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Fetal foot length at delivery as a tool for determining gestation length in non-macerated stillbirths

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Abstract

Objective—To assess whether fetal foot length at autopsy could reliably indicate gestational duration at stillbirth and the effects of maceration on this method.

Methods—The present cross-sectional secondary analysis was part of the Safe Passage Study; all Safe Passage Study participants who experienced a stillbirth at Tygerberg Academic Hospital, Cape Town, South Africa, between August 1, 2007, and January 31, 2015, were eligible to participate. After providing written informed consent for autopsy, the duration of gestation calculated using early ultrasonography and fetal foot length were compared.

Results—There were 69 fetal autopsies included in the present study; placental histology was available for 65. Generally, the gestation length calculated from the first ultrasonography scan correlated well with that calculated from the fetal foot length (Spearman correlation=0.85). However, significant differences were found in the gestation lengths calculated when the fetus was

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Author contributions

EG and JC coordinated all the autopsies, performed the foot-length measurements, collected and labelled the different specimens, collected data from all the reports, and contributing to editing the manuscript. CW performed all the autopsies and contributed to writing and editing the manuscript. DN performed the statistical analyses, designed the figures, and contributed to writing and editing the manuscript. DR and TB examined a portion of the histology slides for quality control and contributed to writing and editing the manuscript. HO was the local principal investigator of the Safe Passage Study, initiated the present study, and contributed to writing and editing the manuscript.

Conflicts of interest

The authors have no conflicts of interest.

macerated ($P<0.001$), or when umbilical cord pathology ($P<0.001$) or maternal vascular malperfusion ($P<0.001$) was the cause of fetal death.

Conclusions—Foot length at stillbirth was a good indicator of gestation length; however, it was a weaker indicator if fetal maceration had occurred.

Synopsis

A correlation was found between using early ultrasonography and fetal foot length to calculate the length of gestation at stillbirth; fetal maceration compromised this.

Keywords

Fetal growth; Foot length; Gestational age; Macerated stillbirth; Maternal vascular malperfusion; Umbilical cord pathology

1. Introduction

Accurate knowledge of gestation length at delivery can be important for a number of reasons, including the identification of preterm deliveries and analyses of stillbirths. A cut-off point for the classification of stillbirths of 28 weeks has been recommended for making comparisons of stillbirth rates internationally; this is in contrast to a delivery weight of 1000 g, which has been used previously [1]. It has been suggested that using a delivery weight of at least 1000 g to define stillbirths, reduces the proportion of stillbirths by 21% compared with using a definition of 28 weeks [2].

Ultrasonography is the ideal method for determining the gestation length for a fetus; however, ultrasonography facilities in many Sub-Saharan African and tropical countries are still inadequate or non-existent [3, 4]. In some countries, only 10%–13% of patients from rural areas have access to imaging technology [3]. According to a review article on the use of ultrasonography in low- and middle-income countries [5], diagnostic imaging in rural and remote areas is often insufficient and sometimes completely non-existent [5]. Consequently, a randomized trial of the effect of including ultrasonography in prenatal care in low-income countries was planned [6]. Additionally, late booking for prenatal care has been identified as occurring commonly in Sub-Saharan Africa [7]; this can further hamper accurate confirmation of the length of pregnancy because the date of last menstruation is not a reliable indicator of pregnancy duration [8].

Measuring fetal foot length is an alternative method for determining gestational duration [9]. This technique has been reported as being used successfully in several low-income countries, including Nepal [10], and Tanzania [11], to identify high-risk conditions such as prematurity or growth restriction that can necessitate additional neonatal care. However, it is uncertain how maceration of the fetus and different causes of stillbirth could affect fetal foot length. It has been hypothesized that data from the Safe Passage Study [12] could be useful in determining how various causes of stillbirth relate to measurements of gestation length made using fetal foot length. The aim of the present study was to assess if foot length at autopsy was a reliable indicator of fetal gestation length following stillbirth; further, the

study investigated how this method of measuring gestation time was affected by different causes of stillbirth and the degree of fetal maceration.

