Prediction of Preterm Birth in Multiple Pregnancies: Development of a Multivariable Model Including Cervical Length Measurement at 16 to 21 Weeks' Gestation

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Abstract

Objective: To develop a multivariable prognostic model for the risk of preterm delivery in women with multiple pregnancy that includes cervical length measurement at 16 to 21 weeks' gestation and other variables.

Methods: We used data from a previous randomized trial. We assessed the association between maternal and pregnancy characteristics including cervical length measurement at 16 to 21 weeks' gestation and time to delivery using multivariable Cox regression modelling. Performance of the final model was assessed for the outcomes of preterm and very preterm delivery using calibration and discrimination measures.

Results: We studied 507 women, of whom 270 (53%) delivered < 37 weeks (preterm) and 66 (13%) < 32 weeks (very preterm). Women with cervical length < 30 mm delivered more often preterm (hazard ratio 1.9; 95% CI 0.7 to 4.8). Other independently contributing predictors were previous preterm delivery, monochorionicity, smoking, educational level, and triplet pregnancy. Prediction models for preterm and very preterm delivery had a c-index of 0.68 (95% CI 0.63 to 0.72) and 0.68 (95% CI 0.62 to 0.75), respectively, and showed good calibration.

Key Words: Cervical length measurement, multiple pregnancy, preterm birth, prediction

Competing Interests: None declared.

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Conclusion: In women with a multiple pregnancy, the risk of preterm delivery can be assessed with a multivariable model incorporating cervical length and other predictors.

Résumé

Objectif : Élaborer un modèle pronostique multivarié (comportant la mesure de la longueur cervicale à 16 - 21 semaines de gestation et d'autres variables) pour ce qui est du risque d'accouchement préterme chez les femmes connaissant une grossesse multiple.

Méthodes : Nous avons utilisé les données issues d'un essai randomisé précédent. Nous avons évalué l'association entre les caractéristiques maternelles et de grossesse (dont la mesure de la longueur cervicale à 16 - 21 semaines de gestation et le délai avant l'accouchement) au moyen du modèle de régression multivariée de Cox. Le rendement du modèle final a été évalué en fonction de critères d'évaluation traitant du moment de l'accouchement (préterme et très préterme) au moyen de mesures d'étalonnage et de discrimination.

Résultats : Nous avons étudié 507 femmes, dont 270 (53 %) ont accouché < 37 semaines (préterme) et 66 (13 %) < 32 semaines (très préterme). Les femmes qui présentaient une longueur cervicale < 30 mm ont plus souvent connu un accouchement préterme (densité de l'incidence, 1,9; IC à 95 %, 0,7 - 4,8). Parmi les autres facteurs prédictifs indépendants, on trouvait les antécédents d'accouchement préterme, la monochorionicité, le tabagisme, le niveau de scolarité et la présence d'une grossesse triple. Les modèles prédictifs pour ce qui est des accouchements préterme et très préterme comptaient un indice C de 0,68 (IC à 95 %, 0,63 - 0,72) et de 0,68 (IC à 95 %, 0,62 - 0,75), respectivement, et présentaient un bon étalonnage.

Conclusion : Chez les femmes qui connaissent une grossesse multiple, le risque d'accouchement préterme peut être évalué au moyen d'un modèle multivarié comportant la mesure de la longueur cervicale et d'autres facteurs prédictifs.

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INTRODUCTION

Preterm birth is one of the major causes of neonatal morbidity and mortality, and occurs more often in multiple than in singleton pregnancies.[1] However, at present individual risk prediction for preterm birth in multiple pregnancies is not applied, thus hampering development, evaluation, and implementation of preventive strategies.

In previous studies, mid-term cervical length (CL) was shown to be a strong predictor for preterm birth in both singleton[2] and multiple pregnancies.[3,4] In women with a singleton pregnancy who had previous preterm delivery, CL measured at 16 weeks' gestation is a good predictor for the risk of preterm birth.[5] Preventive strategies, such as cervical cerclage and administration of progesterone, are effective in the prevention of preterm birth in these singleton pregnancies and can also be introduced at this gestational age.[6,7]

In a systematic review, Condé-Agudelo et al. showed that transvaginal sonographic CL measurement at 20 to 24 weeks' gestation is a good predictor of spontaneous preterm birth in asymptomatic women with twin pregnancies. However, the predictive value of CL measured at a gestational age of 16 to 21 weeks in women with a multiple pregnancy has not been assessed extensively; only three studies, with different cut-off values, have been reported.[3]

In women with a multiple pregnancy, assessment of CL at 22 to 25 weeks is better than assessment at 18 to 21 weeks for predicting preterm delivery before 34 weeks,[8,9] and cervical shortening at a rate of > 2 mm/week between 18 and 25 weeks' gestation is a good predictor for spontaneous preterm birth.[8] However, potential interventions that prevent preterm birth, such as administration of progesterone, should preferably be started before 22 weeks.[6] Current studies of the prevention of preterm birth in women with a multiple pregnancy start interventions before 20 weeks.[10,11] To elucidate individual risk prediction of preterm birth in women with a multiple pregnancy before this time, we evaluated the predictive capacity of CL measurement at 16 to 21 weeks' gestation by developing a prediction model for time to delivery using readily available characteristics, including CL. Therefore, we used data from the AMPHIA trial, a multicentre trial of 17-α hydroxyprogesterone (17P) versus placebo in the prevention of preterm birth in women with multiple pregnancies.[10]

METHODS

We used data collected from the AMPHIA trial assessing the effectiveness of 17P in the prevention of preterm birth in women with a multiple pregnancy (Figure 1).[10] In that study, patients had been randomized to treatment with 17P or placebo at a gestational age of 15 to 19 weeks. Cervical length was measured at randomization or shortly afterwards, but before the start of medication. Unfortunately the AMPHIA protocol did not specify how to measure CL, but the Dutch College of Obstetrics and Gynaecology recommends measuring CL by transvaginal ultrasound in a sagittal view and with an empty maternal bladder, and we can assume that this was the method used.[12] Gestational age and chorionicity were determined at first trimester ultrasound scan.

Exclusion criteria in the AMPHIA trial were congenital abnormalities detected in one of the fetuses, twin-to-twin transfusion syndrome, intrauterine death of one of the fetuses, previous preterm birth under 34 weeks'