Unraveling the Pelvic Floor

Obstetric injury, Symptoms and Imaging Techniques

Leonie Speksnijder

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Unraveling the Pelvic Floor

obstetric injury, symptoms and imaging techniques

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obstetrische schade, symptomen en beeldvorming

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I can do all things through Christ which strengtheneth me (Phil 4:13)

By small and simple things are great things brought to pass (Alma 37:6)

Voor mijn ouders

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CHAPTER

Aims and outline of this thesis and general introduction

AIMS AND OUTLINE OF THIS THESIS

The pelvic floor is important in several bodily functions, such as supporting the abdominal organs, sexual function, continence, passage of urine and stool, and childbearing. Injury to the pelvic floor can lead to dysfunction of these bodily functions. Such dysfunctions or pelvic floor disorders (PFD) may include urinary or anal incontinence, pelvic organ prolapse (POP), pelvic pain, and sexual dysfunction. Although PFD are not life threatening, they can be the cause of significant social and physical restrictions, as well as impact one's psychological well-being, and overall quality of life. In most cases, PFD lead to seeking medical attention. The costs of this medical care are an important part of the total costs of female health care. For example, POP is one of the most common gynecological disorders. The lifetime risk for women of having prolapse surgery is estimated at 10-20%[1-3]. In the Netherlands, approximately 13.000 POP operations are performed, yearly, with the costs adding up to approximately 75 million euros[4]. However, about half of the women with a prolapse do not opt for surgery. The costs for this group are more difficult to calculate. Medical care includes, incontinence pads, pessaries, physiotherapy, etcetera.

Given this information, the aims of this thesis can be summarized in the following:

PART 1: Pelvic floor after vaginal birth

1. To evaluate the association of mediolateral episiotomy with levator avulsion and/ or ballooning with perineal pelvic floor ultrasound (PFUS) and urogynecological complaints in primiparous women without anal sphincter injury.
2. To determine the association between levator hiatal dimensions and female sexual dysfunction after first vaginal delivery.
3. To evaluate whether anal sphincter defects, levator avulsion or levator ballooning on perineal PFUS after obstetric anal sphincter injury (OASI) are associated with severity of anal incontinence. Furthermore, we evaluated whether other factors, such as constipation or altered stool consistency, are associated with symptoms of incontinence after OASI.

PART 2: Pelvic floor imaging with virtual reality

1. To compare levator ani hiatus volume measurements during pelvic floor muscle contraction (PFMC) obtained with conventional perineal PFUS and with virtual reality (VR) imaging. And to establish the reliability and agreement of these measurements.

2. In addition, establish the agreement and reliability of these volume measurements and their relationship with prolapse symptoms and the stage of the pelvic organ prolapse quantification (POP-Q).

Setting and outline of this thesis

For **chapter 2 and 3** we used data of 'EpiLeva study'. The EpiLeva study was a prospective observational cohort study of 204 primiparous with a spontaneous vaginal delivery without anal sphincter tear in Amphia hospital between 2012 and 2015. In **chapter 2**, we compared women with and women without a mediolateral episiotomy and evaluated the association of mediolateral episiotomy with levator ani muscle injury (levator avulsion, ballooning or combined) on perineal PFUS and urogynecological complaints. **Chapter 3** is a secondary analysis of the EpiLeva study, where we analyzed the association of total Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) score, as well as individual sexual complaints (desire, arousal, orgasm, and dyspareunia), with levator hiatal dimensions at rest, maximal Valsalva, and during PFMC on perineal PFUS.

In **chapter 4**, we used the data from the FU-OASIS study. This multicenter prospective observational cohort study was conducted in Amphia hospital and Erasmus Medical center between February 2009 and January 2018. All women with OASI were invited to participate at least 3 months after primary repair. In this study we evaluated whether anal sphincter defects, levator avulsion or levator ballooning with perineal PFUS after OASI are associated with severity of anal incontinence measured with St Mark's incontinence score (SMIS). Furthermore, we also evaluated whether other factors, as constipation (measured with Cleveland Clinic Constipation Score (CCCS) or altered stool consistency (measure with Bristol Stool Scale (BSS) were associated with symptoms of incontinence after OASI.

For **chapter 5 and 6,** we measured levator ani hiatal volumes (in cm^3) semi-automatically by VR imaging using a segmentation algorithm in the I-Space. These measurements were compared with volume measurements on conventional perineal PFUS datasets. We also conducted this study because the I-Space VR system enabled us to visualize perineal PFUS datasets as a 'hologram'. The concave and convex features of the levator ani could be visualized in this hologram, allowing the researcher to measure the actual three-dimensional (3D) volume. These studies were designed to compare levator ani hiatal volume measurements during PFMC, at rest and on maximum Valsalva, measured using conventional perineal PFUS and VR, and to establish the intra- and interobserver agreements of these measurements.

Chapter 5 presents the results of a comparison between measurements of levator ani hiatal volume during PFMC, obtained using conventional perineal PFUS versus these measurements with VR imaging in women without levator avulsion. In **chapter 6**, we present these results at rest and on maximal Valsalva between levator hiatal measurements on perineal PFUS, and compared these with measurements obtained with VR imaging. Furthermore, in **chapter 6**, we aimed to establish whether there is an association between levator ani hiatal volume at rest and on maximum Valsalva, measured using both conventional perineal PFUS and VR, with prolapse symptoms and POP-Q stage.

Chapter 7 contains the general discussion, implications for daily practice and future research.

In **chapter 8 and 9** a summary in English and Dutch is given.

GENERAL INTRODUCTION

The pelvic floor (Figure 1) is an important support structure in the human body and separates the pelvic cavity from the perineum. On the one hand, the pelvic floor must function optimally to prevent incontinence (urine and feces), prolapse, chronic pelvic floor pain and sexual dysfunction. But on the other hand, the passage of the pelvic floor must also be able to take place unhindered, such as for micturition, defecation, sexual activity and vaginal deliveries. An optimal function therefore means an optimal, partly voluntary balance between activation and relaxation.

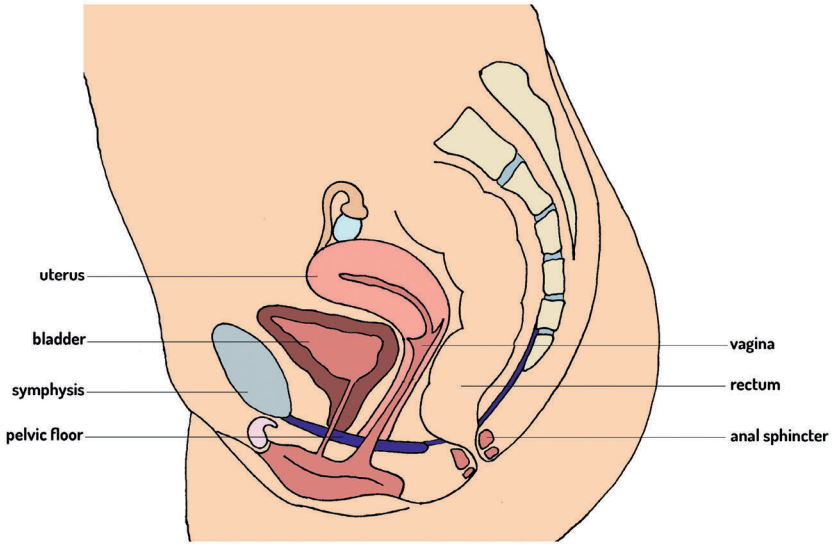

Figure 1 Pelvic floor

Anatomy

The pelvic floor consists of muscle fibers and associated connective tissue. the two sides of levator ani muscle attach peripherally to the pelvic walls and join each other at the midline by connective tissue raphe. It is generally believed that the levator ani muscle (LAM) comprise three separate muscles: the pubococcygeus, puborectalis, and iliococcygeus (Figure 2). The different parts of the LAM are generally described based on the attachments, the course of fibers, and innervation. Together they are the largest components of the bowl- or funnel-shaped structure which span the area below the pelvis like a diaphragm (pelvic diaphragm). The space between the levator muscles is the urogential hiatus or levator hiatus. This space allows the urethra, vagina and anal canal to exit the abdomen. Innervation of the LAM

occurs through the plexus sacralis. Innervation of the puborectal part of the LAM is still a matter of debate, but most likely it is variably innervated by the levator ani nerve and/or pudendal nerve reflecting the poorly demarcated borders between the muscular parts of the LAM[5-7].

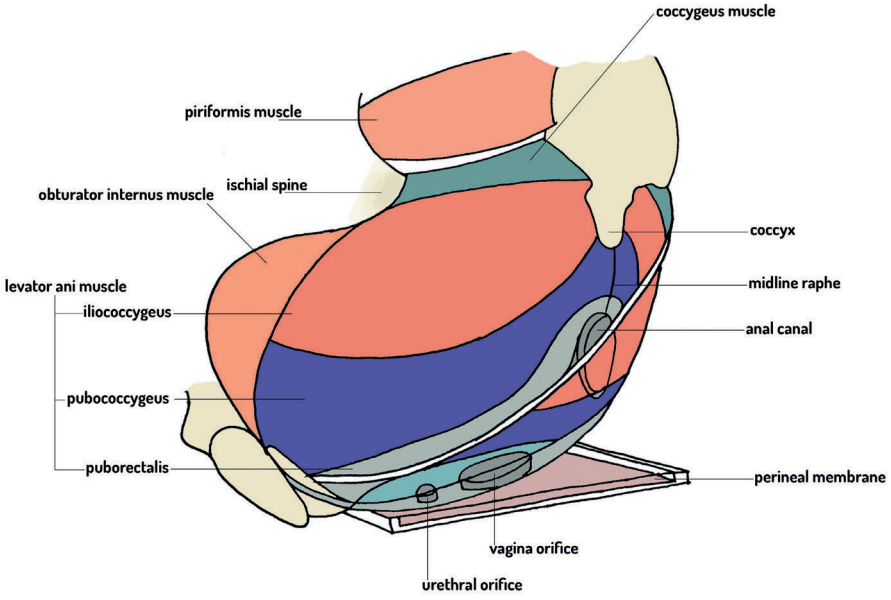

Figure 2 Pelvic floor muscles

Anteriorly the LAM is supported by the perineal membrane and muscles in the deep perineal pouch (Figure 2). The perineal membrane is a thick triangular fascial sheet that fills the space between the arms of the pubic arch, and has a free posterior border (Figure 3).

An imaginary line between the ischial tuberosities divides the perineum into two triangular regions. Anteriorly, the urogenital triangle contains the roots of the external genitalia and the opening of urethra and vagina. Posteriorly, the anal triangle contains the anal aperture (Figure 3). The central anchor point of all musculofibrous components of the pelvic floor is the perineal body (Figure 3). It connects the perineal structures of the urogenital triangle and muscles in the deep perineal pouch, the LAM and the external anal sphincter (EAS). Moreover, it anchors the left and right LAM in the midline. The central tendinous part is barely visible to the naked eye and its function is regularly overlooked. The perineal body is of importance to maintain the correct 3D anatomical relationships. Both the external urethral sphincter and the puborectal muscles can compress the urethra and anorectum optimally when the perineal body is intact [5, 7].

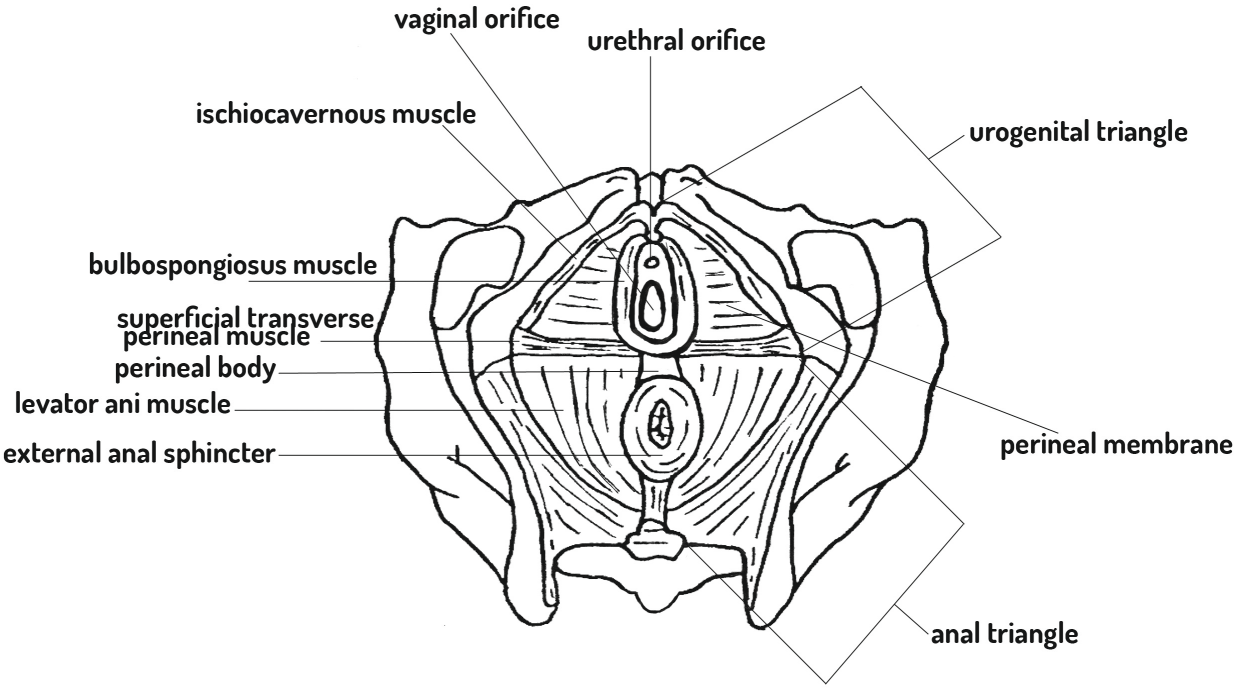

Figure 3 Pelvis, pelvic floor and perineum

The anal triangle includes the anal canal, the anal sphincters, and ischioanal fossae. The anal aperture is centrally located in the anal triangle and is surrounded on either side by ischioanal fossa. The rectum terminates in the anal canal. The anal canal is surrounded by an inner epithelial lining, a vascular subepithelium, anal sphincter complex and fibromuscular supporting tissue. The anal sphincter complex consists two cylindrical layers: the EAS and internal anal sphincter (IAS) separated by the composite longitudinal coat (Figure 4). Although the EAS and IAS form a single unit, both are distinct in structure and function. The IAS forms the inner cylinder and is a thickened continuation of the circular smooth muscle of the bowel and ends at the junction of the superficial and subcutaneous EAS (Figure 4). The outer cylinder, the EAS is made up of skeletal muscle. Structurally, the EAS (Figure 4) is subdivided into three parts: the subcutaneous, superficial and deep. In females, the EAS is shorter anteriorly. The deep EAS blends with the fibers of the puborectalis muscle. The superficial EAS is attached anteriorly to the perineal body and posteriorly to the anococcygeal ligament, which is attached to the tip of the coccyx. The subcutaneous part is circular that surrounds the anal aperture just beneath the skin and may have attachments to the perineal body anteriorly and the anococcygeal ligament posteriorly[6, 7].

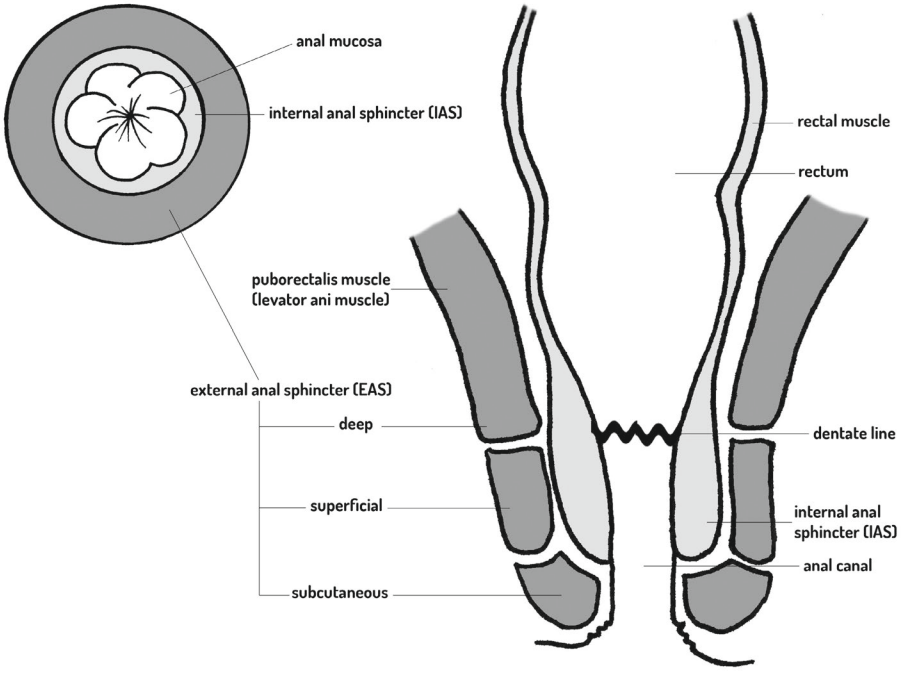

Figure 4 Anal sphincter

Pelvic floor symptoms and injury

Since the pelvic floor is important in various functions as indicated earlier, injury to the pelvic floor can lead to dysfunctions of these various functions. These dysfunctions or PFD can include urinary or anal incontinence, POP, pelvic pain, sexual dysfunction, etcetera.

What is the pathophysiology of PFD? The pathophysiology for PFD is complex. Many factors are involved, such as overactive pelvic floor muscles (PFM), PMF weakness or connective tissue damage. How does this injury or muscle weakness occur? Again, various factors can play a role, such as obesity, chronic increase in intra-abdominal pressure (constipation, heavy physical work, excessive coughing), hormonal changes in menopause, aging, connective tissue diseases, and pelvic floor surgery[8, 9]. One of the most important factors in the etiology of PFD are pregnancy and vaginal delivery[8]. Trauma to the LAM and the anal sphincter are the two most common forms of maternal birth injuries, affecting up to 40% of vaginally parous women[10].

During pregnancy, maternal weight gain and uterine weight increase can lead to an increase in intra-abdominal pressure and thus an overload of the ligamentous structures, fascias, and PFM[11]. The pregnant uterus further leads to an increase in the urethrovesical angle, which in turn leads to an increase in the mobility of the bladder neck and can contribute to the onset of urinary symptoms[12]. Also some authors have shown that an increase in the size of the hiatal area could occur in the antepartum period, which may be a risk factor for POP[13, 14].

During vaginal birth, the fetus needs to pass through the levator hiatus in the pelvic floor. The muscles, connective tissues and nerves can be damaged during this process. During vaginal birth, the LAM are stretched 1.5 to more than 3 times their normal length, depending on the size of both the fetus opening and the PFM[15, 16]. This substantial stretching can injure the LAM by stretch (overdistension, or microtrauma also called levator ballooning) or avulsion (detaching of the muscle insertion from its origin on the inferior pubic ramus, or macrotrauma)[17]. Levator avulsion occurs in 10-36% of women after vaginal delivery[18-20]. Both levator avulsion and levator hiatal ballooning are independent risk factors for female POP and prolapse recurrence[21, 22]. The strong association between POP and LAM injury can be explained to a large extent by a larger levator hiatus and weaker pelvic muscles after levator avulsion or levator overdistention[23].

In addition to damage to the LAM, injury to the anal sphincter complex can also lead to PFD[24, 25]. OASI has been reported in 0.5% to 5% of women

after vaginal delivery[25, 26]. The true incidence is likely much higher due to missed diagnosis and possibly occult tears as well[27, 28]. OASI are associated with increased risk of anal incontinence in both the immediate postpartum period and throughout a women's life[29, 30]. Furthermore, we see that women with OASI have a higher probability of simultaneous LAM injury[31, 32].

In addition, expulsion efforts of the mother during labor and the force uterine contractions exert on the fetal head can lead to stretching and compression of the pelvic nerves. This can lead to ischemia of these nerves followed by temporary or permanent nerve damage[33]. It is believed that nerve lesion during delivery can cause muscle atrophy, altering function and morphology of the pelvic floor[34].

Whether a woman suffers injury to the pelvic floor or anal sphincter during childbirth or not depends on many things. Multiple risk factors have been identified, of which forcipal extraction presents the greatest risk factor[35-38]. Other factors described are advanced maternal age at first delivery, prolonged second stage, an occipitoposterior presentation, fundal expression (Kristeller maneuver)[39], high fetal birth weight, midline episiotomy, and greater fetal head circumference[31, 36, 39-45]. Some protective factors might be upright delivery position[46]. The role of maternal body mass index (BMI), perineal support, and mediolateral episiotomy remains unclear[36-38, 44, 47-49]. However, the angle of placement appears to play an essential role in prevention of injury when placing a mediolateral episiotomy[50, 51].

Optimal primary repair of OASI after childbirth is essential for the reduction of anal incontinence in the long and short term. Repair of the LAM (both ballooning and avulsion) is described by some research groups[52-55]. Unfortunately, at this stage it is still experimental. For this reason, current research efforts are focused on preventing and minimizing these injuries.

Diagnosis of levator ani muscle avulsion, ballooning and residual defect of the anal sphincter (pelvic floor imaging)

Imaging levator ani muscle

The LAM and the levator hiatus can be visualized by Magnetic Resonance Imaging (MRI), perineal 3D/four-dimensional (4D) PFUS or endovaginal ultrasound (EVUS). MRI was the first method to assess LAM and is therefore considered the gold standard for the diagnosis of LAM avulsion[56]. However, the MRI has some shortcomings such as cost, accessibility, and inability to use it in women with claustrophobia or women with metal implants.

In mid-2000 the 3D/4D ultrasound technique was introduced. This technique converts a standard two-dimensional (2D) greyscale ultrasound image into a volumetric dataset (3D) and in 4D interactive dataset. The perineal PFUS allows the investigator to perform an assessment of the LAM and anal sphincter complex[10, 28, 57-59]. Perineal PFUS is more readily available, more accessible, less expensive and invasive in comparison to MRI. Also, women with metal implants and/ or claustrophobia can undergo perineal PFUS[59]. Beside this, perineal PFUS has a good interobserver reliability and can be learned in a short period of time[18, 60-62].

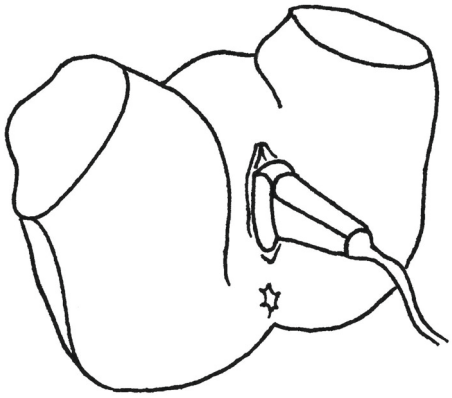

Figure 5 perineal pelvic floor ultrasound (PFUS)

Perineal PFUS is performed after voiding in supine position. An abdominal 4D transducer is placed on the perineum or vulva (Figure 5 shows our method).

A 2D assessment of the pelvic floor is made. In this 2D setting an assessment in longitudinally position (for bladder neck/urethra, prolapse, and LAM assessment) and in transversely (for assessment of anal canal and sphincters) is made (Figure 6).

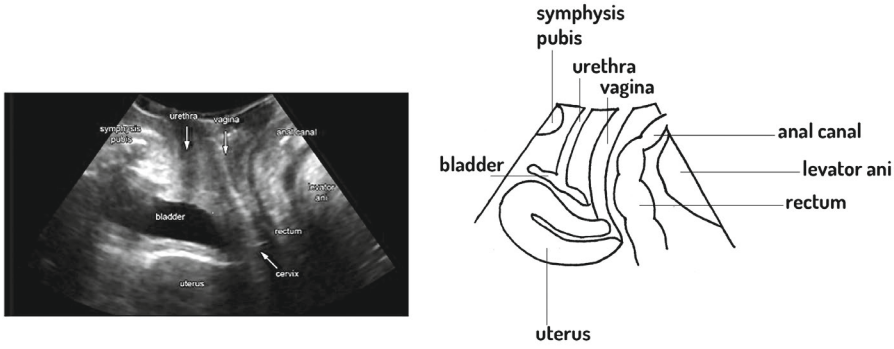

Figure 6 Midsagital 2D assessment of the pelvic floor with pelvic floor ultrasound

After this, a 4D assessment of the pelvic floor is performed. A volume acquisition is performed at rest, at PFMC and at maximum Valsalva maneuver (at least 6 seconds' duration). During post processing, all acquired scans can be manipulated to evaluate the LAM in the plane of the minimal hiatal dimensions[59, 63, 64].

To assess LAM integrity the plane of minimal hiatal dimensions is identified at PFMC. In this plane a tomographic ultrasound imaging (TUI) of the puborectalis component of the LAM, with an interslice interval of 2.5 mm is made (see Figure 7). The diagnosis of levator avulsion is made when at least the three central slices show an abnormal insertion of the puborectalis muscle on the inferior pubic ramus (Figure 7b, c)[59, 62]. Measurement of the levator-urethral gap can be helpful in difficult cases[65].

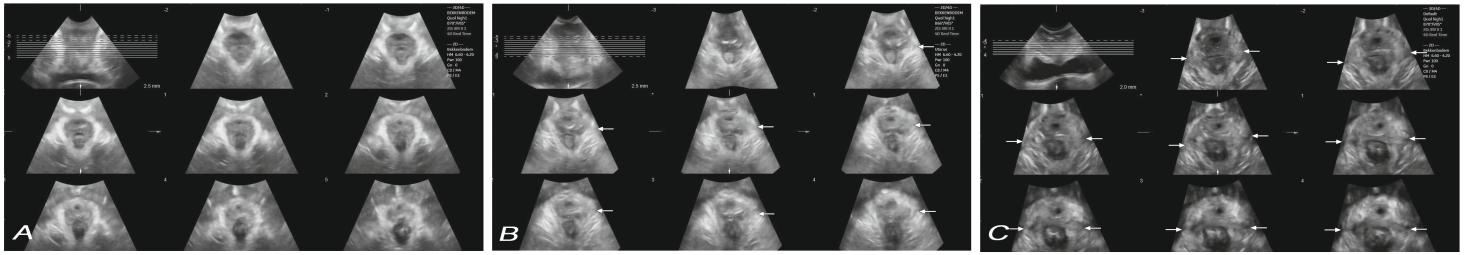

Figure 7 Example of a normal levator ani muscle (A), unilateral (B), and bilateral (C) avulsion of the levator during pelvic floor muscle contraction with perineal pelvic floor ultrasound. Arrow depicts site of avulsion.

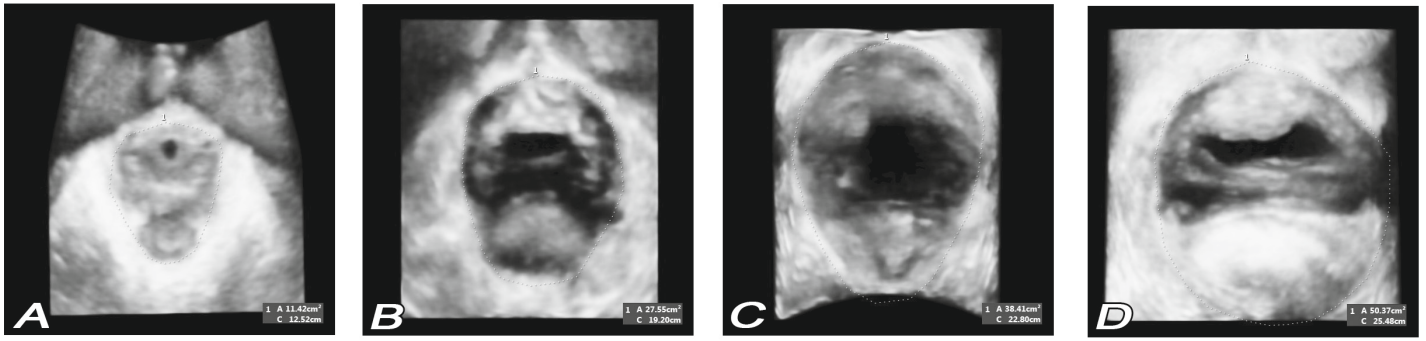

Figure 8 A. normal hiatus during maximum Valsalva maneuver. B, C and D depicts an example of mild, reasonable and severe ballooning.

