Mixed *5* (4%), Black *31* (27%), Other *2* (2%)	White *71* (46%), Asian *32* (21%), Mixed *12* (8%), Black *32* (21%), Other *6* (4%)	**0.007**
Gestational age at delivery (weeks)	40 (1.2)	40 (1.2)	0.48
Mode of delivery	Normal vaginal delivery *48* (42%), forceps delivery *8* (7%), ventouse delivery *19* (17%), elective caesarean *7* (6%), emergency caesarean *32* (28%)	Normal vaginal delivery *69* (45%), forceps delivery *18* (12%), ventouse delivery *25* (16%), elective caesarean *8* (5%), emergency caesarean *33* (22%)	0.58
Episiotomy	Yes *56* (49%)	Yes*72* (47%)	0.62
Perineal laceration	No *6* (8%), first *10* (13%), second *52* (69%), OASIS *7* (9%)	No *11* (10%), first *18* (16%), second *72* (64%), OASIS *12*(11%)	0.89

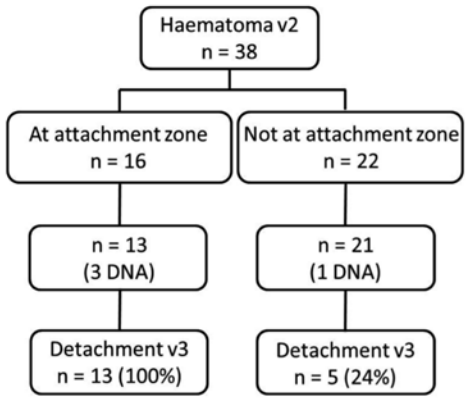
EVUS, Endovaginal Ultrasound; n, number; SD, standard deviation; BMI, body mass index; OASIS, Obstetric Anal Sphincter InjurieS

Haematomas early postpartum

In 27/114 (24%) women hypoechoic areas were identified on EVUS early postpartum (Figures 2, 4). Of these, all delivered vaginally, apart from one woman who underwent an emergency caesarean section at 5 cm dilation for failure to progress. The anatomical distortion seen appeared as a well delineated low reflective focal mass (hypoechoic area) and the features were consistent with a haematoma as described previously in another organ[27]. There was 100% agreement in independent interpretation of haematomas on the scans between the two investigators.

In these 27 women, we found a total of 38 haematomas (11 bilateral, 13 unilateral on the right side and 3 unilateral on the left side). The haematomas that were not at the attachment zone (n=22) (Figure 5) had all resolved three months postpartum, including the haematoma seen following emergency caesarean section. 16 haematomas were at the attachment zone of LAM to the pubic bone, and all of them were seen as LAM avulsion (pubococcygeus part) three months postpartum (Figure 2).

Figure 4 Flowchart of haematomas and LAM avulsions seen early postpartum and three months postpartum

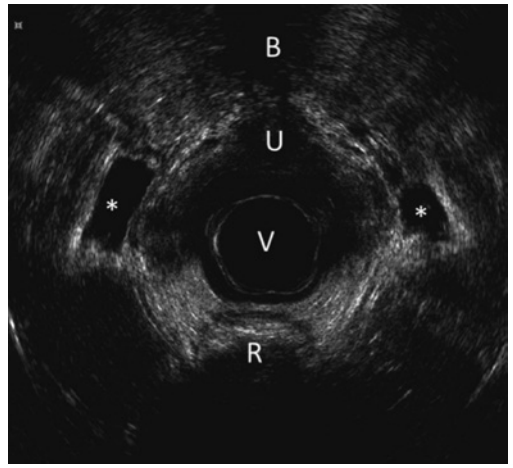


A subdivision was made of haematomas seen at the attachment zone of LAM to the pubic bone, and haematomas that were not seen at the attachment zone.
n, number; v2, visit immediately following delivery; v3, visit three months following delivery; DNA = did not attend.

LAM avulsions three months postpartum

In 23 (23/191=12%) women pubococcygeus LAM avulsion was found three months postpartum. In these 23 women, we found a total of 36 pubococcygeus LAM avulsion (13 bilateral and 10 unilateral). In addition to the 16 pubococcygeus avulsions preceded by a haematoma at the attachment zone, we found another 20 pubococcygeus

Figure 5 Endovaginal ultrasound performed 1 hour following a normal vaginal delivery with a second degree tear: bilateral haematoma is seen away from the attachment to the pubic bone



B, bladder base; U, urethra; V, vagina (probe inside); R, rectum; *, haematoma.

LAM avulsions three months postpartum. 13 of these were not scanned early postpartum. Seven were scanned early postpartum and no haematoma at the attachment zone, but avulsions were seen early postpartum: 5/7 had haematomas away from the attachment zone early postpartum and 2/7 did not have a haematoma at all. Therefore, all pubococcygeus avulsions seen three months postpartum could already be detected early postpartum.

Three months postpartum, avulsion seen at the pubococcygeus level was not seen at the puborectalis level in 16 occasions (16/36=44%). We found three additional puborectalis avulsions, where pubococcygeus was intact. Therefore, the number of avulsions of the puborectalis part three months postpartum was 23 unilateral avulsions, representing 16 women (7 bilateral avulsions).

Episiotomy and instrumental delivery (forceps and ventouse) increased the risk of a haematoma, and a slightly higher BMI was protective (Table 2). Ethnicity was no different between the haematoma and no haematoma group (Table 2) although early postpartum examination rate was different among women from different ethnicities (Table 1).

LUG measurements, hiatus area and hiatus transverse measurements were significantly larger in women with a haematoma early postpartum (Table 3), but only a trend was seen for an increase in hiatus antero-posterior diameter.

Table 2 Demographic differences between women with and without haematoma

Demographics	Haematoma, n=27 Mean (±SD) or *n* (%)	No Haematoma, n=87 Mean (±SD) or *n* (%)	p-value
BMI (kg/m²)	24 (4.6)	27 (5.4)	**0.027**
Age (years)	32 (5.7)	30 (5.1)	0.06
Ethnicity	White *20*(74%), Asian*1* (4%), Mixed *2* (7%), Black *4* (15%)	White *48*(55%), Asian *7*(8%), Mixed *3*(3%), Black *27*(31%), Other *2*(2%)	0.27
Gestational age at delivery (weeks)	40 (1.1)	40 (1.3)	0.60
Mode of delivery	Normal vaginal delivery *13* (48%), forceps delivery *6* (22%), ventouse delivery *7* (26%), emergency caesarean *1* (4%)	Normal vaginal delivery *35* (40%), forceps delivery *2* (2%), ventouse delivery *12* (14%), elective caesarean *7* (8%), emergency caesarean *31* (36%)	**<0.001**
Episiotomy	Yes *18* (69%)	Yes *18* (39%)	**0.012**
Perineal laceration	First *2* (8%), second *20* (77%), OASIS *4* (15%)	No *6* (12%), first *8* (16%), second *32* (65%), OASIS *3*(6%)	0.11

n, number; SD, standard deviation; BMI, body mass index; OASIS, Obstetric Anal Sphincter Injuries

Palpation immediately following delivery identified a total of five bilateral avulsions (score 3) and one unilateral avulsion (score 3) (Table 4). There were 38 unilateral haematomas identified on EVUS. Moreover, not all avulsions identified by palpation were seen as a haematoma early postpartum or as LAM avulsion three months later (Table 4).

Table 3 Differences in hiatus measurements between women with and women without a haematoma

Parameter on EVUS	Haematoma (n=27) Mean (±SD)	No haematoma (n=87) Mean (±SD)	p-value
Levator urethra gap right in cm	2.20 (0.53)	1.89 (0.29)	**<0.001**
Levator urethra gap left in cm	2.15 (0.49)	1.88 (0.27)	**< 0.001**
Hiatus area in cm²	17.74 (3.88)	15.82 (4.01)	**0.030**
Hiatus transverse in cm	4.07 (0.91)	3.61 (0.49)	**0.001**
Hiatus anteroposterior in cm	5.91 (0.73)	5.63 (0.76)	0.09

EVUS, Endovaginal Ultrasound; n, number; SD, standard deviation

Table 4 Overview of abnormalities found on palpation of LAM avulsion immediately following childbirth, compared to haematomas found on EVUS

Subject	Palpation early postpartum left	Palpation early postpartum right	EVUS Haematoma early postpartum left	EVUS Haematoma early postpartum right	EVUS LAM avulsion 3 months postpartum left	EVUS LAM avulsion 3 months postpartum right
1	Grade 3	Grade 3	Yes	Yes	Score 4	Score 4
2	Grade 3	Grade 3	Yes	Yes	Score 4	Score 4
3	Grade 1	Grade 3	No	No	DNA	
4	Grade 3	Grade 3	Yes	Yes	Score 1	Score 3
5	Grade 3	Grade 3	No	No	Score 1	Score 1
6	Grade 3	Grade 3	Yes	No	Score 2	Score 1

LAM, levator ani muscle; DNA, did not attend appointment
For explanation of Grades, see figure 1
Score 1, intact LAM; Score 2, partial avulsion <50%; Score 3, partial avulsion ≥50%; Score 4, complete LAM avulsion

Discussion

One third of primiparous women delivering vaginally develop LAM haematomas within hours of delivery diagnosed using high frequency EVUS. When the haematoma is located in the attachment zone of LAM to the pubic bone, LAM avulsion is always identified three months postpartum. When the haematoma is located away from the attachment zone, LAM avulsion is not seen three months postpartum. However, one third of avulsions are not preceded by a haematoma at the attachment zone, but LAM avulsion was seen early postpartum.

The reported incidence of LAM avulsion in studies conducted early postpartum using TPUS varied between 31%[28] and 39.5%[12]. By contrast, when performing scans at least two months postpartum, the incidence of LAM avulsion varied between 13-22%[8,10,11,13]. The latter incidences correspond better with our present findings; a 12% incidence using EVUS three months postpartum. It appears that early postpartum ultrasound may previously have resulted in over diagnosis of LAM avulsion as haematomas away from the attachment zone can masquerade as avulsions to the unwary. EVUS as a high frequency technique provides very detailed information, which may negate the need for dynamic studies such as squeeze or Valsalva, and might therefore be more reliable immediately postpartum.

We are not aware of another publication in the Medline English literature utilising high frequency EVUS early postpartum to image pelvic floor muscle structures. The sonographic appearance of trauma seen early postpartum was very different from scans acquired before[6] or months after childbirth[24,29]. Therefore, our findings add new information to improve our understanding of the pathogenesis of LAM avulsion, because EVUS was able to differentiate between LAM avulsion and haematomas early postpartum.

Two thirds of LAM avulsions were preceded by formation of a haematoma at the area of torn muscle fibres. An explanation may be that when muscle is torn away from the tendinous attachment, a haematoma is formed, but when the tendon or pubovisceral enthesis is avulsed from the pubic bone no haematoma is formed due to the avascular nature of the trauma[30]. The resolution of haematomas in various locations points to the body's ability to heal itself[31]. As previously evidenced, the pubococcygeus part has to undergo most stretching during childbirth[1]. Although pubococcygeus avulsion with or without haematoma formation is the most catastrophic form of pelvic floor muscle trauma, visualisation of haematomas throughout LAM subdivisions points at global trauma to the whole LAM, which may manifest its effects years after the initial injury[24]. Damage to the puborectalis part can occur incidentally or develop with time, which will be researched in future. LAM avulsion is a risk factor for prolapse, although not all women with prolapse have LAM avulsion[4]. Possibly, women with damage to LAM other than avulsion, such as early

postpartum haematomas away from the attachment zone, will also develop prolapse later in life.

Episiotomy and instrumental delivery rates were significantly higher in women with a haematoma. We found more haematomas on the right side, perhaps related to the right-sided mediolateral episiotomy practised in our unit. One can only speculate whether episiotomy, or the need for episiotomy, leads to a haematoma. We found one haematoma (not at the attachment zone) following an emergency caesarean section, which dissolved three months postpartum. This suggests that labour and fetal head descent during labour could result in haemorrhage and haematoma formation into the LAM, although this appears self-limiting. This finding concurs with previous studies that found LAM trauma following caesarean section[12,32]. There was no difference in haematoma formation in different ethnic groups, which should be interpreted with caution, as significantly less Asian women underwent EVUS early postpartum.

An increased hiatus area and antero-posterior diameter are associated with prolapse[4,33]. Most hiatus measurements were significantly larger in the presence of haematomas, concurring with a study showing substantial irreversible over distension of the levator hiatus on TPUS following childbirth[11]. We speculate that an increase in antero-posterior diameter takes longer to develop. Comparable or larger hiatus measurements after vaginal delivery were found, without sub analysis for LAM avulsion[12,34]. A small remark is that on TPUS hiatal dimensions on Valsalva are generally more valid as measures of prolapse[21] and as a marker of over distension following childbirth[11].

Only a few haematomas or avulsions were identified on palpation. Thus, the majority of LAM trauma early postpartum will be missed when performing palpation only. Possibly a haematoma in combination with oedematous tissue and muscle fibres can be mistaken for muscle bulk or remnants. Moreover, as it is difficult to contract pelvic floor muscles effectively immediately postpartum, it is difficult to accurately diagnose LAM avulsion by palpation. There is one case report of LAM avulsion diagnosed clinically in presence of a large vaginal tear immediately postpartum[14]. As most women do not have a vaginal tear adjacent to the LAM, exploration of sonographic LAM avulsion immediately after delivery would require an incision in the vagina, resulting in more bleeding and scarring. The subsequent management of LAM avulsion in the acute stage remains to be established.

Although the prospective design of this study provides robust and meaningful data, we acknowledge the limitations. Only 78% of women were seen early postpartum, due to organisational difficulties. Almost half of the women seen early postpartum declined EVUS because of pain and discomfort, implying that EVUS will not be suitable for routine screening early postpartum. In addition, more Asian women, who form 15% of our study sample, refused to undergo examinations early

postpartum, which has previously been elaborated[35]. Another limitation is that the haematomas were not further explored by aspiration biopsy, and histological confirmation is lacking. Although we could not measure volumes during post processing of the datasets, the location of a haematoma seems to be the most relevant aspect to predict LAM avulsion.

In conclusion, early postpartum haematomas at the site of LAM attachment to the pubic bone always result in pubococcygeus LAM avulsion three months postpartum. However, one third of avulsions are not preceded by a haematoma at the site of LAM attachment to the pubic bone. Although postpartum repair of these avulsions remains investigational, the current study contributes to the understanding of pathophysiology of LAM avulsion during childbirth.

References

1. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
2. Dietz HP, Lanzarone V. Levator trauma after vaginal delivery. Obstet Gynecol 2005;106:707-12
3. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
4. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
5. Shobeiri SA, LeClaire E, Nihira MA, Quiroz LH, O`Donoghue D. Appearance of the levatorani muscle subdivisions in endovaginal three-dimensional ultrasonography. Obstet Gynecol 2009;114:66-72
6. Shobeiri SA, Rostaminia G, White D, Quiroz LH. The determinants of minimal levator hiatus and their relationship to the puborectalis muscle and the levator plate. BJOG 2013;120:205-11
7. Gainey HL. Post-partum observation of pelvic tissue damage. Am J Obstet Gynecol 1943;46:457-66
8. DeLancey JO, Kearney R, Chou Q, Speights S, Binno S. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. Obstet Gynecol 2003;101:46-53
9. Valsky DV, Lipschuetz M, Bord A, Eldar I, Messing B, Hochner-Celnikier D, et al. Fetal head circumference and length of second stage of labor are risk factors for levator ani muscle injury, diagnosed by 3-dimensional transperineal ultrasound in primiparous women. Am J Obstet Gynecol 2009;201:91.e1-7
10. Shek KL, Dietz HP. Can levator avulsion be predicted antenatally? Am J Obstet Gynecol 2010;202:586.e1-6
11. Shek K, Dietz HP. Intrapartum risk factors for levator trauma. BJOG 2010;117:1485-92
12. Albrich SB, Laterza RM, Skala C, Salvatore S, Koelbl H, Naumann G. Impact of mode of delivery on levator morphology: a prospective observational study with three-dimensional ultrasound early in the postpartum period. BJOG 2012;119:51-60
13. Chan SS, Cheung RY, Yiu AK, Lee LL, Pang AW, Choy KW, et al. Prevalence of levator ani muscle injury in Chinese women after first delivery. Ultrasound Obstet Gynecol 2012;39:704-9
14. Dietz HP, Gillespie AVL, Phadke P. Avulsion of the pubovisceral muscle associated with large vaginal tear after normal vaginal delivery at term. Aust N Z J Obstet Gynaecol 2007;47:341-4
15. Santoro GA, Wieczorek AP, Stankiewicz A, Woźniak MM, Bogusiewicz M, Rechberger T. High-resolution three-dimensional endovaginal ultrasonography in the assessment of pelvic floor anatomy: a preliminary study. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1213-22
16. Santoro GA, Wieczorek AP, Shobeiri SA, Mueller ER, Pilat J, Stankiewicz A, et al. Interobserver and interdisciplinary reproducibility of 3D endovaginal ultrasound assessment of pelvic floor anatomy. Int Urogynecol J 2011;22:53-9
17. van Delft KWM, Shobeiri SA, Thakar R, Schwertner-Tiepelmann N, Sultan AH. Intra- and inter-rater reliability of levator ani muscle biometry and avulsion using three dimensional endovaginal ultrasonography. Ultrasound Obstet Gynecol 2013 doi: 10.1002/uog.13193
18. Kearney R, Miller JM, and DeLancey JOL. Interrater reliability and physical examination of the pubovisceral portion of the levatorani muscle, validity comparisons using MR Imaging. Neurourol Urodyn 2006;25:50-4
19. Dietz HP, Shek C. Validity and reproducibility of the digital detection of levator trauma. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1097-101
20. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
21. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-5
22. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
23. DeLancey JO, Trowbridge ER, Miller JM, Morgan DM, Guire K, Fenner DE, et al. Stress urinary incontinence: relative importance of urethral support and urethral closure pressure. J Urol 2008;179:2286-90

24. Rostaminia G, White D, Hegde A, Quiroz LH, Davila GW, Shobeiri SA. Levator ani deficiency and pelvic organ prolapse severity. Obstet Gynecol 2013;121:1017-24
25. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
26. Dietz HP, Abbu A, Shek KL. The levator-urethra gap measurement: a more objective means of determining levator avulsion? Ultrasound Obstet Gyecol 2008;32:941-5
27. Purushothaman H, Sellars ME, Clarke JL, Sidhu PS. Intratesticular haematoma: differentiation from tumour on clinical history and ultrasound appearances in two cases. Br J Radiol 2007;80:e184-7
28. Blasi I, Fuchs I, D'Amico R, Vinci V, La Sala GB, Mazza V, et al. Intrapartum translabial three-dimensional ultrasound visualization of levator trauma. Ultrasound Obstet Gynecol 2011;37:88-92
29. Rostaminia G, Shobeiri SA, Quiroz LH. Surgical repair of bilateral levator ani muscles with ultrasound guidance. Int Urogynecol J 2013;24:1237-9
30. Kim J, Ramanah R, DeLancey JO, Ashton-Miller JA. On the anatomy and histology of the pubovisceral muscle enthesis in women. Neurourol Urodyn 2011;30:1366-70
31. Drewes PG, Yanagisawa H, Starcher B, Hornstra I, Csiszar K, Marinis SI, et al. Pelvic organ prolapse in fibulin-5 knockout mice: pregnancy-induced changes in elastic fiber homeostasis in mouse vagina. Am J Pathol 2007;170:578-89
32. Novellas S, Chassang M, Verger S, Bafghi A, Bongain A, Chevallier P. MR features of the levator ani muscle in the immediate postpartum following caesarean delivery. Int Urogynecol J 2010;21:563-8
33. Delancey JO, Hurd WW. Size of the urogenital hiatus in the levator ani muscles in normal women and women with pelvic organ prolapse. Obstet Gynecol 1998;91:364-8
34. Falkert A, Endress E, Weigl M, Seelbach-Gobel. Three-dimensional ultrasound of the pelvic floor 2 days after first delivery: influence of constitutional and obstetric factors. Ultrasound Obstet Gynecol 2010;35:583-8
35. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Recruitment of pregnant women in research: Experience from a prospective study. J Obstet Gynaecol 2013;33:442-6

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Levator ani muscle avulsion during childbirth: a risk prediction model

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Abstract

Objective: To establish the incidence of levator ani muscle (LAM) avulsion in primiparous women and to develop a clinically applicable risk prediction model.
Design: Observational longitudinal cohort study
Setting: District General University Hospital, United Kingdom
Population or sample: Nulliparous women at 36 weeks gestation and three months postpartum.
Methods: 4D transperineal ultrasound was performed during both visits. Tomographic ultrasound imaging at maximum contraction was used to diagnose no, minor or major LAM avulsion. A risk model was developed using multivariable ordinal logistic regression.
Main outcome measures: Incidence of LAM avulsion and its risk factors
Results: 269 antenatal women had no LAM avulsion. 71% (n=191) returned postpartum. No LAM avulsion was found after caesarean section (n=48). Following vaginal delivery the overall incidence of LAM avulsion was 21.0% (n=30, 95%CI 15.1-28.4%). Minor and major LAM avulsion were diagnosed in 4.9% (n=7, 95%CI 2.2-9.9%) and 16.1% (n=23, 95%CI 10.9-23.0%) respectively. Risk factors were obstetric anal sphincter injuries (odds ratio 4.4, 95%CI 1.6-12.1), prolonged active second stage of labour per hour (odds ratio 2.2, 95%CI 1.4-3.3) and forceps delivery (odds ratio 6.6, 95%CI 2.5-17.2). A risk model and nomogram were developed to estimate a woman's individual risk: three risk factors combined revealed a 75% chance of LAM avulsion.
Conclusions: 21% of women sustain LAM avulsion during their first vaginal delivery. Our risk model and nomogram are novel tools to estimate individual chances of LAM avulsion. We can now target postnatal women at risk of having sustained LAM avulsion.

Introduction

Defects in pelvic floor muscles following childbirth were first described by Howard Gainey in 1943[1]. Subsequently, the main focus of trauma to the pelvic floor after vaginal delivery shifted to obstetric anal sphincter injuries (OASIS)[2]. However, over the past decade, with the advent of modern imaging techniques, trauma to the pelvic floor muscles has gained a lot of interest. There is evidence that 36% of women with prolapse have an underlying levator ani muscle (LAM) avulsion[3]. This avulsion occurs in 13-36% of women mainly during the first vaginal delivery[4,5,6,7,8,9,10,11] by stretching and tearing of the muscle from the insertion on the inferior pubic ramus[12].

A variety of childbirth related risk factors for LAM avulsion have been described in the literature[13], including operative vaginal delivery[11], forceps delivery[6,10,14], OASIS[6], episiotomy[6], prolonged second stage of labour[6,8,10], increased fetal head circumference[8] and increased maternal age[6]. On the other hand, epidural analgesia is thought to be a protective factor[10]. In a prospective study, Shek et al aimed to describe antepartum predictors of major LAM avulsion[9]. They found that a lower body mass index (BMI) (28 vs. 30 kg/m^2) was the only significant risk factor[9] and were therefore unable to develop an antepartum prediction model.

The primary aim of this study was to establish the incidence of LAM avulsion in primiparous women. Secondly, we aimed to develop a clinically applicable risk prediction model for LAM avulsion.

Methods

Between January 2011 and May 2012 nulliparous women were invited to participate in an observational longitudinal cohort study. This study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87). Women were recruited from the antenatal clinics and parent craft classes at Croydon University Hospital, London, United Kingdom. At the initial contact, they were informed about the project, an information leaflet was given and contact details were collected. At 34 weeks gestation the researcher telephoned them to enquire if they were interested in participating in the study. The inclusion criteria were a singleton pregnancy, maternal age > 18 years, no previous history of pregnancy of more than 20 weeks gestation, and being able to read and understand English. We invited all nulliparous women, to create a sample representative for the normal population. The recruitment process has previously been described in detail[15]. All women gave written informed consent during their first appointment at 36 weeks gestation. Subsequently, participants were invited by telephone, postal mail and electronic mail to book a follow-up appointment three months following childbirth (Figure 1). Demographic

and obstetric details were prospectively collected from the hospital confidential notes.

Women were asked to empty their bladder prior to the ultrasound assessment. 4D transperineal ultrasound (TPUS) was performed in the supine position with knees semi-flexed using GE Voluson 730 system with a 4-8 MHz transabdominal curved array volume transducer, with an acquisition angle of 85 degrees. The midsagittal plane was used to identify the minimal anteroposterior diameter of the levator hiatus, from the posterior margin of the symphysis pubis to the anterior margin of LAM[16,17]. Tomographic ultrasound imaging (TUI) on maximum pelvic floor muscle contraction was used to assess the entire LAM and its attachment to the inferior pubic ramus[18,19]. Eight slices were created in the axial plane, from 5 mm below the plane of minimal hiatal dimensions to 12.5 mm above, at 2.5 mm slice intervals[18,19]. The central three slices were scored as positive or negative for LAM avulsion, using direct visualisation, scoring left and right side separately. The final unilateral score ranged from 0 (no avulsion) to 3 (complete LAM avulsion)[19]. A summed total score for the left and right side (0 – 6) was then assigned and classified as no LAM avulsion (summed score of 0), minor LAM avulsion (summed score of 1 – 3) or major LAM avulsion (summed score of 4 – 6, or a unilateral score of 3) (Figure 2)[6,20]. Blind offline analysis was performed using 4D view version 10.2. Two independent investigators (KvD and KK), blinded for mode of delivery and each other's results, analysed LAM avulsion on all postnatal scans. In presence of discrepancies, consensus was reached by a third investigator (RT). LAM avulsion can be diagnosed reliably using TUI on TPUS at maximum pelvic floor muscle contraction as excellent agreement was found between two raters (Cohen's kappa 0.83 (95% confidence interval 0.59-1.0))[21].

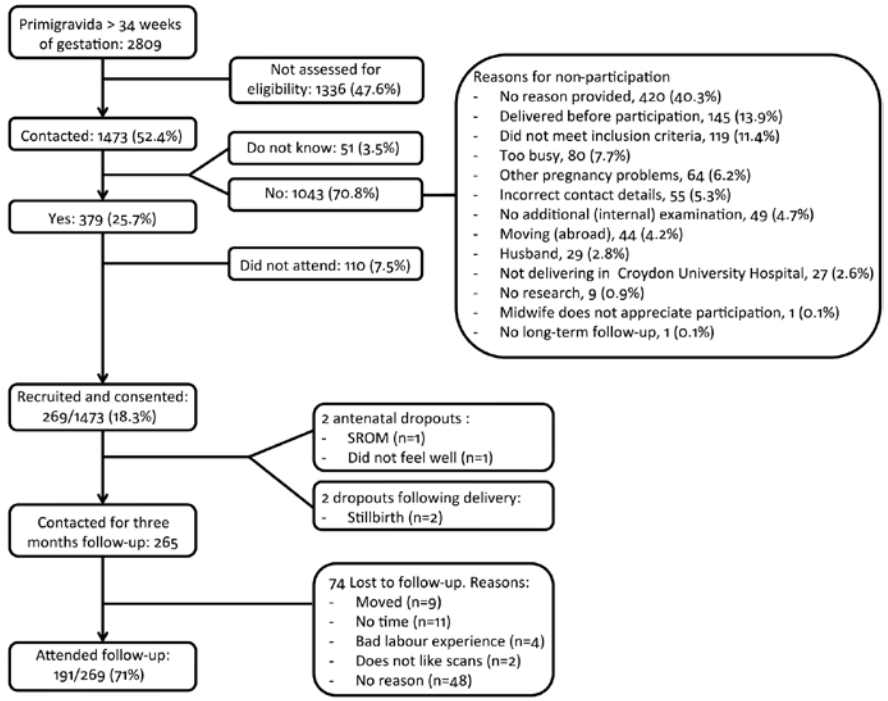
Statistical analysis

On the basis of previous studies on LAM avulsion following childbirth, we determined that we would need to enrol 186 women in order to detect 14% LAM avulsion with a precision (standard error) of 2.5%. A total sample size of 265 was calculated to allow a 30% dropout rate.

To analyse differences in women that attended three months postpartum and were lost to follow up, we used Student t-test, Mann Whitney U test, Chisquare test and Fisher's exact test where appropriate. Demographics and obstetric data to identify risk factors of LAM avulsion were analysed by definition of the three groups (no vs. minor vs. major LAM avulsion), using analysis of variance (ANOVA), applying post-hoc least significant difference procedure for inter-group comparison, Kruskal Wallis test, Chi^2 test and Fisher's exact test where appropriate.

