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Original article

Changing physiology in the first- to third-trimester foetal circulation

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THE HEART IS THE FIRST ORGAN THAT BECOMES fully independent from the mother. Its proper function provides normal development of the cardiovascular system.[1]

Development of the foetal cardiovascular system starts as early as the 3rd week of gestation, when the embryo's length is about 0.4 mm. There are three circulation systems at that time:[2]

- Embryonic circulation, which consists of three veins – anterior, common, and posterior cardinal veins – and three arteries – ventral and dorsal aorta and aortic arch arteries.
- Placental circulation, which consists of the left umbilical vein and umbilical artery.
- Vitelline circulation, which consists of the vitelline artery and vein, which will become the liver circulation in the future foetus: liver sinusoids, portal system, and ductus venosus (Fig. 1).

This period of development is known only from experimental animal studies and specimens of human embryos. It is not possible to examine the human embryo's heart using currently available ultrasound techniques. Some early experience using mice hearts has been presented by Leiden group, but the results are not published yet. The primitive straight heart tube starts to contract at about 4 weeks, but this is not visible. It is possible to see the first contraction using M-mode ultrasound by about 5 weeks, and Doppler trace can be recorded by about 6 weeks.

Early embryology is difficult to study in vivo, and there is considerable experimental research to better understand this stage of development. The proepicardium is a pool of the progenitor cells, which contains those that are necessary for heart development: the fibrous skeleton of the heart, epicardium, and coronary vessels. They are important in the processes of vasculogenesis, angiogenesis, morphogenesis, and remodelling of the cardiovascular matrix. The proepicardium was first described by a Polish researcher Kurkiewicz at the beginning of the 20th century.[3] It is located near the venous pole of the embryonic heart and protrudes into the pericardial cavity. The proepicardium disappears by the end of the 5th week of gestation.

The foetus can only develop successfully if essential nutrient and gaseous exchange occurs with the maternal circulation. Therefore, the next embryological question is how the maternal–foetal circulation is established. Uterine arteries, which arise from the internal iliac arteries, give rise to the spiral arteries that pierce the endometrium. At the beginning of trophoblast development, invading trophoblastic cells create plugs within these spiral arteries, and the villi erode tiny portions of the decidua–intervillous spaces. This early developmental process is, however, still not well understood. Despite this, ultrasound techniques are able to examine the placental and foetal circulation from the late first trimester of pregnancy.

Heart contractions start at 4 gestational weeks, and the earliest Doppler tracings at 6 weeks have confirmed that the heart rate is low at this stage, increasing to 170–180 by the end of the first trimester and then slowing after 12 weeks.[4] The normal heart rate at 14 weeks according to FIGO is between 110 and 150/minute (Fig 2).

The placental circulation can be seen from the 7th week of gestation. Dynamic changes in flow waveforms occur in the umbilical vein and arteries throughout the pregnancy. Before 12–13 weeks, there is absent end-diastolic flow in the umbilical arteries and umbilical vein, and pulsations are observed. Placental resistance slowly decreases during this period and results in an increase in diastolic velocities in the umbilical artery, with resultant decrease in pulsatility index (Fig 3).

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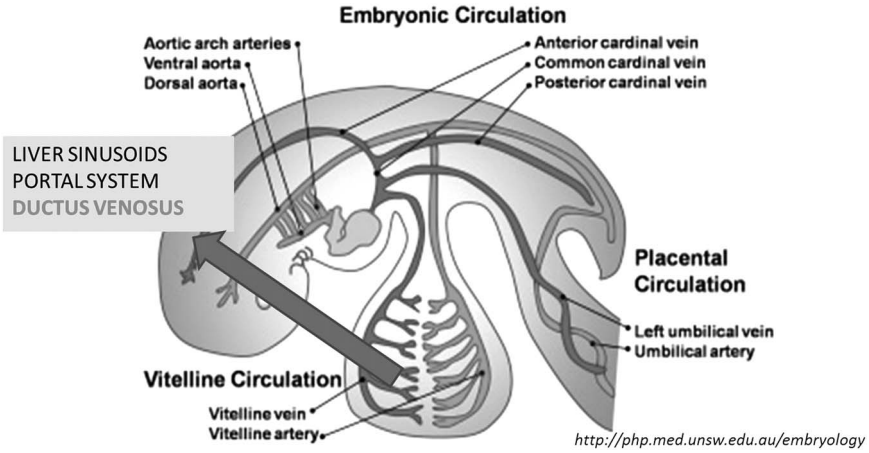

Figure 1.
Early human circulation, the scheme from: http://php.med.unsw.edu.au/embryology with own changes. The embryo at the early 3rd week of gestation, length 0.4 mm.

