Cervical Length, Multifetal Pregnancy Reduction, and Prediction of Preterm Birth

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ABSTRACT: Purpose. To evaluate the application of transvaginal sonography assessment of cervical length before fetal reduction for predicting spontaneous preterm birth in triplet gestations reduced to twins.

Methods. This retrospective study was conducted at the ultrasound unit of a university-affiliated municipal hospital. The study cohort consisted of 25 women with triplet gestations following ovulation induction or assisted-reproduction techniques who underwent fetal reduction to twins. Cervical length was assessed via transvaginal sonography before fetal reduction, and data on pregnancy outcome were retrieved from maternal records and/or maternal interviews.

Results. Cervical length (mean ± SD) at reduction was 4.0 ± 0.85 (range: 1.2–5.5). Five women were excluded from statistical evaluation because pregnancy complications precluded spontaneous delivery. Two of 3 (67%) women with a cervical length of <3.5 cm delivered prior to 33 weeks’ gestation compared with 1/17 (6%) women with a cervical length ≥3.5 cm. This difference was statistically significant (P < 0.05). The sensitivity, specificity, positive predictive value, and negative predictive value of cervical lengths <3.5 cm to predict delivery prior to 33 gestational weeks was 67%, 94%, 67%, and 94%, respectively.

Conclusions. Measurement of cervical length in triplet pregnancies before fetal reduction provides useful predictive information on the risk for preterm delivery.

Keywords: cervical length; sonography; triplets; fetal reduction

The incidence of multifetal pregnancies has increased markedly during the past 20 years because of advancements in assisted reproduction. More recently, in vitro fertilization centers have specifically aimed at decreasing the multiple pregnancy rate through close monitoring of ovulation induction, limitations in the number of embryos transferred, and developments in the technique of blastocyst transfer. Despite these advancements in technology, however, multiple gestations are still a common consequence of assisted-reproductive techniques.

Higher-order multiple gestations are associated with increased morbidity and mortality compared with twin and singleton gestations. Multifetal pregnancy reduction was introduced in an effort to improve the overall pregnancy loss rate, gestational age at delivery, birth weight, neonatal morbidity and mortality rates, and incidence of pregnancy complications that are frequently associated with higher-order gestations. Nevertheless, in spite of the contribution of multifetal pregnancy reduction, a considerable proportion of multifetal births still occur before 34 weeks’ gestation.

Transvaginal sonography for measuring cervical length has been proposed as a means for providing valuable information in the prenatal care of singleton, twin, and triplet gestations. The objective of this study was to evaluate the role of sonographic assessment of cervical length before fetal reduction in predicting spontaneous preterm birth in triplet gestations reduced to twins.

PATIENTS AND METHODS

This study included 25 women with triplet gestations who underwent fetal reduction to twins between February 1999 and May 2001. All pregnancy
reductions were approved by the Institutional Review Board as mandated by national law, and informed consent to participate in the study was obtained from each patient.

All enrollees were evaluated by at least two first-trimester sonographic examinations and early fetal malformation screening. The pregnancies included in this study were trichorionic triamniotic, and no fetal malformations had been detected. All of the pregnancies were reduced by way of a transabdominal, sonographically guided procedure using an intracardiac injection of potassium chloride. All procedures were performed by two experienced operators (JH and AJ) in a similar manner as described elsewhere.\textsuperscript{19,20} No antibiotics were prescribed. Data on pregnancy outcome were obtained from maternal records and/or maternal interviews.

Transvaginal sonographic assessment of cervical length was performed prior to and at the same session of fetal reduction. The patient lay in a dorsal lithotomy position after having emptied her bladder. A transvaginal probe (Sonoline Elegra; Siemens Medical System, Inc., New York, NY) with a dynamic focus of 5–7 MHz was placed in the anterior fornix of the vagina. We aimed to obtain a sagittal view of the cervix and of the endocervical mucosa marking the cervical canal. Whenever the cervical canal appeared curvilinear, the cervical length was the sum of two linear segments. The distance between the external os and the internal os was measured. It was important that the entire cervical canal be visualized and that the two cervical lips were similarly widened. Care was taken to avoid pressure on the cervix. Only the closed portion of the cervical canal was measured. All the measurements were performed by two operators (JH and AJ), and the values were printed on a hard copy. The mean of three repeated measurements was used for study purposes.

