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Reference data representative of normal findings at two-dimensional and three-dimensional gray scale ultrasound examination of the cervix from 17 to 41 gestational weeks

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ABSTRACT

Objectives To create reference values representative of normal findings at two dimensional (2D) and three-dimensional (3D) transvaginal ultrasound examination of the cervix from 17 to 41 gestational weeks (gws), and to determine the agreement between cervical measurements taken by 2D and 3D transvaginal ultrasound.

Methods Cross-sectional study covering 17 to 41 gws in 419 nulliparae and 360 multiparae who delivered at term and underwent 2D and 3D transvaginal ultrasound examination of the uterine cervix. We examined approximately 25 women in each gestational week. The length, anterior-posterior (AP) diameter and width of the cervix and of any cervical funnel, and the AP diameter of the cervical canal were measured. Results were plotted against gestational age. The agreement between 2D and 3D ultrasound results was expressed as the mean (± 2SD) difference between the results of the two methods and as inter-class correlation coefficient (inter-CC).

Results There was excellent agreement between measurements taken by 2D and 3D ultrasound (Inter-CC values 0.80 − 0.98), but measurements of cervical length taken using 3D ultrasound were greater than measurements taken by 2D ultrasound (mean difference –0.04cm ± 0.36). Below 3D measurements are presented. Cervical length did not change substantially between 17 and 32 gws but decreased progressively thereafter. There was no difference in cervical length between nulliparae and multiparae ≤ 32 gws, but from 33 gws the cervix was longer in multiparae. Median cervical length decreased from 3.8 cm (range 0.7 − 6.1) at 17 – 32 gws to 2.3 cm (range 0.4 − 6.0) at 33 – 40 gws in nulliparae and 3.0 cm (range 0.4 − 5.7) in multiparae and to 0.7 cm (range 0.2 − 1.5) at 41 gws in nulliparae and 0.8 cm (range 0.4 − 0.8) in multiparae. Cervical AP diameter and width did not differ between nulliparae and multiparae. Median AP diameter increased from 3.0 cm (range 2.0 − 4.6) at 17 − 30 gws to

3.5 cm (range 1.8 − 5.5) at 31 – 40 gws and to 4.0 cm (range 2.8 − 5.9) at 41 gws. Cervical width was 3.7 cm (range 2.3 − 6.0) at 17 − 30 gws and 4.5 cm (range 2.3 − 6.1) at 31 − 41 gws. The percentage of women with funneling increased from 4% (3/84) at 17 − 18 gws to 63% (12/19) at 41 gws and the percentage of women with an open cervical canal from 19% (15/84) to 72% (13/19). Funneling and opening of the cervical canal were equally common in nulliparae and multiparae.

Conclusion Reference data lay the basis for studies of pathological conditions. Common reference values for nulliparae and multiparae can be used for cervical AP diameter and width from 17 to 41 gws and for cervical length from 17 to 32 gws. Separate reference values for cervical length for nulliparae and multiparae should be used from 33 to 41 gws.

Introduction

Transvaginal ultrasound has been advocated as a good method to assess the uterine cervix and lower uterine segment[1]. Measurement of cervical length and anterior-posterior (AP) diameter and assessment of the inner cervical os by two-dimensional (2D) transvaginal ultrasound has been suggested as a method to predict preterm[2,4], term or post-term delivery[5,6], and outcome of labor induction[7,8].

Three-dimensional (3D) ultrasound imaging is now available for clinical use. With 3D ultrasound a volume of data is acquired and stored. The stored data can be reformatted and analyzed in an infinite number of planes. 3D ultrasound offers a unique possibility to show true coronal and mid-sagittal planes by direct correlation of the views in a multiplanar display. 3D transvaginal ultrasound has been used to measure the cervix in women at risk of preterm delivery[9-11].

Reference values for cervical length as measured by 2D ultrasound in pregnancy have been published[12-20]. The published studies cover different periods of gestation, have different design, and the study populations are mixed and/or small. There are only a few studies where reference values for cervical AP diameter[12,15,17,18] are presented, but to the best of our knowledge no reference values for cervical funneling have been published. In three small studies cervical length[9,10,21] and funneling[9,10] were assessed by 3D ultrasound. However, there are no ultrasound studies presenting reference values for all cervical dimensions i.e., cervical length, AP diameter and width, and size of cervical funnel as assessed either by 2D or 3D ultrasound.

The aim of this study was to establish reference data representative of normal findings at 2D and 3D transvaginal ultrasound examination of the cervix during the second half of pregnancy and to determine the agreement between cervical measurements taken by 2D and 3D ultrasound.

Subjects and methods

The study protocol was approved by the Ethics Committee of the Medical Faculty of Lund University, Sweden. Informed consent was obtained from all participants, after the nature of the procedures had been fully explained.

At our institution all pregnant women are offered one routine ultrasound examination at 18 gestational weeks (gws) and another at 32 gws. Consecutive women coming for a routine scan were asked to participate in this study, i.e., to undergo a transvaginal 2D and 3D ultrasound examination of the cervix once in a predefined gestational week. Inclusion criteria were: singleton pregnancy, gestational age determined by ultrasound fetometry at 12 – 20 gws, live fetus, intact membranes, not in labor and no vaginal bleeding at the time of the ultrasound examination of the cervix, and no previous cone biopsy. The exclusion criterion was spontaneous delivery ≤ 37 gws.

The equipment used was a GE Voluson 730 ultrasound system (General Electrics, Zipf, Austria) equipped with a 2.8 − 10 MHz transvaginal transducer. The field of view was 146°. All women underwent 2D and 3D transvaginal ultrasound examination of the cervix by the first author as described below. The women were examined in the lithotomy position with an empty bladder. The ultrasound probe was slowly introduced into the vagina and care was taken to avoid exerting undue pressure, which may artificially lengthen the cervix. After a satisfactory image of the cervix had been obtained, the probe was withdrawn until the image became blurred. Then the probe was gradually advanced with only enough pressure to restore a satisfactory image. Neither fundal nor suprapubic pressure was applied. A sagittal view of the cervix was obtained where the internal os, the cervical canal and the external os were all visible simultaneously. The image was magnified so that the cervix occupied approximately 75% of the screen. A standardized measurement technique was used. Cervical length was measured from the outer to the inner cervical os, care being taken to include only that segment of the cervical canal that was bordered by the endocervical mucosa [22]. Cervical AP diameter was measured in the same plane as cervical length at the midpoint between the inner and outer cervical os and perpendicular to the longitudinal axis of the cervical canal as previously described[23]. The internal cervical os was described as being closed or open, any opening being called funneling. The length and AP diameter of any funnel were measured as described in a previous publication[23]. An open cervical canal was seen as an anechoic space extending from the internal to the external cervical os. Its AP diameter was measured where it appeared to be at its widest perpendicularly to the longitudinal axis of the cervical canal. All 2D ultrasound measurements were repeated three times, and the mean of the three measurements was used for statistical analysis. Cervical width and cervical funnel width were not measured by 2D ultrasound. The duration of the 2D examinations was approximately 4 min.

After having completed the 2D ultrasound examination, the system was switched into the 3D mode. A sagittal view of the cervix was centralized within the 3D sector appearing on the ultrasound screen. Then the system was switched into the power Doppler mode and an ultrasound volume containing the cervix was acquired by holding the transducer stationary while its crystals were mechanically rotated across the sector with a sweep angle of 90°**.** The original plane of the cervical volume acquisition was the sagittal plane. The acquired volumes were stored on the hard disk of the ultrasound system for later analysis off-line. The following measurements were taken using `any-plane` slicing of the volume acquired: length, AP diameter and width of the cervix and of any cervical funneling and the AP diameter of the cervical canal (Figure 1). The measurements were taken from 3D power Doppler volumes, because power Doppler blood flow indices were used for another study.

Statistical analysis

All measurement results were plotted against gestational age. The statistical significance of differences in continuous data was determined using Mann-Whitney's test or

Kruskall-Wallis test as appropriate. Correlation was determined using Spearman Rank Correlation test. To determine the agreement between cervical measurements obtained by 2D and 3D ultrasound limits of agreement (i.e., mean difference in measurement results ± 2 SD)[24,25] and interclass correlation coefficients (Inter-CC)[26] were calculated. Systematic bias between 2D and 3D ultrasound measurements was determined by calculating the 95% confidence interval of the mean difference (mean difference ± 2 standard errors; SE). If zero lay within this interval no systematic bias was assumed to exist between the two methods. Agreement for categorical data was expressed as Cohen's kappa[27] value. Two tailed p-values are given. Bonferroni correction was used to correct for multiple testing. Statistical calculations were performed using StatView®, version 5 (SAS Institute Inc., USA, 1999) and the Statistical Package for the Social Sciences software (SPSS, version 12.0, Chicago, IL, USA, 2004).

Results

Eight hundred and twenty women agreed to participate and underwent a 2D and 3D transvaginal ultrasound examination of the cervix. Forty-one delivered before 37 gws and were excluded. Our study population includes 419 nulliparae and 360 multiparae, each woman contributing the results of one ultrasound examination to the study. Mean age was 31 years ± 4.2 (SD; standard deviation) and mean body mass index in the first trimester was 25.0 kg/m^2 ± 4.87.

Changes in cervical length, AP diameter and width with advancing gestation are shown in Figures 2-6. Cervical length did not change substantially between 17 and 32 gws and was similar in nulliparae and multiparae. After 32 gws cervical length decreased in both nulliparae and multiparae, but the cervix tended to be substantially longer in multiparae from 33 to 41gws (Figures 2 and 3).

Cervical AP diameter was similar in nulliparae and multiparae and seemed to increase stepwise during pregnancy: unchanged AP diameter from 17 to 30 gws, slightly greater diameter at 31 – 40 gws, and greatest diameter at 41 gws ($p < 0.001$), see Figures 4 and 5.

Cervical width did not differ between nulliparae and multiparae and seemed to increase stepwise during pregnancy. Cervical width was similar from 17 to 30 gws and greater at 31 – 41 gws ($p < 0.0001$), see Figure 6.

Reference values for cervical length, AP diameter and width as measured by 2D and 3D ultrasound are shown in Table 1.

The percentage of women with cervical funneling increased from 17 to 41 gws (Figures 7 and 8). Cervical funneling was equally common in nulliparae and multiparae, 22% (91/419) of nulliparae and 25% (89/360) of multiparae having cervical funneling according to 2D ultrasound and 22% (91/419) of nulliparae and 22% (80/360) of multiparae having cervical funneling according to 3D ultrasound. There was no statistically significant difference in funnel size between multiparae and nulliparae at any gestational age, but funnel size (mean of length and AP diameter for 2D measurements, mean of length, AP diameter and width for 3D measurements) tended to increase slightly with gestational age (correlation between funnel size as measured by 2D ultrasound and gestational age: Rho = 0.18, $p = 0.018$; correlation between funnel size as measured by 3D ultrasound and gestational age: Rho = 0.26, $p < 0.001$). The correlation between funnel width and gestational age was stronger (Rho 0.36, $p < 0.0001$) than that between funnel AP diameter or funnel length and gestational age (Rho 0.15, $p < 0.056$ and Rho 0.14, $p < 0.062$) as measured by 3D ultrasound. Results for funnel size are shown in Table 1.

The proportion of women with an open cervical canal increased with advancing gestation and was similar in nulliparae and multiparae (Figures 9 and 10). Median cervical canal AP diameter as measured both by 2D and 3D ultrasound was 0.2 cm (range 0.1 – 0.8;

10th percentile 0.1, 90th percentile 0.3). The AP diameter of the cervical canal increased slightly with gestational age (Rho = 0.16, p = 0.009, same result for 2D and 3D ultrasound).

The agreement between results of 2D and 3D ultrasound measurements of the cervix was excellent (Table 2), but cervical length measured by 3D ultrasound was greater than cervical length measured by 2D ultrasound.

