A Mother and Child Reunion

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“Few subjects can be conceived calculated to attract…more serious thought and attention on the part of obstetricians, than the bearing of organic disease of the heart upon the condition of the pregnant, parturient, and lying-in woman….and yet scarcely a subject that borders on the mutual region occupied by the obstetric and the pure physician seems to have received less study from either the one or the other. The reason, no doubt, is partly due to the cramping effects of a too rigid specialism….But as every woman has not only a uterus and ovaries, but also a liver, heart, lungs, kidneys, etc....”

Angus Macdonald, 1878

*The Bearings of Chronic Disease of the Heart upon Pregnancy, Parturition, and Childbed*

Pioneering studies and clinical experience long ago identified the major risk factors for adverse pregnancy outcomes in women with congenital heart disease (CHD): functional status, pulmonary vascular disease, systemic ventricular dysfunction and cyanosis.\(^1\)\(^{-4}\) Additional insights have been provided by subsequent observational studies, population-based research and reports of pregnancy in new and evolving populations of women with CHD. These studies have validated and expanded upon earlier observations and provided critical quantitative tools to stratify risk.\(^5\)\(^{-7}\) They have not, however, fundamentally informed our understanding of why a subset of these women and their offspring suffer specific adverse outcomes. There is an increasingly well-described problem with no clear path towards a solution.

Pieper and colleagues present data from a prospective multi-center observational study of predictors of diverse adverse pregnancy outcomes among women with a wide range of congenital heart defects.\(^8\) This represents one of the largest, most detailed clinical and
physiologic studies of pregnancy in women with CHD. The authors introduce a fresh perspective to the topic with a focus on aspects of the physical nutritive bridge between mother and developing fetus, the uterine and umbilical arteries. It is a reflection of the state of interdisciplinary collaboration and communication that this investigation didn’t happen long ago, as the underlying concepts are shared between cardiology and obstetrics, as is the technology (Doppler ultrasound of blood flow in vessels). The authors present clear evidence, using widely applied clinical techniques and variables, that maternal cardiovascular disease adversely influences the uteroplacental circulation with attendant effects on offspring. While this finding may not be entirely unexpected, it is both original and important.

Demonstration of an association between maternal CHD offspring outcomes and readily measured markers of uteroplacental flow should facilitate new avenues of investigation.

Pregnancy for many women with CHD is generally classified as bearing high risk, but the absolute risk of unmanageable maternal clinical events during pregnancy is low for all but a few women with specific diagnoses (e.g., Eisenmenger syndrome). The risk of maternal death during childbirth is over 10-fold higher than in the general population but still on the order of 1-2 deaths per 1,000 deliveries. And while more than one third of pregnancies among CHD patients in the present study involved an offspring event, this high figure was in large part because of a broad definition of offspring event, which also encompassed almost one in five low risk pregnancies in healthy women managed by midwives. Given the low absolute risks, in order to provide adequate statistical power, many studies on pregnancy in CHD include a broad array of unrelated diagnoses such as aortic coarctation, Marfan syndrome and single ventricle Fontan physiology. This favors identification of ‘least common denominator’ maternal risk factors, as there is little reason to suspect that these diagnoses share cardiovascular pathophysiologic mechanisms related
to pregnancy outcome. Pending validation, Doppler measures of the uteroplacental circulation may serve as useful continuous outcome variables to provide additional power and allow more focused attention on smaller samples of populations with relatively homogenous pathophysiology. Further, changes in Doppler flow patterns may provide a way to assess the effect of any specific intervention (e.g., medication to improve vascular function in women with aortic coarctation) and abnormal Doppler flow may identify offspring at risk for subtle developmental effects of maternal CHD. Finally, uteroplacental Doppler findings may have implications for maternal cardiovascular health over the longer term. Since these variables are already commonly measured in clinical care, there are likely extensive existing clinical data for rapid retrospective validation of the present findings and additional investigations.

It is tempting to speculate on novel mechanisms, or at least consider new hypotheses, based on the results presented. For example, while extensive research has explored the relationship between the systemic maternal circulation including arterial vascular dynamics and uteroplacental function, there has been less attention to venous effects. The association between Doppler flow and variables expected to correspond to systemic venous pressure and flow (tricuspid annular plane systolic excursion, atrioventricular valve regurgitation) suggests that the role of venous hemodynamics deserves consideration.

It remains to be seen how these data may influence clinical management. Most of the pregnancies in question are already managed in collaborative care as “high risk” and fetal Doppler examination has an accepted role, as there is evidence that such assessment may improve care. Further study is required to determine whether this test should be applied or interpreted differently for women with CHD compared to how it is used in other types of high risk pregnancy. The data presented also suggest that normal Doppler flow should not be
considered entirely reassuring. The risk of an adverse offspring was almost 2-fold higher among women with an abnormal Doppler pattern, but consideration of absolute risks and pre/post-test probabilities suggests a more cautious interpretation. An adverse offspring outcome occurred in 18.6% of pregnancies among healthy women, compared with 35.4% for all women with CHD. The figure was ~27-30% for women with CHD and normal Doppler (negative likelihood ratio ~0.7), still distinctly higher than the frequency observed among healthy women and only marginally lower than women with CHD overall. Clinical implications of abnormal Doppler flow were similarly modest. The positive likelihood ratio was ~1.8, consistent with only a small increase in the likelihood of having an offspring event based on the results of this test.

If direct clinical and physiological research applications require further thought and investigation, the same cannot be said for a judgment on the significance of the productive close collaboration and cross-fertilization demonstrated between these investigators from distant sub-specialties. While directed towards obstetricians, the 150 year-old quotation above is as applicable to cardiologists, anesthesiologists and others who care for pregnant women with CHD. Developing greater understanding and comfort among cardiologists in thinking about fetal physiology is a critical step in better defining the links between maternal heart disease, fetal development and pregnancy outcomes. It is therefore fitting and encouraging that this manuscript, which predominantly reports on obstetric and offspring variables, is being disseminated in the cardiovascular literature.

Conflict of Interest Disclosures: None.

References:


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