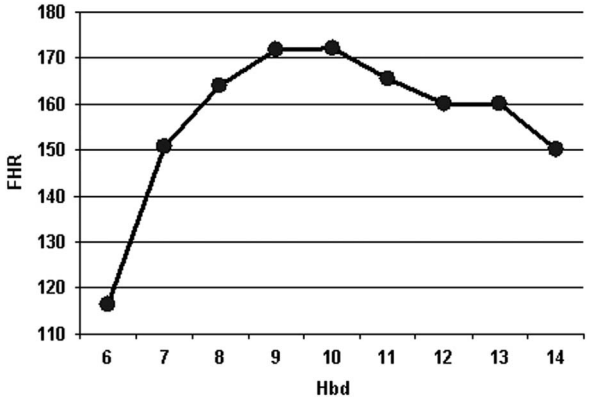

Figure 2.
Foetal heart rate from 6 to 14 weeks of gestation – own data.

From about 11 weeks, umbilical venous flow is laminar and pulsations should only be recorded in pathological circumstances such as foetal hypoxia, foetal heart failure, or some foetal heart defects.

One very important precordial vein is the ductus venosus, which is the vessel directing the oxygenated blood from the placenta to the foetus. There are three waves in the normal tracing: "S" during ventricular systole, "D" during ventricular diastole, and "a" during atrial contraction. In the early first trimester, there is always reversal of the "a" wave, reflecting the relatively high atrial pressure in the embryo's heart during that period of development. From 9 weeks, this "a" wave becomes positive[5] and remains so until the end of pregnancy (Fig 4). A reversal of the "a" wave between 11 and 13.6 weeks may be a sign of aneuploidy or a foetal heart defect.[6] This is one of the chromosomal markers used in the risk calculation for trisomy 21 in the Fetal Medicine Foundation Programme.

Middle cerebral artery flow is characterised by high-resistance flow with a high pulsatility index, which decreases during pregnancy. A lower resistance index is observed in foetuses with left heart obstructive lesions.[7]

There remain some uncertainties in aspects of early embryonic human heart development, particularly the myocardial and coronary circulations. They are thought to be formed by directional growth of vascular protrusions towards the aorta that establish contact with the aortic wall.[8] The process of myocardial morphogenesis and maturation depends on adequate coronary blood supply to the ventricular myocardium.[9] The foetal myocardium is "non-compacted" until about 8–10 weeks when it begins to become compacted, probably because of the coronary circulation, although some aspects of this remain controversial. The exact timing of development of the human coronary circulation is unknown, and thus further study is necessary to fully understand the developmental changes in the embryo between 4 and 10 weeks.

Detailed intracardiac Doppler flow can be recorded from the 6th week of gestation. They were described by Włoch et al[5] in a prospective study. In the 5th week, the heart was not visible, although colour flow could be recorded inside the embryonic heart. From the 6th week, characteristic inflow and outflow Doppler could be recorded, indicating very high end-diastolic pressure in the embryonic ventricle. The monophasic inflow through the atrio-ventricular valve, later valves, was at a higher velocity than that in the ventricular outflow tracts (Fig 5). Filling of the primitive ventricles occurred only during atrial systole, and inflow time was very short. Both isovolumetric contraction time and isovolumetric relaxation time were much longer than later in pregnancy. These Doppler parameters result in a high myocardial performance index (MPI or Tei-index), which gradually decreases towards the end of the first trimester.