Hiatus measurements can be performed to determine the size of the levator hiatus in the rendered image at rest, PFMC and maximum Valsalva maneuver[63]. In maximum Valsalva maneuver an enlarged hiatus can be identified. An enlarged hiatus or ballooning is divided into 4 categories, namely mild (> 25cm^2 – 29.9cm^2), moderate (≥ 30cm^2 – 34.9cm2), reasonable (≥ 35cm^2 – 39.9cm^2) and severe ballooning (≥ 40cm^2) (Figure 8)[66].

Imaging of anal sphincter
Endoanal ultrasound using a high-resolution 10 MHz 360˚ rotational probe is considered the gold standard for anal sphincter assessment in the diagnostic workup for anal incontinence[67]. However, this technique is more bothersome for the patient and this extra equipment is not widely available. Another disadvantage of endoanal ultrasound is that the anatomy is disrupted by the insertion of the rectal endoprobe. This endoprobe leads to shortening of the anal canal and compression or dilation of mucosa, IAS and EAS. In addition, the ability to perform a dynamic assessment of the anal sphincter is a great advantage over endoanal sphincter imaging. During contraction, defects in the sphincter become more visible[68]. Several studies have shown that perineal PFUS is a non-invasive alternative to endoanal ultrasound[58, 59, 69, 70]. In our current studies, the anal sphincter is assessed with a 3-9 mHz 4D microconvex probe (RNA5-9 H48651DB). Unfortunately, this probe is no longer manufactured. Our future studies will therefore be performed with an abdominal or vaginal probe, which is internationally recognized as the standard method for assessing the sphincter with perineal PFUS[59, 69].

To image the anal sphincter, the transducer is rotated 90 degrees and applied to the introitus or ventral aspect of the perineum (Figure 9).

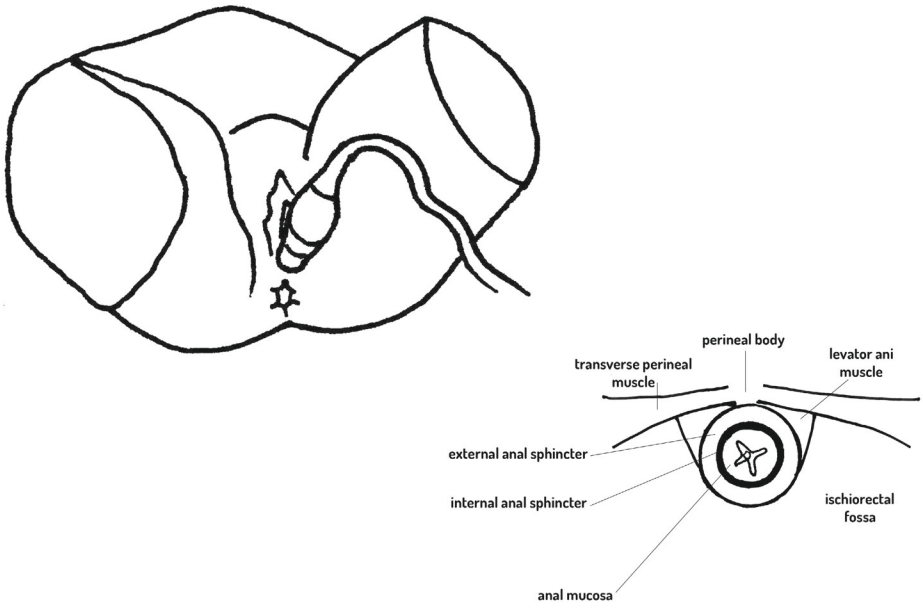

Figure 9 Placement of transducer with perineal pelvic floor ultrasound for assessment of the anal sphincter, and schematic illustration of imaged structures in the resulting coronal or transverse plane.

4D volumes of the anal sphincter are obtained at rest and PFMC. After this, the integrity of the anal sphincter is assessed with TUI of the anal canal. With this TUI, a set of eight slices is obtained from puborectalis loop level (slice 1) to the level of the anodermis (slice 8), with a variable distance between each slide depending on the length of the sphincter, leaving six slices to demonstrate the entire sphincter. A residual sphincter defect of EAS and/or IAS was defined as a discontinuity in the texture of the EAS or IAS of ≥ 30 degrees in at least 4 out of 6 slices (Figure 10)[28, 59, 71].

There are other ultrasound methods for assessing pelvic floor injury, however this introduction has focused on the ultrasound methods used in our studies.

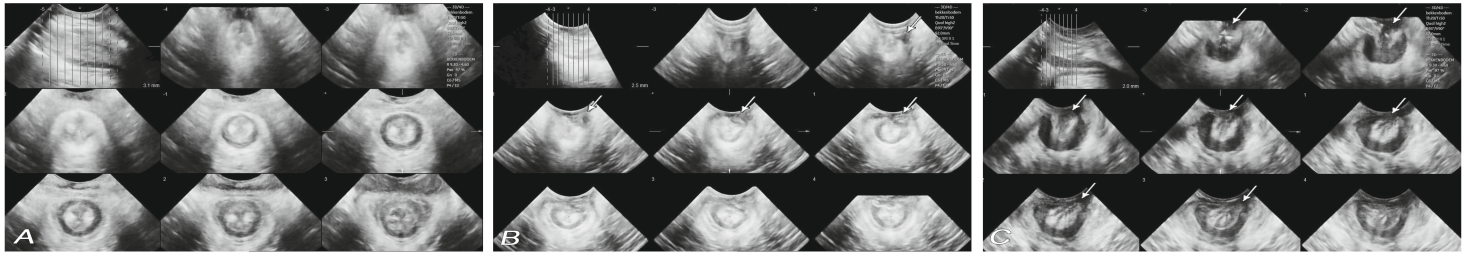

Figure 10 Example of intact anal sphincter (A), residual defect of external anal sphincter (B) and complete residual defect of anal sphincter (internal and external) (C) during maximal pelvic floor muscle contraction with 3D/4D transperineal ultrasound.

Imaging with VR

3D ultrasound has many advantages over 2D ultrasound, however, currently 3D volumes are mainly viewed and assessed using 2D media. These 2D media do not provide depth perception, which is necessary for optimal interpretation of 3D and 4D echo volumes. This is also the case in levator hiatus measurements. It has been postulated that, in real multiplanar MRI construction, the levator hiatus is visualized as a non-Euclidean hyperbolic structure (see Figure 11)[72, 73]. Perineal PFUS measurements are currently performed on 2D rendered images, obtained from data volume analysis of 4D cineloops. The non-Euclidean nature, i.e. the concave and convex shape of the levator hiatus, is therefore not taken into consideration in volume measurements obtained by perineal PFUS. This may overestimate or underestimate the 'real' levator hiatal area.

In 2005, the Bioinformatics department of Erasmus MC in Rotterdam opened a Barco I-Space VR system. The I-Space is a CAVE™-like[74] VR system that provides a 3D environment. The images in the I-Space are generated by eight Barco SIM5 digital light processing (DLP) projectors aimed at the four projection screens (2.60 by 1.95 meters) that form the three walls and floor of a small room. The I-Space uses passive 3D projection using stereoscopic glasses to deliver different images to the left and right eye. Because of this difference in position, each eye has a slightly different point of view. The brain is able to construct one 3D image (i.e. a hologram) from these two projected 2D images. An infrared camera (four in all) is installed in each corner of this room for tracking purposes. The tracking system registers the position and orientation of the joystick and the user's head to give him the correct perspective. The wireless joystick is used to operate the V-Scope volume rendering application[75]. This V-scope application provides interaction and manipulation of the volumetric dataset or hologram. Using the joystick it is possible to rotate, translate, enlarge and cut the hologram. In addition, V-Scope offers several other tools, such as a virtual eraser and tools to perform various biometric and semi-automatic volumetric measurements on the hologram.

These volumetric measurement take into account all three dimensions. This semi-automatic algorithm of V-Scope is based on a region growing approach with both grey level and neighborhood variation thresholds. The user selects the thresholds and places a seed point in the structure of interest. The algorithm will then segment the structure of interest starting from the seed point by adding voxels, i.e. 3D pixels, until voxels exceeding one of the thresholds are reached. Prior to a volume measurement all connecting structures that fall within the threshold values have to be

erased in order to limit the segmentation to the structure of interest. Both hypoechoic and hyperechoic structures can be measured using the segmentation algorithm. Due to the depth perception and simple 3D interaction offered by the I-Space the user can quickly check whether the segmentation is correct. If not, additional seed points can be placed, the volume can be manually grown or shrunk and a brush function can be used to add or delete voxels from the segmentation.

Most 3D imaging modalities, such as 3D prenatal ultrasound data sets, computed tomography (CT), MRI, positron emission tomography (PET), and similar modalities, can be visualized with V-Scope in I-Space. Various other departments of Erasmus Medical Centre use the I-Space in both research and clinical practice[76-79]. CAVE™-like VR systems like the I-Space are available in a very limited number of research centers throughout the world and are costly, but a smaller, low cost desktop VR system are available for use in an outpatient clinical setting[80].

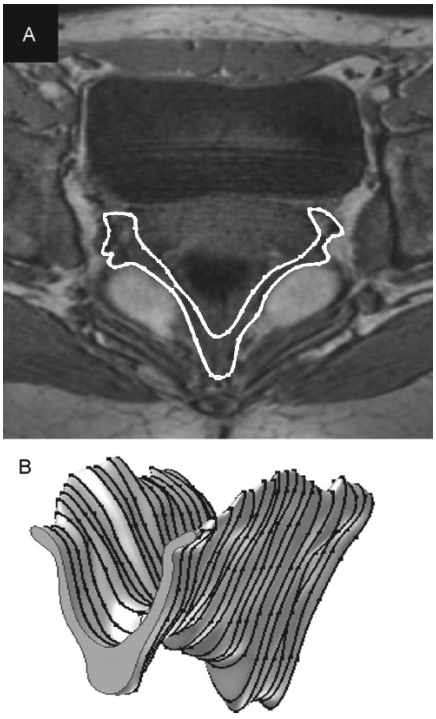

Figure 11 Construction of the pelvic floor model. (A) Levator ani muscle manually outlined from MRI image. (B) 3D computer model generated model from 20 MRI images. MRI, magnetic resonance imaging[73].

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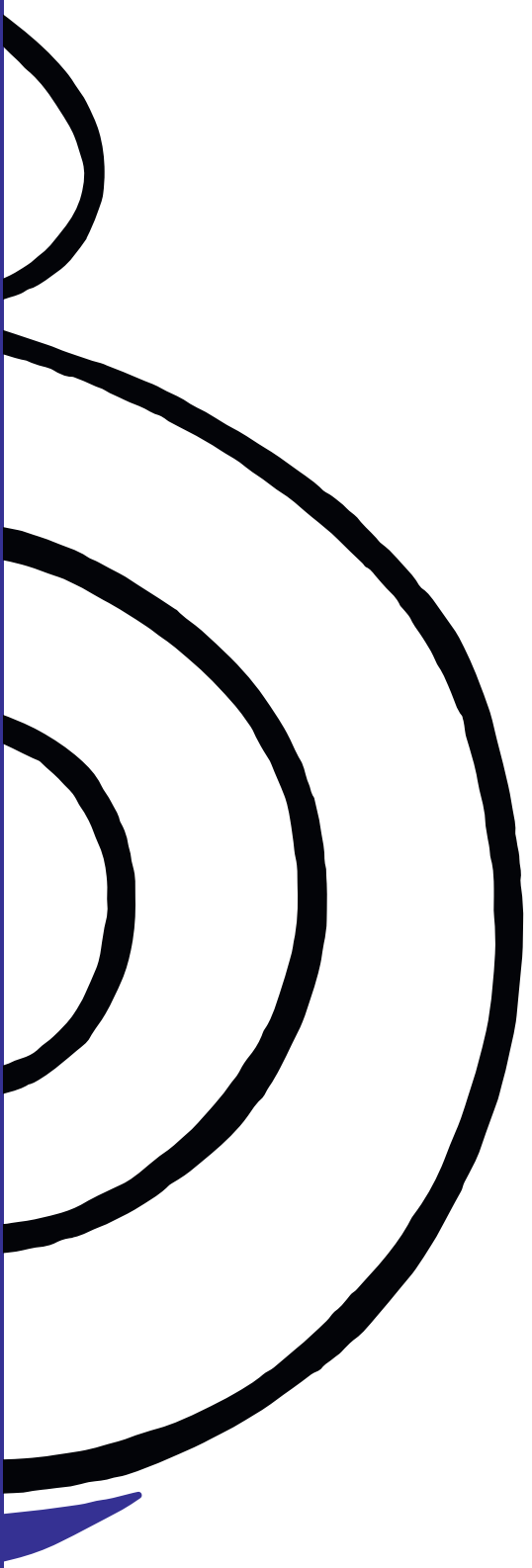

Pelvic floor after vaginal birth

CHAPTER 2

Association of levator injury and urogynecological complaints in women after their first vaginal birth with and without mediolateral episiotomy

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Am J Obstet Gynecol. 2019 Jan;220(1):93.e1-93.e9

ABSTRACT

Background
Pelvic organ prolapse is a common health problem in women and has a negative influence on quality of life. A major cause of pelvic organ prolapse is levator injury.

Objective
The objective of the study was to evaluate the association of mediolateral episiotomy with levator injury (levator avulsion, ballooning, or combined) and urogynecological complaints.

Study Design
A prospective observational cohort study was performed in 204 primiparous women with a spontaneous vaginal delivery without anal sphincter tear in a general hospital between 2012 and 2015. One hundred three of these women had had a mediolateral episiotomy. Validated urogynecological questionnaires and transperineal 3-dimensional/4-dimensional ultrasound were completed after delivery. Outcome measures were levator avulsion, ballooning (hiatal area of more than 25 cm2), and urogynecological questionnaire scores. Statistical analysis was performed using univariate and multiple logistic regression analysis.

Results
The median time at investigation after vaginal delivery was 13 months (range 6–33). Levator injury (avulsion, ballooning, or combined) was identified in 35 of the 103 women who had undergone mediolateral episiotomy (40.0%) and 33 of the 101 women without episiotomy (32.7%) (P = .69). No differences were found in the incidence of levator avulsion 27 (26.7%) vs 23 (22.8%) (P = .53) or in levator ballooning (20 [19.4%] vs 23 [22.8%] (P = .58) between both groups. There was an association between longer duration of the second stage of labor and the incidence of levator avulsion (odds ratio, 1.24 [95% confidence interval, 1.01–1.52]). Nonocciput anterior fetal position increased the risk of levator ballooning and levator injury (odds ratio, 10.19 [95% confidence interval, 1.89–54.91] and odds ratio, 12.16 [95% confidence interval, 1.41–104.38], respectively). No differences in urogynecological complaints were found.

Conclusion
Mediolateral episiotomy is not associated with the occurrence of levator injury or urogynecological complaints in women with a spontaneous vaginal delivery who did not obtain an anal sphincter injury. Levator injury was associated with a prolonged second stage of labor and a nonocciput anterior fetal position.

INTRODUCTION

Pelvic organ prolapse (POP) is a common health problem in women and has a negative influence on quality of life[1, 2]. A major cause of POP is pelvic floor injury during delivery. Specific types of pelvic floor injury include levator avulsion and levator ballooning.

Levator avulsion occurs in 13–36% of women after vaginal delivery. Levator ani muscle overextension or levator ballooning can also be related to POP and is strongly associated with symptoms and clinical signs of prolapse[3-5]. This levator ballooning (a hiatal area of more than 25 cm^2 in Valsalva) occurs in 33% of primiparous women[3, 6, 7]. Both are also associated with a higher recurrence of POP after POP surgery and a decrease in pelvic floor muscle strength[3-6, 8]. Attempts to repair levator injuries so far have not been proven successful[9]. Therefore, prevention is important.

Prevention starts with identifying the risk factors and protective factors for levator avulsion. One possible risk or protective factor is the use of a mediolateral episiotomy during vaginal delivery. A mediolateral episiotomy can reduce the incidence of anal sphincter injury[10]. However, while in regard to protecting the levator ani muscle, some studies have found a causative effect of mediolateral episiotomy on levator avulsion, and others have found a protective effect or no effect[3, 11-14]. Therefore, the influence of a mediolateral episiotomy on levator injury and urogynecological complaints remains unclear.

If there is a potential benefit of mediolateral episiotomy, this must be weighed against its potential adverse effects. The potential adverse effects include unsatisfactory anatomic results, increased blood loss, increased postpartum pain, higher rates of infection, wound dehiscence, and sexual dysfunction[15-18].

This uncertainty regarding the benefits of mediolateral episiotomy led us to the following research questions: is a mediolateral episiotomy a risk factor or a protective factor for levator injuries (levator avulsion, ballooning, or combined) and for the occurrence of urogynecological complaints? Furthermore, we examined whether other determinants were involved (i.e., age, birthweight, etc.). To answer these questions, we used validated questionnaires and transperineal 3-dimensional/4-dimensional (3D/4D) ultrasound in women with and without mediolateral episiotomy after a first, spontaneous vaginal delivery who did not obtain an anal sphincter injury.

MATERIAL AND METHODS

This was a prospective observational cohort study comparing women who received a mediolateral episiotomy and those who did not. Ethical approval for this study was obtained by the medical research ethics committee of the Erasmus Medical Centre (MEC-2012-058).

All women who underwent a first spontaneous vaginal delivery in our hospital with or without mediolateral episiotomy received a written invitation 3 months after their delivery to participate in this study between 2012 and 2015. Women who delivered prematurely, delivered a fetus in noncephalic position, experienced an instrumental vaginal delivery, median episiotomy, obstetric anal sphincter injury, or secondary Caesarean section were not included in the study. The investigators were not involved in the management of the participants' deliveries.

The women who agreed to participate were scheduled for an appointment no sooner than 6 months after delivery at the outpatient clinic. Participants received compensation for their travel and parking expenses.

After obtainment of written informed consent, the patients completed an anonymized standardized questionnaire on urogynecological complaints. A detailed examination of the perineum and 3D/4D transperineal ultrasound investigation were performed. Antenatal, intrapartum and fetal characteristics were retrospectively obtained from the medical file. In The Netherlands the second stage of labor is defined as the time period from the moment of active pushing onward until the delivery of the baby.

Perineal examination
The scar of the mediolateral episiotomy was studied by the investigator (L.S.). The angle, length, and position of the scar against the midline of the posterior fourchette were measured.

Questionnaire
We used the following validated questionnaires: the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12[19], Pelvic Floor Impact Questionnaire-7[20], Urogenital Distress Inventory scale-6[21], Fecal Incontinence Severity Index[22], Incontinence Impact Questionnaire-7[21], and Fecal Incontinence Quality of Life scale[22].

3D/4D transperineal ultrasound

A 3D/4D transperineal ultrasound was performed in the supine position and after voiding using a Voluson E Expert system using a 4–8 MHz RAB abdominal probe (GE Healthcare, Chalfont St Giles, United Kingdom) as previously described by Dietz[23]. The ultrasound volumes were obtained at rest, pelvic floor muscle contraction, and maximal Valsalva. All volumes were obtained by an experienced investigator (L.S.).

Offline analysis of the recorded 3D/4D transperineal ultrasound volumes were performed by 3 experienced investigators (L.S., D.O., A.S.). The investigators were blinded against all clinical data and therefore unaware of the delivery outcome and whether the participant had or had not had a mediolateral episiotomy. Analysis was done using specialized 3D imaging software, 4D View version 17.0 (GE Healthcare).

Levator avulsion was scored using a scoring system based on tomographic ultrasound imaging as previously described by Dietz[24]. Levator avulsion was diagnosed when 3 central slices (reference slice and the slices 2.5 and 5 mm cranial) showed an abnormal muscle insertion[25]. Figure 1 depicts a normal, unilateral, and bilateral levator avulsion on 3D/4D transperineal ultrasound.

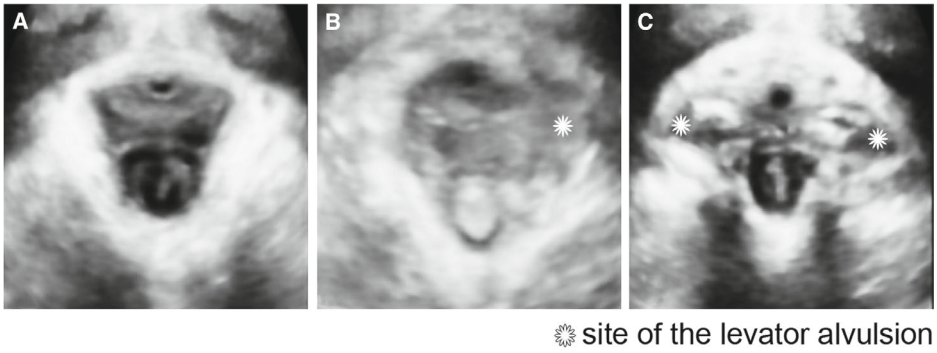

Figure 1 Normal levator, unilateral, and bilateral avulsion of levator during contraction. Example of a normal levator **(A)**, unilateral **(B)**, and bilateral **(C)** avulsion of the levator during contraction with 3D/4D transperineal ultrasound.

The hiatal area was measured during maximum Valsalva. Levator ballooning was scored when the levator hiatal area was >25 cm^2. Previous research indicate that a cut of 25 cm^2 can be defined as abnormal distensibility, or ballooning, of the levator hiatus in relation to complains and clinical prolapse[6, 7]. Figure 2A gives an example of a normal hiatus during maximal Valsalva. Figure 2, B and C, depicts an example of mild and marked levator

ballooning. Women with an avulsion, ballooning, or a combination were scored as having levator injury.

To determine good interobserver and intraobserver reliability of hiatal area measurements, 20 patients were selected at random. All investigators independently performed 3 volume measurements of each data set; the mean measurement was used for comparison. The interobserver intraclass correlations coefficients were above 0.90.

For intraobserver reliability all investigators repeated another 3 measurements at least 2 weeks after the first series in 20 randomly chosen data sets. The mean of these measurements was compared with the mean of the 3 previously obtained measurements from the same 20 data sets. The interobserver intraclass correlations coefficients were above 0.80 (reflects an excellent reliability)[26, 27].

Primary outcome measures were levator avulsion, levator ballooning, and the score of the urogynecological questionnaire.

Statistical analysis

A power analysis was calculated. Previous data regarding the prevalence of a levator avulsion after first vaginal birth have indicated a mean occurrence of approximately 25%[5]. Our hypothesis was that a mediolateral episiotomy reduced the risk of levator avulsion. We considered a difference of 20% to be clinically relevant. We assumed an alpha risk of 5% and a beta risk of 20% (ie, a power of 80%). With these criteria we needed at least 91 women in each group; therefore, we planned to include 100 women in both groups.

Statistical analysis was performed using IBM SPPS Statistics version 20.0. The comparison of means between groups was performed by the Student t test after checking for normal distribution of the variables; otherwise, a Mann-Whitney U test was used. Univariate and multiple logistic regression analysis was used for multiple comparisons of quantitative variables between groups.

For the logistic regression, we controlled for known risk or protective factors for occurrence of obstetric trauma like levator avulsion or obstetric anal sphincter trauma including maternal age, mediolateral episiotomy, duration of second stage of labor, fetal birthweight, and nonocciput anterior fetal head position[5, 28-30].

For the study of categorical variables, Fisher exact and χ2 tests were used as appropriate. For ordinal data the Kruskal-Wallis test was used. A 2-sided value of P < .05 was considered to indicate statistical significance.

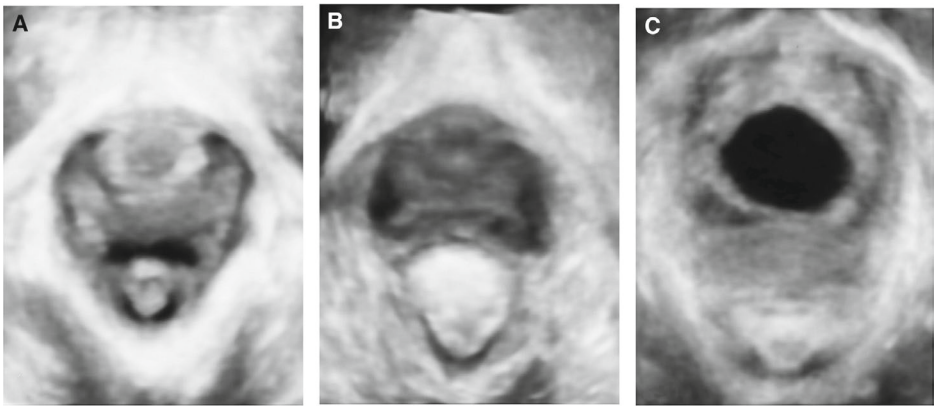

Figure 2 Normal hiatus, mild, and marked levator ballooning during maximal Valsalva. Example of a normal **(A)** hiatus during maximal Valsalva with 3D/4D transperineal ultrasound and mild **(B)** and marked **(C)** levator ballooning.

RESULTS

A total of 2535 women were invited to participate, but only 204 women with a first, spontaneous vaginal delivery (8%) volunteered to participate in our study. Characteristics of participants and nonparticipants are reflected in Table 1. Participants were more likely to be white and had a longer second stage. In nonparticipants more women were induced and received more frequently epidural analgesia.

The median time at investigation after vaginal delivery was 13 months (range, 6–33 months). Women who received a mediolateral episiotomy had experienced more blood loss and a longer duration of the second stage of labor than women with no mediolateral episiotomy (Table 2).

The mediolateral episiotomy was placed at the left side of posterior fourchette. Indications for performing the mediolateral episiotomy were fetal distress (36.6%), failure to progress (18.8%), tight or short perineum (21.8%), or a combination (22.8%). The median angle of the episiotomy against the midline of the posterior fourchette was 35° (range 10–60°). The median length was 3 cm (range, 1.5- 5 cm).

Table 1 Baseline characteristics between participants and nonparticipants

Characteristics	**Study participants (n = 204)**	**Non-participants (n = 2535)**	**P value**
	Mean ± SD or median (IQR) or %	Mean ± SD or median (IQR) or %	
Age, y	30.1 ± 3.9	29.5 ± 4.8	.05
Caucasian ethnicity[a]	91.7%	80.1%	< .05
BMI, kg/m^2	23.2 (21.3–26.3)	23.0 (20.9–26.1)	.64
Mediolateral episiotomy	51%	51%	.52
Birthweight, g	3362 ± 453	3342 ± 470	.55
Blood loss, mL	300 (200–550)	300 (200–500)	.89
Duration of second stage of labor, min[a]	38 (22–55)	31 (18–48)	< .05
0–30	37%	47%	.09
30–60	42%	39%	.45
60–90[a]	17%	11%	< .05
>90 min	4%	3%	.52
Induction[a]	23%	33%	< .05
Use of oxytocin	64%	69%	.09
Use of epidural analgesia[a]	42%	53%	< .05
Occiput anterior fetal head position	3.4%	4.4%	.34

Depending on normal distribution or not either Student *t* test or Mann-Whitney *U* test was used. For the categorical variables, we used the Fisher exact or χ^2 tests. The Kruskal-Wallis was used for ordinal-level dependent variables. Second stage of labor is defined as the time period from the moment of active pushing onward until the delivery of the baby. a p< .05

The episiotomy was placed with a median of 0.5 cm (range 0–2 cm) distance against the midline of the posterior fourchette. Of the women without mediolateral episiotomy, 18% of the women had a first-degree perineal tear, 40% had a second-degree perineal tear, 28% a labial and/or vaginal tear, and 14% had no tear.

