Randomized trial of screening for preterm birth in low-risk women - the preterm birth screening study

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BACKGROUND: Preterm birth is a major cause of perinatal morbidity and mortality. It is unclear whether the introduction of a universal transvaginal ultrasound cervical length screening program in women at low risk for preterm delivery is associated with a reduction in the frequency of preterm birth.

OBJECTIVE: To test the hypothesis that the introduction of a midtrimester universal transvaginal ultrasound cervical length screening program in asymptomatic singleton pregnancies without prior preterm delivery would reduce the rate of preterm birth at <37 weeks of gestation.

STUDY DESIGN: This study was a multicenter nonblinded randomized trial of screening of asymptomatic singleton pregnancies without prior spontaneous preterm birth, who were randomized to either cervical length screening program (ie, intervention group) or no screening (ie, control group). Participants were randomized at the time of their routine anatomy scan between 18 0/7 and 23 6/7 weeks of gestation. Women randomized in the screening group received cervical length measurement. Those who were found to have cervical length ≤25 mm were offered 200 mg vaginal progesterone daily along with cervical pessary. The primary outcome was preterm birth at <37 weeks. The risk of primary outcome was quantified by the relative risk with 95% confidence interval, and was based on the intention-to-screen principle.

RESULTS: A total of 1334 asymptomatic women with singleton pregnancies and without prior preterm birth, were included in the trial. Out of the 675 women randomized in the transvaginal ultrasound cervical length screening group, 13 (1.9%) were found to have transvaginal ultrasound cervical length ≤25 mm during the screening. Preterm birth at <37 weeks of gestation occurred in 48 women in the transvaginal ultrasound cervical length screening group (7.5%), and 54 women in the control group (8.7%) (relative risk, 0.86; 95% confidence interval, 0.59–1.25). Women randomized in the transvaginal ultrasound cervical length screening group had no significant differences in the incidence of preterm birth at less than 34, 32, 30, 28, and 24 weeks of gestation.

CONCLUSION: The introduction of a universal transvaginal ultrasound cervical length screening program at 18 0/6 to 23 6/7 weeks of gestation in singleton pregnancies without prior spontaneous preterm birth, with treatment for those with cervical length ≤25 mm, did not result in significant lower incidence of preterm delivery than the incidence without the screening program.

Key words: cerclage, NICU, pessary, prematurity, preterm birth, progesterone, screening

Introduction

Prematurity is a major cause of perinatal morbidity and mortality.[1] Worldwide, about 15 million babies are born too soon every year, causing 1.1 million deaths, as well as short-term and long-term disability in the survivors.[2,3]

Different strategies have been studied for prevention of preterm birth, including progesterone, cerclage, and cervical pessary.[4–9] Most successful effort to reduce the incidence of preterm delivery have focused on women with risk factors, such as prior preterm birth.[9] However, most preterm deliveries occur in women who have no such history.[1,3] In singleton gestations without prior preterm birth but with short transvaginal ultrasound (TVU) cervical length (CL) the evidence from randomized trials and meta-analyses supports the use of vaginal progesterone,[4,5] whereas evidence on cervical pessary are still unclear.[7] Based on these data, TVU CL at around 18 to 23 weeks of gestation has been proposed for all singleton gestations without prior preterm birth as a universal screening method to identify women at risk of preterm delivery at an early stage.[10] However, the incidence of a short cervix a in low-risk population, such as singletons without prior preterm birth, has been reported to be low, about 1% to 2%, or less,[5,10] and therefore the benefit of a universal screening program is controversial.[10–13]

Several observational studies aimed to examine whether the introduction of such screening was associated with a reduction in preterm birth rate.[11–20] Son et al[11] In a retrospective study concluded that TVU CL screening was associated with a reduction in the frequency of preterm delivery; whereas a large observational study of nulliparous women with singleton pregnancies, by Esplin et al,[13] showed that quantitative vaginal fetal fibronectin and serial TVU CL had low predictive accuracy for preterm delivery, not supporting the routine use of these tests in such subset of women. Despite the conflicting data, no randomized trials of screening have been undertaken so far.

Objective

We aimed to test the hypothesis that the introduction of a midtrimester universal TVU CL screening program in

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AJOG MFM at a Glance

Why was this study conducted?