Discussion

We found cervical length to change very little and not to differ between nulliparae and multiparae between 17 and 32 gws. After 32 gws the cervix shorted but was longer in multiparae than in nulliparae. Thus, it seems justified to use common reference values for cervical length for nulliparae and multiparae from 17 to 32 gws. After 32 gws we would recommend separate reference values for nulliparae and multiparae and separate reference values depending on pregnancy week. Our results with regard to cervical length agree with those reported by Tongsong et al[16] and Brieger et al[15]. Tongsong et al[16] found cervical length not to change substantially between 8 and 31 gws whereafter it decreased. Brieger et al[15] reported decreasing cervical length from 30 gws. Results of other studies are more variable: some found cervical length not to change during pregnancy[12], others found a continuous decrease from 10 to 40gws[13] or from 17 to 37gws[20], others[14] reported that the cervix became longer between 8 and 25 gws and then shortened. In most studies cervical length did not differ between nulliparae and mulltiparae[13,14,20,28,29], in some the cervix was longer in multiparae[17,18]. The discrepant results may be explained by differences in measurement technique, study design, the period in gestation studied, the statistical methods used, and the interpretation of the results. For example, in some studies[13,15,16,19,20,28] a correlation coefficient was used to describe changes in cervical length with gestational age. Only Gramellini et al[13], Murakawa H et al[20] and Brieger et al[15] reported a strong or moderate negative correlation between cervical length and gestational age ($r = 0.92$, $p < 0.001$, $r = 0.4$, $p < 0.001$, and $r = 0.6$, $p < 0.001$), in the other studies [16,19,28] the negative correlation was weak.

In all studies where cervical AP diameter was measured and compared between nulliparae and multiparae it tended to be larger in multiparae[17,18], and in all studies AP diameter increased with gestational age[12,15,17,18]. This is in agreement with our results. The larger cervical AP diameter in multiparae is possibly to be explained by changes in the cervix caused by delivery and then persisting into the next pregnancy. Cervical AP diameter was largest at 41 gws. It is reasonable to believe that women examined at 41gws were closer to delivery than those examined at 37 – 40 gws. The large AP diameter at 41gws might therefore be explained by increasing distension of the lower uterine segment shortly before onset of labor.

Cervical width as measured by 3D ultrasound did not change substantially between 17 and 30 gws, then the cervix became broader. Cervical width did not differ between nulliparae and multiparae. To the best of our knowledge there are no other studies reporting reference values for sonographic cervical width during pregnancy.

In our study funneling was found in 22% of nulliparae and in 24% of multiparae from 17 to 41 gws and was seen as early as at 18 gws. This is similar to the results of Hasegawa and co-workers[28]. They reported that 20% of pregnant women (both nulliparae and multiparae) delivering at term had an open inner cervical os between 15 and 34 gestational weeks. However, funneling at 18 gws was more common in our study (4%) than in a study by Taipale and Hiilesmaa[3] (0.4%). The disagreement might be explained by differences in definition of funneling: we defined funneling as any opening of the inner cervical os, whereas Taipale and Hiilesmaa[3] defined it as a protrusion of the amniotic membranes 3 mm or more into the cervical canal.

An opening of the cervical canal up to 2 mm in diameter was suggested by Cook et al[18] to be a normal finding during pregnancy. We found the cervical canal to be visible at ultrasound examination as early as 17 gws - both in nulliparae and multiparae - but the proportion of women with an open cervical canal increased with advancing gestation up to 70% at 41gws. To the best of our knowledge there are no other studies reporting reference values for sonographic cervical canal diameter during pregnancy.

There was good agreement between measurements taken by 2D and 3D ultrasound. Only cervical length differed systematically between the two methods, measurements of cervical length obtained by 3D ultrasound being greater than those obtained by 2D ultrasound. However, the difference was so small that we believe it to be clinically unimportant. Towner et al[21] also found that cervical length measurements taken by 3D ultrasound were greater than those taken by 2D ultrasound, but their differences were larger than ours (mean 8.0 mm vs. -0.4 mm). The reason for this discrepancy is unclear.

Because the correlation between funnel width and gestational age was stronger than that between funnel AP diameter or funnel length and gestational age, it is possible that measurement of the width of a funnel might be a more useful indicator of cervical ripeness than funnel length or funnel AP diameter.

To sum up, we have created reference values for sonographic cervical measurements in asymptomatic pregnant women who deliver at term. These values can be used as normative guidelines when assessing cervical dimensions by ultrasound during the second half of pregnancy.

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References

1. Sonek JD, Iams JD, Blumenfeld M, Johnson F, Landon M, Gabbe S. Measurement of cervical length in pregnancy: comparison between vaginal ultrasonography and digital examination. *Obstet Gynecol* 1990; **76**: 172- 175.

2. Heath VCF, Southall TR, Souka AP, Elisseou A, Nicolaides KH. Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery. *Ultrasound Obstet Gynecol* 1998; **12**: 312-317.

3. Taipale P, Hiilesmaa V. Sonographic measurement of uterine cervix at 18-22 weeks gestation and the risk of preterm delivery. *Obstet Gynecol* 1998; **92**: 902-907.

4. To MS, Skentou C, Liao AW, Cacho A, Nicolaides KH. Cervical length and funneling at 23 weeks of gestation in the prediction of spontaneous early preterm delivery. *Ultrasound Obstet Gynecol* 2001; **18**: 200-203.

5. Rozenberg P, Goffinet F, Hessabi M. Comparson of the Bishop score, ultrasonographically measured cervical length, and fibronectin assay in predicting time until delivery and type of delivery at term. *Am J Obstet Gynecol* 2000; **182**: 108-113.

6. Ramanathan G, Yu C, Osei E, Nicolaides KH. Ultrasound examination at 37 weeks` gestation in the prediction of pregnancy outcome: the value of cervical assessment. *Ultrasound Obstet Gynecol* 2003; **22**: 598-603.

7. Rovas L, Sladkevicius P, Strobel E, Valentin L. Three-dimensional power Doppler ultrasound assessment of the cervix for prediction of successful induction of labor with prostaglandin in prolonged pregnancy. *J Ultrasound Med;* in press. *2005.*

8. Rane SM, Guirgis RR, Higgins B, Nicolaides KH. The value of ultrasound in the prediction of successful induction of labor. *Ultrasound Obstet Gynecol* 2004; **24**: 538-549.

9. Bega G, Lev-Toaff A, Kuhlman K, Berghella V, Parker L, Goldberg B, Wapner R. Three-dimensional multiplanar transvaginal ultrasound of the cervix in pregnancy. *Ultrasound Obstet Gynecol* 2000; **16**: 351-358.

10. Severi FM, Bocchi C, Florio P, Picciolini E, D`Aniello G, Petraglia F. Comparison of two-dimensional and three-dimensional ultrasound in the assessment of the cervix to predict preterm delivery. *Ultrasound in Med. & Biol* 2003; **9**: 1261-1265.

11. Rozenberg P, Rafii A, Senat MV, Dujardin A, RaponJ, Viie Y. Predictive value of two-dimensional and three-dimensional multiplanar ultrasound evaluation of the cervix in preterm labor. *J Matern Fetal Neonatal Med* 2003; **13**: 237-341.

12. Smith CV, Anderson JC, Matomoros A, Rayburn WF. Transvaginal sonography of cervical width and length during pregnancy. *J Ultrasound Med* 1992; **11**: 465-467.

13. Gramellini D, Fieni S, Molina E, Berretta R, Vadora E. Transvaginal sonographic cervical length changes during normal pregnancy. *J Ultrasound Med*. 2002; **21**: 227-32.

14. Kushnir O, Vigil DA, Izquierdo L, Schiff M, Curet LB. Vaginal ultrasonographic assessment of cervical length changes during normal pregnancy. *Am J Obstet Gynecol* 1990; **162**: 991-993.

15. Brieger GM, Ning XH, Dawkins RR, Ying KQ, Weng C, Chang AM, Haines CJ. Transvaginal sonographic assessment of cervical dynamics during the third trimester of normal pregnancy. *Acta Obstet Gynecol Scand* 1997; **76**: 118-22.

16. Tongsong T, Kamprapanth P, Pitaksakorn J. Cervical length in normal pregnancy as measured by transvaginal sonography. *Int J Gynaecol Obstet* 1997; **58**: 313-315.

17. Zorzoli A, Soliani A, Perra M, Caravelli E, Galimberti A, Nicolini U. Cervical changes throughout pregnancy as assessed by transvaginal sonography. *Obstet Gynecol* 1994; **84**: 960-964.

18. Cook CM, Ellwood DA. A longitudinal study of the cervix in pregnancy using transvaginal ultrasound. *Br J Obstet Gynaecol* 1996; **103**: 16 -18.

19. Hoesli IM, Strutas D, Tercanli S, Holzgreve W. Charts for cervical length in singleton pregnancy. *Int J Gynaecol Obstet* 2003; **82**: 161-165.

20. Murakawa H, Utumi T, Hasegawa I, Tanaka K, Fuzimori R. Evaluation of threatened preterm delivery by transvaginal ultrasonographic measurement of cervical length. *Obstet Gynecol* 1993; **82**: 829-832.

21. Towner D, Boe N, Lou K, Gilbert WM. Cervical length measurements in pregnancy are longer when measured with three-dimensional transvaginal ultrasound. *J Matern Fetal Neonatal Med* 2004; **16**: 167-170.

22. Sonek J, Shellhass C. Cervical sonography: a review. *Ultrasound Obstet Gynecol* 1998; **11**: 71-78.

23. Bergelin I, Valentin L. Patterns of normal change in cervical length and width during pregnancy in nulliparous women: a prospective, longitudinal ultrasound study. *Ultrasound Obstet Gynecol* 2001; **18**: 217-222.

24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307-310.

25. Bland JM, Altman DG. A note on the use of the intraclass correlation coefficient in the evaluation of agreement between two methods of measurement. *Comput. Biol. Med* 1990; **20**: 337-340.

26. Scherjon SA, Kok JH, Oosting H, Zondervan HA. Intra-observer and inter-observer reliability of the pulsatility index calculated from pulsed Doppler flow velocity waveforms in three fetal vessels. *Br J Obstet Gynaecol* 1993; **100**: 134-138.

27. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Measurem* 1960; **20**: 37-46.

28. Hasegawa I, Tanaka K, Takahashi K, Tanaka T, Aoki K, Torii Y, Okai T, Saji F, Takahashi T, Sato K, Fujimura M, Ogawa Y. Transvaginal ultrasonographic cervical assessment for the prediction of preterm delivery. *J Matern Fetal Med* 1996; **5**: 305-309.

29. Andersen HF. Transvaginal and transabdominal ultrasonography of the uterine cervix during pregnancy. *J Clin Ultrasound* 1991; **19**: 77-83.

Legends

Figure 1 Ultrasound images showing cervical measurements taken by two-dimensional ultrasound (images a and b) and by three-dimensional ultrasound (images c and d) a) Cervical length – A, cervical anterior-posterior diameter – B, length of cervical funneling – C, anterior-posterior diameter of funnel – D b) Cervical canal. Anterior-posterior diameter of the cervical canal was measured where it appeared to be at its widest, the measurements being taken perpendicularly to the longitudinal axis of the canal c) Cervical width d) Width of funnel.

Figure 2 Relationship between cervical length as measured by two-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae. Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 3 Relationship between cervical length as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae. Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 4 Relationship between cervical anterior-posterior diameter as measured by two-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 5 Relationship between cervical anterior-posterior diameter as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae Median, 10th, 25th, 75th and 90th percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 6 Relationship between cervical width as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Boxes represent the cervical width of both multiparae and nulliparae. Median, 10th, 25th, 75th and 90th percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 7 Percentage of women with cervical funneling according to two-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.005/13), signifies a statistically significant difference.

