OBSTETRICS

Tissue Doppler echocardiographic markers of cardiac dysfunction in small-for-gestational age fetuses

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OBJECTIVE: The objective of the study was to evaluate echocardiographic markers of cardiac dysfunction in small-for-gestational age (SGA) fetuses with normal umbilical artery Doppler.

STUDY DESIGN: Cardiac function was evaluated in 58 SGA (mean gestational age, 38 weeks) and 58 gestational-age matched normally grown fetuses by conventional echocardiography (peak early [E] and late [A] ratios and myocardial performance index [MPI]), and tissue Doppler imaging (TDI) (annular peak velocities and MPI').

RESULTS: With conventional echocardiography, SGA fetuses had a nonsignificant trend to increased E/A ratios and left MPI compared with controls. TDI demonstrated that SGA fetuses had significantly lower right E' and A' peak velocities and higher MPI' values.

CONCLUSION: These findings further support that a proportion of SGA fetuses have true late-onset intrauterine growth restriction, which is associated with subclinical cardiac dysfunction, as previously described for early-onset intrauterine growth restriction.

Key words: fetal cardiac function, fetal echocardiography, late-onset intrauterine growth restriction, myocardial performance index, small for gestational age, tissue Doppler imaging

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Intrauterine growth restriction (IUGR) caused by placental insufficiency is recognized among the main causes of perinatal morbidity and mortality.[1] Umbilical artery (UA) Doppler has been the mainstay for diagnosing placental insufficiency for 2 decades. Consequently, fetuses with normal UA Doppler, normally defined as small for gestational age (SGA), have long been considered to be constitutionally small fetuses with a good prognosis. However, recent evidence strongly suggests that a remarkable proportion of SGA fetuses share clinical features with early-onset IUGR fetuses, which supports the existence of mild forms of placental insufficiency that are not reflected in the UA Doppler. Thus, SGA fetuses as a group have poorer perinatal results,[2,3] suboptimal neurodevelopment,[4,5] and higher postnatal cardiovascular risk,[6-8] compared with normal-weight newborns of the same gestational age (GA) at delivery. This evidence stresses the need to characterize the pathophysiology and develop biomarkers to identify the subgroup of late-onset IUGR forms among the category of SGA.

Cardiac dysfunction is now recognized among the central pathophysiologic features of human growth restriction.[9-14] In addition, recent evidence supports that cardiac dysfunction might be one of the key mechanisms explaining cardiac programming and the long-described increased cardiovascular mortality in adults who suffered growth restriction in utero.[8] Concerning early-onset IUGR, several studies have demonstrated the presence of echocardiographic and biochemical signs of subclinical cardiac dysfunction, which progress further as the fetal condition deteriorates.[9-13]

Preliminary evidence suggests that SGA fetuses with normal UA Doppler might also present features of cardiac dysfunction. Chaiworapongsa et al[14] demonstrated that 4% of neonates born small for gestational age had detectable cardiac troponin I in umbilical cord blood, suggesting subclinical myocardial injury before birth. Girsen et al[9] evaluated 13 SGA fetuses with normal UA Doppler and found significantly increased levels of atrial natriuretic peptide, a biomarker of cardiac dysfunction, although echocardiographic markers were not significantly different from controls.

In this prospective study, we aimed at confirming and extending previous evidence of the existence of cardiac dysfunction in SGA fetuses with normal UA Doppler. We evaluated cardiac function

