A new reference line for the evaluation of the normal position of the upper two-thirds of the vagina based on MRI: a retrospective study.

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Abstract

Objectives The upper two-thirds of the vagina is most commonly affected by pelvic organ prolapse. This study aims to find a reference line proximate to the axis of this part of the vagina on MRI which is critical but lacking. Design Retrospective cross-section study Setting Two university-affiliated hospital in China (July 2018 - June 2019) Population Six hundred and fourteen women without prolapse Methods Two reference lines were introduced to compare with the upper two-thirds of the vagina on pelvic MRI: the pubococcygeal line (PCL) and a line passing through the inferior pubic symphysis to the midpoint of the third sacral vertebra (PS3L). Main outcome measures The distances and the angles between the vagina and both reference lines were measured. Results: The median distances from the distal, middle, and apical points to the PS3L were -0.5[interquartile range (IQR), -0.9 - 0.0] cm, 0.0[IQR, -0.4 - 0.6] cm, and -0.2[IQR, -0.9 - 0.0] cm, respectively, while the median distances to the PCL were 0.4[IQR, 0.0 - 0.7] cm, 2.1[IQR,1.7 - 2.5] cm, and 3.1[IQR, 2.5 - 3.7] cm, respectively. The median angle between the vagina and the PS3L was significantly smaller than that with the PCL (0.0[IQR, -4.0 - 7.0] degree vs 29.0[IQR, 23.0 - 34.0] degrees, $p<.001$). Conclusions: A line passing through the inferior portion of the pubic symphysis to the third sacral vertebra mostly conforms to the normal upper two-thirds of the vaginal axis.

Tweetable abstract:

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Introduction

Pelvic organ prolapse (POP) is a common, distressing condition[1]. An objective and accurate evaluation of POP is important for diagnosis and treatment, but physical examinations remain limited to anatomical assessments[2]. MRI with high soft-tissue resolution provides a multiplanar depiction of the pelvic anatomy and has been considered a promising complementary diagnostic tool[3-8], but its validation is unsatisfactory[9-10]. As POP is clinically defined as the descent of the anterior, apex, or posterior vaginal walls[11], an in situ reference line for evaluating the vagina is critical but lacking [9-10].

An assessment of the vagina in situ requires an understanding of its supporting structures, which have been divided into three levels[4, 12]. The upper third of the vagina is typically considered to be suspended by the cardinal and uterosacral ligaments[12, 13]. However, the role of the cardinal ligament is controversial but was proven to be a mesentery structure consisting of vessels and nerves[14,15]. The main ligament-like structure of the upper third seems to be the uterosacral ligament. In the middle third of the vagina, the anterior surface

of the vagina and its lateral attachment to the arcus tendineus fasciae of the pelvis form the pubocervical fascia [12]. In the lower third of the vagina, the pubocervical fascia continues anteriorly, merges with the urethra and then attaches to the pubic symphysis. The attachments in the lower third are highly dense such that the lower portion seldom suffers from POP[12]. In summary, the upper two-thirds of the vagina are more commonly clinically and anatomically affected by POP, and to our understanding, the structure seems to be mainly supported by the uterosacral ligament, which extends from the second to the fourth sacral vertebra region to the dorsal margin of the uterine cervix and/or the upper third of the posterior vaginal wall[13], and by the pubocervical fascia, which originates from the anterior surface of the vagina and anteriorly ends at the pubic symphysis[12]. Therefore, we speculate that a line passing through the inferior aspect of the pubic symphysis to the third sacral vertebra might be the closest proxy for the normal upper two-thirds of the vaginal axis (Fig. 1A). Therefore, this article reviews the vaginal anatomic structures of women without POP and analyses the relationship between this line and the vagina on sagittal MR images.

Materials and methods

This retrospective cross-sectional study was approved by the ethical committee of The Fourth Affiliated Hospital of Zhejiang University School of Medicine (08/22/2019, No. K20190046). The requirements for informed consent were exempted. An electronic search of the radiology information system was performed in two hospitals between July 2018 and June 2019 and included all consecutive female inpatients who underwent pelvic MRI. The demographic information was collected from the medical records.