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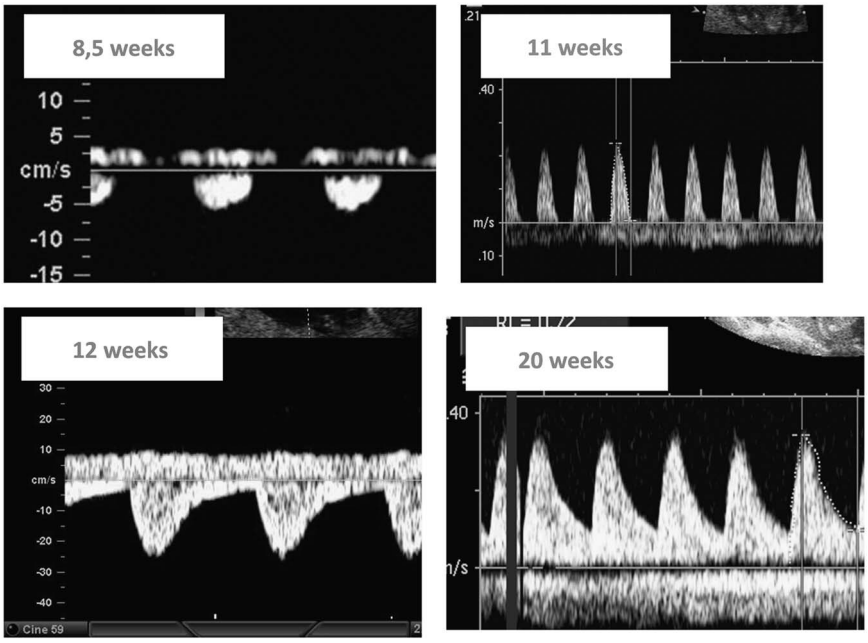

Figure 3.
Changes in the umbilical flow during pregnancy: 8 weeks – pulsations in the umbilical vein, absent end-diastolic flow in the umbilical artery; 11 weeks – laminar flow in the umbilical vein (no pulsations), absent end-diastolic flow in the umbilical artery; 12 weeks – low-velocity diastolic flow in the umbilical artery is recorded; 20 weeks – low placental resistance, low (normal) pulsatility index (PI) in the umbilical artery. PI in the umbilical artery decreases by the end of pregnancy.

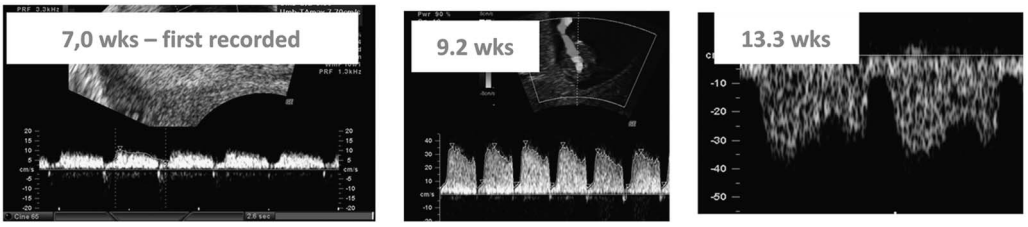

Figure 4.
Ductus venosus flow: 7 weeks – reverse a wave; 9 weeks – positive a wave, low velocity; 13 weeks – normal ductus venosus flow.

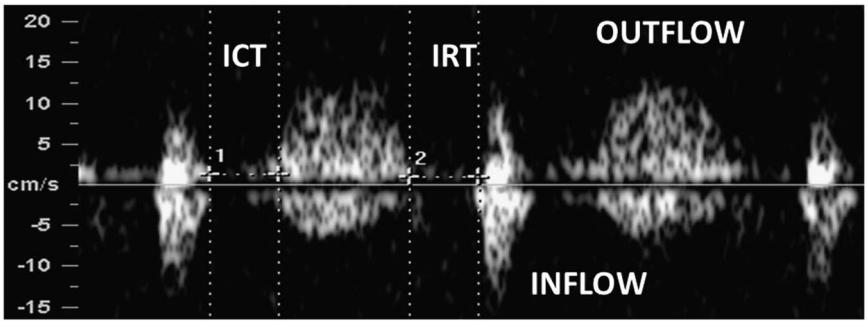

Figure 5.
Early intracardiac flow (courtesy A. Włoch). ICT = isovolumic contraction time; IRT = isovolumic relaxation time (see text for details).

