Fetal congestive heart failure

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KEYWORDS
Fetal; Cardiology; Congestive heart failure; Doppler; Hydrops

Summary
Fetal echocardiography is used in the diagnosis of many forms of congenital heart disease, and in the assessment of the prognosis of cardiac lesions based on their anatomy and presentation in utero. However, the presence of signs of fetal heart failure such as hydrops or valvular regurgitation makes the assessment of prognosis more difficult. A tool for this assessment is the 'cardiovascular profile score', which combines ultrasonic markers of fetal cardiovascular unwellness based on univariate parameters that have been correlated with perinatal mortality. This profile could become the 'heart failure score' and could potentially be used in much the same way as and in combination with the biophysical profile score. This article will present a straightforward method for rapid evaluation of a fetus that may have congestive heart failure.

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The fetal circulation and heart failure

In the fetus, the ventricles pump blood in parallel rather than in series; the left ventricle pumps blood to the aorta and the upper body, and the right ventricle pumps blood to the ductus arteriosus, the lower body and the placenta. The lungs have a high resistance in utero and the placenta fulfills the role of oxygenating the blood and ridding the body of waste. Highly oxygenated blood from the placenta passes to the ductus venosus where a portion bypasses the liver and passes predominantly to the left atrium. The relatively de-oxygenated blood from the upper body passes to the tricuspid valve and then to the ductus arteriosus and lungs. The de-oxygenated blood from the inferior vena cava and the right hepatic veins is directed to the right atrium and predominantly to the tricuspid valve. This distribution of lower body flow is accomplished by the posterior portion of the inferior vena cava connecting directly to the foramen ovale, and the superior portion of the atrial septum, the crista dividers, which overlies the inferior vena cava, effectively dividing it into two streams. Therefore, the presence of three shunts (ductus venosus, foramen ovale and ductus arteriosus) allows the fetal heart to work with two parallel circulations rather than one series circulation. Right and left atrial pressures are almost equal because of the

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presence of the foramen ovale, and right and left ventricular pressures are equal due to the ductus arteriosus. The left ventricle ejects blood into the upper body and cerebral circulation, and the right ventricle ejects blood into the pulmonary arteries and through the ductus arteriosus into the lower body and the placental circulation. The vascular beds of the upper and lower body are connected via the aortic isthmus. As a further consequence of the parallel arrangement of these circulations, ventricular outputs can be different; in the case of obstruction on one side of the heart, the other side is able to increase its work or even to supply the whole circulation alone.1

Factors affecting perinatal cardiac output

As the pulmonary and systemic circulations are separate in the fetus, each ventricle has a stroke volume determined by the individual preload, afterload and contractility of that chamber. Both ventricles have a common heart rate and humeral environment, and the atrial pressures are similar due to the presence of the foramen ovale. The ventricles are linked by the ventricular septum, and have a common arterial pressure due to the widely patent ductus arteriosus. The unique feature of parallel ventricular ejection is that if there is increased afterload of one ventricle, the output of that ventricle will fall and the output of the contralateral ventricle will increase in a compensatory manner. This leads to the commonly observed feature associated with congenital heart disease of disproportionate growth of the normal side of the heart.

Comparisons of myocardial contractility between fetal and adult animals have shown that fetal myocardium develops less active tension than adult myocardium at similar muscle lengths. Structural differences such as less T-tubular system and less organized myofibrils in the fetus are observed, and there are also differences in calcium uptake into the sarcoplasmic reticulum. Decreased sympathetic innervation in immature myocardium could influence the stress response of the myocardium. Fetal myocytes are smaller in size, have less mitochondria, sarcoplasmic reticulum, myofilaments, alpha- and beta-adrenoceptors, and t-tubuli, and higher concentrations of DNA reflecting a larger number of nuclei. In contrast to postnatal life, myocardial growth is the result of an increase in the number of muscle cells rather than an increase in cell size. In the very immature heart, myofilaments are arranged in a more chaotic way, but they become better organized as gestation advances. These morphological differences have been used to explain the reduced ability of the fetal myocyte to contract. The metabolic source of energy for the fetal myocardium is almost exclusively glucose. In adults, fatty acids are the major source of energy for the myocardium. Growth or increased work load in the fetus results in hyperplasia of the myocardium with an increased number of cells, whereas growth of the myocardium after birth is due to increased cell size or hypertrophy (increased protein content of each cell).2

The effect of heart rate on combined ventricular output (CVO) is much more pronounced in utero than in postnatal life.3 For fetal heart rates between 50 and 200 beats/min, the stroke volume of the ventricular chambers can adapt to maintain adequate CVO and tissue perfusion. Heart failure will often occur outside this range.