Exclusion criteria

First, each patient's history was reviewed. Patients who met one of the following criteria were excluded: (1) a previous history of total or subtotal hysterectomy or cervical excision; (2) previous pelvic floor surgery for prolapse or urinary incontinence; (3) a history of prolapse or urinary or faecal incontinence; (4) pregnancy with a gestational age [?] 8 weeks or within 12 months after delivery; and (5) malformation of the female genital tract, such as Mayer-Rokitansky-Küster-Hauser syndrome, although uterine mediastinum was not excluded. Then, the MR images and MRI reports were reviewed. Patients who met one of the following criteria were excluded: (1) a maximum uterine diameter [?] 7 cm, such as multiple uterine fibroids or adenomyosis; (2) any mass or cysts in the pelvis with a diameter [?] 6 cm, such as fibroids, ovarian cysts, or hydrosalpinx; (3) any mass or cysts in the cervix or the cervical canal with a diameter [?] 2 cm; (4) any mass or cysts on the vaginal wall, in the vaginal lumen, or in the area around the vagina with a diameter [?] 2 cm; (5) a maximum diameter of the rectum [?] 3 cm or maximum bladder diameter [?] 6.5 cm on any sagittal images; and (6) poor visibility of the anatomic structures of the landmarks. Finally, the pelvic examination records were carefully reviewed, and any patients with POP were excluded. If surgical treatment was conducted in our hospitals, the corresponding record was also reviewed. Patients with dense, extensive adhesions between the uterus and abdominal wall suggestive of an obvious change in the position of the uterus were excluded.

MR image analysis

Pelvic MRI was performed with a 1.5-Tesla magnet (Sigma, General Electric Medical System, Milwaukee, WI, USA) in the supine position, and no vaginal or rectal contrast was used. The MRI measurements were performed using WebViewer (Greenlander Information Technology, Version 1.0.0.53449). The measurements were performed on the midline or almost midline sagittal plane with a fat-saturated T2-weighted fast recovery fast spin-echo with a repetition time (TR) of 4100-4200 ms and an echo time (TE) of 102-109 ms by a gynaecologist-obstetrician and a radiologist, and any disagreements were discussed. The observers were blinded to the clinical findings, but the patients' ages were not concealed.

The sagittal schematic of the pelvis demonstrates the following anatomical landmarks (Fig. 1). Point P represents the most inferior aspect of the pubic symphysis. Point B represents the bladder neck. Point C represents the most distal edge of the cervix. Point D represents the apex of the tented up posterior fornix.

Two distinct reference lines were used to complete the MRI measurements (Fig. 1). One line was drawn from point P to the midpoint of the third sacral vertebra; we developed and named this line PS3L. The

other line was the pubococcygeal line (PCL), which was drawn from point P to the last coccygeal joint[3].

Points D and C were expected to represent the apical and middle parts of the upper two-thirds of the vagina, respectively. Regarding the distal part, a line was drawn perpendicular to the PS3L from point B; we continued this line into the vaginal area, and the midpoint of the vaginal portion of this line was named point b (Fig. 1A and B). The perpendicular distances from points D, C and b to the PCL and PS3L were measured (Fig. 1B).

The angle between the axis of the upper two-thirds segment of the vagina (a line running through point D to point b) and the PS3L and PCL and the angle between the PCL and PS3L were also measured (Fig. 1C).

Regarding the position locations of points D, C and b relative to the PS3L, a line was drawn perpendicular to the PS3L from points B, C and D, and the points of intersection of the two vertical lines were named b', c, and d. The distances from point P to points b', c, and d were named Pb', Pc, and Pd, respectively (Fig. 1D).

The measurements were performed in centimetres or degrees. If an anatomical landmark or angle was located above a reference line, it had a positive value, and if it was located below the reference line, it had a negative value.

Statistical analysis

The results were analysed with IBM SPSS statistics version 23 for Windows (IBM Corp, Armonk, NY, USA). The age variable was divided into the following three groups: [?] 30 years old, 31 to 49 years, and [?] 50 years. The Kolmogorov-Smirnov test was used to assess the normality of the distribution of the continuous variables. The mean+-standard deviation or median (interquartile range) was used to summarize the results of the continuous data. The categorical variables are presented as percentages and counts. An independent t-test or a Mann-Whitney U test was used for the between-group comparisons of the continuous data, and a chi-square test was used to compare the differences in the categorical data. $P < .05$ was considered indicative of a significant difference.

