Ultrasound Obstet Gynecol 2003; **21**: 441–444
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI:** 10.1002/uog.105

Reference values for an index of fetal aortic isthmus blood flow during the second half of pregnancy

J. RUSKAMP*, J.-C. FOURON*, J. GOSSELIN*, M.-J. RABOISSON*, C. INFANTE-RIVARD† and F. PROULX*

**Fetal Cardiology Unit, Pediatric Cardiology Service, Department of Pediatrics, Ste-Justine Hospital, University of Montreal, and †Department of Epidemiology and Statistics, McGill University, Montreal, Quebec, Canada*

KEYWORDS: aortic isthmus; fetus; flow index

ABSTRACT

Objective *During fetal life, the parallel position of the two cardiac ventricles confers a special status to the aortic isthmus. Flow through the isthmus reflects the balance between the performances of the two ventricles and their respective peripheral impedances. This study proposes a fetal aortic isthmus flow velocity index and its reference values defined on the basis of gestational age (GA).*

Methods *Video recordings of 111 normal fetuses from 18 to 39 weeks of gestation were retrospectively reviewed. An isthmus flow velocity index (IFI) was calculated as follows: IFI = (systolic + diastolic)/systolic velocity integrals. GA-specific reference ranges of IFI were constructed.*

Results *An IFI of 1.33 ± 0.03 was found at 18 weeks. This value decreased slightly but steadily with GA to reach 1.23 ± 0.16 at 39 weeks. This change is mainly related to a decrease in diastolic velocity integrals.*

Conclusion *The proposed IFI provides information on the direction and, indirectly, on the volume of blood flow through the fetal aortic isthmus. Copyright © 2003 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

Experimental[1,2] and clinical[3,4] studies have shown that flow velocity patterns in the aortic isthmus are valid indicators of cardiac and peripheral circulatory conditions during fetal life. The isthmus, localized between the origin of the left subclavian artery and the aortic end of the ductus arteriosus, is indeed the only arterial connection between the two fetal vascular systems positioned in parallel. Any variation in the output of one ventricle[5] or any change in the impedance of one of the peripheral arterial networks[3–6] should inevitably influence the flow pattern through the isthmus. Under normal conditions, the isthmic flow velocity waveforms have been shown to vary concomitantly with physiological changes in ventricular output as well as cerebral and placental vascular resistances[7]. For clinical purposes, what is presently needed is an index that would reflect both the amount and the direction of blood flow through the fetal isthmus. The objective of this study was to propose such an index, together with its normal reference ranges during the second and third trimesters.

METHODS

The data presented in this study were obtained from a retrospective review of the video recordings of 111 fetuses whose ages varied from 18 to 39 weeks of gestation. The data were selected from a computerized database of patients referred to our Fetal Cardiology Unit between 1997 and 2001. All were singleton pregnancies with normal medical and obstetric histories; intrauterine growth was appropriate for gestational age (GA). At least five patients were included for each gestational week. The recordings were obtained on either a Hewlett-Packard Sonos 100 (Hewlett-Packard, Andover, MA, USA) or a XP/10c and Sequoia (Acuson, Mountain View, CA, USA) echocardiographic apparatus. The technique used to obtain a real-time picture of the aortic arch and the isthmus has been described previously[3]. The correct position (a few millimeters beyond the origin of the left subclavian artery) of the sample volume in the aortic isthmus could be confirmed in all cases (Figure 1a). The normal morphology of the fetal heart was also confirmed by the postnatal clinical examination and outcome. Occasional extrasystoles in an otherwise healthy heart were not considered an exclusion criterion. Measurements

Correspondence to: Dr J.-C. Fouron, Ste-Justine Hospital, Service of Cardiology, 3175 Côte Ste-Catherine, Montreal, Quebec H3T 1C5, Canada (e-mail: fouron@sympatico.ca)

