17th World Congress in Fetal Medicine

Fetal growth restriction prognosis: a competing risks model

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Objective

We studied the association of ultrasound indices with the different subtypes of FGR, namely severe and mild. We created modalities to discriminate and follow up this 2 conditions. A personalized competing risks approach is introduced.

Methods

FGR was diagnosed by one or more of the following criteria: Estimated Fetal Weight (EFW)<3rd centile, Fetal Abdominal Circumference (AC)<5 th centile, Umbilical artery pulsatility index (UA)>95 th, Middle cerebral artery pulsatility index (MCA)< 5 th centile, Cerebroplacental ratio (CPR) < 5 th centile and pregnancies dated by a first trimester scan. Only the first assessment of these FGR pregnancies was included in our analysis. The ultrasound parameters were converted to z-scores for the purpose of our analysis according to local standards. We studied the association between ultrasound indices and gestational age at delivery (GA-Delivery) and time from diagnosis to delivery (t) in both severe and mild FGR groups. A logit regression model was used to discriminate the FGR types. Finally a competing risks survival regression model was used to provide individualised prognosis. The competing risks were delivery due to severe FGR or delivery due to mild FGR.

Results

2382 pregnancies that were assessed at 24 to 40 weeks and fulfilled the abovementioned criteria were included in the analysis. Overall 7. 22% of FGRs were classified as severe form while the remaining belong to the mild form. The following parameters were lower in the severe FGR group vs the mild FGR group: zEFW (-2. 23 vs -0. 7 p, 0. 001), zBPD (Biparetial diameter--1. 25 vs -0. 29 p<0. 001), zAC (-1. 93 vs -0. 7 p, 0. 001), zFL (Femur lenght -1. 71 vs -0. 28 p<0. 001), zMCA (-1. 03 vs -0. 8 p=0. 0154), zCPR (-1. 3 vs -0. 9 p<0. 001). zUA was increased in the severe group compared to the mild group (1. 92 vs 0. 49 respectively, p<0. 001). In the mild FGR group zEFW (coef=0. 07, p, 0. 001), zBPD (coef=0. 08, p, 0. 001), zAC (coef=0. 06, p<0. 001), zFL (coef=0. 08, p<0. 001), zCPR (coef=0. 03, p=0. 005), were all positively associated with GA-Delivery. Interestingly zEFW (coef=0. 28, p, 0. 001), zBPD (coef=0. 17, p, 0. 001), zAC (coef=0. 23, p<0. 001), zFL (coef=0. 28, p<0. 001), zCPR (coef=0. 15, p=0. 005) had a steeper association with GA-Delivery in the severe FGR group. zMCA was not related to GA-Delivery in both FGR subtypes and in the whole study population (p=0. 7). Similar trends were observed in the association between ultrasound indices and time from diagnosis to delivery. zCPR, zEFW and gestational age at diagnosis (GA-Diagnosis) may predict 67. 4 % and 76. 2% of severe FGR for 10% and 20% false positive rates respectively (Area under the curve=0. 8417, logit model R2 =0. 31). A marginally but not significantly better model that includes zBPD, zAC, zFL, zUMB, zMCA and GA-Diagnosis identifies 68. 6% and 76. 7% of severe FGR (Area under the curve=0. 8530, logit model R2 =0. 34). A competing risk regression model that includes zCPR (subhazard ratio = 0. 52, p<0. 001), zEFW (subhazard ratio = 0. 48, p<0. 001) and GA-Diagnosis (subhazard ratio = 0. 68, p<0. 001) may provide an individualised prognostic survival curve for severe FGR.

Conclusion

Ultrasound indices already used for FGR diagnosis may be also used to discriminate severe and mild FGR. Ultrasound indices correlate with GA-Delivery and their separation from the average is higher for the severe FGR group. The competing risk model that we present promotes the concept of an individualised approach in managing FGR.