Table 2 Baseline characteristics between women with and without a mediolateral episiotomy

Characteristics	No mediolateral episiotomy		With mediolateral episiotomy		P value
	n	Mean ± SD or median (IQR) or n (%)	n	Mean ± SD or median (IQR) or n (%)	
Age, y	101	30.5 ± 4.2	103	29.8 ± 3.6	.19
Caucasian ethnicity	101	91 (90.1%)	102	96 (93.2%)	.29
BMI, kg/m^2	99	22.7 (21.2–26.3)	101	23.4 (21.3–26.0)	.60
Birth with midwife-led car[e]a	101	9 (8.9%)	103	2 (1.9%)	.03[a]
Birthweight, g	101	3333 ± 468	103	3392 ± 467	.93
Blood loss, mL[a]	101	200 (150–400)	102	355 (218–585)	< .001[a]
Duration of second stage of labor, min[a]	101	34 (17–52)	103	41 (26–61)	.002[a]
0–30		31 (42%)		19 (30%)	.212
30–60		32 (43%)		27 (43%)	1.00
60–90		9 (12%)		14 (22%)	.168
>90		2 (3%)		3 (5%)	.661
Induction	101	24 (23.8%)	103	23 (22.3%)	.81
Use of oxytocin	101	61 (60.4%)	103	70 (68.0%)	.26
Use of epidural analgesia	101	48 (47.5%)	103	37 (35.9%)	.09
Occiput anterior fetal head position	101	97 (96.0%)	103	100 (97.1%)	.68

Depending on normal distribution or not either Student t test or Mann-Whitney U test was used. For the categorical variables, we used the Fisher exact or χ^2 tests. The Kruskal-Wallis was used for ordinal-level dependent variables. Second stage of labor is defined as the time period from the moment of active pushing onward until the delivery of the baby. a p< .05

Levator injury (avulsion, ballooning, or a combination) was identified in 33.3% of all included patients. No difference in levator injury was found between women with and without mediolateral episiotomy (35 (40.0%) vs 33 (32.7%%) (P = .69).

A levator avulsion was identified in 50 of the women (24.5%). Fifty-six percent of the 50 women had an unilateral avulsion, of whom 57% had an avulsion on the left side. There were no significant differences in the incidence of levator avulsion, 27 (26.7%) vs 23 (22.8%) (P = .53), between women with and without mediolateral episiotomy.

Levator ballooning was identified in 43 of all women (21%), of whom 41.9% were without levator avulsion. In the majority of patients (51%), ballooning was classified as mild (>25–29.9 cm2). Twenty-eight percent had moderate ballooning (≥30 to 34.9 cm2), reasonable (≥35 to 39.9 cm2) in 14%, and 7% had severe ballooning (≥40 cm2). There was also no significant difference in the incidence in levator ballooning between both groups (20 (19.4%) vs 23 (22.8%) (P = 0.58).

A multiple logistic regression analysis was used to analyze quantitative variables between different groups (Table 3, Table 4, Table 5). The first group compared women with and women without levator injury (Table 3). A nonocciput anterior fetal head position remained a risk factor for levator injury (adjusted odds ratio [OR], 12.16 [95% confidence interval (CI), 1.41–104.38).

A longer duration of the second stage of labor increased the risk for levator avulsion (OR, 1.24 [95% CI, 1.01–1.52]) (Table 4). Also a nonocciput anterior fetal head position remained a risk factor for levator ballooning (adjusted OR, 10.19 [95% CI, 1.89–54.91]) after correction (Table 5).

Table 3 Crude and adjusted estimations for levator injury, meaning women with an avulsion, ballooning, or a combined injury

Characteristics	No levator injury		Levator injury		*P* value of ANOVA	Nonadjusted OR[a] Odds (95% CI)	*P*value[a]	Adjusted OR[b] Odds (95% CI)	*P*value[b]
	n	Mean ± SD or median (IQR) or n (%)	n	Mean ± SD or median (IQR) or n (%)					
Age, y	136	30.0 ± 4.1	68	30.5 ± 3.5	.31	1.04 (0.96–1.11)	.34	1.02 (0.94-–1.10)	.61
Duration of second stage of labor (every 15 min)	136	34 (21–51)	68	45 (25–60)	.05	1.01 (1–1.02)	.07	1.20 (0.99–1.45)	.06
Mediolateral episiotomy	136	70 (51%)	68	33 (49%)	.58	0.89 (0.50–1.59)	.69	0.84 (0.45– 1.55)	.50
Occiput anterior fetal head position	136	135 (99%)	68	62 (91%)	.35	13.07 (1.54–111)	.02[c]	12.16 (1.42– 104.38)	.02[c]
Birthweight (every 500 g)	136	3377 ± 470	68	3334 ± 418	.56	1.00 (1.00–1.00)	.53	0.84 (0.60–1.19)	.33

ANOVA, analysis of variance; *CI*, confidence interval; *IQR*, interquartile range; *n*, number of patients; *OR*, odds ratio.

[a] Crude logistic regression model; [b] Multiple logistic regression analysis adjusted for age, duration of second stage of labor (the time period from the moment of active pushing onward until the delivery of the baby), mediolateral episiotomy, occiput anterior fetal head position, and birthweight.

[c] Significant *P* value.

Table 4 Crude and adjusted estimations for levator avulsion

Characteristics	No levator avulsion		Levator avulsion		*P* value of ANOVA	Nonadjusted OR[a] OR (95% CI)	*P*value[a]	Adjusted OR[b] OR (95% CI)	*P*value[b]
	n	Mean ± SD or median (IQR) or n (%)	n	Mean ± SD or median (IQR) or n (%)					
Age, y	154	30.4 ± 3.4	50	30.1 ± 4.0	.56	1.03 (0.94–1.11)	.56	1.01 (0.93–1.10)	.85
Duration of second stage of labor (every 15 min)	154	34 (20–52)	50	45 (32–61)	.02[c]	1.01 (1.00–1.03)	.03[c]	1.24 (1.01–1.52)	.04[c]
Mediolateral episiotomy	154	76 (49%)	50	27 (54%)	.67	1.21 (0.64–2.28)	.57	1.10 (0.56–2.16)	.77
Occiput anterior fetal head position	154	151 (98%)	50	46 (92%)	.12	4.38 (0.95–20.27)	.06	4.17 (0.88–19.90)	.07
Birthweight (every 500 g)	154	3372 ± 422	50	3332 ± 463	.62	1.00 (1.00–1.00)	.58	0.82 (0.56–1.21)	.32

ANOVA, analysis of variance; *CI*, confidence interval; *IQR*, interquartile range; *n*, number of patients; *OR*, odds ratio.

[a] Crude logistic regression model; [b] Multiple logistic regression analysis adjusted for age, duration of second stage of labor (the time period from the moment of active pushing onward until the delivery of the baby), mediolateral episiotomy, occiput anterior fetal head position, and birthweight.

[c] Significant *P* value.

Table 5 Crude and adjusted estimations for levator ballooning (>25 cm^2)

Characteristics	No levator ballooning		Levator ballooning		*P* value of ANOVA	Nonadjusted OR[a] Odds (95% CI)	*P*value[a]	Adjusted OR[b] Odds (95% CI)	*P*value[b]
	n	Mean ± SD or median (IQR) or n (%)	n	Mean ± SD or median (IQR) or n (%)					
Age, y	161	30.5 ± 4.1	43	30.6 ± 3.3	.47	1.04 (0.95–1.13)	.43	1.02 (0.94–1.12)	.56
Duration of second stage of labor (every 15 min)	161	37 (22–56)	43	41 (20–55)	.86	1.00 (0.99–1.01)	.94	1.00 (0.80–1.25)	.98
Mediolateral episiotomy	161	83 (52%)	43	20 (50%)	.55	0.82 (0.42–1.60)	.56	0.86 (0.42–1.76)	.68
Occiput anterior fetal head position	161	159 (99%)	43	38 (88%)	.01[c]	10.5 (1.95–55.9)	.01[c]	10.19 (1.89–54.91)	.007[c]
Birthweight (every 500 g)	161	3372 ± 461	43	3325 ± 423	.59	1.00 (1.00–1.00)	.54	0.89 (0.59–1.32)	.55

ANOVA, analysis of variance; *CI*, confidence interval; *IQR*, interquartile range; *n*, number of patients; *OR*, odds ratio.

[a] Crude logistic regression model; [b] Multiple logistic regression analysis adjusted for age, duration of second stage of labor (the time period from the moment of active pushing onward until the delivery of the baby), mediolateral episiotomy, occiput anterior fetal head position, and birthweight.

[c] Significant *P* value.

No differences in urogynecological complaints on the different validated questionnaires were found between women with and without mediolateral episiotomy or between women with or without levator avulsion and/or ballooning (Table 6).

COMMENT

A mediolateral episiotomy is neither a risk factor nor a protective factor for levator injury (levator avulsion, levator ballooning, or combined injury). Our results suggest that levator injury in women is a result of a difficult vaginal delivery, in, for example, a longer second stage or nonocciput anterior position.

The greatest stress on the levator ani muscle occurs when the biggest circumference of the head reaches the level of the levator ani muscle. A possible explanation for our finding therefore might be that damage to the levator ani muscle already occurs before placement of a mediolateral episiotomy.

Previous studies reported conflicting outcomes. Three studies suggested that levator avulsions were more common after mediolateral episiotomy[3, 12, 13]. However, multivariable regression analysis revealed a weaker association of mediolateral episiotomy on avulsion rates. Their data revealed that prolonged second stage of labor, forceps delivery, and occipitoposterior position of the fetal head were associated with a higher incidence of levator avulsions.

Two previous studies found similar outcomes as the present study. However, Cassado *et al*[11] showed a lower number of patients with levator avulsions (12.9%). Possibly their number of studied patients was too small. Our higher proportion of women with levator avulsion (24.5%), is comparable with the study of Valsky *et al*[14], which also found no effect of episiotomy on the levator avulsion rates. Based on these previous and the present study, it seems that there is no association between levator avulsion and mediolateral episiotomy.

Table 6 Differences in urogynecological complaints on the different validated questionnaires between women with or without episiotomy and between women with or without levator injury (levator avulsion, ballooning, or combined injury), levator avulsion, and levator ballooning

Questionnaire	Mediolateral episiotomy		Levator injury		Levator avulsion		Levator ballooning	
	Yes	No	Yes	No	Yes	No	Yes	No
Urogenital Distress Inventory scale-6[20]								
On a scale from 0 to 100, the higher the score, the higher the disability	29 (13–46)	33 (17–46)	33 (17–46)	29 (13–46)	33 (16–46)	29 (13–46)	33 (17–42)	29 (13–48)
Prolapse/Urinary Incontinence Sexual Questionnaire-12[18]								
Maximum: 48 (on a scale from 0 to 48, the lower the score, the higher the disability)	38 (36–41)	38 (34–40)	39 (39–42)	38 (35–41)	39 (35–41)	38 (35–40)	40 (36–42)	38 (35–40)
Pelvic Floor Impact Questionnaire-7[19]								
On a scale from 0 to 300, the higher the score the higher the disability	5 (0–21)	0 (0–14)	5 (0–19)	0 (0–14)	5 (0–14)	0 (0–19)	5 (0–19)	0 (0–14)
Fecal Incontinence Severity Index[21]								
On a scale from 0 to 61, the higher the score, the higher the disability	17 (3–27)	12 (0–27)	16 (16–28)	13 (13–27)	17 (5–27)	12 (0–27)	15 (0–30)	15 (2–27)

Numbers are median (interquartile range [IQR]).

There we no significant differences on the questionnaires with Mann-Whitney U test between the groups ($P < .05$).

In our study group, we also analyzed levator ballooning, considered to be another sign of levator injury. We found that women with levator avulsion have a higher risk of levator ballooning, although some women with ballooning had no avulsion. A possible explanation for why women with levator avulsion have a higher risk of levator ballooning is that they are two self-contained pelvic floor injuries that are strongly associated with each other. One recently published study that also found no difference in hiatal area during maximal Valsalva in women with and without mediolateral episiotomy[31]. Our measured hiatal area during maximal Valsalva was similar with theirs.

In addition to levator injury, we analyzed other urogynecological complaints and potential adverse effects of episiotomy. Mediolateral episiotomy did not influence the frequency of urogynecological symptoms. A potential adverse effect was a higher amount of blood loss at delivery, which is in line with the findings of a previous study[32]. We found no differences in urogynecological complaints between the women with and without levator injury.

A possible explanation for this could be that the mean time of analysis after delivery was 13 months. As we know, pelvic floor symptoms could exacerbate at an older age. Our urogynecological complaints scores were comparable with the score of asymptomatic Dutch women in previously studied groups[19-22].

A key strength of our study is that the 3D/4D transperineal ultrasound was performed on average 13 months after birth. We avoided the risk of an overestimation of the levator avulsions because in examining a patient soon after delivery, a hematoma could be mistaken for a levator avulsion. A study showed that hematomas can dissolve between 6 months and a year after delivery[33, 34]. Another strength is that we included urogynecological complaints and pelvic floor injury other than levator avulsion. No other study has addressed these data. A third strength is that we measured angle, length, and position of the scar against the midline of the posterior fourchette.

There were some limitations in our study. The first limitation is selection bias. Only 8% of invited women participated in our study. The fact that our incidence of levator avulsion is comparable with that in previous studies indicates a representative study group. Also, the score on the different questionnaire represents a normal score, suggesting a representative cohort.

The second limitation is that the measurement of the fetal head circumference is not a standard procedure in our department. Therefore, we cannot analyze the influence of head circumference on levator avulsion or ballooning, although Valsky *et al*[14] have shown that this might be an independent risk factor.

The third limitation is that our mediolateral episiotomy is not a real mediolateral episiotomy when we look at the angle and position of the scar against the midline of the posterior fourchette[35]. The origin of a lateral episiotomy is usually 1–2 cm away from the posterior fourchette and may therefore give less relief of the stretch of the perineum at the point of the posterior fourchette and possibly also on the levator ani muscle[36].

The fourth limitation is that our results can be generalized only to white women after a first and normal vaginal delivery without anal sphincter tear who have undergone restrictive use of mediolateral episiotomy on the left side.

The possibility remains that our sample size was too small to find a significant difference between women who had a mediolateral episiotomy and women who had not in terms of levator injury or urogynecological complaints. Indeed, a greater population size may well be necessary to detect a possible small protective effect of mediolateral episiotomy in preventing levator avulsion or ballooning or urogynecological complaints. Whether or not this is the case, it should be considered if the intervention is worthwhile, given the potential adverse effects that result from this procedure.

In terms of clinical relevance, we conclude that to prevent levator injury like levator avulsion or ballooning and urogynecological complaints in the future, further research should focus on developing a good prediction model for difficult vaginal deliveries that is applicable in daily practice.

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CHAPTER 3

Postpartum sexual function; the importance of the levator ani muscle

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ABSTRACT

Introduction and hypothesis
Pelvic floor muscle function plays an important role in female sexual functioning. Smaller genital hiatal dimensions have been associated with sexual dysfunction, mainly dyspareunia. On the other hand, trauma of the levator ani muscle sustained during childbirth is associated with increased genital hiatus which potentially could affect sexual functioning by causing vaginal laxity. This study aims to determine the association between levator hiatal dimensions and female sexual dysfunction after first vaginal delivery.

Methods
This is a secondary analysis of a prospective observational study. 204 women who had a first, spontaneous vaginal delivery at term between 2012 and 2015 were recruited at a minimum of 6 months postpartum. 13 pregnant women were excluded. We analyzed the association of total PISQ-12 score, as well as individual sexual complaints (desire, arousal, orgasm and dyspareunia), with levator hiatal dimensions at rest, maximum Valsalva and during pelvic floor muscle contraction as measured by 4D transperineal ultrasound. Statistical analysis was performed using lineair regression analysis and Mann Whitney U test.

Results
191 women were evaluated at a median of 11 months postpartum. There was no significant association between total PISQ-12 score and levator hiatal dimensions. Looking at individual sexual complaints, women with dyspareunia had significantly smaller levator hiatal area and anterior-posterior diameter on maximum Valsalva. By using multivariate logistic regression analysis however we found dyspareunia wasn't independently associated with levator hiatal dimensions.

Conclusions
After first vaginal delivery sexual dysfunction is not associated with levator hiatal dimensions as measured by 4D transperineal ultrasound.

INTRODUCTION

Childbirth can have a great impact on the sexual functioning of women. Postpartum sexual functioning is influenced by both psychological changes associated with the transition into parenthood, as well as physical changes, such as perineal trauma[1]. Female sexual dysfunction in the DSM V is subdivided into three broad categories, including: sexual interest/arousal disorder, female orgasmic disorder and genitopelvic pain/penetration disorder, including dyspareunia[2]. Previous literature on postpartum sexual function has focused mainly on the complaint of dyspareunia, which is associated with instrumental delivery and the extend of perineal trauma sustained[3].

Physical birth trauma encompasses more than perineal trauma alone. Following first vaginal delivery 13 - 36% of women sustain trauma of levator ani muscle[4-7]. This trauma can be divided into levator ani muscle avulsion and levator over-distension or a combination of both. Trauma of the levator ani muscle is associated with increased genital hiatus (levator ballooning), decreased pelvic floor contractility and is strongly associated with symptoms and clinical signs of prolapse[4, 6-9] . This potentially could affect sexual functioning, as decreased pelvic floor muscle strength has been associated with worse sexual function[10-12].

Literature on the association of genital hiatus, levator trauma and postpartum sexual functioning is sparse. At short term follow-up levator avulsion was associated with symptoms of vaginal laxity and reduced vaginal sensation, but these complaints did not have appreciable effects on women's sexual functioning[13, 14]. At 1 year postpartum women with persistent levator avulsion had significantly more bothersome symptoms of a loose vagina. A trend towards a spoiled sex life as a result of these symptoms was found, but did not reach significance[15].

On the other hand, smaller hiatal dimensions have been associated with sexual dysfunction as well, mainly dyspareunia. Women with provoked vestibulodynia (PVD) were shown to have smaller relative increases in hiatal area on maximum Valsalva, which is associated with hypertonia from the pelvic floor muscles[16].

The aim of this study was to determine the nature of pelvic floor muscle involvement in women with sexual dysfunction after first vaginal delivery. We hypothesized that larger levator hiatus and decreased contractibility of levator ani muscle is associated with female sexual dysfunction, because

of the association with symptoms of reduced vaginal sensation and vaginal laxity. We also hypothesized that a small hiatus in rest and decreased relaxation is associated with dyspareunia. For this purpose we evaluated the biometry of the levator hiatus at rest, pelvic floor muscle contraction (PFMC) and maximal Valsalva using 3D/4D transperineal ultrasound in relation to sexual complaints.

MATERIALS AND METHODS

This is a secondary analysis of a prospective observational study which aimed to evaluate the association of mediolateral episiotomy with levator injury and urogynecological complaints (EpiLeva study)[17]. All participants were recruited at the Amphia Hospital in Breda, Netherlands, between 2012 and 2015. Women who underwent a first spontaneous, term, vaginal delivery of a singleton in cephalic position were included. Women who delivered prematurely, who delivered a fetus in non-cephalic position, who experienced instrumental vaginal delivery, obstetric anal sphincter injury or caesarean section were not included. The investigators were not involved in the management of the participants' deliveries.

Women who agreed to participate filled out standardized urogynaecological questionnaires, and a detailed examination including 3D/4D transperineal ultrasound was performed at a minimum of six months postpartum[17]. Antenatal and intrapartum characteristics were retrospectively obtained from the patients' medical notes.

Assessment of sexual function

For assessment of sexual function the Dutch validated version of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire-12 (PISQ-12)[18] was used. The PISQ-12 is a 12-item, condition-specific tool for assessing sexual function in women with urinary incontinence and/or pelvic organ prolapse. Responses are measured on a 5-point Likert scale ranging from "never" to "always". The total score ranges from 0 to 48, with higher scores indicating better sexual function. For analysis of sexual function in this study we analyzed total PISQ score as well as individual sexual complaints. To define individual complaints we dichotomized PISQ questions. Dyspareunia was defined as answering "always" or "usually" to question: "Do you feel pain during sexual intercourse?". Reduced desire was defined as answering "seldom" or "never" to question: "How often do you feel sexual desire?". Inability to reach an orgasm as answering "seldom" or "never" to question: "Do you climax (have an orgasm) while having sexual intercourse with your partner?". Reduced arousal was defined as answering "seldom" or "never"

to question: ”Do you feel sexually excited (turned on) when having sexual activity with your partner?”.

3D/4D transperineal ultrasound

3D/4D transperineal ultrasound was performed in supine position and after voiding, using a Voluson E Expert system using a 4-8 MHz RAB abdominal probe (GE Healthcare, Chalfont St. Giles, UK) as previously described by Dietz *et al*[19]. The ultrasound volumes were obtained at rest, PFMC and maximal Valsalva. All volumes were obtained by an investigator experienced in performing 3D/4D transperineal ultrasound.

Offline analysis of the recorded 3D/4D transperineal ultrasound volumes were performed by experienced investigators who were blinded against all clinical and obstetric data[17]. Analysis was done using specialized 3D imaging software, 4D View version 17.0 (GE Healthcare, Chalfont St. Giles, UK). The anterior-posterior (AP) diameter of the levator hiatus, the left-right (LR) transverse diameter of the levator hiatus, and the area of the levator hiatus were measured at rest, PFMC, and at maximal Valsalva (figure 1). Relative change in levator hiatal dimensions between rest and maximum Valsalva ([dimension at maximum Valsalva – dimension at rest / dimension at rest] x 100%), and between rest and PFMC ([dimension at contraction- dimension at rest / dimension at rest] x100%) were computed[16].

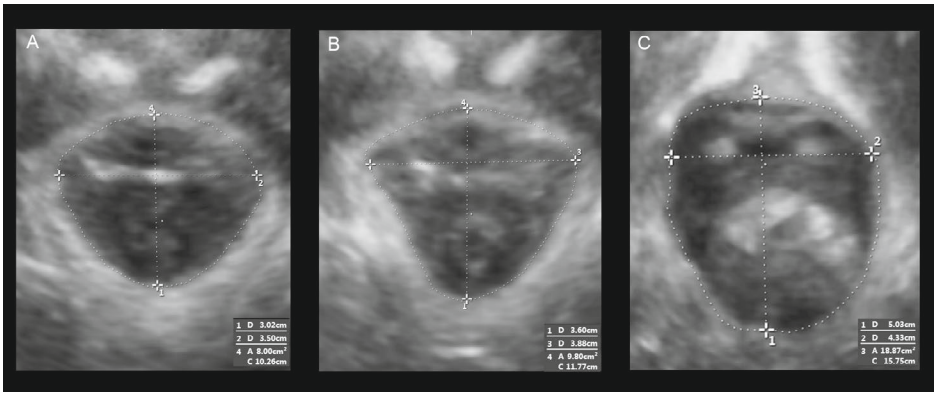

Figure 1 Example of measurement of levator hiatal dimensions in one patient at pelvic floor muscle contraction, at rest and at maximal Valsalva

Statistical analysis

For this analysis we excluded women who were pregnant at the time of examination, as pregnancy has the potential to compromise sexual function and sexual activity[20, 21].

Measurements of hiatal dimensions followed a non-normal distribution. Linear regression analysis was used to compare measurements of hiatal dimensions and total PISQ-12 score. We used R^2 to interpreted the explained variance. Mann Whitney U test was used to compare hiatal dimensions between women with and without individual sexual complaints. Baseline and obstetric factors were compared between women with and without sexual complaints using Student t-test for continues variables, Kendall's tau-c for ordinal variables and chi-square/fisher's exact test for categorical variables. Significant univariate associations were subjected to multivariate analysis using logistic regression analysis.

As this was a secondary analysis of the EpiLeva data, the sample size was determined by the primary end points of the EpiLeva study [17], and not specific to the research question addressed in this article. Statistical analysis was performed using IBM SPSS Statistics version 25. P values < 0,05 were considered statistically significant.

Ethical approval
Ethical approval for this study was obtained by the medical research ethics committee of the Erasmus Medical Centre (MEC-2012-058). Date of approval 11th April 2012.

RESULTS

A total of 2535 women were invited and 204 (8%) agreed to participate in our study. Comparison of baseline characteristics between participants and non-participants were previously described[17]. In summary, participants were more likely to be Caucasian and had a longer second stage of labor. In non-participants more women were induced and more frequently received epidural analgesia. There were no significant differences in age, BMI, episiotomy rate and other obstetrical factors.

Thirteen (6%) women were pregnant at the time of examination and were excluded from the analysis. The median time at investigation after vaginal delivery was 11 months (range 6-33). The baseline and obstetric characteristics of the 191 included women are shown in Table 1.

Table 1 Baseline and obstetric characteristics of 191 included women in N(%)

Baseline		
	Age	30 (20-40)*
	Ethnicity- Caucasian	174 (91%)
	BMI at booking	24 (16-39)*
Obstetric		
	Perineal tear	
	Intact perineum	39 (21%)
	1st degree tear	16 (8%)
	2nd degree tear	38 (20%)
	Episiotomy	98 (51%)

* Mean (range)

Sexual functioning and levator hiatal dimensions

All women had resumed sexual activity at the time of examination. Median (range) of the PISQ-12 was 38 (22-46). In our population 31 (16%) women experienced dyspareunia, 24 (13%) had difficulty reaching an orgasm, 33 (17%) experienced reduced desire, 7 (4%) had a problem with arousal.

Using linear regression analysis we did not find a significant association between total PISQ-12 score and (relative changes in) levator hiatal dimensions, accept for AP diameter at rest (p= 0.014). Larger diameter is associated with higher PISQ-12 score, and thus with better sexual functioning. However, this association is very weak, as < 5% of variance in PISQ score is explained by the AP diameter at rest (R^2 = 0.031).

Table 2 shows the comparison of hiatal dimensions between women with and without dyspareunia. These results indicate that women with dyspareunia had significantly smaller levator hiatal areas and AP diameter on maximum Valsalva. No significant effects were found for LR diameter. Table 3 shows the comparison in relative changes between levator hiatal dimensions between rest and PFMC and between rest and maximal Valsalva in women with and without dyspareunia. This showed no significant differences.

Table 2 Median (range) levator hiatal dimensions at rest, on pelvic floor muscle contraction and on maximal Valsalva in women with and without dyspareunia using Mann Whitney U test

	Dyspareunia N= 31	**No dyspareunia N= 160**	**P value**
Rest			
Hiatal Area	13,12 (7,84 – 20,53)	14,03 (8,18 – 34,13)	0.133
AP diameter (cm)	4,92 (3,01 – 6,06)	5,09 (3,67 – 7,22)	0.074
LR diameter (cm)	3,77 (3,09 – 5,80)	3,92 (2,66 – 6,09)	0.402
Contraction			
Hiatal Area	10,72 (7,13 – 19,39)	10,81 (6,68 – 26,28)	0.149
AP diameter	4,21 (2,87 – 5,54)	4,20 (2,66 – 7,05)	0.328
LR diameter	3,73 (2,64 – 5,46)	3,62 (2,63 – 6,17)	0.450
Valsalva			
Hiatal Area	**16,13 (7,90 – 33,43)**	**18,79 (7,38 – 53,69)**	**0.035**
AP diameter	**5,25 (3,22 – 6,95)**	**5,86 (3,18 – 28,91)**	**0.006**
LR diameter	4,26 (2,83 – 6,78)	4,23 (2,94 – 7,41)	0.467

Table 3 Relative changes (median (range) in levator hiatal dimensions between rest and pelvic floor muscle contraction and between rest and maximal Valsalva in women with and without dyspareunia using Mann Whitney U test

	Dyspareunia N= 31	**No dyspareunia N= 160**	**P value**
Contraction			
Hiatal Area (%)	-16,05 (-44,22 – 5,55)	-18,63 (-55,18 - 69,49)	0,386
AP diameter (%)	- 13,69 (-32,54 – 11,25)	-15,78 (44,12 – 45,66)	0,236
LR diameter (%)	-4,58 (-22,00 – 22,12)	- 7,73 (32,68 – 28,45)	0,149
Valsalva			
Hiatal Area (%)	30,60 (-28,74 – 91,80)	31,87 (-29,78 – 197,87)	0,308
AP diameter (%)	10,25 (-19,04 – 61,79)	15,35 (-21,87 – 456,32)	0,230
LR diameter (%)	7,03 (-28,54 – 53,57)	9,43 (-21,66 – 63,29)	0,479

For the other individual sexual complaints there was no significant difference between levator hiatal dimensions and relative changes in levator hiatal dimensions. There were no significant differences between

women with and without reduced desire, women with and without reduced arousal and women with and without difficulty reaching an orgasm.

Multivariate analysis
We used multivariate analysis to correct for age, BMI at booking, ethnicity (Caucasian vs non Caucasian), postnatal follow-up time (weeks), grade of tear/episiotomy and other sexual complaints including reduced desire, reduced arousal, and difficulty reaching an orgasm. Variables that showed a (near) significant association at univariate analysis were included in a multivariate model. In the final model for dyspareunia we included age, ethnicity, hiatus at maximal Valsava, AP diameter at maximal Valsalva, the presence of reduced desire, and reduced arousal. On multivariate analysis using logistic regression we found dyspareunia was independently significantly associated with younger age, reduced desire, and reduced arousal, but not with hiatal dimensions at maximal Valsalva.