Figure 8 Percentage of women with cervical funneling according to three-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 9 Percentage of women with an open cervical canal according to two-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 10 Percentage of women with an open cervical canal according to three-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure1

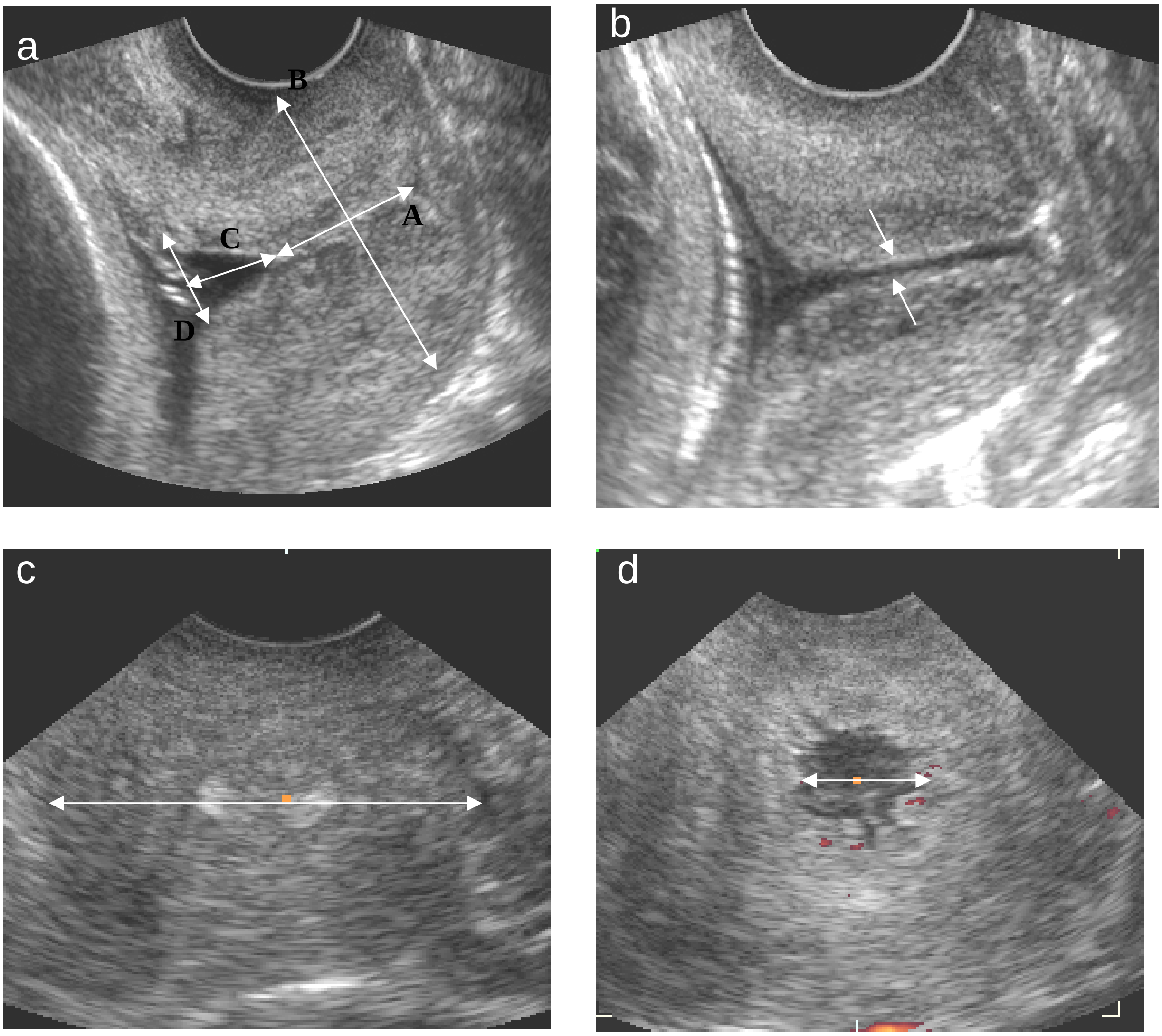
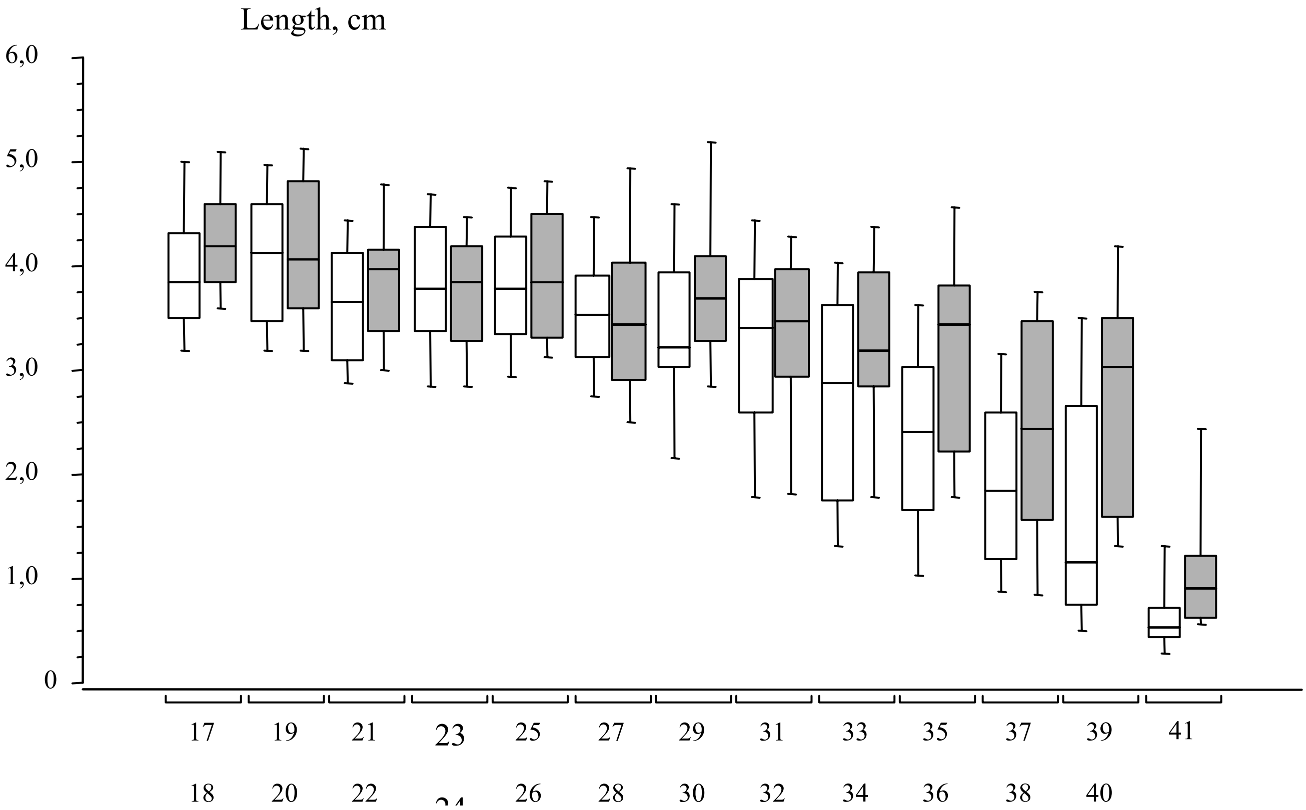


Figure 2



No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.095	0.593	0.223	0.733	0.464	0.706	0.146	0.485	0.081	0.001	0.009	0.003	0.140

Reference data representative of normal findings at two-dimensional and three-dimensional gray scale ultrasound examination of the cervix from 17 to 41 gestational weeks

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ABSTRACT

Objectives To create reference values representative of normal findings at two dimensional (2D) and three-dimensional (3D) transvaginal ultrasound examination of the cervix from 17 to 41 gestational weeks (gws), and to determine the agreement between cervical measurements taken by 2D and 3D transvaginal ultrasound.

Methods Cross-sectional study covering 17 to 41 gws in 419 nulliparae and 360 multiparae who delivered at term and underwent 2D and 3D transvaginal ultrasound examination of the uterine cervix. We examined approximately 25 women in each gestational week. The length, anterior-posterior (AP) diameter and width of the cervix and of any cervical funnel, and the AP diameter of the cervical canal were measured. Results were plotted against gestational age. The agreement between 2D and 3D ultrasound results was expressed as the mean (± 2SD) difference between the results of the two methods and as inter-class correlation coefficient (inter-CC).

Results There was excellent agreement between measurements taken by 2D and 3D ultrasound (Inter-CC values 0.80 − 0.98), but measurements of cervical length taken using 3D ultrasound were greater than measurements taken by 2D ultrasound (mean difference –0.04cm ± 0.36). Below 3D measurements are presented. Cervical length did not change substantially between 17 and 32 gws but decreased progressively thereafter. There was no difference in cervical length between nulliparae and multiparae $\leq$ 32 gws, but from 33 gws the cervix was longer in multiparae. Median cervical length decreased from 3.8 cm (range 0.7 − 6.1) at 17 – 32 gws to 2.3 cm (range 0.4 − 6.0) at 33 – 40 gws in nulliparae and 3.0 cm (range 0.4 − 5.7) in multiparae and to 0.7 cm (range 0.2 − 1.5) at 41 gws in nulliparae and 0.8 cm (range 0.4 − 0.8) in multiparae. Cervical AP diameter and width did not differ between nulliparae and multiparae. Median AP diameter increased from 3.0 cm (range 2.0 − 4.6) at 17 − 30 gws to

3.5 cm (range 1.8 − 5.5) at 31 – 40 gws and to 4.0 cm (range 2.8 − 5.9) at 41 gws. Cervical width was 3.7 cm (range 2.3 − 6.0) at 17 − 30 gws and 4.5 cm (range 2.3 − 6.1) at 31 − 41 gws. The percentage of women with funneling increased from 4% (3/84) at 17 − 18 gws to 63% (12/19) at 41 gws and the percentage of women with an open cervical canal from 19% (15/84) to 72% (13/19). Funneling and opening of the cervical canal were equally common in nulliparae and multiparae.

Conclusion Reference data lay the basis for studies of pathological conditions. Common reference values for nulliparae and multiparae can be used for cervical AP diameter and width from 17 to 41 gws and for cervical length from 17 to 32 gws. Separate reference values for cervical length for nulliparae and multiparae should be used from 33 to 41 gws.

Introduction

Transvaginal ultrasound has been advocated as a good method to assess the uterine cervix and lower uterine segment[1]. Measurement of cervical length and anterior-posterior (AP) diameter and assessment of the inner cervical os by two-dimensional (2D) transvaginal ultrasound has been suggested as a method to predict preterm[2,4], term or post-term delivery[5,6], and outcome of labor induction[7,8].

Three-dimensional (3D) ultrasound imaging is now available for clinical use. With 3D ultrasound a volume of data is acquired and stored. The stored data can be reformatted and analyzed in an infinite number of planes. 3D ultrasound offers a unique possibility to show true coronal and mid-sagittal planes by direct correlation of the views in a multiplanar display. 3D transvaginal ultrasound has been used to measure the cervix in women at risk of preterm delivery[9-11].

Reference values for cervical length as measured by 2D ultrasound in pregnancy have been published[12-20]. The published studies cover different periods of gestation, have different design, and the study populations are mixed and/or small. There are only a few studies where reference values for cervical AP diameter[12,15,17,18] are presented, but to the best of our knowledge no reference values for cervical funneling have been published. In three small studies cervical length[9,10,21] and funneling[9,10] were assessed by 3D ultrasound. However, there are no ultrasound studies presenting reference values for all cervical dimensions i.e., cervical length, AP diameter and width, and size of cervical funnel as assessed either by 2D or 3D ultrasound.

The aim of this study was to establish reference data representative of normal findings at 2D and 3D transvaginal ultrasound examination of the cervix during the second half of pregnancy and to determine the agreement between cervical measurements taken by 2D and 3D ultrasound.

Subjects and methods

The study protocol was approved by the Ethics Committee of the Medical Faculty of Lund University, Sweden. Informed consent was obtained from all participants, after the nature of the procedures had been fully explained.

At our institution all pregnant women are offered one routine ultrasound examination at 18 gestational weeks (gws) and another at 32 gws. Consecutive women coming for a routine scan were asked to participate in this study, i.e., to undergo a transvaginal 2D and 3D ultrasound examination of the cervix once in a predefined gestational week. Inclusion criteria were: singleton pregnancy, gestational age determined by ultrasound fetometry at 12 – 20 gws, live fetus, intact membranes, not in labor and no vaginal bleeding at the time of the ultrasound examination of the cervix, and no previous cone biopsy. The exclusion criterion was spontaneous delivery ≤ 37 gws.