Subsequently, odds ratios were estimated by performing regression analysis on demographics and obstetric data. Ordinal logistic regression analysis was used instead of multinomial logistic regression to maintain the valuable information on

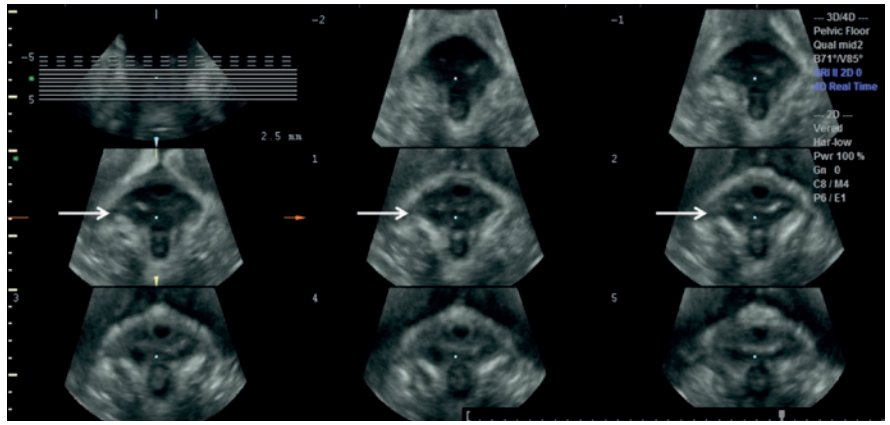
Figure 1 Flowchart of the recruitment process and the attendance of the three months postpartum visit



SROM = spontaneous rupture of membranes.
(Partly reproduced from van Delft et al[15] with permission)

ordering of LAM avulsion severity[22]. All variables with a p-value < 0.20 on univariable ordinal logistic regression were considered for multivariable ordinal logistic regression. The final selection procedure for the multivariable ordinal logistic regression was subsequently based on clinical relevance. Although individual risk prediction is often poor when based on only one factor[23], it is important to avoid over fitting of the model especially with many predictive factors in a small dataset[24]. Accurate selection of predictive factors will result in models with less over fitting and greater generalisability[24,25]. Predictors should be as independent as possible and there should be a possibility to influence subsequent management based on these predictors. Furthermore, when performing regression analyses, the number of events (LAM avulsion) should be ten times the number of prognostic factors included in the model[26].

Figure 2 Tomographic ultrasound imaging: unilateral LAM avulsion on maximum contraction, three months postpartum



Arrows indicate right sided unilateral levator ani muscle avulsion.

Multivariable ordinal logistic regression was applied to estimate adjusted odds ratios for the most relevant variables, in models of all possible combinations of these most relevant variables (all subsets regression). The model with the highest R^2 was selected as the final model. The internal validity of this model was controlled for by performing bootstrap validation. Nomograms were created to estimate an individual woman's risk of LAM avulsion. All analyses were performed using SPSS (version 20.0 SPSS Inc, Chicago, IL, USA) and R (version 2.15.2)[27]. Two-sided P values < 0.05 were considered statistically significant.

Results

1473 out of 2809 eligible women were invited to participate (Figure 1). 269 nulliparous women agreed to participate at a median of 36 weeks of gestation (range 34 – 41 weeks). 71% (n=191) returned for follow-up at a median of 13 weeks postnatal (range 10 – 26 weeks) (Figure 1). Two antenatal women dropped out prior to antenatal ultrasound assessment, all other ultrasound assessments were performed according to protocol. Demographics and obstetric data were compared to assess differences in the follow up and loss to follow up group (Table S1). Non-attenders were somewhat younger (mean age 29.1 vs. 30.7 years, p=0.039), were more often delivered by caesarean section (43% vs. 25%, p=0.043), had fetuses with a significantly smaller birth weight (3185g vs. 3375g, p=0.002) and head circumference (33.8cm vs. 34.3cm, p=0.045) and more episiotomies (61% vs. 43%, p=0.030) were performed.

None of the antenatal women had LAM avulsion. No LAM avulsion was found after caesarean section (n=48). Therefore, the overall incidence of LAM avulsion following a vaginal delivery was 21.0% (n = 30, 95% CI 15.1-28.4%). Minor and major LAM avulsion were diagnosed in 4.9% (n = 7, 95% CI 2.2-9.9%) and 16.1% (n = 23, 95% CI 10.9-23.0%), respectively.

Demographics were not notably different in the three groups (Table 1). Obstetric data revealed a significant association between LAM avulsion and age, duration of active second stage, mode of delivery (forceps delivery), and perineal laceration (OASIS) (Table 1). Six women had forceps delivery and OASIS. One of them had no LAM avulsion and five had major LAM avulsion.

Table 1 Demographics and obstetric details in women with no, minor or major LAM avulsion

	No avulsion (n = 161)	Minor avulsion (n = 7)	Major avulsion (n = 23)	P value
Demographic variables				
Age (years)	30.7 (SD 5.3)	25.0 (SD 6.0)	32.9 (SD 5.3)	**0.003**[B,C]
BMI (kg/m^2)	25.6 (SD 5.7)	25.4 (SD 6.3)	23.3 (SD 2.7)	0.18
Ethnicity - White - Asian - Mixed - Black - Other	 91 (57%) 24 (15%) 6 (4%) 37 (23%) 3 (2%)	 5 (71%) 2 (29%)	 10 (43%) 5 (22%) 2 (9%) 5 (22%) 1 (4%)	0.10
Delivery variables				
Gestational age at delivery (weeks)	40.1 (SD 1.2)	40.0 (SD 1.3)	40.4 (SD 1.0)	0.40
Induction - No - Yes	 111 (69%) 50 (31%)	 4 (57%) 3 (43%)	 20 (87%) 3 (13%)	0.15
Use of oxytocin - No - Yes	 99 (61%) 62 (389%)	 5 (71%) 2 (29%)	 13 (57%) 10 (43%)	0.77
Epidural analgesia - No - Yes	 105 (65%) 56 (35%)	 5 (71%) 2 (29%)	 16 (70%) 7 (30%)	0.88
First stage (min)*	415 (range 35-1271)	310 (range 90-756)	420 (range 62-985)	0.24
Second stage (min)*	60 (range 4-269)	45 (range 27-267)	130 (range 4-260)	0.10

Table 1 Continued

	No avulsion (n = 161)	Minor avulsion (n = 7)	Major avulsion (n = 23)	P value
Delivery variables				
Active second stage (min)*	37 (range 2-209)	45 (range 22-183)	75 (range 2-200)	**0.018[A]**
Mode of delivery - Normal vaginal - Forceps - Ventouse - Elective caesarean - Emergency caesarean	 77 (48%) 10 (6%) 26 (16%) 10 (6%) 38 (24%)	 6 (86%) 1 (14%)	 9 (39%) 10 (43%) 4 (17%)	**<0.001**
Perineal laceration* - No - First degree - Second degree - OASIS	 11 (10%) 14 (12%) 80 (70%) 10 (9%)	 4 (57%) 3 (43%)	 1 (4%) 3 (13%) 11 (48%) 8 (35%)	**0.001**
Episiotomy* - No - Yes	 70 (61%) 45 (39%)	 5 (71) 2 (29%)	 8 (35%) 15 (65%)	0.05
Birth weight (gram)	3362 (SD 413)	3451 (SD 428)	3450 (SD 441)	0.57
Head circumference (cm)**	34.2 (SD 14.4)	34.0 (SD 12.6)	34.4 (SD 18.8)	0.78
Occipito anterior*** - No - Yes	 20 (13%) 136 (87%)	 0 7 (100%)	 4 (17%) 19 (83%)	0.48
Shoulder dystocia**** - No - Yes	 155 (99%) 2 (1%)	 7 (100%) 0	 23 (100%) 0	0.82

ANOVA applying least significant difference if $p<0.05$, Kruskal Wallis applying Mann Whitney U test if $p<0.05$, and chi-square test. Continuous variables are given as means with standard deviations (SDs) or medians with ranges (range); categorical variables are given as numbers with percentages (%). All P-values are two-sided.

[A, B] and [C] statistically significant difference between no and major avulsion ([A]), minor and major avulsion ([B]) and no and minor avulsion ([C]), respectively.

n, number; SD, standard deviation; BMI, Body mass Index; OASIS, obstetric anal sphincter injuries

* not applicable in women that delivered by caesarean section

** missing data in 6 women without LAM avulsion, in 1 woman with minor LAM avulsion and in 1 woman with major LAM avulsion

*** missing data in 5 women without LAM avulsion

**** missing data in 4 women without LAM avulsion

Ordinal logistic regression analysis

Women delivered by caesarean section were excluded from the ordinal logistic regression analysis, because they had not sustained LAM avulsion. The following variables had a p-value < 0.20 on univariable ordinal logistic regression analysis and were considered for multivariable ordinal logistic regression analysis: BMI (OR 0.95, 95%CI 0.87-1.03), mode of delivery (forceps delivery as a risk factor (OR 6.6, 95%CI 2.5-17.2)), second stage of labour (per hour) (OR 1.82, 95%CI (1.00-1.82), active second stage of labour (per hour) (OR 2.17, 95%CI 1.35-3.28), perineal laceration: OASIS (OR 4.4, 95%CI 1.6-12.1), second degree tear (OR 2.6, 95%CI 1.15-5.87) and episiotomy (OR 0.5, 95%CI 0.21-1.07) (Table S2).

Multivariable ordinal logistic regression analysis applying all subsets analyses was performed for three variables, to avoid over fitting in a relatively small number of women with any form of LAM avulsion (n=30)[24], as the ratio number of events to number of prognostic values should be 10:1[26]. The selection procedure for the multivariable analysis was based on clinical relevance of the predictors as explained in the methods. Therefore OASIS, duration of active second stage of labour and forceps delivery were selected from the candidate list of predictors. This resulted in four combined models with crude and adjusted odds ratios (Table 2). Model 1 consisted of: OASIS and active second stage of labour, model 2: OASIS and forceps delivery, model 3: active second stage and forceps delivery, model 4: OASIS, active second stage of labour and forceps delivery.

The odds ratios indicate that (higher values of) these variables increase the likelihood of more severe LAM avulsion. Furthermore, using multivariable ordinal logistic regression analysis, we estimated cumulative odds for the observation of LAM avulsion severity. For example, if two women were identical except for the variable OASIS, the odds for a major LAM avulsion (vs. minor or no LAM avulsion) were 3.1 in case of OASIS. Likewise, the odds for a LAM avulsion (either minor or major) vs. no LAM avulsion were 3.1 times greater than for the woman without OASIS. The three predictive factors used for the prediction model are independent factors. Although, OASIS and forceps delivery have previously been related[2], they have a cumulative effect on the chance of sustaining LAM avulsion, which make them independent factors.

Model 4, consisting of all three variables, resulted in the most reliable risk prediction of having sustained LAM avulsion. This model has an R^2 of 19.2% which suggests how much of LAM avulsion can (19.2%) and how much cannot (80.8%) be explained by the model. The internal validity of the model was evaluated by performing bootstrap validation. The concordance-index (c-index) indicating discrimination for the proposed model (similar to the area under the Receiver Operator Curve in logistic regression) was 0.672. After correction for optimism in the original model the c-index was 0.647 (> 0.70 corresponds to a reasonable model) which implies that you can

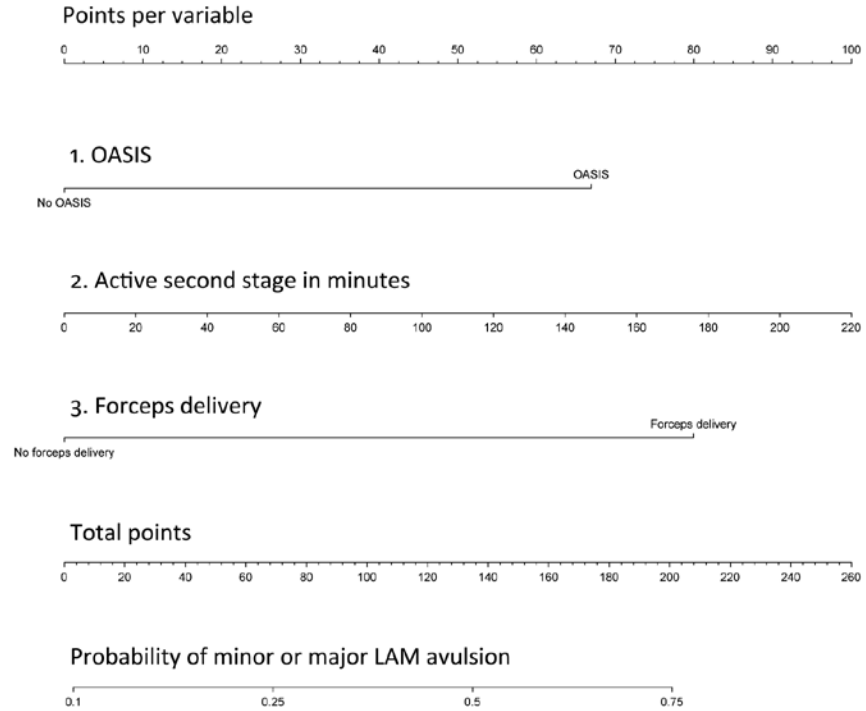
Table 2 Multivariable ordinal logistic regression analysis: crude and adjusted odds ratios for LAM avulsion severity in three categories for primiparous women following vaginal delivery (n=143)

Variables	Crude Odds ratio (95%CI)	p value	Adjusted Odds ratio (95% CI)			
			Model 1, $R^2 = 0.145$	Model 2, $R^2 = 0.167$	Model 3, $R^2 = 0.161$	Model 4, $R^2 = 0.191$
Forceps delivery	6.6 (2.5-17.2) $R^2 = 0.128$	<0.001		5.6 (2.1-15.0)	4.2 (1.5-12.1)	3.8 (1.3-11.1)
OASIS	4.4 (1.6-12.1) $R^2 = 0.069$	0.007	3.5 (1.2-10.1)	3.4 (1.2-9.9)		3.1 (1.01-9.2)
Active second stage (hour)	2.17 (1.35-3.28) $R^2 = 0.102$	0.001	2.05 (1.27-3.09)		1.61 (1.0-2.75)	1.61 (1.06-2.59)
Estimates for the intercepts of the lower and middle categories respectively			1.02, 1.39	-1.08, -0.70	0.72, 1.10	-0.20, 0.19

95% CI, 95% confidence interval; OASIS, obstetric anal sphincter injuries.
Model 1, OASIS and Active second stage of labour; Model 2, OASIS and Forceps delivery; Model 3, Active second stage and Forceps delivery; Model 4, all variables combined in one model.
The crude and adjusted odds ratios were estimated using univariable and multivariable ordinal logistic regression analyses, respectively.

predict better with this risk model than if you had no model at all. The nomogram based on model 4, can be used to estimate a woman's individual risk of having sustained LAM avulsion (Figure 3).

Figure 3 Nomogram to estimate an individual woman's risk of having sustained LAM avulsion (minor or major LAM avulsion)



Nomogram to predict the chance for an individual primiparous woman of having sustained LAM avulsion. For each level of predictive factors, there is a number of points allocated at the point scale above. The total points can be calculated by adding the points of each separate parameter. This number represents the chance of having sustained LAM avulsion during the first vaginal delivery. For example, a woman with Obstetric Anal sphincter injuries (67 points), an active second stage of labour of 120 minutes (55 points) and forceps delivery (79 points) has a total score of 201 points; probability of having sustained minor or major LAM avulsion is 75%. On the other hand, a woman who has been in active second stage of labour for one hour (28 points), without OASIS and without forceps delivery, has a 15% chance of having sustained minor or major LAM avulsion.

Discussion

Main findings

This observational longitudinal cohort study reveals a 21% incidence of LAM avulsion in primiparous women three months following vaginal delivery. The risk factors for LAM avulsion were OASIS, active second stage of labour and forceps delivery. The risk model and nomogram we have described are novel tools to estimate an individual woman's risk of having sustained LAM avulsion.

Strengths and limitations

The strengths of the study were the prospective design and power calculation to establish the incidence of LAM avulsion. Furthermore, the loss to follow up group was similar in demographics and obstetric outcomes to the group that attended both visits. The prospective study design makes the results of the prediction model more reliable[24]. However, we acknowledge the limitations as this study was not powered to develop a prediction model[24,26]. Secondly, the list of predictors was not defined a priori, which would have made the risk of overfitting even smaller. Another limitation is the relatively small number of LAM avulsion, allowing us to only enter three variables in the multivariable ordinal logistic regression analysis[22,26]. Although with small group sizes the risk of over fitting exists[24,25], we have controlled for that by performing bootstrapping to internally validate the discriminatory performance of the model[24]. However, the major limitation of our study is its external validity[24] and we acknowledge that our model needs further evaluation and validation in an external model in a different population. Further work could be done on the prediction model in a study which is adequately powered to develop a risk prediction model. However, for such analysis, risk prediction models as ours can help to establish which risk factors to evaluate in a large sample. Furthermore, the R^2 remains low even for the best model, and consequently most cases of avulsion are not currently predictable.

Interpretation

The incidence of LAM avulsion following vaginal delivery found in our study is in keeping with, and adds credence to other studies revealing a 13-22% incidence using TPUS[7,8,9,10,11] and 18-20% incidence using MRI[4,6] a few months after delivery. Our incidence of 21% in vaginally parous women seems to be a little higher, which is probably because we incorporated minor LAM avulsion, whereas others only reported major LAM avulsion[9,10]. A higher incidence rate of 36% was found by Dietz et al[5]. However, the definition they used was 'a loss of continuity between muscle and pelvic side wall in all volume data sets (rest, squeeze, Valsalva)'[5], which is different from a more recent suggested definition in which TUI at maximum pelvic floor muscle contraction is used to diagnose LAM avulsion[21]. This might explain why later

studies[7,8,9,10,11] using the same definition on TPUS as in our study, have found similar incidence rates of LAM avulsion. This highlights the importance of using standardising terms when research is conducted.

Prediction models for LAM avulsion have been developed for women presenting to tertiary urogynaecology clinics with pelvic floor dysfunction[20,28]. The variables they identified cannot be used for comparison in our study population, because our women are much younger and do not have a history of previous prolapse surgery. We therefore sought to create a prediction model related to childbirth only. Ideally, a prediction model should consist of modifiable factors present prior to childbirth, such as mother's age or BMI, to allow prevention of LAM avulsion. However similar to the findings of Shek et al[9] we were unable to demonstrate any influence of the mentioned antenatal variables on the incidence of LAM avulsion. We therefore developed our model to identify women at risk of having sustained LAM avulsion during their first vaginal delivery. Women delivered by caesarean section were excluded, because none sustained LAM avulsion. Eighty percent of LAM avulsion cannot be explained by our model. This implies that there must be other factors that contribute to LAM avulsion, which we could not identify in our population. However, this can possibly be explained by our relatively small numbers. Nevertheless, OASIS, prolonged second stage of labour and forceps delivery will certainly put women at a high risk of LAM avulsion, which is in keeping with the literature[6,8,10,14].

It has been suggested that prediction models should only be presented when they can be clinically applicable[24]. We therefore developed clinically applicable nomograms based on our risk model, to estimate a woman's individual risk of having sustained LAM avulsion, which can be used in a clinical setting. The presented tools will help to target women at high risk of having sustained LAM avulsion. These women can be offered pelvic floor imaging to confirm or exclude diagnosis of LAM avulsion. If this is confirmed, or if imaging is not available but women are at high risk, they could be advised to initiate intensive lifestyle modification and pelvic floor education to increase pelvic floor muscle strength (PFMS). As we know, these women are at risk of developing POP in the long term[3] and it has been shown that supervised pelvic floor muscle training increases PFMS in women with POP[29]. We speculate that pelvic floor muscle training might prevent or at least delay the onset of symptomatic POP in women following childbirth.

Our model can also help focus on obstetric care with a view to minimising the risk of LAM avulsion as repair of the damage soon after delivery has not been shown to be beneficial[30]. The latest NICE guidelines on Intrapartum Care suggest that birth would be expected to take place within three hours of the start of active second stage of labour[31]. However, our model shows that an active second stage of labour of 180

minutes could increase the chance of sustaining LAM avulsion. Furthermore, we could aim to reduce the need for instrumental delivery. The RCOG Green-top guideline on operative vaginal delivery provides level one evidence on such a strategy including continuous support in labour, upright position, minimised use of epidural analgesia and to start oxytocin in second stage of labour[32]. Hands-on training in the choice and technique of vacuum extraction will enhance the risk of success and minimise the use of forceps[32], the main risk factor for LAM avulsion[6,10,14]. However, we acknowledge that, although the length of the second stage is a proxy marker for feto-maternal disproportion and obstruction, it is not clear that measures to shorten the second stage would reduce the rate of LAM avulsion. Furthermore, the mode of vaginal delivery is likely to be strongly influenced by unmeasured factors relating to obstructed labour. Therefore, the association between forceps and avulsion may be due to confounding by indication, and may perhaps not be a true causal relationship.

Conclusion

21% of women sustain LAM avulsion during their first vaginal delivery. Our risk model shows that OASIS, active second stage of labour and forceps delivery are risk factors. We have developed a nomogram which is a novel tool to estimate an individual woman's risk of having sustained LAM avulsion. This nomogram can help us to target postnatal women at risk and offer them pelvic floor education.

References

1. Gainey HL. Post-partum observation of pelvic tissue damage. Am J Obstet Gynecol 1943;46:457-66
2. Sultan AH, Kamm MA, Hudson CN, Thomas JM, Bartram CI. Anal-sphincter disruption during vaginal delivery. N Engl J Med 1993;329:1905-11
3. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
4. DeLancey JO, Kearney R, Chou Q, Speights S, Binno S. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. Obstet Gynecol 2003;101:46-53
5. Dietz HP, Lanzarone V. Levator trauma after vaginal delivery. Obstet Gynecol 2005;106:707-12
6. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
7. Shek KL, Dietz HP. The effect of childbirth on hiatal dimensions. Obstet Gynecol 2009;113:1272-8
8. Valsky DV, Lipschuetz M, Bord A, Eldar I, Messing B, Hochner-Celnikier D, et al. Fetal head circumference and length of second stage of labor are risk factors for levator ani muscle injury, diagnosed by 3-dimensional transperineal ultrasound in primiparous women. Am J Obstet Gynecol 2009;201:91.e1-7
9. Shek KL, Dietz HP. Can levator avulsion be predicted antenatally? Am J Obstet Gynecol 2010;202:586.e1-6
10. Shek K, Dietz HP. Intrapartum risk factors for levator trauma. BJOG 2010;117:1485-92
11. Chan SS, Cheung RY, Yiu AK, Lee LL, Pang AW, Choy KW et al. Prevalence of levator ani muscle injury in Chinese women after first delivery. Ultrasound Obstet Gynecol 2012;39:704-9
12. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
13. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
14. Krofta L, Otcenasek M, Kasikove E, Feyereisl J. Pubococcygeus-puborectalis trauma after forceps delivery: evaluation of the levator an imuscle with 3D/4D ultrasound. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1175-81
15. van Delft KWM, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Recruitment of pregnant women in research: Experience from a prospective study. J Obstet Gynaecol 2013;33:442-6
16. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-585
17. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
18. Dietz HP. Quantification of major morphological abnormalities of the levator ani. Ultrasound Obstet Gynecol 2007;29:329-334
19. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
20. Lammers K, Fütterer JJ, Inthout J, Prokop M, Vierhout ME, Kluivers KB. Correlating signs and symptoms with pubovisceral muscle avulsions on magnetic resonance imaging. Am J Obstet Gynecol 2013;208:148.e1-7
21. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30
22. Norušis MJ. PASW Statistics 18.0 Advanced Statistical Procedures Companion (2010). Chapter 4 Ordinal Regression. ISBN-10: 0-321-69057-5, ISBN-13: 978-0-321-69057-9. http://www.norusis.com/pdf/ASPC_v13.pdf
23. Riley RD, Hayden JA, Steyerberg EW, Moons KG, Abrams K, Kyzas PA, et al; PROGRESS Group. Prognosis Research Strategy (PROGRESS) 2: prognostic factor research. PLoS Med 2013;10:e1001380
24. Steyerberg EW, Moons KG, van der Windt DA, Hayden JA, Perel P, Schroter S, et al; PROGRESS Group. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. PLoS Med 2013;10:e1001381
25. Harrell FE, Lee KL, Mark DB. Tutorial in biostatistics multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med 1996;15:361-87

26. Simon R, Altman DG. Statistical aspects of prognostic factor studies in oncology. Br J Cancer 1994;69:979-85
27. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2012. ISBN 3-900051-07-0, URL http://www.R-project.org/
28. Dietz HP, Kirby A. Modelling the likelihood of levator avulsion in a urogynaecological population. Aust N Z J Obstet Gynaecol 2010;50:268-72
29. Braekken IH, Majida M, Engh ME, Bø K. Morphological changes after pelvic floor muscle training measured by 3-dimensional ultrasonography: a randomized controlled trial. Obstet Gynecol 2010;115:317-24
30. Dietz HP, Gillespie AVL, Phadke P. Avulsion of the pubovisceral muscle associated with large vaginal tear after normal vaginal delivery at term. Aust N Z J Obstet Gynaecol 2007;47:341-4
31. NICE clinical guidelines – Intrapartum Care (CG55). October 2012
32. RCOG Green-top Guidelines – Operative vaginal delivery (No. 26). January 2011

Supplementary material

Table S1 Demographics and obstetric details in women who have and who have not attended the follow-up visit

	Attended (n = 191)	Did not attend (n = 76)	p value
Demographic variables			
Age (years)	30.7 (SD 5.5)	29.1 (SD 6.4)	**0.039**
BMI (kg/m^2)	25.3 (SD 5.5)	25.6 (SD 4.7)	0.70
Ethnicity - White - Asian - Mixed - Black - Other	 106 (55%) 29 (15%) 10 (5%) 42 (22%) 4 (2%)	 33 (43%) 11 (14%) 7 (9%) 21 (28%) 4 (5%)	0.25
Delivery variables			
Gestational age at delivery (weeks)	40.1 (SD 1.2)	39.8 (SD 1.3)	0.07
Induction* - No - Yes	 135 (71%) 56 (29%)	 52 (69%) 23 (31%)	0.83
Use of oxytocin** - No - Yes	 117 (61%) 74 (39%)	 43 (58%) 31 (42%)	0.64
Epidural analgesia** - No - Yes	 126 (66%) 65 (34%)	 44 (59%) 30 (41%)	0.32
First stage (min)***	408 (range 35-1271)	488 (range 86-1173)	0.61
Second stage (min)***	65 (range 4-269)	53 (range 1-312)	0.83
Active second stage (min)***	40 (range 2-209)	42 (range 1-245)	0.82
Mode of delivery - Normal vaginal - Forceps - Ventouse - Elective caesarean - Emergency caesarean	 92 (48%) 21 (11%) 30 (16%) 10 (5%) 38 (20%)	 25 (33%) 5 (7%) 14 (18%) 5 (7%) 27 (36%)	**0.043**
Perineal laceration*** - No - First degree - Second degree - OASIS	 12 (8%) 21 (15%) 94 (65%) 18 (12%)	 5 (12%) 7 (16%) 30 (70%) 1 (2%)	0.27

Table S1 Continued

	Attended (n = 191)	Did not attend (n = 76)	p value
Delivery variables			
Episiotomy*** - No - Yes	 83 (57%) *62* (43%)	 17 (39%) 27 (61%)	**0.030**
Birth weight (gram)**	3375 (SD 416)	3185 (SD 492)	**0.002**
Head circumference (cm)****	34.3 (SD 1.5)	33.8 (SD 1.8)	**0.045**
Occipito anterior***** - No - Yes	 24 (13%) 162 (87%)	 12 (14%) 56 (86%)	0.85
Shoulder dystocia*** - No - Yes	 185 (99%) 2 (1%)	 67 (100%) 0	1.00

Independent-sample Student's t test, Mann Whitney U test, and chi-square test: continuous variables are given as means with standard deviations (SDs) or medians with ranges (range); categorical variables are given as numbers with percentages (%). All P-values are two-sided.

