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Changes in inferior vena cava blood flow velocity and diameter during breathing movements in the human fetus

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ABSTRACT

Breathing movements in the human fetus cause distinct changes in Doppler flow velocity measurements at arterial, venous and cardiac levels. In adults, breathing movements result in a momentary inspiratory collapse of the inferior vena cava vessel wall. The study objective was to quantify the inferior vena cava flow velocity modulation during fetal breathing movements and to evaluate possible inferior vena cava vessel diameter changes in normal third-trimester pregnancies.

We studied 57 women after oral administration of dextrose (50 g). In 40 fetuses (n = 19, 27–32 weeks and n = 21, 36–39 weeks), fetal inferior vena cava waveforms were obtained during apnea and fetal breathing activity. In 30 fetuses (27–39 weeks) inferior vena cava vessel diameter changes were studied using the M-mode during apnea and breathing movements. Peak and time-averaged velocities of inferior vena cava flow velocity waveforms showed a gestational age-independent increase of 60–160% during breathing activity. A temporary inferior vena cava vessel wall collapse (range, 50–83%) was recorded, which was significantly different from vessel diameter changes during apnea (range, 11–19%). The marked increase of inferior vena cava flow velocities is due to a raised thoraco–abdominal pressure gradient, which may cause a reduction in vessel size and additional volume flow into the right atrium. The significance of the caval index for recognition of elevated right atrial pressure in abnormal human fetal development needs further investigation.

INTRODUCTION

Fetal breathing movements are caused by diaphragmatic contractions, resulting in intrathoracic and intra-abdominal pressure changes[1]. Combined real-time ultrasound and pulsed Doppler studies have demonstrated fetal breathing-dependent flow velocity modulation in the human fetus at arterial[2–4], cardiac[5] and venous levels[2,3,6].

Whereas increased flow velocities have been observed in the inferior vena cava during the inspiratory phase of fetal breathing movements[2,6], no quantitative data are available with respect to the modulation of blood flow velocity or vessel diameter during fetal breathing movements in this vein. In adults, a momentary inspiratory collapse of the inferior vena cava was documented using two-dimensional echocardiography and M-mode[7–9]. The degree of collapse (caval index) correlated well with the right atrial pressure, allowing non-invasive indirect assessment of right heart function[9]. Such information would be also of interest in fetuses suffering from hydrops or growth retardation. In the latter instance, raised retrograde flow in the inferior vena cava during atrial contraction has been established, suggesting increased ventricular pressure or decreased ventricular compliance[10].

The objective of the present study was to quantify the modulation of the inferior vena cava flow velocity waveform and vessel diameter during fetal breathing movements in normal third-trimester pregnancies.

SUBJECTS AND METHODS

A total of 57 women gave informed consent to participate in this study; the protocol was approved by the Hospital Ethics Committee. The gestational age was calculated on the basis of the last menstrual period combined with early ultrasonic measurement of crown–rump length or biparietal diameter. In all 57 women the pregnancy was uneventful resulting in the delivery of a normal infant with a birth weight between the 10th and 90th centile, according to Kloosterman[11]. There were no macroscopically detectable congenital abnormalities.

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Flow velocity recordings (n = 40)

The modulation of fetal inferior vena cava flow velocity waveforms was studied in 40 normal pregnancies at 27–32 weeks (n = 19) and 36–39 weeks (n = 21) of gestation. Oral administration of 50 g glucose induces fetal breathing activity within 30–120 min[12]. Fetal inferior vena cava flow velocity recordings were, therefore, made 1 h after maternal oral administration of 50 g dextrose (Dextro energy®, CPC Benelux, Loosdrecht, The Netherlands).

Fetal inferior vena cava waveform recordings were obtained by means of a combined curved-linear array two-dimensional real-time and pulsed Doppler system with a carrier frequency of 3.5 MHz and a spatial peak temporal average power output of less than 100 mW/cm^2 according to manufacturer's specifications (Hitachi EUB-450, Hitachi Medical Corporation, Tokyo, Japan). The high-pass filter was set at 100 Hz. All measurements were performed by one examiner (T.W.A.H) and with the women in a semi-recumbent position.