In summary, the major determinant of cardiac output is the afterload of the fetal ventricle. Any factor that raises the impedance to ejection will inversely lower the ventricular stroke volume due to its effect on both systolic and diastolic functions. For example, in fetal growth restriction due to placental dysfunction, the combined cardiac output drops due to increased placental resistance.

The transitional circulation

After birth, the function of gas exchange is transferred from the placenta to the lungs. The major changes in the circulation after birth are a decrease in pulmonary vascular resistance and closure of the ductus arteriosus and foramen ovale. The ductus arteriosus closes within 2–3 days in term neonates, and the patency of the ductus arteriosus during this time results in significant left to right shunt. This raises the left atrial pressure and effectively restricts right to left shunting at the atrial level. Shunting through the ductus venosus normally ceases 2–3 days after birth.

The aetiology of hydrops fetalis

Cardiac failure in the fetus

These morphological and functional differences affect the development and presentation of fetal heart failure. End-stage fetal heart failure results in hydrops fetalis. The reduced ability of the fetal heart to contract and generate force, the lower myocardial compliance and the diminished Frank Starling mechanism (the higher dependence of
cardiac output on heart rate, and the lack of adrenoceptors) all contribute to decreased cardiac reserve in response to stress and to higher susceptibility of the fetus for the development of cardiac failure. With increasing atrial pressure, the output of the heart plateaus at a much lower pressure in utero than postnatally.

Several features are responsible for fluid accumulation in fetal tissue. The final common pathway of many different conditions compromising the cardiovascular system is the elevation of ventricular end-diastolic pressure, atrial pressure and central venous pressure. In the fetus, even small increases in venous pressure have been shown to alter fetal organ function. The younger the fetus, the higher is its extracellular water content and the lower is its tissue pressure. Fluid movement between intravascular and extravascular spaces is dependent on intra- and extravascular hydrostatic and oncotic pressures and the fluid filtration coefficient, which is determined by the capillary membrane (in the fetus, this is more permeable for fluid and protein). Albumin concentration, largely responsible for oncotnic pressure, is lower in the fetus and increases with gestational age. All these factors favour fluid movement out of capillaries into the surrounding tissues. Thus, lymphatic drainage of tissue seems to be much more important in the fetus. Elevated venous pressure may reduce lymphatic flow, further favouring the development of hydrops. Decreased arterial blood pressure and elevated filling pressures also trigger hormonal responses such as production of plasma arginine vasopressin (decreases urinary production), angiotensin II (increases fluid accumulation) and atrial natriuretic peptide (increases capillary permeability).

Faced with a fetus with hydrops fetalis, one must first determine if the hydrops is cardiac, inflammatory or metabolic. Many cases of hydrops are now being attributed to fetal systemic infection. New markers include aetiologic agents such as parvovirus or adenovirus. The associated hepatitis with these infections can compromise the protein-producing capability of the fetus, thereby decreasing the fetal oncotic pressure in the vascular space and resulting in fluid loss from the circulation. Immune hydrops must always be considered in the differential diagnosis, but other causes of anaemia can cause hydrops such as haemoglobinopathies. Infections can cause haemolytic anaemia that can be treated by fetal transfusion. High central venous pressure may exceed the oncotic pressure of the interstitial space, causing fluid to pass into spaces such as the abdominal cavity (ascites), pleural or pericardial spaces (effusions) or any of the vital organs. Multiple mechanisms of hydrops may co-exist and the primary cause may not be immediately obvious. Of more importance is the determination of the prognosis of hydrops. This task would be aided by a semiquantitative measure of fetal heart failure. In other words, is this hydrops due to heart failure? In human fetuses, a rising central venous pressure correlates with increasing heart size.

There are several possibilities for the cause of heart failure in the fetus after ruling out fetal infection (Table 1).

<table>
<thead>
<tr>
<th>Table 1 Causes of fetal congestive heart failure</th>
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<tbody>
<tr>
<td>• Fetal arrhythmias</td>
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<tr>
<td>• Anaemia</td>
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<tr>
<td>• Congenital heart disease with valvular regurgitation</td>
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<tr>
<td>• Non-cardiac malformations such as diaphragmatic hernia or cystic hygroma</td>
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<tr>
<td>• Twin–twin transfusion recipient volume and pressure overload</td>
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<td>• Atrioventricular fistula with high cardiac output</td>
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Prognosis of fetal heart failure: markers of fetal mortality

The most useful predictor of perinatal death in fetal hydrops is the presence of umbilical venous pulsations, as the most common pathway of perinatal demise is compromised fetal cardiac output/fetal congestive heart failure (CHF). What follows is a method to detect this entity and to attempt to decide which fetuses should be referred to a fetal centre. Initial data are collected using echocardiography.