The equipment used was a GE Voluson 730 ultrasound system (General Electrics, Zipf, Austria) equipped with a 2.8 − 10 MHz transvaginal transducer. The field of view was 146°. All women underwent 2D and 3D transvaginal ultrasound examination of the cervix by the first author as described below. The women were examined in the lithotomy position with an empty bladder. The ultrasound probe was slowly introduced into the vagina and care was taken to avoid exerting undue pressure, which may artificially lengthen the cervix. After a satisfactory image of the cervix had been obtained, the probe was withdrawn until the image became blurred. Then the probe was gradually advanced with only enough pressure to restore a satisfactory image. Neither fundal nor suprapubic pressure was applied. A sagittal view of the cervix was obtained where the internal os, the cervical canal and the external os were all visible simultaneously. The image was magnified so that the cervix occupied approximately 75% of the screen. A standardized measurement technique was used. Cervical length was measured from the outer to the inner cervical os, care being taken to include only that segment of the cervical canal that was bordered by the endocervical mucosa [22]. Cervical AP diameter was measured in the same plane as cervical length at the midpoint between the inner and outer cervical os and perpendicular to the longitudinal axis of the cervical canal as previously described[23]. The internal cervical os was described as being closed or open, any opening being called funneling. The length and AP diameter of any funnel were measured as described in a previous publication[23]. An open cervical canal was seen as an anechoic space extending from the internal to the external cervical os. Its AP diameter was measured where it appeared to be at its widest perpendicularly to the longitudinal axis of the cervical canal. All 2D ultrasound measurements were repeated three times, and the mean of the three measurements was used for statistical analysis. Cervical width and cervical funnel width were not measured by 2D ultrasound. The duration of the 2D examinations was approximately 4 min.

After having completed the 2D ultrasound examination, the system was switched into the 3D mode. A sagittal view of the cervix was centralized within the 3D sector appearing on the ultrasound screen. Then the system was switched into the power Doppler mode and an ultrasound volume containing the cervix was acquired by holding the transducer stationary while its crystals were mechanically rotated across the sector with a sweep angle of 90°**.** The original plane of the cervical volume acquisition was the sagittal plane. The acquired volumes were stored on the hard disk of the ultrasound system for later analysis off-line. The following measurements were taken using `any-plane` slicing of the volume acquired: length, AP diameter and width of the cervix and of any cervical funneling and the AP diameter of the cervical canal (Figure 1). The measurements were taken from 3D power Doppler volumes, because power Doppler blood flow indices were used for another study.

Statistical analysis

All measurement results were plotted against gestational age. The statistical significance of differences in continuous data was determined using Mann-Whitney's test or

Kruskall-Wallis test as appropriate. Correlation was determined using Spearman Rank Correlation test. To determine the agreement between cervical measurements obtained by 2D and 3D ultrasound limits of agreement (i.e., mean difference in measurement results ± 2 SD)[24,25] and interclass correlation coefficients (Inter-CC)[26] were calculated. Systematic bias between 2D and 3D ultrasound measurements was determined by calculating the 95% confidence interval of the mean difference (mean difference ± 2 standard errors; SE). If zero lay within this interval no systematic bias was assumed to exist between the two methods. Agreement for categorical data was expressed as Cohen's kappa[27] value. Two tailed p-values are given. Bonferroni correction was used to correct for multiple testing. Statistical calculations were performed using StatView®, version 5 (SAS Institute Inc., USA, 1999) and the Statistical Package for the Social Sciences software (SPSS, version 12.0, Chicago, IL, USA, 2004).

Results

Eight hundred and twenty women agreed to participate and underwent a 2D and 3D transvaginal ultrasound examination of the cervix. Forty-one delivered before 37 gws and were excluded. Our study population includes 419 nulliparae and 360 multiparae, each woman contributing the results of one ultrasound examination to the study. Mean age was 31 years ± 4.2 (SD; standard deviation) and mean body mass index in the first trimester was 25.0 kg/m^2 ± 4.87.

Changes in cervical length, AP diameter and width with advancing gestation are shown in Figures 2-6. Cervical length did not change substantially between 17 and 32 gws and was similar in nulliparae and multiparae. After 32 gws cervical length decreased in both nulliparae and multiparae, but the cervix tended to be substantially longer in multiparae from 33 to 41gws (Figures 2 and 3).

Cervical AP diameter was similar in nulliparae and multiparae and seemed to increase stepwise during pregnancy: unchanged AP diameter from 17 to 30 gws, slightly greater diameter at 31 – 40 gws, and greatest diameter at 41 gws ($p < 0.001$), see Figures 4 and 5.

Cervical width did not differ between nulliparae and multiparae and seemed to increase stepwise during pregnancy. Cervical width was similar from 17 to 30 gws and greater at 31 – 41 gws ($p < 0.0001$), see Figure 6.

Reference values for cervical length, AP diameter and width as measured by 2D and 3D ultrasound are shown in Table 1.

The percentage of women with cervical funneling increased from 17 to 41 gws (Figures 7 and 8). Cervical funneling was equally common in nulliparae and multiparae, 22% (91/419) of nulliparae and 25% (89/360) of multiparae having cervical funneling according to 2D ultrasound and 22% (91/419) of nulliparae and 22% (80/360) of multiparae having cervical funneling according to 3D ultrasound. There was no statistically significant difference in funnel size between multiparae and nulliparae at any gestational age, but funnel size (mean of length and AP diameter for 2D measurements, mean of length, AP diameter and width for 3D measurements) tended to increase slightly with gestational age (correlation between funnel size as measured by 2D ultrasound and gestational age: Rho = 0.18, $p = 0.018$; correlation between funnel size as measured by 3D ultrasound and gestational age: Rho = 0.26, $p < 0.001$). The correlation between funnel width and gestational age was stronger (Rho 0.36, $p < 0.0001$) than that between funnel AP diameter or funnel length and gestational age (Rho 0.15, $p < 0.056$ and Rho 0.14, $p < 0.062$) as measured by 3D ultrasound. Results for funnel size are shown in Table 1.

The proportion of women with an open cervical canal increased with advancing gestation and was similar in nulliparae and multiparae (Figures 9 and 10). Median cervical canal AP diameter as measured both by 2D and 3D ultrasound was 0.2 cm (range 0.1 – 0.8;

10th percentile 0.1, 90th percentile 0.3). The AP diameter of the cervical canal increased slightly with gestational age (Rho = 0.16, p = 0.009, same result for 2D and 3D ultrasound).

The agreement between results of 2D and 3D ultrasound measurements of the cervix was excellent (Table 2), but cervical length measured by 3D ultrasound was greater than cervical length measured by 2D ultrasound.

Discussion

We found cervical length to change very little and not to differ between nulliparae and multiparae between 17 and 32 gws. After 32 gws the cervix shorted but was longer in multiparae than in nulliparae. Thus, it seems justified to use common reference values for cervical length for nulliparae and multiparae from 17 to 32 gws. After 32 gws we would recommend separate reference values for nulliparae and multiparae and separate reference values depending on pregnancy week. Our results with regard to cervical length agree with those reported by Tongsong et al[16] and Brieger et al[15]. Tongsong et al[16] found cervical length not to change substantially between 8 and 31 gws whereafter it decreased. Brieger et al[15] reported decreasing cervical length from 30 gws. Results of other studies are more variable: some found cervical length not to change during pregnancy[12], others found a continuous decrease from 10 to 40gws[13] or from 17 to 37gws[20], others[14] reported that the cervix became longer between 8 and 25 gws and then shortened. In most studies cervical length did not differ between nulliparae and mulltiparae[13,14,20,28,29], in some the cervix was longer in multiparae[17,18]. The discrepant results may be explained by differences in measurement technique, study design, the period in gestation studied, the statistical methods used, and the interpretation of the results. For example, in some studies[13,15,16,19,20,28] a correlation coefficient was used to describe changes in cervical length with gestational age. Only Gramellini et al[13], Murakawa H et al[20] and Brieger et al[15] reported a strong or moderate negative correlation between cervical length and gestational age (r = 0.92, $p < 0.001$, r = 0.4, $p < 0.001$, and r = 0.6, $p < 0.001$), in the other studies [16,19,28] the negative correlation was weak.

In all studies where cervical AP diameter was measured and compared between nulliparae and multiparae it tended to be larger in multiparae[17,18], and in all studies AP diameter increased with gestational age[12,15,17,18]. This is in agreement with our results. The larger cervical AP diameter in multiparae is possibly to be explained by changes in the cervix caused by delivery and then persisting into the next pregnancy. Cervical AP diameter was largest at 41 gws. It is reasonable to believe that women examined at 41gws were closer to delivery than those examined at 37 – 40 gws. The large AP diameter at 41gws might therefore be explained by increasing distension of the lower uterine segment shortly before onset of labor.

Cervical width as measured by 3D ultrasound did not change substantially between 17 and 30 gws, then the cervix became broader. Cervical width did not differ between nulliparae and multiparae. To the best of our knowledge there are no other studies reporting reference values for sonographic cervical width during pregnancy.

In our study funneling was found in 22% of nulliparae and in 24% of multiparae from 17 to 41 gws and was seen as early as at 18 gws. This is similar to the results of Hasegawa and co-workers[28]. They reported that 20% of pregnant women (both nulliparae and multiparae) delivering at term had an open inner cervical os between 15 and 34 gestational weeks. However, funneling at 18 gws was more common in our study (4%) than in a study by Taipale and Hiilesmaa[3] (0.4%). The disagreement might be explained by differences in definition of funneling: we defined funneling as any opening of the inner cervical os, whereas Taipale and Hiilesmaa[3] defined it as a protrusion of the amniotic membranes 3 mm or more into the cervical canal.

An opening of the cervical canal up to 2 mm in diameter was suggested by Cook et al[18] to be a normal finding during pregnancy. We found the cervical canal to be visible at ultrasound examination as early as 17 gws - both in nulliparae and multiparae - but the proportion of women with an open cervical canal increased with advancing gestation up to 70% at 41gws. To the best of our knowledge there are no other studies reporting reference values for sonographic cervical canal diameter during pregnancy.

There was good agreement between measurements taken by 2D and 3D ultrasound. Only cervical length differed systematically between the two methods, measurements of cervical length obtained by 3D ultrasound being greater than those obtained by 2D ultrasound. However, the difference was so small that we believe it to be clinically unimportant. Towner et al[21] also found that cervical length measurements taken by 3D ultrasound were greater than those taken by 2D ultrasound, but their differences were larger than ours (mean 8.0 mm vs. -0.4 mm). The reason for this discrepancy is unclear.

Because the correlation between funnel width and gestational age was stronger than that between funnel AP diameter or funnel length and gestational age, it is possible that measurement of the width of a funnel might be a more useful indicator of cervical ripeness than funnel length or funnel AP diameter.

To sum up, we have created reference values for sonographic cervical measurements in asymptomatic pregnant women who deliver at term. These values can be used as normative guidelines when assessing cervical dimensions by ultrasound during the second half of pregnancy.

Acknowledgments

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References

1. Sonek JD, Iams JD, Blumenfeld M, Johnson F, Landon M, Gabbe S. Measurement of cervical length in pregnancy: comparison between vaginal ultrasonography and digital examination. *Obstet Gynecol* 1990; **76**: 172- 175.

2. Heath VCF, Southall TR, Souka AP, Elisseou A, Nicolaides KH. Cervical length at 23 weeks of gestation: prediction of spontaneous preterm delivery. *Ultrasound Obstet Gynecol* 1998; **12**: 312-317.

3. Taipale P, Hiilesmaa V. Sonographic measurement of uterine cervix at 18-22 weeks gestation and the risk of preterm delivery. *Obstet Gynecol* 1998; **92**: 902-907.

4. To MS, Skentou C, Liao AW, Cacho A, Nicolaides KH. Cervical length and funneling at 23 weeks of gestation in the prediction of spontaneous early preterm delivery. *Ultrasound Obstet Gynecol* 2001; **18**: 200-203.

