

Defining the “normal uterus” by ultrasound measurement of uterine lengths, thicknesses, and angles in a population of nulliparous women: the Normal UteRus asSEssment study

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Objective: The existing classifications of congenital uterine anomalies are inconsistent and subject to criticism for various reasons. Noteworthy, there is still no universally accepted definition of normal uterus (NU) based on ultrasound measurements, making it difficult to objectively distinguish the uterine anatomical variants within the population. The purpose of the Normal UteRus asSEssment study was to define the exact three-dimensional (3D) ultrasound measurements of an NU, in terms of uterine lengths, thicknesses, and angles.

Design: This multicenter, prospective cohort study was conducted between January 2021 and May 2024 at 15 European gynecology centers.

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Data regarding any of the subjects in the study has not been previously published unless specified.

Data will be made available to the editors of the journal for review or query upon request.

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Subjects: Women aged 18 to 35 years, nulliparous, with regular menstrual cycles, with no previous attempts to conceive and no known diagnosis of uterine anomalies were considered eligible. Furthermore, they were referred to gynecology units either for routine gynecological evaluation or for gynecological complaints unrelated to fertility.

Exposures: All enrolled patients underwent two-dimensional and 3D transvaginal ultrasound during the proliferative phase of the menstrual cycle (days 11–14). Uterine measurements were obtained in two-dimensional on the mid-sagittal plane and in 3D on a standardized coronal plane, using the interstitial portions of the fallopian tubes as landmarks and ensuring optimal visualization of the uterine isthmus.

Main Outcome Measures: Multiple uterine lengths, thicknesses, and angles were evaluated, expressing their distribution in percentiles. Interrater and intrarater agreements were assessed using the Intraclass Correlation Coefficient.

Results: A total of 442 nulliparous women with a mean age of 25.7 (SD: 4.27) years were enrolled. Key measures obtained included a median fundal indentation of 1.7 mm, with a 90th percentile of 4.8 mm; a median interostial-to-outer-contour distance of 9.1 mm; and a median indentation angle of 161.8°. Collectively, the ultrasound measurements enabled the construction of a detailed model of the NU. Measurement values were consistent across all participating centers. Both interrater and intrarater analyses demonstrated high reproducibility of the measurements.

Conclusions: This study provides the first normative reference values for uterine lengths, thicknesses, and angles in a healthy population of nulliparous women, enabling the objective classification of a normal uterus based on measurable anatomical parameters rather than on arbitrarily established criteria. Further validation in larger and more heterogeneous cohorts is warranted to confirm these findings and to enhance their generalizability. (Fertil Steril® 2025;■:■–■. ©2025 by American Society for Reproductive Medicine.)

Key Words: Normal uterus, congenital uterine anomalies, 3D transvaginal ultrasound, septate uterus, T-shaped uterus

In medicine, normal values are defined as the set of parameters used to interpret the results of a patient's tests. Typically, the normal range for a given test is based on the values observed in 95% of an apparently healthy population (1).

When it comes to uterine morphology, the term *normal* is often used in the literature to generically refer to a uterus that is not characterized by specific congenital malformations. Indeed, although over the years all major gynecological scientific societies have attempted to develop classification algorithms that include all known uterine anatomical variants, a precise, technical definition of *normal uterus* (NU) is still lacking.

The first milestone in the classification of Müllerian anomalies was set in 1988 by an American Fertility Society (AFS) committee chaired by Veasy C. Buttram, Jr. (2). The AFS classification has been widely adopted for years, although the morphological criteria for an NU were not specified. Later, in 2005, Oppelt et al. (3) proposed a method for combining female genital malformations, inspired by the Tumor, Node, and Metastasis classification used for cancers, namely Vagina-Cervix-Uterus-Adnexa-associated Malformation. However, an accurate definition of normal uterine shape was still lacking in this system as well (3).

A breakthrough in this field occurred in 2013 with the publication of the European Society of Human Reproduction and Embryology (ESHRE)/European Society for Gynaecological Endoscopy (ESGE) classification (4), which offered the advantage of combining uterine body anomalies with cervical and vaginal anomalies, and introduced the concept of the NU. More specifically, the three new core ESHRE/ESGE classes were U0, the *NU*; U1, the *dysmorphic uterus*; and U2, the *septate uterus* (further subdivided into U2a, *partial*, and U2b, *complete*). Higher classes included more complex anomalies.

Notably, the arcuate uterus, considered a normal uterine variant in both the historical AFS classification (2) and its 2021 update (5), despite being assigned to a separate class,

was eliminated in the ESHRE/ESGE system. Based on this classification (4), an NU is defined as “a uterus having either straight or curved interostial line, but with an internal indentation at the fundal midline not exceeding 50% of the uterine wall thickness”, with no reference to additional specific uterine measurements such as lengths, thicknesses, or angles. In contrast, a uterus is considered septate when it has a “normal uterine outline and an internal indentation at the fundal midline exceeding 50% of the uterine wall thickness” (4).