DISCUSSION

This study aimed to determine the association between levator hiatal dimensions and relative changes in levator hiatal dimensions, and sexual dysfunction after first vaginal delivery. All women were sexual active at time of investigation. Sixteen percent of women experienced dyspareunia, 13% had difficulty reaching an orgasm, 17% experienced reduced desire, and 4% had a problem with arousal. Postpartum sexual dysfunction (including dyspareunia) is identified in 41–83% of women at 2–3 months postpartum[1]. Longer term data beyond six months postpartum is sparse. There is great variability in the literature on the reported prevalence rates of particular sexual dysfunctions due to differences in definition of sexual dysfunction, degree of severity, and differences in age groups. Similar to our data, prevalence rates for women in the general population vary from 17% to 55% for low levels of sexual desire; from 8% to 28% for arousal and lubrication problems; from 16% to 25% for orgasmic dysfunction; and from 14% to 27% for dyspareunia[22].

We hypothesized that women that experience sexual complaints show significant differences in levator hiatal dimensions and relative changes in these dimensions on PMFC and maximal Valsalva, when compared to women without sexual complaints. However, our results showed that 11 months after first vaginal delivery hiatal dimensions are not predictive of overall sexual dysfunction as measured by PISQ-12. When we studied individual sexual complaints we found that dyspareunia was associated with smaller hiatal dimensions at Valsalva on univariate analysis, but on

multivariate analysis, hiatal dimensions were not an independent risk factor for dyspareunia.

Previous studies showed that at 5 months after delivery, levator ani muscle avulsion and levator over-distension did not have appreciable effects on women's sexual functioning related to sexual activity, sensation on intercourse, arousal and orgasm[14]. And although women with persistent levator avulsion had significantly higher bothersome symptoms of a loose vagina at 1 year postpartum, these symptoms had no impact on their sexual life[15]. Although levator avulsion was associated with larger hiatal areas on transperineal ultrasound in these studies, the association between the different levator hiatal dimensions and sexual function was not examined. A study by Aydin *et al*[23] did correlate levator hiatal dimensions and sexual dysfunction, in non-symptomatic sexually active premenopausal women. An increase in AP diameter of the levator hiatus during maximal Valsalva was weakly associated with worse sexual functions, particularly desire, arousal, and orgasm domains[23]. Our study demonstrates that after first vaginal delivery hiatal dimensions were not associated with arousal, desire or orgasm. And although not significant on multivariate analysis, we did find that women with dyspareunia had smaller hiatal dimensions at Valsalva rather than larger dimensions, which could be a sign of higher pelvic floor muscle tone.

The etiology of sexual dysfunction is multifactorial, including emotional, physical and psychological causes. Changes in the dimensions and contractility of the pelvic floor might be the main cause of sexual dysfunction only in a subgroup of women. Perineal pain resulting from perineal trauma, fear of pain on resumption of intercourse or psychological stress associated with changes in family structure following childbirth, could possibly cause an increase in pelvic floor muscle tone in the postpartum period. Previously studies have shown that levator hiatal dimensions are smaller in women diagnosed with provoked vestibulodynia (PVD). In a study by Thibault *et al*[16], women were diagnosed with PVD when complaining about pain around the vaginal opening upon attempted vaginal penetration for a minimum of six months. The diagnosis was confirmed by using a standardized cotton-swab test. Women with PVD had smaller hiatal dimensions at rest, on PFMC and on maximum Valsalva than controls. Furthermore, these women had smaller relative increases in hiatal area on maximum Valsalva, which is associated with hypertonia from the pelvic floor muscles.

When dyspareunia is caused by, or maintained as a result of, pelvic floor hypertonia without anatomical causes, first-line treatment consist of

education, tactile desensitization and pelvic floor physiotherapy possibly in combination with psychological or sexuological consultation. When first-line treatment fails, more invasive interventions can be considered. One of these invasive interventions is injection with botulinium toxin A (BTA) in the pelvic floor muscles. When injected intramuscularly BTA produces a localized, partial and reversible chemical denervation of the muscle which results in localized muscle weakness or paralysis. There is some low grade evidence that injection of BTA in the hypertonic pelvic floor muscles decreases pelvic floor resting pressure as measured by manometry, and improves dyspareunia in women with therapy resistant chronic pelvic pain[24, 25]. Pelvic floor ultrasound might play a role in the future in the diagnostic work-up of women with dyspareunia. A cut of value for high muscle tone needs to be determined. These women with high muscle tone could be a subgroup of women with dyspareunia that might benefit from BTA injections.

To the best of our knowledge this is the first study to evaluate the association of sexual complaints and the biometry of the levator hiatus and relative changes of the puborectalis muscle using 3D/4D transperineal ultrasound in the postpartum period. All women in our study filled out the validated PISQ-12 questionnaire. The women included in our study did not have an increased risk for sexual dysfunction postpartum, as women who had instrumental delivery or third- or forth degree perineal tearing were excluded[1]. Furthermore, the researchers who conducted the study, were blinded against all clinical and obstetric data during analysis of the ultrasound data, hereby reducing bias.

There were also some limitations to our study. First, there is a possibility of selection bias. Only 8% of invited women participated in our study. Lack of time and fear for the examination were reasons most mentioned for non-participation. This might have led to a higher participation of women with complaints or complications. However, the percentage of women reporting sexual complaints in our study, does not exceed the incidence reported in previous literature, suggesting a representative cohort[22]. Participants were more likely to be Caucasian, but didn't differ in age and BMI compared to non-participants. We therefore feel that our results can be generalized to other populations of mainly Caucasian women who had a first spontaneous vaginal delivery at term. A second limitation is our sample size. As this was a secondary analysis of the EpiLeva data, the sample size was determined by the primary end points of the EpiLeva study, and not specific to the research question addressed in this article[17]. It might be that our sample size was too small to evaluate a significance association between the biometry of the levator hiatus and sexual complaints. A third limitation is

the fact that we did not ask about sexual functioning before and during pregnancy. However, due to the design of our study it was impossible to prospectively collect these data as it would have required inclusion of study participants at the first antenatal booking. When information on pre-pregnancy sexual functioning was obtained retrospectively in the postpartum period, it might have been subjective to recall bias.

Finally, the PISQ-12 questionnaire may not be the best questionnaire to identify sexual dysfunction in our cohort of postpartum women. The PISQ-12 is validated to assess sexual function in women with urinary incontinence and/or pelvic organ prolapse, but has previously also been used to evaluate sexual function after vaginal delivery[26, 27]. The EpiLeva study was conducted to assess the association of mediolateral episiotomy with levator injury and urogynecological complaints. This is why we chose to use the PISQ-12 questionnaire. However, the frequency of pelvic organ prolapse and urinary incontinence symptoms in our study population was low. As the PISQ-12 does not provide cut-off values discriminating between normal sexual function and sexual dysfunction, we dichotomized answers of questions to what we considered to be relevant complaints. For future research on this topic a more general female sexual function questionnaire could be considered, for example the Female Sexual Function Index (FSFI).

In conclusion we can state that sexual dysfunction at 11 months postpartum is not independently associated with levator hiatal dimensions or relative changes between levator hiatal dimensions as measured by 3D/4D transperineal ultrasound. Although women with dyspareunia had smaller hiatal dimensions at maximum Valsalva, suggesting a higher pelvic floor muscle tone, on multivariate analysis this association was not significant. Sexual dysfunction in the postpartum period is multifactorial and can have many different psychological as well as physical causes. Changes in hiatal dimensions of the pelvic floor could be one of the causes for sexual dysfunction in a certain group, but further research is necessary to identify these women.

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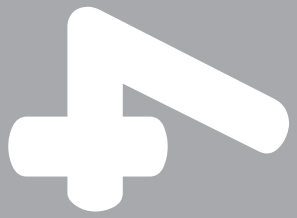
CHAPTER



Which factors are associated with anal incontinence after obstetric anal sphincter injury?

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ABSTRACT

Objectives
Obstetric anal sphincter injury (OASI) is an important factor in the etiology of anal incontinence. This study aimed to evaluate whether anal sphincter defects, levator avulsion or levator ballooning after OASI are associated with severity of anal incontinence. Furthermore, we evaluated whether factors as constipation and altered stool consistency are associated with symptoms of incontinence after OASI.

Methods
In this multicenter prospective observational cohort study, women with OASI were invited to participate at least 3 months after primary repair. All women completed validated questionnaires including St Mark's incontinence score, Bristol stool scale (BSS) and Cleveland clinic constipation score (CCCS) and underwent four-dimensional (4D) transperineal ultrasound for assessment of the levator ani muscle and anal sphincter.

Results
In total, 220 women were included. Median follow-up was 4 months (range, 3–98 months). Univariate linear regression analysis showed an association of St Mark's incontinence score with a residual defect of external anal sphincter (EAS) (β 1.55 (95% CI, 0.04–3.07); P = 0.045), higher parity (β 0.85 (95% CI, 0.02–1.67); P = 0.046, BSS (β 1.28 (95% CI, 0.67–1.89); P < 0.001) and CCCS (β 0.36 (95% CI, 0.18–0.54); P < 0.001). However, multivariate linear regression found an association of St Mark's incontinence score only with BSS (β 1.50 (95% CI, 0.90–2.11); P < 0.001) and CCCS (β 0.46 (95% CI, 0.29–0.63); P < 0.001).

Conclusions
Residual defects of the EAS, detected on 4D transperineal ultrasound, are associated with severity of anal incontinence symptoms measured using St Mark's incontinence score 4 months after OASI repair. Furthermore, clinical factors such as constipation and altered stool consistency appear to influence this association and may therefore play a more important role in clinical management.

INTRODUCTION

Anal incontinence is a debilitating condition with a significant social and economic impact that reduces quality of life. Obstetric anal sphincter injury (OASI) is one of the main causes of anal incontinence in women that may lead to problems in the early postpartum period as well as in the years thereafter. Primary repair of OASI is essential for anal continence and has been shown to prevent long-term morbidity[1]. Unfortunately, even after primary repair, residual defects of the anal sphincters may occur, associated with ongoing anal incontinence years after the initial injury[2-7]. In addition to optimal function and full integrity of the anal sphincters, optimal condition of the levator ani muscle is also important for anal continence[2, 7].

Previous studies in children and elderly women have shown that chronic diarrhea, constipation, irritable bowel syndrome and low consumption of dietary fibre are all associated with anal incontinence[8-13]. Unfortunately, none of these studies included women after OASI. Studies on the association of factors such as stool consistency or constipation with the development of anal incontinence in women with a history of OASI are scarce. As these factors are relatively easy to manage, they may be targeted in the prevention and eventual treatment of anal incontinence and improvement of quality of life of women after OASI. To bridge this knowledge gap, we performed a multicentre prospective observational study to assess whether residual anal sphincter or levator ani muscle defects, assessed using transperineal ultrasound, are associated with severity of anal incontinence symptoms measured using St Mark's incontinence score in women after OASI. A secondary objective was to evaluate whether potentially modifiable factors such as stool consistency and constipation are associated with anal incontinence.

METHODS

This was a multicenter prospective observational cohort study of women who had a primary repair of OASI between February 2009 and January 2018. All women were invited for a follow-up visit at least 3 months after childbirth, during which a four-dimensional (4D) transperineal ultrasonography was routinely performed. The women were also invited to complete the following questionnaires: the Bristol stool scale (BSS), the Cleveland clinic constipation score (CCCS) and St Mark's incontinence score, which was done just before, during or after this follow-up visit. Written informed consent was obtained from all participants. Women were included only if they had at least undergone St Mark's incontinence score

assessment and transperineal ultrasound from the anal sphincter. Ethical approval for this study was obtained from the medical research ethics committee of the Erasmus Medical Centre (MEC-2015-425). The study was performed in either the Erasmus Medical Centre in Rotterdam or the Amphia Hospital in Breda, The Netherlands.

Data collection

Antenatal, intrapartum and neonatal characteristics were obtained from the individual patient records. 4D transperineal ultrasound was performed by an experienced investigator using a Voluson E Expert system or Voluson 730 Expert system with a 4-8 MHz transducer for examination of the levator ani muscle and a 3-9 MHz 4D micro convex probe (RNA5-9 H48651DB) for examination of the anal sphincter (GE Healthcare, Zipf, Austria). All volumes of the levator ani muscle were obtained in supine position after voiding, at rest, on maximal pelvic floor muscle contraction and on maximum Vasalva maneuver. Volumes of the anal sphincter were obtained at rest and on maximum pelvic floor muscle contraction. The integrity of the levator ani muscle and anal sphincter was assessed using ultrasound volumes of the levator ani muscle on maximum pelvic floor muscle contraction.

Anal sphincter integrity was visualized in the axial images of the anal canal with tomographic ultrasound imaging, which was used to obtain a set of eight slices from the level of the puborectalis loop (slice 1) to the level of the anodermis (slice 8), with a variable distance between each slide depending on the length of the sphincter, leaving six slices to delineate the entire sphincter[14]. A residual sphincter defect of external anal sphincter (EAS) and/or internal anal sphincter (IAS) was defined as a discontinuity in the texture of the EAS or IAS of ≥ 30° in at least four out of six slices (Figure 1)[15].

Levator avulsion was defined as an abnormal muscle insertion in three central slices on tomographic ultrasound imaging (reference slice and the 2.5 and 5 mm cranial slices). The hiatal area was measured in a rendered volume during maximum Valsalva maneuver[16]. Levator ballooning was defined as hiatal area of > 25 cm^2[2; 17]. Ballooning was divided into four categories: mild (> 25cm^2 – 29.9cm^2), moderate (≥ 30cm^2 – 34.9cm2), marked (≥ 35cm^2 – 39.9cm^2) and severe (≥ 40cm^2)[17].

Three experienced investigators (L.S, D.M.J.O. and A.B.S.) performed offline analysis using specialized software (4D view version 18, GE Healthcare). All investigators were blinded to the clinical data. To determine interobserver reliability between the investigators, a random test–retest series of 20 volumes was performed and Fleiss's kappa coefficients were obtained.

After the test-retest series, the remaining volumes were divided among the investigators. In the case of inconclusive evaluation by one investigator, sphincter volumes were discussed between all investigators until consensus was reached. Interobserver and intraobserver reliability of the hiatal area measurements and levator integrity evaluation had been determined in previous research[18].

Outcomes

The St Mark's incontinence score was used as the primary outcome to assess the severity of anal incontinence symptoms[19]. The total score ranges from 0 to 24, with a score of 0 indicating perfect continence and 24 indicating total anal incontinence. For the analysis of secondary outcomes, several St Mark's incontinence score questions were dichotomized. Fecal incontinence was defined as liquid and/or solid stool incontinence (score 1 or higher). Flatal incontinence was defined as difficulty controlling flatus present 'sometimes' (score 2) to 'all the time' (score 4).

Covariates

Residual defect of the EAS or IAS and levator avulsion or ballooning were covariates determined from the ultrasound data. The BSS was used as an instrument to score stool consistency[20]. The BSS scoring card contains images of stool types ranging from the hardest (type 1) to the softest (type 7). Constipation was defined by the sum of the CCCS[21]. In this system, the scores ranges from 0 to 30, with higher scores representing more severe symptoms. Other covariates, including grade of OASI, maternal age, body mass index, time between delivery and postnatal ultrasound and parity were selected based on their known association with anal incontinence[4-6, 8, 13].

Statistical methods

Scores with a normal distribution were analyzed using Student's t-test, while skewed data were analyzed using the Mann–Whitney U-test. Unadjusted univariate linear regression analysis was used to study the association between all covariates and total St Mark's incontinence score. Covariates with $P < 0.1$ on univariate analysis were selected for multivariate linear regression analysis. Logistic regression analysis was performed separately to assess the possible independent association of fecal and flatal incontinence with all covariates. To assess significant covariates, multivariate logistic regression analysis was performed using stepwise backward elimination using the Wald test, with a value of 0.1 as the threshold for elimination. Analysis was performed using SPPS Statistics, version 20 (SPSS Inc., Chicago, IL, USA); two-sided $P < 0.05$ was taken to indicate statistical significance.

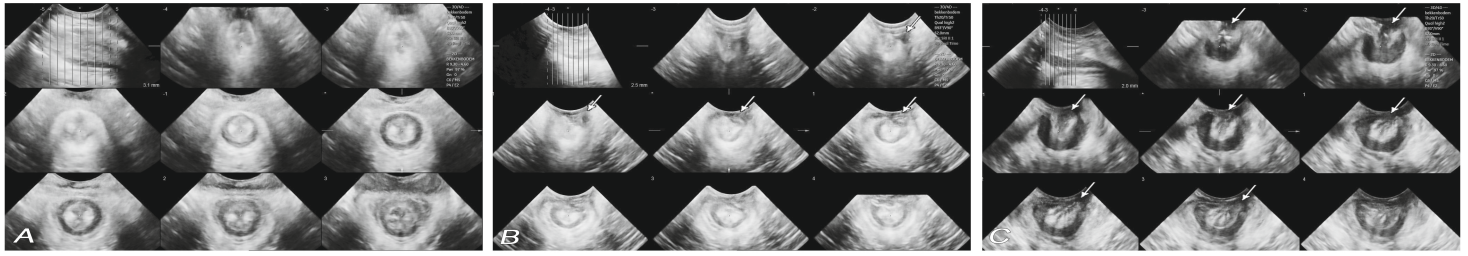

Figure 1 Tomographic ultrasound images obtained by four-dimensional transperineal ultrasound during maximum pelvic floor muscle contraction, showing: (a) intact anal sphincter, (b) residual defect (arrows) of the external anal sphincter and (c) complete residual defect (arrows) of the anal sphincter (internal and external).

RESULTS

Of the 321 women who were invited to participate, 68.5% (*n* = 220) were enrolled in the study (Figure 2). All participants were examined between 3 and 98 months after vaginal delivery, with a median follow-up of 4 months. Of these 220 women, 65% were primiparous. Six (2.7%) women had sustained their second OASI. In 23.2% of cases the woman had a ventouse delivery. Most women (73.6%) had a Grade 3A or 3B OASI. The repair technique for OASI depended on the experience of the attending physician and the degree of rupture. Baseline characteristics of all participants are provided in Table 1.

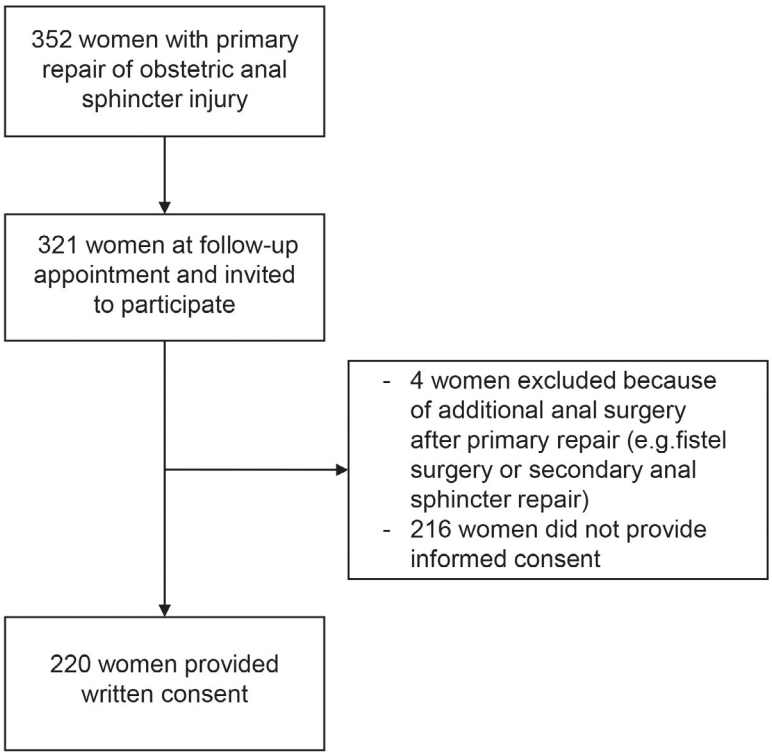

Figure 2 Flowchart summarizing study population. OASI, obstetric anal sphincter injury.

Table 1 Baseline characteristics of 220 women who had primary repair of obstetric anal sphincter injury (OASI)

Variable	
Maternal age at investigation (years)	31.6 ± 3.8
Body mass index (kg/m^2)	23.6 (21.4-26.2)
History of OASI	6 (2.7)
Time at investigation after vaginal delivery (months) (median (range))	4 (3-98)
Parity (median (range))	1 (1-4)
Gestational age at delivery (weeks)	40+0 (39+2 to 40+6)
Birth weight (g)	3600 ± 423
Ventouse delivery	51 (23.2)
Episiotomy	85 (38.6)
Occiput posterior position	16 (7.3)
Shoulder dystocia	11 (5)
Median duration second stage (min)	44 (18-69)
Degree of OASI	
3A	57 (25.9)
3B	105 (47.7)
3C	43 (19.5)
4	11(5.0)
Unclassified 3rd degree tear	4 (1.8)
Repair technique OASI	
Overlapping	88 (40.0)
End-to end	96 (43.6)
Unknown	36 (16.4)

Data are given as mean ± SD, median (interquartile range) or n (%) except where indicated.

The interobserver test–retest series for transperineal three-dimensional (3D)/4D ultrasound data yielded a Fleiss' kappa of 0.69 (95% CI, 0.43-0.95) for the EAS and 0.74 (95% CI, 0.48-0.99) for IAS integrity evaluation. Thirty-six (16.4%) women had a residual defect of the EAS and 42 (19.1%) had a residual defect of the IAS. Thirty-one (14.1%) had a residual defect of both EAS and IAS. Levator avulsion (both uni- and bilateral) was identified in 96 (43.6%) women, of whom 75 (78.1%) had bilateral avulsion. The median

hiatal area during maximal Valsalva maneuver was 22.7cm^2 (interquartile range (IQR), 18-27.6 cm^2). Levator ballooning was identified in 79 (35.9%) women, categorized as mild in 47%, moderate in 25%, marked in 14% and severe in 14% of cases[17].

Table 2 Univariate and multivariate linear regression analyses of association between St Mark's incontinence score and covariates in AQ20 women after obstetric anal sphincter injury (OASI)

Covariate	**Univariate analysis**		**Multivariate analysis***	
	β (95% CI)	**P**	**Adjusted β (95% CI)**	**P**
Maternal age at ultrasound (years)	0.07 (-2.96 to 6.47)	0.39	N/A	N/A
Body Mass Index (kg/m^2)	0.05 (-0.10 to 0.20)	0.53	N/A	N/A
Parity	0.85 (0.02 to 1.67)	0.046	0.60 (-2.67 to 1.46)	0.17
Grade of OASI	0.35 (-0.35 to 1.04)	0.33	N/A	N/A
Time between delivery and postnatal 4D ultrasound (months)	-0.26 (-0.56 to 0.00)	0.09	-0.02 (-0.06 to 0.02)	0.30
Residual EAS defect	1.55 (0.04 to 3.07)	0.045	1.05 (-0.45 to 2.55)	0.17
Residual IAS defect	0.97 (-0.47 to 2.40)	0.19	N/A	N/A
LAM avulsion (unilateral and/or bilateral)	0.31 (-0.83 to 1.45)	0.59	N/A	N/A
Hiatal area during maximum Valsalva manuever (cm^2)	-0.01 (-0.08 to 0.07)	0.89	N/A	N/A
Bristol Stool Scale	1.28 (0.67 to 1.89)	< 0.001	1.50 (0.90 to 2.11)	< 0.001
CCCS	0.36 (0.18 to 0.54)	< 0.001	0.46 (0.29 to 0.63)	< 0.001

*Covariates for multivariate linear regression analyses included parity, time between delivery and postnatal ultrasound, residual defect of external anal sphincter (EAS), Bristol Stool Scale and Cleveland Clinic constipation score (CCCS) and were selected based on P < 0.1 on univariate analysis. All P-values are two-sided. 4D, four-dimensional; IAS, internal anal sphincter; LAM, levator ani muscle; N/A, not applicable.

Table 3 Univariate and multivariate analysis of association of clinical and sonographic covariates with fecal and flatal incontinence in women after obstetric anal sphincter injury

		Fecal incontinence					Flatal incontinence				
Covariate	**n**	**No (n=170)**	**Yes (n=50)**	**Crude OR (95% CI)**	**aOR (95% CI)***	**P**	**No (n=148)**	**Yes (n=72)**	**Crude OR (95% CI)**	**aOR (95% CI)***	**P**
Residual EAS defect	36	20 (11.8)	16 (32)	3.53 (1.66- 7.51)	3.87 (1.61-9.31)	0.011	19 (12.8)	17 (23.6)	2.10 (1.02- 4.34)	N/A	N/A
Residual IAS defect	42	26 (15.3)	16 (32.0)	2.61 (1.26-5.39)	N/A	N/A	22 (14.9)	20 (27.8)	2.20 (1.11- 4.38)	1.61 (0.72-3.64)	0.27
LAM avulsion (unilateral or bilateral)	96	75 (44.1)	21 (42.0)	0.92 (0.49- 1.74)	N/A	N/A	58 (39.2)	38 (52.8)	1.73 (0.98- 3.06)	2.58 (1.28- 5.22)	0.007
Hiatal area on maximum Valsalva maneuver (cm2)	218	22.7 (9.6-48.3)	22.7 (6.4-43.1)	1.00 (0.96-1.04)	N/A	N/A	22.2 (9.6-45.6)	23.8 (6.4-48.3)	1.02 (0.99- 1.06)	N/A	N/A
Major anal sphincter tear‡	54	40 (23.5)	14 (28.0)	1.32 (0.64- 2.70)	N/A	N/A	35 (23.6)	19 (26.4)	1.15 (0.60-2.20)	N/A	N/A
Age at ultrasound (years)	220	32 (18-41)	33 (26-43)	1.05 (0.97- 1.15)	N/A	N/A	32 (23-41)	32 (18-43)	1.05 (0.97- 1.15)	N/A	N/A
Multiparity	76	53 (31.2)	23 (46.0)	1.88 (0.99- 3.58)	N/A	N/A	47 (31.8)	29 (40.3)	1.45 (0.81-2.60)	N/A	N/A
BSS	188	3 (1-6)	4 (2-7)	1.91 (1.31-2.78)	2.18 (1.44-3.28)	< 0.001	3 (1-6)	4 (2-7)	1.62 (1.16- 2.27)	2.02 (1.38- 2.96)	0.02
CCCS	184	3 (0-16)	4 (0-20)	1.13 (1.02-1.24)	1.21 (1.08-1.34)	< 0.001	3 (0-16)	5 (0-20)	1.14 (1.04-1.25)	1.24 (1.11- 1.38)	< 0.001

Covariates are displayed as median (interquartile range) or *n* (%). *Multivariate analysis of fecal incontinence was adjusted for residual defect of external anal sphincter (EAS), Bristol Stool Scale (BSS) and Cleveland Clinic constipation score (CCCS). †Multivariate analysis of flatal incontinence was adjusted for residual defect of internal anal sphincter (IAS), levator ani muscle (LAM) avulsion, BSS and CCCS. ‡Major anal sphincter tear was defined as Grade 3C or 4 (damage to both EAS and IAS). Selection of covariates for multivariate regression was based on a stepwise backward elimination using the Wald test with a value of 0.1 as a threshold for elimination. aOR, adjusted odds ratio; N/A, not applicable; OR, odds ratio.

The median reported St Mark's incontinence score was 3 (IQR, 1-6). Women with a residual defect of the EAS had a higher St Mark's incontinence score than did women without a sphincter defect (2 *vs* 3.5; P= 0.02). There was no difference in St Mark's incontinence score between women with a second OASI and women with only one OASI. Table 2 presents the univariate and multivariate linear regression analyses of the association between total St Mark's incontinence score and all covariates. In our model, 23% of all anal incontinence was predicted by the following covariates: parity, time between delivery and postnatal 4D ultrasound, residual defect of EAS, BSS and CCCS.

There were 50 (22.7%) women with and 170 (77.3%) without fecal incontinence. Flatal incontinence was present in 72 (32.7%) women and absent in 148 (67.3%) women. Table 3 presents univariate and multivariate analyses of the association of all covariates with fecal and flatal incontinence. Residual defect of EAS, BSS and CCCS predicted 23% of fecal incontinence in our cohort. Residual defect of IAS, levator avulsion (unilateral and/or bilateral), BSS and CCCS predicted 21% of flatal incontinence.