Statistical analysis was performed at the Department of Statistics at Tel Aviv University. SPSS computer software was used. An ROC curve analysis was performed to determine the best cervical length cut-off and showed that a cervical length of 3.3 cm would have a sensitivity of 100% and a specificity of 67%. Using these criteria, we would not have had any false-negative cases. The cut-off of 3.5 cm that we had arbitrarily chosen results in a sensitivity of 94% and a specificity of 67%. Correlations between gestational age at fetal reduction, gestational age at delivery, and cervical length before reduction were evaluated using Pearson correlations. The Fisher exact test was performed to compare groups. A $P$ value less than 0.05 was considered significant.

RESULTS

Pregnancies were achieved via ovulation induction ($n = 7$) or assisted-reproduction techniques ($n = 18$). The mean ($\pm$SD) maternal age at reduction was 30.5 $\pm$ 2.7 years, and the mean gestational age at reduction was 15.9 $\pm$ 0.3 weeks. The mean cervical length at reduction was 4.0 $\pm$ 0.85 cm (range: 1.2–5.5). Five women were excluded from statistical evaluation because of pregnancy complications that precluded spontaneous delivery (late abortion [$n = 1$], abruptio placentae [$n = 1$], intra-uterine growth restriction [$n = 2$], pre-eclamptic toxemia [$n = 1$]). The data collected for the remaining 20 women were evaluated statistically.

Two of 3 (67%) women with a cervical length of less than 3.5 cm delivered before 33 weeks’ gestation compared with 1 of 17 (6%) women with a cervical length of 3.5 cm or more (cervical length of 3.6 cm). This difference was statistically significant ($P < 0.05$). The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of a cervical length less than 3.5 cm to predict delivery before 33 gestational weeks were 67%, 94%, 67%, and 94%, respectively. In two women, a cerclage was performed at 21 and 23 weeks’ gestation because of cervical shortening and dilatation: their cervical lengths at reduction were 1.2 cm and 3.5 cm, respectively. The first patient delivered at 32 weeks’ gestation, and the second patient delivered at 36 weeks’ gestation.

When we excluded from the analysis the two women who underwent a cervical cerclage, it was noted that 1 of 2 (50%) women with a cervical length of less than 3.5 cm had delivered before 33 weeks’ gestation compared with 1 of 16 (6%) women with a cervical length of 3.5 cm or more (cervical lengths of 3.6 cm). This difference was not statistically significant. The sensitivity, specificity, PPV, and NPV of a cervical length less than 3.5 to predict delivery before 33 gestational weeks was 50%, 94%, 50%, and 94%, respectively. Cervical length and gestational age at fetal reduction were not significantly correlated with gestational age at delivery, whether or not the data of the two women who underwent cervical cerclage were included in the assessment.

DISCUSSION

Few studies have provided information on cervical length in triplet pregnancies or have addressed the potential value of measuring this parameter for the predictive value of preterm birth in multifetal pregnancies. Ramin et al.\textsuperscript{15} performed serial transperineal measurements of cervical length beginning at 10 weeks’ gestation. They reported...
that the mean cervical length was significantly shorter from as early as 20 weeks in 11 pregnancies that had delivered before 33 weeks compared with 6 pregnancies that had delivered after 33 weeks. They also noted that cervical length in triplet gestations progressively shortened with advancing gestational age and that the mean cervical length in triplet gestations was significantly shorter than that reported for singleton gestations. Guzman et al.\textsuperscript{16} examined 51 triplet pregnancies that were followed up longitudinally on 274 occasions with serial transvaginal sonography between 15 and 28 weeks’ gestation. They found that a cervical length of <2.5 cm between 15 and 20 weeks’ gestation had a sensitivity, specificity, PPV, and NPV of 25%, 100%, 100%, and 72%, respectively, for predicting spontaneous delivery before 32 weeks’ gestation. Ramin et al.\textsuperscript{15} did not establish a cervical length cut-off, nor did they determine the efficacy of this parameter for the prediction of spontaneous preterm birth. Guzman et al.\textsuperscript{16} had set a cutoff of 2.5 cm or less. Using this cut-off, the sensitivity, specificity, PPV, and NPV of the current study to predict delivery before 33 gestational weeks were 33.3%, 100%, 100%, and 89.5%, respectively—results similar to those reported by Guzman et al.\textsuperscript{16}