Shortly after the publication of the ESHRE/ESGE classification, the Congenital Uterine Malformation by Experts group proposed new criteria (6, 7) for the diagnosis of a septate and T-shaped uterus based on three-dimensional (3D) uterine measurements, with the aim of refining the differentiation between normal and abnormal uterus. Herein, the “normality” of the uterus was assessed solely based on indentation depth, indentation angle, and uterine fundal wall thickness, without consideration of any other uterine parameters (6, 7).

Finally, in 2021, an American Society for Reproductive Medicine (ASRM) task force updated the historical AFS classification and established ultrasound cut-off values to differentiate the septate uterus from the normal or arcuate uterus (5). Based on this classification, a septum must measure more than 1 cm in length from the bicornual line to the leading edge of the septum and form an angle of less than 90°. Conversely, if the indentation measures less than 1 cm and the angle is greater than 90°, the uterus is classified as either normal or arcuate. However, even in this case, uterine normality was defined solely by fundal indentation and its angle. Furthermore, the updated ASRM classification does not include a separate category for dysmorphic or T-shaped uteri (5).

As this overview highlights, the available classifications of congenital uterine anomalies appear inconsistent with each other and are subject to criticism for various reasons. For instance, some investigators (8) have raised concerns

about the potential overtreatment of uterine septa when applying the ESHRE/ESGE classification instead of the ASRM criteria. Although these concerns are somewhat understandable, it is equally noteworthy that the cut-off values differentiating normal or arcuate uterus from a septate uterus have been set arbitrarily in all classifications, making any therapeutic strategy unsupported by real-world evidence.

Against this background, the purpose of the Normal UteRus asSEssment (NURSE) study was to define, for the first time, the exact 3D ultrasound parameters of an NU, in terms of uterine lengths, thicknesses, and angles, based on real-world data from a population of nulliparous women.

MATERIALS AND METHODS

Study design

This multicenter, prospective cohort study was conducted between January 2021 and May 2024 at 15 European gynecology centers. The participating centers, selected for their high level of expertise in gynecological ultrasound and reproductive surgery, are listed in Supplemental File 1, available online. This study was conducted and reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (9) and Guidelines for Reporting Reliability and Agreement Studies (10).

Ethics Committee approval and data protection

The Committee for Ethics in Medicine of the Ministry of Health of the Republic of Slovenia granted the Promoter center approval to carry out this study on December 22, 2020, under registration number 0120-388/2020/10. Subsequently, all other participating centers obtained approval from their local, regional, or national ethics committees. All enrolled patients were informed about the study and provided written consent.

Each patient included in the study was pseudonymized using two numbers separated by a dot: the first number indicated the referring center, whereas the second was the consecutive patient enrollment number (e.g., 4.22 means collaborating center 4, 22nd patient enrolled). Data are protected in accordance with Articles 6, 7, 9, and 89 of the General Data Protection Regulation.

Patients

Women aged 18–35 years, nulliparous, with regular menstrual cycles, with no previous attempts to conceive and no known diagnosis of uterine anomalies were considered eligible. Furthermore, they were referred to gynecology units either for routine gynecological evaluation or for gynecological complaints unrelated to fertility. All patients were recruited consecutively at each participating center. Exclusion criteria were nonnulliparous women; prior or new diagnosis of acquired uterine anomalies, such as myomas and adenomyosis; new diagnosis (made by the study team) of congenital uterine anomaly of class U4 or higher, based on the ESHRE/ESGE classification (4); history of uterine surgery; and intrauterine hormonal device or other

ongoing long-term hormonal therapy, such as contraceptive pills.

Transvaginal ultrasound technique

All enrolled patients underwent two-dimensional (2D) and 3D transvaginal ultrasound. Based on the previous experience of Saravelos and Li (11), all ultrasound examinations were performed during the proliferative phase of the menstrual cycle (days 11–14), when the endometrium exhibits a typical trilaminar appearance and the margins between the endometrium and myometrium are clear and sharp. The choice of this narrow time frame within the menstrual cycle for performing ultrasound evaluations aimed to avoid bias related to cyclic endometrial thickness variability. Additionally, the secretory phase was avoided because of the significant increase in interstitial distance and consequent flattening of angles that occur during this phase (11).

Once the mid-endometrial line was displayed in the 2D mid-sagittal projection, volume acquisition was performed with the maximum angle of the region of interest. Patients were asked to hold their breath during volume acquisition to avoid artifacts (3–6). Images and volumes (.vol or .mvl for General Electric [GE] or Samsung ultrasound machines, respectively) were stored to allow subsequent offline examinations, as well as to enable the same or another sonographer to repeat the measurements at least 1 month later (intrarater and interrater agreement).

Uterine measurements in 2D were taken on the mid-sagittal projection, whereas those in 3D were taken on a standardized coronal plane, using the interstitial portions of the fallopian tubes as landmarks and ensuring optimal visualization of the uterine isthmus.

Ultrasounds and subsequent measurements were performed by sonographers with high expertise in the 3D technique (MG, AA, AV, AXH, US, CB, BZ, LM, MA, MH, GJ, AK, LA, SV, FB, TT).

All transvaginal ultrasound evaluations were performed using GE Voluson (GE Healthcare, Zipf, Austria) and Samsung (Samsung Medison Co., Ltd., Seoul, Korea) ultrasound machines.