Results

Patient characteristics

In total, 3545 consecutive patients who underwent pelvic MRI from July 2018 to June 2019 were reviewed. Of these patients, 2931 met the exclusion criteria, and 614 cases remained in the final analysis (Fig. 2). The study sample had a median age of 43 [range: 17 to 76] years and a median body mass index of 22.4 [range: 15.6 to 38.8] kg/m^2. In total, 63.5% (390/614) of the patients had laparoscopic or transabdominal surgery records. The enrolled patients were stratified by age, with 120 patients aged [?] 30 years, 282 patients aged between 31 and 49 years, and 212 patients aged [?] 50 years old. The differences in height, weight, BMI and position of uterus among these three groups were limited as shown in Table S1. However, the parity times significantly differed among the groups ($p < .001$). The women aged [?] 50 years had the highest rate of multiparity (49.1%, 104/212) and highest rate of vaginal delivery (92.9%, 197/212) but the lowest rate of nullipara (0.9%, 2/212). The women aged between 31 and 49 years were mostly primiparous (59.6%, 168/282), and the vaginal delivery rate was 52.8% (149/282), while the women aged [?] 30 years were mostly nulliparous (79.2%, 95/120), and the vaginal delivery rate was only 12.5% (15/120). These findings are presented in Table S1.

Assessment of the relationships among the PS3L, PCL and vaginal axis

The MRI measurements are also summarized in Table S1. The length of the PS3L was longer than that of the PCL (median, 12.8 cm vs 10.1 cm; $p < .001$). The median angle between the PS3L and PCL (PS3L-PCL angle) was 27.0 [interquartile range (IQR), 24.0 – 30.0] degrees, ranging from 13.0 to 41.0 degrees. When stratified by age, no significant differences were observed in the lengths of both reference lines among the

subgroups ($p > .05$), and no significant differences were observed in the PS3L-PCL angle in the subgroup analysis ($p > .05$) (Table S1).

The median distances from the distal, middle, and apical points of the upper two-thirds of the vagina to the PS3L were -0.5 [IQR, -0.9 - 0.0] cm, 0.0 [IQR, - 0.4 - 0.6] cm, and -0.2 [IQR, -0.9 - 0.0] cm, respectively, in the total sample (Table S1). These points showed a trend of a relatively concentrated distribution along the PS3L, and this trend was observed in all age subgroups (Fig. S1), especially in the women aged [?] 30 years (with median distances from these three points to the PS3L of 0.0 [IQR, -0.5- 0.0] cm, 0.0 [IQR, 0.0 - 0.7] cm, and -0.2 [IQR, -0.8 - 0.0] cm) and the women aged 31 to 49 years (with distances of -0.4 [IQR, -0.7- 0.0] cm, 0.0 [IQR, -0.4 - 0.7] cm, and 0.0 [IQR, -0.8 - 0.2] cm). In the women aged [?] 50 years, the distances from all three points to the PS3L were slightly lower than those in the two younger groups ($p < .01$) (Table S1, Figs. 3 and S1), with median distances of -0.8 [IQR, -1.2 - -0.5] cm, 0.0 [IQR, -0.6 - 0.3] cm, and -0.7 [IQR, -1.1 - 0.0] cm.

The median distances from the distal, middle, and apical points of the upper two-thirds of the vagina to the PCL were 0.4 [IQR, 0.0 - 0.7] cm, 2.1 [IQR, 1.7 - 2.5] cm, and 3.1 [IQR, 2.5 - 3.7] cm, respectively (Table S1). Because both the PS3L and PCL originate from the most inferior aspect of the pubic symphysis, the distal point of the upper two-thirds of the vagina was also close to the PCL, but the middle and apical points gradually shifted upward away from the PCL, and this trend was observed in all age subgroups (Fig. S1). The locations of all three points to the PCL in the women aged [?] 50 years were also slightly lower than those in the two younger groups ($p < .001$), although the difference was limited to no greater than 1 cm (Table S1, Figs. 3 and S1).