SD, standard deviation; BMI, Body Mass Index; OASIS, obstetric anal sphincter injuries
* missing data in one woman that did not attend follow-up
** missing data in two women that did not attend follow-up
*** not applicable in women that delivered by caesarean section
**** missing data in 8 women that attended follow-up and in 7 women that did not attend follow-up
***** missing data in 5 women that attended follow-up and in 12 women that did not attend follow-up

Table S2 Univariable ordinal logistic regression analysis, excluding women who delivered via caesarean section (n=48)

	p-value	Odds ratio (95% confidence interval)
Demographic variables		
Age (years)	0.22	1.05 (0.97-1.13)
Ethnicity	0.55	1.10 (0.81-1.49)
BMI (kg/m^2)	0.16*	0.95 (0.87-1.03)
Delivery variables		
Gestational age at delivery (weeks)	0.18	1.27 (0.89-1.81)
- Forceps delivery	<0.001*	6.6 (2.5-17.2)
- Ventouse delivery	0.27	1.85 (0.60-5.68)
First stage of labour (hour)	0.30	1.06 (0.94-1.13)
Second stage of labour (hour)	0.015*	1.82 (1.00-1.82)
Active second stage of labour (hour)	0.001*	2.17 (1.35-3.28)
Induction	0.42	1.48 (0.55-4.02)
Oxytocin	0.37	0.68 (0.30-1.55)
Epidural analgesia	0.78	0.88 (0.37-2.12)
Birth weight	0.21	1.001 (1.00-1.002)
Head circumference	0.56	1.008 (0.98-1.03)
Tear grade	0.020*	1.71 (1.09-2.69)
- Second degree tear	0.022*	2.59 (1.15-5.87)
- OASIS	0.007*	4.4 (1.6-12.1)
Episiotomy	0.07*	0.47 (0.21-1.07)

95% CI, 95% confidence interval; OASIS, obstetric anal sphincter injuries.
* variables evaluated clinically for multivariable ordinal logistic regression analysis

8

The relationship between postpartum levator ani muscle avulsion and signs and symptoms of pelvic floor dysfunction

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Abstract

Objective: To establish the relationship between postpartum levator ani muscle (LAM) avulsion and signs and/or symptoms of pelvic floor dysfunction (PFD).
Design: Observational longitudinal cohort study
Setting: District General University Hospital, United Kingdom
Population or sample: Primigravida at 36 weeks gestation and three months postpartum
Methods: Pelvic floor muscle strength (PFMS) and pelvic organ prolapse were assessed clinically using validated methods. Transperineal ultrasound was performed to identify LAM avulsion and measure hiatus dimensions. Validated questionnaires evaluated sexual function, urinary and faecal incontinence.
Main outcome measures: PFD signs and symptoms related to LAM avulsion
Results: 269 primigravida without LAM avulsion participated and 71% (n=191) returned postpartum. LAM avulsion was found in 21% of vaginal deliveries (n=30, 95%CI 15.1-28.4%). Women with minor and major avulsion had worse PFMS ($p<0.038$) and more anterior compartment prolapse (maximum stage 2) ($p<0.024$). Antenatal hiatus antero-posterior diameter on ultrasound was significantly smaller in women sustaining avulsion ($p=0.011$). Postnatal measurements were significantly increased following avulsion. Women with major avulsion were less sexually active at both antenatal and postnatal periods ($p<0.030$). These women had more postnatal urinary incontinence and symptoms such as reduced vaginal sensation and 'too loose vagina'. No postnatal differences were found for faecal incontinence, prolapse symptoms or quality of life. Differences in variables only correlated slight-fair with avulsion severity.
Conclusions: 21% sustain LAM avulsion during first vaginal delivery with significant impact on signs and symptoms of PFD. As avulsion has been described as the missing link in the development of prolapse, longer term follow-up is vital.

Introduction

Pelvic organ prolapse (POP) is a common condition and the life time risk of a woman undergoing surgery for POP is 11-20%[1,2,3]. Anatomical POP recurrence occurs in 40% of women in the operated compartment, with a re-operation rate of 9.7% due to symptomatic recurrence[4]. The main contributor for POP is vaginal delivery with damage to the levator ani muscle (LAM)[5,6]. A recent review has shown that this damage diagnosed on transperineal ultrasound (TPUS) a few months following childbirth occurs in 13-36% of women[7]. A 2.4 to 2.9 fold increase of anatomical cystocele recurrence has been shown in women with LAM avulsion, although not all women were symptomatic[8,9].

In addition to POP[5,6,10], women with LAM avulsion are at risk of a reduction in pelvic floor muscle strength (PFMS)[11,12,13] and an increased vaginal hiatus[14,15,16]. Although the literature is ambiguous, these anatomical changes may lead to symptoms of pelvic floor dysfunction (PFD). Although the relationship between LAM avulsion and faecal[17,18,19,20] and urinary incontinence[21,22,23,24,25] has been evaluated, sexual function has not been studied in relation to LAM avulsion. We are not aware of a study in the literature that has utilised validated methods for objective and subjective assessment of PFD in relation to LAM avulsion before and after childbirth.

The aim of this study was to establish the relationship between postpartum LAM avulsion and signs and/or symptoms of PFD.

Methods

Between January 2011 and May 2012, primigravid women were invited to participate in an observational, longitudinal, cohort study to establish the prevalence of LAM defects during childbirth and to correlate these with pelvic floor symptoms and muscle strength. We invited consecutive primiparous women, to create a sample representative for the normal population. The inclusion criteria were a singleton pregnancy, maternal age $>$ 18 years, no previous history of pregnancy of more than 20 weeks gestation, and being able to read and understand English. The recruitment process has previously been described[26,27], and our study sample was representative for the local population[26]. This study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87). Clinical examination was carried out in the supine position with knees semi-flexed. Women were asked to empty their bladder prior to the examination. PFMS was assessed by digital palpation, inserting the index-finger approximately 4 cm into the vagina. The strength was graded using the modified Oxford scale (MOS), on a six point scale (0 – 5)[28], for which substantial inter-rater agreement has been found[29]. POP assessment was performed

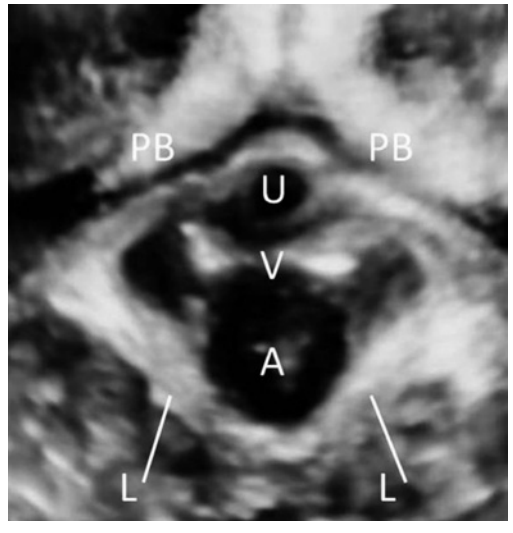
using the validated International Continence Society POP-Q staging method[30,31]. Rigorous investigator training and observation by the principal investigator (RT) minimised measurement and technique variability.

3D/4D TPUS was performed using the GE Voluson 730 system with a 4-8 MHz transabdominal curved array volume transducer, with an acquisition angle of 85 degrees. Imaging was performed at rest, at maximum pelvic floor muscle contraction and at maximum Valsalva manoeuvre. Blind offline analysis was performed using 4D view version 10.2. The cineloops were reviewed in the midsagittal view to identify the plane of the minimal hiatal dimensions[32]. This is the minimal distance from the posterior margin of the symphysis pubis to the anterior margin of the levator plate[29,32]. Tomographic Ultrasound Imaging (TUI) on maximum pelvic floor muscle contraction was used to assess the entire LAM and its attachment to the inferior pubic ramus as previously described[27,33]. Two independent investigators (KvD and KK), blinded for findings on assessment and each other's results, analysed the TUI in postnatal scans for LAM avulsion. Consensus was reached by a third investigator (RT). Using direct visualisation, the central three slices were scored as positive or negative for LAM avulsion, scoring left and right side separately[33,34]. The unilateral score ranged from 0 (no avulsion) to 3 (complete LAM avulsion)[34]. Reliability analyses have shown excellent agreement between two raters (Cohen's kappa 0.83, 95% confidence interval 0.59-1.0) when diagnosing LAM avulsion using TUI on TPUS at maximum pelvic floor muscle contraction[35]. A summed total score for either side (0 – 6) was assigned and categorised as no LAM avulsion (summed score 0), minor LAM avulsion (summed score 1 – 3) or major LAM avulsion (summed score 4 – 6, or a unilateral score 3) (Figure S1)[10,27,36].

The rendered image (Figure 1 and Figure 2) was used to perform hiatus measurements in the axial plane of the minimal hiatal dimensions. Sectional planes could be used instead, as the rendered volume is not available on all ultrasounds. Hiatus area and hiatus antero-posterior diameter (AP) were measured at rest, at maximum pelvic floor muscle contraction and at maximum Valsalva manoeuvre[32]. All measurements in the rendered image were performed by one investigator (KvD) and a test-retest series was done by a second investigator (KK).

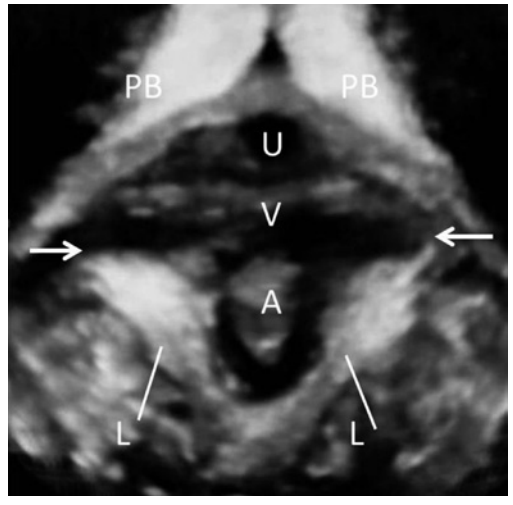
Previously validated questionnaires were administered to assess bowel, urinary and sexual function in the third trimester of pregnancy and three months postpartum. The St Mark's incontinence (SMIS) scoring system was used for faecal incontinence: a total score was calculated adding up the separate scores of frequency of faecal urgency, faecal incontinence, flatus incontinence and impact on lifestyle (range 0 – 24)[37,38]. The International Consultation Incontinence Questionnaire Short Form (ICIQ-SF) was used for urinary incontinence: a total score was calculated including frequency, amount that leaks and interference with everyday life (range 0 – 21) and urinary incontinence was defined as ICIQ-SF $>$ 0, and sub analysis was performed

Figure 1 Normal antenatal levator hiatus in rendered volume, at rest



PB, pubic bone; U, Urethra; V, vagina; A, Anus; L, levator ani muscle.

Figure 2 Abnormal postnatal levator hiatus in rendered volume, at rest



PB, pubic bone; U, Urethra; V, vagina; A, Anus; L, levator ani muscle.
Arrows indicate bilateral LAM avulsion.

to assess when urine leaks[39]. ICIQ-VS was used for vaginal symptoms and sexual matters and all subscales of this questionnaire were analysed separately[40].

Statistical analysis

Based on previous studies on LAM avulsion following childbirth, we enrolled 269 women to detect 14% incidence of LAM avulsion (including allowance for a 30% drop-out rate) with a precision of 2.5%[27]. The same cohort of primiparous women was used to establish the relationship between LAM avulsion and PFD in the present study.

All analyses were performed by definition of the three groups (no LAM avulsion (summed score 0) vs. minor LAM avulsion (summed score 1 – 3) vs. major LAM avulsion (summed score 4 – 6, or a unilateral score 3)). Outcomes of digital assessment, ultrasound assessment and the validated questionnaires were analysed before and after childbirth. To assess antenatal and postnatal differences between the three independent groups, we used analysis of variance (ANOVA), applying post-hoc least significant difference procedure for inter-group comparison, Kruskal Wallis test, Chi^2 test and Fisher's exact test where appropriate. To assess differences between the antenatal and postnatal visit for each variable, comparisons within groups were performed using paired Student t-test and Wilcoxon Signed rank test where appropriate. We hypothesised that the differences between antenatal and postnatal PFD assessment would depend on the severity of LAM avulsion. To assess whether there was an association between the severity of pelvic floor dysfunction and the severity of LAM avulsion, Pearson's rho was used for normally distributed continuous data, Spearman's rank for continuous data that were not normally distributed and Kendall's tau b for categorical data. An increasing rank correlation implies increasing agreement between two variables. Correlation ranges from -1 (perfect disagreement) to +1 (perfect agreement), where 0 refers to completely independent rankings. SPSS version 20.0 was used (SPSS Inc, Chicago, IL, USA) and two-sided p values < 0.05 were considered statistically significant.

Results

269 primigravid women participated at a median of 36 weeks of gestation (range 34 – 41 weeks) and 71% (n=191) returned for follow-up at a median of 13 weeks (range 10 – 26 weeks). All women, except three, underwent examination and filled in the validated questionnaires. Two women did not undergo the antenatal examination and dropped out, and one woman declined vaginal examination at follow-up. Women who attended the three months follow-up had a mean age of 30.7 years (SD 5.5), mean BMI was 25.3 (SD 5.5), the majority was from a white ethnic background (55%, n=106)[27]. 75% (n=143) delivered vaginally and 25% (n=48) had a caesarean section. A more detailed description of demographics and obstetric details to assess differences in the follow-up and lost to follow up group was described previously[27].

Test-retest analyses for the performed measurements on TPUS in the rendered image revealed moderate-good correlation for hiatus area (ICC 0.45-0.61) and good correlation for hiatus antero-posterior diameter (ICC 0.64-0.80).

None of the antenatal women had LAM avulsion and LAM avulsion was not found after caesarean section (n=48). The overall incidence of LAM avulsion following first vaginal delivery was 21.0% (n=30, 95% CI 15.1-28.4%); 4.9% (n=7, 95% CI 2.2-9.9%) for minor LAM avulsion and 16.1% (n=23, 95% CI 10.9-23.0%) for major LAM avulsion[27]. Further analysis of the present study is based on three groups of primiparous women divided into: no avulsion (n=113), minor LAM avulsion (n=7), and major LAM avulsion (n=23).

Clinical assessment (Table S1)

Antenatal and postnatal PFMS were lower in women with minor and major LAM avulsion (mean 3.0 and 2.4 respectively), compared to women without LAM avulsion (mean 3.6 and 3.1 respectively) ($p<0.038$). PFMS of women with no and major LAM avulsion decreased significantly following childbirth. However, the differences between antenatal and postnatal assessment did not correlate with LAM avulsion severity. No significant differences between the three groups were found on POP-Q examination performed during pregnancy. Postpartum, significantly more prolapse was found in women with no and major LAM avulsion on POP-Q assessment for points Ba (anterior compartment), C (central compartment) and Bp (posterior compartment). Women with major LAM avulsion had more anterior compartment prolapse following childbirth ($p<0.024$). However LAM avulsion severity correlated only slightly with differences between antenatal and postnatal anterior compartment prolapse. Maximum POP-Q stage was 2. Genital hiatus increased in all groups following childbirth and perineal body length decreased in all groups, without differences between groups and no correlation with LAM avulsion was found.

Ultrasound assessment (Table 1)

On antenatal TPUS, no difference in hiatus area measurements was found between the three groups. However, a significantly smaller hiatus antero-posterior (AP) diameter at rest was found in women that were going to sustain LAM avulsion ($p=0.011$).

Following childbirth, hiatus area decreased in women without LAM avulsion and increased in women with LAM avulsion. Postnatal hiatus area at rest was not significantly different between the three groups. Significantly larger areas were found for women with LAM avulsion on images acquired at maximum pelvic floor muscle

Table 1 Hiatus measurements on ultrasound assessment in women with no, minor or major LAM avulsion

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
Area - rest (cm^2)				
- Antenatal	16.1 (SD 3.1)	14.1 (SD 2.8)	15.0 (SD 4.4)˚	p=0.15
- Postnatal	15.3 (SD 3.3)	15.2 (SD 2.6)	15.6 (SD 3.8)˚	p=0.91
- Difference	-0.7 (SD 2.7)*	1.0 (SD 2.9)	0.8 (SD 3.5)	ρ=-0.21
AP - rest (cm)				
- Antenatal	5.7 (SD 0.7)	5.2 (SD 0.8)	5.3 (SD 0.9)˚	**p=0.011[A]**
- Postnatal	5.5 (SD 0.8)	5.3 (SD 0.6)	5.3 (SD 0.7)˚	p=0.61
- Difference	-0.2 (SD 0.5)*	0.2 (SD 0.7)	Δ 0.1 (SD 0.7)	ρ=-0.22
Area - contraction (cm^2)				
- Antenatal	12.6 (SD 2.4)˚	12.4 (SD 2.8)	11.9 (SD 3.5)˚	p=0.58
- Postnatal	12.5 (SD 2.7)˚	13.9 (SD 2.7)	14.2 (SD 3.2)	**p=0.020[A]**
- Difference	-0.04 (SD 2.2)	1.4 (SD 2.6)	2.3 (SD 4.5)*	ρ=-0.32
AP - contraction (cm)				
- Antenatal	4.7 (SD 0.7)˚	4.4 (SD 0.6)	4.4 (SD 0.9)˚	p=0.25
- Postnatal	4.6 (SD 0.7)˚	4.7 (SD 0.7)	4.7 (SD 0.6)	p=0.81
- Difference	-0.1 (SD 0.5)	0.3 (SD 0.5)	0.3 (SD 0.8)	ρ=-0.22
Area - Valsalva (cm^2)				
- Antenatal	20.5 (SD 6.0)˚˚˚	17.3 (SD 3.7)	20.0 (SD 7.2)˚	p=0.38
- Postnatal	20.5 (SD 6.4)˚	21.0 (SD 5.6)	23.7 (SD 6.5)˚˚	**p=0.049[A]**
- Difference	1.6 (SD 46.2)	3.7 (SD 3.6)*	4.1 (SD 7.2)*	ρ=-0.29
AP - Valsalva (cm)				
- Antenatal	6.3 (SD 1.0)˚˚˚	5.6 (SD 0.9)	6.0 (SD 1.1)˚	p=0.20
- Postnatal	6.1 (SD 0.9)˚	6.0 (SD 0.9)	6.2 (SD 1.0)˚˚	p=0.76
- Difference	-0.2 (SD 0.8)*	0.3 (SD 0.7)	0.2 (SD 0.9)	ρ=-0.19

Continuous variables are given as means with standard deviations (SDs); categorical variables are given as numbers with percentages (%). For antenatal and postnatal variables: ANOVA applying least significant difference if $p<0.05$. [A, B] and [C] statistically significant difference between no and major avulsion ([A]), minor and major avulsion ([B]) and no and minor avulsion ([C]), respectively. All P-values are two-sided. Pearson's ρ was used to assess the association between the difference of antenatal and postnatal variables in relation to LAM avulsion. *= significant difference between antenatal and postnatal variables per group.
AP= hiatus antero-posterior diameter.
˚ = one scan of the group could not be analysed
˚˚ = two scans of the group could not be analysed
˚˚˚ = four scans of the group could not be analysed

contraction and maximum Valsalva manoeuvre. Fair correlation was found between the increase in hiatus area and LAM avulsion severity. Following childbirth, hiatus AP diameter decreased in women without LAM avulsion and increased in women with LAM avulsion. Fair correlation was found between the increase of hiatus AP diameter and LAM avulsion severity. Overall, the changes in AP diameter were less distinct than the changes in hiatus area measurements.

Subjective assessment (Table S2)

A significant increase in faecal incontinence was seen in women with and women without LAM avulsion, mainly due to an increase in flatus incontinence. As such, no trend was found between faecal incontinence and LAM avulsion severity. Impact on quality of life was not different between the three groups.

Urinary incontinence score was higher in women who were to sustain LAM avulsion. Women without LAM avulsion had a significant improvement in urinary symptoms following childbirth, which was not found in women with LAM avulsion. The latter had significantly more urinary incontinence three months postnatal, with a higher total score. No trend was found between urinary incontinence and LAM avulsion severity. Before and after childbirth, the majority of women had urinary incontinence related to stress urinary incontinence (n=54, 74%; and n=32, 64% respectively).

No antenatal differences were found for vaginal symptoms. Following childbirth, women with major LAM avulsion had a significant increase in the bothersome symptom of a reduced vaginal sensation and the difference between antenatal and postnatal assessment correlated slightly with LAM avulsion severity. Furthermore, women with LAM avulsion had significantly more symptoms of a 'too loose vagina' following childbirth and the differences between antenatal and postnatal assessment correlated slightly with LAM avulsion severity. In all three groups, prolapse symptoms did not significantly differ following childbirth. Significantly fewer women who were going to sustain a major LAM avulsion during delivery were sexually active in the third trimester of pregnancy (39% major LAM avulsion vs. 86% minor LAM avulsion vs. 65% no LAM avulsion, p=0.029). Less women with major LAM avulsion had resumed sexual intercourse within three months following delivery (43% major LAM avulsion vs. 100% minor LAM avulsion vs. 71% no LAM avulsion, p=0.004). However, none of the vaginal symptoms reported interfered with their sex-life. Overall, antenatal interference of vaginal symptoms with everyday life was significantly higher in women who were going to sustain a major LAM avulsion. This was not significant anymore following childbirth, and the differences between antenatal and postnatal assessment did not correlate with LAM avulsion severity.

Discussion

Main findings

This study shows the relationship between postpartum LAM avulsion and PFD using validated techniques for objective and subjective assessment. A smaller antenatal hiatus antero-posterior diameter was associated with a significant increased risk of postnatal LAM avulsion. Less PFMS, more anterior compartment prolapse and a larger hiatus were found in women with minor and major LAM avulsion following childbirth. Women with major LAM avulsion had more urinary incontinence, without differences in faecal incontinence. Furthermore, women with major LAM avulsion had more bothersome vaginal symptoms, and had less sexual intercourse before and after childbirth.

Strengths and limitations

The strengths are the prospective design and the use of validated methods to assess PFD related to LAM avulsion. We evaluated PFD objectively and subjectively, as signs and symptoms do not always correlate[41,42]. When analysing LAM avulsion and hiatus measurements on ultrasound, the investigators were blinded to delivery details, clinical examination and each other's results. Furthermore, the statistical significant differences presented during postnatal assessment were often not related to changes between antenatal and postnatal assessment. Therefore, differences between antenatal and postnatal assessment did not correlate well with LAM avulsion severity. This highlights the merits of performing prospective studies, as we have done.

We acknowledge the limitations of this study. We could not perform a power calculation based on the validated assessment techniques, as they have not been previously used in relation to LAM avulsion and childbirth. The current sample size was based on a power calculation to detect the incidence of LAM avulsion following first delivery, which will be published elsewhere[27]. Secondly, we acknowledge that the group size of minor LAM avulsion was small.

Interpretation

Antenatal and postnatal PFMS were significantly less in women with LAM avulsion. The postnatal difference did not correlate with LAM avulsion severity, suggesting that there may be another mechanism responsible for the worsening PFMS. Although our psychometric properties of PFMS were good, we acknowledge that there is debate in the literature and therefore this should be taken into consideration during interpretation of this score. An increase of PFMS during pregnancy, followed by a reduction in strength postpartum has previously been described[43]. Although worsening of POP following vaginal delivery has previously been demonstrated in prospective studies[18,42,44],

this was not related to LAM avulsion. Our study revealed more anterior compartment prolapse for women with LAM avulsion. Although women were asymptomatic and maximum POP-Q stage was 2, this study provides baseline data to evaluate future POP development. Previous studies in prolapse patients have revealed a reduced PFMS in women with LAM avulsion[11,12]. Moreover, supervised pelvic floor muscle training to increase PFMS in women with POP can improve severity of prolapse and reduce prolapse symptoms[45].

Postnatal hiatus area was significantly larger in women with major LAM avulsion (except at rest), compared to women without LAM avulsion. The explanation is two-fold. Firstly, diagnosis of LAM avulsion appears to be most reliable on maximum contraction[35], as LAM avulsion becomes more obvious on contraction. Secondly, as the LAM has been stretched to a larger extent when avulsion has occurred[46], we speculate that this can lead to muscle that stretches easier even three months later. However, the correlation between increase in hiatus area and LAM avulsion severity was fair. Another new finding is that women with a smaller antenatal antero-posterior diameter at rest are at greater risk of sustaining LAM avulsion during delivery. Although this is only a geometric measure, it does support the hypothesis that as LAM has to stretch more to allow passage of the fetus, it would increase the risk of avulsion from the inferior pubic ramus[46].

Our findings on objective assessment are in accordance with the literature where POP, enlarged hiatus and LAM avulsion are inter-related[5,6,10,14,16,47].

In contrast to another study performed postpartum[18], we found that both women with and without major LAM avulsion had significantly more faecal incontinence, without differences between groups. As shown previously we expected women with major avulsions to report more faecal incontinence as the incidence of OASIS was higher (n=8/30)[27]. Although two studies among older women showed an association between faecal incontinence and LAM avulsion[17,19], another study in a tertiary referral centre showed the opposite[20].

The incidence of urinary incontinence prior to childbirth can be explained by the physiological changes that occur during pregnancy and the load of the gravid uterus predisposing women to urinary incontinence. However, we could not explain why women that were to sustain LAM avulsion had more antenatal urinary incontinence. Women with LAM avulsion persisted to have more stress urinary incontinence than women without LAM avulsion. Other postpartum studies found that women with LAM avulsion had more urinary incontinence, although no antenatal values were available[21,22]. Contradictory findings have been published regarding urinary incontinence and LAM avulsion in prolapse patients[23,24,25]. We speculate that women with LAM avulsion have an earlier onset of stress urinary incontinence, which might balance out with age.

Women with LAM avulsion were less sexually active prior to childbirth and their vaginal symptoms interfered with their everyday life. We cannot offer an explanation for this and attribute it to a coincidental finding. A recent review reports a 41-83% prevalence of postpartum sexual dysfunction, especially following instrumental vaginal delivery and perineal trauma[48]. However, vaginal symptoms and sexual function have not previously been evaluated in women with LAM avulsion postpartum. Lack of vaginal sensation has been shown to occur after vaginal delivery[44], which is worse in women with LAM avulsion. Furthermore, these women feel that their vagina is too loose, which concurs with the enlarged hiatus found on TPUS. Women with these vaginal symptoms and associated major LAM avulsion were less likely to resume sexual intercourse postpartum. This might not necessarily be an independent factor as women with LAM avulsion sustained more severe perineal trauma which could explain delayed resumption of sexual intercourse. Future follow-up may show whether overall bother with vaginal symptoms including sexual intercourse in women with LAM avulsion persists.

Previous studies have shown that minor LAM avulsion behaved like no LAM avulsion[34]. However, differences between antenatal and postnatal objective and subjective assessment were not obviously associated with LAM avulsion severity. We can therefore not draw conclusions regarding the impact of minor LAM avulsion. Furthermore, the minor LAM avulsion group was small as stated in the limitations, which hampers conclusions in this respect.

A smaller antenatal hiatus antero-posterior diameter could be a predictor of LAM avulsion, although this needs further evaluation in future studies. The presented changes in objective and subjective assessment can be incorporated in the management of women with LAM avulsion. We can now target women with LAM avulsion and provide intensive lifestyle modification, education and pelvic floor muscle training[45]. Together with weaker pelvic floor muscles, we found more anterior compartment prolapse and larger hiatus in women with major LAM avulsion. We also found more vaginal symptoms and urinary incontinence in women with LAM avulsion. These symptoms can be addressed during postnatal counselling[48]. Longer term follow-up is vital to establish the pattern of resolution, on-going and de novo symptoms of PFD. Furthermore, as LAM avulsion has been described as the missing link in the development of POP we need to establish if women with LAM avulsion progress to overt prolapse and therefore longer term follow-up is planned.