The fetal inferior vena cava was visualized in a sagittal view directly under the fetal spine, to the right of and parallel to the descending aorta. The sample volume (2–4 mm) was placed under two-dimensional ultrasonic guidance immediately proximal to the right atrium[13]. Waveforms were only accepted if the interrogation angle between the Doppler beam and assumed direction of blood flow was less than 30°. Fetal breathing movements were recognized by the combined motion of the fetal diaphragm, thorax and abdomen with two-dimensional real-time ultrasound. Continuous fetal breathing was considered present when the interval between two consecutive breathing movements was ≤ 6 s. At least three consecutive inferior vena cava waveforms were recorded on hard copies during apnea. Since during breathing activity these three waveforms were not completed within three to five cardiac cycles, two to three hardcopies were collected during that particular breathing period. Waveforms were only recorded during high-amplitude fetal breathing movements. No distinction was made between the inspiratory and expiratory phase of the breathing cycle. After each individual analysis, the three values per parameter were combined and the mean value was calculated for each fetus.

Using an xy-tablet and a microcomputer (Olivetti M24), with a specially designed program, the following parameters were calculated: time-averaged velocity (cm/s), time velocity integral (cm), peak velocity (cm/s) and percentage time velocity integral during reverse flow[10], calculated from: [(time velocity integral during reverse flow)/(time velocity integral during forward flow)] × 100%.

Vessel diameter recordings (n = 30)

The vessel diameter changes in the inferior vena cava during apnea and fetal breathing movements were studied in a group of 30 normal pregnancies using time motion recording (M-mode). The gestational age was 27–39 weeks (median 36 weeks). Recordings were obtained approximately 10 mm below the fetal diaphragm to avoid interference from diaphragmatic movements. The inferior vena cava was again visualized under the fetal spine in a sagittal scanning plane. Simultaneous real-time and M-mode recording should demonstrate inferior vena cava vessel wall reflections both during fetal breathing activity and apnea. A special effort was made to reduce any movement from the mother and examiner during recording and to ensure differentiation between the fetal inferior vena cava and abdominal aorta. The transducer was angled laterally and medially to record the maximum inferior vena cava vessel size. All recordings were performed by one examiner (T.W.A.H.). Also here, vessel diameter changes were studied 1 h after maternal oral administration of 50 g dextrose (Dextro energy®, CPC Benelux, Loosdrecht, The Netherlands) to ascertain the occurrence of breathing movements. The inferior vena cava diameters during apnea and fetal breathing movements were measured, from hard copies, using a ruler allowing a measuring accuracy of 0.25 mm. A maximum measuring error of 0–0.5 mm was accepted and the percentage collapse (caval index) was calculated. The 'caval respiratory index' was defined as the percentage decrease in diameter of the inferior vena cava with inspiration[9].

Statistics

Data from all groups are presented as the mean ± SD. Paired t-tests were used to compare flow velocity waveforms and caval respiratory indices obtained during fetal breathing movements and apnea. Using linear regression analysis, comparison was made between time-averaged velocity, time velocity integral, peak velocity, percentage reverse flow, caval respiratory index and gestational age during fetal breathing activity. The Wilcoxon signed-rank test was applied to compare the standard deviations between the apneic and breathing-modulated data. Probability values < 0.05 were considered statistically significant.

RESULTS

Inferior vena cava flow velocities

Maternal glucose loading induced regular fetal breathing movements in all 57 subjects. Modulation of inferior vena cava waveforms occurred in each instance and was characterized by near obliteration of the typical three-component waveform pattern (systolic and early diastolic forward flow and late diastolic retrograde flow[10]), resulting in a profile as demonstrated in Figure 1. It was possible, however, to analyze these obliterated waveforms with sufficient accuracy for the parameters which are shown in Table 1.

Absent reverse flow was observed during apnea in two fetuses at 27–32 weeks' gestation (10.5%) and in five fetuses at 36–39 weeks' gestation (24%). During breath-

Table 1 Inferior vena cava flow velocity waveform parameters during apnea and fetal breathing movements at 27–32 weeks and 36–39 weeks of gestation (mean ± SD)

	27–32 weeks		*36–39 weeks*	
	Apnea	*Fetal breathing movements*	*Apnea*	*Fetal breathing movements*
Time-averaged velocity (cm/s)	26 ± 3	49 ± 11	29 ± 7	55 ± 9
Peak velocity (cm/s)	49 ± 6	93 ± 18	54 ± 9	83 ± 11
Time velocity integral (cm)	11 ± 2	27 ± 9	13 ± 3	31 ± 9
Percentage reverse flow	12 ± 3	11 ± 4	10 ± 3	9 ± 4