Ultrasound measurements

Measures were taken as follows:

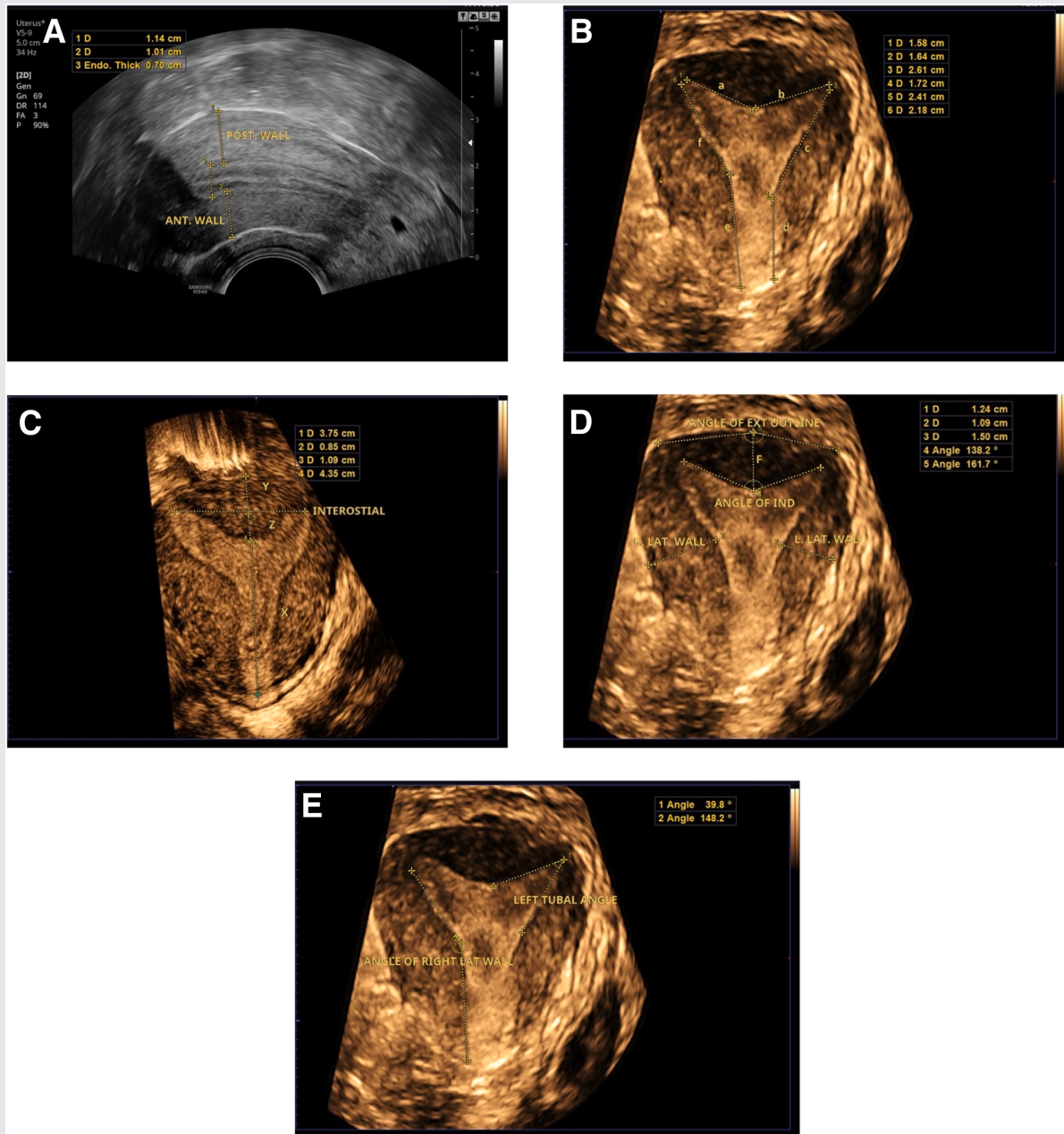
On 2D mid-sagittal projection:.

- Anterior and posterior wall thicknesses, measured at the level of maximum thickness (Fig. 1A).
- Endometrial thickness, defined as the maximum measurable endometrial thickness (Fig. 1A).

On 3D coronal projection:.

- Distances *a* to *f* (Fig. 1B):
 - *a*: from the right tubal ostium to the apex of the mid indentation.
 - *b*: from the apex of the mid indentation to the left tubal ostium (in the case of a perfectly straight fundus, values of *a* and *b* were equal and each represented 50% of the interstitial distance).
 - *c*: from the left tubal angle to the left lateral wall angle.

FIGURE 1



Ultrasound measurements. (A) Two-dimensional mid-sagittal projection. D1: posterior wall; D2: anterior wall; D3: endometrial thickness. (B) Three-dimensional (3D) coronal projection. D1 to D6 correspond to a to f, respectively. (C) 3D coronal projection. D1: interstitial distance; D2: z value; D3: y value; D4: x value. (D) 3D coronal projection. D1: F; D2: left lateral wall thickness; D3: right lateral wall thickness; 4: angle of indentation; 5: angle of external outline. (E) 3D coronal projection. Left tubal angle and right lateral wall angle.