5. Rozenberg P, Goffinet F, Hessabi M. Comparson of the Bishop score, ultrasonographically measured cervical length, and fibronectin assay in predicting time until delivery and type of delivery at term. *Am J Obstet Gynecol* 2000; **182**: 108-113.

6. Ramanathan G, Yu C, Osei E, Nicolaides KH. Ultrasound examination at 37 weeks` gestation in the prediction of pregnancy outcome: the value of cervical assessment. *Ultrasound Obstet Gynecol* 2003; **22**: 598-603.

7. Rovas L, Sladkevicius P, Strobel E, Valentin L. Three-dimensional power Doppler ultrasound assessment of the cervix for prediction of successful induction of labor with prostaglandin in prolonged pregnancy. *J Ultrasound Med;* in press. *2005.*

8. Rane SM, Guirgis RR, Higgins B, Nicolaides KH. The value of ultrasound in the prediction of successful induction of labor. *Ultrasound Obstet Gynecol* 2004; **24**: 538-549.

9. Bega G, Lev-Toaff A, Kuhlman K, Berghella V, Parker L, Goldberg B, Wapner R. Three-dimensional multiplanar transvaginal ultrasound of the cervix in pregnancy. *Ultrasound Obstet Gynecol* 2000; **16**: 351-358.

10. Severi FM, Bocchi C, Florio P, Picciolini E, D`Aniello G, Petraglia F. Comparison of two-dimensional and three-dimensional ultrasound in the assessment of the cervix to predict preterm delivery. *Ultrasound in Med. & Biol* 2003; **9**: 1261-1265.

11. Rozenberg P, Rafii A, Senat MV, Dujardin A, RaponJ, Viie Y. Predictive value of two-dimensional and three-dimensional multiplanar ultrasound evaluation of the cervix in preterm labor. *J Matern Fetal Neonatal Med* 2003; **13**: 237-341.

12. Smith CV, Anderson JC, Matomoros A, Rayburn WF. Transvaginal sonography of cervical width and length during pregnancy. *J Ultrasound Med* 1992; **11**: 465-467.

13. Gramellini D, Fieni S, Molina E, Berretta R, Vadora E. Transvaginal sonographic cervical length changes during normal pregnancy. *J Ultrasound Med*. 2002; **21**: 227-32.

14. Kushnir O, Vigil DA, Izquierdo L, Schiff M, Curet LB. Vaginal ultrasonographic assessment of cervical length changes during normal pregnancy. *Am J Obstet Gynecol* 1990; **162**: 991-993.

15. Brieger GM, Ning XH, Dawkins RR, Ying KQ, Weng C, Chang AM, Haines CJ. Transvaginal sonographic assessment of cervical dynamics during the third trimester of normal pregnancy. *Acta Obstet Gynecol Scand* 1997; **76**: 118-22.

16. Tongsong T, Kamprapanth P, Pitaksakorn J. Cervical length in normal pregnancy as measured by transvaginal sonography. *Int J Gynaecol Obstet* 1997; **58**: 313-315.

17. Zorzoli A, Soliani A, Perra M, Caravelli E, Galimberti A, Nicolini U. Cervical changes throughout pregnancy as assessed by transvaginal sonography. *Obstet Gynecol* 1994; **84**: 960-964.

18. Cook CM, Ellwood DA. A longitudinal study of the cervix in pregnancy using transvaginal ultrasound. *Br J Obstet Gynaecol* 1996; **103**: 16 -18.

19. Hoesli IM, Strutas D, Tercanli S, Holzgreve W. Charts for cervical length in singleton pregnancy. *Int J Gynaecol Obstet* 2003; **82**: 161-165.

20. Murakawa H, Utumi T, Hasegawa I, Tanaka K, Fuzimori R. Evaluation of threatened preterm delivery by transvaginal ultrasonographic measurement of cervical length. *Obstet Gynecol* 1993; **82**: 829-832.

21. Towner D, Boe N, Lou K, Gilbert WM. Cervical length measurements in pregnancy are longer when measured with three-dimensional transvaginal ultrasound. *J Matern Fetal Neonatal Med* 2004; **16**: 167-170.

22. Sonek J, Shellhass C. Cervical sonography: a review. *Ultrasound Obstet Gynecol* 1998; **11**: 71-78.

23. Bergelin I, Valentin L. Patterns of normal change in cervical length and width during pregnancy in nulliparous women: a prospective, longitudinal ultrasound study. *Ultrasound Obstet Gynecol* 2001; **18**: 217-222.

24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **1**: 307-310.

25. Bland JM, Altman DG. A note on the use of the intraclass correlation coefficient in the evaluation of agreement between two methods of measurement. *Comput. Biol. Med* 1990; **20**: 337-340.

26. Scherjon SA, Kok JH, Oosting H, Zondervan HA. Intra-observer and inter-observer reliability of the pulsatility index calculated from pulsed Doppler flow velocity waveforms in three fetal vessels. *Br J Obstet Gynaecol* 1993; **100**: 134-138.

27. Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Measurem* 1960; **20**: 37-46.

28. Hasegawa I, Tanaka K, Takahashi K, Tanaka T, Aoki K, Torii Y, Okai T, Saji F, Takahashi T, Sato K, Fujimura M, Ogawa Y. Transvaginal ultrasonographic cervical assessment for the prediction of preterm delivery. *J Matern Fetal Med* 1996; **5**: 305-309.

29. Andersen HF. Transvaginal and transabdominal ultrasonography of the uterine cervix during pregnancy. *J Clin Ultrasound* 1991; **19**: 77-83.

Legends

Figure 1 Ultrasound images showing cervical measurements taken by two-dimensional ultrasound (images a and b) and by three-dimensional ultrasound (images c and d) a) Cervical length – A, cervical anterior-posterior diameter – B, length of cervical funneling – C, anterior-posterior diameter of funnel – D b) Cervical canal. Anterior-posterior diameter of the cervical canal was measured where it appeared to be at its widest, the measurements being taken perpendicularly to the longitudinal axis of the canal c) Cervical width d) Width of funnel.

Figure 2 Relationship between cervical length as measured by two-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae. Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 3 Relationship between cervical length as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae. Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 4 Relationship between cervical anterior-posterior diameter as measured by two-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 5 Relationship between cervical anterior-posterior diameter as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Filled boxes represent the cervical length of multiparae, open boxes represent that of nulliparae Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 6 Relationship between cervical width as measured by three-dimensional ultrasound and gestational age in completed gestational weeks (gws). Boxes represent the cervical width of both multiparae and nulliparae. Median, 10^{th}, 25^{th}, 75^{th} and 90^{th} percentiles are shown. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 7 Percentage of women with cervical funneling according to two-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.005/13), signifies a statistically significant difference.

Figure 8 Percentage of women with cervical funneling according to three-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 9 Percentage of women with an open cervical canal according to two-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure 10 Percentage of women with an open cervical canal according to three-dimensional ultrasound examination in relation to gestational age in completed gestational weeks (gws). Filled boxes represent multiparae, and open boxes represent nulliparae. No., number of women; p-values refer to comparison between nulliparae and multiparae. Using Bonferroni correction a p-value < 0.0038 (0.05/13), signifies a statistically significant difference.