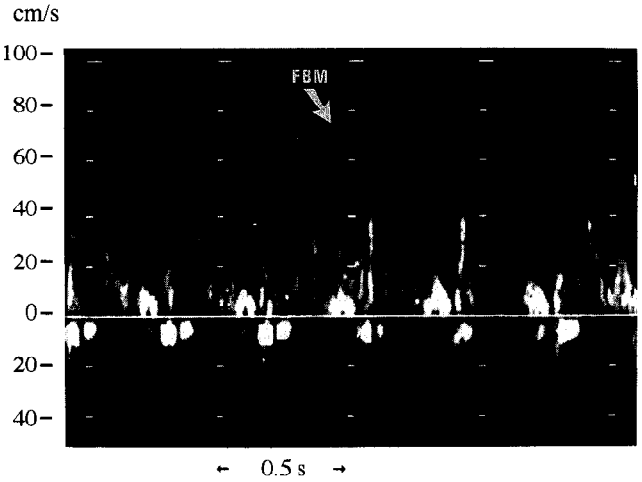

Figure 1 Normal inferior vena cava flow velocity waveforms modulated by a fetal breathing movement (FBM) in a 37-week-old fetus

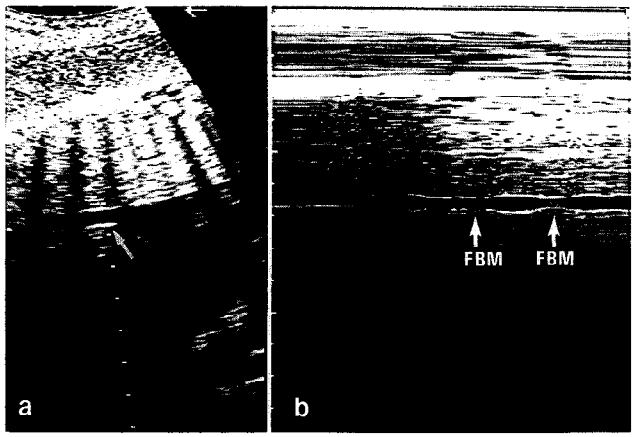

Figure 2 The inferior vena cava vessel walls during fetal breathing activity; (a) sample site (see arrow); (b) M-mode recording of vessel diameter changes during apnea and during two fetal breathing movements (FBM)

ing activity, no reverse flow could be established in four cases (10%).

A statistically significant increase ($p < 0.001$) for time-averaged velocity, peak velocity and time velocity integral in the inferior vena cava was demonstrated during breathing movements when compared with apnea (Table 1). This increase was in the range of 60–160%. The percentage reverse flow during fetal breathing movements, if present, was not significantly different between the two states. The changes observed for each flow velocity parameter were not statistically significantly different between the two gestational age groups. The standard deviation of all parameters was increased ($p < 0.01$) during breathing activity compared with the apneic phase in both groups.

Inferior vena cava vessel diameters

In the group of 30 women studied by time motion recording, a temporary collapse of the inferior vena cava vessel wall during fetal breathing movements could be established in 27 fetuses (88%) (Figure 2). The vessel diameter collapse took place immediately beneath the diaphragm over a length of approximately 5–10 mm. This collapse occurred during downward movement of the diaphragm, indicating the inspiratory phase of the breathing cycle. Diameter measurement could be established with an estimation up to 0.25 mm, leaving an estimation error in the range of 0–0.5 mm. This resulted in a maximum collapse estimation error of 17.5%. The caval index, representing the percentage of vessel collapse during fetal breathing movement, did not correlate with gestational age. All data were, therefore, lumped together, resulting in a mean value of 70.1 ± 8.3% (range 50–83%). During apnea, inferior vena cava vessel pulsations demonstrated diameter reduction of only 14% (range, 11–19%). This difference is statistically significant ($p < 0.001$).

DISCUSSION

This study demonstrates that fetal breathing movements influence the fetal hemodynamics at the level of the right atrium and inferior vena cava. Increased flow velocities were documented during breathing activity as compared with the apneic state in the range of 60–160%, which is remarkably higher than in other cardiovascular structures. For instance, in the descending aorta a 2–40% modulation has been demonstrated[2], in the ductus arteriosus, 10–33%[4] and in the foramen ovale, 69–117%[5]. We hypothesize that this increase of flow velocities during breathing movements at the level of the inferior vena cava is caused by a raised pressure difference between the thorax and abdomen, resulting in a reduction in the inferior vena cava vessel diameter and an increase of blood volume directed to the right atrium. Extra blood could originate from the hepatic vascular bed as it is squeezed into the inferior vena cava during the temporary increase of intra-abdominal pressure. This is in accordance with our preliminary observation that blood flow velocities in the hepatic veins were also greatly increased during fetal breathing movements (unpub-

lished data). Also at the level of the foramen ovale, raised flow velocities were established during fetal breathing activity. This was attributed to increased volume flow, since no diameter reduction could be detected at that particular level[5]. It was proposed that the source of this additional volume flow could be either the inferior vena cava or the ductus venosus as part of fetal venous return. This study suggests that an increased amount of blood is drawn from the inferior vena cava into the right atrium.