Gergolet. Ultrasound definition of normal uterus. *Fertil Steril* 2025.

- d: from the left lateral wall angle to the external opening of the cervix (os) (left margin).
- e: from the external cervical os (right margin) to the right lateral wall angle.
- f: from the right lateral wall angle to the right tubal angle.
- Interstitial distance (Fig. 1C): the distance between the two tubal ostia, measured at the transition between the isthmic portions of the fallopian tubes.
- Fundal indentation (z) (Fig. 1C): distance from the apex of the cavity indentation to the midpoint of the interstitial line.

- Interstitial-to-outer-contour distance (y) (Fig. 1C): from the midpoint of the interstitial line to the outer contour. Notably, in cases of bicorporal uterus where the outer contour lies below the interstitial line, the value of y is negative.
- Uterine length (x) (Fig. 1C): from the top of the uterine cavity to the external cervical os.
- Fundal thickness (F) (Fig. 1D): from the apex of the cavity indentation to the outer contour, crossing the interstitial line at its midpoint. Conceptually, $F = z + y$.
- Left (L) and right (R) lateral wall thicknesses (Fig. 1D): measured at the point of maximum thickness.
- Angle of indentation (Fig. 1D): internal angle of the uterine fundus.
- Angle of external outline (Fig. 1D), considered $>180^\circ$ in the case of a concave fundus and $<180^\circ$ in a convex fundus.
- Left and right lateral wall angles (Fig. 1E): angle between distances c and d on the left side, and between e and f on the right side of the uterus.
- Left and right tubal angles (Fig. 1E): angle between distances b and c on the left side, and between f and a on the right side of the uterus.

Sample size

Sample size estimation was based on preliminary measurements taken by the first author, with particular focus on the interstitial distance. An average value of 27.6 mm with an SD of 5.5 mm (27.6 ± 5.5 mm) was obtained. The study aimed to achieve an accuracy of 0.1 SD in defining the normal size and shape of the uterus. A total of 384 subjects were required to reach this level of precision with a 95% confidence level.

Statistics

Summary statistics for all measured distances and angles were calculated and reported as means, SDs, medians, minimum and maximum values, and percentiles (1st, 3rd, 5th, 10th, 50th, 90th, 95th, 97th, and 99th). The distributional properties of the measurements were visualized using violin plots with a Gaussian kernel (12, 13). Intraclass correlation coefficients (ICCs) were calculated using a two-way random-effects model with absolute agreement to assess both interrater and intrarater reliability. The ICC values were interpreted as follows (14): <0.40 , poor agreement; 0.40 – 0.59 , fair; 0.60 – 0.74 , good; and 0.75 – 1.00 , excellent. All statistical analyses were performed using IBM SPSS Statistics v29 and R (Armonk, New York, USA) (12). A *P*-value $< .05$ was considered statistically significant.

Interrater and intrarater reliability

Three sonographers from different collaborating centers re-evaluated 10 of their own ultrasound measurements at least one month after the initial assessment. In total, 30 repeated measurements were obtained for intrarater reliability.

For interrater reliability, two different sonographers independently measured the same ultrasound volume. Each pair of operators evaluated 10 volumes, and three pairs from different centers were included, resulting in a total of 30 interrater repeated measurements.

RESULTS

The normal uterus

A total of 2,861 patients were assessed for eligibility. Of these, 2,397 did not meet the inclusion criteria and 22 declined to participate. Consequently, 442 nulliparous women were enrolled in the study. The mean age of participants on the day of ultrasound examination was 25.7 ± 4.27 years (mean $\pm$ SD).

All acquired uterine measurements are presented in Table 1. In particular, regarding the parameters most commonly considered essential for distinguishing a normal from an abnormal uterus, we found the following: the median fundal indentation (z) was 1.7 mm, with a 90th percentile of 4.8 mm; the median interstitial-to-outer-contour distance (y) was 9.1 mm; the median left tubal angle was 50.0° ; the median right tubal angle was 48.0° ; and the median indentation angle was 161.8° . Figure 2 displays the distribution of the first four parameters. Additionally, as shown in Supplemental Figure 1 (available online), the values for these parameters were substantially homogeneous across all participating centers.

Collectively, the ultrasound measurements enabled the construction of a detailed model of the NU, illustrated in Fig. 3A.

Interrater and intrarater agreements

Interrater and intrarater reliability were assessed for all acquired uterine measurements, demonstrating overall substantial reproducibility. Specifically, interrater agreement (Supplemental Table 1, available online) was excellent for most parameters; good for anterior wall thickness, angle of external outline, and left lateral wall angle; fair for left lateral wall thickness (L); and poor for right lateral wall thickness (R), with an ICC of 0.389, just below the threshold for fair agreement. Intrarater agreement (Supplemental Table 2) was also excellent for most measurements, with the following exceptions: good agreement for right lateral wall thickness (R); fair agreement for left lateral wall thickness (L).