This study aimed to test the hypothesis that the introduction of a second trimester universal transvaginal ultrasound cervical length (TVU CL) screening program in asymptomatic singleton pregnancies without prior preterm delivery would reduce the rate of preterm birth at less than 37 weeks of gestation.

Key findings

Preterm birth at less than 37 weeks of gestation occurred in 48 women in the TVU CL screening group (7.5%), and 54 women in the control group (8.7%) (relative risk, 0.86; 95% confidence interval, 0.59−1.25). Women randomized in the TVU CL screening group had no significant differences in the incidence of preterm birth at less than 34, 32, 30, 28, and 24 weeks of gestation.

What does this add to what is known?

The introduction of a universal ultrasound cervical length screening program at 18 0/6 to 23 6/7 weeks of gestation in singleton pregnancies without a prior preterm birth, with treatment for those with cervical length ≤25 mm, did not result in significant lower incidence of preterm delivery than the incidence without the screening program.

asymptomatic singleton pregnancies without prior spontaneous preterm delivery would reduce the rate of preterm birth at less than 37 weeks of gestation.

Materials and Methods

Study design and participants

This study was a multicenter nonblinded randomized trial of asymptomatic singleton pregnancies without prior spontaneous preterm birth conducted in 2 centers in Italy (University of Naples Federico II and University of Campania Luigi Vanvitelli). The study was conducted from July 2018 to December 2022. The trial was approved by the local ethics committee at each participating center. All participants in the trial provided written informed consent. The trial protocol is available in the Supplemental Figure.

All patients with singleton gestations without prior spontaneous preterm birth, defined as spontaneous preterm delivery between 16 0/7 and 36 6/7 weeks of gestation, were eligible for randomization. Exclusion criteria were as follows: multiple pregnancies; spontaneous preterm delivery in a prior pregnancy; rupture of membranes at the time of randomization; known major fetal structural or chromosomal abnormality; symptoms of preterm labor or miscarriage (eg, low back pain, abdominal contractions) at the time of randomization; and cerclage or pessary in situ, or vaginal bleeding, at the time of randomization.

Participants were randomized to either TVU CL screening program (ie, intervention group) or no screening (ie, control group). Women were approached and consented at the time of their routine second trimester scan between 18 0/7 and 23 6/7 weeks of gestation, after the anatomy scan was completed and major fetal abnormalities ruled out. Gestational age was judged from the menstrual history and confirmed by measurement of fetal crown-rump length at a first trimester scan.

Randomization and masking

After written informed consented was obtained from the eligible participants, the women were randomly allocated to either the TVU CL screening or control group. The trial coordinator did not have access to the randomization sequence. The study was open label because of the nature of the intervention; however, the data analysts were blinded to the allocated treatment group.

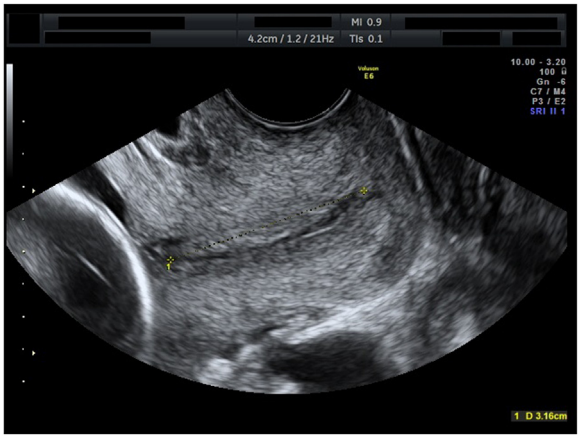
Interventions

The women randomized in the TVU CL screening group were asked to empty the bladder, undress from the waist down and to lie on an examination bed. The cervix was measured by operators with certification of competence in the technique (Fetal Medicine Foundation Certificate of Competence in Cervical Assessment). The length of the cervix was measured with a transvaginal real-time ultrasound probe placed in the anterior fornix of the vaginal. Endocervical canal length was measured as the distance between the internal and external os, by using a straight line with calipers placed at the notches made by the internal os and external os (Figure 1).[17−19] Three anatomic landmarks defined the appropriate sagittal view: the internal os, the external os, and the endocervical canal. The image was enlarged while visualizing the 3 landmarks simultaneously. This procedure was repeated 3 times. After a baseline TVU CL was measured, fundal pressure was applied for 30 seconds as a provocative maneuver. TVU CL was measured during and after the fundal pressure. Only the shortest TVU CL measurement was recorded.[18]