References

1. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-6
2. Smith FJ, Holman CD, Moorin RE, Tsokos N. Lifetime risk of undergoing surgery for pelvic organ prolapse. Obstet Gynecol 2010;116:1096-100
3. de Boer TA, Slieker-Ten Hove MC, Burger CW, Kluivers KB, Vierhout ME. The prevalence and factors associated with previous surgery for pelvic organ prolapse and/or urinary incontinence in a cross-sectional study in The Netherlands. Eur J Obstet Gynecol Reprod Biol 2011;158:343-9
4. Miedel A, Tegerstedt G, Mörlin B, Hammerström M. A 5-year prospective follow-up study of vaginal surgery for pelvic organ prolapse. Int Urogynecol J 2008;19:1593-601
5. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
6. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
7. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
8. Dietz HP, Chantarasorn V, Shek KL. Levator avulsion is a risk factor for cystocele recurrence. Ultrasound Obstet Gynecol 2010;36:76-80
9. Weemhoff M, Vergeldt TFM, Notten K, Serroyen J, Kampschoer PHNM, Roumen FJME. Avulsion of puborectalis muscle and other risk factors for cystocele recurrence: a 2-year follow-up study. Int Urogynecol J 2012;23:65-71
10. Lammers K, Fütterer JJ, Inthout J, Prokop M, Vierhout ME, Kluivers KB. Correlating signs and symptoms with pubovisceral muscle avulsions on magnetic resonance imaging. Am J Obstet Gynecol 2013;208:148.e1-7
11. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-636
12. Steensma AB, Konstantinovic ML, Burger CW, de Ridder D, Timmerman D, Deprest J. Prevalence of major levator abnormalities in symptomatic patients with an underactive pelvic floor contraction. Int Urogynecol J 2010;21:861-7
13. Dietz HP, Shek KL, Chantarasorn V, Langer SE. Do women notice the effect of childbirth-related pelvic floor trauma? Aust N Z J Obstet Gynaecol 2012;52:277-81
14. Abdool Z, Shek KL, Dietz HP. The effect of levator avulsion on hiatal dimension and function. Am J Obstet Gynecol 2009;201:89.e1-5
15. Shek KL, Dietz HP. The effect of childbirth on hiatal dimensions. Obstet Gynecol 2009;113:1272-8
16. Dietz HP, Franco AVM, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand 2012;91:211-14
17. Weinstein MM, Pretorius DH, Jung SA, Nager CW, Mittal RK. Transperineal 3-dimensional ultrasound imaging for detection of anatomical defects in the anal sphincter complex muscles. Clin Gastroenterol Hepatol 2009;7:205-11
18. Heilbrun ME, Nygaard IE, Lockhart ME, Richter HE, Brown MB, Kenton KS, et al. Correlation between levatorani muscle injuries on magnetic resonance imaging and fecal incontinence, pelvic organ prolapse, and urinary incontinence in primiparous women. Am J Obstet Gynecol 2010;202:488.e1-e6
19. Lewicky-Gaupp C, Brincat C, Yousuf A, Patel AD, DeLancey JO, Fenner DE. Fecal incontinence in older women: are levator ani defects a factor? Am J Obstet Gynecol 2010;202:491.e1-e6
20. Chantarasorn V, Shek KL, Dietz HP. Sonographic detection of puborectalis muscle avulsion is not associated with anal incontinence. Aust N Z J Obstet Gynaecol 2011;51:130-5
21. DeLancey JO, Kearney R, Chou Q, Speights S, Binno S. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. Obstet Gynecol 2003;101:46-53
22. Dietz HP, Lanzarone V. Levator trauma after vaginal delivery. Obstet Gynecol 2005;106:707-12
23. Dietz HP, Kirby A, Shek LK, Bedwell PJ. Does avulsion of the puborectalis muscle affect bladder function? Int Urogynecol J 2009;20:967-72

24. Dietz HP, Kirby A. Modelling the likelihood of levator avulsion in a urogynaecological population. Aust N Z J Obstet Gynaecol 2010;50:268-72
25. Morgan DM, Cardoza P, Guire K, Fenner DE, DeLancey JOL. Levator ani defect status and lower urinary tract symptoms in women with pelvic organ prolapse. Int Urogynecol J 2010;21:47-52
26. van Delft KWM, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Recruitment of pregnant women in research: Experience from a prospective study. J Obstet Gynaecol 2013;33:442-6
27. Van Delft KWM, Thakar R, Sultan AH, Schwertner-Tiepelmann N, Kluivers KB. Levator ani muscle avulsion during childbirth: a risk prediction model. Accepted for publication in BJOG
28. Laycock J. Clinical evaluation of the pelvic floor. In Pelvic floor re-education, Principles and practice, Schüssler B, Laycock J, Norton PA, Stanton SL, eds. Springer-Verlag: London, 1994; 42 48
29. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
30. Bump RC, Mattiasson A, Bø K, Brubaker LP, DeLancey JO, Klarskov P, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol 1996;175:10-7
31. Hall AF, Theofrastous JP, Cundiff GW, Harris RL, Hamilton LF, Swift SE, et al. Interobserver and intraobserver reliability of the proposed International Continence Society, Society of Gynecologic Surgeons, and American Urogynecologic Society pelvic organ prolapse classification system. Am J Obstet Gynecol 1996;175:1467-70
32. Dietz HP, Shek C, Clarke B. Biometry of the pubovisceral muscle and levator hiatus by three-dimensional pelvic floor ultrasound. Ultrasound Obstet Gynecol 2005;25:580-585
33. Dietz HP. Quantification of major morphological abnormalities of the levator ani. Ultrasound Obstet Gynecol 2007;29:329-334
34. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
35. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30
36. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
37. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut 1999;44:77-80
38. Roos AM, Sultan AH, Thakar R. St. Mark's incontinence score for assessment of anal incontinence following obstetric anal sphincter injuries (OASIS). Int Urogynecol J Pelvic Floor Dysfunct 2009;20:407-10
39. Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. Neurourol Urodyn 2004;23:322-30
40. Price N, Jackson SR, Avery K, Brookes ST, Abrams P. Development and psychometric evaluation of the ICIQ Vaginal Symptoms Questionnaire: the ICIQ-VS. BJOG 2006;113:700-12
41. Mouritsen L, Larsen JP. Symptoms, bother and POPQ in women referred with pelvic organ prolapse. Int Urogynecol J 2003;14:122-7
42. Glazener C, Elders A, Macarthur C, Lancashire RJ, Herbison P, Hagen S, et al; ProLong Study Group. Childbirth and prolapse: long-term associations with the symptoms and objective measurement of pelvic organ prolapse. BJOG 2013;120:161-8
43. Elenskaia K, Thakar R, Sultan AH, Scheer I, Beggs A. The effect of pregnancy and childbirth on pelvic floor muscle function. Int Urogynecol J 2011;22:1421-7
44. Elenskaia K, Thakar R, Sultan AH, Scheer I, Onwude J. Effect of childbirth on pelvic organ support and quality of life: a longitudinal cohort study. Int Urogynecol J 2013;24:927-37
45. Braekken IH, Majida M, Engh ME, Bø K. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. Am J Obstet Gynecol 2010;203:170.e1-7
46. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40

47. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80
48. Leeman LM, Rogers RG. Sex after childbirth: postpartum sexual function. Obstet Gynecol 2012;119:647-55

Supplementary material

Table S1 Digital assessment in women with no, minor or major LAM avulsion

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
MOS Right				
- Antenatal∞	3.6 (SD 1.2)	3.0 (SD 1.0)	3.0 (SD 1.7)	p=0.09
- Postnatal∞	3.1 (SD 1.2)	2.3 (SD 1.7)	2.4 (SD 1.6)	**p=0.034**[A]
- Difference¥	-0.5 (SD 1.0)*	-0.7 (SD 1.6)	-0.6 (SD 1.2)*	ρ=0.03
MOS Left				
- Antenatal∞	3.7 (SD 1.2)	2.9 (SD 0.9)	3.1 (SD1.6)	**p=0.042**[A]
- Postnatal∞	3.2 (SD 1.2)	2.4 (SD 1.6)	2.6 (SD1.6)	**p=0.037**[A]
- Difference¥	-0.4 (SD 1.0)*	-0.4 (SD 1.4)	-0.5 (SD 1.2)*	ρ=0.03
POP-Q measurements				
Aa in cm				
- Antenatal∞∞	-2.7 (SD 0.4)	-2.9 (SD 0.4)	-2.6 (SD 0.5)	p=0.37
- Postnatal∞∞	-2.3 (SD 0.7)	-2.6 (SD 0.8)	-1.8 (SD 0.9)	**p=0.023**[A,B]
- Difference¥	0.4 (SD 0.7)*	0.3 (SD 1.0)	0.8 (SD 0.9)*	ρ=-0.16
Ba in cm				
- Antenatal∞∞	-2.7 (SD 0.5)	-2.9 SD 0.4)	-2.6 (SD 0.5)	p=0.23
- Postnatal∞∞	-2.3 (SD 0.7)	-2.6 (SD 0.8)	-1.8 (SD 0.9)	**p=0.021**[A,B]
- Difference¥	0.4 (SD 0.7)*	0.3 (SD 1.0)	0.7 (SD 0.9)*	ρ=-0.15
C in cm				
- Antenatal∞∞	-8.5 (SD 0.9)	-8.7 (SD 0.8)	-8.6 (SD 0.9)	p=0.84
- Postnatal∞∞	-7.9 (SD 1.4)	-8.4 (SD 1.0)	-7.7 (SD 1.6)	p=0.45
- Difference¥	0.7 (SD 1.5)*	0.3 (SD 1.4)	0.9 (SD 1.6)*	ρ=-0.04
Gh in mm				
- Antenatal∞	34.0 (SD 6.6)	28.6 (SD 3.8)	35.0 (SD 7.2)	p=0.08
- Postnatal∞	36.4 (SD 5.9)	37.1 (SD 5.7)	36.3 (SD 6.8)	p=0.95
- Difference¥	2.4 (SD 6.5)*	8.6 (SD 5.6)*	1.3 (SD 6.3)	ρ=0.02
Pb in mm				
- Antenatal∞	31.6 (SD 5.9)	28.6 (SD 4.8)	31.1 (SD 6.7)	p=0.41
- Postnatal∞	26.2 (SD 5.4)	22.9 (SD 6.4)	25.9 (SD 5.1)	p=0.27
- Difference¥	-5.4 (SD 6.6)*	-5.7 (SD 6.7)	-5.2 (7.6)*	ρ=-0.01
Tvl in cm				
- Antenatal∞∞	10.0 (SD 0.2)	10.0 (no variation)	10.0 (SD 0.2)	p=0.86
- Postnatal∞∞	9.9 (SD 0.4)	9.7 (SD 0.5)	9.7 (SD 0.8)	p=0.24
- Difference¥	0.1 (SD 0.5)*	0.3 (SD 0.5)	0.3 (SD 0.8)	ρ=0.13
Ap in cm				
- Antenatal∞∞	-2.9 (SD 0.3)	-3.0 (no variation)	-3.0 (no variation)	p=0.44
- Postnatal∞∞	-2.7 (SD 0.5)	-3.0 (no variation)	-2.4 (SD 0.7)	p=0.05
- Difference¥¥	0.2 (SD 0.5)*	Constant (SD 1.0)	0.6 (SD 0.7)*	ρ=-0.14

Table S1 Continued

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
POP-Q measurements				
Bp in cm				
- Antenatal∞∞	-2.9 (SD 0.3)	-3.0 (no variation)	-3.0 (SD 0.2)	p=0.81
- Postnatal∞∞	-2.7 (SD 0.6)	-3.0 (no variation)	-2.4 (SD 0.7)	p=0.05
- Difference¥¥	0.3 (0.5)*	Constant (SD 1.0)	0.5 (0.7)*	ρ=-0.12
D in cm				
- Antenatal∞∞	-9.9 (SD 0.5)	-9.9 (SD 0.4)	-9.9 (SD 0.5)	p=0.85
- Postnatal∞∞	-9.8 (SD 0.5)	-9.7 (SD 0.5)	-9.7 (SD 0.8)	p=0.69
- Difference¥	0.1 (SD 0.6)*	0.1 (SD 0.7)	0.2 (SD 0.7)	ρ=-0.06

Continuous variables are given as means with standard deviations (SDs); categorical variables are given as numbers with percentages (%). For antenatal and postnatal variables: ANOVA applying least significant difference if p<0.05 (indicated with ∞), Kruskal Wallis applying Mann Whitney U test if p<0.05 (indicated with ∞∞). [A, B] and [C] statistically significant difference between no and major avulsion ([A]), minor and major avulsion ([B]) and no and minor avulsion ([C]), respectively. All P-values are two-sided. To assess the association between the difference of antenatal and postnatal variables in relation to LAM avulsion: Pearson's ρ (indicated with ¥), Spearman's rank (indicated with ¥¥).
*= significant difference between antenatal and postnatal variables per group; MOS= modified oxford scale; Aa= point located in the midline of the anterior vaginal wall; Ba= most descended edge of anterior vaginal wall; C= most descended edge of cervix; Ap= point located in the midline of the posterior vaginal wall; Bp= most descended edge of posterior vaginal wall; D= douglas; Gh= genital hiatus; Pb= perineal body; tvl= total vaginal length

Table S2 Validated questionnaires in women with no, minor or major LAM avulsion

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
Faecal incontinence (St. Mark's incontinence Score)				
Total score FI				
- Antenatal∞∞	0.7 (SD 1.9)	1.3 (SD 1.7)	0.2 (SD 0.7)	p=0.09
- Postnatal∞∞	1.4 (SD 3.5)	0.0 (no variation)	1.4 (SD 2.6)	p=0.28
- Difference¥¥	0.8 (SD 3.5)*	-1.3 (SD 1.7)	1.2 (SD 2.5)*	ρ=-0.06
Faecal urgency				
- Antenatal∞∞	0.3 (SD 1.0)	0.4 (SD 1.1)	0.0 (no variation)	p=0.30
- Postnatal∞∞	0.6 (SD 1.3)	0.0 (no variation)	0.2 (SD 0.7)	p=0.42
- Difference¥¥	0.3 (SD 1.3)*	-0.4 (SD 1.1)	0.2 (SD 0.7)	ρ=0.02
FI (solid)				
- Antenatal∞∞	0.1 (SD 0.5)	0.0 (no variation)	0.0 (SD 0.2)	p=1.0
- Postnatal∞∞	0.1 (SD 0.4)	0.0 (no variation)	0.0 (SD 0.2)	p=0.86
- Difference¥¥	0.1 (SD 0.5)*	0.0 (no variation)	0.0 (SD 0.2)	ρ=0.00
FI (liquid)				
- Antenatal∞∞	0.0 (no variation)	0.0 (no variation)	0.0 (no variation)	p=1.0
- Postnatal∞∞	0.1 (SD 0.6)	0.0 (no variation)	0.1 (SD 0.6)	p=0.82
- Difference¥¥	0.1 (SD 0.6)	0.0 (no variation)	0.1 (SD 0.6)	ρ=-0.02
Flatus incontinence				
- Antenatal∞∞	0.3 (SD 1.0)	0.9 (SD 1.2)	0.2 (0.7)	p=0.06
- Postnatal∞∞	0.4 (SD 1.1)	0.0 (no variation)	0.8 (1.5)	p=0.19
- Difference¥¥	0.1 (SD 1.3)	-0.9 (SD 1.2)	0.7 (SD 1.3)*	ρ=-0.10
Impact quality of life				
- Antenatal∞∞	0.1 (SD 0.4)	0.0 (no variation)	0.0 (no variation)	p=0.77
- Postnatal∞∞	0.2 (SD 0.7)	0.0 (no variation)	0.1 (0.5)	p=0.74
- Difference¥¥	0.1 (SD 0.6)*	0.0 (no variation)	0.1 (SD 0.5)	ρ=-0.01
Urinary incontinence (ICIQ-SF)				
Urinary incontinence				
- Antenatal	53 (47%)	6 (86%)	14 (61%)	p=0.08
- Postnatal	34 (30%)	3 (43%)	13 (57%)	**p=0.048**
- Difference¥¥¥	-19 (17%)	-3 (43%)	-1 (4%)	ρ=0.04
Total score UI				
- Antenatal∞∞	2.7 (SD 3.3)	7.1 (SD 5.6)	3.5 (SD 3.3)	**p=0.031[C]**
- Postnatal∞∞	1.8 (SD 3.3)	4.0 (SD 6.6)	3.4 (SD 3.7)	**p=0.037[A]**
- Difference¥¥	-0.9 (SD 4.0)*	-3.1 (SD 3.5)	-0.0 (SD 3.9)	ρ=-0.07
Vaginal symptoms (ICIQ-VS)				
Dragging pain				
- Antenatal∞∞	0.9 (SD 1.0)	1.3 (SD 1.1)	1.0 (SD 0.9)	p=0.45
- Postnatal∞∞	0.3 (SD 0.6)	0.6 (SD 1.1)	0.4 (SD 0.8)	p=0.70
- Difference¥¥	-0.6 (SD 1.0)*	-0.7 (SD 1.2)	-0.6 (SD 1.1)*	ρ=0.02

Table S2 Continued

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
Vaginal symptoms (ICIQ-VS)				
Bother				
- Antenatal∞∞	1.8 (SD 2.4)	2.9 (SD 3.1)	2.0 (SD 2.2)	p=0.52
- Postnatal∞∞	0.7 (SD 1.7)	1.4 (SD 3.0)	1.2 (SD 2.4)	p=0.70
- Difference¥¥	-1.1 (SD 2.5)*	-1.4 (SD 1.4)*	-0.9 (SD 3.0)	ρ=0.02
Soreness				
- Antenatal∞∞	0.7 (SD 0.9)	1.0 (SD 1.0)	0.7 (SD 0.9)	p=0.57
- Postnatal∞∞	0.6 (SD 0.8)	0.9 (SD 1.2)	0.8 (SD 1.2)	p=0.92
- Difference¥¥	0.0 (SD 0.9)	-0.1 (SD 1.1)	0.0 (SD 0.9)	ρ=-0.03
Bother				
- Antenatal∞∞	1.4 (SD 2.0)	2.7 (SD 3.5)	2.1 (SD 2.8)	p=0.42
- Postnatal∞∞	1.6 (SD 2.2)	2.3 (SD 3.4)	2.0 (SD 3.2)	p=0.87
- Difference¥¥	0.1 (SD 2.4)	-0.4 (SD 1.9)	-0.2 (SD 2.5)	ρ=0.03
Reduced sensation				
- Antenatal∞∞	0.3 (SD 0.6)	0.4 (SD 0.8)	0.2 (SD 0.5)	p=0.61
- Postnatal∞∞	0.3 (SD 0.5)	0.3 (SD 0.8)	0.5 (SD 0.7)	p=0.08
- Difference¥¥	0.0 (SD 0.6)	-0.1 (SD 0.9)	0.3 (SD 0.8)*	ρ=-0.16
Bother				
- Antenatal∞∞	0.6 (SD 1.3)	1.4 (SD 3.0)	0.6 (SD 1.6)	p=0.64
- Postnatal∞∞	0.7 (SD 1.7)	0.3 (SD 0.8)	1.7 (SD 2.6)	**p=0.049[A]**
- Difference¥¥	0.2 (SD 1.8)	-1.1 (SD 3.0)	1.0 (SD 2.8)	ρ=-0.15
Too loose				
- Antenatal∞∞	0.2 (SD 0.5)	0.6 (SD 1.0)	0.4 (SD 0.7)	p=0.27
- Postnatal∞∞	0.3 (SD 0.6)	0.6 (SD 0.8)	0.7 (SD 0.8)	**p=0.017[A]**
- Difference¥¥	0.1 (SD 0.7)	0.0 (SD 1.0)	0.3 (SD 1.1)	ρ=-0.13
Bother				
- Antenatal∞∞	0.7 (SD 1.8)	2.6 (SD 4.4)	1.3 (SD 2.1)	p=0.28
- Postnatal∞∞	0.9 (SD 1.9)	1.4 (SD 2.3)	1.7 (SD 2.2)	p=0.07
- Difference¥¥	0.2 (SD 2.3)	-1.1 (SD 3.9)	0.5 (SD 2.7)	ρ=-0.08
Lump inside vagina				
- Antenatal∞∞	0.1 (SD 0.4)	0.3 (SD 0.8)	0.3 (SD 0.9)	p=0.44
- Postnatal∞∞	0.2 (SD 0.7)	0.0 (no variation)	0.5 (SD 1.2)	p=0.34
- Difference¥¥	0.1 (SD 0.8)	-0.3 (SD 0.8)	0.2 (SD 1.6)	ρ=0.04
Bother				
- Antenatal∞∞	0.2 (SD 0.6)	0.7 (SD 1.9)	0.7 (SD 2.1)	p=0.34
- Postnatal∞∞	0.5 (SD 1.6)	0.0 (no variation)	1.0 (SD 2.5)	p=0.35
- Difference¥¥	0.3 (SD 1.7)	-0.7 (SD 1.9)	0.3 (SD 3.5)	ρ=0.06
Lump outside vagina				
- Antenatal∞∞	0.1 (SD 0.4)	0.3 (SD 0.8)	0.0 (no variation)	p=0.13
- Postnatal∞∞	0.2 (SD 0.6)	0.0 (no variation)	0.2 (SD 0.7)	p=0.58
- Difference¥¥	0.1 (SD 0.7)	-0.3 (SD 0.8)	0.2 (SD 0.7)	ρ=-0.02

Table S2 Continued

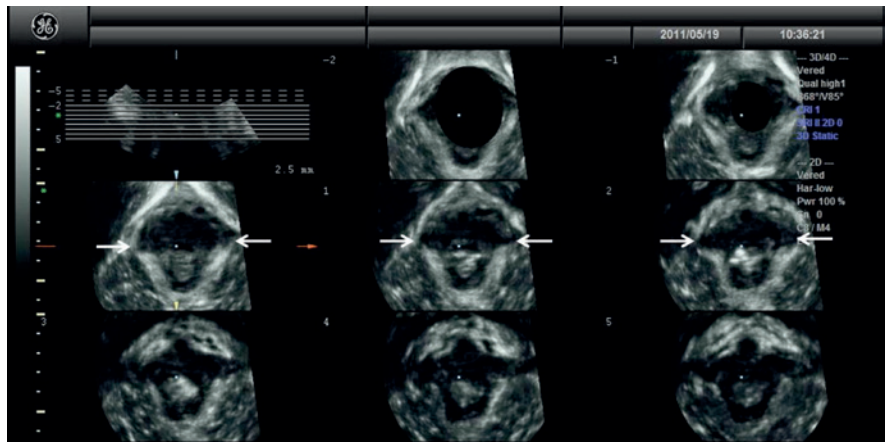
	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
Vaginal symptoms (ICIQ-VS)				
Bother - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.1 (SD 0.7) 0.4 (SD 1.4) 0.3 (SD 1.6	 0.7 (SD 1.9) 0.0 (no variation) -0.7 (SD 1.9)	 0.0 (no variation) 0.7 (SD 2.3) 0.7 (SD 2.3)	 p=0.13 p=0.56 ρ=-0.02
Dry - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.6 (SD 0.8) 0.6 (SD 0.9) 0.0 (SD 0.8)	 1.0 (SD 1.0) 1.6 (SD 1.3) 0.6 (SD 1.5)	 0.7 (SD 1.1) 0.5 (SD 0.8) -0.2 (SD 1.0)	 p=0.52 p=0.06 ρ=-0.01
Bother - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 1.2 (SD 2.0) 1.5 (SD 2.2) 0.3 (SD 1.8)	 2.9 (SD 3.4) 3.4 (SD 3.4) 0.6 (SD 2.4)	 0.9 (SD 1.8) 1.3 (SD 2.5) 0.4 (SD 2.0)	 p=0.25 p=0.15 ρ=0.00
Finger to open bowels - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.0 (no variation) 0.1 (SD 0.2) 0.0 (SD 0.3)	 0.0 (no variation) 0.0 (no variation) 0.0 (no variation)	 0.0 (no variation) 0.0 (no variation) 0.0 (no variation)	 p=1.0 p=0.58 ρ=0.06
Bother - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.0 (no variation) 0.1 (SD 0.7) 0.1 (SD 0.7)	 0.0 (no variation) 0.0 (no variation) 0.0 (no variation)	 0.0 (no variation) 0.0 (no variation) 0.0 (no variation)	 p=1.0 p=0.58 ρ=0.09
Too tight - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.5 (SD 0.8) 0.5 (SD 0.8) 0.0 (SD 1.0)	 0.4 (SD 0.8) 0.7 (SD 1.3) 0.3 (SD 0.5)	 0.5 (SD 1.1) 0.5 (SD 1.0) 0.0 (SD 1.3)	 p=0.83 p=0.82 ρ=-0.05
Bother - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.9 (SD 1.8) 1.0 (SD 1.8) 0.1 (SD 2.2)	 0.7 (SD 1.9) 2.1 (SD 3.7) 1.4 (SD 2.7)	 1.0 (SD 2.1) 0.7 (SD 1.7) -0.2 (SD 3.0)	 p=0.83 p=0.61 ρ=-0.01
Sexual matters				
Sex life at present - Antenatal - Postnatal - Difference¥¥¥	 73 (65%) 82 (73%) 9 (8%)	 6 (86%) 7 (100%) 1 (14%)	 9 (39%) 10 (43%) 1 (4%)	 **p=0.029** **p=0.004** ρ=-0.16
Interference vaginal symptoms¦ - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.4 (SD 0.6) 0.6 (SD 0.8) 0.3 (SD 0.7)*	 0.8 (SD 0.8) 0.7 (SD 0.8) -0.3 (SD 0.8)	 0.2 (SD 0.4) 1.2 (SD 1.0) 1.1 (SD 1.4)	 p=0.13 p=0.11 ρ=-0.07

Table S2 Continued

	No avulsion (n = 113)	Minor avulsion (n = 7)	Major avulsion (n = 23)	p-value
Sexual matters				
Bother¦ - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 1.1 (SD 2.2) 1.9 (SD 2.6) 1.0 (SD 2.5)*	 2.3 (SD 2.6) 2.7 (SD 3.0) -0.5 (SD 2.9)	 0.6 (SD 1.1) 4.1 (SD 3.8) 3.5 (SD 4.4)	 p=0.16 p=0.08 ρ=-0.04
Relationship affected¦ - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.2 (SD 0.4) 0.2 (SD 0.5) 0.1 (SD 0.5)	 0.3 (SD 0.5) 0.4 (SD 0.8) -0.2 (SD 0.8)	 0.2 (SD 0.4) 0.3 (SD 0.6) 0.3 (SD 0.5)	 p=0.42 p=0.81 ρ=0.01
Bother¦ - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 0.7 (SD 1.9) 0.8 (SD 1.8) 0.2 (SD 2.4)	 1.7 (SD 2.9) 1.9 (SD 3.3) -0.8 (SD 4.0)	 0.7 (SD 1.7) 0.9 (SD 2.4) 1.3 (SD 2.5)	 p=0.39 p=0.77 ρ=0.00
Sex life spoilt¦ - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 1.0 (SD 2.1) 1.7 (SD 2.4) 0.7 (SD 2.8)*	 1.3 (SD 1.8) 0.9 (SD 1.5) -0.3 (SD 2.4)	 0.8 (SD 1.1) 2.1 (SD 2.8) 1.8 (SD 3.1)	 p=0.39 p=0.72 ρ=0.02
Interference everyday life - Antenatal∞∞ - Postnatal∞∞ - Difference¥¥	 1.0 (SD 1.8) 1.3 (SD 2.1) 0.3 (SD 2.6)	 2.4 (SD 3.2) 1.4 (SD 1.4) -1.0 (SD 2.6)	 1.7 (SD 2.0) 1.9 (SD 2.3) 0.2 (SD 2.9)	 **p=0.010[A,C]** p=0.34 ρ=0.05

Continuous variables are given as means with standard deviations (SDs), although not all variables show a normal distribution; categorical variables are given as numbers with percentages (%). For antenatal and postnatal variables: Kruskal Wallis applying Mann Whitney U test if p<0.05 (indicated with ∞∞), and chi-square test. [A, B] and [C] statistically significant difference between no and major avulsion ([A]), minor and major avulsion ([B]) and no and minor avulsion ([C]), respectively. All P-values are two-sided.
To assess the association between the difference of antenatal and postnatal variables in relation to LAM avulsion: Spearman's rank (indicated with ¥¥), and Kendall's tau b: ¥¥¥
*= significant difference between antenatal and postnatal variables per group; ¦ = number represents women who are sexually active
FI = faecal incontinence; UI = urinary incontinence

Figure S1 Bilateral levator ani muscle avulsion on tomographic ultrasound imaging



Arrows indicate bilateral LAM avulsion.

9

The natural history of levator avulsion one year following childbirth: a prospective study

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Submitted

Abstract

Objective: To establish the natural history of levator avulsion in primiparous women within one year following childbirth and correlate this to signs and symptoms of pelvic floor dysfunction.

Methods: 269 nulliparous women were evaluated prospectively at 36 weeks gestation, three months and one year postnatal. Validated methods assessed pelvic floor muscle strength, pelvic organ prolapse, ultrasound measurements of hiatus dimensions and levator avulsion, and questionnaires for sexual function, urinary and anal incontinence. Pattern differences over time were evaluated using linear mixed models.

