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Fetal Movement Counting and Perinatal Mortality: A Systematic Review and Meta-analysis

The article by Bellussi et al in the February 2020 issue[1] caught my attention, because its conclusions run counter to decades of traditional teaching about educating pregnant women to be alert to fetal movement patterns. Additionally, all experienced clinicians can recall a small number of pregnancies rescued after an alert of decreased fetal movement by the mother. The authors have addressed some of the limitations of their analysis; namely, the exact nature and audit of fetal movement counting was variable among the studies, and ease of access to intervention was probably variable as well. Nevertheless, the conclusion that educating women regarding fetal movement was not associated with an improvement in pregnancy outcomes was startling.

Of course, this is not an observational analysis but one based on a variety of interventions, because this is the only ethical way to proceed. The salutary effect of these interventions cannot, therefore, be directly measured. One could interpret the significant increase in low 5-minute Apgar scores as a surrogate marker for a positive effect in the study group, thus trading morbidity for mortality. The price of this strategy is a modest increase in preterm births, induction of labor, and cesarean births.

A doubling of the study and control groups maintaining identical proportions of perinatal deaths, the CI of the risk ratio no longer touches 1.0 and the result is significant. Nearly 400,000 patients is not large enough of a group to study such a rare event. I can live with the potential of a 15% decrease in perinatal mortality.

Another large study of this issue seems unlikely. For the time being, it may be prudent to continue to educate pregnant women to observe fetal movement patterns. It may lead to an increase in obstetric interventions whose positive effects will be difficult to measure.

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In Reply:

We thank Dr. Porreco very much for his letter regarding our article in the February 2020 issue.[1] We agree with him that, in fact, our data should not run counter to current recommendations. In fact, the original conclusion of our study when we first submitted it was that instructing pregnant women on fetal movement counting in the second and third trimester is associated with a nonsignificant 8% decrease in perinatal mortality. We also stated that, although the 8% decrease in the incidence of perinatal mortality between the intervention and control groups was not statically significant, some could argue that it could be clinically significant. Globally, there are more than 5 million annual perinatal deaths, about 2.5 million stillbirths, and 2.5 million neonatal deaths.[2,3] Even if fetal movement counting could prevent just 10% of these deaths, that would mean that about 6,250 children would be saved from stillbirth or neonatal mortality every year, about 17 per day, in the world.

Indeed, one could interpret the significant increase in low 5-minute Apgar scores as a surrogate marker for a positive effect in the fetal movement counting group, thus trading morbidity for mortality. The price of maternal routine fetal movement counting is a modest increase in preterm births, induction of labor, and cesarean births. As Dr. Porreco states, it may be prudent to continue to educate pregnant women to observe fetal movement patterns; it may lead to an increase in obstetric interventions, but with positive effects in terms of an 8% decrease in perinatal mortality.

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Editor's Note: *The objective of the systematic review and meta-analysis by Bellussi et al was to assess the association of fetal movement counting with perinatal mortality. Dr. Berghella, in the response to Dr. Porreco's Letter to the Editor, is correct that the original version of the manuscript reported a "nonsignificant difference" of 8% in the rate of perinatal mortality among women randomized to fetal movement counting and that, in response to reviewer and editorial comment, the final article does not include language that suggested an improvement in perinatal mortality. The results of this meta-analysis and the primary contributing article do not reject the null hypothesis; in other words, there is no reduction in perinatal mortality. There were small increases in preterm birth, induction of labor, and cesarean births. Although we may all wish that this ubiquitous pregnancy intervention would decrease perinatal deaths, the data do not support this. Numeric differences are not the same as significant differences.*

Effects of Selective Exclusion of Patients on Preterm Birth Test Performance

The article by Boniface et al[1] in the December 2019 issue provides an overview of recent studies using emerging technologies to study preterm birth. However, it does not distinguish between research attempting to first discover a biomarker to predict an adverse pregnancy outcome and research designed to validate the clinical utility of a marker being made available for clinical decision making.

The nested case–control methodology, where cases are defined by an early gestational age cutoff and compared with a term control group, is a well-established approach. It is particularly suited for exploratory, discovery, and development work at the cutting edge where resources (both sample number and financial support) are often limited. We readily acknowledge that limiting the gestational age, creating a gap, will augment the perceived characteristics of putative markers. Boniface et al do not sufficiently point out to the reader that this is the intended point of this type of analysis. When attempting to sort through thousands of putative makers–the so-called "P>N problem," where the number of variables in a data set is much larger than the sample size–the nested case–control methodology is efficient and effective. This is particularly true in perinatal epidemiology, where cases defined at an earlier gestational age are more likely to be homogeneous with regard to pathogenesis. In this situation, the nested case–control methodology is more likely to bring out candidate markers that can then be explored in subsequent studies. The authors' simulation demonstrates this point nicely. Indeed, it is common practice in research to explore the tails of distributions, that is, abnormal compared with normal, in a binary fashion before narrowing to include where the gradient between the two actually switches. Few if any phenomena in biology are simply binary. A prospective trial with a sufficient sample size where the markers are tested commensurate with how they would be used in clinical practice (an ungapped analysis) is appropriate before a product is used for clinical decision making. However, the studies cited by the authors do not appear to reflect products in this stage of development (Weiner C, Zhou H, Cuckle H, Ramsey R, Egerman R, Dong Y. 321: FuturebirthTM- prediction of future preterm birth <33w and preeclampsia/eclampsia <34w by 16w using a novel test in asymptomatic women [abstract]. Am J Obstet Gynecol 2017;216:S196).[2–7] Instead, these publications represent an appropriate early stage in the identification and characterization of putative markers.

Five of the seven references cited by the authors represent markers that are in commercial development (Weiner C et al. Am J Obstet Gynecol 2017;216:S196.).[2,3,5,7] As such, they could represent potential competition for each other or any other company proposing the use of a biomarker for the prediction of preterm birth. Boniface et al may want to acknowledge this perspective as a consideration in their overall assessment and message to the reader.

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