The distributions of these measurements when using the PS3L as a reference line were more concentrated than those using the PCL (Fig. 3).

The median angle between the PS3L and the upper two-thirds of vaginal axis (PS3L-vaginal angle) was 0.0 [IQR, -4.0 - 7.0] degrees and ranged from -27.0 to 30.0 degrees (Table S1). The PS3L seemed to be nearly parallel to the vaginal axis, and this trend was observed in all age subgroups (Fig. S1), especially in the women aged [?] 30 years (with a PS3L-vaginal angle of 0.0 [IQR -6.5 - 3.0] degrees) and the women aged 31 to 49 years (with an angle of 0.0 [IQR, -0.3 – 6.0] degrees). In the women aged [?] 50 years, the PS3L-vaginal angle (mean angle, 3.2 degrees +- 9.5) was slightly larger than that in the two younger groups ($p < .05$), but the difference was limited (Table S1).

The median angle between the PCL and the vaginal axis (PCL-vaginal angle) was 29.0 [IQR, 23.0 - 34.0] degrees, ranged from 2.0 to 60.0 degrees and was significantly larger than the PS3L-vaginal angle ($p < .001$). The PCL and the vaginal axis demonstrated an acute angulation, and this trend was observed in all age subgroups (Fig. S1). In the women aged [?] 30 years, this angle was slightly smaller than that in the two older groups ($p < .001$), although the difference was limited (Table S1).

The median distances of Pb', Pc, and Pd were 2.4 [IQR, 2.1- 2.6] cm, 4.5 [IQR, 3.9- 5.3] cm, and 7.7 [IQR, 7.0- 8.5] cm and were nearly one-fifth, two-fifths, and three-fifths of the length of the PS3L, respectively (Table S1). All positions of the three marker points in the 614 patients relative to the PS3L are shown in Fig. 4.

Discussion

Main findings

In this study, the anatomical structures of the vagina were distinctly displayed on MRI. A reference line that passes through the inferior aspect of the pubic symphysis to the midpoint of the third sacral vertebra was introduced and named PS3L. The marker points representing the distal, middle, and apical points of the upper two-thirds of the vagina showed relatively concentrated distributions along this line, and the median distances from these points to the line were -0.5 cm, 0.0 cm, and -0.2 cm. Additionally, the vaginal axis lay nearly parallel to this line, and the median angle between the line and the vaginal axis was 0.0 degree. These

trends were observed in all age subgroups, indicating that the reference line PS3L approximates the axis of the normal upper two-thirds of the vagina.

Strengths and limitations

Maintaining normal anatomical appearances in situ is a prerequisite for well-functioning pelvic organs. Pelvic organ prolapse (POP) mostly occurs in the upper two-thirds of the vagina. Although the vaginal shape and dimensions have been previously studied[16], the method used to evaluate this part of the vagina in situ is seldom reported but could be of great clinical value. This study is the first to attempt to introduce a line for an in situ evaluation of the upper two-thirds of the vagina on MRI.

Limitations exist in our study. First, this study adopted a retrospective cross-sectional design; the clinical examinations were not always performed by experienced physicians familiar with POP quantification. Second, not all patients had a transabdominal or laparoscopic surgical record, which was important for identifying dense, extensive adhesions between the pelvic and abdominal walls that may potentially change the direction of the vagina. Finally, MRI was conducted in the supine position in all patients in this study; thus, the results may not reflect pelvic organ positions in the standing position[17].