Patients in the TVU CL screening group, who were found to have TVU CL ≤25 mm were offered prophylactic therapy with daily 200 mg micronized natural vaginal progesterone capsules.[4,5] In this subset of women, cervical pessary was also offered.[20] Those who were found to have TVU CL ≤5 mm were offered a speculum examination. If the membranes were visible or cervical dilatation was ≥1.5 cm, physical examination-indicated cerclage,[21] along with vaginal progesterone[4] was offered (Figure 2). Cervical cerclage was performed according to the McDonald technique, with the use of perioperative indomethacin and antibiotic administration. Cerclage and pessary were removed at 36 weeks, or earlier if clinically indicated.[20,22]

Patients with TVU CL between 25.1 mm and 29.9 mm were asked to return for 1 follow-up CL measurement after 7 days; if TVU CL was ≤25 mm on follow-up ultrasonogram, vaginal progesterone, along with cervical pessary, was prescribed.[10] If the TVU CL was >25 mm no further follow-up was recommended (Figure 2).

FIGURE 1
Transvaginal ultrasound image of a long cervix



The internal and external os are visible, along with the entire endocervical canal. Endocervical canal length is measured as the distance between the internal and external os, by using a straight line with calipers placed at the notches made by the internal os and external os.

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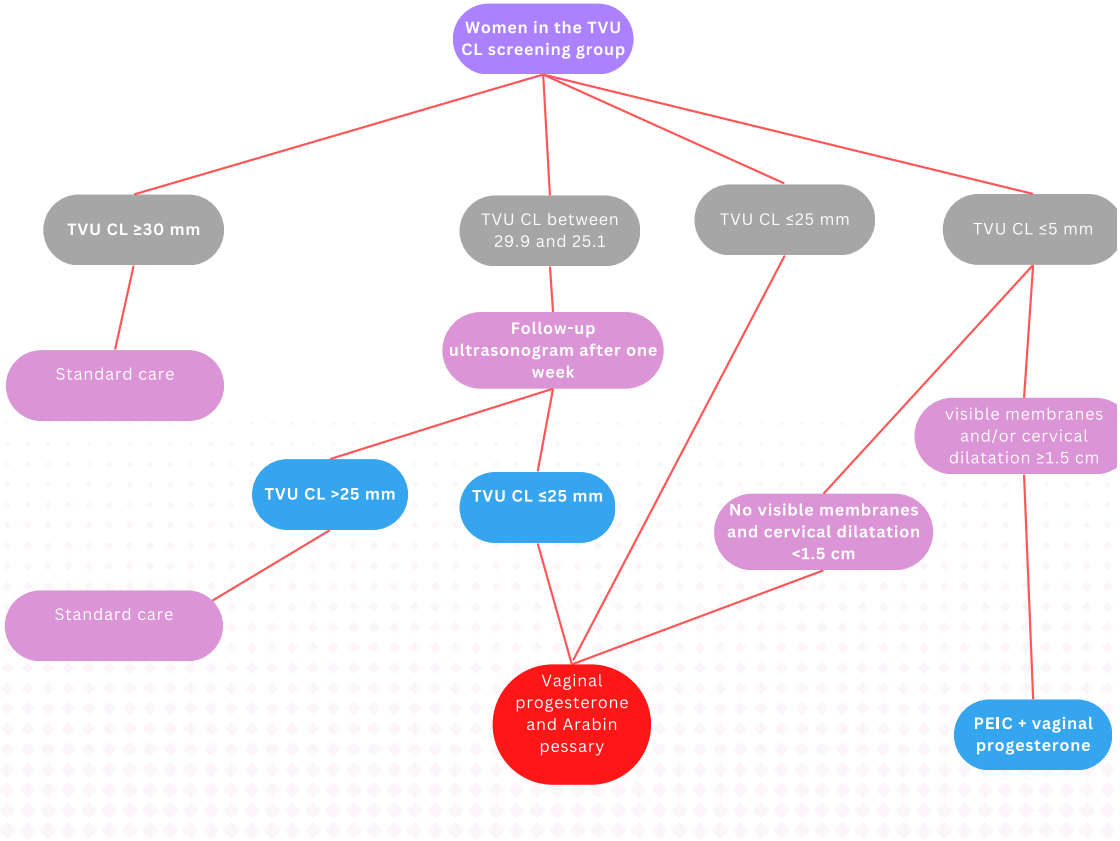
Primary and secondary outcomes

