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Echocardiographic evaluation before and after cardiac transplantation

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TRANSPLANTATION OF THE HEART REMAINS A viable option not only as primary treatment for hypoplastic left heart syndrome, but also for end-stage problems after the Norwood sequence of palliations. In this review, I discuss the pre-operative, intra-operative, and post-operative echocardiographic evaluation of these patients, with special emphasis on hemodynamic and functional assessment as well as surveillance for rejection and coronary arterial disease.

Preoperative evaluation

Hypoplastic left heart syndrome, a term coined by Noonan and Nadas, refers to a complex of congenital cardiac anomalies affecting the left side of the heart.[1] The special characteristics defining this syndrome are an underdevelopment of the left ventricle and ascending aorta, coupled with abnormalities of the aortic and mitral valves. The syndrome, however, is far from homogeneous. Within the spectrum of malformation, nonetheless, it is usual to recognize four combinations:

- Combined aortic and mitral atresia,
- Aortic atresia with mitral stenosis,
- Aortic stenosis with mitral atresia,
- Combined aortic and mitral stenosis.

When there is aortic atresia, then almost always there is associated severe hypoplasia of the ascending aorta, which usually measures less than 2.5 mm in diameter. In the presence of aortic stenosis, however, the ascending aorta typically measures between 3 and 5 mm in diameter. When aortic atresia is associated with a ventricular septal defect,[2] the ascending aorta may be of normal size, as may the left ventricle, and these cases should not be considered as part of the syndrome. Aortic coarctation, with a well-defined posterior shelf, is present in about four-fifths of cases.[3] The left atrium is usually small, and its walls are thickened. In some cases, endocardial fibroelastosis is present in the left atrium, and may extend to involve the pulmonary veins, leading to diffuse pulmonary venous disease. The interatrial communication can be obstructed, and in this setting the atrium can be decompressed by pathways such as the so-called levo-atriocardinal vein,[4] or fenestrations to the coronary sinus. Careful systematic echocardiographic evaluation, therefore, is important to recognize all the above features, if present, in preparation for either cardiac transplantation or the Norwood operation. It is also important to exclude associated anomalies that may be the underlying reason for the left-sided hypoplasia. These include totally anomalous pulmonary venous connection, severe restriction or premature closure of the oval foramen, and interruption of the aortic arch. Knowledge of these anatomic details for those preparing for transplantation helps when harvesting the important sections of heart required to reconstruct the left atrium, superior and inferior caval veins, and the aortic arch.

Intra-operative echocardiogram

During the transplantation, the descending aorta of the donor is anastomosed to the descending aorta of the recipient below the level of the arterial duct. The brachiocephalic arteries of the recipient are anastomosed as a single "Carrel" patch to the arch of the donor. The modification of the standard technique for orthotopic transplantation described by Bailey et al.[5] results in biatrial enlargement, and gives a characteristic hourglass shape to the right atrium.

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The transesophageal echocardiogram is the mainstay of intraoperative evaluation. The anastomotic suture line gives rise to a typical echo-dense ridge. The newer bicaval surgical approach is associated with better preservation of atrial morphology,[6] but it is essential to check the anastomoses of the both caval veins to rule out any obstruction. The entire aortic arch can be imaged particularly well with the multiplane probe. The left atrial anastomosis is then imaged, as well as all four pulmonary veins, again to identify any evidence of obstruction or distortion.

Qualitative assessment is made of both right and left ventricular systolic function. Regional abnormalities of wall motion can be determined from the transgastric short axis views, and the midesophageal 4-chamber and 2-chamber views.

Color Doppler interrogation of the atrioventricular and the arterial valves will reveal any significant regurgitation. Residual pulmonary hypertension is common in the patients with long waiting times, excessive flow of blood to the lungs, and significant restriction of the oval foramen. Pulmonary arterial pressures can be quantified from the velocity of the regurgitant jet through the tricuspid valve using Bernoulli's equation.

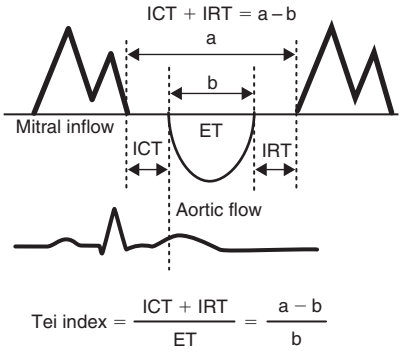


Figure 1.
The formula for calculating the Tei index.