2. Materials and methods

The present cross-sectional secondary analysis included data from the Safe Passage Study; the Safe Passage Study is part of the Prenatal Alcohol in SIDS and Stillbirth Network and was developed to test the hypothesis that prenatal alcohol exposure was associated with increased risk of stillbirth and/or sudden infant death syndrome [12]. The multicenter parent trial, performed between August 1, 2007, and January 31, 2015, enrolled individuals aged at least 16 years with singleton or twin pregnancies at least 6 weeks in duration who were able to communicate in Afrikaans or English. From these study data, the present secondary analysis included data from autopsies performed at Tygerberg Hospital, Cape Town, South Africa, following stillbirth. The parent study was approved by the Health Research Ethics Committee of Stellenbosch University, Stellenbosch, South Africa (approval number N06/10/210), and written informed consent was obtained from all participants and, where possible, the father of the fetus/neonate. To be included in the present secondary analysis, further specific written informed consent for fetal autopsy and data inclusion was required. A copy of the signed consent form, in the participants own language, was given to participants to keep. The process used to obtain informed consent for the present analysis has been described previously [13].

Clinical, placental, and autopsy findings were used to categorize the cause of each stillbirth according to a specific classification system used in the study; the main cause could be classified as fetal, placental, maternal, external, or undetermined [14]. At autopsy, a plastic Vernier caliper was used to measure fetal foot length; measurements of both feet were made by two medical technologists (E.G. and J.C.) and the mean foot length was calculated. Measurements were taken from the heel to the tip of the longest toe; this was most commonly the first toe but was the second toe on some occasions. The caliper was positioned against the tissue gently to prevent any compression. Additionally, the caliper was placed perpendicular to the leg to avoid any flexing of the ankle. The tables of Maroun and Graem [15] were used to derive the gestational duration from the foot length, based on recommendations by Conway et al. [16].

The pathologists performing fetal autopsies received no information regarding pregnancy or delivery apart from the accurate gestational duration at delivery, derived from the first ultrasonography examination during pregnancy. Pathologists were masked to any prenatal alcohol exposure during pregnancy and received no information on any clinical variables that could have resulted in stillbirth. Maceration was categorized as absent when there was a virtual absence of desquamation or discoloration of the skin, mild, moderate, or severe [17].

All stillbirths were discussed in detail during regular conference calls that included the pathology subcommittee of the Safe Passage Study to decide specific causes, in accordance with the parent study classification schema [14]. As there were many different subcategories of causes of death, these were classified into the basic categories of maternal vascular

malperfusion, umbilical cord conditions, infection, placental abruption, congenital anomalies, and a mixed group of other fetal, maternal and placental disorders.

All data were entered into a spreadsheet using Excel 2016 (Microsoft, Redmond, WA, USA) and statistical analyses were performed using Statistica version 13.0 (Dell, Round Rock, TX, USA). Descriptive analyses were performed to identify outliers; subsequently, continuous variables were compared with either analysis of variance or repeated-measures analysis of variance using the compound symmetry assumption. Bonferroni multiple comparisons were used to identify significant differences among the means. The Spearman rank correlation (r) was used to measure correlations between repetitions of several response variables. Intra-class correlations for agreement and consistency were also reported.

3. Results

Fetal foot length autopsy data were available for 69 fetuses (35 female and 34 male) and placental histology was available for 65. Bilateral foot lengths were measured in 66 fetuses; one foot was measured for three stillbirths but the laterality was not specified. The mean maternal age was 25.4 years; the mean ultrasonography-derived length of gestation was 110 days (15^{+5} weeks) and 205 days (29^{+2} weeks) at the first prenatal visit and at delivery, respectively (Table 1). The mean foot length-derived gestation length at delivery was 190 days (27^{+1} weeks). The mean fetal weights at delivery and autopsy were 1152 g and 1020 g, respectively (Table 1). The mean length of fetuses' right and left feet were 50.4 mm and 50.3 mm, respectively. A highly significant correlation was found between the ultrasonography- and foot length-derived gestation length at delivery ($r=0.85$; $P<0.001$) (Figure 1). Highly significant correlations were also recorded between delivery and autopsy weight ($r=0.97$; $P<0.001$), weight at autopsy and foot length ($r=0.96$; $P<0.001$), and weight at autopsy and placental weight ($r=0.75$; $P<0.001$).

No maceration was recorded in 33 (48%) fetuses at post-mortem examination; 22 (32%) had mild maceration and 14 (20%) had severe maceration. A difference of 4 days was observed in ultrasonography- and foot length-derived gestation length among fetuses exhibiting no maceration; however, significant differences in gestation were recorded when mild (19 days) or severe maceration (34 days) were recorded (Figure 2).