Figure1

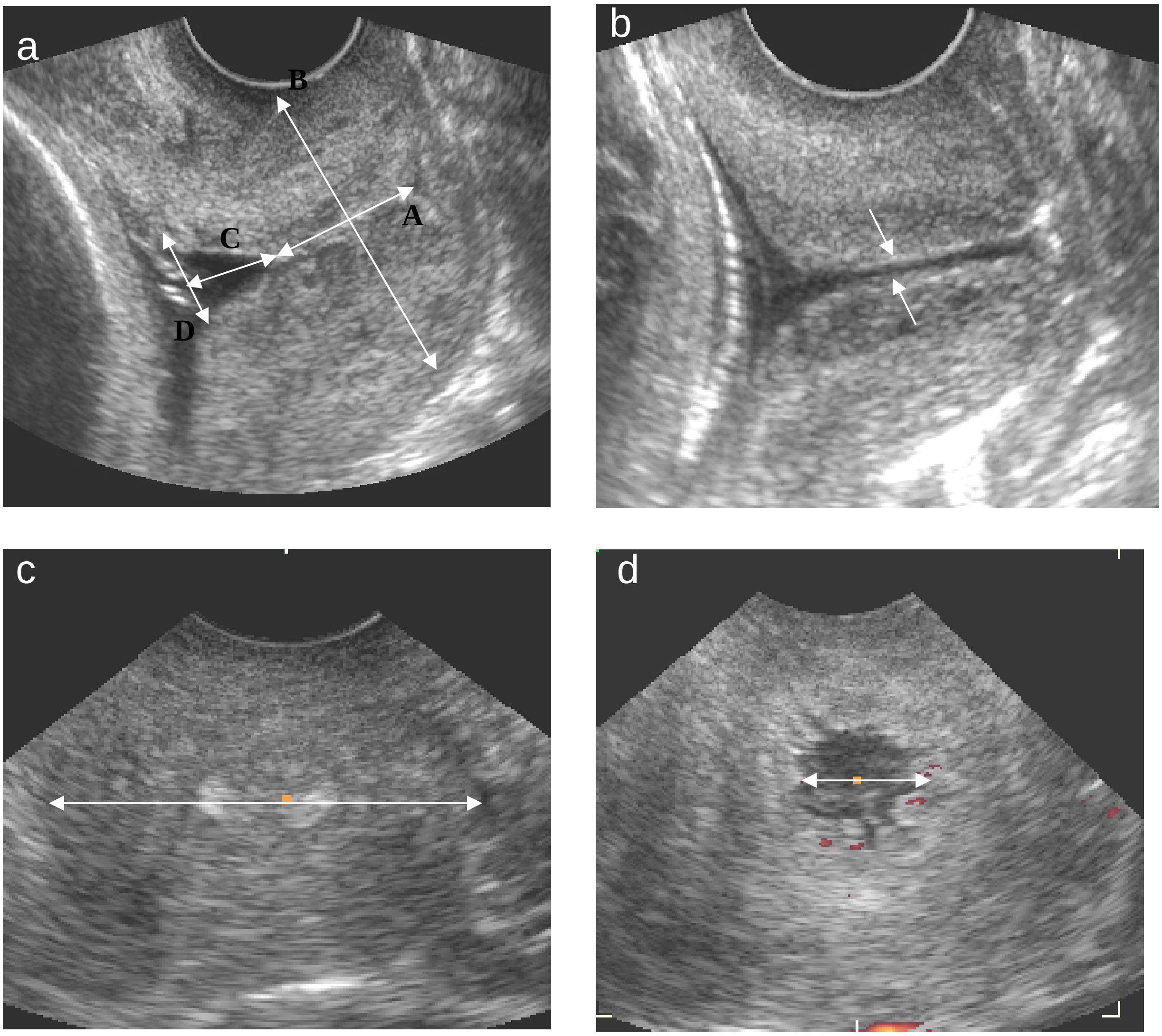
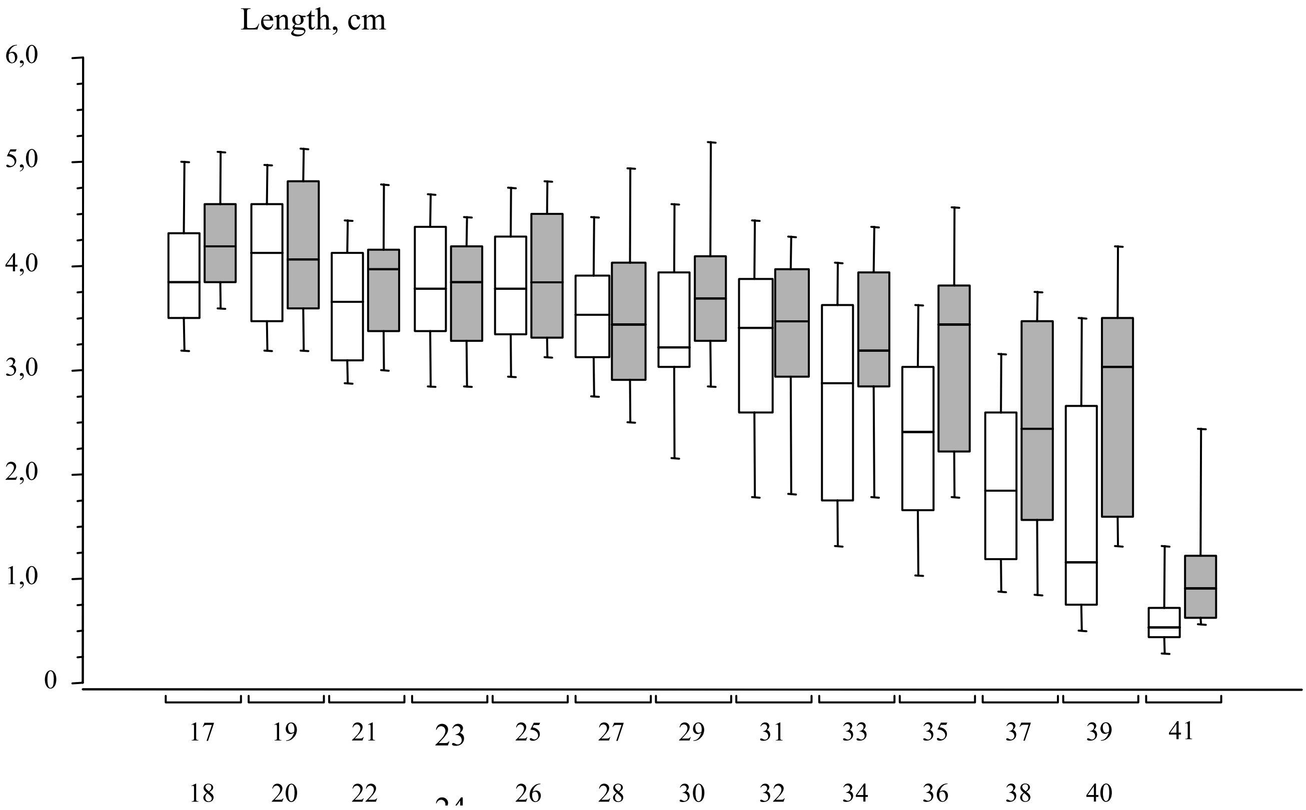
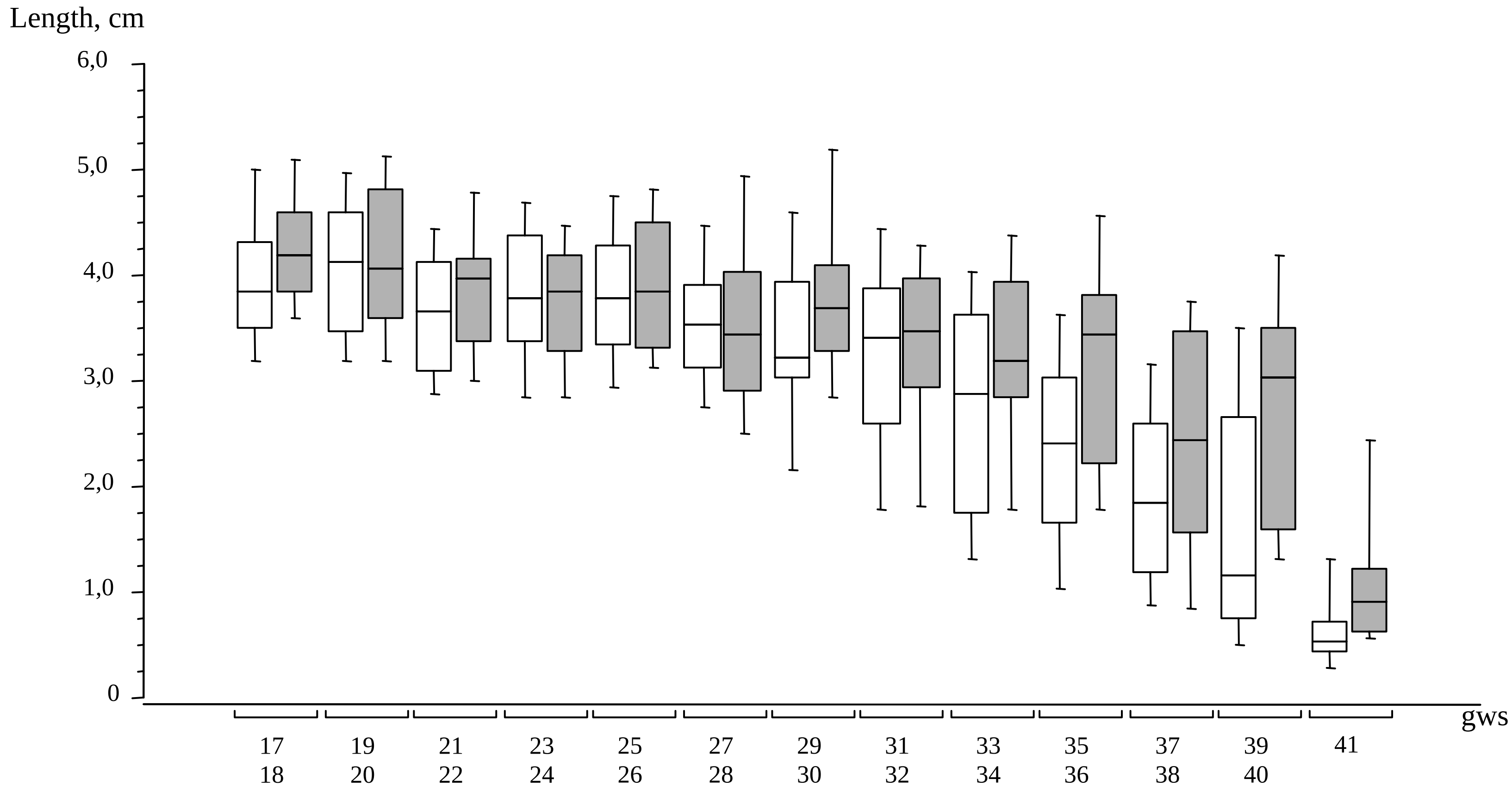


Figure 2



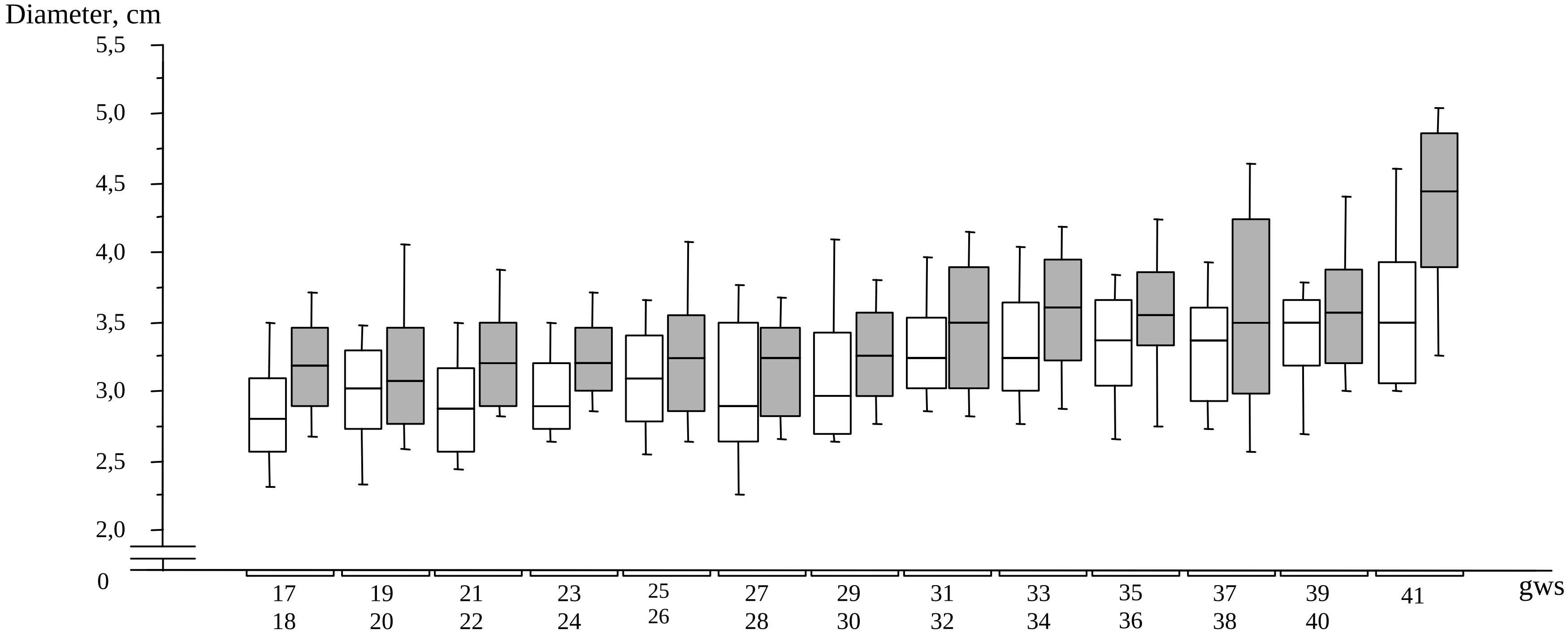
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.095	0.593	0.223	0.733	0.464	0.706	0.146	0.485	0.081	0.001	0.009	0.003	0.140

Figure 3



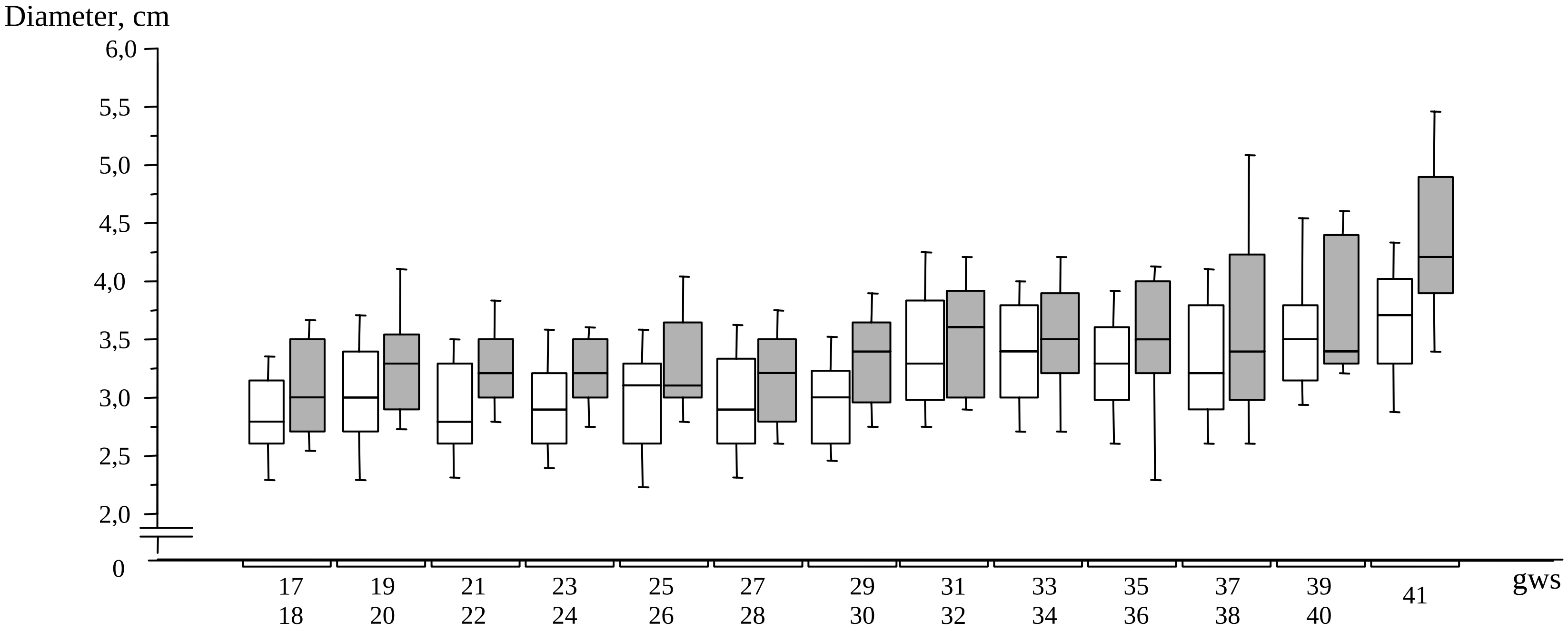
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.124	0.227	0.368	0.795	0.331	0.187	0.155	0.485	0.049	0.001	0.007	0.005	0.185