Determining the influence of fetal reduction on cervical length in triplet pregnancies would require a comparison of cervical length in triplet pregnancies with and without fetal reduction. No such study has been reported to date. Rebarber et al.\textsuperscript{21} compared the cervical length in the remaining twin gestations of 35 women who underwent multifetal pregnancy reduction to the cervical length in twin gestation of 83 women without multifetal pregnancy reduction. The cervical length did not differ significantly between the two groups at any gestational age interval. At 14–19 weeks, the median was 3.9 cm (range: 2.4–6.0 cm) in the multifetal pregnancy reduction group versus 3.7 cm (range 3.1–4.7 cm) in the twin group ($P = 0.15$). Neither cervical length cut-off values nor the efficacy of this parameter for the prediction of spontaneous preterm were determined in their study. Guzman et al.\textsuperscript{22} longitudinally evaluated 131 women carrying twins using transvaginal sonography in a manner similar to the one they had used in triplet pregnancies. A cervical length of 2 cm or less between 15 and 20 weeks had a sensitivity, specificity, PPV, and NPV of 40%, 99%, 80%, and 95%, respectively, to predict delivery before 32 gestational weeks. Interestingly, a shorter cervical length cutoff (2.0 cm) in twin pregnancies compared with the cut-off set for triplets at the same gestational age yielded similar predictive values for spontaneous preterm delivery.

Applying cut-offs of different cervical lengths for different gestational ages with different gestational age as the end point causes some confusion when using the above-mentioned studies for making clinical decisions for women with a multifetal pregnancy and a sonographically determined short cervix. This is especially true when cervical length is evaluated before fetal reduction. Should we intervene at a certain cervical length? What intervention should we use? Bedrest? Tocolytic therapy? Cerclage? Few interventional trials have been based on endovaginal cervical length measurements. To our knowledge, bedrest and tocolytic therapy were not evaluated in women with a sonographically determined short cervix. Two relatively small prospective randomized trials involving either singleton gestations alone\textsuperscript{23} or primarily singleton gestations (89%)\textsuperscript{24} have yielded conflicting results regarding the efficacy of a cerclage placement in women with sonographic evidence of cervical shortening. Newman et al.\textsuperscript{25} determined the impact of cerclage placement on obstetric outcome in twin gestations with a shortened cervical length. They prospectively studied 147 consecutive twin pregnancies of women who underwent transvaginal sonographic cervical length measurements between 18 and 26 weeks’ gestation. Cerclage was offered to women with a cervical length of 2.5 cm or less. A comparison of 21 women who received a cerclage with 12 women who had a mid-trimester cervical length of 2.5 cm or less but declined a cerclage failed to reveal any significant difference in obstetric outcome.

In the Ramin et al. study,\textsuperscript{15} the cerclage performed in two women was placed before 18 gestational weeks when funneling of membranes was noted and the cervical length fell below 2.5 cm. The outcome of these pregnancies was not reported. Three cerclages were performed in Guzman et al.’s study\textsuperscript{16} at a median gestational age of 21 weeks (range 15–24 weeks), a preoperative cervical length of 0.56 cm (range: 0.46–1.13 cm), and a gestational age at delivery of 28 weeks (range: 26–34 weeks’ gestation). In the study of To et al.,\textsuperscript{17} three patients with the shortest cervical lengths (6 mm, 14 mm, and 15 mm) had elective placement of cervical
sutures and they delivered at 28, 34, and 27 weeks, respectively. In our study, cerclage was performed in two women at 21 and 23 weeks’ gestation because of cervical shortening and dilation. Cervical length at reduction was 1.2 and 3.5 cm, respectively. The first patient delivered at 32 weeks’ gestation, and the second patient delivered at 36 weeks’ gestation. From these data, the extent to which this treatment is useful in prolonging triplet pregnancies with or without fetal reduction is uncertain.

In conclusion, measurement of cervical length in triplet pregnancies before reduction may provide predictive information on spontaneous early preterm delivery. Additional studies are needed to determine the specific cut-off values and to evaluate the efficacy of different interventions.

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REFERENCES