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Editorial

Fontan pregnancy and the placenta: More information needed

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The survival of those born with a single ventricle has improved dramatically over the past 50 years, largely as a result of the widespread use of the Fontan operation and more recently refinements in staging of the palliative surgery pathway. As a result the average age of people with a Fontan circulation is increasing, [1] and many more women are entering their child bearing years. Despite a significant physical and psychosocial burden, many aspire to parenthood and this number will increase over the coming years.

The Fontan circulation is characterized by an elevated central venous pressure and a cardiac output that is restricted by limited preload and is low-normal or reduced at rest. Importantly there is a limited capacity to increase cardiac output in response to exercise and most likely also to the physiological stress of pregnancy. It is evident from a number of case series that pregnancy is associated with maternal complications, with a significant minority developing heart failure and arrhythmia. In addition postpartum hemorrhage is common. Maternal mortality is low in published reports, but given the paucity of data and the selection bias inherent in these types of studies, assessment of individual patient risk is challenging. Moreover the long term effect of pregnancy on the Fontan circulation is yet to be defined [2].

The Fontan pregnancy is associated with a high miscarriage rate (≥50%), and a considerable risk of perinatal morbidity and mortality, much of which relates to prematurity. Factors responsible for premature delivery are doubtless multifactorial and include induction for maternal or fetal health reasons, and premature rupture of membranes – the latter perhaps implicating functional or anatomic placental abnormalities [3]. Nevertheless, given the limited cardiac output reserve and elevated venous pressure inherent in the Fontan circulation, utero-placental insufficiency is likely to play an important role. Certainly, fetal growth restriction (FGR) is frequently reported. In a recent retrospective multicenter review, over 50% of newborns were small for gestational age with one third having a birthweight less than the 5th percentile. When compared to babies born to mothers with other forms of heart disease, those from a Fontan pregnancy had the lowest median gestational age-adjusted weight percentile [4].

Hence the article from Phillips and colleagues detailing a small number of pregnancies where pathological examination of the placenta was undertaken is of considerable interest [5]. Although non-consecutive, the authors state that there was no specific clinical or outcome bias associated with the request for pathological examination. Supporting this statement, the maternal and perinatal profile of the 13 pregnancies described is similar to that reported in larger case series: placental abruption, premature rupture of membranes and FGR occurred in a not insignificant minority. Only 2 pregnancies delivered at term, and the median birth weight was 2.2 kg. Nevertheless selection bias cannot be discounted, and the frequency of the placental abnormalities reported needs to be interpreted in that light. There was a considerable variation in placental weight, but the primary finding was of subchorionic fibrin deposition. Although patchy subchorionic fibrin deposition is frequently seen in the near-term and term placenta, the magnitude of deposition described in this publication appears to be outside the usual range. The authors speculate that excessive fibrin deposition may be due to venous stasis secondary to elevated venous resistance and hypothesize that this could impair fetal perfusion through vascular compression. Caution is needed when interpreting this finding. A degree of subchorionic fibrin deposition is frequently seen in placentas submitted for routine examination, and is generally considered a nonspecific finding. This is in contrast to peri- and inter-villous fibrin deposition that is known to be associated with utero-placental dysfunction and pre-eclampsia [6]. Moreover the understanding of the pathogenesis of placental abnormalities and their relation to outcome is limited [3]. The authors also report abnormal insertion of the fetal membrane, known as circummargination, in 4 of the 13 cases. Placentas with this pathology often show large blood-type fibrin depositions at the margin that are thought to arise as a consequence of antenatal hemorrhage and haematoma formation.. There may be an association with placental abruption and premature rupture of membranes. Villous hypoplasia, a finding associated with placental dysfunction, was reported in 4 cases, one of whom had preeclampsia.