Figure 4



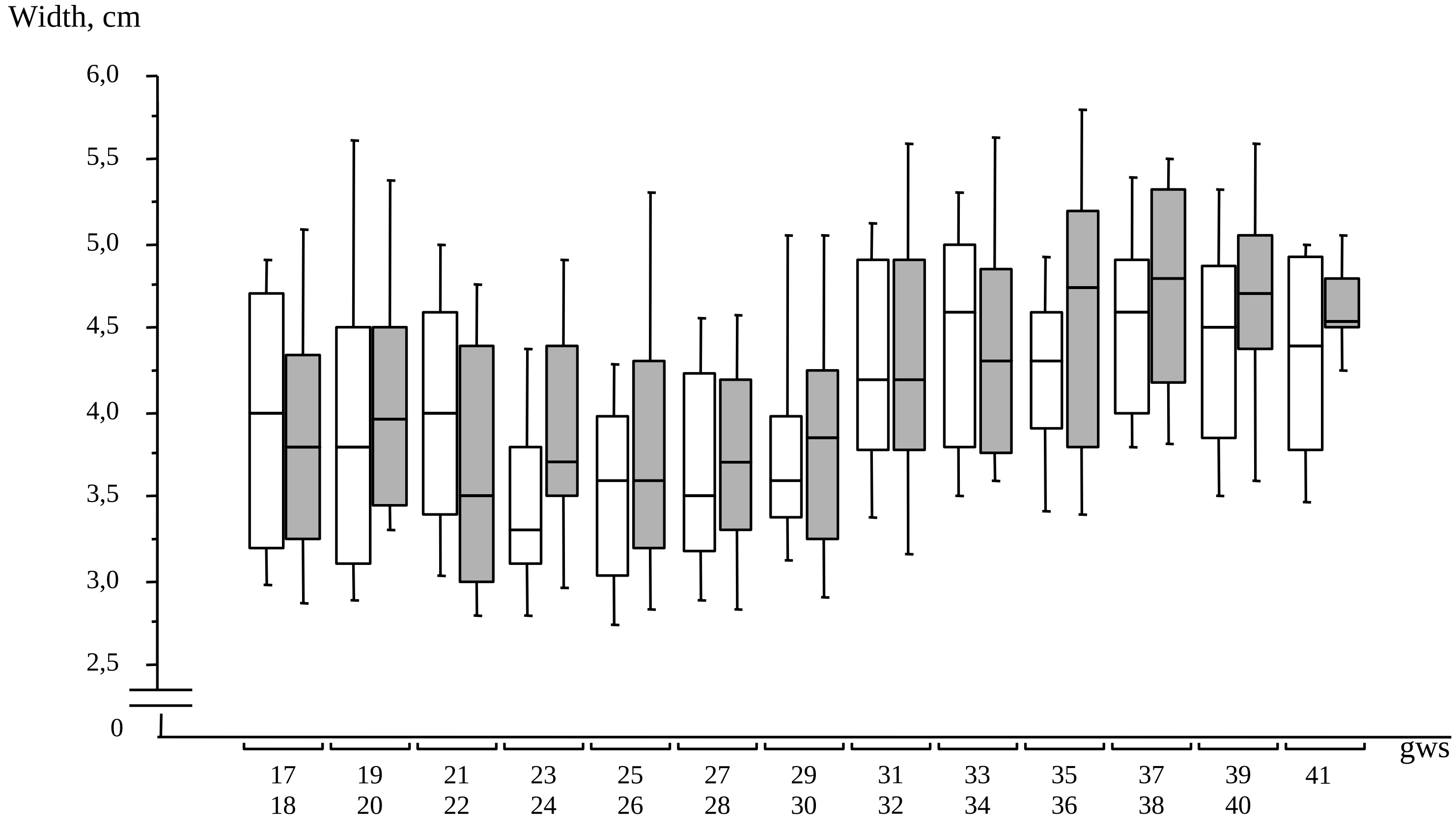
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.001	0.129	0.004	0.002	0.245	0.309	0.357	0.214	0.080	0.068	0.025	0.054	0.034

Figure 5



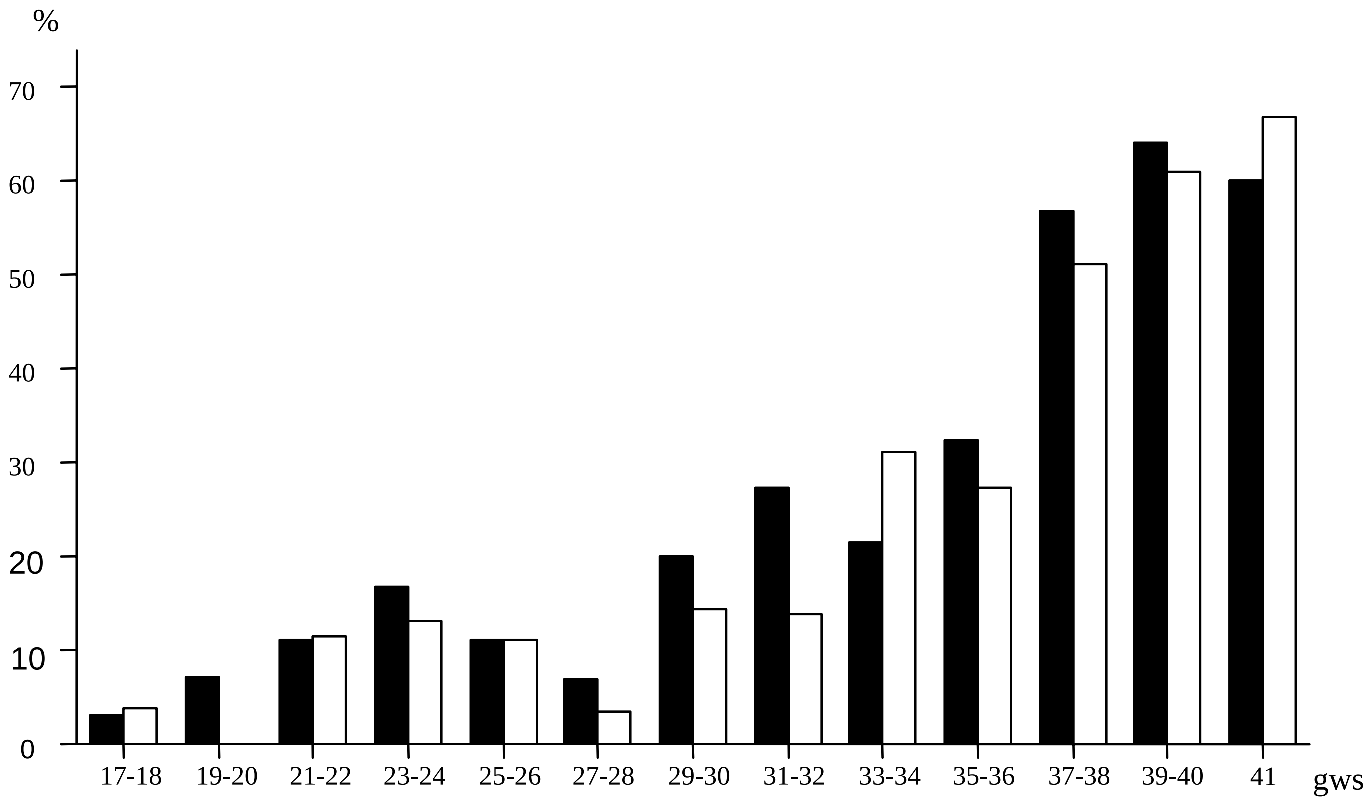
No nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.072	0.039	0.013	0.002	0.024	0.138	0.016	0.582	0.343	0.267	0.079	0.491	0.044

Figure 6



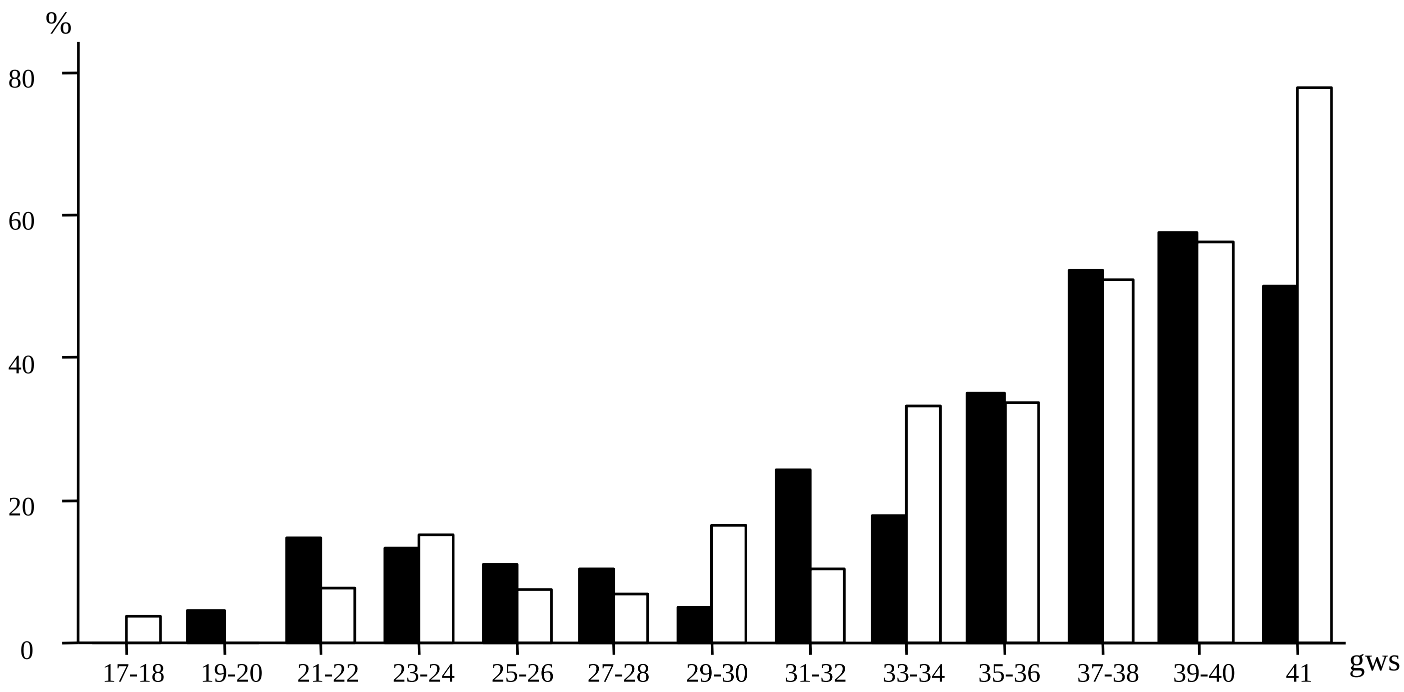
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.658	0.377	0.145	0.015	0.199	0.512	0.804	0.789	0.815	0.067	0.290	0.166	0.154