DISCUSSION

Only residual defects of the EAS was associated with higher St Mark's incontinence score. However, it was not the strongest predictor of the severity of anal incontinence symptoms 4 months after OASI. Our findings show that stool consistency (i.e. BSS) and constipation (i.e. CCCS) have a greater predictive value for the severity of anal incontinence symptoms in the short term. Moreover, subgroup analysis showed a significant association of fecal or flatal incontinence with stool consistency and constipation. This offers opportunities for improving the quality of life of affected women by modifying stool consistency and treating constipation.

Our study had several limitations that need to be addressed. Inclusion bias cannot be ruled out because of the inclusion rate of 69%. In theory, women with complaints may have been more motivated to attend their follow-up visit. However, the median St Mark's incontinence score in our cohort was comparable with that reported in previous studies, which suggests that our study group is comparable with the groups in earlier studies[2, 7]. Another limitation is that our results could have been influenced by the chosen imaging technique. Endoanal ultrasound is considered the gold standard for evaluation of anal sphincter muscle integrity in patients with anal incontinence. A recent study by Taithongchai *et al.*[22] showed that 4D transperineal ultrasound does not always agree with endoanal

ultrasound in detecting residual defects of the EAS and IAS. However, other studies have indicated that transperineal ultrasound can be considered as a valuable non-invasive alternative of endoanal ultrasound[23, 24]. Furthermore, transperineal ultrasound imaging allows the possibility of direct assessment of the levator ani muscle. Other limitations were the absence of predelivery data on pelvic floor symptoms and the short time of follow-up.

The data from our study group with regard to St Mark's incontinence score and rates of faecal incontinence and levator avulsion are in agreement with the findings of previous studies in this area[2, 7, 24-27]. We found no relationship between the grade of OASI and severity of incontinence symptoms. Whether the grade of OASI affects symptoms of incontinence has been inconclusive in previous research[4, 6, 7, 25, 28, 29]. A major difficulty is that studies in the field of anal incontinence are difficult to compare because of the use of different scoring methods for clinical symptoms and ultrasound features. Unfortunately, earlier studies that used the same St Marks scoring system to assess the severity of anal incontinence in women after OASI used different, arbitrarily chosen cut-off values[2, 30]. Therefore, objective results may differ and comparison of the outcome may be less reliable between the studies.

Although we found no association between levator avulsion and anal incontinence severity, we did find an association between levator avulsion and flatal incontinence. A possible explanation for this association might be that an optimal function of levator ani is mandatory in order to control flatus. This could explain why the rate of women with flatal incontinence was much higher than the rate of women with anal sphincter defects and why flatal incontinence was only moderately associated with anal sphincter damage in other studies[31, 32].

Our findings with regard to the association between severity of anal incontinence and fecal consistency and constipation corroborate previous studies, which revealed a similar association in both women and men[8, 13, 33]. Bharucha *et al.*[8] even found that the strongest risk factor for anal incontinence in women older than 39 years was bowel disturbances and not obstetric injury. Given the lack of successful treatment options for residual defects of the anal sphincters and levator ani muscle and the long-term, serious morbidity experienced by young women with anal incontinence after OASI, other options to improve the quality of life are needed. As both abnormal stool consistency and constipation are relatively easy to treat, this may offer possible treatment options in affected women. Finding out about stool consistency and constipation using questionnaires like BSS

and CCCS in women with symptoms of anal incontinence after OASI is therefore important. Future studies may explore whether stool consistency and constipation are also a significant predictors of the severity of anal incontinence after OASI in long-term follow-up, or whether residual defects of anal sphincter or levator ani muscle defects are more predictive. In addition, we should investigate whether management of stool consistency and constipation with various treatment options leads to a reduction in the severity of anal incontinence.

In the future, it will be necessary to achieve an internationally validated scoring system for symptoms of anal incontinence with a clear cut-off for significant complaints. This would help to compare the findings of different studies and evaluate treatments. This might also apply to the international standardization of endoanal or transperineal ultrasound assessment of anal sphincter integrity.

CONCLUSION

Residual defects of the EAS, detected on 4D transperineal ultrasound, are associated with the severity of anal incontinence symptoms measured using St Mark's incontinence score 4 months after OASI repair. Furthermore, clinical factors such as constipation and altered stool consistency appear to influence this association and may therefore play a more important role in clinical management.

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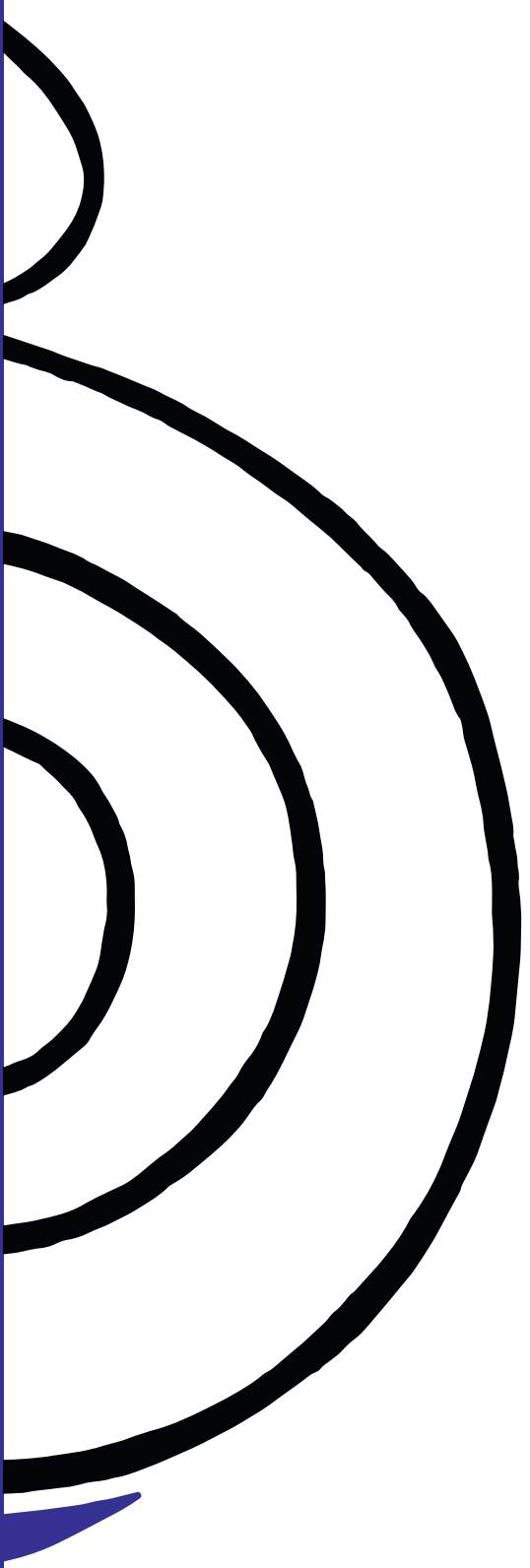
PART II



Pelvic floor imaging with virtual reality

CHAPTER 5

Agreement and reliability of pelvic floor measurements during contraction using three-dimensional pelvic floor ultrasound and virtual reality

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ABSTRACT

Objectives

Virtual reality is a novel method of visualizing ultrasound data with the perception of depth and offers possibilities for measuring non-planar structures. The levator ani hiatus has both convex and concave aspects. The aim of this study was to compare levator ani hiatus volume measurements obtained with conventional three-dimensional (3D) ultrasound and with a virtual reality measurement technique and to establish their reliability and agreement.

Methods

100 symptomatic patients visiting a tertiary pelvic floor clinic with a normal intact levator ani muscle diagnosed on translabial ultrasound were selected. Datasets were analyzed using a rendered volume with a slice thickness of 1.5 cm at the level of minimal hiatal dimensions during contraction. The levator area (in cm^2) was measured and multiplied by 1.5 to get the levator ani hiatus volume in conventional 3D ultrasound (in cm^3). Levator ani hiatus volume measurements were then measured semi-automatically in virtual reality (cm^3) using a segmentation algorithm. An intra- and interobserver analysis of reliability and agreement was performed in 20 randomly chosen patients.

Results

The mean difference between levator ani hiatus volume measurements performed using conventional 3D ultrasound and virtual reality was 0.10 (95% CI, – 0.15 to 0.35) cm^3. The intraclass correlation coefficient (ICC) comparing conventional 3D ultrasound with virtual reality measurements was > 0.96. Intra- and interobserver ICCs for conventional 3D ultrasound measurements were > 0.94 and for virtual reality measurements were > 0.97, indicating good reliability for both.

Conclusion

Levator ani hiatus volume measurements performed using virtual reality were reliable and the results were similar to those obtained with conventional 3D ultrasonography.

INTRODUCTION

Pelvic floor disorders affect a substantial number of women worldwide. The levator ani muscle is thought to be of great importance for pelvic organ support[1]. It has been shown that abnormal distensibility of the levator ani hiatal dimension (i.e. 'ballooning') is associated with an increased risk of pelvic organ prolapse[2, 3].

In the 1980s, magnetic resonance imaging (MRI) was the only available imaging method capable of assessing the levator ani muscle *in vivo*[4]. However, cost, availability and contraindications limited the implementation of MRI in clinical practice. With the introduction of three-dimensional (3D) pelvic floor ultrasound imaging in the 1990s a non-invasive and more practical technique for assessing levator ani morphology has become possible[5, 6]. Furthermore four-dimensional (4D) dynamic ultrasound can be performed, which allows the investigator to perform measurements during rest, contraction and Valsalva maneuver. Previous studies indicate that 3D ultrasound can be used for obtaining levator ani hiatus volumes instead of MRI[7, 8].

Silva-Filho *et al.*[9] generated a 3D computer model derived from MRI imaging visualizing the different aspects of the levator ani and showed that the levator area can be visualized as a non-Euclidean hyperbolic structure. They illustrated the different dimensions of the levator ani for the anterior, middle and posterior compartments at different sections through the hiatal area, as well as for patients with and without prolapse. These findings were supported by Kruger *et al.*[10], who compared MRI with 3D ultrasound imaging and found that investigators previously assumed that the minimal dimensions of the hiatus can be measured in a flat plane. However, the 3D nature of the hiatus means that the true levator hiatus occupies a warped (non-Euclidean) plane and that hiatal measurements may be subject to systematic error if performed in a flat (Euclidean) plane.

Measurements of the levator ani hiatus with 3D ultrasound are performed in two dimensions (2D) using a rendered volume, single plane measurements and/or volume contrast imaging with different slice thickness. The non-Euclidean nature, i.e. the concave and convex shape of the levator hiatus as described by Silva-Filho *et al.*[9] and Kruger *et al.*[10] is not taken into consideration in volume measurements using transperineal ultrasound. Therefore, the levator hiatal area visualized and measured in 2D might overestimate or underestimate the 'real' dimensions of the levator hiatal area.

By using the I-Space virtual-reality system (which has already been successfully used for 3D prenatal ultrasonography[11, 12]) the concave and convex features of the levator can be visualized, allowing the investigator to represent better the true (3D) appearance of the levator hiatus and measure it more effectively.

The aim of this study was to compare levator ani hiatus volume measurements performed using conventional 3D ultrasound with those performed using a virtual reality application and to establish the agreement and reliability of both techniques.

METHODS

In 2008, 100 symptomatic patients attending a tertiary pelvic floor clinic with a normal levator ani were selected. A normal levator ani was defined as an intact levator ani attachment in eight slices when utilizing the tomographic ultrasound imaging technique described by Dietz[13]. All had undergone a standardized interview and pelvic floor ultrasound imaging in the supine position and after voiding, using a Voluson 730 Expert system with a 4–8-MHz RAB transabdominal probe (GE Medical Systems, Zipf, Austria) as previously described by Dietz[5]. Offline analysis of the levator ani hiatus during maximal contraction was performed blinded, without knowledge of the patient's history.

Conventional 3D ultrasound measurements

Offline conventional 3D ultrasound measurements were performed using specialized 3D imaging software, 4D View version 9.0 (GE Medical Systems). A rendered volume with a slice thickness of 1.5 cm was obtained at the level of minimal hiatal dimensions during contraction (Figure 1)[6]. In 4D View the levator ani area of this rendered dataset is measured in cm^2. The slice thickness of the rendered volume was set at 1.5 cm; therefore the conventional volume measurements in cm^2 were multiplied by 1.5 to get the levator ani hiatus volume in cm^3. These conventional volume measurements were later compared with the levator ani hiatus volume measured in virtual reality (cm^3).

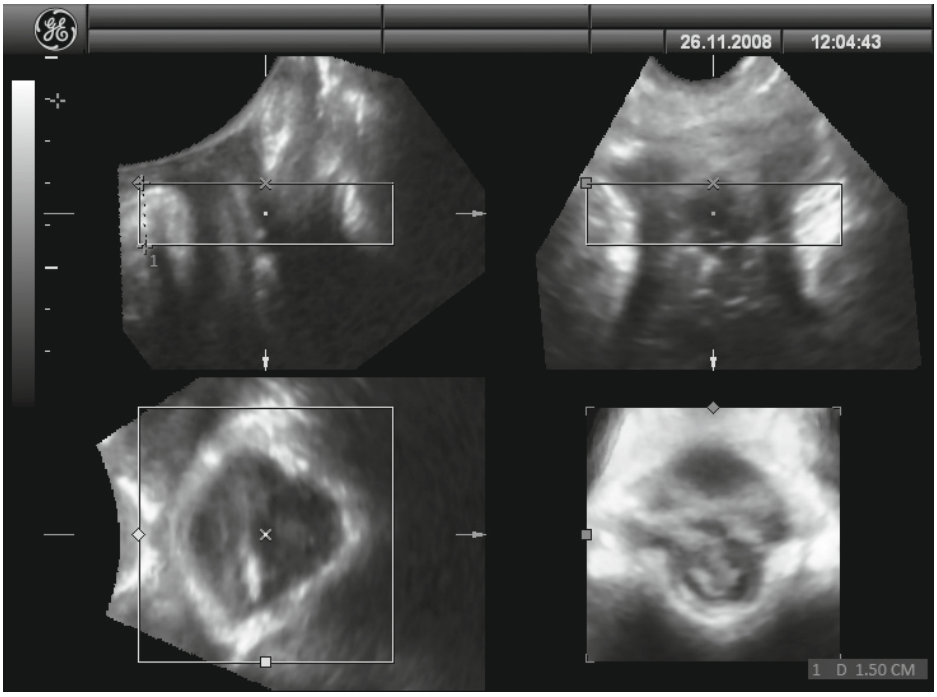

Figure 1 Rendered volume (slice thickness 1.5 cm) of a normal levator ani as seen and measured using 4D View.

Virtual reality measurements

We performed levator ani hiatus volume measurements in virtual reality by storing the 3D datasets as Cartesian volumes in 4D View. These 3D datasets were then visualized in the I-Space, a so-called four-walled CAVE™-like (Cave Automatic Virtual Environment) virtual reality system[14]. In the I-Space a researcher is surrounded by computer-generated stereo images, which are projected by eight high-quality digital light processing projectors onto three walls and the floor of a small room. With V-Scope[15], a volume-rendering application developed in-house, an interactive hologram of the ultrasound image is created and can be manipulated and measured by means of a virtual pointer, controlled by a wireless joystick (Figure 2). The hologram must be viewed through glasses with polarizing lenses to create the perception of depth. Hereby, the I-Space allows medical professionals to view and interact with their volumetric data in all three dimensions, which provides them with views much more like those they will experience during surgery[16, 17].

To perform volume measurements, a flexible and robust segmentation algorithm that is based on a region-growing approach in combination with

a neighborhood variation threshold was implemented[18]. This algorithm has been modified to handle the speckles in ultrasound data by smoothing the gray-level data[19].

Prior to the levator ani hiatus volume measurement, the 3D datasets were enlarged, rotated and cropped. The outside of the puborectalis has to be 'brushed away' with an eraser to avoid segmentation of parts other than the levator ani. The hypoechoic inside of the levator ani was then chosen by placing a seed point after selecting an upper and lower gray-level threshold and an upper threshold for the standard deviation of the voxel neighborhood. If the volume measurement was incomplete, the user could manually grow (or shrink) the segmented region with a spherical, free hand 'paint brush' to add voxels to or delete voxels from the segmented structure when necessary[11, 12, 19]. Figure 3 shows the complete volume, displayed in blue, as measured in virtual reality.

Agreement and reliability

The conventional 3D ultrasound and virtual reality levator ani hiatus volume measurements of all 100 patients were performed by one operator (L.S.) and repeated three times, which is standard in the clinical application of ultrasound measurements. The mean of the three levator ani hiatus volume measurements obtained using conventional 3D ultrasound and that obtained in virtual reality were used for comparison between the two methods.

For calculating interobserver reliability and agreement of both conventional 3D ultrasound and virtual reality levator ani hiatus volume measurements, 20 datasets of randomly chosen patients were selected. Investigators L.S. and A.B.S. independently performed three volume measurements of each dataset and the mean was used for comparison. We randomly selected these patients with the help of a research randomizer (http://www. randomizer.org/form.htm).

To assess intraobserver reliability and agreement of both conventional 3D ultrasound and virtual reality measurements, L.S. performed another three measurements in 20 randomly chosen datasets, and the mean of these measurements was compared with the mean of the three measurements previously obtained by L.S from the same 20 datasets. The second series of measurements was performed at least 2 weeks after the first series to prevent recollection bias.

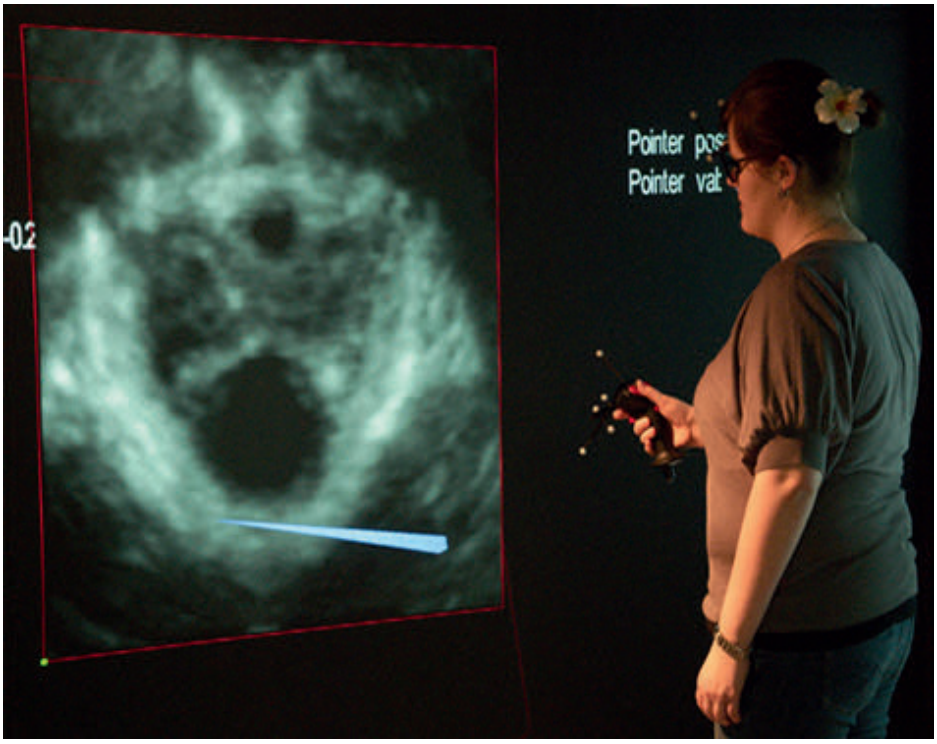

Figure 2 Operator examining the levator ani muscle using the I-Space virtual reality system.

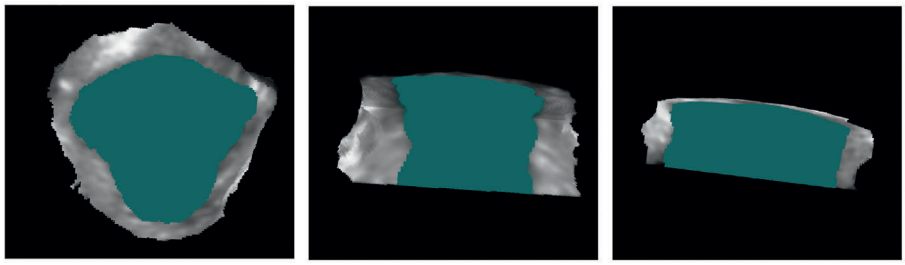

Figure 3 Two-dimensional virtual reality images of a volume measurement of the levator hiatal area, displayed in blue, showing the axial (a), coronal (b) and midsagittal (c) planes. The concave–convex shape of the hiatus can be observed.

Statistical analysis

Statistical analysis was performed using SPSS/PC version 15.0 (SPSS Inc., Chicago, IL, USA). Two-sided $P < 0.05$ was considered to be statistically significant. The same statistics were used to compare the virtual reality and conventional 3D measurements, as well as to determine inter- and intraobserver variability. The mean difference (95% CI), limits of agreement

(mean difference ± (1.96 × SD) and intraclass correlation coefficients (ICC) were calculated. Bland–Altman plots were used to determine whether the difference was influenced by the magnitude of the measurements[20-22]. An ICC of 0.81–1.00 was considered to reflect excellent reliability[23, 24].

Table 1 Baseline characteristics of the 100 symptomatic women attending tertiary pelvic floor clinic and included in the study

Characteristic	Value
Age (years)	57 (22–79)
Nulliparous	7 (7)
Urinary incontinence (all types)	21 (21)
Prolapse complaints	13 (13)
Fecal incontinence	19 (19)
Anal sphincter rupture during childbirth	4 (4)
Fistula	2 (2)
Evacuation problems	2 (2)
Pain	7 (7)
No urogenital complaints	6 (6)
Combination of urinary incontinence, prolapse complaints, evacuation problems and fecal incontinence	26 (26)

Data are given as median (range) or *n* (%).

RESULTS

The baseline clinical characteristics of all the women who underwent pelvic floor ultrasound imaging are presented in Table 1.

The mean levator ani hiatus volume measurements of all 100 patients on conventional 3D ultrasound and virtual reality were 21.65 ± 3.38 cm^3 and 21.75 ± 4.79 cm^3, respectively. Table 2 shows the results of the comparison between conventional 3D ultrasound and virtual reality levator ani hiatus volume measurements. The mean difference between the two measurement techniques was not significantly different from zero and good agreement was observed, with an ICC of 0.968.

Figure 4 illustrates the relationship between conventional 3D ultrasound measurements and virtual reality measurements in all 100 patients, with

the Bland–Altman plot showing no variation in differences between the two techniques in relation to the magnitude of the measurements.

The intra- and interobserver reliability and agreement of the two measurement techniques (*n* = 20) are also shown in Table 2, with good agreement observed for all comparisons. The intra- and interobserver ICCs for conventional 3D ultrasound levator ani hiatus volume measurements in the 20 randomly chosen datasets were both > 0.94 and those for virtual reality measurements were > 0.97.

Table 2 Results of comparison between conventional three-dimensional (3D) ultrasound and virtual reality levator ani hiatus volume measurements and intra- and interobserver reliability and agreement of the two measurement techniques

Comparison	***n***	**Mean (SD) (cm^3)***	**Mean diff. (95% CI) (cm^3)†**	**95% limits of agreement (cm^3)‡**	**ICC (95% CI)**
Conventional 3D ultrasound vs virtual reality	100	21.70 (4.92)	0.10 (–0.15 to 0.35)	– 2.36 to 2.56	0.968 (0.952–0.978)
Intraobserver repeatability of 3D ultrasound measurements	20	22.16 (5.76)	– 0.90 (–1.69 to – 0.10)	– 4.23 to 2.43	0.948 (0.851–0.980)
Intraobserver repeatability of virtual reality measurements	20	20.56 (4.07)	0.12 (–0.21 to 0.45)	– 1.26 to 1.51	0.986 (0.965–0.994)
Interobserver agreement of 3D ultrasound measurements	20	22.06 (5.79)	– 0.71 (–1.38 to – 0.44)	– 3.52 to 2.09	0.964 (0.899–0.986)
Interobserver agreement of virtual reality measurements	20	20.49 (4.04)	0.27 (–0.13 to 0.67)	– 1.40 to 1.94	0.977 (0.944–0.991)

* Mean of three measurements.

† Mean difference = first minus second measurement of L.S. in intraobserver analysis and mean difference = first measurement of L.S. minus measurement of A.B.S. in interobserver analysis.

‡ Limits of agreement = mean difference ± (1.96 × SD).

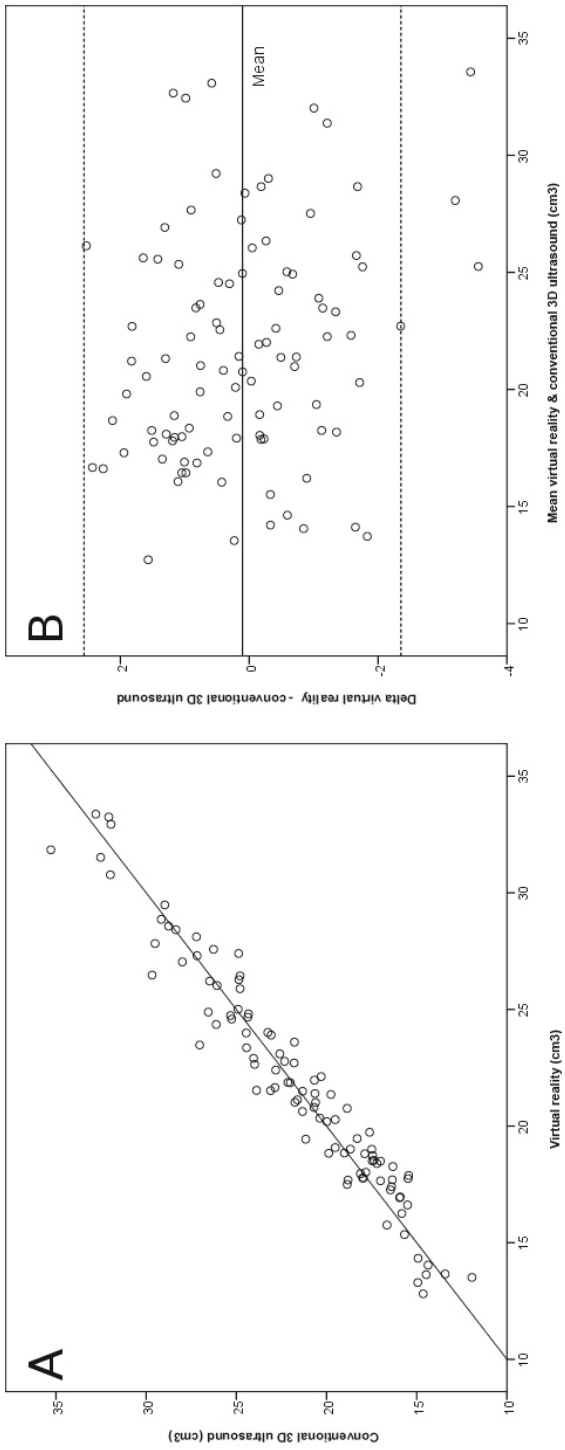

Figure 4 (a) Scatterplot showing relationship between conventional three-dimensional (3D) ultrasound measurements and virtual reality measurements in all 100 symptomatic patients attending a tertiary pelvic floor clinic.(——), Line of equality. (b) Bland–Altman plot showing agreement between conventional 3D ultrasound and virtual reality levator ani hiatus measurements in all 100 patients. Mean (——) and 95% limits of agreement (·····) are shown.

DISCUSSION

This study indicates that there is an excellent ICC value for levator ani hiatus volume measurements performed with conventional 3D ultrasound and with virtual reality. This investigation demonstrates that the conventional 3D ultrasound measurements do not differ significantly from the virtual reality volume measurements during contraction. We also conclude that there is excellent intra- and interobserver reliability of both conventional 3D ultrasound and virtual reality levator ani hiatus volume measurements. The mean intra- and interobserver differences of conventional 3D ultrasound levator ani hiatus volume measurements show some bias, but as indicated by the ICCs this does not affect reliability. The means of the second volume measurements in conventional 3D ultrasound of L.S. are smaller than the means of the first, and the volume measurements of A.B.S. are smaller than the first measurements of L.S. This bias maybe explained by the fact that A.B.S. is a more experienced investigator of the levator ani and can therefore better determine the tissue/hiatus interface of the levator ani; over time L.S. became more experienced, explaining the smaller measurements the second time.