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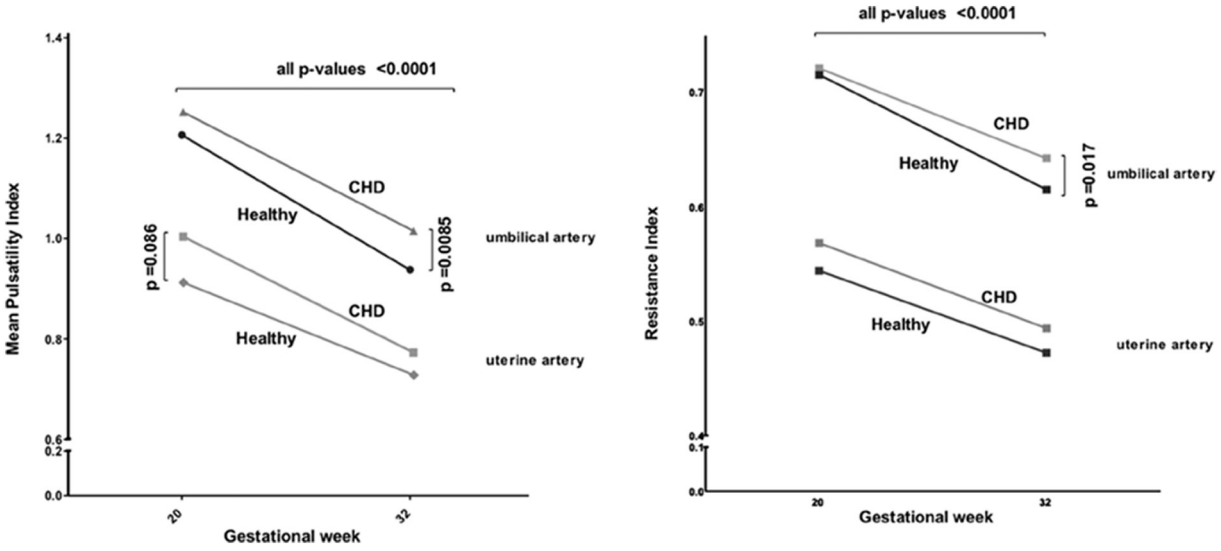

Fig. 1. Uteroplacental Doppler flow parameters: pulsatility index and resistance index of mean of right and left uterine artery and of umbilical artery at 20 and 32 weeks of pregnancy, in women with CHD and healthy women. Mean PI (left) and mean RI (right) differed significantly between 20 and 32 weeks, in both uterine and umbilical artery and in healthy controls and CHD patients (as represented by the horizontal line indicating all *P* values < 0.0001). Significant differences in separate analyses comparing groups at 20 weeks and at 32 weeks are indicated by vertical lines with *P* values. CHD indicates congenital heart disease; PI, pulsatility index; and RI, resistance index [9].
Reproduced with permission from: P. G. Pieper, A. Balci, J. G. Aarnoudse, M et al., Uteroplacental blood flow, cardiac function, and pregnancy outcome in women with congenital heart disease, Circulation. 128 (2013) 2478–2487. https://doi.org/10.1161/circulationaha.113.002810. Fig. 1.

There is a growing understanding of the detrimental effect of cardiac dysfunction on placental function, and its impact on fetal well-being [7]. Doppler measures of uteroplacental blood flow, particularly indices of placental vascular resistance, provide an indirect measure of placentation, the process by which trophoblasts invade the spiral artery walls resulting in arterial dilatation and low vascular resistance in the placental bed. Abnormalities in this process result in abnormal uteroplacental flow and resistance, and are associated with the development of preeclampsia, FGR and an elevated perinatal mortality risk. Woman with uteroplacental flow dysfunction (UFD) are more likely to have undiagnosed heart disease, and occult abnormalities of cardiac structure and function including left ventricle hypertrophy and diastolic dysfunction [8]. Importantly the ZAHARA II study demonstrated that women with congenital heart disease have a higher incidence of UFD. Furthermore UFD correlated with measures of maternal left and right heart function and with pregnancy outcome (Fig. 1) [9]. Few women with a Fontan circulation were included in that study, but given that the obstetric and perinatal complication risk profile is more severe in the Fontan pregnancy than most other forms of congenital heart disease, it is not unreasonable to suspect that UFD is prevalent in this population. Recent publications from the same group linking maternal right heart dysfunction (and presumably elevated central venous pressure and limited cardiac output reserve), to UFD add further support to this concept [10].

The dilemma for the cardiologist and maternal fetal medicine physician advising a woman with a Fontan circulation lies in the assessment of Fontan pregnancy risk. The placenta is a newly recognized part of the puzzle, and further information is needed to ascertain the relationship between the unique characteristics of the Fontan circulation and abnormalities of uteroplacental physiology. It is likely that a better understanding of how measures of Fontan circulation health – including ventricular function, central venous pressure, and cardiac output reserve – interact with and influence placental function and structure will assist risk assessment and management of pregnancy in this high-risk population.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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