In a previous study of inferior vena cava velocities during apnea, the time-averaged velocity displayed a positive correlation, and percentage reverse flow a negative correlation, with gestational age[13]. No such correlation could be established in the present study during fetal breathing activity. This and the presence of large standard deviation values in all breathing-modulated waveform parameters could be the result of several factors. First, distinct vessel diameter reductions (range, 50–83%) together with flow velocity increases in the range of 60–160% were documented. Second, a breathing-related obliteration of the normal three-component waveform, in particular the systolic and early diastolic forward flow component, made it difficult to compare absolute flow velocity values. Finally, in this study no discrimination was made between fetal behavioral states or the type of fetal breathing movements[14]. Especially, the depth of breathing is likely to be a component of considerable variance. Therefore, waveforms were only selected from a period of continuous high-amplitude breathing activity.

To our knowledge, this is the first description of human fetal inferior vena cava vessel wall collapse during the inspiratory phase of fetal breathing movements. Unsuccessful recording was due to the inability to document both vessel walls, but also in these cases a clear collapse of the inferior vena cava during breathing movements could be observed. In adults, this vessel size reduction was already postulated as early as 1941 by Holt[15]. Brecher demonstrated in dogs that two stages could be observed in the response to application of negative pressure in the inferior vena cava[16]: first, a 'depleting stage', characterized by a continuous reduction of the vein's filling state, resulting in increased venous outflow, and, second, a collapsed stage which occurred during greater pressure gradients. Wexler and colleagues[17] described the collapse of the human inferior vena cava in healthy adults during inspiration, leading to an increase of flow velocity and a reduction of blood flow during the Valsalva maneuver[17]. Veins coursing through the abdomen are often compressed by different organs and by the intra-abdominal pressure, so that usually they are at least partially collapsed to an elliptical or slit-like state; veins inside the thorax are not collapsed, because the negative pressure inside the chest distends these veins[18]. Venous pressure in the fetal inferior vena cava is higher than in the adult, but it is assumed that the fetal inferior vena cava vessel section is also slightly elliptical. Because of the limitations in ultrasonic diameter measurement, an exact quantification in fetal inferior vena cava collapse was not the purpose of this study. The observed diameter changes, however, suggest a similar physiological explanation for the reduction of the inferior vena cava vessel diameter in the fetus as in the adult. Some of the physical laws concerning fluid dynamics and laminar blood flow are thought to be different in associations with changes in vessel diameter. The fact, however, that very similar data have been observed in animals and adults, using accurate measurement equipment, gives reason to extrapolate these physiological explanations to the human fetus.

When in normal adults inspiration augments venous return, the increased blood flow is derived from the central capacitance venous system. As flow through the inferior vena cava increases and, therefore, intraluminal pressure decreases, the diameter of this highly compliant vessel decreases[9]. In adults with right heart dysfunction, however, the normal inspiratory increase in venous return is limited by cardiac enlargement and decreased right ventricular compliance[7]. Flow in the inferior vena cava is impeded by increased right-sided cardiac filling pressures. This results, on the one side, in an increased inferior vena cava diameter and, on the other side, in a decrease of inspiratory caval collapse. Our preliminary data obtained from four hydropic fetuses with congenital heart pathology (Ebstein's anomaly ($n = 2$), combined foramen ovale obstruction and aortic valve stenosis, and supraventricular tachycardia) support the presence of such a mechanism in the human fetus. Vessel diameter studies in these unborn infants with presumed increased right atrium pressure demonstrated no detectable collapse of the inferior vena cava during breathing movements. We suggest that in their case the increased heart volume and ascites may also play a role in the prevention of effective diaphragmatic contraction by mechanical interference and/or changes in interthoraco-abdominal pressure gradient. More pathological cases are needed to evaluate the possible use of the caval index as a diagnostic tool for recognition of elevated right atrial pressure in the human fetus.

In conclusion, flow velocity waveforms in the inferior vena cava are markedly increased during fetal breathing movements. These changes are independent of gestational age and could be due to a raised pressure gradient between thorax and abdomen, resulting in a reduction in the inferior vena cava vessel diameter and additional volume flow being directed to the right atrium. Inspiratory collapse of the inferior vena cava vessel wall, as described in the adult, was documented for all normally developing fetuses. The significance of the 'caval index' for the recognition of elevated right atrial pressure in abnormal human fetal development (hydrops, cardiac anomalies) needs further investigation.

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