- Cardiac size/thoracic size: cardiac area/thoracic area (C/T) ratio (normal 0.25–0.35) or C/T circumference ratio (normal < 0.5).
- Venous Doppler: inferior caval (or hepatic venous) (increased atrial reversal) and umbilical cord vein (pulsations).
- Four-valve Doppler: any valvular leaks should be evaluated further.

If there are abnormalities in any of these measurements, a cardiac cause or associated physiological problem may be present and detailed study is indicated to rule out serious cardiovascular involvement.

The cardiovascular system provides a large volume of information about the wellbeing of the fetus. It is accessible because of rapid technological developments in non-invasive techniques,
particularly ultrasound. The fetus has become the new patient of the decade due to the rapid changes in ultrasonic technologies and other fetal assessment techniques. The fetal biophysical profile is useful to detect changes in fetal wellbeing, especially heart failure due to abnormal heart rate. The decision to deliver a fetus prematurely due to cardiac changes must be made in the context of the risks both pre- and postnatally. Most associations between cardiovascular changes and the function of other organs in the fetus have yet to be defined. Therefore, any assessment demands a co-ordinated team approach between perinatologists, cardiologists and neonatologists.

The definition of fetal CHF is similar to that after birth; i.e. inadequate tissue perfusion. Inadequate cardiac output results in a series of complex reflexes and adaptations to improve forward flow or to direct blood to vital organs. This state can be described as a deficiency of blood flow to the tissues such that certain reflexes are triggered for survival of the fetus. One is the secretion of an excess of circulating catacholamines, produced in response to peripheral vascular detection of abnormal perfusion. Powerful hormonal reflexes are triggered, including those that control salt and water retention, in an attempt to increase myocardial preload and adrenocorticoid excess, which mobilizes additional calories for the increased metabolic demand. It is now known that the fetus is capable of activating cytokines and secreting the endothelin, troponin T. The maturational changes of the systemic vascular bed with gestational age are not known, but it is thought that vasoconstriction of the fetal systemic resistance vessels occurs in response to stress at some point in the pregnancy. How this affects compensation in the fetal circulation is currently being investigated.

Ventricular function in the fetus

Right ventricular function in the human fetus has received the most attention because this ventricle is most likely to show an abnormality during clinical situations associated with increased work load. Some examples of right ventricular problems are summarized below to illustrate an approach to ventricular function in the fetus. The right ventricle is a large contributor to the work output of the fetal myocardium because of the large volume and pressure work it performs. The earliest signs of altered function in the fetal heart are a reflection of right heart haemodynamics. For example, isolated right atrial enlargement is a sign of many abnormalities, especially early in gestation. This may be because the right atrium is at the centre of the fetal circulation. Flow from the superior vena cava passes to the tricuspid valve directed by the right venous valve inside the right atrium. Flow from the left hepatic veins and the ductus venosus crosses inferiorly across the right atrium to reach the foramen ovale and the left atrium. Normal flow from the right atrium to the left atrium reflects a normal right atrial to left atrial pressure gradient. Any increase in flow to the heart, such as with anaemia or arteriovenous fistula, will translate into enlargement of the right atrium. The right ventricle pumps primarily to the lower body and placenta, and right atrial pressure elevation will result from any increase in the resistance faced by this ventricle.

Cardiac function can be estimated using the Tei index or myocardial performance index. This is calculated using the filling time of the atrioventricular valve and the ejection time of the ventricle. The index is calculated as shown in Fig. 1.

Fetal congestive heart failure

The diagnosis of fetal CHF must be addressed in a clinical fashion, similar to that after birth. There are multiple potential causes of CHF (Table 1). The final common pathway to fetal death is poor tissue perfusion and acidosis. The clinical state of CHF in the fetus can be characterized by findings in at least five categories obtained during the ultrasonographic examination. Each of these categories is worth 2 points in a 10-point scoring system for assessment of the cardiovascular system. Abnormalities in the cardiovascular profile score may occur prior to the clinical state of hydrops fetalis. The five categories are hydrops, umbilical venous
Doppler, heart size, abnormal myocardial function, and arterial Doppler.

Within specific disease entities, the attending physician places more emphasis on certain aspects when predicting the prognosis. As always, this information can only comprise a portion of the total picture and must be integrated by the attending physician into the diagnostic and treatment plan for the patient.

The cardiovascular profile score gives a semi-quantitative score of fetal cardiac wellbeing, and uses known ultrasound markers that have been correlated with poor fetal outcome (Appendix 1 and Table 2).11 This profile is normal if the score is 10, and signs of cardiac abnormalities result in a decrease of the score from normal. For example, if there are hydrops with ascites and no other abnormalities, there would be a deduction of 1 point for hydrops (ascites but no skin oedema) and no deductions for the other categories (i.e. a score of 9 out of 10).