Interpretation

Several reference lines have been proposed to stage POP on MRI, but to the best of our knowledge, no reference lines represent the axis of the normal vagina[9,10]. In this study, we compared the PS3L with the pubococcygeal line (PCL). The PCL is the most widely used and recommended reference line for POP staging with MRI[3,9]. Traditionally, in situations in which the bladder neck and vaginal vault or distal edge of the cervix descend below the PCL on MRI, the diagnosis of prolapse is established[3]. As shown in this study, the PCL was under the vaginal axis, which is consistent with previous studies[3,9]. In fact, the PCL was thought to approximate the axis of the levator plate[18]. Other lines, such as the midpubic line and the perineal line, were introduced and were expected to correspond to the level of the hymen[19,20]. The hymen is the fixed reference point recommended by the International Continence Society and is used by urogynaecologists to stage POP[11]. Clinically, successful surgical treatment for prolapse from an anatomical perspective has been defined as no apical descent greater than one-third into the vaginal canal or anterior or posterior vaginal wall beyond the hymen[21]. However, the plane of the hymen is anterior to the pubic bone and crosses the urethral meatus[4]. Evaluations of POP based on these lines are not in situ assessments and could result in underestimation, further leading to incomplete or incorrect surgery. Nearly one-third of patients undergoing surgery for POP repair were estimated to require reoperation within 4 years after the initial surgery[22]. After prolapse surgery, new pelvic floor symptoms may develop, while preexisting pelvic floor symptoms may improve, worsen, or remain unchanged[21].

In this study, the measurements based on the PS3L showed superiority over those based on the PCL because they were more concentrated, that mainly because relative to the PCL, the PS3L has an orientation that mostly conforms to the normal vaginal anatomy, and in situ evaluation may reduce deviations to a certain degree. Therefore, quantifying POP based on the PS3L may be more likely to allow quantification and grading of the extent of POP.

However, the measurements still showed variation in these parameters, even in the young women, possibly because the uterosacral ligament is attached anteriorly mostly but not exclusively on the posterior aspect of the cervicovaginal junction[23], posteriorly broadly to the first three sacral vertebrae and variably to the fourth sacral vertebra[24]. In addition, the definitive role of paravaginal support in the middle third of the vagina and its contribution to the development of prolapse are still unknown[25,26]. In this study, the vaginal points in the elderly women were slightly lower than those in the younger women. Ageing, multiparity, and especially previous vaginal delivery are high risk factors for POP[27], and a moderate degree of prolapse in continent women based on MRI has been reported due to its ability to measure actual pelvic organ descent[19,28]. However, in most cases, overall, as shown in this study, the PS3L may represent the axis of the normal upper two-thirds of the vagina

Conclusions

A reference line passing through the most inferior aspect of the pubic symphysis to the midpoint of the third sacral vertebra mostly conforms to a normal upper two-thirds of the vaginal axis, enabling the objective and accurate assessment of this part of the vagina in situ, which could be valuable for surgical planning, postsurgical follow-ups and assessing whether a repair surgery is more suitable. However, how to use this line as a reference for POP staging remains unclear, and further prospective studies are needed.

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Contribution to Authorship

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Manuscript is approved for publication by all authors, All the authors listed have agreed to be accountable for all aspects of the work..

Details of Ethics Approval

This cross-sectional study was approved by the Ethical Committee of The Fourth Affiliated Hospital Zhejiang University School of Medicine (08/22/2019, No. K20190046).

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References

1. Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J et al. Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008; 300:1311-16.

2. Barber MD, Maher C. Epidemiology and outcome assessment of pelvic organ prolapse. Int Urogynecol J 2013; 24:1783-90.

3. El SR, Alt CD, Maccioni F, Meissnitzer M, Masselli G, Manganaro L et al. Magnetic resonance imaging of pelvic floor dysfunction - joint recommendations of the ESUR and ESGAR Pelvic Floor Working Group. Eur Radiol 2017; 27:2067-85.

4. Maglinte DD, Bartram CI, Hale DA, Park J, Kohli MD, Robb BW et al. Functional imaging of the pelvic floor. Radiology 2011; 258: 23-39.

5. El SR, El MS, Farag A, Morsy MM, Abdel AM. Pelvic floor dysfunction: assessment with combined analysis of static and dynamic MR imaging findings. Radiology 2008; 248:518-30.

6. Stoker J, Halligan S, Bartram CI. Pelvic floor imaging. Radiology 2001; 218:621-41.

7. Healy JC, Halligan S, Reznek RH, Watson S, Phillips RK, Armstrong P. Patterns of prolapse in women with symptoms of pelvic floor weakness: assessment with MR imaging. Radiology 1997; 203:77-81.