DISCUSSION

The objective of the present study was to establish a reference set of uterine measurements that would enable healthcare providers to define a uterus as normal objectively, rather than by exclusion from other classes or relying on arbitrarily established criteria. The added value of our study, compared with previous reports in the literature (2–5), lies in the quantitative definition of uterine lengths, thicknesses, and angles of an NU. It is worth noting that the reported values are based on ultrasound measurements and may not

TABLE 1

Uterine measurement results.

	Percentiles													
	Mean	Median	SD	Min	Max	1st	3rd	5th	10th	50th	90th	95th	97th	99th
Endometrial thickness	6.6	6.3	2.8	1.00	15.90	1.9	2.0	2.3	3.0	6.4	10.2	11.6	12.6	14.4
Interostial distance	27.6	27.1	6.0	12.0	50.0	15.7	17.9	18.4	20.3	27.1	35.3	38.7	40.3	44.5
a	13.9	14.0	3.2	6.3	26.0	7.5	8.5	9.1	10.0	13.9	17.9	19.8	20.7	23.8
b	13.9	13.8	3.2	1.2	26.3	7.1	8.4	9.3	10.0	13.8	18.0	19.7	20.9	23.4
c	18.8	16.3	8.0	5.2	51.4	7.9	9.0	9.6	10.9	16.3	31.0	35.2	38.0	43.0
d	25.4	25.0	8.7	6.0	52.9	8.2	10.2	12.0	14.7	25.1	37.0	40.0	42.6	46.7
e	25.4	25.2	8.6	6.3	49.0	9.6	10.9	12.4	14.6	25.4	37.3	40.6	42.5	45.1
f	19.0	17.1	7.6	6.0	51.4	7.6	9.1	10.0	11.4	17.1	30.4	34.9	36.0	43.7
Anterior wall thickness	12.5	12.4	2.8	4.3	23.9	6.8	7.9	8.3	9.0	12.4	16.0	18.0	18.7	20.0
Posterior wall thickness	13.2	12.7	3.2	1.0	26.5	7.3	8.0	8.7	9.8	12.8	17.5	19.4	20.0	22.7
F	11.3	11.0	3.1	2.8	24.7	5.8	6.4	6.8	7.8	11.0	15.0	16.5	18.0	22.3
L	14.9	14.6	3.4	6.7	29.6	8.4	9.4	10.1	11.0	14.6	19.2	21.4	23.1	25.7
R	14.9	14.5	3.4	6.1	29.5	8.1	9.7	10.1	11.0	14.5	19.3	20.6	22.2	25.8
z	2.2	1.7	3.1	0.0	35.4	0.0	0.0	0.0	0.0	1.7	4.8	6.7	8.8	15.4
y	9.3	9.1	2.7	0.0	22.7	2.1	5.0	5.6	6.4	9.1	12.6	14.0	14.9	16.4
x	43.4	43.0	10.2	15.9	71.5	20.4	25.4	27.7	30.5	43.1	56.0	61.0	64.8	69.3
Angle of indentation	159.7	161.8	18.4	49.4	180.0	92.2	121.5	129.2	139.0	161.8	180.0	180.0	180.0	180.0
Angle of external outline	151.6	151.2	11.8	114.0	180.0	123.0	126.8	131.4	137.6	151.1	167.6	172.0	176.9	179.3
Right lateral wall angle	149.9	150.8	12.8	101.5	178.3	116.7	123.9	126.0	132.2	150.5	165.5	169.0	171.4	176.4
Left lateral wall angle	150.3	151.0	11.5	106.3	180.0	120.4	127.0	131.5	135.7	151.0	164.6	169.0	170.9	177.3
Left tubal angle	48.8	50.0	17.9	10.3	101.5	11.9	15.2	18.5	25.7	50.3	71.3	77.5	81.4	91.9
Right tubal angle	48.4	48.0	18.6	8.1	148.2	11.3	15.6	17.8	23.4	48.0	71.1	77.7	81.0	94.5

Note: Data are expressed in millimeters (lengths and thicknesses) or degrees (angles). The uterine measurements commonly considered most important in differentiating a normal uterus from an abnormal one are reported in red.

Gergolet. Ultrasound definition of normal uterus. Fertil Steril 2025.

correspond exactly to anatomical dimensions observed in surgical or anatomical reference specimens.