### Hydrops

Hydrops fetalis, in early stages, may present with ascites, pleural effusion, pericardial effusion or a combination. In advanced hydrops, generalized skin oedema is seen easily on the scalp and abdominal wall. In scoring hydrops for the cardiovascular profile score, one point is deducted for early hydrops and two points for skin oedema.

- Ascites, pleural or pericardial effusion minus 1 point
- Skin oedema minus 2 points

### Umbilical and ductus venosus Doppler

Studies in human fetuses have shown that alterations in central venous blood velocity patterns are an accurate reflection of abnormalities in cardiac haemodynamics.12 The abnormal pulsatility pattern consists of increased velocity of blood flow. Reversal away from the heart during atrial contraction has been reported in fetuses with CHF, and may be a sign of increased end-diastolic pressure in the ventricles of the failing heart. Abnormal inferior vena cava flow velocity patterns have been described in several fetal pathological conditions including anaemia, non-immune hydrops and arrhythmias, and in severely growth-retarded fetuses characterized by the absence of end-diastolic flow in the umbilical artery. The compromised fetus with acidosis is known to manifest abnormalities of venous Doppler including atrial reversal in excess of normal in the inferior vena cava at the junction with the right atrium and increased pulsatility in the ductus venosus. The prognostic importance of these abnormalities has been confirmed in fetuses with intra-uterine growth retardation and fetuses with hydrops. An increased A/S ratio in the ductus venosus (peak atrial reversal divided by the peak filling wave during ventricular systole) appears to be the most useful sign in quantifying the increased atrial contraction in fetuses with growth retardation. Normally, the ratio of the area of atrial reversal to the area of entire forward flow should be less than 7%. Transmission of venous pulsations into the portal and umbilical circulation correlates with increasing degrees of cardiac compromise. Tulzer et al. studied the cardiac factors related to prognosis in hydrops, and noted that umbilical venous pulsations could stand in for a number of cardiac variables in predicting prognosis, including ventricular shortening fraction, ejection velocities and percentage inferior vena cava atrial reversal.13 Abnormal venous Doppler progresses retrograde from the heart in the following order:

- Increased atrial reversal in the inferior vena cava.
- Ductus venosus atrial reversal.
- Portal venous atrial pulsations.
- Umbilical venous atrial pulsations.

The end-stage finding of abnormal venous Doppler is atrial pulsations in the umbilical cord vein. This finding of so-called ‘diastolic block’ predicts perinatal mortality. So-called ‘double venous pulsations’ is an ominous sign (the umbilical vein velocity resembles the inferior vena cava). Venous

### Table 2: Summary of cardiovascular profile score

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
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<tbody>
<tr>
<td>Hydrops: effusion – minus 1 point (pt); skin oedema – minus 2 pts</td>
<td></td>
</tr>
<tr>
<td>Venous Doppler: atrial reversal in ductus venosus – minus 1 pt; atrial pulsations in umbilical vein – minus 2 pts</td>
<td></td>
</tr>
<tr>
<td>Heart size: C/T area ratio &gt; 0.35 – minus 1 pt; &gt;0.5 or &lt;0.20 – minus 2 pts</td>
<td></td>
</tr>
<tr>
<td>Cardiac function: RV/LV shortening fraction 0.28 – minus 1 pt; tricuspid valve regurgitation (holosystolic) – minus 1 pt; mitral regurgitation – minus 1 pt; pulmonary or aortic valve regurgitation – minus 1 pt; valve regurgitation dP/dt 400 mmHg/s – minus 2 pts; ventricular hypertrophy – minus 1 pt; monophasic filling – minus 2 pts</td>
<td></td>
</tr>
<tr>
<td>Umbilical artery: absent end-diastolic velocity – minus 1 pt; reversed diastolic velocity – minus 2 pts</td>
<td></td>
</tr>
</tbody>
</table>

The maximum deduction for each category is 2 points.
pulsations are not normal in the portal vein and such a finding may precede umbilical venous pulsations. The most useful site for sampling in the abdomen is the ductus venosus, which can be identified by its location and colour Doppler acceleration blood velocity pattern.

To assess the venous system consistently, pulsed Doppler sampling is obtained in the inferior vena cava, the ductus venosus, the umbilical vein in the abdomen and the umbilical cord vein as part of each serial examination. Transmission of the atrial reversal into the ductus venosus and later into the portal and cord vein sites over time suggests progression of heart failure. The cardiovascular profile score has deductions for abnormal venous Doppler as shown below.

- Ductus venosus atrial reversal minus 1 point
- Umbilical venous atrial pulsations minus 2 points

The maximum deduction in this category, as for the other categories, is 2 points.