Foetal heart inflow Doppler is monophasic, initially occurring in late diastole; however, between 9 and 11 weeks, the E waves gradually appear in the atrio-ventricular inflow Doppler tracing (Fig 6). The early E wave shows very low velocities that gradually increase but remain lower than the late filling A wave until birth and early infancy. We know from experimental studies that the myocardium alters at the same time and it may be that evolution of intracardiac flow between 6 and 10 weeks is

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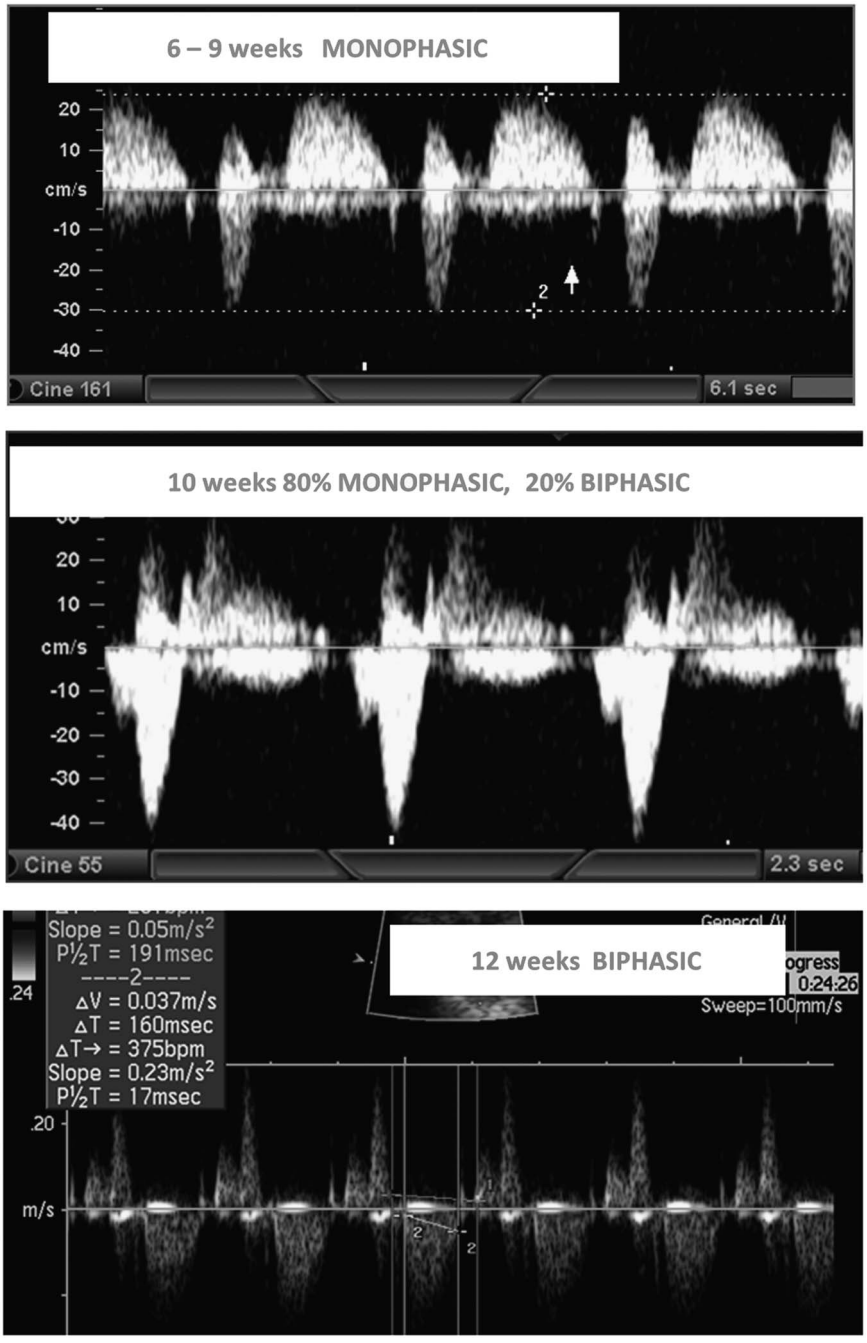

Figure 6.
Atrio-ventricular valves inflow from 6 to 12 weeks of pregnancy: 6–9 and 10 weeks – courtesy of A. Włoch; between 6 and 9 weeks – monophasic inflow during atrial contraction; 10 weeks – in 20% foetuses small E wave in the early diastole appears. Since 11–12 weeks until the end of pregnancy – biphasic atrio-ventricular inflow.

dependent on the correct development of the coronary circulation.