Accepted: 26 November 2002

 ORIGINAL PAPER

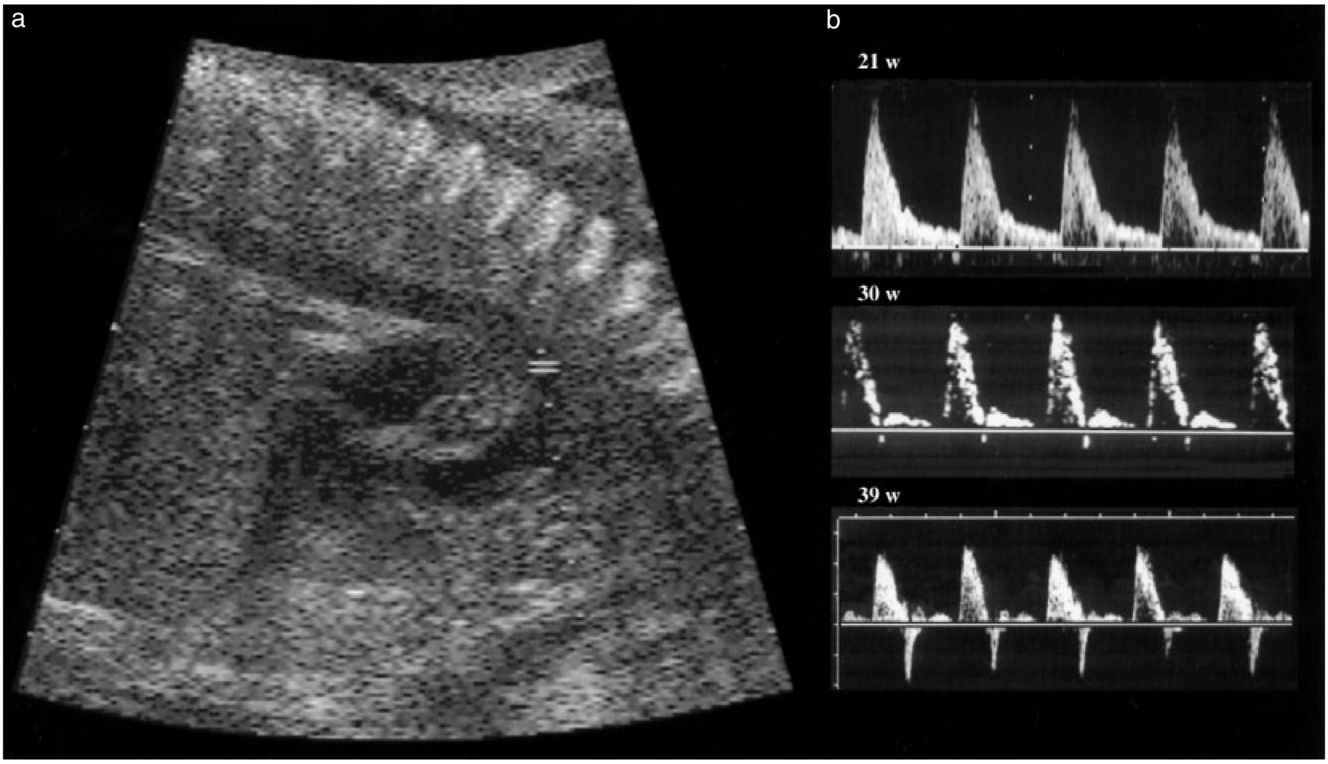

Figure 1 (a) Real-time ultrasound image of the aortic arch showing the position of the Doppler sample volume in the isthmus. (b) Examples of Doppler flow velocity waveforms in the aortic isthmus, illustrating the progressive fall in the antegrade diastolic velocities as gestation progresses. At 30 weeks (w), a brief end-systolic reverse wave is observed, which increases as gestation progresses.

were always made during apnea and regular sinus rhythm. The proposed isthmic flow index (IFI) was calculated by dividing the sum of the systolic (S) and diastolic (D) Doppler flow integrals by the systolic flow integral: IFI = (S + D)/S.

Statistical analysis

Prior to defining reference ranges for the index, test–retest (1 month interval between the two measures) and interobserver reliabilities were measured on 30 recordings covering all the GAs in the study; interobserver reliability was based on the comparison of the IFI measured independently by two observers, each without knowledge of the results obtained by the other. Intraclass coefficient (ICC)[8] and 95% confidence intervals (CIs) were calculated. To ensure that data obtained from Acuson and Hewlett-Packard equipment were similar, a paired *t*-test was applied on IFI values calculated on 14 patients with both types of equipment. Then, the reference values for the IFI were estimated using the method proposed by Royston[9,10] and implemented in the STATA package[11]. This approach is based on regression modeling of both the mean and the standard deviation (SD) across GA. The rationale is that both the mean and the SD will change smoothly with age, so the method of analysis must reflect this observation. Linear regressions were fitted separately to the mean and the SD as a function of GA. Values for the 95% CIs were calculated to evaluate the precision of the 2.5th and 97.5th centiles.

RESULTS

The ICC for test–retest reliability was 0.94 (95% CI 0.86–0.97, $F = 16.23$, $P < 0.001$) while it was 0.98 (95% CI 0.96–0.99, $F = 55.03$, $P < 0.001$) for interobserver reliability. No difference was found between data obtained from the two types of echographic equipment: for the Hewlett-Packard: IFI = 1.33 ± 0.05, for the Acuson: IFI = 1.33 ± 0.06; $P > 0.05$.

With respect to the IFI, a few trends could be observed. Up to approximately 30 weeks of gestation an antegrade flow was recorded during the entire cardiac cycle in the aortic isthmus. After 30 weeks, an end-systolic incisura appeared which progressively increased resulting in a brief reversal of flow towards the end of gestation. This pattern corresponds to previous observations[7] and is illustrated in Figure 1. The mean and SD for the IFI values were modeled as linear functions of GA and the equations for the fitted lines are shown in Box 1. We checked the model using the Shapiro–Wilk *W*-test for normality; $P = 0.76$, thereby confirming the normal distribution. Box 1 also shows how to estimate the desired centiles curves: for the 5th and 95th centile curves, K is 1.645; for the 10th and 90th centile curves, K is 1.28. The GA-related reference ranges for the IFI are given in Table 1. An IFI of 1.33 ± 0.03 was found at 18 weeks. This value decreased slightly but steadily with GA and reached 1.23 ± 0.16 at 39 weeks. From this reference table constructed according to the method proposed by Wright and Royston[11] *Z*-scores could be calculated as: (measurement – mean)/SD.