The most common causes of stillbirth were maternal vascular malperfusion and infection in 14 and 15 fetuses, respectively. Umbilical cord lesions were the cause of stillbirth in 11 fetuses; these consisted of torsion in three, non-acute flow restriction in three, hypercoiling in two, and prolapse, velamentous with marginal insertion, and hematoma in one fetus each. Among the 15 fetuses where infection was the cause of stillbirth, 14 were caused by acute chorioamnionitis and one was caused by syphilis. The placental abruption-caused stillbirths (12 fetuses) included acute abruption as the cause of stillbirth for 11 fetuses and chronic abruption for one fetus. Among the seven congenital anomalies recorded in the study cohort, trisomy 18 affected two fetuses, ventriculomegaly affected two, and one stillbirth was caused by each of absent corpus callosum, osteogenesis imperfecta, and multiple congenital anomalies, including absent tibia, fibula, and diaphragmatic hernia. Among the 10 other fetuses, massive perivillous fibrin deposition, massive histiocytic intervillitis, and drug-

induced cardiomyopathy were the cause of stillbirth in one fetus each; the cause of stillbirth remained undetermined for seven fetuses (Supplementary material S1).

Among stillbirths caused by maternal vascular malperfusion, a significant mean difference of 29 days was observed in the ultrasonography- and foot length-derived gestation length (208 days vs 179 days; $P<0.001$); a significant difference of 25 days was also observed among stillbirths caused by umbilical cord anomalies (212 days vs 187 days; $P<0.001$). Among the 10 fetuses not grouped by stillbirth cause, a similar significant difference of 21 days was observed (224 days vs 203 days; $P=0.026$). No significant differences were observed among the other stillbirth groupings described above (Figure 3).

The length of gestation calculated from the fetal foot length was lower than the ultrasonography-derived gestation time among all stillbirth groupings except for stillbirths caused by placental abruption (Figure 3).

4. Discussion

To the best of our knowledge, the present study was the first to compare discrepancies in estimates of gestation length made using early ultrasonography or fetal foot length and to use the cause of stillbirth to stratify the data. Overall, a strong correlation was recorded between the two measurement methods, with the foot-length method yielding somewhat lower estimates.

Given that growth restriction occurs frequently among stillborn fetuses [18], a specific delivery weight cut-off value lacks sufficient accuracy for determining the length of pregnancy in the event of stillbirth, particularly at lower pregnancy lengths. By way of example, stillbirth in the USA has been defined using a delivery weight of at least 500 g; in comparison with using a definition of at least 22 weeks of pregnancy, this weight-based definition corresponds to recording 40% fewer stillbirth events [2]. Consequently, it has been recommended that length of pregnancy be used to define stillbirth in place of delivery weight [1].

The degree of maceration can be used as a rough indicator of the fetal death-to-delivery interval [17]. In the present study, the difference in fetal gestation length estimates made using early-ultrasonography or fetal foot length was 4 days when no maceration was recorded; however, this increased to 19 and 34 days when there was mild or severe maceration, respectively. Therefore, foot length should be interpreted with caution when maceration is recorded as this could be unrepresentative of the actual gestation length at fetal death.

The difference in gestation-duration calculations in the presence of maternal vascular malperfusion is not surprising; it has been demonstrated that the accuracy of foot length-derived estimates of gestation is affected by intrauterine growth restriction [19]. Additionally, in a large study [20] that consisted of more than 5000 foot-length measurements made between 15 weeks and 37 weeks of pregnancy, it was found that foot length was affected by intrauterine growth restriction. Consequently, foot length as a proxy for gestation length should be interpreted with caution if maternal vascular malperfusion is

identified. It should also be noted that fetal death of a growth-restricted fetus could have occurred several weeks prior to delivery.

An unexpected finding of the present study was the difference in gestation-length calculations when cord anomalies were the cause of fetal death; to the best of our knowledge, this has not been reported in the literature previously. It is suggested that, with the exception of acute prolapse, most conditions affecting umbilical cord venous flow, such as hypercoiling, oligohydramnios, long cord, and entanglement, are more likely to be chronic in nature. In addition, mechanical umbilical cord obstruction predisposes a fetus to placental fetal vascular thrombosis and stillbirth [21]. These conditions are likely to cause fetal death prior to the onset of labor or to be preceded by growth restriction, as demonstrated by the significant difference in the gestation lengths calculated in the present study. The small difference in gestation lengths among fetuses with placental abruption or infection as the cause of fetal death can be explained more easily because delivery usually occurs soon after the onset of these events [22, 23]. However, different specific congenital anomalies could exert specific effects on the difference in gestation calculations using the two methods [24].