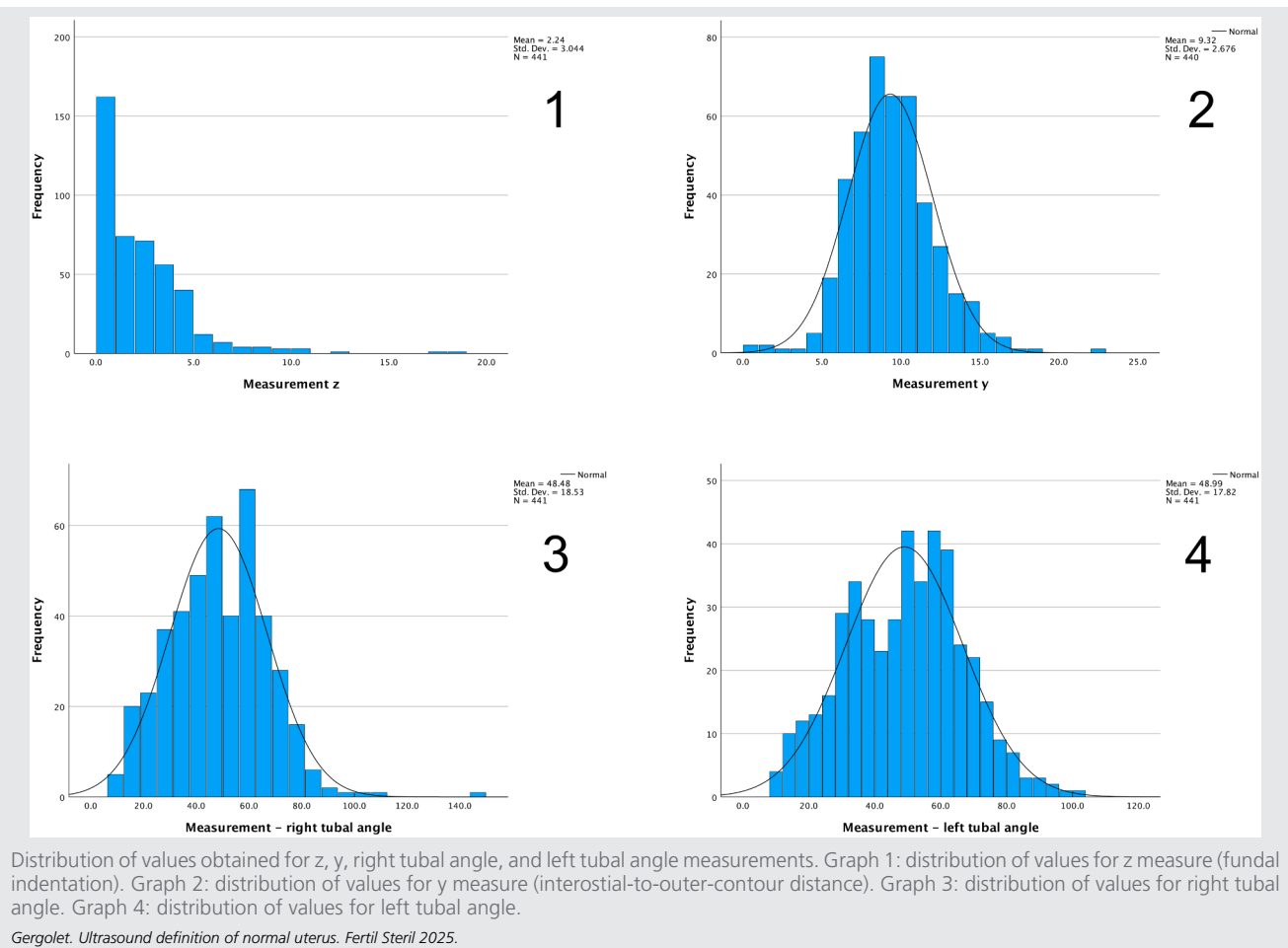
Among all the uterine parameters assessed, those most commonly considered critical in differentiating a NU from an abnormal uterus are highlighted in red in Table 1 and are discussed next.

First and foremost, we found a median fundal indentation (z) of 1.7 mm, with the 90th percentile at 4.8 mm, and a median indentation angle of 161.8°, whereas the median distance from the interostial line to the outer uterine contour (y) was 9.1 mm. These parameters represent some of the most debated aspects among existing classifications, primarily because they contribute to defining different cut-offs for distinguishing a normal from a septate uterus (4, 5). Our findings are supported by several studies that have reported comparable normal uterine measurements. Bajka and Badir (15) found an average fundal thickness of 10.92 ± 1.86 mm in 45 nulliparous women whose uteri were considered normal based on their criteria. In their review, Detti et al. (16) proposed a 5.9 mm cut-off for subseptation length as the most sensitive threshold for diagnosing septate uteri requiring treatment and predicting an associated early pregnancy loss. The investigators (16) also acknowledged that the ASRM 10-mm cut-off is more restrictive and may lead to the under-treatment of clinically relevant subseptations. Finally, a cross-sectional study (17) evaluating uterine morphology in women with and without polycystic ovary syndrome (PCOS) reported mean fundal indentations of 0.0 ± 0.2 mm in infertile non-PCOS women and 2.2 ± 0.4 mm in the

PCOS group. Indentation angles were also more acute in women with PCOS compared with controls (162.9° vs. 175.2°, respectively). All of these findings are highly consistent with our own observations.