Results: 147 women (55%) attended at one year; 109 following vaginal and 38 following cesarean delivery. 13/21 (62%, 95%CI 41-79%) levator avulsions three months postnatal had healed at one year. Following vaginal delivery, nine (8%, 95%CI 4.2-15.1%) had persistent levator avulsion. Most changes in symptoms and signs of pelvic floor dysfunction occurred between the antenatal and three months postnatal visit, without improvement after one year. Anterior vaginal wall prolapse was associated with vaginal delivery. Women with persistent levator avulsion had significantly worse deterioration patterns of muscle strength, hiatus measurements and more vaginal symptoms (too loose vagina / lump sensation). However, evidence of pelvic floor dysfunction was also related to healed levator avulsion. At one year, subjective anal and urinary incontinence did not differ between groups.

Conclusions: 62% of levator avulsions acquired during vaginal delivery healed within one year. Although women with healed and persistent levator avulsion had signs and symptoms of pelvic floor dysfunction, women with persistent levator avulsion showed worse patterns.

Introduction

Levator ani muscle avulsion is associated with pelvic organ prolapse (POP) and hiatal ballooning[1,2,3,4,5]. An underlying levator avulsion has previously been found in 36% of women with POP[2]. Although not always symptomatic, women with levator avulsion have higher odds of developing cystocele recurrence[6,7].

A review of the literature has revealed that 13-36% of women undergoing their first vaginal delivery sustain levator avulsion[8]. In a recent longitudinal study using transperineal ultrasound (TPUS) van Delft et al identified levator avulsions in 21% of women following their first vaginal delivery[9]. The association of levator avulsion with signs and symptoms of pelvic floor dysfunction has been shown using validated assessment methods three months postpartum[10]. However, long term follow-up is vital to follow the development in pelvic floor dysfunction[10].

Only two studies on levator avulsion reviewed women twice following childbirth. Shek et al used TPUS four months and two to three years postnatal[11]. They found that two out of twelve (17%) levator avulsions diagnosed four months postnatal had healed at follow-up, although levator distensibility had not regressed[11]. Branham et al used magnetic resonance imaging six weeks and six months postnatal and found that women with more extensive levator injury did not heal, whereas approximately 50% of less extensive injuries had healed[12].

The aim of this study was to establish the natural history of levator avulsions within one year following childbirth and to correlate these findings with signs and symptoms of pelvic floor dysfunction.

Materials and methods

In this prospective longitudinal cohort study, nulliparous women were invited to participate between January 2011 and May 2012, by a dedicated research fellow. Recruitment took place in the antenatal clinics and parent craft classes of Croydon University Hospital, United Kingdom. The inclusion criteria were a singleton pregnancy, maternal age > 18 years, no previous history of pregnancy of more than 20 weeks gestation, and being able to read and understand English. The recruitment process to achieve 265 participants has been described previously[9,13]. This study was approved by the National Research Ethics Service South West London committee (REC 10/H0806/87). All women gave written informed consent before participation and were invited for the follow-up appointments three months and one year postnatal, via telephone, electronic mail and/or postal mail. The results of the three months postpartum visit have previously been described[9,10].

All assessments were carried out according to the same protocol, with women in supine position and knees semi-flexed. Investigator training and observation by the

principal investigator (RT) was carried out before commencing the study to minimise measurement and technique variability.

Women were asked to empty their bladder prior to the assessment. Pelvic floor muscle strength (PFMS) was assessed by digital palpation, inserting the index-finger approximately 4 cm into the vagina. PFMS was graded using the Modified Oxford Scale, on a six point scale (0 – 5)[14], which has a substantial inter-rater agreement[15]. POP was assessed using the validated International Continence Society POP-Q staging method[16].

3D/4D TPUS was performed using the GE Voluson 730 system with a 4-8 MHz curved array volume transducer, with an acquisition angle up to 85 degrees. Images were acquired at rest, maximum pelvic floor contraction and maximum Valsalva maneuver. Offline analysis was carried out using 4D view version 10.2. The minimal antero-posterior diameter was identified in the midsagittal plane as previously described[15]. The rendered image was used to perform hiatus area and antero-posterior diameter measurements in the axial plane[15]. All measurements were performed by one investigator (KvD), blinded to delivery details and clinical assessment. A test-retest series of 20 scans by a second investigator (KK) revealed moderate to good correlation for the measurements (ICC 0.45-0.80)[10].

Tomographic Ultrasound Imaging on maximum pelvic floor contraction was used to assess levator attachment to the pubic bone[9,10,17,18]. Each side was scored separately and the final unilateral score ranged from 0 (no avulsion) to 3 (complete avulsion)[9,10,17,18]. Reliability of diagnosing levator avulsion on maximum pelvic floor contraction has previously been shown to be excellent (Cohen's kappa 0.83, 95% confidence interval 0.59-1.0)[17] and to be most clinically relevant[18]. We assigned a summed total score for the left and right side (0 – 6) and these were classified as no levator avulsion (summed score of 0), minor levator avulsion (summed score of 1 – 3) or major levator avulsion (summed score of 4 – 6, or a unilateral score of 3)[9,10]. Two independent investigators (KvD and KK), blinded for delivery details, clinical assessment, each other's results and previous ultrasound results, analysed levator avulsion. Discrepancies were reviewed by a third blinded investigator (RT) to reach consensus.

Validated questionnaires were administered to assess bowel, urinary and sexual function. Anal incontinence was scored using the St. Mark's incontinence scoring system: all separate scores of frequency of faecal urgency, faecal incontinence, flatus incontinence and impact on quality of life were added up to a total score ranging between 0 and 24[19,20]. Urinary incontinence was evaluated using the International Consultation Incontinence Questionnaire Short Form (ICIQ-SF): all separate scores of frequency, amount that leaks and interference with everyday life were added up to a total score ranging between 0 and 24[21]. Vaginal symptoms and sexual matters were addressed using the International Consultation Incontinence

Questionnaire Vaginal Symptoms (ICIQ-VS) questionnaire: a separate analysis was performed for all subscales. Frequency ranged from never (score 0) to all of the time (score 4) and bothersome scores ranged from not at all (score 0) to a great deal (score 10)[22]. Higher scores indicated poorer outcomes in all three questionnaires.

Statistical analysis

Based on a review of the data, four groups were defined at one year follow-up: 1= cesarean section without levator avulsion, 2= vaginal delivery without levator avulsion, 3= healed levator avulsion, 4= persistent levator avulsion. SPSS version 20.0 was used (SPSS Inc, Chicago, IL, USA) and two-sided p-values <0.05 were considered statistically significant.

To analyse differences between groups for demographic and obstetric data, we used analysis of variance (ANOVA), applying the post-hoc least significant difference procedure for the between-group comparisons, or Kruskal-Wallis, with pair wise comparisons between groups using Mann-Whitney U tests if $p<0.05$, and Chi-square and Fisher's exact test where appropriate.

To minimise effects of missing data we used a mixed model on the prospectively gathered longitudinal data of the clinical and ultrasound assessment findings, using all available data from the three visits for the four different groups. We evaluated pattern differences over time with a linear mixed model, in which the outcome was modeled as a function of group, visit (antenatal, three months and one year postnatal) and the interaction between group and visit. An unstructured covariance matrix was used to account for the repeated measures design of the study. If the interaction between visit and group was statistically significant, the changes from visit one to two and the changes from visit two to three were compared between the groups. For cross-sectional comparisons between the four groups at one year follow-up, we used analysis of variance (ANOVA), applying the post-hoc least significant difference procedure for the between-group comparisons.

The scores on the validated questionnaires were not normally distributed and were analysed separately. Changes between visits were calculated, and Kruskal-Wallis tests were used to evaluate whether these changes were statistically significantly different between the groups. If $p<0.05$, pair wise comparisons between groups were performed using Mann-Whitney U tests. Chi-square and Fisher's exact test were used where appropriate. Kruskal-Wallis tests were also applied for the cross-sectional comparisons between the four groups at one year follow-up.

The graphs to support the results were plotted using means.

Results

269 women were recruited, of which 191 (71%) attended at three months follow-up at a median of 13 weeks postnatal (range 10 – 26 weeks). 147 (55%) women attended the one year follow-up visit (Figure 1) at a median of 52 weeks postpartum (range 46 – 72). Of these, 48% (n=70) had a spontaneous vaginal delivery, 27% (n=39) had an assisted vaginal delivery and 26% (n=38) delivered by cesarean section. 138/269 women (51%) attended both postnatal visits. Nine women attended at one year, but had missed the three months follow-up visit. None of the women had another delivery within the time-frame. 12/147 (8.2%) women were pregnant at a median of 15 weeks (range 6 – 36) at one year follow-up. Mean age of attendees was 31.2 years (SD 5.6) and mean BMI was 25.8 kg/m^2 (SD 5.7). Attendees of the one year follow-up visit were older (31.2 vs. 29.2 years, p=0.006), and delivered babies with a higher birth weight (3398 vs. 3228 grams, p=0.002).

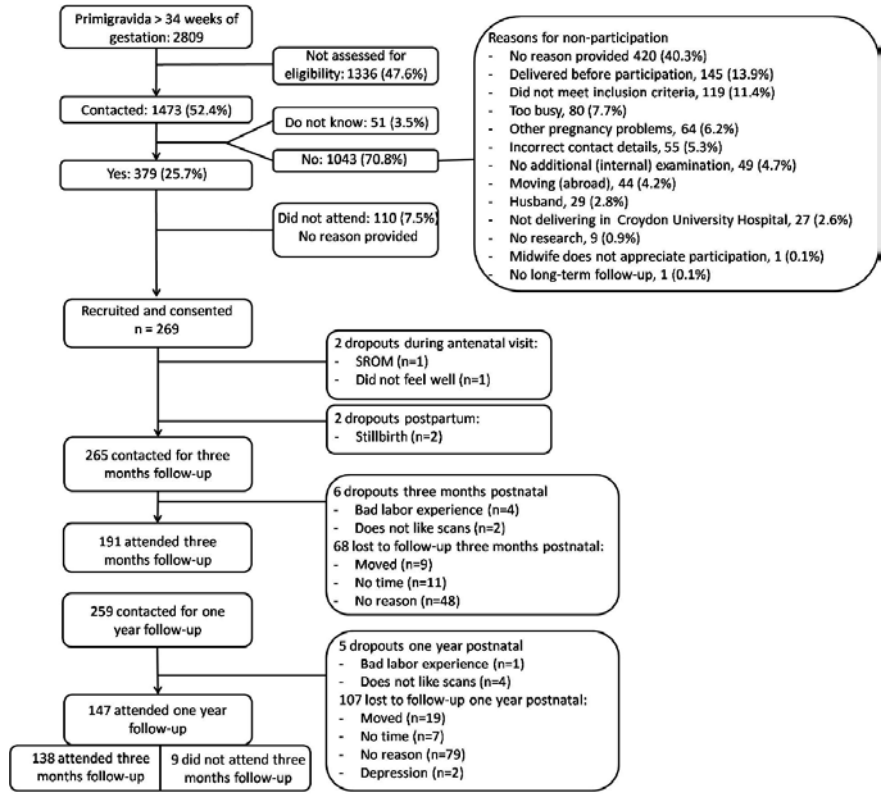
Levator avulsion

21/30 (70%) women with levator avulsion at three months follow-up, attended at one year. 13/21 (62%, 95%CI 41-79%) levator avulsions healed completely and 1/21 (5%, 95%CI 0-24%) improved from major to minor avulsion (Table 1). 6/21 women (29%) had persistent major avulsion and one woman had persistent minor avulsion at one year follow-up. One of the investigators found one new minor avulsion at one year follow up, which appeared to be an artefact when re-evaluating the ultrasound images by the independent third investigator. Of the 9 women who attended at one year follow-up and had not attended at three months, we found one major levator avulsion. The discrepant scans between three months and one year follow-up were jointly reviewed (KvD, RT, KK), but no changes had to be made to the diagnosis made three months postpartum. When comparing the antenatal and the one year postnatal ultrasound assessment, the healed levator avulsions at one year follow-up did not look as pristine as their antenatal levator appearance.

We did not find any levator avulsion following cesarean section (n=38). Following a vaginal delivery (n=109), the overall incidence of levator avulsion at one year follow-up was nine (8%, 95% CI 4.2-15.1%), minor avulsion two (2%, 95% CI 0.1-6.9%), major avulsion seven (6%, 95% CI 2.9-12.9%) (Figure 2).

Thus, women were subdivided into four groups: cesarean section (n=38), any vaginal delivery without levator avulsion (n=87), healed levator avulsion (n=13) and persistent levator avulsion (n=9). The number of patients per group were similar for all graphs: antenatal numbers were 38, 87, 13 and 9; three months postnatal numbers were 36, 83, 13 and 8; and one year follow-up numbers were 38, 87, 13 and 9 for the cesarean section group, vaginal delivery without levator avulsion group, healed levator avulsion group and persistent levator avulsion group respectively.

Figure 1 Flowchart of women who attended the one year follow-up visit



SROM = spontaneous rupture of membranes. Nine women attended the one year follow up visit, but did not attend the three months follow up visit. This flowchart is partly adapted from previous publications[9,13]

Women with persistent levator avulsion had a significantly longer active second stage of labor (p=0.030). Furthermore, these women were significantly more often delivered by forceps delivery (p<0.001), underwent more episiotomies (p=0.022) and sustained significantly more obstetric anal sphincter injuries (OASIS) (p=0.010).

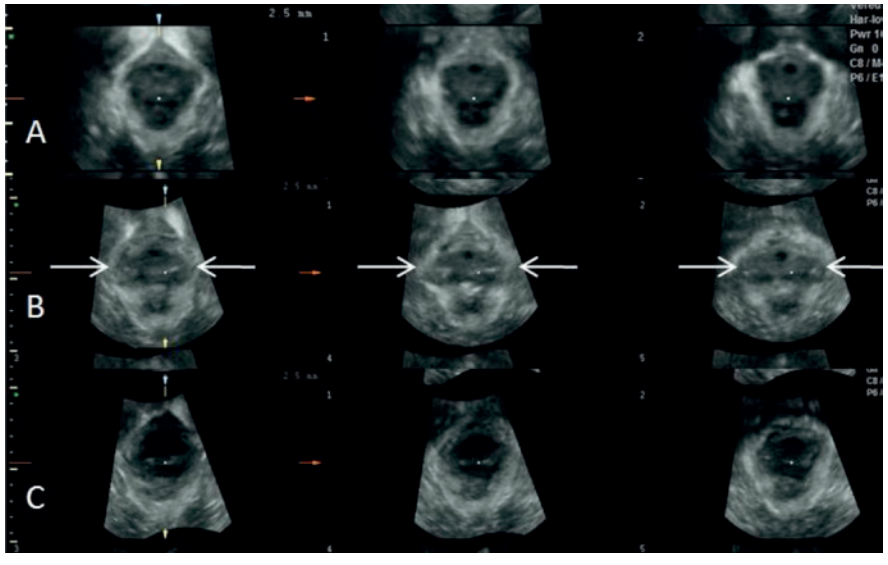
Objective assessment (Table 2)

Significant differences in PFMS patterns over time were found between the four groups (p<0.001) (Figure 3). PFMS was significantly reduced three months postnatal in women who delivered vaginally; however, an increase in PFMS was seen following cesarean section (p<0.05). PFMS continued to deteriorate significantly within the first year after delivery in women with persistent levator avulsions only, resulting in a

Table 1 Healing of levator avulsion one year following childbirth compared to three months following childbirth

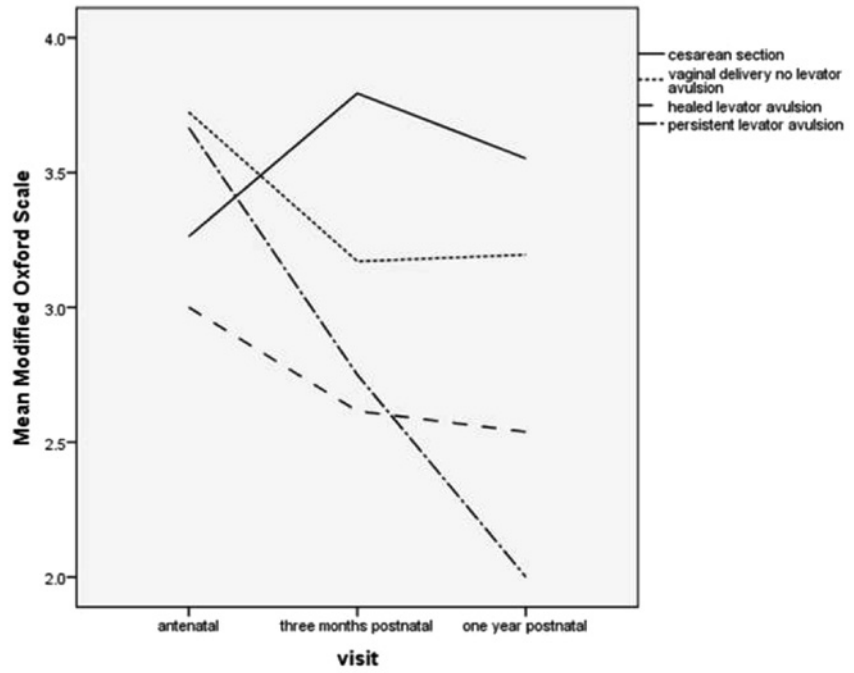
Levator avulsion (n=269)		Three months follow-up			
		No avulsion (n=161)	Minor avulsion (n=7)	Major avulsion (n=23)	Not attended (n=78)
One year follow-up	No avulsion (n=138)	117	4	9	8
	Minor avulsion (n=2)	0	1	1	0
	Major avulsion (n=7)	0	0	6	1
	Not attended (n=122)	44	2	7	69

Figure 2 Levator avulsion on transperineal ultrasound (tomographic ultrasound imaging)



A: Normal antenatal insertion of the levator muscle at maximum pelvic floor muscle contraction
B: Bilateral levator avulsion (indicated by the arrows) three months following first vaginal delivery at maximum pelvic floor muscle contraction.
C: A shot of the same woman one year following first vaginal delivery at maximum pelvic floor muscle contraction. No levator avulsion can be seen anymore

Figure 3 Longitudinal analysis of pelvic floor muscle strength: mean modified Oxford scale

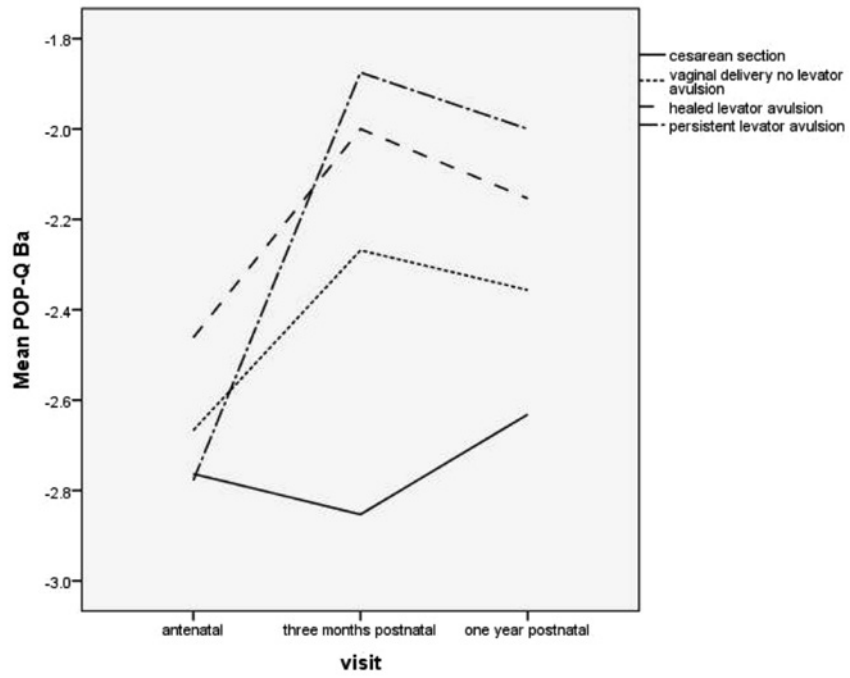


significant difference when compared to women without levator avulsions ($p<0.047$). However, no significant difference was found between women with healed and persistent levator avulsions ($p=0.09$).

The maximum POP-Q stage was 2 in all groups. Figure four shows a significant difference in anterior vaginal wall prolapse (POP-Q Ba) patterns between the four groups over time ($p=0.002$). An increase in anterior vaginal wall prolapse at three months occurred more frequently in women delivered vaginally, compared to the cesarean section group, resulting in significant differences between the four groups ($p<0.013$). No significant change was found between three months and one year postnatal. Furthermore, no significant pattern differences were found in the central and posterior compartment.

Figure five reveals a significant difference in patterns of hiatus area measurements performed on TPUS at rest, contraction and Valsalva between the four groups over time ($p<0.001$). Changes occurred within three months postnatal and were significantly worse in women with persistent levator avulsions, when compared to women without levator avulsions ($p<0.003$). However, no significant difference was

Figure 4 Longitudinal analysis of anterior vaginal wall prolapse (POP-Q Ba in centimeters)



POP-Q Ba = anterior vaginal wall prolapse

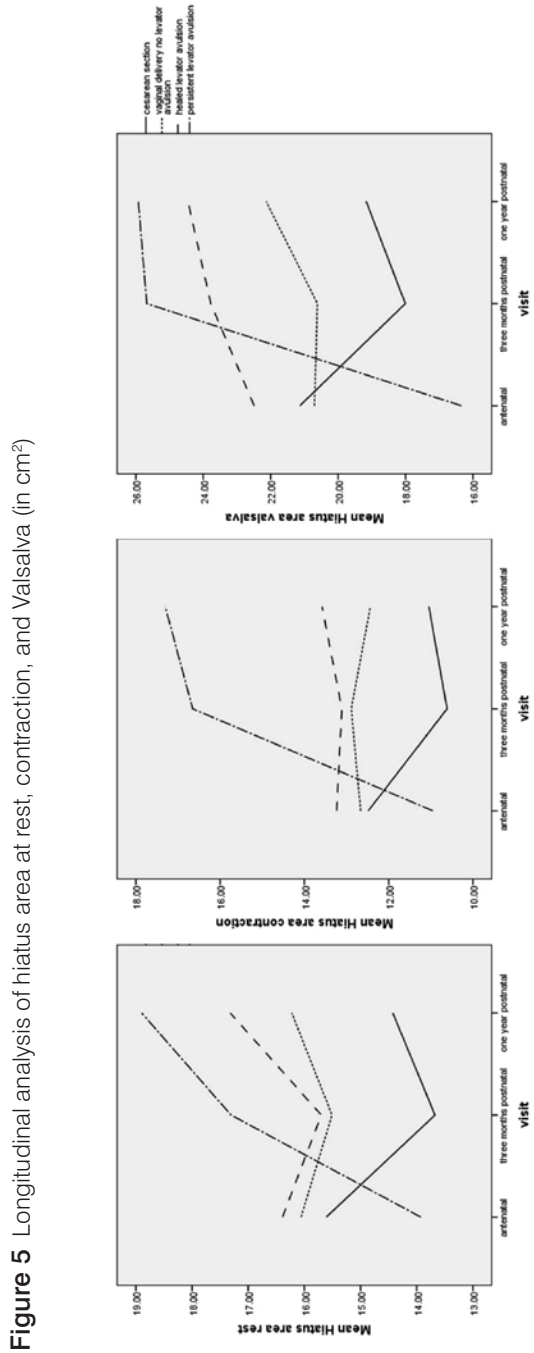
found between women with healed and persistent levator avulsions. No significant postnatal regression or deterioration of hiatus distensibility was seen in any of the groups. Patterns for hiatus antero-posterior diameter performed on TPUS at rest, contraction and Valsalva between the four groups were different over time ($p<0.003$) (Figure 6).

Subjective assessment (Table 2)

The anal incontinence patterns differed significantly between the four groups ($p<0.018$) (Figure 7). Women with persistent levator avulsions had a significant increase in anal incontinence within three months postnatal, but reverted to the antenatal values at one year.

Figure eight demonstrates significantly different patterns in total urinary incontinence score between the four groups ($p<0.050$). An initial significant decrease in urinary incontinence was seen for women delivered by cesarean section and an initial

Figure 5 Longitudinal analysis of hiatus area at rest, contraction, and Valsalva (in cm^2)



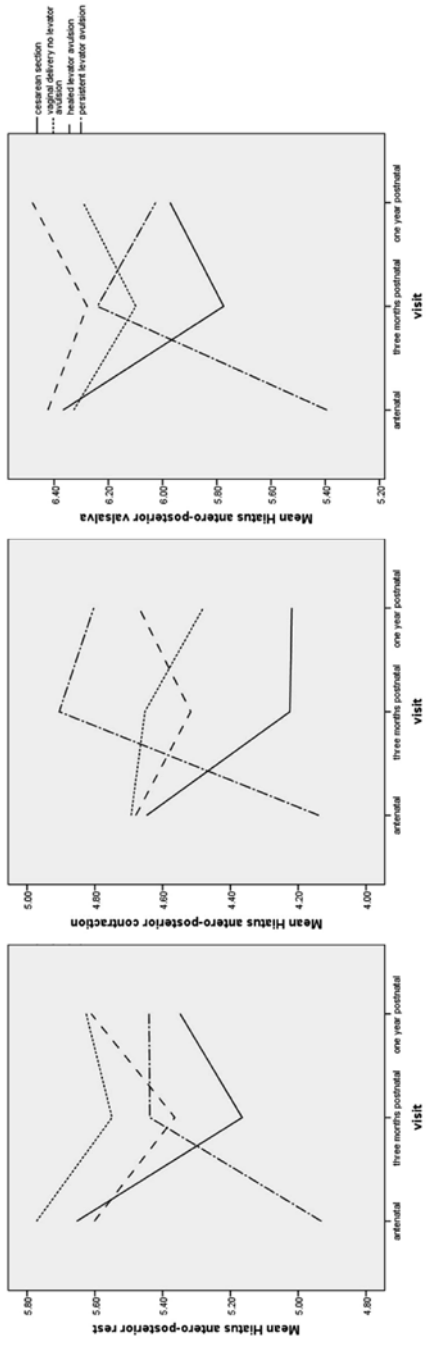
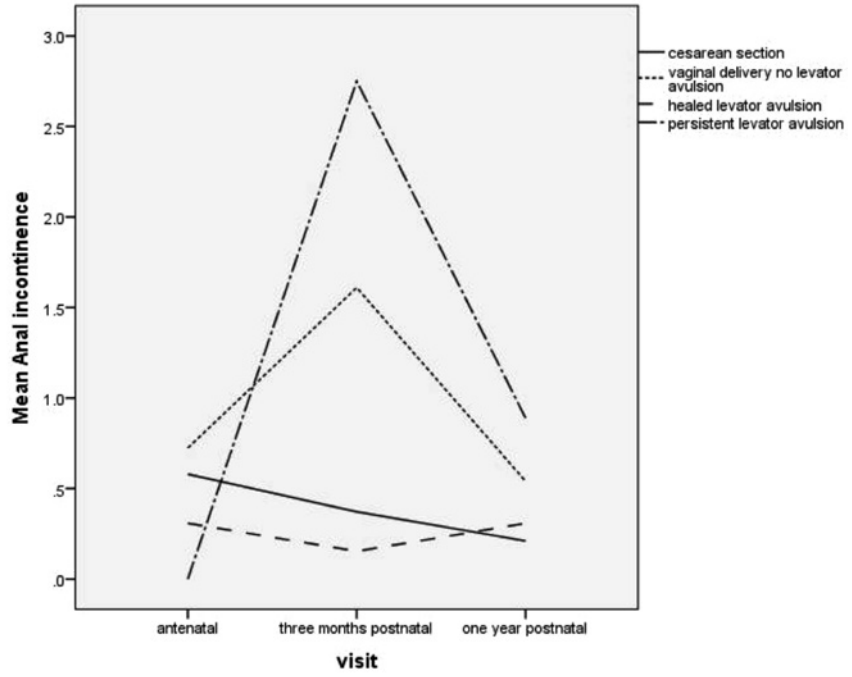


Figure 6 Longitudinal analysis of hiatus antero-posterior diameter at rest, contraction, and Valsalva (in cm)

Figure 7 Longitudinal analysis of anal incontinence using the St. Mark's incontinence score



significant increase in urinary incontinence was seen in women with persistent levator avulsions. The prevalence of daily urinary incontinence at one year follow-up was 8% for women with a cesarean section and healed levator avulsions, 3% following a vaginal delivery without levator avulsion and none of the women with persistent levator avulsion had daily urinary incontinence, revealing no significant difference between the four groups ($p=0.60$).