The primary outcome was preterm birth at less than 37 weeks of gestation. The prespecified secondary outcomes were preterm birth at less than 34, 32, 30, 28, and 24 weeks; and neonatal outcomes, including birthweight, admission to neonatal intensive care unit, neonatal death (death of a live-born baby within the first 28 days of life); perinatal death (either intrauterine fetal death or neonatal mortality); and a composite of adverse perinatal outcome (defined as at least 1 of the following: necrotizing enterocolitis, intraventricular hemorrhage grade 3 or higher, respiratory distress syndrome, bronchopulmonary dysplasia, retinopathy of prematurity requiring therapy, blood-culture proven sepsis, and neonatal death).

FIGURE 2
Management of women in the transvaginal ultrasound screening group



PEIC, physical examination-indicated cerclage; *TVU CL*, transvaginal ultrasound cervical length.

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Sample size calculation

Calculation of the sample size was based on the following considerations: an incidence of preterm birth <37 weeks in women with singleton gestations without prior spontaneous preterm birth of 6.7%,[11] and decrease in preterm birth by 50%[20] by the introduction of the TVU CL screening and treatment with vaginal progesterone and pessary for patients with short cervix.[4,20] We determined that a sample size of 1334 patients would provide a statistical power of 80% with a 2-sided alpha level of .05.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) v. 19.0 (IBM Inc., Armonk, NY). Data are shown as mean±standard deviation (SD), or as number (percentage). Univariate comparisons of dichotomous data were performed with the use of the chi-square test with continuity correction. Comparisons between groups were performed with the use of the *t* test to test group means with SD by assuming equal within-group variances.

The primary analysis was an intention—to-treat comparison of the treatment assigned at randomization. The effect of the TVU CL screening on the cumulative incidence of each outcome was quantified as the relative risk (RR) with 95% confidence interval (CI).