Postoperative echocardiogram

Hemodynamic assessment

Right ventricular dilation and dysfunction are common within several days of transplantation.[7] They are mainly due to exposure of the donor right ventricle to the elevated pulmonary vascular resistance encountered in some recipients.[7] The tendency is for this right ventricular dilation and dysfunction to eventually improve over time. Significant tricuspid regurgitation is also common. Several factors have been postulated, and include transient right ventricular dysfunction, and right ventricular dilation with concomitant dilation of the annulus of the tricuspid valve secondary to the elevated pulmonary vascular resistance found in the peri-operative period.[8] Late sudden development of significant tricuspid regurgitation may be due to damage to the subvalvar apparatus during endomyocardial biopsy.[9,10]

Right ventricular systolic function is assessed using the method of acoustic quantification,[11] or by planimetry. The area fractional shortening is measured by these methods. The index of myocardial performance, also known as the Tei index, is a relatively new method of measuring global systolic and diastolic function, and is the ratio of the sum of the isovolumic times against the ventricular ejection time[12] (Fig. 1). The index is said to be independent of heart rate and load, and requires no geometric assumptions, making it suitable for measuring both left and right ventricular function.[12] The normal index for children is 0.32 ± 0.03 for the right ventricle, and 0.35 ± 0.03 for the left ventricle[13] (Fig. 2).

Left ventricular systolic dysfunction within a few days of transplantation is usually due to injuries

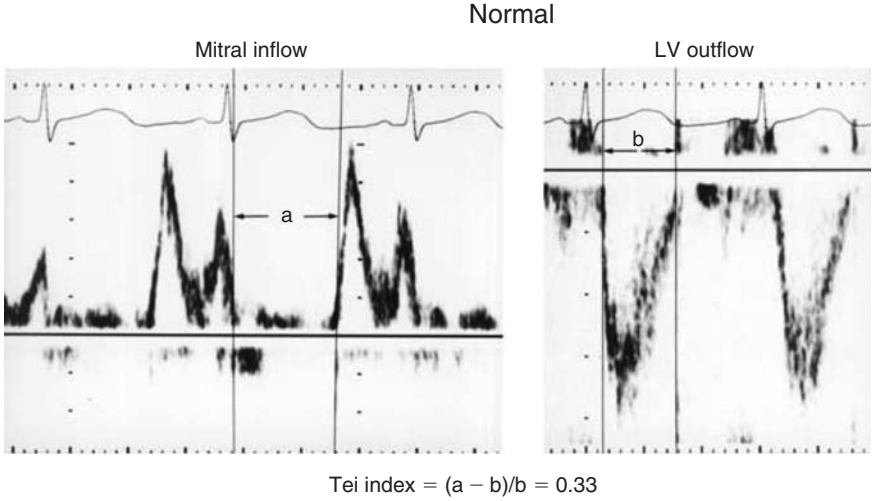


Figure 2.
Pulse wave Doppler depiction of the myocardial performance index (Tei index) in children. The normal index for the right ventricle is 0.32 ± 0.03, and for the left ventricle is 0.35 ± 0.03.

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incurred during preservation of the donor organ. The pattern of diastolic filling is variable. It is influenced by factors including loading conditions, ventricular hypertrophy, acute rejection and myocardial edema and fibrosis.[14] The increase in left ventricular mass and mural thickness shortly after transplantation represent the effects of myocardial ischemia and edema. These appearances are independent of rejection of the allograft. The use of steroids, cyclosporin, and tacrolimus, as well as hypertension, may all be contributory. Later acute increases in left ventricle mass and myocardial thickness, however, may be attributable to rejection.[15] Left ventricular systolic function is measured as the shortening and ejection fractions, and by using the Tei index. Diastolic function is assessed using the mitral inflow pulsed Doppler, the E/A ratio, isovolumic times, and more recently using tissue Doppler methods[16] (Fig. 3).