Women with persistent levator avulsions had significantly higher bothersome symptoms of a 'too loose vagina' three months postnatal ($p<0.002$) (Figure 9), which did not change within the first year postnatal. Although changes over time were not significant, women with persistent levator avulsions had significantly more bothersome symptoms of a sensation of a lump inside ($p<0.001$) and outside ($p<0.033$) the vagina at one year follow-up. In all groups, >75% of women had sexual intercourse in the past four weeks, without a significant difference between the four groups. A trend towards sex life being 'spoilt due to vaginal symptoms' was found for women with persistent levator avulsions ($p=0.05$). However, no significant difference was found in interference of vaginal symptoms with everyday life.

Table 2 Cross-sectional comparisons between the four groups at one year follow-up

	Cesarean section, no avulsion (n=38)	Any vaginal delivery, no avulsion (n=87)	Healed avulsion at one year (n=13)	Persistent avulsion at one year (n=9)	p value
Signs of pelvic floor dysfunction					
Modified Oxford Scale	3.6 (SD 1.4)	3.2 (SD 1.1)	2.5 (SD 1.7)	2.0 (SD 0.7)	**0.002**[C,E]
POP-Q Ba in cm	-2.6 (SD 0.5)	-2.4 (SD 0.6)	-2.2 (SD 1.0)	-2.0 (SD 0.7)	**0.027**[A,C]
Hiatus area in cm^2 (rest)	14.4 (SD 3.3)	16.2 (SD 3.1)	17.3 (SD 3.1)	18.9 (SD 5.5)	**0.001**[A,B,C,E]
Hiatus area in cm^2 (squeeze)	11.1 (SD 2.5)	12.4 (SD 2.5)	13.6 (SD 2.7)	17.3 (SD 6.1)	**<0.001**[A,B,C,E,F]
Hiatus area in cm^2 (Valsalva)	19.2 (SD 5.7)	22.1 (SD 6.5)	24.5 (SD 5.7)	25.9 (SD 8.0)	**0.006**[A,B,C]
Hiatus antero-posterior in cm (rest)	5.35 (SD 0.81)	5.63 (SD 0.77)	5.61 (SD 0.72)	5.44 (SD 0.89)	0.32
Hiatus antero-posterior in cm (squeeze)	4.22 (SD 0.73)	4.48 (SD 0.61)	46.7 (SD 0.66)	4.80 (SD 0.89)	**0.036**[A,B,C]
Hiatus antero-posterior in cm (Valsalva)	5.97 (SD 1.08)	6.29 (SD 1.03)	6.48 (SD 0.92)	6.03 (SD 0.91)	0.30
Symptoms of pelvic floor dysfunction					
Total score anal incontinence	0 (range 0, 5)	0 (range 0, 9)	0 (range 0, 2)	0 (range 0, 4)	0.27
Total score urinary incontinence	0 (range 0, 21)	0 (range 0, 15)	0 (range 0, 14)	4 (range 0, 9)	0.55
Too loose vagina – frequency	0.21 (SD 0.6)	0.28 (SD 0.5)	0.38 (SD 0.5)	0.89 (SD 0.9)	**0.032**[C,E]
Too loose vagina – bother	0.89 (SD 2.5)	0.63 (SD 1.3)	1.0 (SD 1.5)	2.78 (SD 3.2)	**0.030**[C,E]
Lump inside vagina – frequency	0.03 (SD 0.2)	0.05 (SD 0.3)	0.23 (SD 0.6)	0.56 (SD 1.0)	**<0.001**[C,D,E]
Lump inside vagina – bother	0.13 (SD 0.8)	0.13 (SD 0.9)	0.46 (SD 1.4)	1.67 (SD 3.3)	**<0.001**[C,D,E]
Lump outside vagina – frequency	0.03 (SD 0.2)	0.06 (SD 0.4)	0.15 (SD 0.6)	0.56 (SD 1.3)	**0.032**[C,E]
Lump outside vagina – bother	0.16 (SD 1.0)	0.15 (SD 1.0)	0.38 (SD 1.4)	1.33 (SD 3.3)	**0.032**[C,E]

ANOVA applying least significant difference if $p<0.05$, Kruskal Wallis applying Mann Whitney U test if $p<0.05$, and chi-square test. Continuous variables are given as means with standard deviations (SDs) or medians with ranges (range).
All P-values are two-sided. n = number; SD= standard deviation; p = p-value for statistical significance; Ba = most descended edge of anterior vaginal wall
[A, B, C, D, E] and [F] statistically significant difference, between cesarean section and vaginal delivery without levator avulsion ([A]), cesarean section and healed levator avulsion ([B]), cesarean section and persistent levator avulsion ([C]), vaginal delivery without levator avulsion and healed levator avulsion ([D]), vaginal delivery without levator avulsion and persistent levator avulsion ([E]) healed levator avulsion and persistent levator avulsion ([F]) respectively.

Figure 8 Longitudinal analysis of urinary incontinence using the ICIQ-SF

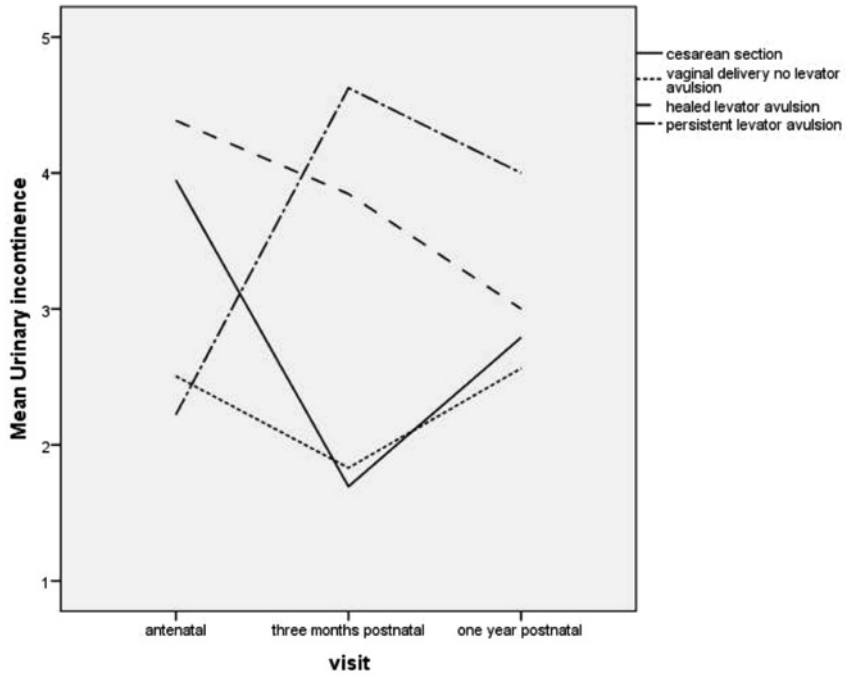
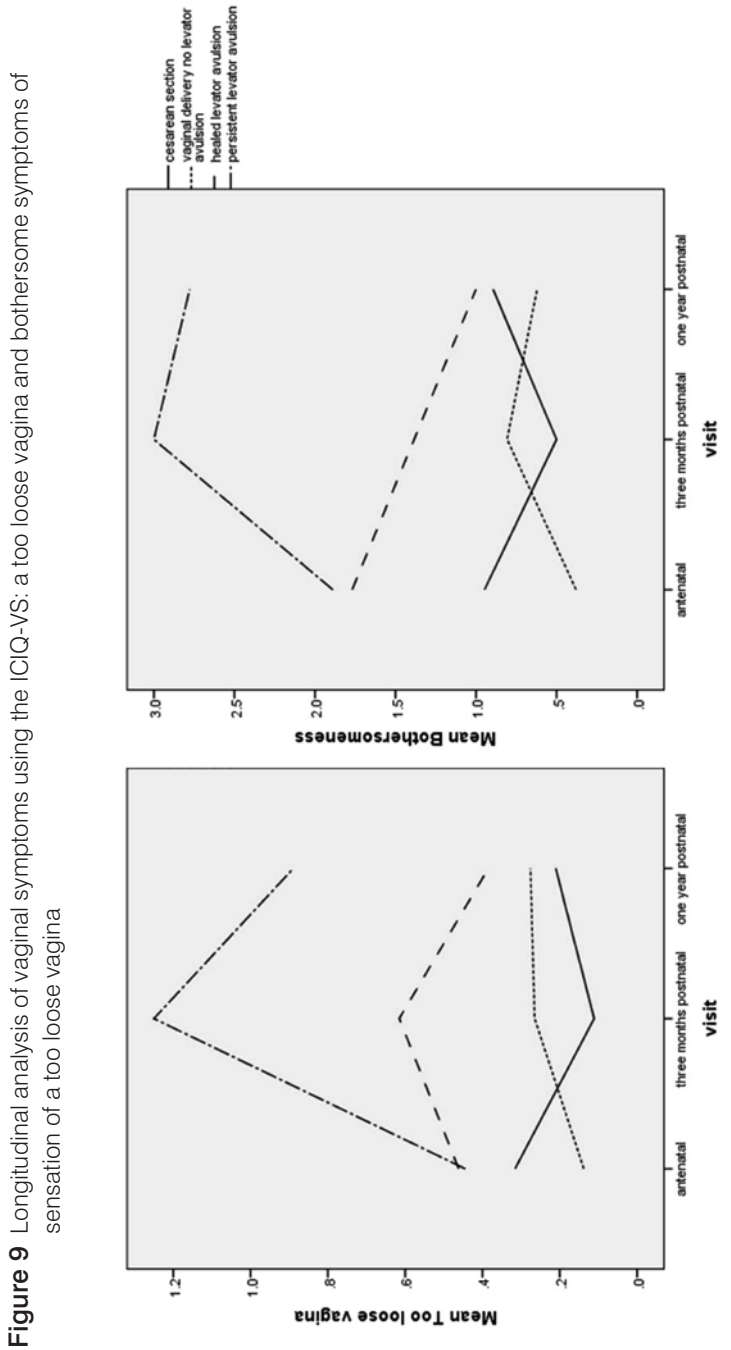


Figure 9 Longitudinal analysis of vaginal symptoms using the ICIQ-VS: a too loose vagina and bothersome symptoms of sensation of a too loose vagina



Discussion

62% of levator avulsions in primiparous women healed within one year following childbirth. Women with persistent levator avulsions showed worse patterns of reduction in PFMS, enlarged hiatus, more prolapse symptoms and deteriorated sexual matters, compared to women with healed levator avulsions. Most changes in pelvic floor dysfunction occurred between the antenatal and three months postnatal visit, emphasizing the impact of childbirth. We did not see regression or deterioration of the variables at one year compared to three months, except for a decrease in PFMS in women with persistent levator avulsions.

Healing of levator avulsion has previously been identified prospectively in 17% of avulsions 2-3 years postnatal[11]. However, Shek et al had less women with levator avulsion at the second postpartum visit (n=12, 38% vs. n=21, 70%), subsequent deliveries were included, and minor avulsions were not included[11]. Another study revealed 50% healing of less extensive avulsions using MRI six weeks and six months postnatal[12]. Risk factors for persistent levator avulsion (OASIS, forceps delivery, prolonged second stage) were similar to three months postnatal[9]. We found no evidence that younger women were more likely to recover[12]. Nerve reinnervation and levator recovery is less likely once levator avulsion has reached a certain severity[12]. In our study, most healed levator avulsions were minor avulsions. Furthermore, anatomical improvement of levator appearance on ultrasound could be scar formation[11]. Elastic fibers allow the vagina to expand during parturition and renewal of these fibers is crucial to restore pelvic organ support postpartum[23]. The time-frame for this dynamic restoration process is unknown and may explain the variation in rates of healed levator avulsion. Given the demonstration of spontaneous healing, it is questionable whether there is merit in attempting to repair acute levator avulsion at the time of delivery[24,25].

Objective assessment

PFMS deteriorated significantly in women with persistent levator avulsion only, concurring with studies showing an association between weaker PFMS and levator avulsion in prolapse patients[26,27]. Significantly more POP has been found following vaginal delivery but not following cesarean section[28], which we found for anterior vaginal wall prolapse. We could not confirm an association between levator avulsion and POP[2].

Although hiatus measurements increased in all women with levator avulsion, postnatal measurements increased more in persistent levator avulsion. Thus, pelvic floor distension is more distinct in persistent compared to healed levator avulsion. A trend was found for smaller antenatal measurements and persistent levator avulsion, suggesting that more stretch of the levator during childbirth predisposes to avulsion[29].

We confirmed that levator distensibility had not regressed in healed and persistent levator avulsion[11]. Our current findings raise further questions regarding the aetiology of POP as associations between hiatus distension at Valsalva and POP have been made[5]. PFMS reduction and increased hiatus measurements in women with healed levator avulsion, might suggest their risk of developing POP in future[3,4,5]. This could possibly explain why 'only' 36% of prolapse patients have levator avulsions[2]. However, the spontaneous course of levator avulsion and pelvic floor dysfunction in the longer term remains to be established.

Subjective assessment

Although there are contradictory associations between anal incontinence and levator avulsion[30], we found an association three months postnatal, but not at one year. This can be due to the high OASIS rate in women with persistent levator avulsion and their treatment in our dedicated perineal clinic[31]. We confirmed no postnatal increase in urinary incontinence, irrespective of mode of delivery[28]. Similarly, no association between levator avulsion and urinary incontinence was found in prolapse patients[32,33].

Women with persistent levator avulsions had significantly more bothersome vaginal symptoms ('too loose vagina', 'feeling of lump'), possibly due to an enlarged hiatus. Furthermore, these women tend to have more sexual problems, which should be addressed in gynecology clinics.

Strengths and limitations

Strengths are the longitudinal prospective design with antenatal inclusion, large sample size, and validated methods. Levator avulsion was diagnosed independently by two blinded investigators. We acknowledge the limitations as 55% attended at one year, despite great efforts. Levator avulsions were subdivided into healed and persistent, but no further subdivision was made for minor and major avulsion, as the numbers would have become too small.

In conclusion, 62% of levator avulsions healed within the first year postnatal. Women with healed and persistent levator avulsions have signs and symptoms of pelvic floor dysfunction, although worse for women with persistent levator avulsions. Longer term follow-up is planned to monitor the development of pelvic floor dysfunction and to evaluate the impact of subsequent deliveries.

References

1. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
2. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
3. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80
4. Abdool Z, Shek KL, Dietz HP. The effect of levator avulsion on hiatal dimension and function. Am J Obstet Gynecol 2009;201:89.e1-5
5. Dietz HP, Franco AVM, Shek KL, Kirby A. Avulsion injury and levator hiatal ballooning: two independent risk factors for prolapse? An observational study. Acta Obstet Gynecol Scand 2012;91:211-4
6. Dietz HP, Chantarasorn V, Shek KL. Levator avulsion is a risk factor for cystocele recurrence. Ultrasound Obstet Gynecol 2010;36:76-80
7. Weemhoff M, Vergeldt TFM, Notten K, Serroyen J, Kampschoer PHNM, Roumen FJME. Avulsion of puborectalis muscle and other risk factors for cystocele recurrence: a 2-year follow-up study. Int Urogynecol J 2012;23:65-71
8. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
9. Shek KL, Chantarasorn V, Langer S, Dietz HP. Does levator trauma 'heal'? Ultrasound Obstet Gynecol 2012;40:570-5
10. van Delft KWM, Thakar R, Sultan AH, Schwertner-Tiepelmann N, Kluivers KB. Levator ani muscle avulsion during childbirth: a risk prediction model. Accepted for publication in BJOG
11. van Delft KWM, Sultan AH, Thakar R, Schwertner-Tiepelmann N, Kluivers KB. The relationship between postpartum levator ani muscle avulsion and signs and symptoms of pelvic floor dysfunction. Accepted for publication in BJOG
12. Branham V, Thomas J, Jaffe T, Crockett M, South M, Jamison M, Weidner A. Levator ani abnormality 6 weeks after delivery persists at 6 months. Am J Obstet Gynecol 2007;197:65.e1-6
13. van Delft KWM, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Recruitment of pregnant women in research: Experience from a prospective study. J Obstet Gynaecol 2013;33:442-6
14. Laycock J. Clinical evaluation of the pelvic floor. In Pelvic floor re-education, Principles and practice, Schüssler B, Laycock J, Norton PA, Stanton SL, eds. Springer-Verlag: London, 1994; 42–48
15. van Delft K, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
16. Hall AF, Theofrastous JP, Cundiff GW, Harris RL, Hamilton LF, Swift SE, et al. Interobserver and intraobserver reliability of the proposed International Continence Society, Society of Gynecologic Surgeons, and American Urogynecologic Society pelvic organ prolapse classification system. Am J Obstet Gynecol 1996;175:1467-70
17. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30.
18. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
19. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. Gut 1999;44:77-80
20. Roos AM, Sultan AH, Thakar R. St. Mark's incontinence score for assessment of anal incontinence following obstetric anal sphincter injuries (OASIS). Int Urogynecol J Pelvic Floor Dysfunct 2009;20:407-10
21. Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. Neurourol Urodyn 2004;23:322-30
22. Price N, Jackson SR, Avery K, Brookes ST, Abrams P. Development and psychometric evaluation of the ICIQ Vaginal Symptoms Questionnaire: the ICIQ-VS. BJOG 2006;113:700-12

23. Drewes PG, Yanagisawa H, Starcher B, Hornstra I, Csiszar K, Marinis SI, et al. Pelvic organ prolapse in fibulin-5 knockout mice: pregnancy-induced changes in elastic fiber homeostasis in mouse vagina. Am J Pathol 2007;170:578-89
24. Dietz HP, Gillespie AV, Phadke P. Avulsion of the pubovisceral muscle associated with large vaginal tear after normal vaginal delivery at term. Aust N Z J Obstet Gynaecol 2007;47:341-4
25. van Delft K, Thakar R, Shobeiri SA, Sultan AH. Levator haematoma at the attachment zone as an early marker for levator ani muscle avulsion. Ultrasound Obstet Gynecol 2013. doi: 10.1002/uog.12571.
26. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-636
27. Steensma AB, Konstantinovic ML, Burger CW, de Ridder D, Timmerman D, Deprest J. Prevalence of major levator abnormalities in symptomatic patients with an underactive pelvic floor contraction. Int Urogynecol J 2010;21:861-7
28. Elenskaia K, Thakar R, Sultan AH, Scheer I, Onwude J. Effect of childbirth on pelvic organ support and quality of life: a longitudinal cohort study. Int Urogynecol J 2013;24:927-37
29. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
30. Lammers K, Fütterer JJ, Prokop M, Vierhout ME, Kluivers KB. Diagnosing pubovisceral avulsions: a systematic review of the clinical relevance of a prevalent anatomical defect. Int Urogynecol J 2012;23:1653-64
31. Thakar R, Sultan AH (2007). Postpartum problems and the role of a perineal clinic. In: Sultan AH, Thakar R, Fenner DE (eds). Perineal and anal sphincter trauma. Springer, London, pp 65–79
32. Dietz HP, Kirby A, Shek LK, Bedwell PJ. Does avulsion of the puborectalis muscle affect bladder function? Int Urogynecol J 2009;20:967-72
33. Morgan DM, Cardoza P, Guire K, Fenner DE, DeLancey JOL. Levator ani defect status and lower urinary tract symptoms in women with pelvic organ prolapse. Int Urogynecol J 2010;21:47-52

10

General discussion

General discussion

The main focus of this thesis was the description of the results of a prospective longitudinal cohort study focusing on the impact of childbirth on the levator ani muscle (LAM) and the relation to signs and symptoms of pelvic floor dysfunction (PFD). Furthermore, this thesis evaluated three different assessment techniques of the LAM, all of which can be easily used in outpatient settings.

The general discussion highlights and discusses the main results, with implications to daily clinical practice and recommendations for future research.

To provide insight into the trials and tribulations of recruiting pregnant women for this longitudinal study, we identified factors that influenced recruitment (Chapter 2). Four out of five women declined to participate in the study, with 40% providing no reason for their decision not to participate. We found that women should be screened for eligibility prior to definite enrolment and flexible appointment times should be available to accommodate preferences of busy women. Furthermore, involvement of an Asian woman's husband is relevant as they tend to involve them in their decision making, and the researcher should be gentle and explain possible benefits for the participant. Previous studies have shown the importance of consistent staff[1] and possible adverse effects when intrusive procedures are involved[2], both applicable to our study. Furthermore, as this research project was carried out in urban London where many different ethnicities live together, the approached women often had a different ethnicity than the dedicated research fellow[3], posing challenges on the recruitment process. However, after 17 months the recruitment process was completed.

Assessment of levator ani muscle avulsion

Different techniques have been described to assess the LAM and to diagnose LAM avulsion. The simplest of these techniques is palpation with the examining finger. The imaging techniques are magnetic resonance imaging (MRI), transperineal ultrasound (TPUS), and endovaginal ultrasound (EVUS).

Clinical assessment

Inter-rater reliability analysis of pelvic floor muscle strength (PFMS) and palpation of LAM avulsion have been described in Chapter 3. PFMS was assessed by vaginal palpation using the index finger, and scored on the 6-point modified Oxford scale, ranging from no contraction to strong muscle contraction[4]. Inter-rater reliability analysis in 25 nulliparous women revealed substantial agreement (Kappa 0.66) between two investigators, which is higher than results from previous studies[5,6].

Vaginal palpation to diagnose LAM avulsion has previously been described[7,8]. Inter-rater studies have revealed acceptable reliability, albeit with a substantial

learning curve[7,8]. As this palpation technique has not been standardised, we implemented a new grading system to assess LAM attachment, using a four-point scale ranging from intact muscle to not intact muscle. Excellent inter-rater reliability was found in nulliparous women (Kappa 0.90), suggesting that this technique can be readily learned and reliably incorporated into clinical practice and research after appropriate training. However, ideally this inter-rater reliability analysis needs to be repeated in parous women.

Previous research has shown that the presence of LAM avulsion is associated with a significant reduction in PFMS, including differences between the left and right side of the LAM, due to avulsion[9]. However, we found side differences in PFMS in 16% of women with intact LAM on TPUS, suggesting that side differences in PFMS do not necessarily correlate with LAM avulsion. Using our classification system, up to 20% of nulliparous women would have been scored as having some form of LAM avulsion. This indicates the natural variation of muscle insertion, as no LAM avulsion was diagnosed on TPUS. On the other hand, this could possibly suggest that palpation is futile, as none of these nulliparous women had LAM avulsion on TPUS.

The findings on palpation directed us to evaluate imaging techniques to assess the LAM to prevent possible false-positive findings.

Imaging techniques

Over a decade ago, MRI was firstly used to image the LAM. Cadaveric studies demonstrated the correlation between detailed LAM anatomy seen on MRI and fresh cadavers[10]. This imaging technique was thereafter perceived to be the gold standard, as it was the only available technique. Lammers et al have shown good inter-rater reliability for hiatus measurements and diagnosis of LAM avulsion[11]. Further studies have shown the association between LAM avulsion seen on MRI and pelvic organ prolapse (POP)[12]. The capability of MRI to distinguish between different tissues is still superior to other imaging techniques, but possibly with limited clinical relevance[13]. Disadvantages such as costs and limited availability can be overcome with pelvic floor ultrasound. Currently, TPUS and EVUS are accessible, easy to use in outpatient settings, and at lower costs. Both ultrasound techniques have the ability of manipulating acquired images using post-processing software.

3D/4D TPUS is the most frequently used technique to image the LAM. Inter-rater studies have revealed good correlation for hiatus measurements and diagnosis of LAM avulsion[14,15]. TPUS has the possibility of dynamic studies: maximum contraction for LAM avulsion[14,16] and maximum Valsalva for enlarged hiatus[17], which are both associated with signs and symptoms of POP[17,18].

3D EVUS is an upcoming technique, which has been authenticated in cadaveric sections, unlike TPUS. Although EVUS can be perceived as intrusive, it has the advantage of placement of the high frequency probe directly next to the tissue of

interest negating the need for contraction while providing very detailed information on pelvic floor structures[19,20]. The first reliability studies on hiatus measurements in nulliparous women revealed good results[21,22]. Chapter 4 describes reliability analysis of hiatus measurements and diagnosis of LAM avulsion using EVUS in nulliparous and primiparous women. Intraclass correlation coefficients on intra- and inter-rater analysis respectively were: hiatus area 0.95 and 0.86-0.88, hiatus transverse diameter 0.90 and 0.16-0.74, and hiatus antero-posterior diameter 0.91 and 0.73-0.80. Both intra- and inter-rater analysis revealed acceptable limits of agreement for hiatus measurements. The correlation of specific LAM avulsion was excellent on intra- and inter-rater analysis. Our findings suggest that EVUS is a reliable tool in the assessment of hiatus measurements and LAM avulsion in nulliparous and primiparous women. We would therefore encourage its use in research studies involving childbirth and evaluation of this technique in women with recurrent prolapse. Recent research has confirmed the relationship between LAM avulsion diagnosed on EVUS and POP[23]. Furthermore, a significant decrease in hiatus measurements was found 12 months following POP surgery[24]. However, more studies would be welcome to enhance the clinical validation of the technique.

Comparison of assessment techniques

Due to the dramatic upsurge in imaging modalities in recent years, it is important to standardise assessment techniques to enable evaluation and comparison of techniques. Furthermore, comparative studies, preferably in the same cohort of women, will gain more insight in the ultrasound techniques, and might help us in future to determine a gold standard. Some comparisons have been made between MRI and TPUS revealing moderate to good correlation for hiatus measurements[25,26,27] and diagnosis of LAM avulsion[27].

Chapter 5 describes the comparison of hiatus measurements and diagnosis of LAM avulsion between TPUS and EVUS in the same group of nulliparous and primiparous women. The intraclass correlation coefficient when comparing TPUS and EVUS was 0.76-0.79 for hiatus area, 0.51-0.59 for the transverse diameter, and 0.70-0.72 for the antero-posterior diameter. Although acceptable limits of agreement were observed for the hiatus measurements, EVUS measurements were generally smaller. These differences could possibly be related to TPUS measurements being taken in the rendered image and EVUS measurements in a non-rendered image. We have to bear this in mind when comparing images or when suggesting cut-off points. Similar correlation results were found for nulliparous and primiparous women, in spite of primiparous women having sustained LAM avulsion during childbirth. Nonetheless, it is of utmost importance to acquire an image with all landmarks visible. Overall agreement between both ultrasound techniques in diagnosing LAM avulsion was 95%, revealing an intraclass correlation coefficient of 0.72 (good correlation). Our

findings imply that TPUS and EVUS can be used interchangeably to analyse hiatus measurements and to diagnose LAM avulsion.

Both ultrasound techniques can be used in outpatient settings by a clinician. However, the simplest way to diagnose LAM avulsion would be with the finger. As the inter-rater reliability was excellent in nulliparous women, we continued to perform this assessment. This enabled us to determine agreement of digital assessment with TPUS and EVUS (Chapter 5). Palpation had a high specificity (99%) and a low sensitivity (26-28%) when compared to both ultrasound techniques. These findings confirm previous studies comparing palpation with MRI[7] and TPUS[8]. Similar to their conclusions, we concluded that palpation is not a good screening tool as it underestimates true LAM avulsion. Therefore palpation cannot substitute ultrasound, because many positive findings are actually false positives. However, when the test result is negative, LAM is very likely to be intact and palpation might therefore be helpful in excluding LAM avulsion.

Recommendations in diagnosing LAM avulsion

As palpation underestimates true LAM avulsion, it is not a good screening tool and therefore cannot substitute ultrasound. Both ultrasound techniques are easy to use in outpatient settings and correlate well. Therefore, TPUS and EVUS can be used interchangeably to perform hiatus measurements and to diagnose LAM avulsion. Which technique will be used depends upon the preferences of the clinician. For example, if very detailed information of pelvic floor structures is desirable, we would recommend using EVUS. However, if the aim is to assess ballooning, which is associated with POP and LAM avulsion[17], it would be better to use TPUS as dynamic studies are not possible with EVUS.

The second part of this discussion will explore the relation between LAM avulsion and childbirth in depth and will thereby illustrate the characteristics of each assessment technique.

The levator ani muscle and childbirth

Levator ani muscle avulsion

Previous studies with different sample sizes have found a 13-36% incidence of LAM avulsion following the first vaginal delivery[28]. To establish the incidence of LAM avulsion, we studied primigravid women in our prospective longitudinal cohort study (Chapter 7). As hypothesised, we found that none of these primigravid women had LAM avulsion prior to the first delivery. Women were subsequently seen at three postnatal time points: early postpartum (within four days), three months postpartum and one year postpartum. This enabled us to describe the patterns of LAM avulsion seen at the different time points, and their evaluation over time.