Results

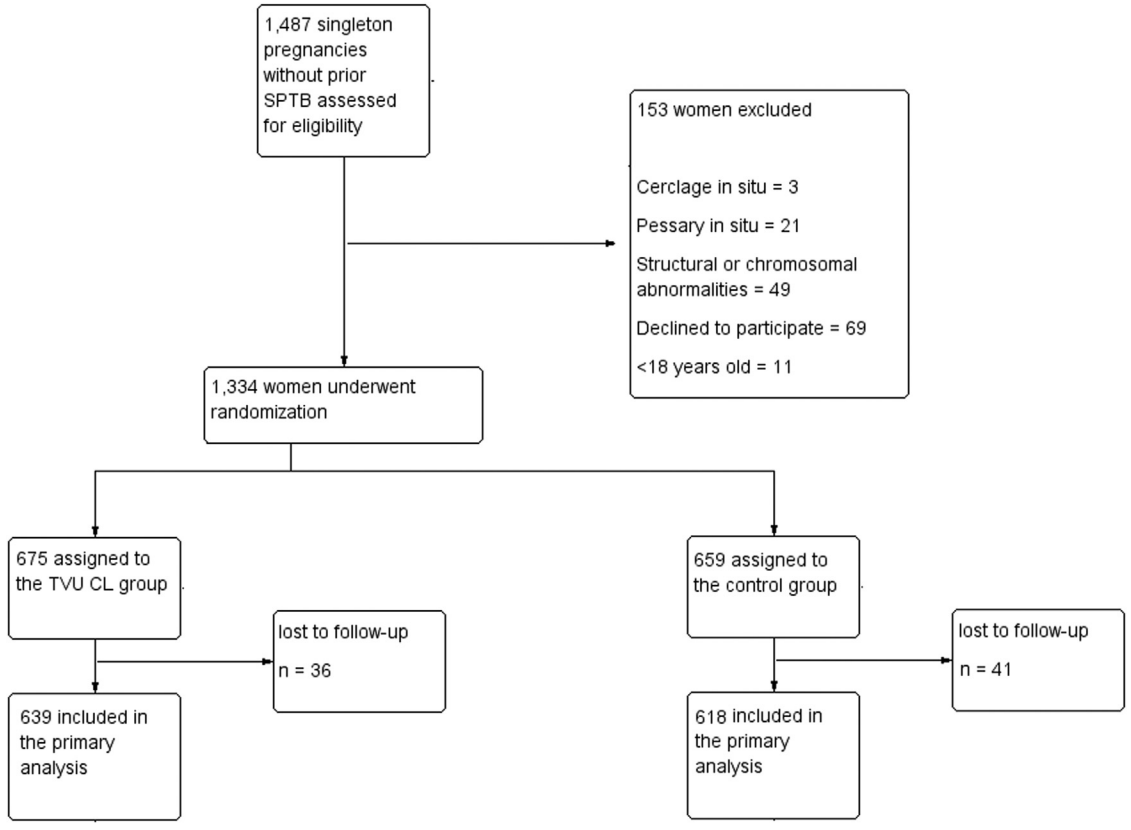
Trial population

During the study period, 1334 asymptomatic women with singleton pregnancies without prior spontaneous preterm birth at 18 0/6 to 23 6/7 weeks of gestation agreed to take part in the study, underwent randomization, and were enrolled in the trial. Of these, 675 (50.6%) were randomized to the TVU CL screening group, and 659 (49.4%) to the control group. Seventy-seven were lost to follow-up; therefore, primary and secondary outcomes were available for 1257 of 1334 (94.2%) women (Figure 3).

In Table 1, we show the baseline demographic and clinical characteristics for each group. No significant differences between the TVU CL screening group and the control group were reported. The mean gestational age at randomization was about 20.7 weeks in both groups (Table 1).

Out of the 675 women randomized in the TVU CL screening group, 636 (94.2%) had TVU CL ≥30 mm, and 13 (1.9%) were found to have TVU CL

FIGURE 3
CONSORT Study flow-chart



TVU CL, transvaginal ultrasound cervical length.

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TABLE 1
Characteristics of the included women

Characteristics	TVU CL screening n=675	Control group n=659
Age, y (mean±SD)	31.6±5.5	32.1±5.5
Ethnicity: Caucasian, n (%)	571 (84.6%)	554 (84.1%)
BMI, kg/m^2 (mean±SD)	25.8±5.3	25.4±5.3
Smoking, n (%)	70 (10.4%)	62 (9.4%)
Nulliparous, n (%)	450 (66.7%)	446 (67.7%)
GA at randomization, wk (mean±SD)	20.7±0.8	20.7±0.8
Chronic hypertension, n (%)	32 (4.7%)	24 (3.6%)
Pregestational DM, n (%)	12 (1.8%)	13 (2.0%)
Cold knife conization	8 (1.2%)	3 (0.5%)
LEEP	6 (0.9%)	4 (0.6%)
Lost to follow-up,[a] n (%)	36 (5.3%)	41 (6.2%)

Data are presented as number (percentage) or as mean±SD.

BMI, body mass index; *DM*, diabetes mellitus; *GA*, gestational age; *LLEP*, loop electrosurgical excision procedure; *SD*, standard deviation; *TVU CL*, transvaginal ultrasound cervical length.

[a] For the primary outcome.

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≤25 mm during the screening. All of them received vaginal progesterone, and 11 of 13 received cervical pessary (Supplemental Table 1). One with CL of 22 mm refused the pessary; and 1 with CL of 4 mm had cervical dilatation ≥1.5 cm at speculum examination and received transvaginal cerclage along with vaginal progesterone. Of the women, 26 (1.9%) had TVU CL between 25.1 mm and 29.9 mm. All of them had repeated scan in 1 week. Twenty-four of 26 had TVU CL >25 at the follow-up scan; 1 had TVU CL of 24 mm and received vaginal progesterone; and 1 had TVU CL of 5 mm with cervical dilatation ≥1.5 cm and received cervical cerclage, along with vaginal progesterone (Supplemental Table 1; Table 2). In the control group, 1 woman underwent placement of cervical cerclage because of the incidental finding of cervical dilation on physical examination after randomization.