Cardiomegaly

Enlargement of the cardiac chambers is a universal sign of heart failure. This is also true in the fetus, but few of the mechanisms are understood. It is likely that neural humoral reflexes are triggered, resulting in retention of extracellular volume leading to increased end-diastolic volume of the ventricles. At some point, this increased ventricular size indicates increased end-diastolic pressure. However, unlike the postnatal human, it is uncommon to encounter persistent tachycardia with signs of catecholamine excess. It is possible that the levels of humoral agents are modified by the fetal–maternal exchange mechanisms that exist when the placenta is functioning normally.

The most common cardiac chamber to express enlargement as a sign of impending cardiac failure is the right atrium. The reasons for this relate to the many causes for heart failure, but the right atrium is a final pathway for blood flow returning to the heart and will manifest enlargement in situations of relative foramen obstruction, volume overload, tricuspid valve regurgitation, and increased afterload. Increased size of the right atrium may be due to increased right ventricular end-diastolic pressure, that may itself be due to increased afterload or coronary insufficiency. The right ventricle may be more susceptible to increased work because of the nature of the afterload and the resulting increased demands for oxygen in the face of increased chamber wall stress. It is generally believed that increased atrial wall stress without increased ventricular work does not lead to clinical difficulties in the fetus. Such a situation could be an early marker of cardiac decompensation and may predispose to supraventricular arrhythmias. Secretion of atrial natriuretic peptide could be a marker of this finding.

The technique for measuring fetal heart size as the heart area:chest area ratio is shown in Fig. 2. Cardiomegaly is defined as a heart area:chest area ratio > 0.35 at any time in gestation. A heart rate that is slower than normal or a persistent rapid heart rate leads to cardiomegaly. The time frame of the onset of arrhythmia may therefore be estimated by the effect on cardiac size. For example, an intermittent arrhythmia that has appeared recently would not be expected to cause cardiac enlargement.

In utero, the heart area can be compared easily with the thorax area, and the ratio should be less than one-third and greater than one-quarter in the presence of normal chest development. In fetuses with cystic adenomatoid malformation, a small $C/T$ ratio ($<0.2$) is associated with a poor prognosis.

$C/T$ area ratio = cardiac area/ chest area (normal 0.2–0.35).

$C/T$ circumference ratio = cardiac circumference/ chest circumference (normal < 0.5).

- Mild cardiomegaly: area ratio > 0.35 minus 1 point
- Severe cardiomegaly: area ratio > 0.50 minus 2 points
- Small heart ratio (<0.2) minus 2 points
Abnormal myocardial function

Cardiac function is assessed indirectly by global shortening (and thickening) of the walls of the ventricles, and by the function of the atrioventricular and semilunar valves. Both the right and left ventricles should shorten their diameters more than 28% in systole compared with diastole. Measurements of cardiac dimensions with time are performed using M-mode echocardiography. The shortening fraction of a ventricle is calculated by taking the difference between the diastolic (DD) and systolic dimensions (SD) and dividing by the diastolic dimension.

Fractional shortening

\[
\frac{(DD - SD)}{DD} \quad \text{(normal > 0.28)}
\]

An abnormal shortening fraction could reflect myocardial compromise or an increase in the fetal ventricular workload. Regardless, an increase in DD is often related to a decrease in shortening fraction, and should be regarded as an indication for more intensive monitoring.

The atrioventricular and semilunar valves are competent in the normal fetus. If regurgitation is detected, it is usually a sign of altered cardiovascular physiology. Since tricuspid valve regurgitation is common after birth, one may speculate that the fetal right ventricle is well adapted to systemic pressure work. Therefore, valvular competence is normal and tricuspid valve regurgitation is only present where there is increased ventricular wall stress. Trace tricuspid regurgitation, defined as non-holosystolic regurgitation lasting for at least 70 ms, is not normal. This may be the first sign of a problem but has little prognostic importance. Holosystolic tricuspid regurgitation is abnormal and always indicates the need for further investigation. When regurgitation is detected by colour Doppler, it must be confirmed and graded by pulsed Doppler. Hydrops and fetal death can occur with congenital diseases of the tricuspid valve. Regurgitation of other valves is usually a sign of more advanced CHF and may occur in the moribund fetus with acidosis and severe heart failure as a sign of myocardial compromise. Tricuspid valve regurgitation can be a reversible sign of heart failure, as seen in fetuses with successful in-utero therapy for anaemia or tachycardia. Progression to mitral valve regurgitation is always a sign of fetal CHF and usually means that a significant increase in left ventricular wall stress is present. With severe myocardial failure, support for the semilunar valves is compromised and pulmonary or aortic valve regurgitation can occur.