To assess the LAM early postpartum, we used high frequency EVUS to provide very detailed information on pelvic floor structures (Chapter 6). Moreover, images acquired at rest are more applicable soon after delivery, as we could not expect these women to perform a proper pelvic floor contraction, which is the recommended method of diagnosing LAM avulsion on TPUS[14]. Almost half of the women seen early postpartum declined EVUS because of pain and discomfort, implying that EVUS will not be suitable for routine screening early postpartum. Twenty-four percent of women were found to have well delineated, hypoechoic areas consistent with haematomas in the LAM. All except one (an emergency caesarean section) had delivered vaginally. There was 100% agreement in diagnosing haematomas. All haematomas away from the LAM attachment zone to the pubic bone resolved, including the woman delivered by emergency caesarean section. All haematomas at the attachment zone manifested as LAM avulsions three months postnatal. However, only 2/3 of LAM avulsions seen three months postnatal were preceded by a formation of a haematoma at the area of torn muscle fibres early postpartum. In the other cases, evidence of LAM avulsion was seen early postpartum without the formation of a haematoma. We hypothesised that when muscle is torn away from the tendinous attachment, a haematoma is formed[29]. However, when the tendon or pubovisceral enthesis is avulsed from the pubic bone no haematoma is formed due to the avascular nature of the trauma[29]. The incidence of haematomas early postpartum is much higher than the incidence of LAM avulsion three months postpartum in our study. It therefore appears that early postpartum ultrasound may previously have resulted in over diagnosis of LAM avulsion[30,31] as haematomas away from the attachment zone can masquerade as LAM avulsions to the unwary.

Palpation of LAM avulsion in the postnatal ward was not a good screening tool, especially because these women were not able to contract their pelvic floor muscles properly. Besides, as most women do not have a vaginal tear adjacent to the LAM[32], exploration of sonographic LAM avulsion immediately postpartum would require an incision in the vagina, resulting in more bleeding and scarring. Therefore, the subsequent management of LAM avulsion in the acute stage remains to be

established. Furthermore, until repair of these avulsions becomes feasible, early postpartum imaging will remain largely a research tool.

We incorporated a visit three months postpartum using TPUS at maximum pelvic floor contraction, to establish the incidence of LAM avulsion (Chapter 7). A power calculation revealed an intended sample size of 265 women, including a 30% drop-out rate. A number of 191 women were seen before and after childbirth, and therefore our data on the incidence of LAM avulsion are expected to be reliable. 25% of women were delivered by a caesarean section, and as hypothesised we did not find any LAM avulsion following caesarean section. Therefore the incidence of LAM avulsion following vaginal delivery was 21% (95%CI 15.1-28.4%). Minor and major LAM avulsion were diagnosed in 4.9% (n=7) and 16.1% (n=23) respectively. Our results are in keeping, and add credence to other recent studies revealing a 13-22% incidence a few months postnatal[28].

Very little research has been carried out on LAM avulsion longer after childbirth. Chapter 9 outlines the one year follow-up of the same cohort to establish the natural history of LAM avulsion within one year following childbirth. 147 (55%) women attended one year postnatal. 13/21 (62%) women with LAM avulsion diagnosed three months postnatal had healed completely at one year follow-up. Therefore, persistent LAM avulsion was seen in 9/109 (8%) women one year following a vaginal delivery. The percentage of women with healed LAM avulsion was much lower in two other studies[33,34], which could be due to differences in the used imaging techniques and timing of follow-up.

Hypothesis on the healing of levator ani muscle avulsion

As previously evidenced, the pubococcygeus part of the LAM has to undergo most stretching during childbirth[35]. Although pubococcygeus avulsion with or without haematoma formation seems to be the most catastrophic form of pelvic floor muscle trauma, visualisation of haematomas throughout LAM subdivisions points at global trauma to the whole LAM. Mice studies about POP and pelvic organ support have shown the body's ability to heal itself in certain individuals and circumstances[36]. Elastic fibers are needed to allow the vagina to expand during parturition and renewal of these fibers is crucial to restore pelvic organ support postpartum[36]. Currently, it is uncertain whether elastic fibers represent connective tissue or muscle fibers and what their appearance on ultrasound would be. Furthermore, it is uncertain which time-frame is applicable to this dynamic restoring process of the pelvic floor. On the other hand, healing of LAM avulsion seen on ultrasound one year postnatal could be due to scar formation between the pubic bone and the LAM[34]. Recovery and nerve reinnervation are thought to be unlikely once LAM avulsion has reached a certain severity[33]. We can confirm this hypothesis as most healed levator avulsions were minor avulsions at three

months in our cohort. Nevertheless, it can well be hypothesised that any LAM trauma seen at any time point following childbirth, although appeared to be healed later, may put a woman at risk of developing POP. This hypothesis could then explain why 'only' 36% of women with POP have LAM avulsion[18]. However, the further spontaneous course of levator avulsion remains to be established.

Risk factors for levator ani muscle avulsion

Risk factors for LAM avulsion were evaluated using the number of LAM avulsions diagnosed three months postpartum (Chapter 7). In this sample, the three most relevant risk factors were obstetric anal sphincter injuries (OASIS), prolonged active second stage of labour and forceps delivery. These risk factors have been found by others in previous studies[37,38,39,40], and have been confirmed in our analysis of persistent LAM avulsion one year following childbirth. Similar to others, we were not able to develop a prediction model based on antenatal risk factors[41]. However, by combining the three identified risk factors, we developed a nomogram to estimate an individual woman's risk on having sustained LAM avulsion during childbirth. In presence of all three risk factors, the individual woman has a 75% chance of having sustained LAM avulsion. Our nomogram can be used during labour to optimise management in the delivery suite by reducing the length of active second stage and the need for forceps deliveries. The royal green-top guideline (Royal College of Obstetricians and Gynaecologists) on operative vaginal delivery provides level one evidence on such a strategy including continuous support in labour, upright position, minimised use of epidural analgesia and to start oxytocin in the second stage of labour[42]. Furthermore, hands-on training in choice and technique of vacuum extraction will enhance the risk of success of vacuum extraction and minimise the use of forceps[42]. Although prolonged active second stage and forceps delivery are proxy markers for feto-maternal disproportion and obstruction, we acknowledge that it is not clear whether the proposed measures will reduce the rate of LAM avulsion.

Levator ani muscle avulsion and pelvic floor dysfunction

To assess the clinical relevance of having sustained LAM avulsion during childbirth, we incorporated validated methods to perform an objective and subjective assessment of PFD in our cohort of women (Chapter 8,9).

PFMS was significantly reduced in women with LAM avulsion, and PFMS deteriorated further in women with persistent LAM avulsion at one year follow-up. Previous studies in prolapse patients have also revealed a reduced PFMS in women with LAM avulsion[43,44]. Increased POP stage was found in women with LAM avulsion three months postnatal. However, at one year follow-up, women with healed or persistent LAM avulsion did not have more POP than women with a vaginal delivery without LAM avulsion. The maximum POP-Q stage was two.

Hiatus measurements at contraction and valsalva increased postnatal, probably due to the ease of muscle stretch following delivery. Significantly larger hiatus area measurements were found in women with LAM avulsion three months postpartum. Hiatus area measurements were largest in women with persistent LAM avulsion at one year follow-up. In all groups, LAM distensibility did not regress at one year follow-up confirming the results of a previous study[34]. Women with a smaller antenatal antero-posterior diameter at rest on TPUS were at greater risk of sustaining (persistent) LAM avulsion. This supports the hypothesis that extensive stretching of the LAM during childbirth to allow passage of the fetus predisposes to LAM avulsion[35].

The reduction in PFMS and the changes on ultrasound assessment seen in women with healed and persistent LAM avulsion, might suggest that both groups are at risk of developing POP in future[17,45]. This strengthens our hypothesis why 'only' 36% of women with prolapse have LAM avulsions[18].

Heilbrun et al[46] found an association between faecal incontinence and LAM avulsion three months postnatal. In our study, a temporarily increase in faecal incontinence was seen for women with persistent LAM avulsion, which improved within the first year following childbirth. We hypothesised that this pattern was seen because of the large number of women with persistent LAM avulsion that sustained OASIS during childbirth. As part of routine practice in our hospital, women with OASIS were seen in a dedicated perineal clinic, from which conservative management was started in presence of faecal incontinence[47].

Three months postnatal, women with LAM avulsion had significantly more urinary incontinence, which was mainly stress urinary incontinence, although no significant difference between groups was found one year following childbirth. Furthermore, no association between urinary incontinence and LAM avulsion has been found in studies with prolapse patients[48,49].

Women with LAM avulsion had more vaginal symptoms three months postnatal, such as 'reduced vaginal sensation' and 'too loose vagina'. Women with LAM avulsion were less likely to resume sexual intercourse within three months postpartum. This is most likely not an independent factor as women with LAM avulsion sustained more severe perineal trauma which could explain their delayed resumption of sexual intercourse[50]. One year postnatal, over 75% of all women had had sexual intercourse in the previous four weeks. However, the sex life of women with persistent LAM avulsion was affected by their vaginal symptoms (too loose vagina and feeling of a lump inside and/or outside the vagina), but women with healed LAM avulsion were not affected. At all time-points the vaginal symptoms in women with (persistent) LAM avulsion correlated with the enlarged hiatus found on TPUS.

The implementation of pelvic floor muscle training during and after pregnancy to prevent PFD has previously been suggested[51]. As illustrated we found that women

with LAM avulsion had a significant increase in signs and symptoms of PFD. However, signs and symptoms of PFD were more distinct in women with persistent LAM avulsion at one year follow-up. This development is expected to continue in the long term. Our nomogram presented in Chapter 7 can be used in a clinical setting to target postnatal women at risk of having sustained LAM avulsion. As these women already have PFD in the short term and are at risk of developing POP in the long term[18], they can be offered pelvic floor imaging to confirm or exclude the diagnosis of LAM avulsion. It has been shown that supervised pelvic floor muscle training increases PFMS in women with POP[52,53]. Although no randomized controlled trials for pelvic floor muscle exercises are available in relation to LAM avulsion and childbirth, it can be expected that women with healed and persistent LAM avulsion benefit from pelvic floor muscle exercises to reduce their signs as well as their symptoms of PFD. Therefore, women with LAM avulsion could be advised to initiate intensive lifestyle modification and pelvic floor education to increase PFMS. We speculate that pelvic floor muscle training might prevent or at least delay the onset of symptomatic POP and other forms of PFD.

Strengths and limitations

Our prospective longitudinal cohort study was carried out following a sample size calculation to establish the incidence of LAM avulsion. The sample size was reached and thus sufficiently large to draw our conclusions. Standardised protocols to acquire and analyse the ultrasounds were used throughout the entire study. For each ultrasound technique, LAM avulsion was analysed by two independent investigators and consensus was reached by a third investigator, all blinded for delivery details, clinical examination and each other's findings on ultrasound. This implies that there was certainty about the diagnosis made. Large numbers, including women following childbirth in which LAM avulsion and subsequent distortions of the landmarks could be expected, were used for the reliability analyses. Reliability was assessed using the intra class correlation coefficient and limits of agreement, to control for close agreement between measurements rather than correlation only[54]. Besides MRI and TPUS, EVUS has now become a well described technique to reliably analyse the LAM. Validated methods were used to perform an objective and subjective assessment of PFD in relation to LAM avulsion following childbirth. Despite great efforts, the one year follow-up rate was lower than the three months follow-up rate, due to a variety of reasons, such as moved houses or no time. However, almost 3 out of 4 women did not provide a reason for her non-attendance. Limitations of the reliability studies and the studies on the validated assessment methods were the relatively low incidence of LAM avulsion, and short term POP and pelvic floor dysfunction, as this study was carried out in a cohort of low risk postnatal women.

Conclusions

- Women from different ethnicities and age groups gave a wide variety of reasons for non-participation in a longitudinal study in pregnancy, however 40% gave no reason for non-participation (Chapter 2).
- Assessments of pelvic floor muscle strength and levator ani muscle attachment to the pubic bone are reproducible in nulliparous women (Chapter 3).
- 3D endovaginal ultrasound is a reproducible tool in the assessment of hiatus measurements and levator ani muscle avulsion in parous women (Chapter 4).
- Transperineal and endovaginal ultrasound can be used interchangeably to analyse hiatus measurements and to diagnose levator ani muscle avulsion (Chapter 5).
- Digital palpation underestimates true levator ani muscle avulsion and therefore cannot substitute ultrasound (Chapter 5, 6).
- Two out of three levator ani muscle avulsions three months postnatal are preceded by a haematoma at the site of attachment to the pubic bone seen on ultrasound within hours following childbirth (Chapter 6).
- The true incidence of levator ani muscle avulsion following first vaginal delivery is 21% when assessed three months postnatal (Chapter 7)
- Sixty-two percent of levator ani muscle avulsions heal within one year following childbirth (Chapter 9).
- Risk factors for levator ani muscle avulsion are obstetric anal sphincter injuries, prolonged active second stage of labour and forceps delivery (Chapter 7,9).
- Healed, and more so persistent LAM avulsion are associated with signs and symptoms of pelvic floor dysfunction one year postnatal (Chapter 8,9).

Topics for future research

An increase in studies using endovaginal ultrasound in women with levator ani muscle avulsion could enhance the clinical validation of the technique. Furthermore, this technique has not been compared to magnetic resonance imaging.

The use of MRI can be considered to further evaluate and gain more detailed insight in the understanding of healing of levator ani muscle avulsion following childbirth.

Further evaluation is needed to see whether a smaller antenatal hiatus ante-ro-posterior diameter as seen on transperineal ultrasound could be a predictor of levator ani muscle avulsion.

Longer term follow-up would enable us to follow the development of pelvic floor dysfunction. Furthermore, the influence of subsequent deliveries in women with levator ani muscle avulsion has not been determined. Both aspects will be addressed in a three year follow-up study of the same cohort.

The proposed risk model to estimate a woman's individual risk of having sustained levator ani muscle avulsion has been validated internally, but not externally in a different population. This risk model can also help researchers to select a group of women at high risk of levator ani muscle avulsion, to be able to study larger numbers of women with levator ani muscle avulsion.

References

1. Zielinski R, Ackerson K, Misiunas RB, Miller JM. Feasibility of a longitudinal study of women anticipating first pregnancy and assessed by multiple pelvic exams: recruitment and retention challenges. Contemp Clin Trials 2010;31:544-8
2. Hilden M, Sidenius K, Sidenius K, Langhoff-Roos J, Wijma B, Schei B. Women's experiences of the gynecologic examination: factors associated with discomfort. Acta Obstet Gynecol Scand 2003;82:1030-6
3. Gilliss CL, Lee KA, Gutierrez Y, Taylor DT, Beyene Y, Neuhaus J, et al. Recruitment and retention of healthy minority women into community-based longitudinal research. J Womens Health Gend Based Med 2001;10:77-85
4. Laycock J. Clinical evaluation of the pelvic floor. In Pelvic floor re-education, Principles and practice, Schüssler B, Laycock J, Norton PA, Stanton SL, eds. Springer-Verlag: London, 1994;42-8
5. Bø K, Finckenhagen HB. Vaginal palpation of pelvic floor muscle strength: inter-test reproducibility and comparison between palpation and vaginal squeeze pressure. Acta Obstet Gynecol Scand 2001;80:883-7
6. Ferreira CH, Barbosa PB, de Oliveira Souza F, Antônio FI, Franco MM, Bø K. Inter-rater reliability study of the modified Oxford Grading Scale and the Peritron manometer. Physiotherapy 2011;97:132-8
7. Kearney R, Miller JM, DeLancey JO. Interrater reliability and physical examination of the pubovisceral portion of the levator ani muscle, validity comparisons using MR imaging. Neurourol Urodyn 2006;25:50-4
8. Dietz HP, Shek C. Validity and reproducibility of the digital detection of levator trauma. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:1097-101
9. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-6
10. Strohbehn K, Ellis JH, Strohbehn JA, DeLancey JO. Magnetic resonance imaging of the levator ani with anatomic correlation. Obstet Gynecol 1996;87:277-85
11. Lammers K, Kluivers KB, Vierhout ME, Prokop M, Fütterer JJ. Inter- and intraobserver reliability for diagnosing levator ani changes on magnetic resonance imaging. Ultrasound Obstet Gynecol 2013. doi: 10.1002/uog.12462
12. DeLancey JO, Morgan DM, Fenner DE, Kearney R, Guire K, Miller JM, et al. Comparison of levator ani muscle defects and function in women with and without pelvic organ prolapse. Obstet Gynecol 2007;109:295-302
13. Lammers K, Prokop M, Vierhout ME, Kluivers KB, Fütterer JJ. A pictorial overview of pubovisceral muscle avulsions on pelvic floor magnetic resonance imaging. Insights Imaging 2013 doi 10.1007/s13244-013-0261-9
14. Dietz HP, Steensma AB. The prevalence of major abnormalities of the levator ani in urogynaecological patients. BJOG 2006;113:225-30
15. Majida M, Braekken IH, Umek W, Bø K, Saltyte Benth J, Ellstrøm Engh M. Interobserver repeatability of three- and four-dimensional transperineal ultrasound assessment of pelvic floor muscle anatomy and function. Ultrasound Obstet Gynecol 2009;33:567-73
16. Dietz HP, Bernardo MJ, Kirby A, Shek KL. Minimal criteria for the diagnosis of avulsion of the puborectalis muscle by tomographic ultrasound. Int Urogynecol J 2011;22:699-704
17. Dietz HP, Shek C, De Leon J, Steensma AB. Ballooning of the levator hiatus. Ultrasound Obstet Gynecol 2008;31:676-80
18. Dietz HP, Simpson JM. Levator trauma is associated with pelvic organ prolapse. BJOG 2008;115:979-84
19. Shobeiri SA, LeClaire E, Nihira MA, Quiroz LH, O`Donoghue D. Appearance of the levator ani muscle subdivisions in endovaginal three-dimensional ultrasonography. Obstet Gynecol 2009;114:66-72
20. Shobeiri SA, Rostaminia G, White D, Quiroz LH. The determinants of minimal levator hiatus and their relationship to the puborectalis muscle and the levator plate. BJOG 2013;120:205-11
21. Santoro GA, Wieczorek AP, Stankiewicz A, Woźniak MM, Bogusiewicz M, Rechberger T. High-resolution three-dimensional endovaginal ultrasonography in the assessment of pelvic floor anatomy: a preliminary study. Int Urogynecol J 2009;20:1213-22

22. Santoro GA, Wieczorek AP, Shobeiri SA, Mueller ER, Pilat J, Stankiewicz A, et al. Interobserver and inter-disciplinary reproducibility of 3D endovaginal ultrasound assessment of pelvic floor anatomy. Int Urogynecol J 2011;22:53-9
23. Rostaminia G, White D, Hegde A, Quiroz LH, Davila GW, Shobeiri SA. Levator ani deficiency and pelvic organ prolapse severity. Obstet Gynecol 2013;121:1017-24
24. Lone F, Thakar R, Sultan AH, Stankiewicz A. Prospective evaluation of change in levator hiatus dimensions using 3D endovaginal ultrasound before and 1 year after treatment for female pelvic organ prolapse. Int Urogynecol J 2013;24:1287-93
25. Kruger JA, Heap SW, Murphy BA, Dietz HP. Pelvic floor function in nulliparous women using three-dimensional ultrasound and magnetic resonance imaging. Obstet Gynecol 2008;111:631-8
26. Majida M, Braekken IH, Bø K, Benth JS, Engh ME. Validation of three-dimensional perineal ultrasound and magnetic resonance imaging measurements of the pubovisceral muscle at rest. Ultrasound Obstet Gynecol 2010;35:715-22
27. Zhuang RR, Song YF, Chen ZQ, Ma M, Huang HJ, Chen JH, et al. Levator avulsion using a tomographic ultrasound and magnetic resonance-based model. Am J Obstet Gynecol 2011;205:232.e1-8
28. Schwertner-Tiepelmann N, Thakar R, Sultan AH, Tunn R. Obstetric levator ani muscle injuries: current status. Ultrasound Obstet Gynecol 2012;39:372-83
29. Kim J, Ramanah R, DeLancey JO, Ashton-Miller JA. On the anatomy and histology of the pubovisceral muscle enthesis in women. Neurourol Urodyn 2011;30:1366-70
30. Blasi I, Fuchs I, D'Amico R, Vinci V, La Sala GB, Mazza V, et al. Intrapartum translabial three-dimensional ultrasound visualization of levator trauma. Ultrasound Obstet Gynecol 2011;37:88-92
31. Albrich SB, Laterza RM, Skala C, Salvatore S, Koelbl H, Naumann G. Impact of mode of delivery on levator morphology: a prospective observational study with three-dimensional ultrasound early in the postpartum period. BJOG 2012;119:51-60
32. Dietz HP, Gillespie AVL, Phadke P. Avulsion of the pubovisceral muscle associated with large vaginal tear after normal vaginal delivery at term. Aust N Z J Obstet Gynaecol 2007;47:341-4
33. Branham V, Thomas J, Jaffe T, Crockett M, South M, Jamison M, et al. Levator ani abnormality 6 weeks after delivery persists at 6 months. Am J Obstet Gynecol 2007;197:65.e1-6
34. Shek KL, Chantarasorn V, Langer S, Dietz HP. Does levator trauma 'heal'? Ultrasound Obstet Gynecol 2012;40:570-5
35. Lien KC, Mooney B, DeLancey JOL, Ashton-Miller JA. Levator ani muscle stretch induced by simulated vaginal birth. Obstet Gynecol 2004;103:31-40
36. Drewes PG, Yanagisawa H, Starcher B, Hornstra I, Csiszar K, Marinis SI, et al. Pelvic organ prolapse in fibulin-5 knockout mice: pregnancy-induced changes in elastic fiber homeostasis in mouse vagina. Am J Pathol 2007;170:578-89
37. Kearney R, Miller JM, Ashton-Miller JA, DeLancey JO. Obstetric factors associated with levator ani muscle injury after vaginal birth. Obstet Gynecol 2006;107:144-9
38. Krofta L, Otcenasek M, Kasikove E, Feyereisl J. Pubococcygeus-puborectalis trauma after forceps delivery: evaluation of the levator ani muscle with 3D/4D ultrasound. Int Urogynecol J Pelvic Floor Dysfunct 2009;20:1175-81
39. Valsky DV, Lipschuetz M, Bord A, Eldar I, Messing B, Hochner-Celnikier D, et al. Fetal head circumference and length of second stage of labor are risk factors for levator ani muscle injury, diagnosed by 3-dimensional transperineal ultrasound in primiparous women. Am J Obstet Gynecol 2009;201:91.e1-7
40. Shek K, Dietz HP. Intrapartum risk factors for levator trauma. BJOG 2010;117:1485-92
41. Shek KL, Dietz HP. Can levator avulsion be predicted antenatally? Am J Obstet Gynecol 2010;202:586.e1-6
42. RCOG Green-top Guidelines – Operative vaginal delivery (No. 26). January 2011
43. Dietz HP, Shek C. Levator avulsion and grading of pelvic floor muscle strength. Int Urogynecol J Pelvic Floor Dysfunct 2008;19:633-6
44. Steensma AB, Konstantinovic ML, Burger CW, de Ridder D, Timmerman D, Deprest J. Prevalence of major levator abnormalities in symptomatic patients with an underactive pelvic floor contraction. Int Urogynecol J 2010;21:861-7

45. Abdool Z, Shek KL, Dietz HP. The effect of levator avulsion on hiatal dimension and function. Am J Obstet Gynecol 2009;201:89.e1-5
46. Heilbrun ME, Nygaard IE, Lockhart ME, Richter HE, Brown MB, Kenton KS, et al. Correlation between levator ani muscle injuries on magnetic resonance imaging and fecal incontinence, pelvic organ prolapse, and urinary incontinence in primiparous women. Am J Obstet Gynecol 2010;202:488.e1-e6
47. Thakar R, Sultan AH (2007). Postpartum problems and the role of a perineal clinic. In: Sultan AH, Thakar R, Fenner DE (eds). Perineal and anal sphincter trauma. Springer, London, pp 65–79
48. Dietz HP, Kirby A, Shek LK, Bedwell PJ. Does avulsion of the puborectalis muscle affect bladder function? Int Urogynecol J 2009;20:967-72
49. Morgan DM, Cardoza P, Guire K, Fenner DE, DeLancey JOL. Levator ani defect status and lower urinary tract symptoms in women with pelvic organ prolapse. Int Urogynecol J 2010;21:47-52
50. Leeman LM, Rogers RG. Sex after childbirth: postpartum sexual function. Obstet Gynecol 2012;119:647-55
51. Boyle R, Hay-Smith EJ, Cody JD, Mørkved S. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database Syst Rev 2012;10:CD007471. doi:10.1002/14651858.CD007471.pub2
52. Braekken IH, Majida M, Engh ME, Bø K. Morphological changes after pelvic floor muscle training measured by 3-dimensional ultrasonography: a randomized controlled trial. Obstet Gynecol 2010;115:317-24
53. Braekken IH, Majida M, Engh ME, Bø K. Can pelvic floor muscle training reverse pelvic organ prolapse and reduce prolapse symptoms? An assessor-blinded, randomized, controlled trial. Am J Obstet Gynecol 2010;203:170.e1-7
54. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. Ultrasound Obstet Gynecol 2003;22:85-93

11a

Summary

Summary

Chapter 1 described the general outline of the thesis. The levator ani muscle provides support to the pelvic floor in order to prevent pelvic floor dysfunction and pelvic organ prolapse. The aim of the prospective longitudinal study was to establish the prevalence of levator ani muscle defects sustained during childbirth and to correlate these defects with pelvic floor symptoms and pelvic floor muscle strength. The secondary aim of the study was to compare different techniques to assess the levator ani muscle.

The recruitment process has been described in **Chapter 2**, with the aim to identify factors that could influence recruitment. Women were recruited by a dedicated research fellow using a face-to-face approach. Out of 1473 women approached, 269 (18.3%) agreed to participate and 1043 (70.8%) declined. Forty percent (n=420) did not provide a reason for non-participation. Most often mentioned reasons were 'being too busy', 'other pregnancy problems', 'no additional (internal) examination', 'moving (abroad)', and 'husband'. Age and ethnicity influenced the reasons for non-participation. The information obtained in this study can now be used by researchers recruiting women for comparable studies, to enhance recruitment and participation of eligible patients.

Inter-rater reliability of digital assessment of the levator ani muscle was evaluated using a sample of 25 nulliparous women, as presented in **Chapter 3**. The modified Oxford scale was used to assess pelvic floor muscle strength and substantial agreement was found (kappa=0.66). A novel classification system was used to assess levator ani muscle attachment to the pubic bone and almost perfect agreement was found (kappa=0.90). However, 20% of women had some form of levator ani muscle abnormality using the scoring system on digital assessment, although transperineal ultrasound revealed no levator ani muscle avulsion. It appeared that these results are reproducible in nulliparous women and the techniques can be reliably incorporated into clinical practice and research after appropriate training.

The assessment of the levator ani muscle has previously been evaluated using 3D endovaginal ultrasound in nulligravid women. Endovaginal ultrasound is a high-frequency technique providing detailed information on the pelvic floor structures. **Chapter 4** described the use of this technique in nulliparous and primiparous women to assess intra- and inter-rater reliability of levator ani muscle biometry and avulsion. 169 antenatal scans, 83 scans performed early postpartum and 75 scans three months postpartum were analysed by two independent investigators using a standardised protocol. Measurements were taken and levator ani muscle attachment

was scored (pubococcygeus and puborectalis part): 1= intact, 2= partial avulsion <50%, 3= partial avulsion >50%, 4= complete avulsion. Correlation was excellent for hiatus area, good for hiatus antero-posterior diameter, fair-moderate for hiatus transverse diameter, thickness of the levator and levator urethra gap, all with similar limits of agreement. Correlation for levator ani muscle avulsion was excellent. Therefore, 3D endovaginal ultrasound seemed to be a reliable tool in the assessment of hiatus measurements and levator ani muscle avulsion in parous women. Endovaginal ultrasound could be used in research studies involving the pelvic floor.