We believe that the small mean inter- and intraobserver differences of 0.71 cm^3 and 0.90 cm^3 that we found in this study for conventional 3D ultrasound do not have any clinical significance, as our mean hiatal dimension was 21.7 cm^3 (14.47 × 1.5). These results are comparable with those of previous studies. Shek and Dietz[25] found a mean hiatal dimension during contraction of 11.6 ± 2.24 cm^2 in 296 nulliparous women and Braekken *et al.*[26] showed a mean hiatal dimension at contraction of 14.70 cm^2 in 17 healthy volunteers.

It is notable that the ICC values for both the intra- and interobserver 3D ultrasound measurements are lower than those ICC values for the virtual reality measurements, indicating a better reliability for measurements with virtual reality. This may be explained by the fact that discrimination of the pubic bone and the inside margins of the levator ani hiatus are better visualized in virtual reality. In contrast to subjective selection of the margins of the levator ani using conventional 3D ultrasound, in virtual reality a large portion of the levator ani hiatus was selected by 'the computer system' automatically planting a seed point. It is questionable whether these differences between ICC values are clinically relevant.

To study the reliability and agreement of both measuring techniques we chose to select volumes obtained on maximal levator contraction, because these are usually well defined volumes. Also, we considered

that in contraction the convex–concave shape of the levator hiatus would be more clearly outlined. Because of this, we expected to obtain a larger difference between conventional 3D ultrasound and virtual reality measurements. However, this study shows only small differences, which were not systematic and not statistically significant. So, although we had assumed that we would detect larger differences between conventional ultrasound and virtual reality it might be that the shape of the levator hiatus in contraction is not the best volume for detecting these differences.

That our study only focused on volumes obtained during contraction could also be considered a limitation. For clinical use, measurements of volumes obtained on Valsalva maneuver are of more importance, i.e. for assessing the risk of developing prolapse and determining the risk of developing recurrent prolapse[3, 27]. Therefore further investigation is necessary to see whether volumes obtained on Valsalva might show larger differences between the two methods. Another factor to be considered is that the results found in this study reflect the fact that the current measurements performed using ultrasound display a good representation of the non-Euclidean shape of the levator hiatus.

Previous studies for determining the reliability of measurements during contraction of the levator hiatus in conventional 3D ultrasound have been done. Majida *et al.*[24] showed an interobserver ICC of 0.92 with limits of agreement of – 4.05 to 3.13 in 17 healthy women. Chen *et al.*[28] found an interobserver ICC of 0.807 (95% CI, 0.581–0.918) in 96 patients for the levator hiatus area during contraction on conventional 3D ultrasound. Braekken *et al.*[26] showed an intraobserver ICC of 0.79 (95% CI, 0.50–0. 92) of the levator hiatus area during contraction on conventional 3D ultrasound. Our interobserver ICCs and limits of agreement are comparable with those found by Majida *et al.*[24], but better than those reported by Chen *et al.*[28]. Our intraobserver ICCs are a lot higher than those of Braekken *et al.*[26]. This may be explained by the small number of women investigated.

No previous studies comparing conventional 3D ultrasound with virtual reality for levator ani hiatus volume measurements during contraction have been reported. In addition, no previous studies to determine the reliability and agreement of levator ani hiatus volume measurements during contraction using virtual reality have been performed. A drawback of this study is that, unfortunately, CAVE-like virtual reality systems are currently only available in a very limited number of research centers throughout the world. For this type of measurement to become clinically feasible, smaller, low-cost desktop virtual reality systems will have to be introduced

in the hospital environment. Further investigation is also needed to observe possible differences at rest and during Valsalva maneuver, in women with abnormal levator ani anatomy, and their relationship with pelvic floor symptoms.

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CHAPTER 07

Agreement and reliability of pelvic floor measurements during rest and on maximum Valsalva maneuver using three-dimensional translabial ultrasound and virtual reality imaging

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ABSTRACT

Objectives

Imaging of the levator ani hiatus provides valuable information for the diagnosis and follow-up of patients with pelvic organ prolapse (POP). This study compared measurements of levator ani hiatal volume during rest and on maximum Valsalva, obtained using conventional three-dimensional (3D) translabial ultrasound and virtual reality imaging. Our objectives were to establish their agreement and reliability, and their relationship with prolapse symptoms and POP quantification (POP-Q) stage.

Methods

One hundred women with an intact levator ani were selected from our tertiary clinic database. Information on clinical symptoms were obtained using standardized questionnaires. Ultrasound datasets were analyzed using a rendered volume with a slice thickness of 1.5 cm, at the level of minimal hiatal dimensions, during rest and on maximum Valsalva. The levator area (in cm^2) was measured and multiplied by 1.5 to obtain the levator ani hiatal volume (in cm^3) on conventional 3D ultrasound. Levator ani hiatal volume (in cm^3) was measured semi-automatically by virtual reality imaging using a segmentation algorithm. Twenty patients were chosen randomly to analyze intra- and interobserver agreement.

Results

The mean difference between levator hiatal volume measurements on 3D ultrasound and by virtual reality was 1.52 cm^3 (95% CI, 1.00–2.04 cm^3) at rest and 1.16 cm^3 (95% CI, 0.56–1.76 cm^3) during maximum Valsalva ($P < 0.001$). Both intra- and interobserver intraclass correlation coefficients were ≥ 0.96 for conventional 3D ultrasound and > 0.99 for virtual reality. Patients with prolapse symptoms or POP-Q Stage ≥ 2 had significantly larger hiatal measurements than those without symptoms or POP-Q Stage < 2.

Conclusions

Levator ani hiatal volume at rest and on maximum Valsalva is significantly smaller when using virtual reality compared with conventional 3D ultrasound; however, this difference does not seem clinically important.

INTRODUCTION

It has been shown that enlargement of the levator ani hiatus, so-called 'ballooning', is associated with an increased risk of pelvic organ prolapse for all three pelvic compartments[1-3]. Furthermore, it is associated with prolapse recurrence after previous prolapse surgery[4]. Therefore, imaging of the levator ani hiatus, especially on maximum Valsalva, can be of great value in the diagnosis and follow-up of patients with symptoms of pelvic organ prolapse.

The levator ani hiatus can be visualized using magnetic resonance imaging (MRI) or three-dimensional (3D) translabial or endovaginal ultrasonography[5-7]. However, there may be some limitations. It has been postulated that, in real multiplanar MRI construction, the levator hiatus is visualized as a non-Euclidean hyperbolic structure[8, 9]. 3D translabial ultrasound measurements are currently performed on two-dimensional (2D) rendered images, obtained from data volume analysis of 3D/four-dimensional (4D) cineloops. The non-Euclidean nature, i.e. the concave and convex shape of the levator hiatus, is therefore not taken into consideration in volume measurements obtained by 3D translabial ultrasound. This may overestimate or underestimate the 'real' levator hiatal area.

The I-Space is a virtual reality system which enables 3D ultrasound datasets to be visualized as a 'hologram'[10]. The concave and convex features of the levator ani can therefore be visualized, allowing the investigator to measure the actual 3D volume. The I-Space has been used successfully for studies on prenatal ultrasonography[10, 11] and this technique has recently been applied in a study on 3D translabial pelvic floor ultrasound[12]. This study showed that measurements of levator ani volume during contraction using virtual reality were reliable and comparable to conventional 3D ultrasound measurements[12].

For clinical use, it is important to obtain measurements of the levator ani hiatal volume at rest and especially during maximum Valsalva, because examination during maximum Valsalva determines the severity of prolapse[1, 13].

This study was designed to compare levator ani hiatal volume at rest and on maximum Valsalva, measured using conventional 3D translabial ultrasound and virtual reality, and to establish the intra- and interobserver agreements of these measurements. Furthermore, we aimed to establish whether there is an association between levator ani hiatal volume at

rest and on maximum Valsalva, measured using both conventional 3D translabial ultrasound and virtual reality, with prolapse symptoms and pelvic organ prolapse quantification (POP-Q) stage.

METHODS

Patients

The patient sample was the same as that in our previous publication[12] and comprised 100 female patients with an intact levator ani muscle (diagnosed by translabial pelvic floor ultrasound with the method of Dietz *et al*.[14]) who were selected randomly from the database of our tertiary pelvic floor clinic. All patients had undergone an interview using a standardized questionnaire, concerning medical history, urinary function, prolapse symptoms and bowel function. Prolapse symptoms were defined as complaints of pelvic discomfort and/or vaginal bulging. A clinical examination was performed, including POP-Q staging[15].

The current study was performed several years after our previous study[12] and some patient information was not well known in the first study. We therefore acquired additional patient characteristics or slightly different information.

Pelvic floor ultrasound imaging, with the patient in the supine position and after voiding, was performed at rest and during maximum Valsalva, using a Voluson 730 Expert system with a 4–8-MHz RAB abdominal probe (GE Healthcare, Chalfont St Giles, UK) as described by Dietz *et al*.[16]. The maximum Valsalva was defined as a forced expiration against a closed glottis[17], with a relaxed pelvic floor, for at least 6 s. Care was taken to avoid levator co-contraction. Offline analysis of the levator ani hiatus was performed blinded to the patient's history or clinical information.

Conventional three-dimensional ultrasound measurements

Conventional 3D ultrasound datasets were analyzed offline using a rendered volume, with a slice thickness of 1.5 cm at the level of minimal hiatal dimensions, at rest and on maximum Valsalva (Figure 1). The levator area (cm^2) at rest and on maximum Valsalva was measured using specialized 3D imaging software, 4D View version 9.0 (GE Healthcare), and the value was multiplied by 1.5 to obtain the conventional 3D ultrasound levator ani hiatus volume (cm^3). These conventional volume measurements were later compared with volume measurements obtained using virtual reality (cm^3).

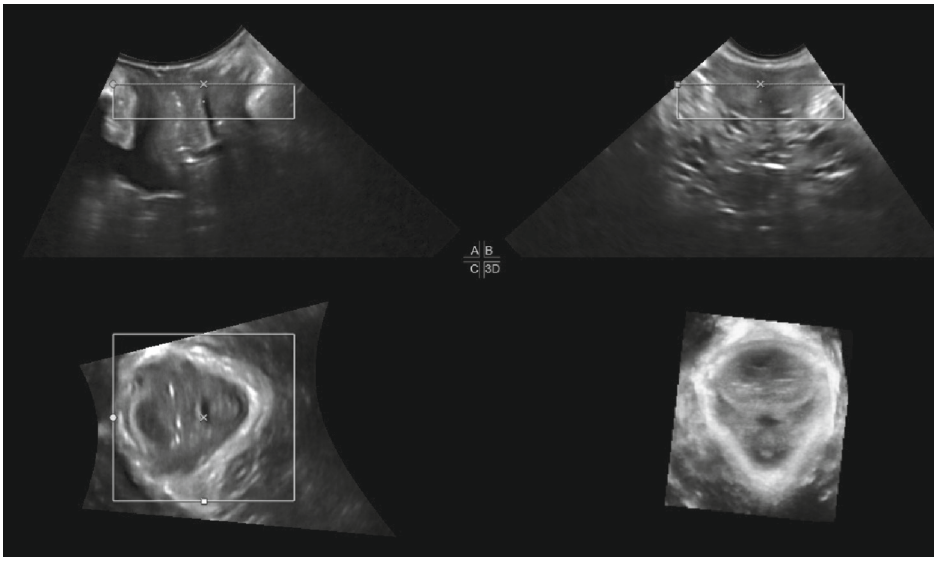

Figure 1 Rendered ultrasound volume (slice thickness of 1.5 cm) of a normal levator ani hiatus as seen and measured using 4D View.

Virtual reality measurements

We measured the levator ani hiatal volume using virtual reality by storing the 3D datasets as Cartesian volumes using 4D View. These 3D datasets were then visualized in the I-Space, a so-called four-walled CAVE™ (Cave Automatic Virtual Environment)[18] like virtual reality system, as described previously in our study on pelvic floor measurement during contraction[12].

In the I-Space, a researcher is surrounded by computer-generated stereo images, which are projected by eight high-quality digital light-processing projectors onto three walls and the floor of a small room. The I-Space allows medical professionals to view and interact with their volumetric data in all three dimensions. With the V-Scope[19] application (a volume-rendering application developed in-house), an interactive 'hologram' of the ultrasound image is created and can be manipulated and measured in all three dimensions by means of a virtual pointer, controlled by a wireless joystick. The interactive hologram is viewed with depth perception, using the same type of glasses with polarizing lenses that are used for 3D movies (Figure 2).

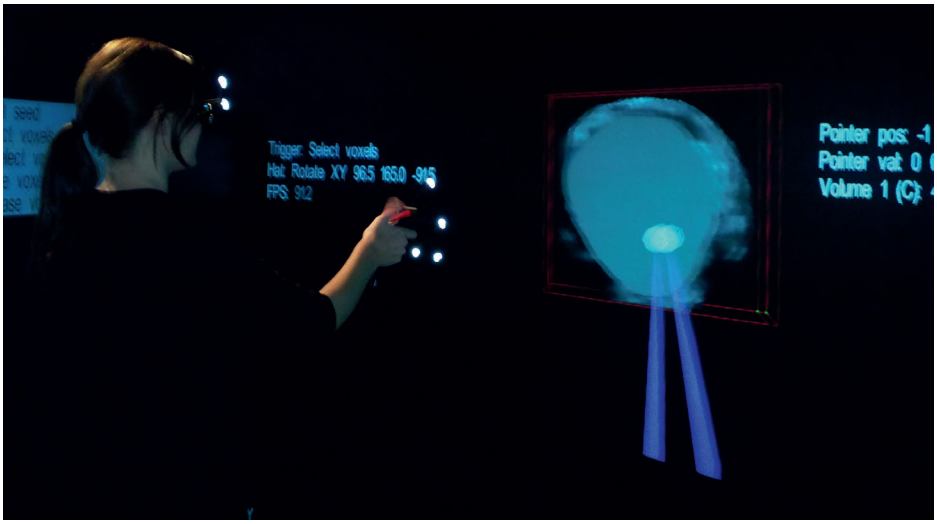

Figure 2 Operator in the I-Space virtual reality system examining the levator ani hiatus.

The levator ani volumes were enlarged, rotated and cropped. The outside of the puborectalis muscle was 'brushed' away with the eraser function to avoid segmentation of parts outside the levator ani. The hypoechoic inside of the levator ani was then selected by placing a seed point for the region growing segmentation algorithm, after setting an upper and lower gray-level threshold and an upper threshold for the standard deviation of the voxel's neighborhood. If the volume measurement is incomplete, the user can enlarge or shrink the segmented region manually with a spherical, free-hand 'paint brush', to add or delete voxels to or from the segmented structure as necessary. Figure 3 shows a complete virtual reality image (displayed in gray) of a volume measurement of the levator hiatal area during rest.

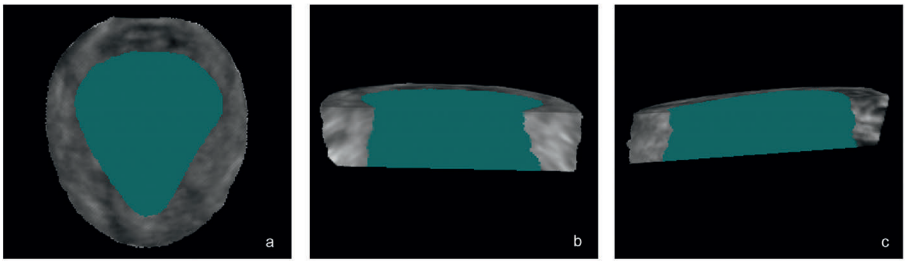

Figure 3 Two-dimensional virtual reality image of a volume measurement of the levator hiatal area, displayed in gray, showing axial (a), coronal (b) and midsagittal (c) planes. The concave and convex shape of the hiatus can be observed.

Agreement and reliability
Conventional 3D ultrasound and virtual reality volume measurements, at rest and on maximum Valsalva, in all 100 patients were performed by one operator (C.S.B.) and repeated three times, which is standard in the clinical application of ultrasound measurements. The mean of the three measurements obtained using 3D ultrasound and those obtained by virtual reality were used for comparison between the two imaging methods.

For calculating the interobserver reliability and agreement of both conventional 3D ultrasound and virtual reality, levator ani hiatal volume datasets from 20 randomly chosen patients were selected. Both investigators, C.S.B. and L.S., independently performed three volume measurements on each dataset by both imaging methods; the mean measurement was used for comparison.

To assess intraobserver reliability and agreement of both conventional 3D ultrasound and virtual reality, C.S.B. performed another three measurements in 20 randomly chosen datasets. The mean of these measurements was compared with the mean of the three previously obtained measurements by C.S.B. from the same 20 datasets. The second series of measurements by C.S.B. were performed at least 2 weeks later than the first to prevent recollection bias.

C.S.B. was performing these measurements in both 4D View and the I-Space for the first time and L.S. had only performed these measurements previously in a prior study on levator ani hiatus measurements during contraction. Both were trained in 4D View by A.B.S., who is experienced in pelvic floor measurements in 4D View but not with virtual reality.

Statistical analysis
Statistical analysis was performed using IBM SPSS Statistics version 20.0 (IBM, Armonk, NY, USA)**.** A two-sided *P*-value < 0.05 was considered to indicate statistical significance.

To compare measurements obtained using virtual reality with those on conventional 3D ultrasound, and determine the inter- and intraobserver variability, we calculated the mean difference, 95% CI of the mean difference, limits of agreement (mean difference ± 1.96 SD) and the intraclass correlation coefficient (ICC). Bland–Altman plots were used to determine whether the difference was influenced by the magnitude of the measurements[20, 21]. An ICC value of 0.81–1.00 was considered to reflect excellent reliability[22, 23].

The associations between prolapse symptoms, pelvic organ prolapse on POP-Q, conventional 3D ultrasound and virtual reality measurements were analyzed using the mean difference and 95% CI. For this analysis, we included only patients without a history of prolapse surgery.

RESULTS

Baseline clinical characteristics of the patients are presented in Table 1. Mean levator hiatal volume measurements at rest obtained with conventional 3D ultrasound and with virtual reality were 27.96 ± 5.91 and 26.44 ± 6.00 cm^3, respectively (Table 2). The mean difference between measurements was 1.52 cm^3 (%95 CI, 2.04–1.00 cm^3) ($P < 0.001$; Figure 4a). Mean levator hiatal volume measurements on maximum Valsalva obtained with conventional 3D ultrasound and with virtual reality were 36.90 ± 10.50 and 35.74 ± 9.63 cm^3, respectively (Table 2). The mean difference was 1.16 cm^3 (%95 CI, 1.76–0.56 cm^3) ($P < 0.001$; Figure 4b).

Table 1 Baseline characteristics of 100 symptomatic women with normal levator ani hiatus attending a tertiary pelvic floor clinic

Characteristic	Value
Age (years)	57 (22–79)
Nulliparous	7
Previous prolapse surgery	19
Urinary incontinence (all types)	21
Prolapse symptoms	15
Fecal incontinence	20
Prior obstetric anal sphincter injury	5
Fistula	2
Obstructed defecation	2
Pain	7
No urogenital complaints (fibroids)	1
Combination of urinary incontinence and/or prolapse symptoms and/or obstructed defecation and/or fecal incontinence	27

Data are given as median (range) or *n*.

Table 2 Measurements of levator ani hiatal volume at rest and on maximum Valsalva, by conventional three-dimensional (3D) ultrasound and by virtual reality imaging in 100 symptomatic women attending a tertiary pelvic floor clinic

Variable	3D ultrasound		Virtual reality	
	At rest (cm^3)	On maximum Valsalva (cm^3)	At rest (cm^3)	On maximum Valsalva (cm^3)
All patients (*n* = 100)	27.96 ± 5.91	36.90 ± 10.50	26.44 ± 6.00	35.74 ± 9.63
Nulliparae (*n* = 7)	23.19 ± 4.01	28.54 ± 11.40	22.49 ± 4.43	27.72 ± 9.28
Parae (*n* = 93)	28.32 ± 5.88	37.53 ± 10.22	26.74 ± 6.01	36.35 ± 9.28
Prolapse symptoms* (*n* = 23)	28.87 ± 4.76	41.39 ± 9.58	26.92 ± 4.50	39.97 ± 9.42
No prolapse symptoms* (*n* = 58)	27.47 ± 6.31	34.96 ± 10.96	26.11 ± 6.62	33.76 ± 9.34
POP-Q Stage ≥ 2* (*n* = 33)	29.16 ± 6.15	43.46 ± 11.02	27.60 ± 7.13	41.09 ± 9.51
POP-Q Stage < 2* (*n* = 48)	26.98 ± 5.64	32.20 ± 8.11	25.46 ± 5.14	31.69 ± 7.91

Data are given as mean ± SD.* Only patients without history of prolapse surgery. POP-Q, pelvic organ prolapse quantification.

Parous women had significantly larger levator ani hiatal volume measurements on 3D ultrasound at rest and on maximum Valsalva than did nulliparous women, with mean differences of 5.13 cm^3 (95% CI, 0.62–9.63 cm^3) (*P* = 0.03) and 8.99 cm^3 (95% CI, 0.98–17.00 cm^3) (*P* = 0.03), respectively (Table 2). Volume measurements in virtual reality were only significantly larger in parous than in nulliparous women when measured during maximum Valsalva, with a mean difference of 8.63 cm^3 (95% CI, 1.30–15.95 cm^3) (*P* = 0.02). At rest, the difference in volume measurements did not reach statistical significance (*P* = 0.07).

Patients with prolapse symptoms had significantly larger levator ani hiatal volume measurements during maximum Valsalva on both conventional 3D ultrasound and on virtual reality when compared with those without

symptoms, with a mean difference of 6.43 cm^3 (95% CI, 1.25–11.60 cm^3) (P = 0.02) and 6.21 cm^3 (95% CI, 1.62–10.80 cm^3) (P = 0.01), respectively. At rest, the difference in volume measurements in patients with *vs* those without prolapse symptoms did not reach statistical significance (P = 0.34 and P = 0.59, respectively).

Patients with POP-Q Stage ≥ 2 had significantly larger levator ani hiatal volume measurements during maximum Valsalva on conventional 3D ultrasound and on virtual reality, compared with patients with POP-Q Stage < 2; the mean differences were 11.26 cm^3(95% CI, 7.03–15.49 cm^3) (P < 0.01) and 9.40 cm^3 (95% CI, 5.54–13.27 cm^3) (P < 0.01), respectively (Table 2).

For the analysis to determine an association between levator ani hiatal volume, measured at rest and on maximum Valsalva by conventional 3D translabial ultrasound and by virtual reality, with prolapse symptoms, we included all patients with symptoms of prolapse (n = 23) who had no history of previous prolapse surgery. Fifteen patients had only symptoms of prolapse (Table 1), whereas the other eight patients also had other complaints such as urinary incontinence, shown in Table 1 as combination of urinary incontinence and/or prolapse symptoms and/or obstructed defecation and/or fecal incontinence.

Intraobserver and interobserver intraclass correlations coefficients for levator ani hiatal volume measurements were ≥ 0.96 for conventional 3D ultrasound and > 0.99 for virtual reality (Table 3). Bland–Altman plots showing the agreement between hiatal volume measurements obtained at rest and on maximum Valsalva are shown in Figure 5.

Figure 4 Scatterplots showing relationship between levator ani hiatal volume, at rest (a) and during maximum Valsalva maneuver (b), measured by conventional three-dimensional (3D) ultrasound (US) and by virtual reality imaging (VR) in 100 symptomatic women attending a tertiary pelvic floor clinic. The line of equality is shown.

Table 3 Intra- and interobserver agreement for measurements of levator ani hiatal volume at rest and on maximum Valsalva maneuver, obtained by three-dimensional ultrasound and by virtual reality imaging in 20 women selected randomly from study group

	ICC (95% CI)	
Method	**At rest**	**On maximum Valsalva**
Intraobserver		
Ultrasound	0.982 (0.957–0.993)	0.949 (0.914–0.968)
Virtual reality	0.995 (0.988–0.998)	0.991 (0.977–0.996)
Interobserver		
Ultrasound	0.960 (0.901–0.984)	0.998 (0.995–0.999)
Virtual reality	0.993 (0.982–0.997)	0.987 (0.969–0.995)

ICC, intraclass correlation coefficient.

DISCUSSION

This study demonstrates that volume measurements obtained by conventional 3D translabial ultrasound can be compared with virtual reality imaging for research investigation of levator ani hiatal volume at rest and on maximum Valsalva. Furthermore, it demonstrates that levator hiatal measurements obtained using virtual reality are significantly smaller than those obtained using conventional 3D ultrasound, at rest and on maximum Valsalva. It shows excellent inter- and intraobserver agreement for both imaging techniques. Furthermore, a positive association was found between parity, prolapse symptoms and POP-Q Stage ≥ 2 and levator ani hiatal volume measurements, especially on maximum Valsalva.

Our hiatal area measurements in cm^2 in patients with no levator avulsion were comparable to measurements of previous published research[24].

The results of this study are in line with those of our previous study[12], comparing levator ani hiatal measurements during contraction using conventional 3D ultrasound with virtual reality (mean difference of 0.10 cm^3 (95% CI, −0.15 to 0.35 cm^3; P = 0.41). However, this difference was not significant, contrary to the differences found in the present study. This may be explained by the fact that differences in measurements can be greater when the volumes are larger, because volumes measured during contraction are smaller than those measured at rest or on maximum Valsalva. Although statistically significant, we believe that the small

Figure 5 Bland–Altman plots showing agreement between levator ani hiatal volume, at rest (a) and during maximum Valsalva maneuver (b), measured by conventional three-dimensional (3D) ultrasound (US) and by virtual reality imaging (VR) in 100 symptomatic women attending a tertiary pelvic floor clinic. Mean (——) and 95% limits of agreement (·-·-·-·) are shown.

differences of 1.52 and 1.16 cm^3 that we found would be unlikely to have clinical consequences.

Virtual reality imaging is a unique way to visualize ultrasound data with perception of depth and offers the possibility for measuring non-planar structures. To our knowledge, this is the first study to compare conventional 3D translabial ultrasound visualization with virtual reality for levator ani hiatal volume measurements obtained at rest and on maximum Valsalva.

Unfortunately, CAVE™-like virtual reality systems such as the I-Space are currently only available in a limited number of research centers throughout the world and are costly. A smaller, low-cost desktop virtual reality system is currently available for use in an outpatient clinical setting[25].

Both operators found that measuring volumes in virtual reality was easier to learn than with 4D View. One of the advantages of virtual reality is that the levator ani volumes can be enlarged, rotated and cropped. Discrimination of the pubic bone and the inner margins of the levator ani hiatus are better visualized in virtual reality. In contrast to selecting subjectively the margins of the levator ani as for conventional 3D ultrasound, in virtual reality, a large portion of levator ani hiatus is selected automatically by the computer system after planting a seed point.

In this study, the intraobserver and interobserver ICC values for virtual reality measurements were slightly better than those for conventional 3D ultrasound measurements; however, both were excellent. The slightly better ICCs for virtual reality measurements might be explained by the abovementioned advantages of measuring in virtual reality. It is questionable whether these differences between ICC values are clinically relevant.

Using both methods, parous women had significantly larger levator ani hiatal volumes on maximum Valsalva compared with nulliparous women. We expect to find pelvic floor changes after a vaginal birth. Our levator ani hiatal volume measurements in nulliparous women are comparable to those of previously published research[26-28]. A recent study showed that vaginal parity was associated strongly with hiatal area measurements on conventional 3D ultrasound during maximum Valsalva[26].

Patients with prolapse complaints and patients with clinical signs of prolapse also had significantly larger volume measurements on maximum Valsalva utilizing both imaging methods. These findings are in concordance with those of previous studies, which showed that the size of the levator

hiatus is strongly associated with both signs and symptoms of pelvic organ prolapse and recurrence[1-3]. We see this association in both 3D translabial ultrasound measurements and in virtual reality, which indicates that normal 3D translabial ultrasound can be used to obtain these measurements.