TABLE 2
Cervical length measurements (in mm) in the transvaginal ultrasound screening group

TVU CL screening N=675	
≥30	636 (94.2%)
<30 and >25	26 (3.9%)
≤25	13 (1.9%)
≤20	7 (1.0%)
≤15	5 (0.7%)
≤10	3 (0.4%)
≤5	1 (0.1%)
1 week ultrasound follow-up scan N=26	
>25	24 (92.3%)
≤25	2 (7.7%)
≤5	1 (3.8%)

Data are presented as number (percentage).

TVU CL, transvaginal ultrasound cervical length.

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Primary outcome

Preterm birth at less than 37 weeks of gestation occurred in 48 patients in the TVU CL screening group (7.5%), and 54 women in the control group (8.7%) (RR, 0.86; 95% CI, 0.59−1.25) (Table 3).

Secondary outcomes

Patients randomized in the TVU CL screening group had no significant differences in the incidence of preterm birth at less than 34, 32, 30, 28, and 24 weeks of gestation (Table 3, Supplemental Table 2). Perinatal outcomes were also not different between the 2 groups (Table 3).

Adverse events

There were no cases of serious vaginal trauma or adverse events during insertion or removal of the transvaginal probe. In the TVU CL screening group, 11 women (1.6%) reported pelvic pain, and 34 women (5.0%) reported pelvic discomfort. No women had vaginal bleeding or spotting during or soon after the ultrasound scan (Supplemental Table 3).

Discussion

Principal findings

This randomized trial of screening aimed to test the hypothesis that the introduction of a midtrimester universal TVU CL screening program in asymptomatic singleton pregnancies without prior preterm delivery would reduce the

TABLE 3
Maternal and perinatal outcomes

Outcomes	TVU CL screening n=639	Control group n=618	RR or MD (95% CI)	*P* value
PTB <37 wk[a]	48 (7.5%)	54 (8.7%)	0.86 (0.59–1.25)	.43
PTB <34 wk	14 (2.2%)	14 (2.3%)	0.97 (0.46–2.01)	.93
PTB <32 wk	9 (1.4%)	10 (1.6%)	0.87 (0.36–2.13)	.76
PTB <30 wk	6 (0.9%)	7 (1.1%)	0.83 (0.28–2.45)	.72
PTB <28 wk	3 (0.5%)	5 (0.8%)	0.58 (0.14–2.42)	.45
PTB <24 wk	0	2 (0.3%)	0.19 (0.01–4.02)	.29
Threatened PTL	28 (4.4%)	37 (6.0%)	0.73 (0.45–1.18)	.20
Birth weight (g)	3239±550	3208±572	0.72 (0.50–1.05)	.09
NICU	44 (6.9%)	59 (9.5%)	0.72 (0.50–1.05)	.09
Neonatal death	3 (0.5%)	4 (0.6%)	0.73 (0.16–3.23)	.67
Intrauterine fetal death	1 (0.2%)	1 (0.2%)	0.97 (0.06–15.43)	.98
Second trimester pregnancy loss[b]	0	1 (0.2%)[b]	0.32 (0.01–7.90)	.49
Composite perinatal outcome[c]	19 (3.0%)	26 (4.2%)	0.71 (0.40–1.26)	.24
NEC	0	1 (0.2%)	0.32 (0.01–7.90)	.49
IVG grade 3 o 4	1 (0.2%)	2 (0.3%)	0.48 (0.04–5.32)	.55
RDS	12 (1.9%)	19 (3.1%)	0.61 (0.30–1.25)	.18
BPD	1 (0.2%)	3 (0.5%)	0.32 (0.03–3.09)	.33
ROP	0	3 (0.5%)	0.14 (0.01–2.67)	.19
Sepsis	6 (0.9%)	9 (1.4%)	0.64 (0.23–1.80)	.40

Data are presented as number (percentage) or as mean±standard deviation.

BPD, bronchopulmonary dysplasia; *CI*, confidence interval; *GA*, gestational age; *IVH*, intraventricular hemorrhage; *MD*, mean difference; *NEC*, necrotizing enterocolitis; *NICU*, neonatal intensive care unit; *PTB*, preterm birth; *PTL*, preterm labor; *RDS*, respiratory distress syndrome; *ROP*, retinopathy of prematurity requiring therapy; *RR*, relative risk.