Regarding the interostial distance, it can be conceptualized as the baseline of an isosceles triangle, with the apex opposite the base forming the indentation angle (Fig. 1C and D). On the basis of the updated ASRM classification (5), a septate uterus is defined by an indentation angle of 90° or less. Given that the median interostial distance in our study was 27.1 mm, a fundal indentation (z) greater than 13.55 mm would be required to generate an indentation angle of 90° or less, thereby classifying the uterus as septate under ASRM criteria (5). Such a z value would be higher than the 98th percentile observed in our population, potentially leading to an underestimation of uterine septa. On the other hand, our findings, which show normal indentations ranging from 0 to 4.8 mm and a median interostial-to-outer contour distance (y) of 9.1 mm, are also not fully consistent with the ESHRE/ESGE definition of a septate uterus (Class U2), which considers an indentation exceeding 50% of y as diagnostic. When applying the ESHRE/ESGE criteria to our cohort, all uteri with z values exceeding 4.55 mm (i.e., y/2, which corresponds to approximately the 87th–88th percentile in our sample) would be classified as septate, potentially resulting in an overestimation of uterine septa. In conclusion, although our 90th percentile for the z value more closely approaches the ESHRE definition of a septate uterus than the ASRM criteria, it does not provide sufficient diagnostic

FIGURE 2



accuracy. Rather, it underscores the urgent need to refine existing classifications through the adoption of shared criteria based on objective measurements. Such a new definition should strike a balance between the high specificity of the ASRM criteria and the high sensitivity of the ESHRE/ESGE criteria, thereby more accurately reflecting the range of normal anatomical variation and minimizing both underdiagnosis and overdiagnosis.

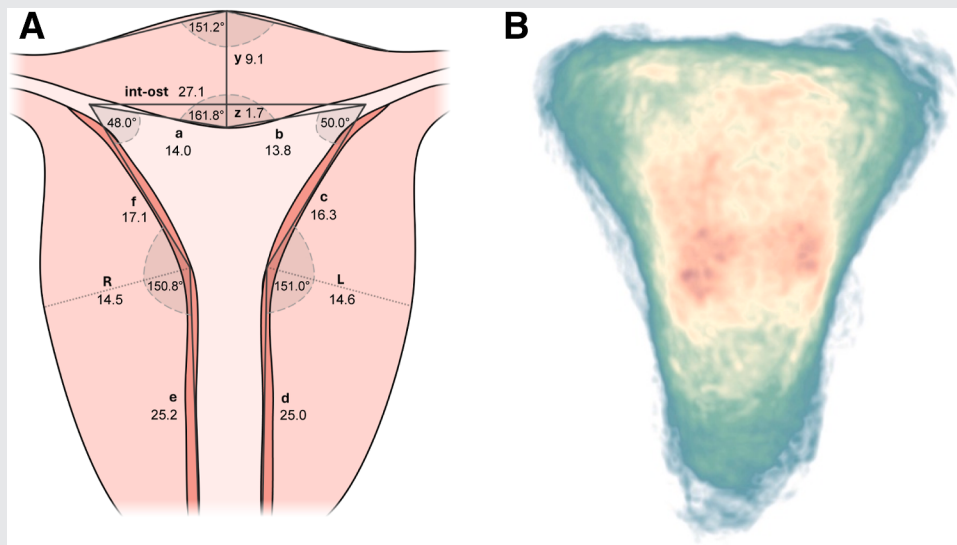
Finally, in our model, the right and left tubal angles had median values of 48.0° and 50.0°, respectively, imparting a delta-shaped configuration to the uterine cavity. Uteri with tubal angles of 20° or less typically exhibit T- or Y-shaped internal contours and are considered abnormal (4). At hysteroscopic evaluation, such uteri usually present with a long, tubular cervix and the lower uterine cavity constricted by fibromuscular rings around the proximal and medial segments. In addition, the tubal ostia are positioned laterally and can be visualized only by rotating a 30-degree hysteroscope near the uterine fundus toward each side. Alonso Pacheco et al. (18, 19) proposed the “rule of 10,” a simple and effective method for describing and classifying T-shaped uteri. In contrast, the Congenital Uterine Malformation by

Experts criteria are more complex and selective and may fail to identify a nonnegligible proportion of abnormalities or clear deviations from the normal shape (7).

Another relevant finding of our study is the essentially homogeneous distribution of measurements across the participating centers (Supplemental Fig. 1), supporting the concept that 3D ultrasound is a straightforward and highly reproducible diagnostic technique. This is further corroborated by the excellent interrater and intrarater agreement observed for most uterine measurements (Supplemental Tables 1 and 2). Notably, the two parameters with the lowest levels of agreement, both interrater and intrarater, were the left and right lateral wall thicknesses (L and R). Accordingly, low intrarater and interrater agreements for lateral walls were also reported by Saravelos et al. (20). This may be attributed to the difficulty in identifying precise landmarks for reproducible measurements, particularly when the lateral wall angles approach 180°.

Pooled together, the results from our ultrasound measurements enabled us to outline the precise identikit of an NU, as illustrated in Figure 3A, successfully addressing a critical knowledge gap through an evidence-based approach.

FIGURE 3



Model of normal uterus built using measurements obtained manually in the present study (A) and by automatic segmentation and alignment (B).
 Gergolet. Ultrasound definition of normal uterus. *Fertil Steril* 2025.

Interestingly, in another recent study from our group (21), we introduced a novel method to automatically segment and align uterine shapes from 3D ultrasound data. Specifically, we trained an nnU-Net deep learning model, which achieved high accuracy, and developed an alignment method based on a combination of standard geometric techniques. As part of the *UterUS* study, an ongoing project conducted in parallel with the present research, we are using the volumes acquired during the NURSE study to automatically reconstruct the shape of an NU. Preliminary results, illustrated in Figure 3B, show a uterine profile that closely resembles the one obtained by manually acquired measurements in the current study.