Some potential limitations of this study should be acknowledged. The studied group of patients was heterogeneous. We do not believe that this influenced the measurements obtained with conventional 3D ultrasound and virtual reality or the inter- and intraobserver ICCs. However, it might have influenced the association found between clinical complaints and prolapse severity with levator ani hiatal volume measurements. Furthermore, measurements obtained during maximum Valsalva may be biased by the fact that levator co-activation can occur during maximum Valsalva. This would provide a smaller levator ani hiatal volume measurement during maximum Valsalva than is the true volume when there is no co-activation.

In conclusion, virtual reality is a novel method for visualizing ultrasound data which has the benefit of depth perception. This offers the possibility for measuring non-planar structures, such as the pelvic floor. This study demonstrates that measurement of levator ani hiatal volume on virtual reality imaging at rest and on maximum Valsalva is reliable and correlates with clinical symptoms and signs of prolapse on POP-Q, in patients with a normal levator ani. Current measurements of the levator ani hiatus by conventional 3D ultrasound in patients with an intact levator ani muscle are reliable and only differ slightly from those measured with virtual reality. Further research is warranted to determine whether these small differences will either increase or decrease in patients with levator ani avulsion or defect and therefore become of clinical importance.

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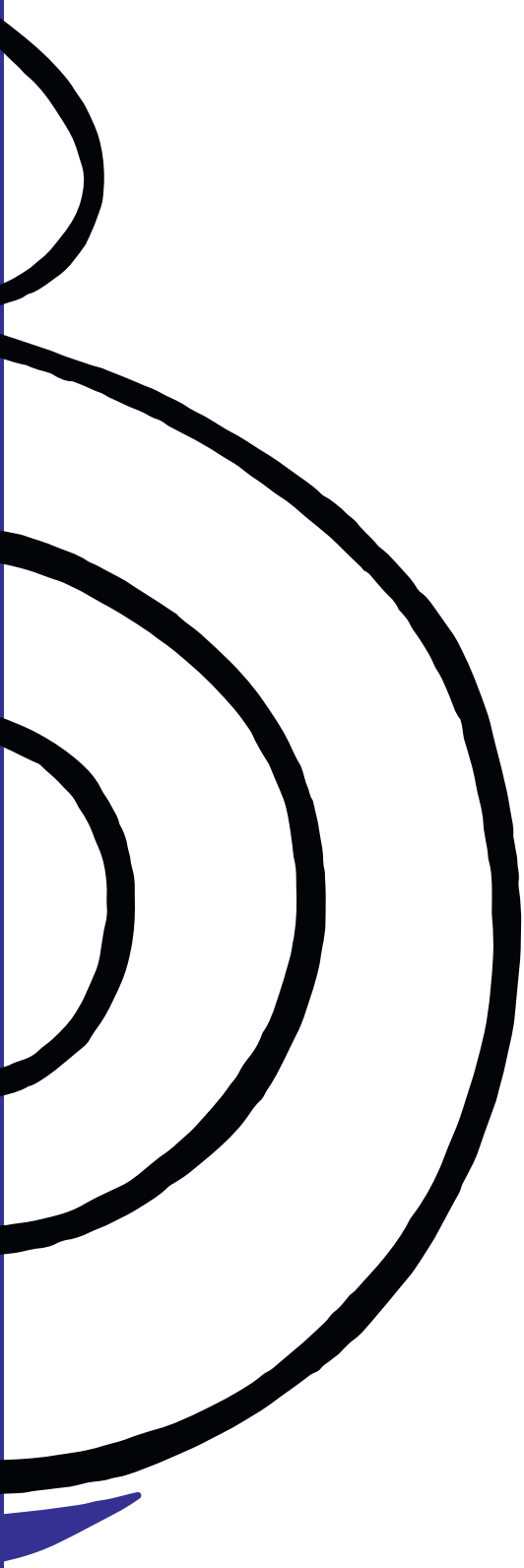
PART III



General Discussion, Summary and Appendices

CHAPTER 7

General discussion, implications for daily practice and future research

The focus of this thesis is the development of pelvic floor injury and complications after vaginal delivery leading to complaints. This was studied in a group of women after a normal vaginal delivery without complications and in a group of women with obstetric sphincter injury. In addition, we studied a new form of pelvic floor imaging and whether it was reliable and feasible.

Pelvic floor injury

A major cause of pelvic floor disorders (PFD) are pelvic floor injury and muscle weakness[1-5]. PFD may imply pelvic floor prolapse, anal or urinary incontinence, and recurrent pelvic floor prolapse after prolapse surgery. Pelvic floor injury and muscle weakness are mainly caused by pregnancy and vaginal delivery[6]. The most common form of pelvic floor injury after childbirth is damage to the anal sphincter and the levator ani muscle (LAM). This injury affects up to 40% of vaginally parous women[7].

This pelvic floor injury can be visualized in different ways nowadays, such as (dynamic) magnetic resonance imaging (MRI) or three dimensional (3D)/ four dimensional (4D) ultrasound imaging. The work of Delancey[5, 8-10], Dietz[3, 11-13], and Sultan[14-17] has done much to draw attention to the role of pelvic floor injury, and especially LAM injury and anal sphincter defects for the development of PFD. The LAM can be injured by stretch (overdistension or microtrauma) or avulsion (disruption of the muscle or macrotrauma)[18]. The strong association between pelvic organ prolapse and LAM injury can be explained to a large extent by a larger levator hiatus and weaker pelvic muscles after levator avulsion[19].

By combining images with general history, obstetric history, urogynecological complaints of the woman, and regular urogynecological examination, we are learning more and more on the pathophysiology of PFD.

Pelvic floor imaging

The first studies of the LAM were performed with MRI[8], but the availability of 3D/4D ultrasound imaging since 2004 has made imaging of pelvic floor injury possible with an easier, cheaper, non-invasive and more accessible method. Currently, pelvic floor ultrasound (PFUS) is a proven and useful procedure for evaluating the pelvic floor, including the urethra, bladder, vagina, uterus if possible, anorectum and LAM[20]. One of the LAM ultrasound assessments is used to measure levator ani hiatus at rest, during maximal pelvic floor contraction, and maximum Valsalva maneuver. These measurements of the levator ani hiatus are performed in two dimensions (2D) using a rendered volume at the level of minimal hiatal dimensions.

The non-Euclidean nature, i.e. the concave and convex shape of the levator hiatus as described by Silva-Filho *et al*.[21] and Kruger *et al.*[22] , is not taken into account in volume measurements with this method. This allows the 2D visualized and measured hiatal region of the levator to overestimate or underestimate the "true" dimensions of the hiatal region of the levator. This may also have consequences in clinical practice.

On March 24, 2005, the Bioinformatics department of Erasmus MC in Rotterdam opened a Barco I-Space virtual reality (VR) system. This system allowed researchers to visualize ultrasonic data sets with depth perception ("real 3D"). This method also offered the possibility to measure non-planar structures, such as the pelvic floor. In our two studies with virtual reality, we compared 3D/ 4D volume measurements obtained with ultrasound with volume measurements obtained using virtual reality. We found no clinically relevant differences between the levator hiatus measurements measured with perineal PFUS or virtual reality. Therefore, we currently believe that virtual reality does not currently add value in the assessment of the pelvic floor.

While ultrasound machines are easily accessible in gynecological practice, PFUS is hardly used in daily urogynecological practice. PFUS is still more a research tool than a tool in clinical practice. In the most recent practice guideline, it was stated that PFUS examinations should only be performed if there is a valid medical reason[20]. However, this reason is not always clear in the daily clinical practice. Moreover, many colleagues find learning and applying the PFUS a challenge. Hopefully, the availability of online training and automatic levator hiatus measurement and LAM integrity assessment can improve the use of this technique [23]. In my opinion, PFUS does play a role as the first additional examination in women with PFD. PFUS should at least be performed in women with complex PFD (multiple urogynecological symptoms especially shortly after childbirth, difficult delivery or premenopausal age). Furthermore, I would recommend to perform PFUS assessment in women with a multicompartment pelvic organ prolapse. As well as those women with chronic pelvic pain (especially after previous pelvic floor (implant) surgery) and those with recurrent prolapse or urinary incontinence after previous pelvic floor surgery. Imaging also helps women with PFD to observe what is happening in the pelvic floor and how this can be related to her symptoms. As mentioned previously, pelvic floor imaging, including PFUS, has enabled us to understand more about the pathophysiology of pelvic floor injury and PFD. Future research may help us unravel even more about this pathophysiology and determine its optimal treatment.

Treatment of Pelvic floor injury

Attempts to repair LAM injuries directly after the delivery have so far have been unsuccessful. There is currently no clear indication for repair and also long-term outcomes are missing[24-27]. Fortunately, obstetric anal sphincter injury is often noticed after delivery. Primary repair of OASI has proven essential for anal continence, and prevents long-term morbidity[28]. Unfortunately, even after primary repair residual defects of the anal sphincters may occur, associated with ongoing anal incontinence years after the initial injury[29-34]. In addition, we know that, despite primary repair after obstetric sphincter injury, women are more likely to have pelvic floor symptoms in the short and longer term than women without obstetric sphincter injury. Therefore, prevention of both kind of injuries is important.

Risk and protective factors of pelvic floor injury

Prevention can be applied if we know the risk and protective factors for the occurrence of pelvic floor injury and PFD. Previous research showed that risk factors for the occurrence of this injury include forcipal extraction, advanced maternal age at first delivery, extended second stage of birth, non- occiput anterior presentation, fundal expression (Kristeller maneuver), high birth weight, midline episiotomy, and large head circumference of the fetus. However, it is not yet known which other factors play a role in the occurrence or prevention of this damage, as there is still insufficient evidence or conflicting outcomes. This is, for example, the case with maternal body mass index (BMI), perineal support and mediolateral episiotomy[35-41].

In our first cohort study, EpiLeva[42], we found that a mediolateral episiotomy is neither a risk factor nor a protective factor for LAM injury (levator avulsion, levator ballooning or combined injury). No differences in urogynecological complaints were found between women who had undergone a mediolateral episiotomy or women without a medial episiotomy. We also saw no difference in symptoms between women with or without a levator avulsion and/ or ballooning and women. In this group we looked more closely at sexual dysfunction and the role of levator injury (avulsion and/or ballooning) and levator function[43]. We concluded that after first vaginal delivery sexual dysfunction is not associated with levator hiatal dimensions as measured by perineal PFUS.

Our results suggest that LAM injury in women is a result of a difficult vaginal delivery, for example a longer second stage or non- occiput anterior position. Usually symptoms of PFD dot not arise until decades after the pelvic floor injury has occurred. In our study, the mean time of analysis

was 13 months which may be too early to see a difference in PFD or sexual dysfunction. A much longer follow-up period would be best but is a 30 to 40 year follow-up feasible? And how can you include the effect of new pregnancies and deliveries? What would be an acceptable risk for women to take into account to assess the possibility of developing pelvic floor complaints? What do women want themselves? Therefore these questions involve a complex issue to which an unambiguous answer cannot be expected. Later on I will come back on these questions and how we might possibly include the known risk factors in our shared decision-making with pregnant patients.

In our second cohort study, FU-OASIS, we evaluated whether anal sphincter defects, levator avulsion or levator ballooning with perineal PFUS after OASI were associated with severity of anal incontinence[44]. Furthermore, we evaluated whether factors such as constipation or altered stool consistency are associated with symptoms of incontinence after OASI. We concluded that residual defects of external sphincter, detected on perineal PFUS, are associated with severity of anal incontinence symptoms measured using St Mark's incontinence score 4 months after OASI repair. Furthermore, several clinical factors, such as constipation and altered stool consistency, appeared to have a greater association and may therefore play a more important role in clinical management. However, here too there is the problem of the short follow-up duration and the fact that we know that complaints can often arise after years.

Other factors associated with pelvic floor disorders

Research has shown that constipation and bowel disease are significant risk factors that are often not considered in PFD and in patients with anal incontinence[45-48]. Two studies by Johannessen *et al.*[46, 49] have shown that bowel disease and bowel evacuation problems were associated with a higher prevalence of anal incontinence from late first pregnancy to six years postpartum. In a large population-based survey of elderly community-dwelling Americans, complaints of fecal incontinence were common[50]. Of the respondents 1 in 7 reported previously experiencing fecal incontinence, whereas 1 in every 20 had a fecal incontinence event within the past week. Fecal incontinence is an age-related disorder and often prevalent among those with Crohn's disease, ulcerative colitis, celiac disease, irritable bowel syndrome, diabetes, and concomitant constipation and diarrhea. Additionally, they found that those with recent diarrhea or chronic idiopathic constipation have significantly more severe fecal incontinence symptoms[50]. In our FU-OASIS study we also found the association between anal incontinence severity and fecal consistency and constipation. This

corroborates with findings in previous studies that revealed a similar association in both women and men [51-53]. Bharucha *et al.* even found that the strongest risk factor for anal incontinence in women older than 39 years was bowel disorders and not obstetric injury[52]. Having optimal stool consistency and preventing constipation is something we need to assess and possibly treat in women after obstetric sphincter injury and with anal incontinence or PFD.

Besides the effects of pregnancy, childbirth, constipation and bowel disease, we also must (as far as possible) take into account other factors that increase the chance of developing pelvic floor injury and PFD. These factors are obesity, chronic increase in intra-abdominal pressure (strenuous physical work, excessive coughing), hormonal changes in menopause, aging, connective tissue disorders and pelvic floor surgery[6, 54].

Preventing pelvic floor disorders

Which general factors may be preventive for PFD? First of all, is there a role for primary prevention through pelvic floor muscle training (PFMT)? There is Level 1a evidence that PFMT is effective in treating PFD, but the role of PFMT in the primary prevention PFD is less clear[55-57]. In any case, we know that general exercise and PFMT during pregnancy have no negative effect on length of labor or mode of delivery[58]. Many women start PFMT during pregnancy, postpartum or when they have pelvic floor complaints. More research is needed to determine whether correct use of the pelvic floor and optimal pelvic floor function in the preconception protects against future PFD.

Secondly, in our opinion, the development of pelvic floor injury and PFD should be considered as is a multiple hit model. One factor might not have that much influence, but combining several factors together may imply greatly increased risk of injury and PFD. The more factors we can prevent or improve, the smaller the chance of injury and PFD in the future. It is therefore not difficult to understand that the associations found are inconsistent when only one or two risk factors are studied. There is a lack of systematic reviews reporting on more than two risk factors predicting PFD later in life[59]. In order to better predict which women are more at risk of complaints in the future. We need to obtain larger datasets for the assessment of which multiple risk factors is related to develop PFD in order to arrive at a better prediction and well-founded advice[60].

One way to achieve these large data sets is to implement pregnancy and delivery (PCB) outcome sets developed by the International Consortium for

Health Outcomes Measurement (ICHOM) [61]. This PCB outcome set includes clinical outcomes and patient reported outcome measures (PROMs). The clinical outcomes are maternal and neonatal mortality and morbidity, stillbirth, preterm birth and birth injury. The PROMs measure health-related quality of life, mental health, mother-child attachment and self-esteem, success with breastfeeding, incontinence (anal and urinary), and satisfaction with care and birth experience. Using this PCB outcome set can help standardize the assessment of key outcomes in perinatal care[62]. This should lead to quality improvement and optimization of the care process in perinatal care. The goal is to achieve an optimal balance between patient outcomes and healthcare costs (value-based care). PFD is part of PROMs in this PCB outcome set. The last PROMs are measured 6 months after delivery. However a longer follow-up duration would be better. Despite the short follow-up period, linking PROMs to maternal and obstetric data is expected to produce interesting results. These outcomes might lead to better risk selection and outcomes for future pregnant women in areas such as PFD. It is also important that global patient-centered standard outcomes by ICHOM are introduced for PFD. Currently, there is only an ICHOM Standard Set for Overactive Bladder[63]. In these ICHOM Standard Set for prolapse, urinary incontinence or anal incontinence, the obstetric data and other risk factors for PFD as described above should be included.

Lifestyle and pelvic floor disorders

Many risk factors for PFD can be influenced by adjusting our lifestyle[64]. Therefore, it is important to screen for these lifestyle factors. But these lifestyle adjustments are easier said than done. All these problems are multifactorial and there are no simple answers here either. In order to achieve effective individual and social change, it is important to understand why is it so difficult to stop smoking, to reduce obesity and intestinal complaints such as constipation, and to start a family at a younger age and make the ‘better’ choice. Further research into new effective tools and treatments and optimal implementation of existing tools and treatments to guide patients with these problems is and remains necessary. But perhaps we also need to adjust our expectations, because it is realistic to live a symptom-free life into old age.

We would like to take a closer look specifically at obesity. In high-income countries, such as the Netherlands, we have had an increase in the number of overweight and obese women for many years even in their fertile stage of life[65]. We also see that nearly half of all pregnant women in the US gain weight more than recommended, especially those who are already overweight or obese before pregnancy[66]. Obesity and weight gain during

pregnancy beyond existing recommendations have been associated with the development of gestational diabetes (GDM). Pregnancies affected by GDM pose a risk to both mother and child as the risk of a longer second stage, surgical vaginal delivery, fetal macrosomia and shoulder dystocia is higher[67]. All these risks are related to the development of pelvic floor injury during vaginal delivery[15, 35-38, 68-72]. There is also evidence that GDM itself leads to an increased risk of pelvic floor complaints, such as urinary incontinence and weakness of the pelvic floor muscles (PFM), sometimes as early as two years after birth[73, 74]. The story thereby continues, the children of women with GDM have a higher risk of developing obesity and type 2 diabetes at a young age[75]. This is how the negative cycle is passed on to the future generation.

One way to reduce this risk is by adjusting various lifestyle factors. In an attempt to prevent perinatal complications, previous studies investigated the effect of lifestyle behavior modification during pregnancy. While these interventions were successful in limiting weight gain during pregnancy, they were unsuccessful in reducing GDM, pre-eclampsia and fetal macrosomia in obese women. In contrast, data from large population studies indicate that lowering the body mass index to normal weight before a subsequent pregnancy does lead to a reduction in GDM and fetal macrosomia[76, 77]. Therefore, a lifestyle intervention that starts during the preconception might be promising in reducing pregnancy and birth complications and thereby provide a more promising start for the future generation[78]. But, a one-size-fits-all approach does not work and we know from several studies that permanent lifestyle changes are difficult[79, 80]. Success or failure in initiating and sustaining lifestyle changes is determined by the complex interplay of internal and external factors. Identifying and optimizing these factors can not only result in more effective and personalized treatment, but can also reduce social stigma for patients. In certain cases (BMI >40kg/m2 or >35kg/m2 with an obesity associated comorbidity), surgical treatment is recommended for obesity[81]. Bariatric surgery has been shown to produce remarkable health improvement and to reduce mortality[81]. In women with PFD, there was a significant impact on reducing urinary incontinence, anal incontinence, and pelvic organ prolapse after bariatric surgery[82]. These encouraging data need to be put in the context of potential risks and side-effects of surgery, which for some patients can be distressing or disabling.

Prevention of pelvic floor injury in childbirth

As mentioned earlier, another option for prevention of pelvic floor injury and PFD is by identifying risk factors or protective factors during childbirth and adjusting policy accordingly.

One of the most substantial risk factors for pelvic floor injury is forcipal extraction[83, 84]. Whilst in many other countries we see a decrease in forceps delivery there are still others where it is the first choice even before vacuum[85]. The reason for maintaining this competence is that guidelines indicate that obstetricians need to be confident and competent in the use of both instruments[86]. A recent Cochrane review concluded that there is a place for both forceps and vacuum births[87]. From PFD and pelvic injury point of view, it has been proven better to switch to vacuum assisted vaginal deliveries[84]. But perhaps from the pelvic floor perspective, we should stop assisted vaginal delivery altogether to prevent pelvic floor injury. Other risk factors for PFD and injury are an extended second stage of birth, abnormal occiput presentation and fetal macrosomia, often result in this assisted vaginal delivery.

Another way to potentially reduce risk is intrapartum use of combined abdominal and transperineal ultrasound. Several studies conclude that intrapartum ultrasound can be used in women at the beginning of the second stage to determine whether they have an increased risk of a caesarean section[88-90]. This type of ultrasound may also predict in women during extended second stage of labor the likelihood of a 'successful' vaginal delivery. New studies are now being conducted, including the introduction of an "intrapartum app" to predict the feasibility of a vaginal delivery[91]. These results allow also help identifying women with a higher risk of pelvic floor injury. These developments could then be used for prevention purposes.

We should study the duration of the second stage of labor time (including active pushing phase). The Dutch[92] and American[93] obstetric guideline for normal vaginal delivery currently indicate an increase in maternal and neonatal complications with an expulsion duration of more than 3 hours in nulliparous and 2 hours in multiparous women[94-96]. No normal progression time limit on delivery has been reported. Furthermore, none of the studies included the risk of the occurrence of maternal pelvic floor injury in addition to OASI.

Another relatively common risk factor for maternal pelvic floor injury is fetal macrosomia[97-99]. There is a strong association of fetal macrosomia with maternal and neonatal complications, and they are a relatively common occurrence. There are no clear guidelines for pregnant women and the obstetric care providers to enable a clear management plan for delivery. The possible explanation for the lack of recommendations is an ineffective prenatal prediction of macrosomia and insufficient evidence about the best policy to follow when macrosomia is suspected[99-101].There is some

evidence suggesting that induction of labor in women with suspected fetal macrosomia (> 4 kg) may potentially reduce neonatal complications[99, 101-103]. Future research should investigate whether induction prevent maternal pelvic floor injury and neonatal complications associated with fetal macrosomia without the increase of failed induction. In addition, it must be investigated from which gestational age this induction can best be performed. In our opinion cesarean section should be strongly considered with an estimated birth weight above 5 kg or above 4.5 kg in case of (gestational) diabetes to avoid injury to both mother and child.

Risk calculation and optimal counseling of pregnant women in relation to pelvic floor disorders

Recently a validated screening tool, UR-CHOICE risk calculator, was developed to identify pregnant women with high risk for PFD after delivery. This tool can help with counselling women regarding PFD prevention (http://riskcalc.org/UR_CHOICE/)[104, 105]. The validation of the screening tool is based on two large cohorts with a total of 8754 women with self-reported PFD 12 and 20 years after childbirth in in the United Kingdom/New Zealand cohort and in the Swedish Register. Unfortunately, it was limited on information whether women already had PFD during pregnancy besides urinary incontinence[59, 104, 105]. In addition, this tool was designed for pregnant women and did not take into account the risk factors for PFD associated with childbirth. Therefore, knowledge on the interaction of risk factors both related to pregnancy and delivery are still missing. The advantage of this model is that it gives different percentages that can be used in shared decision-making. The disadvantage is that no clear cut-off or user instructions are given with regard to these percentages.

Many people, including health professionals themselves, find it difficult to understand and apply information about health and disease risk rates in daily practice[106]. The typical risk communication (numbers, bar graph, verbal label) seems to provoke undervaluation of risk. In general people are often unrealistically optimistic when making estimates[107]. It is more common for a pregnant women to assume that only others suffer pelvic floor injury during childbirth or that she has better physical qualities to give birth without injury. With this general tendency toward optimism, people use three general rules of estimation, called heuristics[108]. The first general rule is that the ease with which we can remember the previous situation influences how we will assess the new situation. This is called availability heuristic. The second general rule has to do with how the predicted situation resembles a previous situation (experienced yourself, from the media or our environment). This is called representativeness heuristic. And

the third general rule is that we make our risk assessment based on the first information we have received. This is called anchor heuristics.

So pregnant woman with PFD or pregnant women surrounded by friends or relatives with PFD will assess the risk differently to the pregnant woman without PFD and friends or relatives without PFD. However, during her pregnancy, the pregnant woman is inundated with mostly all positive propaganda about pregnancy and vaginal childbirth. The involved healthcare professionals may also contribute to this positive propaganda. It is of importance not to underestimate the influence of social media. In my daily practice as healthcare professional, I often hear from women with PFD that they were unaware that PFD could occur at any age. And also women often say that they were not aware that pregnancy and vaginal childbirth play an important role in the development of pelvic floor complaints. Women also indicate that they find it difficult to talk about pelvic floor complaints. They often feel that their complaints are not taken seriously by their health professionals. Women are often surprised when they dare to share their PFD, that many women in their environment experience similar complaints.

Current prenatal care often lacks objective health information about the pelvic floor and PFD. Patient education in this area needs to be improved. Insufficient information and misconceptions about pelvic floor and PFD are the biggest barriers for seeking needed care by women with pelvic floor complaints. Research has shown that concerns about negatively affecting women's preferences for delivery method (increase in caesarean section rate) are unfounded[109-111]. Most women, even female urogynecologist themselves, prefer vaginal delivery. However, among female urogynecologists, there is great interest in participating in a risk stratification process to approach delivery in an individualized and risk-adapted way[111]. Shared decision-making in obstetrics can improve outcomes for women. Shared decision-making is only possible if all women receive clear, objective information about pregnancy, childbirth and pelvic floor complaints. Patients and healthcare professionals need to work together to achieve this form of shared decision-making. Future research should indicate the most effective and positive way to accomplish this[112].

Implications for daily practice

- PFUS should be implemented as the first additional examination in women with PFD. In any case, PFUS should be performed in women with complex PFD or an increased risk of PFD, such as in women with multiple urogynecological symptoms, especially at a young age and after a complicated delivery (eg after OASI).

- Women should be offered a consultation with an urogynecologist and certified pelvic physiotherapist after a complicated delivery and certainly after an OASI (between 3-6 months after delivery) after the first regular follow-up postpartum. Because these women have an increased risk of persistent pelvic floor injury and PFD. During this consultation it is important to ask about bowel function (the consistency of the feces, obstructive defecation and constipation) and to assess the sexual history.
- From a maternal point of view, forceps or fundal expression (Kristeller maneuver) should no longer be used during vaginal delivery. A mediolateral episiotomy should not be placed to prevent LAM injury. Restrictive use plays a role in prevention of OASI. A median episiotomy should not be used.
- Constipation and bowel disease should be included in pregnancy and delivery outcome set of ICHOM.
- Prevention of PFD is key. General risk factors for PFD can be influenced by ongoing lifestyle changes. However, the major risk factor for PFD, pregnancy and delivery, must be approached from an objective, individualized and risk-based assessment.
- The main obstetric outcome measure should be a healthy child and an optimally functioning mother with a low probability of PFD in the short and long term. To achieve this, there is an urgent need for optimal cooperation between women, midwives, obstetricians and urogynecologists.
- Every (pregnant) woman has the right to objective and reliable health information about the pelvic floor and the development and occurrence of PFD. Current patient education in this area needs to be improved.

Future research

- Research should be conducted into effective identification of fetal macrosomia during pregnancy and delivery. And if we can better estimate fetal macrosomia, future research should focus on whether early induction, and if so, from what gestational age is best to prevent maternal pelvic floor injury (both LAM and anal sphincter injury) and neonatal complications associated with fetal macrosomia.
- More research is needed on intrapartum combined abdominal and transperineal ultrasound as a tool to predict the feasibility of vaginal delivery. It may also be possible to predict the risk of pelvic floor injury after delivery in this way.
- We need larger datasets with longer follow-up (30-40 years). Several risk factors for PFD including imaging data must be included in this dataset. This research should lead to an improved PFD risk calculator

than the currently available UR-CHOICE along with shared decision-making tools and. This should lead to an improved PFD risk calculator than the currently available UR-CHOICE, along with shared decision-making tools for counseling in the most positive and effective way in all pregnant women.

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CHAPTER 8

Summary

PART I PELVIC FLOOR AFTER VAGINAL BIRTH

In the first part of this thesis (**chapter 2- 4**) we examined risk factors for the development of pelvic floor (residual) damage and urogynecological complaints after a vaginal delivery with and without obstetric anal sphincter injury (OASI). With perineal pelvic floor ultrasound (PFUS) we diagnosed pelvic floor (residual) injury. Pelvic floor injury to the puborectalis levator ani and anal sphincter was assessed. Levator injury was defined as levator avulsion, levator ballooning, or a combination of both. Anal sphincter damage was defined as a residual defect of the external and/ or internal anal sphincter. Pelvic floor function was also studied at by calculating the relative change in levator hiatus dimensions between Valsalva and rest and between contraction and rest. Urogynecological complaints were assessed on the basis of various validated urogynecological questionnaires.