[a] Primary outcome; [b] Due to cervical insufficiency; [c] Composite perinatal outcome, including at least 1 of the following: NEC, IVH grade 3 or 4, RDS, BPD, ROP, blood-culture proven sepsis, or neonatal death.

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rate of preterm birth at less than 37 weeks of gestation. The trial protocol included treatment for women with TVU CL ≤25 mm, repeated ultrasound after 1 week for those with TVU CL between 26 mm and 29 mm, and standard care for those ≥30 mm. We found no significant benefits associated with a policy of universal screening. However, a nonsignificant decrease by 14% and by 27% were found for preterm birth, and neonatal death, respectively.

Strengths and limitations

The major limitation of our trial was the open-label study design. This limitation could have affected medical decision-making, such as the decision to perform physical examination to rule out acute cervical insufficiency in the control group.

The rate of preterm birth in both the control (8.7%) and the intervention group (7.5%) was higher than expected (6.7%).[11] Sample size was based on an expected 50% reduction in preterm birth rate[20] based on TVU CL, and subsequent treatment with pessary and progesterone. However, our data showed that screening was associated with a nonsignificant 14% reduction from 8.7% to 7.5% (RR, 0.86). This may have led to a type II error and need for a larger sample size. Based on these data, a sample size of 16228 participants (8114 for each group) would provide a statistical power of 80% with a 2-sided alpha level of .05. Therefore, this trial was underpowered for the primary outcome.

Women in the TVU CL group received treatment in case of short cervix. Along with vaginal progesterone, women with short cervix were also offered cervical pessary.[20] Use of cervical pessary in this subset of women is not currently offered routinely.[23] This issue raises the question of the external generalizability of the findings in the countries where cervical pessary is not recommended, for example, in the United States.[24]

Unlike previous trials aiming to reduce the risk of preterm birth with therapy such as cerclage, pessary, progesterone, or vitamin supplementations compared to no such therapy or placebo,[5–9,25–28] we studied in a randomized trial a screening program based on TVU CL measurement at the time of the anatomy scan. A screening trial aims at finding new ways to detect and diagnose medical conditions at an early stage in asymptomatic patients.

Our protocol for women who were found to be positive with the screening test included vaginal progesterone and cervical pessary for those with TVU CL ≤25 mm, and cerclage for those with visible membranes or cervical dilatation ≥1.5 cm at speculum exam.

To our knowledge, this may be the first randomized trial investigating the effect of a universal TVU CL screening program in asymptomatic singleton gestations. Previous trials on TVU CL have studied different populations, including symptomatic singletons with preterm labor,[29] or twin pregnancies.[30] These populations represent less than 10% of all pregnant women, and the vast minority of all preterm deliveries.[1] Previous nonrandomized cohort studies aimed to examine whether the introduction of a policy of universal TVU CL screening in singleton pregnancies without a history of spontaneous preterm birth in a prior pregnancy was associated with a reduction in the preterm birth rate.[11,15] However, these

studies are limited by the retrospective nonrandomized approach, the lack of protocol for women who were found to be positive with the screening test, and provided conflicting results.

In our study, about 2% of the women screened were found to be positive with the screening test, that is, They were found to have TVU CL ≤25 mm. This rate is slightly higher than the rate found in previous studies.[11−13,15] This may be explained by the different characteristics of the women studied, as well as by the fact that nonrandomized studies can be influenced by selection bias. Indeed, our rate of short TVU CL is similar to the rate found in randomized trials evaluating vaginal progesterone or cervical pessary for a short cervix.[5,20,31−35] Moreover, in previous studies, women with TVU CL between 25.1 mm and 29.9 mm were not routinely offered follow-up ultrasonogram.[11−13,15] These women can still be at high risk of preterm birth in case of shortened TVU CL.[32] In our cohort 1.9% of the enrolled women had TVU CL between 25.1 mm and 29.9 mm (n=26). Of them 2 of 26 (7.7%) experienced cervical shortening of ≤25 mm. Boelig et al[36] Aimed to determine the utility of follow-up cervical length screening in otherwise low-risk women with singleton pregnancies with a midtrimester cervical length measurement of 26 mm to 29 mm through the assessment of the rate of short cervix (≤25 mm) on follow-up ultrasound and subsequent delivery outcomes. In their 2-year retrospective cohort, approximately 15% of women with a midtrimester CL measurement of 26mm to 29 mm experienced cervical shortening of ≤25 mm before 24 weeks of gestation, and had significantly higher preterm delivery than those with initial cervical length of ≥30 mm.[36]