8. Fitzgerald J, Richter LA. The role of MRI in the diagnosis of pelvic floor disorders. Curr Urol Rep 2020; 21:26.

9. Broekhuis SR, Futterer JJ, Barentsz JO, Vierhout ME, Kluivers KB. A systematic review of clinical studies on dynamic magnetic resonance imaging of pelvic organ prolapse: the use of reference lines and anatomical landmarks. Int Urogynecol J Pelvic Floor Dysfunct 2009; 20:721-29.

10. Xie B, Chen L, Xue Z, English EM, Fenner DE, Gaetke-Udager K et al. Comparison of measurement systems for posterior vaginal wall prolapse on magnetic resonance imaging. Int Urogynecol J 2019; 30:1269-77.

11. Haylen BT, Maher CF, Barber MD, Camargo S, Dandolu V, Digesu A et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic organ prolapse (POP). Int Urogynecol J 2016; 27:655-84.

12. DeLancey JO. Anatomic aspects of vaginal eversion after hysterectomy. Am J Obstet Gynecol 1992; 166:1717-28.

13. Ramanah R, Berger MB, Parratte BM, DeLancey JO. Anatomy and histology of apical support: a literature review concerning cardinal and uterosacral ligaments. Int Urogynecol J 2012; 23:1483-94.

14. Hockel M, Horn L, Fritsch H. Association between the mesenchymal compartment of uterovaginal organogenesis and local tumour spread in stage IB–IIB cervical carcinoma: a prospective study. The Lancet Oncology 2005; 6:751-56

15. Zhao X, Chen G, Lei L, Wu X, Liu S, Wang J et al. Key anatomies of Delaney's three levels of vaginal support theory: an observation in laparoscopic surgery. Zhejiang Da Xue Xue Bao Yi Xue Ban 2018; 47:329-37.

16. Luo J, Betschart C, Ashton-Miller JA, DeLancey JOL. Quantitative analyses of variability in normal vaginal shape and dimension on MR images. Int Urogynecol J2016;27:1087-95.

17. Grob A, Heuvel JO, Futterer JJ, Massop D, Veenstra VNA, Simonis F et al. Underestimation of pelvic organ prolapse in the supine straining position, based on magnetic resonance imaging findings. Int Urogynecol J 2019; 30:1939-1944.

18. Yang A, Mostwin JL, Rosenshein NB, Zerhouni EA. Pelvic floor descent in women: dynamic evaluation with fast MR imaging and cinematic display. Radiology 1991; 179:25-33.

19. Singh K, Reid WM, Berger LA. Assessment and grading of pelvic organ prolapse by use of dynamic magnetic resonance imaging. Am J Obstet Gynecol 2001; 185:71-77.

20. Fauconnier A, Zareski E, Abichedid J, Bader G, Falissard B, Fritel X. Dynamic magnetic resonance imaging for grading pelvic organ prolapse according to the International Continence Society classification: which line should be used? Neurourol Urodyn 2008; 27:191-97.

21. Barber MD, Brubaker L, Burgio KL, Richter HE, Nygaard I, Weidner AC et al. Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse: the OPTIMAL randomized trial. JAMA 2014; 311:1023-34.

22. Wu JM, Matthews CA, Conover MM, Pate V, Jonsson FM. Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery. Obstet Gynecol 2014; 123:1201-06.

23. Vu D, Haylen BT, Tse K, Farnsworth A. Surgical anatomy of the uterosacral ligament. Int Urogynecol J 2010; 21:1123-28.

24. Buller JL, Thompson JR, Cundiff GW, Krueger SL, Schon YM, Bent AE. Uterosacral Ligament: Description of Anatomic Relationships to Optimize Surgical Safety. Obstet Gynecol 2001; 97:873-79

25. Arenholt L, Pedersen BG, Glavind K, Glavind-Kristensen M, DeLancey J. Paravaginal defect: anatomy, clinical findings, and imaging. Int Urogynecol J 2017; 28:661-73

26. Larson KA, Hsu Y, Chen L, Ashton-Miller JA, DeLancey JO. Magnetic resonance imaging-based three-dimensional model of anterior vaginal wall position at rest and maximal strain in women with and without prolapse. Int Urogynecol J 2010; 21:1103-09.