Foetal heart function can be examined from the 11th week of gestation, and in the author's experience cardiac anatomy can be evaluated in about 90% foetuses during that period,[10] and function can be measured in the majority of foetuses. We have reported that the myocardial performance index is a very good method for evaluation of the foetal heart function during the first few weeks of pregnancy (Fig 7). It is repeatable and can be evaluated by experienced foetal sonographers. Normal values have been reported by our team for foetuses between 11.0 and 13.6 weeks[11] and from 14 weeks until the end of pregnancy.[12]

Examination of the foetal cardiovascular system is possible from 11 weeks of gestation and a full

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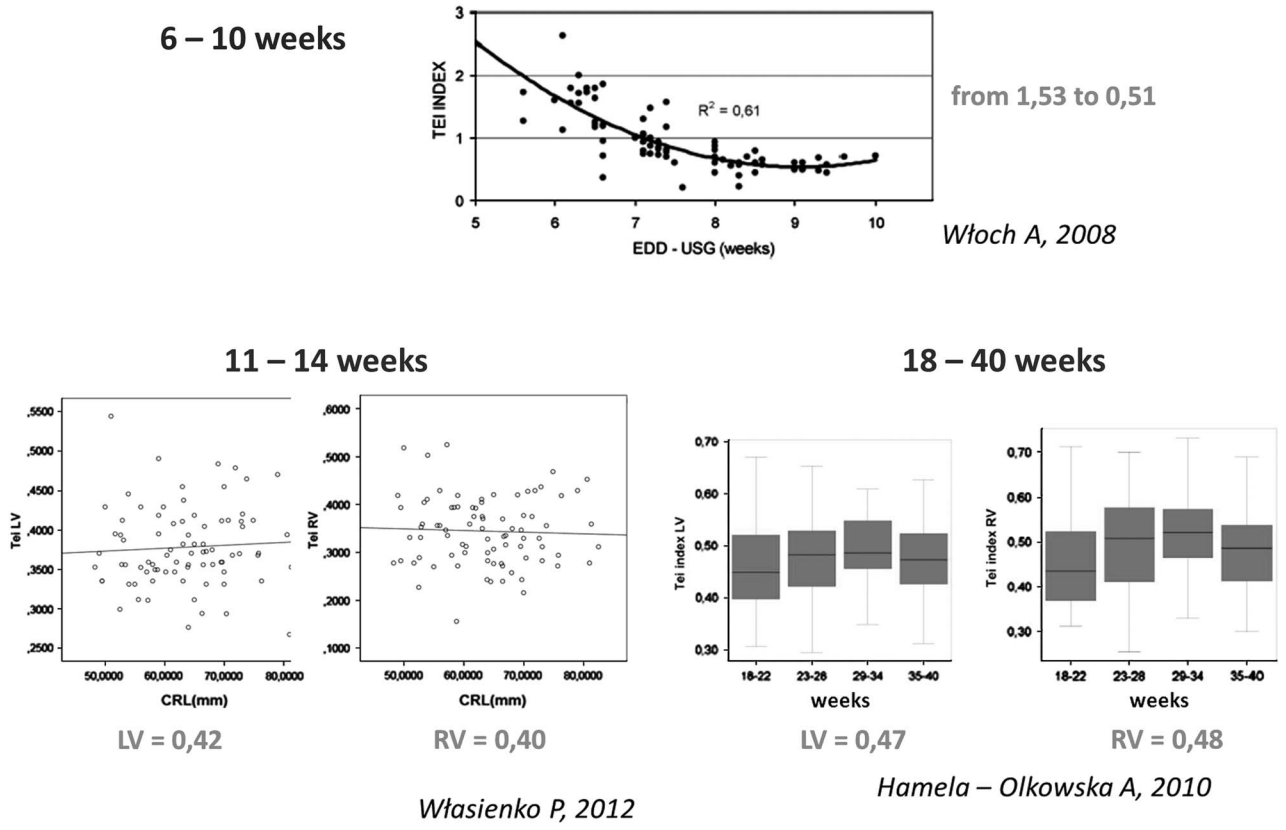

Figure 7.
Myocardial performance index (Tei index, MPI) in different periods of pregnancy – Polish data.

examination includes peripheral arterial blood flows, Doppler of the precordial veins, as well as intracardiac Doppler. Foetal shunts at the level of the foramen ovale and arterial duct are important for foetal well-being. Foetal haemodynamics were described by Rasanen et al[13] who confirmed that right ventricular output is slightly higher than the left ventricular output. The biggest change occurs in the third trimester, when left ventricular output is 40% and right ventricular output is 60% of the combined cardiac output. They calculated pulmonary flow from the sum of left and right pulmonary artery flow and calculated it to be about 20% of the combined cardiac output. In the third trimester of pregnancy, foramen ovale flow was about 34% of the combined cardiac output, and arterial duct flow was about 39% of the combined cardiac output. This is an important observation, because based on this finding it is easy to understand why restriction of the foramen ovale or arterial duct leads to rapid compromise in foetal haemodynamics.