In **chapter 2**, we examined whether there was an association of mediolateral episiotomy with levator injury (levator avulsion, ballooning, or combined) and urogynecological complaints. This was done in an observational study of women with a spontaneous, full term vaginal delivery in cephalic position without anal sphincter tear. 50% had a mediolateral episiotomy and the other half did not. The median time at investigation after vaginal delivery was 13 months (range 6–33). Many women had levator injury (avulsion, ballooning or combination) after normal vaginal delivery, namely 35 (40.0%) of the 103 women with a mediolateral episiotomy and 33 (32.7 %%) of 101 women with no mediolateral episiotomy (p = 0.69). No differences were found in the incidence of levator avulsion or in levator ballooning between both groups. There was an association between longer duration of the second stage of labor and the incidence of levator avulsion. Non-occiput anterior fetal position increased the risk of levator ballooning and levator injury. No differences in urogynecological complaints were found between women who had undergone mediolateral episiotomy or women without mediolateral episiotomy. We also saw no difference in symptoms between women with levator avulsion and/ or ballooning and women without levator avulsion and/ or ballooning.

Optimal pelvic floor muscle function plays an important role in female sexual functioning. In **chapter 3** we examined whether there was an association between levator hiatal dimensions and female sexual dysfunction after first vaginal delivery. This sexual function was assessed using the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) validated questionnaire. We analyzed the association of total PISQ-12 score, as well as individual sexual complaints (desire, arousal, orgasm and dyspareunia), with

levator hiatal dimensions at rest, maximum Valsalva and during pelvic floor muscle contraction, including relative changes between these measurement. There were no significant association between total PISQ-12 score and levator hiatus dimensions. Looking at individual sexual complaints, women with dyspareunia had significantly smaller levator hiatal area and anterior-posterior diameter on maximum Valsalva. By using multivariate logistic regression analysis however we found dyspareunia wasn't independently associated with levator hiatal dimensions. We concluded that, after first vaginal delivery, sexual dysfunction is not associated with levator hiatal dimensions as measured by perineal PFUS.

Women with OASI after their vaginal delivery are at greater risk of levator avulsion or ballooning than women without OASI. OASI is also an important factor in the etiology of anal incontinence. In **chapter 4** we evaluated whether anal sphincter defects, levator avulsion or levator ballooning after OASI is associated with severity of anal incontinence. The severity of the anal incontinence was determined using the St Mark's incontinence score. Furthermore, we evaluated whether other factors, such as constipation or altered stool consistency, are associated with symptoms of incontinence after OASI. Constipation was scored using the Cleveland Clinic Constipation Score and faecal consistency using the Bristol Stool Scale. Median follow-up was 4 months (range 3-98 months). Univariate linear regression analysis showed an association between higher St Mark's incontinence score with a residual defect of external anal sphincter, higher parity, longer time between delivery and postnatal perineal PFUS, higher BSS and higher CCCS. However, multivariate linear regression only found an association between higher St Mark's incontinence score with higher BSS and higher CCCS. We found that residual defects of external sphincter, detected on perineal PFUS, are associated with severity of anal incontinence symptoms measured using St Mark's incontinence score 4 months after OASI repair. Furthermore, several clinical factors, such as constipation and altered stool consistency, appeared to have a greater association and may therefore play a more important role in clinical management.

PART II PELVIC FLOOR IMAGING: VIRTUAL REALITY

In the second part of this thesis (**chapter 5- 6**), we compared conventional perineal PFUS with virtual reality imaging. At that time, virtual reality was a new method for visualizing ultrasound datasets in which depth perception could be displayed. This method offered the possibility to measure non-planar structures, such as the pelvic floor.

In **chapter 5** we found that measurements of levator ani hiatal volume during maximum pelvic floor contraction in women without levator avulsion using virtual reality were reliable with an intraclass correlation coefficient (ICC) comparing conventional perineal PFUS with virtual reality measurements of > 0.96. The intra- and interobserver ICCs for conventional perineal PFUS measurements were > 0.94 and for virtual reality measurements were > 0.97, indicating good reliability for both. Also, the levator ani hiatus volume measurements performed using virtual reality results were similar to those obtained with conventional perineal PFUS (mean difference of 0.10 (95% CI, – 0.15 to 0.35) cm^3.

Then, in **chapter 6**, we compared measurements of levator ani hiatal volume at rest and on maximum Valsalva, obtained using conventional perineal PFUS and virtual reality imaging. Our objectives were to establish their agreement and reliability, and their relationship with prolapse symptoms and Pelvic Organ Prolapse Quantification (POP-Q) stage. The mean difference between levator hiatal volume measurements on perineal PFUS and by virtual reality was 1.52 cm^3 (95% CI, 1.00–2.04 cm^3) at rest and 1.16 cm^3 (95% CI, 0.56–1.76 cm^3) during maximum Valsalva ($P < 0.001$). Both intra- and interobserver intraclass correlation coefficients were > 0.95 for conventional perineal PFUS and > 0.99 for virtual reality. Patients with prolapse symptoms or POP-Q Stage ≥ 2 had significantly larger hiatal measurements than those without symptoms or POP-Q Stage < 2. This study demonstrated that measurement of levator ani hiatal volume on virtual reality imaging at rest and on maximum Valsalva are reliable and correlate with clinical symptoms and signs of prolapse on POP-Q, in patients with a normal levator ani. Current measurements of the levator ani hiatus with conventional perineal PFUS in patients with an intact levator ani muscle were reliable and differ only slightly from those measured with virtual reality, which we considered to be of no clinical relevance.

In the general discussion of this thesis, **chapter 7**, we emphasized the main findings and their implications for clinical practice and discussed suggestions for future research.

CHAPTER 6

Samenvatting

DEEL 1 DE BEKKENBODEM NA VAGINALE BARING

In het eerste deel (**hoofdstuk 2- 4**) van dit proefschrift hebben we gekeken naar risicofactoren op het ontstaan van bekkenbodem(rest)schade en urogynaecologische klachten na een vaginale bevalling met en zonder totaalruptuur. De diagnostiek naar de bekkenbodem(rest)schade werd verricht met behulp van perineale bekkenbodemechografie (perineale PFUS). Bekkenbodem(rest)schade aan de musculus puborectalis levator ani en anale sphincter werden beoordeeld. Schade aan de levator ani werd gedefinieerd als een levator avulsie, levator ballooning of een combinatie van beiden. Schade aan de anale sphincter werd gedefinieerd als een restdefect van de externe en/of interne anale sphincter. Daarnaast werd gekeken naar de functie van de bekkenbodem door het berekenen van de relatieve verandering tussen metingen van de levator ani gedurende maximale Valsalva en rust en tussen contractie en rust. Urogynaecologische klachten werden beoordeeld aan de hand van diverse gevalideerde vragenlijsten.

In **hoofdstuk 2** keken we of er een associatie was tussen het zetten van een mediolaterale episiotomie en de kans op het verkrijgen van levator schade en urogynaecologische klachten. Dit werd gedaan in een zo zuiver mogelijke groep, namelijk primipara, aterme bevallen met een kind in hoofdligging zonder kunstverlossing. De helft van deze groep kreeg een mediolaterale episiotomie. De mediane duur na de bevalling was 13 maanden (range 6-33). Veel vrouwen hadden levator schade (avulsie, ballooning of combinatie) na een normale vaginale baring, respectievelijk 35 (40.0%) van de 103 vrouwen met een mediolaterale episiotomie en 33 (32.7%) van de 101 vrouwen zonder mediolaterale episiotomie (p = 0.69). We zagen ook geen verschil in aantal levator avulsies of levator ballooning tussen deze groepen. We vonden een associatie tussen langere uitdrijvingsduur en het optreden van een levator avulsie. Bij een bevalling met een hoofdligging anders dan een achterhoofdligging met achterhoofd voor, zagen we een verhoogd risico op levator ballooning en levatorschade. We zagen geen verschil in urogynaecologische klachten in vrouwen met een mediolaterale episiotomie of vrouwen zonder mediolaterale episiotomie. Ook zagen we geen verschil in klachten tussen vrouwen met levator avulsie en/of ballooning en vrouwen zonder levator avulsie en/of ballooning.

Een optimale bekkenbodemfunctie speelt ook een essentiële rol in seksueel functioneren. In **hoofdstuk 3** hebben we gekeken of er een associatie was tussen metingen van de levator hiatus (inclusief relatieve verandering in metingen van de levator hiatus tussen maximale Valsalva en rust en tussen contractie en rust) en seksuele functie na een eerste vaginale baring. Deze

seksuele functie werd beoordeeld met behulp van de Pelvic Organ Prolapse/ Urinary Incontinence Sexual Questionnaire (PISQ-12), een gevalideerde vragenlijst. Er werd geen significante associatie gevonden tussen totale PISQ-12 score en metingen van levator hiatus. Vrouwen met dyspareunie hadden een significant kleinere hiatus en anterior-posterior diameter tijdens maximale Valsalva, echter in multivariate analyse was dit niet meer geassocieerd met het hebben van dyspareunie. Wij concludeerden dat seksuele disfunctie na de eerste vaginale bevalling niet geassocieerd is met metingen van de levator hiatus middels perineale PFUS.

Vrouwen met een totaalruptuur bij hun vaginale bevalling hebben een verhoogde kans op een levator avulsie of ballooning vergeleken met vrouwen zonder een totaalruptuur. Het hebben van een totaalruptuur in de voorgeschiedenis leidt ook tot een verhoogde kans op anale incontinentie. In **hoofdstuk 4** hebben we bekeken of echoscopische restdefecten van de anale sphincter, levator avulsie of ballooning geassocieerd zijn met de ernst van de anale incontinentie. De ernst van de anale incontinentie werd bepaald met behulp van de St. Mark's incontinentie score. Verder hebben we onderzocht of andere factoren, zoals obstipatie of veranderde consistentie van de ontlasting, geassocieerd zijn met symptomen van de anale incontinentie na een totaalruptuur. Obstipatie werd gescoord aan de hand van de Cleveland Clinic Constipation Score (CCCS) en de consistentie van de feces met de Bristol Stool Scale (BSS).

De mediane follow-up was 4 maanden (range 3-98). Bij univariate analyse vonden we een associatie tussen de hoogte van de St. Marks's incontinentiescore en de aanwezigheid van een restdefect van de externe anale sphincter, een hogere pariteit, een langere tijd tussen de bevalling en postnatale transperineale echografie, een hogere BSS en een hogere CCCS. Echter bij multivariate analyse vonden we alleen een associatie tussen hoogte van de St. Mark's incontinentiescore en hogere BSS en/of CCCS. Wij concludeerde dat restdefecten van de externe sfincter geassocieerd zijn met de ernst van anale incontinentie. Echter klinische factoren, zoals obstipatie en dunnere consistentie van de ontlasting zijn sterker geassocieerd en kunnen daarom een belangrijkere rol spelen bij de behandeling van anale incontinentie na een totaalruptuur.

DEEL 2 BEELDVORMING VAN DE BEKKENBODEM MET BEHULP VAN VIRTUAL REALITY

In het tweede deel (**hoofdstuk 5- 6**) van dit proefschrift hebben we de conventionele perineale PFUS vergeleken met beeldvorming van de bekkenbodem met behulp van virtual reality. Virtual reality was op dat moment een nieuwe methode voor het visualiseren van echogegevens waarbij dieptewaarneming kan worden weergegeven. Dit bood de mogelijkheid om niet-vlakke structuren te meten, zoals de bekkenbodem.

In **hoofdstuk 5** toonden we aan dat volumemetingen van de levator hiatus gedurende maximale bekkenbodemcontractie in vrouwen zonder een levator avulsie met behulp van virtual reality en conventionele perineale PFUS betrouwbaar waren met een intraclass correlatiecoëfficiënt (ICC) van > 0.96. De intra- en interobserver ICC's voor conventionele perineale PFUS metingen waren > 0.94 en voor metingen met behulp van virtual reality > 0.97, wat duidt op een goede betrouwbaarheid voor beide metingen. De volumemetingen van de levator hiatus met conventionele perineale PFUS en metingen met behulp van virtual reality waren vergelijkbaar met een gemiddeld verschil van 0.10 cm^3. Daarna beschrijven en vergelijken we in **hoofdstuk 6** de volumemetingen van de levator hiatus met conventionele perineale PFUS en met behulp van virtual reality in rust en tijdens maximale Valsalva. Het gemiddelde verschil tussen volumemetingen van de levator hiatus met conventionele perineale PFUS en metingen met behulp van virtual reality was 1.52 cm^3 in rust en 1.16 cm^3. Zowel de intra- als interobserver intraclass correlatiecoëfficiënten waren > 0.96 voor conventionele perineale PFUS en > 0.99 voor metingen met behulp van virtual reality. Patiënten met verzakkingssymptomen of Pelvic Organ Prolapse Quantification (POP-Q) stadium ≥ 2 hadden een significant grotere volumemeting dan vrouwen zonder symptomen of POP-Q stadium ≥ 2.

We concludeerden dat volumemetingen van de levator hiatus met virtual reality betrouwbaar zijn en correleren met klinische symptomen en tekenen van verzakking op basis van POP-Q, bij patiënten met een normale levator ani. Tevens concludeerden we dat volumemetingen van de levator hiatus met conventionele perineale PFUS bij patiënten zonder levator avulsie betrouwbaar zijn en slechts in geringe mate verschillen van volumemetingen gemeten met behulp van virtual reality, een verschil dat wij als niet klinisch relevant beschouwen.

In de algemene discussie van dit proefschrift, **hoofdstuk 7**, legden we de nadruk op de belangrijkste bevindingen en hun implicaties voor de klinische praktijk en bespraken we suggesties voor toekomstig onderzoek.

CHAPTER A

Appendices

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LIST OF ABBREVIATIONS

2D	two-dimensional
3D	three-dimensional
4D	fourth-dimensional
AC	fetal abdominal circumference
BMI	body mass index
BSS	Bristol stool scale
CCCS	Cleveland clinic constipation score
CI	confidence interval
CT	computed tomography
DLP	digital light processing
EAS	external anal sphincter
EFW	estimated fetal weight
EVUS	endovaginal ultrasound
FISI	fecal incontinence severity index
GDM	gestational diabetes
IAS	internal anal sphincter
ICC	interclass correlation coefficients
ICHOM	international consortium for health outcomes measurement
IIQ-7	incontinence impact questionnaire
LAM	levator ani muscle
MC	medical centre
MEC	medical ethical committee
MRI	Magnetic Resonance Imaging
OASI	obstetric anal sphincter injury
OR	odds ratio
PCB	pregnancy and delivery
PET	positron emission tomography
PFD	pelvic floor disorders
PFIQ-7	pelvic floor impact questionnaire
PFM	pelvic floor muscles
PFMC	pelvic floor muscle contraction
PFMT	pelvic floor muscle training
PFUS	pelvic floor ultrasound
PISQ-12	pelvic organ prolapse/urinary incontinence sexual questionnaire
POP	pelvic organ prolapse
POP-Q	pelvic organ prolapse quantification
PROMs	patient reported outcome measures
SD	standard deviation
SMIS	St. Mark's incontinence score
TUI	tomographic ultrasound imaging
UDI-6	urogenital distress inventory scale
VR	virtual reality

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PHD PORTFOLIO

Name PhD student: Leonie Speksnijder
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Research school: NIHES
PhD period: 2015-2021
Promotor: Prof. Dr. E.A.P. Steegers
Copromotor: Dr. A.B. Steensma en Dr. D.M.J. Oom

Summary of PhD training and teaching activities		**Workload (ECTS)**
General courses		
2017, 2021	e-BROK herregistratie	1.0
2017	Practical Biostatistics (Tilburg, Clinical Research unit)	2.0
2016	English Biomedical Writing and Communication (Erasmus MC)	3.0
2016	Research integrity in science (Erasmus MC)	0.3
2016	Endnote (Erasmus MC)	0.3
2014	PC Female Urology & Urogynaecology	0.5
2014	Teach the Teacher II	0.3
2013	Basiscursus regelgeving & organisatie voor Klinisch Onderzoek (BROK)	2.0
2013	Evidence Based Medicine (DOO, Erasmus MC)	1.0
2012	Communicatie (DOO, Erasmus MC)	0.5
2010	The Short Introduction Course on Statistics & Survival Analysis for MD's	0.4
Attended seminars, conferences and workshops		
2015-2021	Biannual meetings of Werkgroep Bekkenbodem, NVOG	1.0
2019, 2021	Post ICS/IUGA Netherlands	0.5
2019	53rd NVOG Gynaecongres, Utrecht	0.5
2019	29th World Congres on Ultrasound in Obstetrics and Gynecology, Berlin, Germany	1.0
2018	43rd annual meeting of the International UroGynecological Association, Vienna, Austria	1.0
2017	42nd annual meeting of the International UroGynecological Association, Vancouver, Canada	1.0
2017	22nd Nederlands-Vlaams Doelencongres Infertiliteit, Gynaecologie en Obstetrie Congres, Rotterdam, Netherlands	0.5

Summary of PhD training and teaching activities		Workload (ECTS)
2016	48th NVOG Gynaecongres, Eindhoven, Netherlands	0.5
2016	9th annual scientific meeting of the European UroGynecological Association, Amsterdam, Netherlands	1.0
2015	40th annual meeting of the International UroGynecological Association, Nice, France	1.0
2015	46th NVOG Gynaecongres, Arnhem, Netherlands	0.5
2014	44th NVOG Gynaecongres, Leeuwarden, Netherlands	
2012	VVAA Time- en stressmanagement, Utrecht, Netherlands	0.5
2012	41e NVOG Gynaecongres, Den Haag, Netherlands	0.5
2011	40e NVOG Gynaecongres, Arnhem, Netherlands	0.5
2011	41st annual meeting of the International Continence Society, Glasgow, UK	1.0
2011	39e NVOG Gynaecongres, Zwolle, Netherlands	0.5
Presentations at (inter) national conferences		
2019	29th World Congress on Ultrasound in Obstetrics and Gynecology, Berlin, Germany	1.0
2016	9th Annual scientific meeting of the European UroGynecological Association, Amsterdam, The Netherlands	2.0
2011	41st annual meeting of the International Continence Society, Glasgow, UK	1.0
2010	40th NVOG Gynaecongres, Arnhem, Netherlands	0.5
2010	20th World congress on Ultrasound in Obstetrics and Gynecology, Prague, Czech Republic	0.5
Posters		
2016	9th Annual scientific meeting of the European UroGynecological Association, Amsterdam, The Netherlands	1.0
2010	35th annual meeting of the International UroGynecological Association, Toronto, Canada	0.3

Summary of PhD training and teaching activities		Workload (ECTS)
Teaching		
2020-2021	Supervisor of urogynecology differentiation in residency training of Obstetrics and Gynecology, Cluster Rotterdam	2.0
2017-2019	Supervisor of N.W.C.M de Jong during her clinical nurse specialist training	2.0
2016-2021	Member 'voortgangstoets commissie' NVOG. Create exam questions for postgraduate progress testing for O&G training	4.0
2016-2021	Supervising and teaching of regular interns and residents Obstetrics and Gynecology, Amphia, Breda	4.0
2017-2021	Class 'Herstel van episiotomie en baringskanaalletsels' Hands-on training, Koninklijke Nederlandse Organisatie van Verloskundigen (KNOV)	2.0
2011-2019	Supervising research students: Charlotte Biesmeijer, Denise de Vos and Marit Schmidt, Erasmus MC, Rotterdam	3.0
2021	Presentation for Master Pelvic Physical Therapy (MPelPT), Avans hogeschool, Breda	1.0
2020	Presentation at urogynecology region meeting on OASI, Amphia, Breda	0.3
2017	Presentation and hands-on training: prevention of OASI and suturing mediolateral episiotomy, Annature, Amphia, Breda	1.0
2016	Presentation and organization of multidisciplinary pelvic floor care after delivery, Amphia, pelvic floor therapists and VSV, Breda	1.0
2016	Post ICS/IUGA 2016 oral presentation and hands-on training, Bunnik, Utrecht	1.0
2013, 2016	Hands-on training suturing OASI, Erasmus MC, Rotterdam	0.5
Miscellaneous		
2016	Prize for best poster at 9th Annual scientific meeting of the European UroGynecological Association, Amsterdam, The Netherlands	
2010-2016	Obstetrics and Gynecology residency training, Cluster Rotterdam. Supervisors: Prof.dr. C.W. Burger, dr. M.J. Ten Kate-Booij, dr. M.K.G Dijksterhuis, M. Bongers. Differentiation urogynecology	
Total ECTS		51.4

DANKWOORD

In dit proefschrift komen zowel mijn liefde voor de verloskunde als de bekkenbodem samen. Mijn onderzoek heeft bijgedragen aan de visie dat een vaginale baring niet perse het hoogste doel is. Het effect van de baring op de bekkenbodem dient te worden meegenomen in het lange termijn perspectief. Deze afweging is complex en brengt onzekerheid voor vrouwen en betrokken hulpverleners.

Het schrijven van dit proefschrift was - naast mijn fulltimebaan, moeder worden en andere life-events - een van de moeilijkste dingen in mijn leven. Je eigen aanjager moeten zijn, dat vraagt iets van je. Promoveren heeft mij geleerd om ergens in vastbijten, in kleine stapjes door te gaan en niet altijd te ver vooruit te willen kijken. Het traject was pittig, maar heeft mij verrijkt als mens, arts en wetenschapper. Ik ben ervan overtuigd dat losse artikelen minder zeggen dan het geheel. Het geheel leidt tot meer discussie. Gelukkig schrijf je een proefschrift niet alleen, daarvoor heb ik hulp van allerlei mensen gehad, bewust en onbewust. Bij deze wil ik graag onderstaande personen bedanken voor hun bijdrage.

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Mijn copromotor Anneke Steensma. Lieve Anneke, in 2009 arriveerde ik in het Erasmus MC als arts-assistent niet in opleiding (ANIOS) met één duidelijk doel: in opleiding komen tot gynaecoloog. Daar hoorde ook een publicatie bij. Jij was bezig met het afronden van je eigen proefschrift en had mogelijk wel een onderzoek voor mij. Dat was het begin van een lange samenwerking. In het begin moest ik wel even wennen aan je directe (en soms best pittige) communicatie, alsook aan de overrompelende hoeveelheid informatie waardoor ik soms de draad even kwijt was. Inmiddels weet ik hoe ik je moet lezen én heb ik ervaren dat je een hart van goud hebt. Ik heb jouw vertrouwen, geduld en steun ook privé het afgelopen decennium enorm gewaardeerd!

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Beste gynaecologen, arts-assistenten, verloskundigen, verpleegkundigen en iedereen met wie ik verder heb samengewerkt in het Erasmus MC, Na twee jaar in het Reinier Graaf was het tijd voor een vervolgstap als ANIOS in het Erasmus MC. Iedereen overtuigen dat ik uit het geschikte hout was gesneden om gynaecoloog te worden was best een uitdaging. De combinatie van een grote afdeling met veel gynaecologen en arts-assistenten en verregaande subspecialisatie maakten dat er tijd nodig was om het draagvlak te krijgen dat nodig was om voorgedragen te worden voor een opleidingsplaats. Ik ben er nog steeds trots op dat mijn voordracht breed gedragen werd en ik de door mij felbegeerde opleiding in kon stromen in dit cluster.

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Twee jaar later was ik terug in het Erasmus MC, maar nu als AIOS, een paar jaar ouder en een hoop ervaring rijker. De duidelijke stagestructuur in combinatie met de academische kritische blik maakte verdere verdieping in de verschillende subspecialisaties mogelijk. Ik moet nog steeds lachen als ik eraan terugdenk dat veel stagebegeleiders zeiden dat ik niet in elk subspecialisme professor hoefde te worden. Ondertussen was ik gestart met het EpiLeva onderzoek en begon mijn interesse in de urogynaecologie te groeien. Het werd langzaam duidelijk dat hier mijn grootste interesses samenvielen: de verloskunde, functionele klachten en de operatieve gynaecologie.

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Beste gynaecologen, arts-assistenten, verloskundigen, verpleegkundigen en iedereen met wie ik verder heb samengewerkt in het Maxima Medisch Centrum, Mijn 6 maanden bij jullie waren een verrijking op zowel professioneel als persoonlijk vlak. In deze korte tijd heb ik mij een onderdeel van jullie team gevoeld. Mijn leergierigheid, nieuwsgierigheid en passie voor ons vak zijn enorm aangewakkerd door jullie. Jullie innovatiegeest en nieuwsgierigheid sieren jullie. Ik wil jullie bedanken dat jullie mij deze verdiepingsstage gedurende 6 maanden geboden hebben. In het bijzonder wil ik noemen Leon Mulders (wat een energie, maar ook aanmoediging gaf jij), Joggem Veen (dank voor het verrijken van mijn kennis in de urogynaecologie, maar ook je voorbeeld in netwerken met andere specialisten), Marlies Bongers (als opleider en trainer van de sacrocolpopexie) en Peggy Geomini (woorden schieten te kort voor hoeveel jij voor mij hebt betekent na de geboorte van Fabian en het starten als jonge gynaecoloog).

Beste gynaecologen, arts-assistenten, verloskundigen, verpleegkundigen en iedereen met wie ik verder heb samengewerkt en nog samenwerk in het Amphia Ziekenhuis te Breda, Toen ik in 2011 bij jullie mocht starten als AIOS, voelde het als een warm bad. Ik hoopte dan ook dat ik ooit een blijvend onderdeel van jullie team mocht zijn. In 2016 ben ik gestart als jonge klare en nieuw vakgroeplid in onze fijne vakgroep. Er zijn al wat wisselingen geweest, maar ik ben trots om bij deze ambitieuze maar ook gezellige vakgroep te horen. Ook het werken met de overige collega specialisten, verloskundigen, arts-assistenten, verpleegkundigen, et cetera maken nog steeds dat ik blij ben om onderdeel van het Amphia te zijn. Hoewel iedereen wel een bijdrage heeft geleverd in mijn opleiding en mijn werkzaamheden als gynaecoloog nu, wil ik enkele mensen in het bijzonder bedanken.

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ABOUT THE AUTHOR

Leonie Speksnijder was born on June the 29th 1982 in Rotterdam, the Netherlands as the eldest daughter of Peter Speksnijder and Marianne Koorevaar. She grew up in Ridderkerk together with her three brothers. After secondary school at the Farel College, Ridderkerk (1994-2000), she started medical school at the Erasmus University in Rotterdam, the Netherlands. In medical school, her interest in obstetrics and gynecology (O&G) led to the conduct of a research internship at the obstetrics department on the intravenous use of the calcium-channel blocker nicardipine as second-line treatment in severe, early-onset pre-eclamptic patients. She graduated in 2006 and started working in 2007 as an O&G resident at the Reinier de Graaf hospital in Delft, the Netherlands (Dr. W.A. ter Harmsel and Dr. H.A. Bremer). In 2009 she started working as an O&G resident at Erasmus Medical Center in Rotterdam, the Netherlands (Prof. dr. Th.J.H. Helmerhorst and Prof. dr. C.W. Burger). At this time, she conducted research on pelvic floor ultrasound in virtual reality with dr. A.B. Steensma, which resulted in a publication in 2012. In 2010, she started her O&G training at the Amphia hospital in Breda, the Netherlands (Dr. M.G.K. Dijksterhuis and Dr. D.N.M. Papatsonis) and thereafter in the Erasmus Medical Centre in Rotterdam (Prof.dr. C.W. Burger and Dr. M.J. Ten Kate-Booij). Meanwhile, during her O&G training she started the EpiLeva study. In 2015 this resulted in a PhD project under supervision of Prof. dr. E.A.P. Steegers with Dr. A.B. Steensma and Dr. D.M.J. Oom as co- supervisors. During her last two years of training, she differentiated herself in urogynecology. She conducted this urogynecology differentiation at the Amphia hospital (Dr. D. Gietelink), Maxima Medical Centre in Veldhoven/ Eindhoven (Prof. dr. M.Y. Bongers and Drs. J. Veen) and Erasmus MC (Dr. A.B. Steensma). She finished her specialization on June 26th 2016. In October of the same year she started her work as a gynecologist at the Amphia hospital in Breda, Netherland with subspecialization in urogynecology and obstetrics. Leonie is married since July 25th 2001 to Paul de Jong. Together they have a daughter (Mirthe Geertje (2013) and a son (Fabian Bram (2016). They live in Breda, the Netherlands.

Unraveling the Pelvic Floor