27. Handa VL, Blomquist JL, McDermott KC, Friedman S, Munoz A. Pelvic floor disorders after vaginal birth: effect of episiotomy, perineal laceration, and operative birth. Obstet Gynecol 2012; 119:233-239.

28. Hodroff MA, Stolpen AH, Denson MA, Bolinger L, Kreder KJ. Dynamic magnetic resonance imaging of the female pelvis: the relationship with the pelvic organ prolapse quantification staging system. J Urol 2002; 167:1353-55.

Table S1 Demographic characteristics and MRI measurements in the study sample	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**
Variables	**All patients enrolled (n= 614)**	**group**	**group**	**group**	*P* **value for between-group comparisons**	*P* **value for between-group comparisons**	*P* **value for between-group comparisons**
		[?] 30 years (n=120)	**31-49 y (n=282)**	**[?]50 y (n=212)**	**[?]30 y vs 31-49y**	**[?]30 y vs[?]50 y**	**31-49 y vs[?]50 y**
Age, y [a]	43 (32, 54) [a]	28 (26, 29) [a]	39 (34, 45) [a]	57 (53, 62) [a]	.000 [c]	.000 [c]	.000 [c]
Height, cm [a]	160 (156, 163) [a]	161 (158, 165) [a]	160 (156, 163) [a]	158 (156, 162) [a]	.001 [c]	.000 [c]	.152[c]
Weight, kg [a]	56.8 (51.0, 64.0) [a]	54 (49, 62) [a]	56 (51, 62) [a]	59 (53, 64) [a]	.060 [c]	.000 [c]	.000 [c]
BMI, kg/m^2 [a]	22.4 (20.3, 24.9) [a]	20.5 (19.1, 22.9) [a]	22.3 (20.3, 24.4) [a]	23.4 (21.6, 25.8) [a]	.000 [c]	.000 [c]	.000 [c]
Parity, range	0-6	0-2	0-5	0-6			
Nulliparous, n (%)	137 (22.3%)	95 (79.2%)	40 (14.2%)	2 (0.9%)	0.000[e]	0.000[e]	0.00[e]

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primiparous, n (%)	290 (47.2%)	16 (13.3%)	168 (59.6%)	106 (50.0%)			
Multiparous, n (%)	187 (30.5%)	9 (7.5%)	74 (26.2%)	104 (49.1%)			
Vagina delivery, n (%)	361 (58.8%)	15 (12.5%)	149 (52.8%)	197 (92.9%)	0.000[e]	0.000[e]	0.00[e]
Position of uterus					0.675 [e]	0.106 [e]	0.033 [e]
Anteposition	355 (57.8%)	75 (62.5%)	173 (61.3%)	107 (50.5%)			
Retroposition	199 (32.4%)	36 (30.0 %)	80 (28.4%)	83 (39.2%)			
Mesoposition	60 (9.8%)	9 (7.5%)	29 (10.3%)	22 (10.4%)			
PS3L, cm	12.8 (12.3, 13.5) [a]	12.8 (± 0.9) [b]	12.8 (± 0.8) [b]	13.0 (± 0.8) [b]	.809 [d]	.086[d]	.059 [d]
PCL, cm	10.1 (9.5, 10.6) [a]	10.0 (± 1.0) [b]	10.1 (± 0.8) [b]	10.1 (± 0.9) [b]	.546[d]	.542[d]	.937 [d]
PS3L-PCL angle, degree	27.0 (24.0, 30.0) [a]	27.5(± 4.6)[b]	27.0 (24.0, 31.0) [a]	27.0 (23.5, 29.0) [a]	.682[c]	.081 [c]	.091[c]
PS3L-vaginal angle, degree	0.0 (- 4.0, 7.0) [a]	0.0 (-6.5, 3.0) [a]	0.0 (-3.0, 6.0) [a]	3.2 (± 9.5)[b]	.023[c]	.000 [c]	.032 [c]
PCL-vaginal angle, degree	29.0 (23.0, 34.0) [a]	26.2 (± 7.6) [b]	30.0 (± 8.6) [b]	29.0 (24.0, 37.0) [a]	.000 [d]	.000 [c]	.841[c]
b-PS3L, cm	-0.5 (-0.9, 0.0) [a]	0.0 (-0.5, 0.0) [a]	-0.4 (-0.7, 0.0) [a]	-0.8 (-1.2, -0.5) [a]	.002 [c]	.000 [c]	.000 [c]
C-PS3L, cm	0.0 (-0.4, 0.6) [a]	0.0 (0.0, 0.7) [a]	0.0 (-0.4, 0.7) [a]	0.0 (-0.6, 0.3) [a]	.233[c]	.000 [c]	.000 [c]
D-PS3L, cm	-0.2 (-0.9, 0.0) [a]	-0.2 (-0.8, 0.0) [a]	0.0 (-0.8, 0.2) [a]	-0.7 (-1.1, 0.0) [a]	.707[c]	.002 [c]	.000 [c]