Fouron[14] proposed a novel concept that the only arterial shunt in the foetus is the aortic isthmus, and not the arterial duct. He proved this in a clinical situation, intrauterine growth restriction, in which flow across the aortic isthmus correlated well with placental flow.

It is important to understand the normal foetal flow patterns through different parts of foetal circulation. The acceleration time of arterial flow is because of the vascular resistance against which the heart is pumping. The shortest acceleration time is in the pulmonary artery: it is slightly longer in the aorta and longest in the arterial duct where blood is pumped to the descending aorta against very low placental resistance.

Flow tracing is characteristic in the veins; in normal circulation, there is always flow towards the heart in the pulmonary veins and venous duct, whereas there is always a small negative "a" wave in the systemic veins. A negative "a" wave in the pulmonary veins may be seen in foetuses with hypoplastic left heart syndrome and restrictive forman ovale and a deep negative "a" wave in the systemic veins in foetuses with severe heart failure.

To evaluate foetal well-being and foetal circulatory condition, Huhta created the concept of the cardiovascular profile score (Fig 8). A healthy foetus has a total of 10 points: for each ultrasound sign one or two points are subtracted.[15] This score is very useful in every day clinical work, because it combines obstetric and cardiac signs, and thus the evaluation of foetal condition is more precise.

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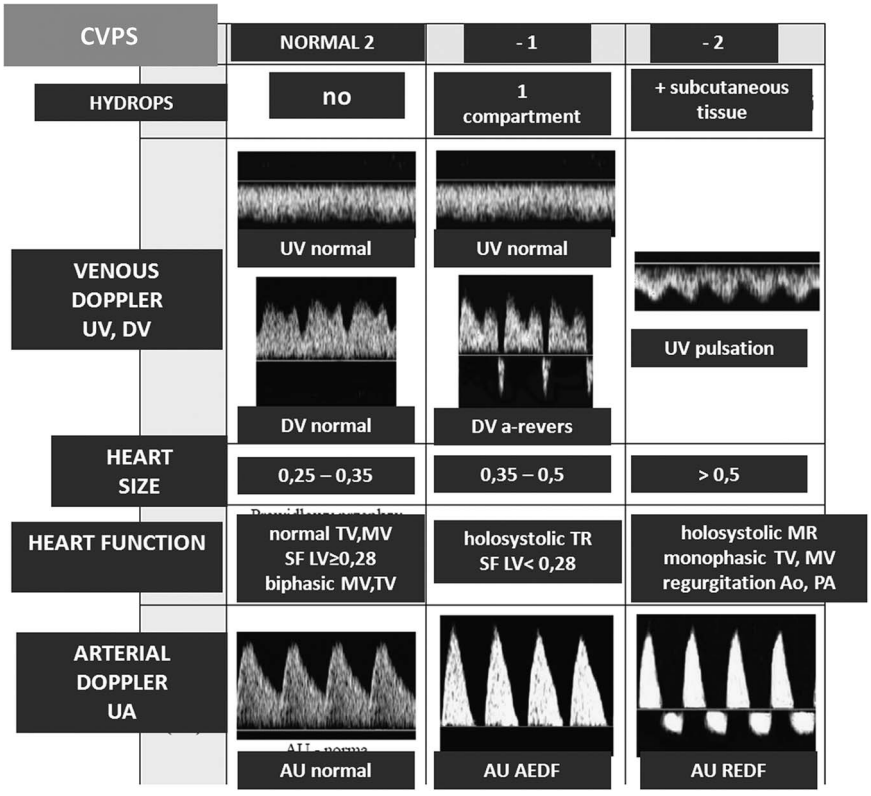

Figure 8.
Cardiovascular profile score developed by J. Huhta.

Conclusions

The quickest and the most profound changes in foetal circulation occur in the early first trimester. All functional changes are strictly connected with morphological ones, but not all of them are well understood. The development of the coronary circulation seems to be the most important for atrio-ventricular valve flow and improvement in foetal heart function. By late first trimester, development of the heart is finished, but further changes are dependent on flow distribution. Evaluation of the foetal and placental circulation is essential to understand the physiological and pathophysiological changes in the foetal cardiovascular system.

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