Results in the context of what is known

A meta-analysis of 5 trials showed that the administration of vaginal progesterone to asymptomatic low risk singleton gestations with a midtrimester TVU CL ≤25 mm reduces the risk of preterm birth and neonatal morbidity and mortality.[5] This evidence has generated controversy regarding universal TVU CL screening for preterm birth prevention in a low-risk population.

Given the current controversy and the lack of randomized trials, national organizations do not currently recommend universal TVU CL screening in this subset of women. The American College of Obstetricians and Gynecologists,[33] and The Royal College of Obstetricians and Gynecologists along with the National Institute for Health and Care Excellence,[34] made no recommendation on TVU CL screening. Controversially, The Society for Maternal Fetal Medicine recommends routine TVU CL screening for women with singleton pregnancy and prior preterm birth, with serial assessment of the cervix every 1 or 2 weeks from 16 weeks until 24 weeks of gestation[10]; but stated that the issue of universal TVU CL screening in women without prior preterm birth remains a subject of debate, and therefore cannot yet be universally mandated.[10] The European Association of Perinatal Medicine,[35] affirmed that singleton gestations with prior spontaneous preterm birth may be monitored safely with a policy of TVU CL screening as compared with a policy of routine history-indicated cerclage, but acknowledge the lack of strong data on TVU CL screening in women with no prior preterm birth.

Clinical implications

Our trial provided evidence that the introduction of a screening program based on TVU CL measurement at 18 0/6 to 23 6/7 weeks of gestation, along with treatment for those with short CL, does not reduce the incidence of preterm birth. The lack of benefit may come from the low rate of short cervix in the low-risk population (less than 2%), and <0.5% rate of very short cervix (Table 2). In addition, the nonsignificant trend for benefit for the primary outcome (RR, 0.86; Table 3), and for the composite perinatal outcome (RR, 0.71; Table 3) raises the question of the statistical power of the study, and the need for larger sample sizes in future trials. Based upon 27% decrease in neonatal death, about 5000 babies lives would be saved every year, in a countries, such as the United States with 3.66 million births per year,[1] and rate of neonatal death of 5.6 infant per 1000 births, corresponding with 20,538 infant deaths in the 2022.[37] Our trial also showed a trend for benefit in reduction of threatened preterm labor (PTL) by 27%. Threatened preterm labor is a complication of pregnancy usually associated with significant cost and inpatient admission.[38−41]

Conclusions

In summary, the introduction of a universal TVU CL screening program at 18 0/6 to 23 6/7 weeks of gestation in asymptomatic singleton pregnancies without a history of spontaneous preterm birth, with treatment for those with TVU CL ≤25 mm, did not result in significant lower incidence of preterm birth than the incidence without the screening program. Given the nonsignificant benefits associated with such screening, future larger multicenter trials are needed. ■

CRediT authorship contribution statement

Gabriele Saccone: Writing − review & editing, Writing − original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Giuseppe Maria Maruotti:** Writing − review & editing, Investigation. **Maddalena Morlando:** Writing − review & editing, Investigation. **Silvia Visentin:** Writing − review & editing. **Carlo De Angelis:** Writing − review & editing. **Laura Sarno:** Writing − review & editing, Investigation, Methodology. **Erich Cosmi:** Writing − review & editing. **Francesco Torcia:** Writing − review & editing. **Flavia Costanzi:** Writing − review & editing. **Elisabetta Gragnano:** Writing − review & editing. **Giorgia Bartolini:** Writing − review & editing. **Marco La Verde:** Writing − review & editing, Investigation. **Felice Borelli:** Writing − review & editing, Investigation, Methodology, Investigation, Formal analysis, Data curation. **Fabiana Savoia:** Writing − review & editing, Investigation. **Antonio Schiattarella:** Writing − review &

editing, Investigation. **Pasquale De Franciscis:** Writing – review & editing, Investigation. **Mariavittoria Locci:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Maurizio Guida:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2023.101267.

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