Strengths and limitations

The main strengths of this study include its originality, the multicenter and prospective design, the sizable number of patients enrolled, and the evaluation of both inter- and intra-rater agreement. An additional strength lies in its cross-sectional structure, which allowed for the acquisition of real-world measurements derived from routine clinical practice.

However, several limitations should be acknowledged. First, a degree of variability related to patients' physical characteristics (such as height and weight) was unavoidable. Second, although we did not conduct a specific subanalysis, the use of different ultrasound machines may have introduced minor variations in image reconstruction and, consequently, in the resulting measurements. Lastly, our study population consisted of a selected cohort of European women, which may limit the generalizability of our findings to populations with different demographic and ethnographic

characteristics. This underscores the need for confirmatory studies in more diverse cohorts.

CONCLUSION

We precisely defined, based on real-world data, the shape of an NU in terms of ultrasound uterine lengths, thicknesses, and angles. Our model may enable healthcare providers to classify a uterus as normal directly and objectively, rather than by exclusion from higher classes or relying on arbitrarily set criteria.

Linking abnormal uterine cavities to primary or secondary infertility was beyond the scope of the present study. Moreover, any deviations from the values reported here should not be considered indications for corrective uterine surgery. All these aspects require further investigation in future research.

Overall, the results of the present study should be considered as a foundation for future investigations on Müllerian anomalies, aiming to provide a reproducible scientific model and to aid in identifying potential reproductive and obstetric adverse effects associated with abnormal uterine measurements.

CRedit Authorship Contribution Statement

Marco Gergolet: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Conceptualization. Pierpaolo Nicoli: Writing – review & editing, Investigation. Eda Vrtačnik Bokal: Formal analysis, Conceptualization. Ivan Verdenik: Formal analysis, Data curation. Attilio di Spiezio Sardo: Investigation. Brunella Zizolfi: Investigation. Anjeza Xholly: Investigation. Angelo Cagnacci: Investigation. Umberto Scovazzi: Investigation.

Alessandro Arena: Investigation. Paolo Casadio: Investigation. Giuseppe Sorgente: Investigation. Stephan Gordts: Investigation. Rudi Campo: Investigation. Sotirios Saravelos: Methodology, Investigation. Carmina Bermejo: Investigation. Lubomir Mikulašek: Investigation. Sara Brucker: Investigation. Gertruda Jonaityte: Investigation. Kristin Katharina Rall: Investigation. Markus Hoopmann: Investigation. Anna Kougioumstidou: Investigation. Apostolos Athanasiadis: Investigation. Luis Alonso Pacheco: Investigation. Francesca Buonomo: Investigation. Martina Colombin: Investigation. Luca Savelli: Investigation. Giulia Magnarelli: Investigation. Luca Gianaroli: Investigation. Maribel Acien: Investigation. Raquel Ortiz-Escribano: Investigation. Lorenza Driul: Investigation. Anna Biasioli: Investigation. Martina Gergolet: Formal analysis, Data curation. Attila Vereczkey: Investigation. Eva Boneš: Software. Matija Marolt: Software. Žiga Lesar: Software. Ciril Bohak: Software. Recai Pabuccu: Investigation. Theodoros Theodoridis: Investigation. Grigoris Grimbizis: Supervision, Conceptualization. Amerigo Vitagliano: Writing – review & editing, Conceptualization.

Declaration of Interests

M.G. has nothing to disclose. P.N. has nothing to disclose. E. V.B. has nothing to disclose. I.V. has nothing to disclose. A. di.S.S. has nothing to disclose. B.Z. has nothing to disclose. A.X. has nothing to disclose. A.C. has nothing to disclose. U.S. has nothing to disclose. Al.A. has nothing to disclose. P.C. has nothing to disclose. G.S. has nothing to disclose. S. G. has nothing to disclose. R.C. has nothing to disclose. S. S. has nothing to disclose. C.B. has nothing to disclose. L. M. has nothing to disclose. S.B. has nothing to disclose. G. J. has nothing to disclose. K.K.R. has nothing to disclose. M.H. has nothing to disclose. A.K. has nothing to disclose. A.A. has nothing to disclose. L.A.P. has nothing to disclose. F.B. has nothing to disclose. M.C. has nothing to disclose. L.S. has nothing to disclose. G.M. has nothing to disclose. L.G. has nothing to disclose. M.A. has nothing to disclose. R.O.-E. has nothing to disclose. L.D. has nothing to disclose. A.B. has nothing to disclose. Mart.G. has nothing to disclose. A.V. has nothing to disclose. E.B. has nothing to disclose. M. M. has nothing to disclose. Ž.L. has nothing to disclose. C.B. has nothing to disclose. R.P. has nothing to disclose. T.T. has nothing to disclose. G.G. has nothing to disclose. Am.V. has nothing to disclose.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be found online at <https://doi.org/10.1016/j.fertnstert.2025.07.1220>.

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