The filling pattern of the ventricles in diastole is an indicator of the diastolic function of the heart. Monophasic filling of the ventricles is a sign of compromised diastolic function and severe fetal heart failure.

Several disease states are now being identified where thickening of the ventricular chambers (myocardial hypertrophy) occurs in the absence of congenital ventricular outflow obstruction. This is assessed by measurement of the end-diastolic wall thickness of the left ventricle and comparison with the normal values for age. Any left ventricular posterior wall thickness greater than or equal to 4 mm is abnormal. The most severe cases of fetal hypertension have been detected in the larger twin in twin—twin transfusion syndrome; a mortality rate of over 70% is common. It appears that early identification of hypertrophy in the larger twin can be useful in patient management. Treatment strategies to separate the placental communications may prevent hydrops in the larger fetus and result in improved survival. Postnatally, neonatal hypertension can be severe and life threatening. Regardless of the aetiology, thickening of the fetal ventricles could restrict the cardiac reserve before or after birth. As cardiac hypertrophy can occur rapidly but takes weeks or months to resolve, its identification is an important marker of a cardiovascular system at risk. Abnormalities of diastolic function could be expected and should be excluded by comparing the filling patterns of the ventricles using pulsed Doppler with standardized normal values. One rule of thumb is that the A-wave of ventricular filling should always be greater than the E-wave; if it is higher or is indistinguishable, a detailed cardiac study should be performed.

Echocardiography has long depended on shortening of the ventricles to assess systolic function. However, it is known that shortening is inversely proportional to afterload of the heart and intense vasoconstriction and redistribution of flow are the rule in fetal CHF. Better methods for the assessment of cardiac work, including pressure and flow data, are needed. Fetal \( \frac{dP}{dt} \) measurement is feasible when valvular regurgitation is present, and Doppler assessment of diastolic function may be useful in detecting compromised myocardial function. Poor prognosis is associated with a \( \frac{dP}{dt} \) value < 400 mmHg/s.
Right ventricle/left ventricle shortening fraction < 0.28 minus 1 point
- Tricuspid valve regurgitation (holosystolic) minus 1 point
- Mitral regurgitation (holosystolic) minus 1 point
- Ventricular hypertrophy minus 1 point
- Pulmonary or aortic valve regurgitation minus 1 point
- Monophasic ventricular filling minus 2 points
- Atrioventricular valve regurgitation dP/dt > 400 mmHg/s minus 2 points

The maximum deduction in this category, as for the other categories, is 2 points.

Arterial Doppler: redistribution of fetal cardiac output

It is well established that blood velocities measured by Doppler echocardiography in the umbilical artery and in other peripheral vascular beds can be used as an indirect indicator of relative vascular impedances. Findings of an increased pulsatility index in the umbilical artery and descending aorta, and a decreased index in the middle cerebral artery, are non-invasive signs of redistribution of flow. It is important to recognize that a pulsed Doppler finding in one portion of the circulation is affected by changes in the rest of the circulation. For example, if there is significant aortic valvular regurgitation in the fetus, the diastolic reversal in the descending aorta and the increased pulsatility index in the umbilical artery are secondary to this change in the heart and do not reflect peripheral resistance alone.

The most common cause of elevated vascular resistance in the fetus is placental dysfunction secondary to vasculopathy leading to asymmetrical growth retardation. This complex pathophysiological state is poorly understood but there is evidence that hypoxaemia occurs due to placental dysfunction, and nutrition is compromised severely enough to impair growth. Once the normal pattern of growth is disturbed (usually asymmetrical such that the brain continues to grow but the body does not), the fetus is at risk of organ damage from hypoxaemic/ischaemic injury. The umbilical artery manifests this problem with a loss or reversal of diastolic blood flow. There is redistribution of flow to the brain (so-called 'brain sparing') due to reflex vasodilatation of the cerebral vessels. This is manifested by a decrease in the pulsatility index in the middle cerebral artery such that diastolic flow is relatively increased (pulsatility index less than 2 standard deviations below the mean for gestational age).

In a fetus with hypoxaemia, the peripheral fetal vessels are vasoconstricted and the larger arteries are thought to be non-compliant compared with normal fetuses with increased blood pressure. In other words, this is a physiological state characterized by increased vascular resistances and, at end stage, decreased cardiac output. Right ventricular enlargement occurs in some cases.

The vasoactive autacoids nitric oxide and prostacyclin occur in decreased amounts with endothelial cell damage in the placenta. Preliminary studies in pregnant women with high pulsatility indices during Doppler ultrasound measurement of umbilical blood flow velocity have revealed that maternal administration of the nitric-oxide-donating drug glyceryl trinitrate decreases the pulsatility index by reducing vasoconstriction in the fetal extracorporeal circulation. Further capability to treat placental vascular disease will benefit from advances in understanding endothelial cell function in pulmonary and other vascular beds. Therefore, altered vascular impedances can be a marker of impending heart failure in the fetus.