Figure 7



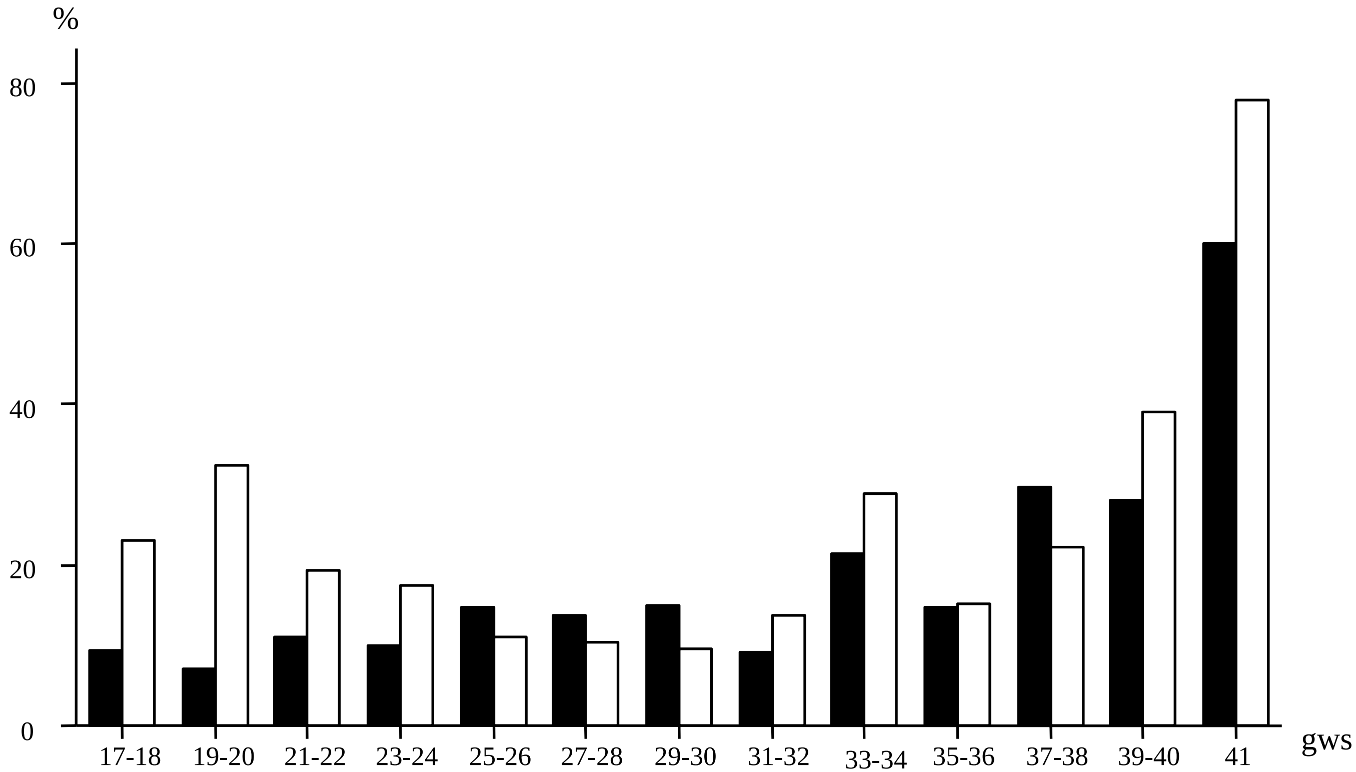
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.861	0.112	0.964	0.661	0.968	0.551	0.633	0.194	0.374	0.652	0.611	0.824	0.762

Figure 8



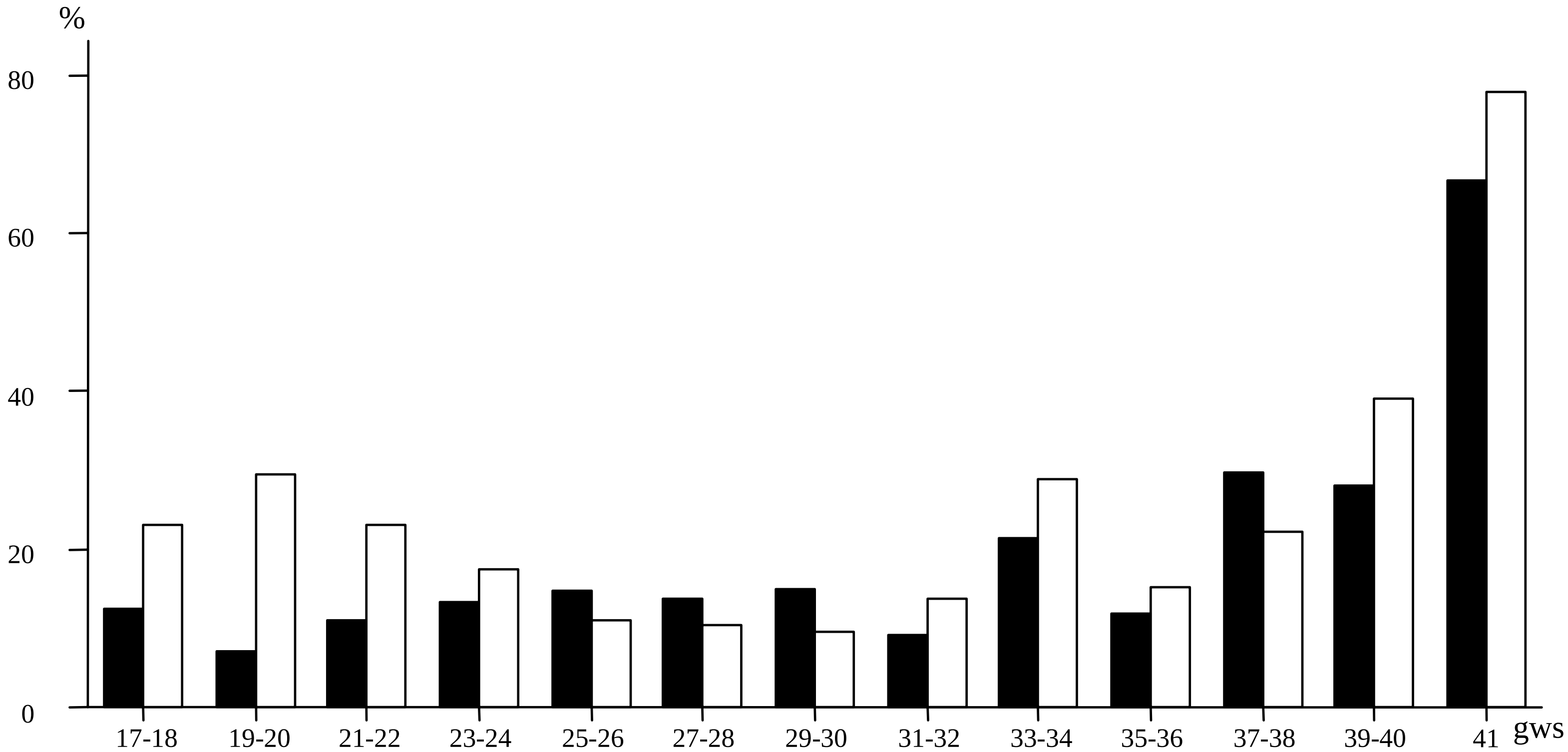
No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.261	0.274	0.411	0.822	0.641	0.642	0.631	0.151	0.153	0.821	0.674	0.753	0.212

Figure 9



No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.111	0.015	0.409	0.371	0.685	0.686	0.591	0.559	0.476	0.959	0.438	0.414	0.405

Figure 10



No. nulliparae	52	34	26	46	27	29	21	29	45	33	45	23	9
No. multiparae	32	28	27	30	27	29	20	33	28	34	37	25	10
p-value	0.231	0.027	0.246	0.632	0.685	0.686	0.592	0.559	0.476	0.684	0.438	0.414	0.598

Table 1 Reference values for cervical parameters assessed by two-dimensional and three-dimensional ultrasound

	2D ultrasound			3D ultrasound		
	All	Nulliparae	Multiparae	All	Nulliparae	Multiparae
Cervical length (cm)						
17 – 32 gws						
median	3.8			3.8		
range	0.7 – 6.0			0.7 – 6.1		
10th, 90th percentiles	2.8 – 4.7			2.8 – 4.7		
33 – 34 gws						
median		2.9	3.2		3.0	3.3
range		0.7 – 5.8	1.3 – 5.0		0.6 – 6.0	1.4 – 4.6
10th, 90th percentiles		1.3,4.1	1.8, 4.4		1.0 – 4.1	2.4 – 4.4
35 – 36 gws						
median		2.4	3.4		2.1	3.3
range		0.9 – 4.2	1.1 – 6.0		0.8 – 4.0	1.4 – 5.7
10th, 90th percentiles		1.0, 3.6	1.8, 4.6		1.1 – 3.6	1.9 – 4.5
37 – 38 gws						
median		1.8	2.4		2.2	2.8
range		0.4 – 4.1	0.6 – 4.9		0.6 – 3.7	0.5 – 5.0
10th, 90th percentiles		0.9, 3.2	0.8, 3.8		1.0 – 3.3	1.4 – 4.0
39 – 40 gws						
median		1.2	3.0		1.3	3.0
range		0.3 – 4.3	0.7 – 4.4		0.4 – 4.5	0.6 – 4.8
10th, 90th percentiles		0.5, 3.5	1.3, 4.2		0.7 – 3.5	1.5 – 3.9
41 gws						
median		0.5	0.9		0.7	0.8
range		0.2 – 1.6	0.5 – 3.5		0.2 – 1.5	0.4 – 3.4
10th, 90th percentiles		0.3, 1.3	0.6, 2.4		0.3 – 1.3	0.5 – 2.7

cont.

Table 1 Continued

	2D ultrasound			3D ultrasound		
	All	Nulliparae	Multiparae	All	Nulliparae	Multiparae
Cervical AP diameter						
17 – 30 gws						
median	3.0			3.0		
range	2.0 – 4.9			2.0 – 4.6		
10^{th}, 90^{th} percentiles	2.5, 3.6			2.4, 3.7		
31 – 40 gws						
median	3.5			3.5		
range	1.9 – 5.2			1.8 – 5.5		
10^{th}, 90^{th} percentiles	2.7, 4.1			2.7, 4.2		
41 gws						
median	3.9			4.0		
range	2.9 – 5.1			2.8 – 5.9		
10^{th}, 90^{th} percentiles	3.0, 5.0			3.0, 4.9		
Cervical width						
17 – 30 gws						
median				3.7		
range				2.3 – 6.0		
10^{th}, 90^{th} percentiles				2.9 – 4.9		
31 – 41 gws						
median				4.5		
range				2.3 – 6.1		
10^{th}, 90^{th} percentiles				3.5 – 5.5		

cont.

Table 1 Continued

	2D ultrasound			3D ultrasound		
	All	Nulliparae	Multiparae	All	Nulliparae	Multiparae
Cervical funnel length	*n = 180*			*n = 171*		
17 – 41 gws						
median	0.6			0.6		
range	0.2 – 3.0			0.2 – 2.3		
10th, 90th percentiles	0.4, 1.3			0.3, 1.5		
Cervical funnel AP diameter	*n = 180*			*n = 171*		
17 – 41 gws						
median	0.8			0.8		
range	0.3 – 2.4			0.3 – 2.8		
10th, 90th percentiles	0.5, 1.5			0.4, 1.6		
Cervical funnel width				*n = 171*		
17 – 41 gws						
median				1.0		
range				0.3 – 3.2		
10th, 90th percentiles				0.6, 2.0		

gws, gestational weeks; AP, anterior-posterior diameter.

Table 2 Differences between the two-dimensional and three-dimensional ultrasound measurements of the cervix

	Inter - method difference in cm				
	Mean	95% CI	Limits of agreement	Inter-CC	Kappa
Cervical length	-0.044	-0.070 – (-) 0.018	-0.754 – 0.666	0.98	
Cervical AP diameter	-0.007	-0.033 – 0.019	-0.717 – 0.703	0.90	
Funnel length	0.027	-0.017 – 0.071	-0.519 – 0.573	0.89	
Funnel AP diameter	-0.023	-0.083 – 0.037	-0.783 – 0.737	0.80	
AP diameter of cervical canal	- 0.001	-0.007 – 0.005	-0.075 – 0.073	0.96	
Presence of funnel					0.93

CI, confidence interval; Inter-CC, inter-class correlation coefficient; AP, anterior-posterior.