Box 1 Regression equations used to generate the table of fitted centiles of isthmic flow index

IFI: Mean = 1.41 – 0.0047 * GA
SD = −0.076 + 0.006 * GA,

where GA is the gestational age in weeks and IFI the isthmic flow index.

Centiles = mean + K * SD, where K is the corresponding centile of the standard Gaussian distribution and SD is the standard deviation.

2.5th centile = mean − 1.96 * SD
97.5th centile = mean + 1.96 * SD

DISCUSSION

Circulatory indices proposed in the literature such as the systolic/diastolic ratio, the pulsatility index (PI)[12] and the resistance index[13] are useful for indirect assessment of the impedance of vascular networks. In a previous report, the formula used for the PI calculation was applied in the assessment of aortic isthmus flow[7]. The PI, however, assesses the downstream impedance of a single vascular bed while the amount and direction of flow through the aortic isthmus is influenced not only by the balance between the impedance of the two vascular systems situated in parallel but also by the systolic performance of their respective ventricular pump. This point is particularly obvious with the appearance of reverse diastolic flow in the isthmus. In this condition, the PI keeps increasing and does not precisely indicate the presence or size of the reverse flow component.

Table 1 Normal values for the isthmic flow index

GA (weeks)	*Mean*	*95% CI*	*SD*
18	1.327	1.263–1.392	0.033
19	1.323	1.247–1.399	0.039
20	1.318	1.230–1.406	0.045
21	1.313	1.213–1.413	0.045
22	1.309	1.197–1.420	0.057
23	1.304	1.180–1.428	0.063
24	1.299	1.164–1.435	0.069
25	1.295	1.147–1.442	0.075
26	1.290	1.130–1.449	0.081
27	1.285	1.114–1.456	0.087
28	1.280	1.097–1.464	0.094
29	1.276	1.081–1.471	0.100
30	1.271	1.064–1.478	0.106
31	1.266	1.047–1.485	0.112
32	1.262	1.031–1.493	0.118
33	1.257	1.014–1.500	0.124
34	1.252	0.997–1.507	0.130
35	1.247	0.981–1.514	0.136
36	1.243	0.964–1.521	0.142
37	1.238	0.948–1.529	0.148
38	1.233	0.931–1.536	0.154
39	1.229	0.914–1.543	0.160

CI, confidence interval; GA, gestational age; SD, standard deviation.

The IFI, as designed, is particularly sensitive to changes in the direction of diastolic flow. Essentially, three patterns are possible: type I: the index is higher than 1, meaning that antegrade flow is present both in systole and diastole; the higher the index, the greater would be the volume of diastolic forward flow; an index of 1 would correspond to an absence of diastolic flow. Type II: the index is lower than 1 but higher than 0, expressing a reversal of diastolic flow but with a predominant antegrade flow in systole; the closer the index is to 0, the greater is the diastolic retrograde component. An IFI above 0, therefore, means that flow through the isthmus is still predominantly antegrade. An index of 0 would occur when forward and reverse velocity integrals are equal and the resultant flow through the isthmus is null. Finally, in type III, the IFI is negative, below 0, meaning that the forward systolic flow is decreased and retrograde diastolic flow increased to the point that net flow through the isthmus is retrograde.

The present paper shows that the majority of normal fetuses have a type I flow pattern in the aortic isthmus; at the end of gestation however, a type II pattern can occasionally be observed. The reason for the progressive decrease of the IFI throughout the second half of pregnancy, as shown in Table 1, is in all likelihood the reflection of physiological hemodynamic events taking place at the same time. During the third trimester, a steady fall has been documented in the impedance of the cerebral circulation[14]; this alone could explain the decrease in diastolic flow integrals recorded during this period since the direction of flow through the aortic isthmus is influenced by the relative impedance of the two parallel vascular systems. Concerning the brief retrograde flow noted at the end of gestation, experimental studies on term ovine fetuses have also shown the same flow reversal at the level of the isthmus; this pattern was related to a delayed onset and longer acceleration time of the ductus flow velocity at the isthmus–ductus junction[15].

A previous report[4] has shown that during placental circulatory insufficiency leading to intrauterine growth restriction, retrograde net blood flow in the aortic isthmus corresponding to a type III IFI was associated with an increased pulsatility in the ductus venosus blood velocity waveforms suggestive of fetal cardiac dysfunction. The IFI is therefore proposed as a clinical tool for the objective assessment of the severity of conditions that not only alter the balance between the upper and lower body peripheral vascular impedance such as placental circulatory insufficiency, but also disturb the relative performance of the two ventricular pumps.

ACKNOWLEDGMENT

J. Ruskamp was the recipient of a fellowship from the Dutch Heart Association.

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