Fetal brain sparing is a marker of cardiac output redistribution that is sensitive for the detection of significant hypoxaemia and placental dysfunction. Whether this will be useful for detecting the presence of acidosis in the fetus is being investigated. There is evidence that reversal of diastolic flow in the umbilical artery, if confirmed, may be a significant risk factor for abnormal outcomes.

- Absent end-diastolic flow in the umbilical artery + brain sparing minus 1 point
- Reversed end-diastolic flow in the umbilical artery minus 2 points

Cardiovascular profile score (Appendix 1)

As shown in the last five sections, a profile can be developed of the fetal circulatory responses. The cardiovascular profile score is comprised of two points from each of five categories used in serial studies to provide a method of uniform physiological assessment. By taking a multivariate approach, this type of multifactorial score can combine assessment of direct and indirect markers of cardiovascular function. Initial validation of the cardiovascular profile score in hydrops

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\( ^a \) Increased middle cerebral artery diastolic velocity.
was shown by Falkensammer and Huhta. Seven fetuses with hydrops, including three with congenital heart disease, showed correlation between the cardiovascular profile score and the myocardial performance index (Tei index). Right ventricular and left ventricular Tei indices were assessed in normal fetuses and showed no change with gestational age. Hofstaetter and Huhta measured the cardiovascular profile score in 59 fetuses with hydrops. Mortality was 21/59. The average score in those who died pre- or postnatally was 4.9, whereas the average score in the survivors was 6.5.

Makikallio et al. studied 75 growth-restricted fetuses and reported six deaths; the average cardiovascular profile score in those who died was 4.5. Cord blood biochemical markers including NT-proANP, NT-proBNP and NT troponin levels were elevated with CHF and correlated inversely with the cardiovascular profile score (personal communication).

Medical treatment of fetal heart failure

Treatment of fetal cardiovascular problems can be classified into five of the most common subgroups based on the aetiology of CHF: (1) abnormal peripheral impedances causing redistribution of flow and growth failure; (2) high output due to anaemia or arteriovenous fistula; (3) primary or secondary valvular regurgitation; (4) heart failure due to myocardial dysfunction; and (5) tachycardia/bradycardia. Interventions aimed at improving the effective cardiac output are also aimed at prolonging pregnancy and preventing prematurity and prenatal asphyxia.

The rapidity with which a disease progresses determines the urgency with which treatment should occur. This is because the myocardial response to increased wall stress will be either adequate or inadequate depending on the severity, timing and duration of the insult, coronary perfusion, the nutritional state of the fetus, and other problems in the pregnancy.

Usual treatment of placental dysfunction is designed to improve the vascular impedance of the placenta and to increase the flow of oxygenated blood to the fetus. Bedrest, improved nutrition and maternal oxygen may lead to an improvement in placental function. Tocolytic medications may relax the placenta and improve its function. Myocardial support for advanced growth restriction has not been proposed, partly because validation of diagnostic methods is lacking. Studies of ventricular ejection force in growth restriction have shown that both ventricles have decreased ejection force. Advanced heart failure in this setting with severely decreased arterial paO2 and poor nutrition is manifested by non-specific signs of increased right ventricle and right atrium size, atrial reversal in the venous Doppler pattern, and altered forward flow velocities.

Treatment of decreased ventricular shortening with digoxin is controversial. Digoxin is known to decrease the catecholamine response to CHF; if there is diastolic dysfunction in the fetus, this may improve filling and reduce filling pressures. When there is cardiomegaly (see above for criteria), it is rational to use transplacental treatment of the fetus to support the myocardium if the pregnancy will be continuing for long enough for medication levels to reach therapeutic levels. Digoxin has been used in such circumstances due to its antiadrenergic benefits and the significant experience that has been gained about its safety in pregnancy. The author uses lanoxin (Lanoxicaps) 0.2 mg orally two to four times per day based on maternal serum levels, with a trough level of 1.0–2.0 to avoid any maternal side effects. In fetuses with arteriovenous fistula or intractable anaemia and heart failure, the author also uses digoxin to support the heart. In a review of clinical experience, digoxin was used to treat 12 fetuses with abnormal cardiovascular profile scores of 7 or less. It appeared to limit the progression of CHF in fetuses with an abnormal cardiovascular system due to CHD or non-cardiac malformations, but was not effective once hydrops was present (B. Cuneo, personal communication).

If the afterload is high, an increase in oxygen consumption could result from increased inotropy without improved myocardial perfusion.

