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Fetal growth restriction classification: a mixture model approach

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Objective

We aimed to classify pregnancies with fetal growth restriction (FGR) by modeling the distribution of gestational age at delivery (GA-Delivery) in relation to the gestational age at diagnosis (GA-Diagnosis). We examined the association of the proposed classification with fetal and neonatal outcome.

Methods

FGR was diagnosed by one or more of the following criteria: Estimated Fetal Weight<3rd centile, Fetal Abdominal Circumference <5 th centile, Umbilical artery pulsatility index>95 th, Middle cerebral artery pulsatility index < 5 th centile, Cerebroplacental ratio < 5 th centile and pregnancies dated by a first trimester scan. Only the first assessment of these FGR pregnancies was included in our analysis. We fitted a dynamic bivariate mixture of 2 Gaussian distributions model to describe the skewed GA-Delivery distribution in relation to GA-Diagnosis. To improve the fit of the model we allowed the proportion of each component to depend on GA-Diagnosis according to a logit regression model. We analyzed the data within a Bayesian framework. Markov chain Monte Carlo simulations implemented in OpenBugs were applied.

Results

2382 pregnancies that were assessed at 24 to 40 weeks and fulfilled the abovementioned criteria were included in the analysis. The distribution of GA-Delivery in relation to GA-Diagnosis was nearly uniform Gaussian for term diagnosed FGRs. However for FGR pregnancies diagnosed earlier the distribution of GA-Delivery was heavily skewed towards preterm birth. The earlier the diagnosis the more prominent the skewness. The heavy left tail of the GA-Delivery essentially constituted the one component of the mixture distribution. We modelled the proportion of the components as a function of GA-Diagnosis. The proportion of the term delivered pregnancies increased exponentially from 26% to 97% at 24 to 42 weeks according to a logit function. The intersection point of the 2 dynamic Gaussian distributions defined 2 forms of FGR fetuses. The first form (overall 172 out of 2382 cases, 7. 22%) had an mean of GA-Diagnosis 30. 06 (range 24 to 34. 71), mean of GA-Delivery 32. 92 (range 25. 4 to 36. 7) mean time from diagnosis to delivery (t) 2. 86 weeks (range 0 to 11. 4). The respective features for the second form (overall 2210 out of 2382 cases, 92. 78%) were: mean of GA-Diagnosis 32. 6 (range 24 to 40. 43), mean of GA-Delivery 38. 67 (range 34. 8 to 42. 14), mean time from diagnosis to delivery (t) 6. 02 weeks (range 0 to 14. 57). Intrauterine demise occurred in 2. 3% of the first form (severe FGR) and in the 0. 22% of the cases in the second form (mild FGR) (chi square, p<0. 001). Neonatal deaths occur in the 4. 6% of the severe form compared to 0. 09% of the mild form (chi square, p<0. 001). The mild form had significantly higher Apgar score and pH values and less admissions in the neonatal intensive care unit.

Conclusion

The classification that arises from the presented dynamic mixture model reduces the proportion of severe FGRs and correlates well with the fetal and the neonatal outcome. The flexibility of this model describes the overlapping features of the 2 FGR subtypes. The expected proportion of severe FGRs depends on gestational age at diagnosis.