After confirming the utility of endovaginal ultrasound we aimed to compare this technique to transperineal ultrasound, which is more widely used, in **Chapter 5**. 269 nulliparous women and 191 primiparous women underwent digital palpation, endovaginal ultrasound and transperineal ultrasound to assess the diagnostic accuracy between the three techniques. Hiatus measurements were performed at rest by one investigator. Correlation was good for hiatus area and antero-posterior diameter, moderate for transverse diameter and levator urethra gap and poor for levator thickness. Endovaginal ultrasound measurements were generally smaller, with acceptable limits of agreement for hiatus measurements. Levator ani muscle avulsion was diagnosed on transperineal ultrasound when the three central slices on tomographic ultrasound imaging were avulsed at contraction, and on endovaginal ultrasound if >50% was avulsed at rest. Two independent blinded investigators analysed levator avulsion and a third investigator resolved discrepancies. Overall agreement between both ultrasound techniques in diagnosing levator avulsion was 95%; correlation 0.72 (95%CI 0.67-0.76). Palpation of levator ani muscle avulsion using the previously presented grading system had a high specificity (99%) and a low sensitivity (26-28%). This study concluded that transperineal and endovaginal ultrasound can both be used interchangeably to analyse hiatus area and antero-posterior diameter and to diagnose levator avulsion. Palpation underestimated true avulsion and therefore could not substitute ultrasound, but could be used in excluding levator ani muscle avulsion.

Childbirth causes overstretching of the levator ani muscle predisposing to avulsion of the pubic bone. **Chapter 6** evaluated the relationship between haematomas and levator ani muscle avulsions using high frequency endovaginal ultrasound and palpation early and late postpartum. No levator ani muscle avulsions were found in 269 nulliparous women. Following childbirth, 114 women agreed to undergo examination within four days postpartum. 27 of them had well delineated, hypoechoic areas consistent with haematomas (100% agreement between two investigators); 26 following vaginal delivery, one following emergency caesarean section. In total, 38 haematomas were found (11 bilateral, 16 unilateral). Haematomas away from the

levator ani muscle attachment zone to the pubic bone (n=22) resolved. Haematomas at the attachment zone (n=16) manifested as pubococcygeus avulsions three months postpartum. In addition to these 16 avulsions, we found another 20 avulsions three months postpartum: thirteen were not scanned early postpartum and in seven no haematoma but avulsion was seen early postpartum. Palpation was unreliable early postpartum as only seven avulsions were diagnosed. We therefore concluded that haematomas at the site of levator ani muscle attachment to the pubic bone always result in avulsion diagnosed three months postpartum. However, one third of avulsions were not preceded by a haematoma at the site of LAM attachment to the pubic bone.

Chapter 7 established the true incidence of levator ani muscle avulsion in primiparous women three months following childbirth using transperineal ultrasound. A sample size of 265 including a dropout rate was used to detect 14% levator ani muscle avulsion. No levator ani muscle avulsions were found in 269 nulliparous women. Seventy-one percent (n=191) were seen three months postpartum. No levator ani muscle avulsion was found after caesarean section (n=48). Seven women had minor avulsion and 23 women had major avulsion, revealing a total incidence of 21% (95%CI 15.1-28.4%) following vaginal delivery. The second aim was to develop a clinically applicable risk prediction model, using multivariate ordinal logistic regression analysis. Risk factors were obstetric anal sphincter injuries, prolonged active second stage and forceps delivery. A risk model and nomogram were developed to estimate a woman's individual risk: the three risk factors combined revealed a 75% chance of levator ani muscle avulsion. From this study it is concluded that these new tools can help us to optimise management in the delivery suite and also target postnatal women at risk of having sustained levator ani muscle avulsion.

Chapter 8 was a continuation of chapter 7 and described the relationship between levator ani muscle avulsion and signs and/or symptoms of pelvic floor dysfunction three months following childbirth. Validated methods were used for objective and subjective assessment of pelvic floor dysfunction. Reduced pelvic floor muscle strength ($p<0.038$) and more pelvic organ prolapse (maximum stage 2) ($p<0.024$) were found in women with levator ani muscle avulsion. Antenatal hiatus antero-posterior diameter on transperineal ultrasound was significantly smaller in women sustaining levator ani muscle avulsion ($p=0.011$). Postnatal measurements on transperineal ultrasound were significantly increased in women with levator ani muscle avulsion. Women with major avulsion were less sexually active and had more postnatal urinary incontinence and symptoms such as reduced vaginal sensation and 'too loose vagina'. No postnatal differences were found for faecal incontinence, prolapse symptoms or quality of life. Differences in variables only correlated slight-fair

with avulsion severity. To conclude, women with levator ani muscle avulsion had more signs and symptoms of pelvic floor dysfunction three months following first vaginal delivery.

The one year follow-up of the same cohort of women has been described in **Chapter 9**. The aim was to establish the natural history of levator ani muscle avulsion in primiparous women within one year following childbirth using transperineal ultrasound. 147 women (55%) attended at one year; 109 following vaginal and 38 following caesarean delivery. Thirteen out of twenty-one (62%, 95%CI 41-79%) levator ani muscle avulsions three months postnatal had healed at one year. Following vaginal delivery, nine women (8%, 95%CI 4.2-15.1%) had persistent levator ani muscle avulsion. The secondary aim was to assess the relation of healed and persistent levator ani muscle with signs and symptoms of pelvic floor dysfunction analysed by pattern differences over time between groups. Most changes in pelvic floor dysfunction occurred between the antenatal and three months postnatal visit, without improvement after one year. Anterior vaginal wall prolapse was associated with vaginal delivery. Women with persistent levator avulsion had significantly worse deterioration patterns of muscle strength, hiatus measurements and more vaginal symptoms (too loose vagina / lump sensation). At one year, subjective anal and urinary incontinence did not differ between groups. Although women with persistent levator ani muscle avulsion had more signs and symptoms of pelvic floor dysfunction, women with healed levator ani muscle avulsion had pelvic floor dysfunction as well. This might explain why not all women with prolapse have levator ani muscle avulsion on ultrasound, shining new light on the pathogenesis of levator ani muscle avulsion and prolapse. Longer term follow-up is needed to monitor the development of pelvic floor dysfunction and to evaluate the impact of subsequent deliveries.

Chapter 10 described the highlights of the thesis and discussed the main results. Furthermore, implications to daily clinical practice and recommendations for future research have been made.

11b

Samenvatting

Samenvatting

Hoofdstuk 1 geeft een algemene introductie op het proefschrift. De levator ani spier maakt onderdeel uit van de bekkenbodem. De bekkenbodem moet zich bij mictie, defecatie, coitus en een bevalling kunnen openen, en geeft de overige tijd steun aan de bekkenorganen. Het doel van de bekkenbodem is dus het adequaat laten functioneren van de bekkenorganen en voorkomen van verzakking.

De gegevens die ten grondslag liggen aan het huidige proefschrift zijn verzameld in een prospectieve longitudinale studie. Het doel was het vaststellen van de prevalentie van defecten aan de levator ani spier ontstaan tijdens de bevalling en om deze defecten te correleren aan risicofactoren tijdens de bevalling, bekkenbodem klachten en de kracht van de bekkenbodemspier. Het tweede doel van deze studie was het vergelijken van verschillende technieken om de levator ani spier te beoordelen.

Het inclusieproces voor deze studie is beschreven in **Hoofdstuk 2**. Het doel van de studie was om de factoren die inclusie beïnvloeden te identificeren. Vrouwen werden persoonlijk door de onderzoekster gevraagd voor deelname aan het onderzoek. Van de 1473 benaderde vrouwen hebben 269 (18.3%) vrouwen ingestemd met deelname en 1043 (70.8%) hebben geweigerd. Veertig procent (n=420) heeft geen reden gegeven waarom ze niet wilden deelnemen. De meest genoemde redenen om niet mee te doen waren ‘te druk zijn’, ‘andere zwangerschapsproblemen’, ‘geen extra (gynaecologisch) onderzoek’, ‘verhuizen (naar het buitenland)’ en ‘echtgenoot’. Vrouwen van verschillende leeftijden namen deel. Alhoewel, vooral vrouwen tussen de 31 en 35 jaar hadden geen tijd, wilden geen gynaecologisch onderzoek en schatten de kans groot dat zij gingen verhuizen. Vrouwen met een gemengde achtergrond namen het vaakst deel. Vrouwen met een Aziatische achtergrond het minst vaak, waarbij ze in verhouding het vaakst als reden aangaven dat de partner niet akkoord was. De resultaten van deze studie kunnen gebruikt worden voor optimalisatie van het werven van deelnemers voor vergelijkbare studies.

Inter-rater betrouwbaarheid van digitale palpatie en beoordeling van de levator ani spier is geëvalueerd in een steekproef van 25 zwangere vrouwen, zoals gepresenteerd in **Hoofdstuk 3**. The gemodificeerde Oxford schaal is gebruikt om de kracht van de bekkenbodem spier te scoren en er werd substantiële overeenstemming gevonden (kappa=0.66). Met een nieuw classificatie systeem om de aanhechting van de levator ani spier aan het schaambeen te beoordelen werd een bijna perfecte overeenstemming gevonden (kappa=0.90). Als er bij transperineale echo geen avulsie van de levator ani spier werd gezien, werd desondanks bij 20% van de vrouwen kleine abnormaliteiten van de levator ani spier gevonden met het classificatie systeem. De technieken zijn reproduceerbaar bij zwangere vrouwen en kunnen, na gepaste training, worden opgenomen in de klinische praktijk en wetenschappelijk onderzoek.

De levator ani spier werd in de volgende studie beoordeeld met 3D endovaginale echo bij vrouwen vóór en na hun eerste bevalling. Endovaginale echo levert gedetailleerde informatie op over bekkenbodem structuren. **Hoofdstuk 4** beschrijft de betrouwbaarheid van het bepalen van de biometrie en avulsie van de levator ani spier binnen en tussen beoordelaars, bij zwangere vrouwen en vrouwen na hun eerste bevalling. 169 echo's tijdens de zwangerschap, 83 echo's binnen vier dagen na de bevalling en 75 echo's drie maanden na de bevalling zijn geanalyseerd door twee onafhankelijke beoordelaars waarbij een gestandaardiseerd protocol is gebruikt. Verschillende metingen aan de spier en hiatus werden gedaan. De levator ani spier werd beoordeeld (pubococcygeus en puborectalis deel) als: 1= intact, 2= partiële avulsie <50%, 3= partiële avulsie >50%, of 4= complete avulsie. Correlatie was uitstekend voor hiatus oppervlakte, goed voor antero-posterior diameter, redelijk voor hiatus transverse diameter, dikte van de levator ani spier en levator urethra gap, zonder structurele bias. Correlatie voor aanwezigheid van avulsie van de levator ani spier was uitstekend. Daarom lijkt de 3D endovaginale echo een betrouwbaar instrument voor de beoordeling van hiatus metingen en avulsie van de levator ani spier, ook na een bevalling. Endovaginale echo kan dus gebruikt worden in bekkenbodem onderzoek.

Na het bevestigen van de reproduceerbaarheid van de endovaginale echo, hebben we deze techniek vergeleken met de transperineale echo in **Hoofdstuk 5.** De transperineale echo wordt wereldwijd het meest frequent toegepast in de dagelijkse kliniek en wetenschappelijk onderzoek. 269 zwangere vrouwen, waarvan 191 (71%) vrouwen na hun eerste bevalling werden teruggezien, ondergingen digitale palpatie, endovaginale echo en transperineale echo om de overeenkomst van de drie diagnostische technieken te vergelijken. Hiatus metingen zijn verricht in de rust-opname door één onderzoeker. Correlatie was goed voor hiatus oppervlakte en antero-posterior diameter, matig voor transverse diameter en levator urethra gap en slecht voor spier dikte. De metingen bij de endovaginale echo waren over het algemeen kleiner, zonder structurele bias. Levator ani spier avulsie werd gediagnosticeerd op de transperineale echo gedurende contractie als de drie centrale doorsneden op tomografische beoordeling een avulsie toonden, en op de endovaginale echo gedurende de rust-opname als >50% geavulseerd was. Twee onafhankelijke geblindeerde onderzoekers hebben avulsie van de levator geanalyseerd en een derde onderzoeker heeft de discrepanties opgelost. De algehele overeenstemming tussen beide echo technieken in het diagnosticeren van levator avulsie was 95%; correlatie 0.72 (95%CI 0.67-0.76). Palpatie van levator ani spier avulsie met gebruik van het eerder gepresenteerde classificatie systeem had een hoge specificiteit (99%) en een lage sensitiviteit (26-28%). Deze studie concludeert dat transperineale en endovaginale echo beiden gebruikt kunnen worden om de hiatus oppervlakte en

antero-posterior diameter te meten en om levator avulsie te diagnosticeren. Palpatie onderschat de aanwezigheid van een avulsie en kan daarom de echo's niet vervangen, maar kan wel gebruikt worden voor het uitsluiten van een levator ani spier avulsie.

Een vaginale baring veroorzaakt overrekking van de levator ani spier hetgeen kan leiden tot avulsie van de aanhechting van de spier van het schaambeen. In **Hoofdstuk 6** werd de relatie tussen haematomen en levator ani spier avulsies geëvalueerd, waarbij gebruikt werd gemaakt van de endovaginale echo en palpatie direct na de bevalling en drie maanden na de bevalling. Er werden zoals verwacht geen levator ani spier avulsies gevonden bij zwangere vrouwen en vrouwen bevallen middels keizersnede. 114/199 vrouwen (57%) stemden in met het onderzoek binnen vier dagen na de bevalling. 27/114 (24%) vrouwen hadden duidelijk omlijnde hypoechogene gebieden gelijkend op haematomen (100% overeenstemming tussen twee onderzoekers); 26% na een vaginale baring en één na een spoed keizersnede bij vijf centimeter ontsluiting. In totaal zijn er 38 haematomen gevonden (11 bilateraal, 16 unilateraal). Haematomen die niet direct bij de aanhechting van de levator ani spier aan het schaambeen (n=22) zichtbaar waren, resorbeerden spontaan. Haematomen direct in de nabijheid van de aanhechting van de levator ani spier aan het schaambeen (n=16) manifesteerden zich steeds als avulsies van het pubococcygeus deel na drie maanden. Naast deze 16 avulsies, hebben we nog 20 avulsies gevonden drie maanden postpartum: 13/20 vrouwen (65%) hadden geen echoscopische beoordeling direct na de bevalling en in zeven gevallen (35%) was er geen haematoom maar avulsie gezien meteen na de bevalling. Palpatie was onbetrouwbaar direct postpartum, omdat slechts zeven avulsies (30%) gediagnosticeerd waren. We concludeerden daarom dat haematomen bij de aanhechtingen van de levator ani spier aan het schaambeen altijd resulteerden in avulsie gediagnosticeerd drie maanden na de bevalling. Een derde van de avulsies (30%) werd echter niet voorafgegaan door een haematoom op de plaats van de aanhechting van de levator ani spier aan het schaambeen.

In **Hoofdstuk 7** is de incidentie van avulsie van de levator ani spier beschreven bij vrouwen drie maanden na de eerste bevalling, beoordeeld op de transperineale echo. De grootte van de benodigde onderzoeksgroep was 265, om 14% levator ani spier avulsie betrouwbaar te detecteren. Geen van de 269 zwangere vrouwen had levator ani spier avulsie. Een-en-zeventig procent (n=191) is terug gezien drie maanden na de bevalling. Er werd geen levator ani spier avulsie gezien na een keizersnede (n=48). Zeven vrouwen (4.9%, 95%CI 2.2-9.9%) hadden partiële avulsie en 23 vrouwen (16.1%, 95%CI 10.9-23.0%) hadden complete avulsie, waarbij de totale incidentie na een vaginale baring 21% was (n=30, 95%CI 15.1-28.4%). Het tweede doel was het ontwikkelen van een klinisch toepasbaar risico predictie model,

met het gebruik van multivariabele ordinale logistische regressie analyse. Risicofactoren voor avulsie waren obstetrische anale sphincter schade, verlengde actieve uitdrijvingsfase en een tangverlossing. Een risico model en nomogram zijn ontwikkeld om het individuele risico van een vrouw te kunnen inschatten: in aanwezigheid van de drie risicofactoren was de kans op een levator ani spier avulsie 75%. Uit deze studie kunnen we concluderen dat deze nieuwe instrumenten ons kunnen helpen om het beleid in de verloskamers te optimaliseren en om postnatale vrouwen met een risico op het hebben van een levator avulsie te detecteren.

Hoofdstuk 8 was een voortzetting van hoofdstuk 7 en beschreef de relatie tussen levator ani spier avulsie en tekenen en/of klachten van bekkenbodem dysfunctie drie maanden na de bevalling. Gevalideerde meetmethoden zijn gebruikt voor objectieve en subjectieve beoordeling van bekkendbodem dysfunctie. Verminderde spierkracht van de bekkenbodem ($p<0.038$) en meer verzakking van de vagina voorwand (maximum stadium 2) ($p<0.024$) werden gevonden bij vrouwen met levator ani spier avulsie. Antenatale hiatus antero-posterior diameter op de transperineale echo was voor de bevalling kleiner bij die vrouwen die een levator ani spier avulsie zouden gaan oplopen tijdens de bevalling ($p=0.011$). Alle echo metingen waren na de bevalling juist significant toegenomen bij vrouwen met levator ani spier avulsie. Vrouwen met complete levator ani spier avulsie waren minder sexueel actief voor en na de bevalling ($p<0.030$). Deze vrouwen hadden meer postnatale urine incontinentie en symptomen zoals verminderde vaginale sensatie en ‘te wijde vagina’. Er waren geen postnatale verschillen gevonden voor faecale incontinentie, verzakkingsklachten en kwaliteit van leven. We concludeerden dat vrouwen met levator ani spier avulsie meer tekenen en klachten hadden van bekkenbodem dysfunctie drie maanden na de eerste bevalling.

De vervolgonderzoeken van hetzelfde cohort een jaar na de bevalling zijn beschreven in **Hoofdstuk 9**. Het doel was om het natuurlijke beloop van levator ani spier avulsie in het eerste jaar na de bevalling vast te stellen door middel van de transperineale echo. 147 vrouwen (55%) werden gezien na een jaar; 109 (74%) na een vaginale baring en 38 (26%) na een keizersnede. Dertien van de één-en-twintig (62%, 95%CI 41-79%) levator ani spier avulsies die drie maanden na de bevalling werden vastgesteld waren geheeld na een jaar. Na een vaginale baring hadden negen vrouwen (8%, 95%CI 4.2-15.1%) persisterende levator ani spier avulsie. Het tweede doel van de studie was de beoordeling van de groepen met genezen levator ani spier avulsie en met persisterende levator ani spier avulsie in relatie tot bekkenbodem dysfunctie. Analyses zijn gedaan op basis van patroon verschillen door de tijd in de verschillende groepen. De grootste veranderingen in bekkenbodem dysfunctie ontstonden tussen de controle vóór de bevalling en de controle drie maanden na de bevalling, zonder verbetering na een jaar. Verzakking van de voorwand was

geassocieerd met een vaginale baring. Vrouwen met persisterende levator avulsie hadden significant slechtere patronen met betrekking tot spierkracht, hiatus metingen en vaginale symptomen (te wijde vagina en balgevoel in vagina). Bij de jaarcontrole verschilden voorkomen van faecale en urine incontinentie niet tussen de groepen. Alhoewel vrouwen met persisterende levator ani spier avulsie de meeste tekenen en klachten van bekkenbodem dysfunctie hadden, werd dit patroon ook bij vrouwen met genezen levator ani spier avulsie gezien. Dit kan een deel van de verklaring zijn van het feit dat niet alle vrouwen met een verzakking levator ani spier avulsie hebben op de echo. We hopen hiermee nieuw licht te kunnen werpen op de pathogenese van levator ani spier avulsie en verzakking. Lange termijn controles zijn essentieel om de ontwikkeling van bekkenbodem dysfunctie te monitoren en om de impact van volgende bevallingen te evalueren.

Hoofdstuk 10 beschreef de hoogtepunten van de thesis waarbij de belangrijkste resultaten zijn besproken. Verder zijn implicaties voor de dagelijkse klinische praktijk en aanbevelingen voor verder onderzoek gemaakt.

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Bibliography

Bibliography

- **van Delft KWM**, Bremer GL. Puerperal fever; Detection of the source. NTOG 2009;122:299-301 [Dutch]
- Hendriksen MTJ, **van Delft KWM**, Bremer GL, Mertens HJMM. Patient satisfaction in treatment for cervical pathology. Oncology Letters 2011;2:439-43
- **van Delft KWM**, Mertens HJMM, Treatment strategies in intermediate cervical neoplasia: implications of radical surgery. Oncology Letters 2011;2:575-8
- **van Delft KWM**, Thakar R, Sultan AH. Re: Levator avulsion using a tomographic ultrasound and magnetic resonance-based model. Am J Obstet Gynecol 2012;206:e7
- **Van Delft KWM**. Urogynaecology Digest. Int Urogynecol J 2012;23:1809-10
- **van Delft K**, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Recruitment of pregnant women in research. J Obstet Gynaecol 2013;33:442-6
- **van Delft K**, Schwertner-Tiepelmann N, Thakar R, Sultan AH. Inter-rater reliability of assessment of levator ani muscle strength and attachment to the pubic bone in nulliparous women. Ultrasound Obstet Gynecol 2013;42:341-6
- **van Delft K**, Thakar R, Shobeiri SA, Sultan AH. Levator haematoma at the attachment zone as an early marker for levator ani muscle avulsion. Ultrasound Obstet Gynecol 2013. doi: 10.1002/uog.12571
- **van Delft K**, Shobeiri SA, Thakar R, Schwertner-Tiepelmann N, Sultan AH. Intra- and inter-rater reliability of levator ani muscle biometry and avulsion using three-dimensional endovaginal sonography. Ultrasound Obstet Gynecol 2013. doi: 10.1002/uog.13193
- **van Delft K**, Thakar R, Sultan AH, Schwertner-Tiepelmann N, Kluivers KB. Levator ani muscle avulsion during childbirth: a risk prediction model. Accepted for publication in BJOG
- **van Delft K**, Thakar R, Sultan AH, Schwertner-Tiepelmann N, Kluivers KB. The relationship between postpartum levator ani muscle avulsion and signs and symptoms of pelvic floor dysfunction. Accepted for publication in BJOG

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Dear Isabelle, you are the new Urogynaecology research fellow in Croydon University Hospital. We worked together for a few months to ensure a proper handover. I hope I have introduced you to the research world in Croydon appropriately. Good luck!

Dear Karin, as the Urogynaecology research fellow in Nijmegen, you have been so good to me by answering all my questions and I enjoyed exchanging ideas. I look forward to work with you during our Obs&Gynae residency in Nijmegen.

Dear Jan Willem de Leeuw, thank you for giving me the opportunity to go to London. Without that opportunity I would not have been here today to defend my thesis. I enjoyed working in Ikazia Hospital and I would like to thank all colleagues there. I mention Inge van Hooft separately as she has been my outlet when drinking red wine and eating 'bitterballen'.

I would like to thank the gynaecologists of the Orbis Medical Centre in Sittard, and Helen Mertens in particular, supervisor of my final rotation in Obstetrics and Gynaecology. This internship was the foundation of my career and I would like to thank you for your inspiration and motivation.

I would like to thank Emma Fenton as she has been really excellent in designing the cover of my PhD book! It is amazing. You are a sweet friend, thank you!

Dear Sarene, what a bliss that you lived in the same accommodation in Croydon. I enjoyed drinking wine and talking French with you and all other things that should not be mentioned here.

Dear Eefje, you are a great friend and I really appreciate your point of view on things. We were about to live in the same city after all, but you decided to move to Rotterdam! I would like to thank you for being my friend for many years already and I look forward to many more years.

Dear Inge, you are very inspirational and I always enjoy our conversations and dinners. Thank you for visiting me twice in London (who could resist the Olympics…!) and I hope that we will plan many more trips!

I would like to thank the girls (or should I say ladies….!) from Amicitia as they are great friends and we had an amazing time (studying) in Maastricht. I will never forget all our adventures and happiness. I still enjoy meeting up with you and I hope we will keep that up!

Dear medical friends! Malou, we chose the same career-path for gynaecology. I enjoyed being neighbours, visiting you in the USA when you did your research there and all the rest. Janneke, we had such amazing times in Nepal and in Australia. Although we have both lived abroad, we stayed in touch and I hope we will increase the frequency now we are both back in The Netherlands. Céline, you have been a very good friend and together we explored travelling abroad in Thailand and Malaysia, followed by more adventures!

Dear family van Benthum, thank you for welcoming me in your family. I know that your son has not chosen the easiest relationship initially by having to travel to London every month. However, Amsterdam-Beers is almost equal! We already had good times together, including nice celebrations and tasty dinners, thank you for your generous hospitality!

I would like to thank my family for being interested in the research and work I have been doing, although I know it is sometimes hard to understand! I would like to thank Oma van Delft in particular as she is such a wonderful lady. I appreciate your interest and although times have been tough, you are always a great support for everybody.

Dearest mom and dad, you have always been very interested in the things I did. I might have shifted my own borders, but yours as well: school in Den Bosch, studying in Maastricht, travelling around the world and working in Rotterdam. In 2010 you received my phone call that I was asked to start a research post abroad. What a relief that abroad was London and not further away! We had amazing times in London together, with Joris, with René and Trudy and with Inge, Wouter, Rik and Roseri. I can imagine that it was hard at times to understand what I was doing, although 'catching babies' was a nice way of putting it. Thank you for all the fun and your love and support in good times and in bad times!

Dearest Inge and Rik, my sweet sister and brother. You are very special to me! Therefore, I am absolutely grateful that you are here today together with me, as my 'Ushers', to help me whilst defending my thesis. We had so many fun times together over the past years, in The Netherlands and in London. Times are changing and we don't live as far away anymore, which makes me happy! Wouter and Roos, you two really belong to our family and it is great to have you around.

Dear Joris, you are extremely special to me. When we first met on the wedding in a sports hall in Germany, I never realised that we were going to start a long-distance relationship. We have been travelling back and forth for almost two years. Although you have not helped me with the content of this project, you have been a great motivational support in your own way. The way you approach people and tackle problems ('think in solutions') is admiring. I so much enjoy our time together and I am a very happy girl! Thanks a million!

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Curriculum Vitae

Curriculum Vitae

Kim van Delft werd geboren op zondag 7 oktober 1984 te Arnhem. Samen met haar zusje Inge en haar broertje Rik groeide ze op in het Brabantse Drunen. In 2002 haalde zij haar gymnasium-diploma aan het Stedelijk Gymnasium te Den Bosch. In 2003 begon zij aan de studie Geneeskunde aan de Universiteit van Maastricht, na eerst een jaar Algemene Gezondheidswetenschappen te hebben gestudeerd. In die jaren is zij actief geweest in het Maastrichtse studentenleven, onder andere als Praeses van het onafhankelijk dames dispuut Amicitia.

Tijdens de co-schappen werd de aandacht herverdeeld met de focus op de studie. Haar passie reizen kon gecombineerd worden met de co-schappen. Zo is zij naar Nepal geweest voor een co-schap Oogheelkunde. Tijdens de reguliere co-schappen en een keuze co-schap Gynaecologie in Mount Gambier, South Australia ontdekte zij de passie voor gynaecologie. Haar semi-arts stage heeft zij gedaan in het Orbis Medical Centre in Sittard onder begeleiding van Dr. Helen Mertens. Daar deed zij ook haar wetenschappelijke stage naar behandeling van cervicale intraepitheliale neoplasie. Na het afronden van de studie geneeskunde startte zij in 2009 als ANIOS Obstetrie & Gynaecologie in het Ikazia Ziekenhuis in Rotterdam. In augustus 2010 vroeg de opleider aldaar, Dr. Jan-Willem de Leeuw, of zij interesse had om onderzoek te gaan doen in London.

En zo kwam het dat zij in januari 2011 startte als Research Fellow Urogynaecology in Croydon University Hospital, London, United Kingdom. Deze grote prospectieve cohortstudie naar de levator ani spier werd uitgevoerd onder supervisie van Miss Ranee Thakar en Mr Abdul Sultan. Het onderzoek wat aldaar verricht is, heeft in samenwerking met het UMC St. Radboud te Nijmegen geresulteerd in het huidige proefschrift.

Op 1 april 2014 zal zij beginnen aan de opleiding tot gynaecoloog in het Canisius Wilhelmina Ziekenhuis in Nijmegen.

In haar vrije tijd speelt ze graag hockey en reist ze het liefst de wereld over.
Ze woont samen met Joris van Benthum in Utrecht.