Pericardial effusions are commonly seen after cardiac transplantation. The plausible explanation is the mismatch in size between the donor and recipient hearts.[17] Although this usually does not suggest allograft rejection, the late development of new onset pericardial effusion may be indicative of this complication.[17]

Echocardiographic surveillance for rejection

The non-invasive nature, and relative simplicity, of echocardiography have driven efforts towards developing algorithms for the diagnosis of rejection. The cellular changes that occur in the myocardium during rejection, such as increased ventricular mass, inflammatory edema, and myocardial necrosis lead to measurable changes using cross-sectional, M-mode, and Doppler techniques. In the post-cyclosporin era, however, a lot of these measures have been rendered obsolete, since cellular rejection in the current era is associated with less edema and inflammation. Diastolic dysfunction is the earliest manifestation of rejection. Using data derived from multiparametric M-mode interrogation, comprising static and dynamic

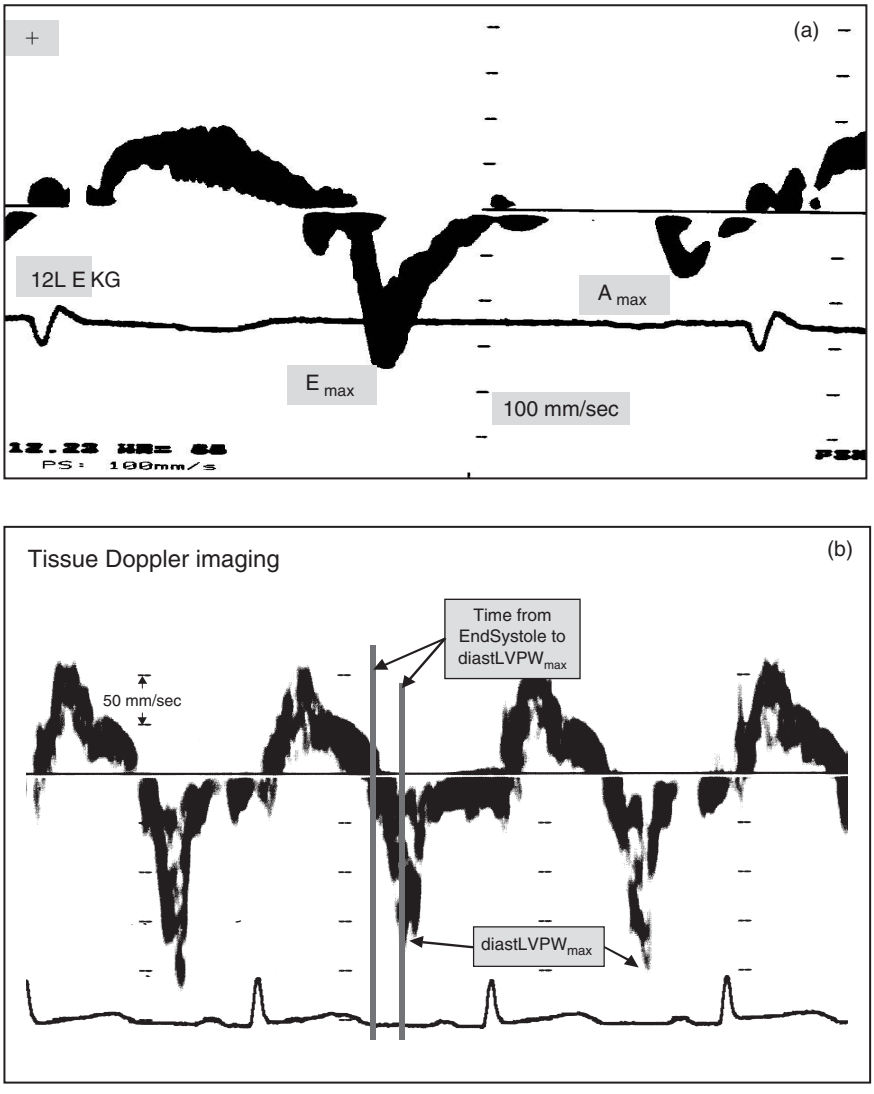


Figure 3.
Pulsed wave tissue Doppler evaluation of (a) the mitral valvar annular velocity and (b) the left ventricular posterior wall. E_{max}: early diastolic filling, A_{max}: late diastolic filling.