Several ways of measuring foot length have been described previously, including using a plastic ruler, measuring tape, or measuring from a paper footprint; the plastic ruler has been described as the best of these options [10]. However, in the present study, a Vernier caliper was used because it was regarded as the most accurate clinical tool for measuring short distances between objects and the measurements have previously been demonstrated to have good inter- and intra-operator variability [25]. Although the mean length of the left and right foot differed by only 0.06 mm, differences of up to 5 mm were recorded. Measuring both feet and using the mean value to determine gestation length could eliminate inaccurate measurements arising from differences in the length of the left and right foot.

The limitations of the present study were the small cohort, resulting in some of the statistical analyses being underpowered, and the inclusion of different medical conditions within the same groups. Generally, the gestation length was underestimated when calculated using the foot length; this appeared to be due to poor fetal growth and fetal death occurring considerably prior to delivery. Further, it was difficult to determine the degree of growth restriction prior to fetal death, as this could also have contributed to the differences in gestation calculations. However, the Safe Passage Study provided a unique opportunity to use detailed follow-up data from pregnancies and stillbirth fetal autopsies; consequently, it was possible to compare the two measurement techniques. Despite a larger study cohort being desirable, regular autopsy is not feasible or recommended in low-income countries; with the Safe Passage Study completed, it is unlikely that a similar opportunity in a low-income country will be available.

In the International Classification of Diseases 10th revision, delivery weight was given priority over gestation length in defining stillbirth, and crown–heel lengths of at least 35 cm and at least 25 cm were described as suitable alternatives to delivery weights of 1000 g and 500 g as indicators of gestations of at least 28 weeks and 22 weeks, respectively [26].

However, in clinical practice, measuring fetal length is difficult without a suitable length board and could result in erroneous measurements.

The data from the present study suggested that foot-length measurements could provide an accurate estimate of gestation length in non-macerated fetuses following stillbirths. Additionally, if data are only available from early ultrasonography and not later ultrasonography for non-macerated fetuses, making comparisons between the ultrasonography-derived and foot length-derived gestation length could provide a good indication of the role in fetal death played by growth restriction. Measuring foot length to estimate gestation length in stillbirth could be a valuable tool, especially in low-income countries where early ultrasonography examinations are not routinely available.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Correlation between the lengths of gestation at delivery calculated from ultrasonography data and using fetal foot length. Spearman correlation 0.85; $P < 0.001$. Intra-class correlation for agreement 0.836 (95% CI 0.556–0.924); intra-class correlation for consistency 0.885 (95% CI 0.820–0.927). The solid line denotes the regression line and the broken line denotes the $y=x$ line. Abbreviation: CI, confidence interval.

Figure 2.

Effect of maceration on the difference in gestation length calculated using either ultrasonography data or fetal foot length. Significant differences in the calculated gestation were recorded if there was mild (19 days) or severe maceration (34 days); current effect $F(2, 66) 17.154$; $P < 0.001$. Whiskers denote 95% confidence intervals and duplicated letters above whiskers indicate an absence of a significant difference.

Figure 3.

Effect of different causes of stillbirth on the difference in gestation length calculated using either ultrasonography data or fetal foot length. Significant differences were recorded for UP ($P<0.001$), Cord ($P<0.001$), and other ($P=0.026$) causes of fetal death. Whiskers denote 95% confidence intervals and duplicated letters above whiskers indicate an absence of a significant difference. Abbreviations: UP, maternal vascular malperfusion; Cord, cord pathology; I, infection; AB, placental abruption; Cong ab, congenital anomalies.

Table 1

Patients and stillbirth characteristics.

Variable	Value ^a
Maternal age, y (n=69)	25.4±6.0 (25.0) (16–41) [21–29]
Delivery weight, g (n=64)	1152±854 (830) (190–3500) [480–1615]
Weight at autopsy, g (n=67)	1020±775 (659) (169–3160) [425–1466]
Placental weight, g (n=65)	218±119 (187) (50–586) [132–275]
Foot length, mm (n=69)	50.7±14.2 (45.5) (28.0–84.5) [40–62]
Gestation at booking, d (n=69) ^b	110±37 (111) (49–215) [84–128]
Ultrasonography-derived gestation at delivery, d (n=69)	205±44 (195) (146–300) [168–239]
Foot length-derived gestation at delivery, d (n=69)	190±40 (175) (131–293) [160–222]

^aValues are given as number or mean±SD (median) (range) [interquartile range].

^bMeasured using ultrasonography.