Table S1 Demographic characteristics and MRI measurements in the study sample	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**	**Table S1 Demographic characteristics and MRI measurements in the study sample**
b-PCL, cm	0.4 (0.0, 0.7) [a]	0.7 (0.4, 0.9) [a]	0.4 (0.0, 0.8) [a]	0.3 (0.0,0.6) [a]	.000 [c]	.000 [c]	.000 [c]
C-PCL, cm	2.1 (1.7,2.5) [a]	2.2 (± 0.6) [b]	2.2 (± 0.6) [b]	1.8 (± 0.7) [b]	.698 [d]	.000 [d]	.000 [d]
D-PCL, cm	3.1 (2.5,3.7) [a]	3.1 (± 0.8) [b]	3.3 (± 0.9) [b]	2.7 (2.1, 3.3) [a]	.009[d]	.000 [c]	.000 [c]
Pb', cm	2.4 (2.1, 2.6) [a]	2.4 (2.2, 2.6) [a]	2.3 (± 0.4)[b]	2.4 (2.2, 2.6) [a]	.002 [c]	.445[c]	.002 [c]
Pc, cm	4.5 (3.9, 5.3) [a]	4.4 (3.9, 5.5) [a]	4.5 (3.9, 5.5) [a]	4.5 (± 0.9)[b]	.568[c]	.102[c]	.176[c]
Pd, cm	7.7 (7.0, 8.5) [a]	7.8 (± 1.1) [b]	8.0 (± 1.1) [b]	7.2 (6.7, 7.8) [a]	.181[d]	.000 [c]	.000 [c]
Pb'/PS3L	0.18 (± 0.03) [b]	0.19 (± 0.03) [b]	0.18 (± 0.03) [b]	0.18 (± 0.03) [b]	.001 [d]	.179[d]	.014[d]
Pc/PS3L	0.35 (0.30, 0.42) [a]	0.36 (0.31, 0.46) [a]	0.35 (0.30, 0.42) [a]	0.35 (± 0.07)[b]	.524[c]	.049 [c]	.062[c]
Pd/PS3L	0.59 (0.54, 0.67) [a]	0.60 (0.55, 0.70) [a]	0.62 (0.55, 0.69) [a]	0.56 (± 0.08)[b]	.286 [c]	.000 [c]	.000 [c]

Footnote: BMI, Body mass index; *PS3L,* the distance from the most inferior margin of the symphysis pubis to the midpoint of the third sacral vertebra*; b-PS3L, C-PS3L, D-PS3L,* represent the perpendicular distances from point b , C, D to PS3L*; PCL*pubococcygeal line; *b-PCL, C-PCL, D- PCL* represent the perpendicular distances from point b, C, D to PCL. *Pb', Pc, Pd*represent the distances from points b', c, and d to the inferior aspect of the pubic symphysis*; Pb'/PS3, Pc/PS3, Pd/PS3* represent the proportions of Pb', Pc, Pd to the length of PS3L. Positive values indicate that an anatomical landmark or angle was located above a reference line

[a] Data given as median (interquartile range).[b] Data given as mean (± standard deviation).[c] The Mann-Whitney U test was used for between-group comparisons. [d] The chi-square test T was used for between-group comparisons. [e] The chi-square test was used for between-group comparisons. $P < .05$ was considered indicative of a significant difference.

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