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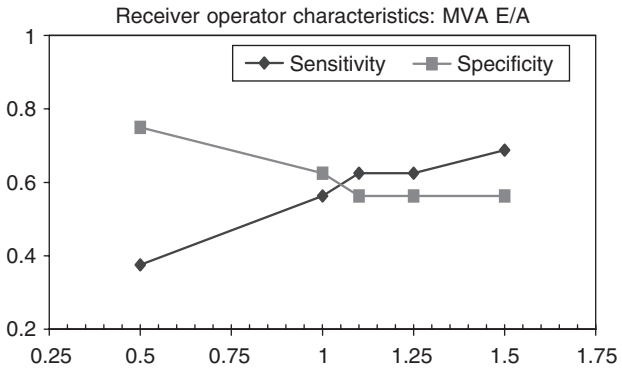


Figure 4.
A graph of mitral valvar annular E′/A′ ratio on the x-axis versus sensitivity/specificity on the y-axis.

diastolic parameters as well as data concerning systolic function, Boucek et al.[18,19] showed that a high percentage of episodes of significant rejection can be detected using echocardiography. This has been shown to be more predictive and reproducible than the older Doppler parameters, such as shortened isovolemic time and increased velocity of the early phase of left ventricular filling.[18,19]

Tissue Doppler assessment of diastolic dysfunction

Tissue Doppler is a new method of assessing diastolic and systolic function.[20] We employ these principles serially to assess diastolic function in all our transplanted patients. Whereas conventional Doppler techniques measure the velocity of the flow of blood in the cardiac chambers and vessels using signal of high velocity but low amplitude, tissue Doppler measures the velocity of the motion of the myocardial wall using signals of low velocity and high amplitude, and uses low pass filters to eliminate the high velocity signals from the flow of blood. The method uses cross-sectional and M-mode images displayed in colour, as well as pulse wave techniques, to quantify myocardial movement.[21]

Using this technique, we recently evaluated mitral valvar annular velocities, and the extent of thinning of the inferior wall of the left ventricle, in 37 children undergoing cardiac transplantation over a period of 2 years.[22] We compared our data with findings from endomyocardial biopsies, assessed using the grades of the International Society of Heart and Lung Transplantation, performed within 24 h, and digitized M-mode scores. We found that the maximal diastolic velocities recorded from the left ventricular inferior wall did not correlate with rejection, this being in contrast to recently published data in adults where good correlation was found between velocities derived using tissue Doppler and rejection of recent onset.[23] Our study, however, showed that mitral valvar annular velocities, particularly the ratio of early to late filling, were significantly decreased with rejection. As a single parameter, a ratio of less than 1.1 was highly predictive of rejection if the ratio prior to the onset of suspected rejection had been greater than 1.1 (Fig. 4).

Recognition of post-transplantation coronary arterial disease

There is considerable interest in the so-called allograft vasculopathy because of its importance as a cause of late death in patients surviving more than 5 years after transplantation.[24] In the current era of treatment with cyclosporin and tacrolimus, when survival is considerably improved, the focus on methods reliably to diagnose such coronary arterial disease has increased immensely. Most centers currently rely on coronary angiography for diagnosis. The value of invasive screening methods has been called into question, however, because there is no specific therapy for the disease.[25,26] The role of screening programs, therefore, is to identify patients at risk for eminent death, and hence to be considered for re-transplantation.

The diffuse and concentric nature of the disease within the coronary arteries has resulted in considerable underestimation by angiography.[27] This has provided the rationale for the use of intravascular ultrasound for its detection. A number of recent studies have identified this technique as a more sensitive reference, and it has now become the method of choice for the early detection of the complication.[28] Its major weakness is that it is an invasive test involving cardiac catheterization, and the analysis is limited to the main epicardial coronary arteries.[29]

Dobutamine stress echocardiography has evolved as the technique that best provides the opportunity serially to evaluate for the presence of inducible myocardial ischemia.[30,31] Because the disease is primarily one involving small vessels that cannot be visualized angiographically, assessment based on dynamically induced ischemia should provide useful information by unmasking microvascular disease. There is increasing interest, therefore, in the ability of this test to predict future catastrophic cardiac events in transplanted patients. Pahl et al.[30] showed that the test can safely be performed in children, with minimal side effects and complications. Normal findings indicate a good prognosis, with a negative predictive value of 90–95%.[26]

Conclusion

Since the introduction of cyclosporin, considerable emphasis has been placed on markers indicative of acute changes in diastolic function as a means of early detection of rejection. Multi-parametric M-mode

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echocardiographic assessments have correlated with significant rejection.[18,19,32] The use of newer Doppler techniques, in particular tissue Doppler, is very promising. These techniques may, in the future, replace current tedious modalities of non-invasive testing for rejection. The potential role of stress echocardiography, particularly dobutamine stress echocardiography, is now being appreciated as the non-invasive method of choice, since it not only allows identification of patients at risk for major cardiac events, but also permits assessment of the progression of post-transplantation coronary arterial disease.[29–31]

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