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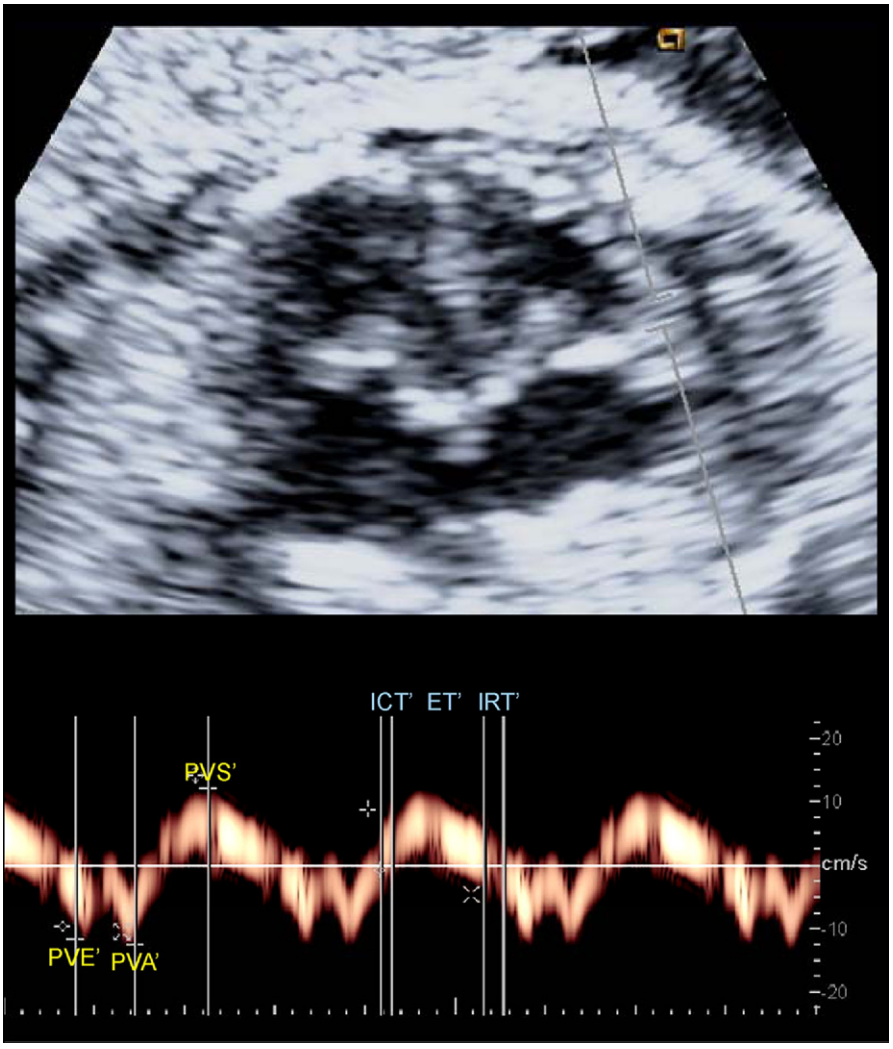
FIGURE 1
Measurement of peak velocities and times by pulsed TDI in the right annulus



TDI, tissue Doppler imaging.

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parameters by means of conventional echocardiography and by tissue Doppler imaging, which has been shown to have a higher sensitivity to detect subclinical fetal cardiac dysfunction than conventional Doppler.[15-18] We compared a group of 58 late-onset SGA fetuses with 58 normal fetuses matched for gestational age.

Materials and Methods

Study populations

The study population included 58 SGA fetuses and 58 controls. Patients were selected from women who attended the Department of Maternal-Fetal Medicine at Hospital Clinic in Barcelona. The study protocol was approved by the local ethics committee, and patients provided their written informed consent.

In all pregnancies, gestational age was calculated based on the crown-rump length at the first-trimester ultrasound.[19] SGA was defined as an estimated fetal weight below the 10th centile, according to local reference curves[20] together with UA pulsatility index (PI) below the 95th centile.[21] The last examination before delivery was used for statistical analysis. The control group consisted of 58 normally grown fetuses matched with cases by gestational age at ultrasound (±1 week). Exclusion criteria were structural/chromosomal anomalies or evidence of fetal infection.

All patients underwent ultrasonographic examination using a Siemens Sonoline Antares (Siemens Medical Systems, Malvern, PA). Basic Doppler examination included UA, middle cerebral artery, and uterine arteries. Cerebral vasodilation was defined as middle cerebral artery PI below the fifth centile. The cerebroplacental ratio was calculated as described previously.[22] At delivery, gestational age, mode of delivery, birthweight, birthweight centile, Apgar score, and umbilical pH were recorded.

Cardiac function was assessed in all cases and controls by conventional echocardiography and tissue Doppler imaging (TDI).

Conventional echocardiography

Conventional echocardiography included ductus venosus (DV) PI (DV-PI), peak early (E) and late (A) transvalvular filling velocities, and myocardial performance index (MPI). DV-PI was measured either in a midsagittal view of the fetal thorax or in a transversal plane through the upper abdomen prior to its entrance to the inferior vena cava, positioning the Doppler gate at the DV isthmic portion.[23] Atrioventricular flows were obtained from a basal or apical 4-chamber view, placing the pulsed Doppler sample volume just below valve leaflets, and left and right E/A ratios were calculated.[24] Left MPI was obtained using the clicks of mitral and aorta valves as landmarks, as previously described.[25] The following time periods were calculated: isovolumetric contraction time (ICT), ejection time (ET), and isovolumetric relaxation time (IRT). Finally, the MPI was calculated as (ICT + IRT)/ET.

Tissue Doppler imaging

TDI was obtained in real time using a 2-10 MHz phased-array transducer. In a 4-chamber-view, sample volumes were placed in the basal part of the left ventricular wall (mitral annulus), interventricular septum, and right ventricular wall (tricuspid annulus). The insonation ul-