Terbutaline appears to hold promise as an inotropic and chronotropic agent, but studies of possible negative effects on the fetal myocardium are needed. At the present time, the author uses digoxin for fetal cardiac failure due to arrhythmias and high output states such as fistula and anaemia. In a recent case of acardiac twinning where the normal fetus was supporting two circulations, digoxin appeared to improve cardiac function and resulted in a prolonged and successful gestation for the normal twin.

Laser treatment of the twin–twin communications or cord ligation with acardiac twins can be applied to improve cardiac failure.

With anaemia, it is possible to transfuse the fetus via the umbilical vein. The diagnosis of fetal anaemia can be made using the middle cerebral artery peak velocity. With anaemia, the cardiac
output is increased with a reduced oxygen-carrying capacity.

When fetal valvular regurgitation is present on a congenital basis, it could be useful to decrease the afterload of the fetal ventricles, as is done in infants with a similar problem. However, medications that reduce the afterload, such as angiotensin-converting-enzyme inhibitors, are known to be dangerous to fetuses. A reduction of catecholamine levels could have a useful effect, and digoxin could affect this situation.

When myocardial dysfunction is seen without obvious reasons and fetal infection has been excluded, an inherited form of cardiomyopathy of either the left or right ventricle may be present in utero. The author uses digoxin for these patients provided that there is no sign of ventricular ectopy or tachycardia.

In pregnancies where the mother has significant levels of anti-Rho and anti-La antibodies, the author recommends dexamethasone 4 mg daily if there are signs of valvular regurgitation, heart block, valvulitis, myocardial dysfunction, myocardial echogenicity or effusion. Early use of this medication may prevent progression of heart block and myocardial injury later in life.

Conclusions

Diagnosing fetal heart failure is challenging due to difficulty in knowing how well the fetal myocardium is performing under changing loading conditions. By combining information from obstetric and cardiological evaluations, perinatal cardiologists can assess whether it is likely that the function abnormality is transient or permanent. The aetiology cannot always be known but the differential between infectious, inherited, congenital or toxic aetiologies can be tested.

After birth, the prognosis will depend on the diagnosis and the evolution of the functional abnormality over time. The long-term outcome will be dependent on whether or not the insult is reversible and whether there were periods of ischaemia and/or brain injury.

Fetal cardiac findings must be integrated into clinical management of the fetus by perinatologists. The cardiovascular profile score can be used to communicate between visits and specialists to assess the urgency of abnormalities and the prognosis.Serial studies using the cardiovascular profile score are necessary to determine the value of this test. With it, uniform treatment strategies can be planned.

Practice points

- Heart failure can be diagnosed in fetuses and the severity can be estimated.
- Serial studies with emphasis on venous Doppler can be useful in management.
- Transplacental treatment of fetal heart failure could result from accurate diagnosis and fetal/maternal stratification.

Appendix 1

Cardiovascular profile score (10 points = normal)

<table>
<thead>
<tr>
<th>Normal</th>
<th>-1 point</th>
<th>-2 points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrops</td>
<td>None (2 pts)</td>
<td>Ascites or pleural effusion or pericardial effusion</td>
</tr>
<tr>
<td>Venous Doppler (umbilical vein and ductus venosus)</td>
<td>UV (2 pts)</td>
<td>UV</td>
</tr>
<tr>
<td>Heart size (heart area/chest area)</td>
<td>&gt;0.20 and &lt;0.35 (2 pts)</td>
<td>0.35–0.50 &gt;0.50 or &lt;0.20</td>
</tr>
<tr>
<td>Cardiac function</td>
<td>Normal TV and MV RV/LV S.F. &gt;0.28 Biphasic diastolic filling (2 pts)</td>
<td>Holosystolic TR or RV/LV S.F. &lt;0.28 Holosystolic MR or TR dP/dt 400 or monophasic filling</td>
</tr>
<tr>
<td>Arterial Doppler (umbilical artery)</td>
<td>UA (2 pts)</td>
<td>UA (AEDV)</td>
</tr>
</tbody>
</table>

The heart failure score is 10 if there are no abnormal signs and reflects 2 points for each of five categories: hydrops; venous Doppler; heart size; cardiac function; and arterial Doppler. AEDV, absent end-diastolic velocity; dP/dt, change in pressure over time of TR jet; DV, ductus venosus; LV, left ventricle; MR, mitral valve regurgitation; MV, mitral valve; pts, points; S.F., ventricular shortening fraction; TR, tricuspid valve regurgitation; TV, tricuspid valve; REDV, reversed end-diastolic velocity; RV, right ventricle; UV, umbilical vein.
References

22. Hofstaetter C, Huhta JC. Outcome assessment in hydrops fetalis using a cardiovascular score. Poster presentation at the Society of Pediatric Research, Baltimore, MD; May 7, 2002 [Abst].