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Review

The echocardiographic risk assessment of donor hearts for consideration of transplantation

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ABSTRACT

Pediatric patients waiting for heart transplantation experience the highest waiting list mortality compared to all other age groups and across all solid organ waiting lists. A significant number of potential donor hearts go unutilized every year due to "marginal" quality. Echocardiography is one of the single most important tools for the examination of donor heart function. Echocardiography can identify donor hearts that can be used successfully in transplantation despite the presence of clinical factors that could lead to exclusion. The echocardiographic risk assessment of donor hearts for consideration of transplantation involves an understanding of the donor's clinical status and mechanism of brain death, the role of serial echocardiogram, and the recognition of the limitations of echocardiography. This review looks at donor cardiac function and the echocardiographic assessment in general, discusses the growing role for serial echocardiography, and examines the correlation between echocardiographic findings and patient outcomes. The limitations of donor echocardiography are also discussed as well strategies to improve the quality of donor echocardiograms.

1. Introduction

Pediatric patients waiting for heart transplantation experience the highest waiting list mortality compared to all other age groups across all solid organ waiting lists [1]. This can be at least partially attributable to the number of pediatric donor hearts that go unutilized every year. It is difficult to quantify the exact number of potential donor hearts that go unutilized; however, limited reports in the literature range as high as 35–40% [2,3] with a report out of Korea quoting an unutilized rate as high as 72% [4]. Given the donor: recipient imbalance and the reality of waitlist mortality, it is incumbent upon us to explore donor organ utilization and optimize all possible factors to maximize donor organ availability.

All potential cardiac donors should undergo a full echocardiographic examination and it can be argued that this is the single most important tool for examination of donor heart function [5]. Echocardiography is the optimal method of imaging a potential donor heart. It is only mildly invasive and can be done with minimal risk to brain dead organ donors. The equipment is portable, does not emit ionizing radiation and does not require administration of nephrotoxic contrast [6]. Echocardiography can provide an accurate assessment of structural abnormalities, including left ventricular hypertrophy, valvar disease or anomalies and congenital heart defects. Quantitative assessments of global left ventricular size and contractility can be measured as well as qualitative assessments of right ventricular contractility.

Transthoracic echocardiographic assessment of potential hearts for transplantation was first reported in 1988 and is now performed on almost all potential cardiac donors. Gilbert and colleagues [7] were successful in showing in their cohort that in the absence of transthoracic echocardiogram, 29% of donor hearts would have been excluded based on clinical criteria alone (ex: chest trauma, prolonged hypotension, cardiac arrest). However, with only mild abnormalities on echocardiogram, these hearts went on to successful transplantation. Prior to this, selection involved a review of the present and past medical history of the donor, invasive monitoring of donor heart function with central and venous and pulmonary artery catheters and direct surgical inspection.

This chapter will take a look at the echocardiographic risk assessment of donor heart quality. We will review donor cardiac function and the echocardiographic assessment in general, discuss the growing role for serial echocardiography, and examine the correlation between echocardiogram findings and patient outcomes. The limitations of donor echocardiography will also be discussed as well strategies to improve quality of donor echocardiograms. As literature on pediatric donor echocardiograms remains limited, most of what we know and will present in this chapter comes from our adult counterparts.

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2. Donor Cardiac Function and Echocardiographic Assessment

Failure to use donor hearts is multifactorial; however, left ventricular dysfunction has been described in the literature as the most common single cause responsible for unused organs [8] accounting for approximately 25% of unused hearts [9,10,11]. Left ventricular dysfunction is common (38–57%) in potential pediatric donors [12,13]. When compared to pediatric donors without cardiac dysfunction, the proportion of procured hearts was significantly lower in those with cardiac dysfunction (56% vs. 84%) [13]. Left ventricular dysfunction is a common finding in patients with intracranial pathologies and brain death. Both animal and human studies have shown that following a severe neurologic injury resulting in brain death, there is sympathetic nervous system activation leading to an immediate release of catecholamines into the circulation [14,15]. This catecholamine storm is followed by myocardial ischemia and significant ventricular dysfunction with the right ventricular myocardium often being more affected than the left ventricle; however, it is often reversible. Echocardiography is important for assessing the degree of dysfunction with the challenge of distinguishing the donor hearts whose dysfunction is transient or reversible from those that manifest primary graft failure post-transplant.

Regional dysfunction or regional wall motion abnormalities have been defined as contractile dysfunction of some but not all left ventricular segments [16]. In adults, it most commonly occurs as a result of coronary artery disease and is therefore irreversible and a common reason that a donor heart is precluded from transplantation. Regional wall motion abnormalities have been reported in 20–42% of potential adult donors with a subarachnoid hemorrhage or brain injury [6,17]. However, studies have shown a difference in pattern of dysfunction compared to coronary artery disease suggesting that these abnormalities are of a different entity and are therefore potentially reversible. Regional wall motion abnormalities in pediatrics are also largely unrelated to coronary artery disease and therefore commonly reversible. In 147 adult patients with sub-arachnoid hemorrhage and absence of coronary artery disease, who underwent echocardiograms, Zaroff and colleagues [16] found global or regional left ventricular dysfunction in 30 (20%) patients. Regional wall motion abnormalities were observed in 21/30 patients and covered multiple arterial territories with relative preservation in apical function. Global left ventricular dysfunction was observed in 9/30 patients and in 5 of these patients apical function was again preserved when compared to the base. Similar findings were reported in a study of 66 adult patients who died of brain injury, where 28 (42%) of whom were found to have global or segmental left ventricular dysfunction that was not predicted by clinical and electrocardiographic examination [17]. Interestingly, most of these patients also had preserved apical left ventricular function. This sparing is thought to be related to the distribution of myocardial sympathetic nerve terminals with a relative paucity at the apex of the left ventricle, resulting in a reduced susceptibility to the catecholamine storm. This is an important fact as it must be kept in mind that if the interpreting cardiologist uses the M-mode technique, which places emphasis on basal septal contractile function to measure left ventricular ejection fraction, the result may underestimate the true systolic function of the left ventricle [6].

Although the data is limited, it appears that left ventricular systolic and diastolic dysfunction are common findings in potential pediatric heart transplant donors as well. In a study looking at 23 potential pediatric heart transplant donors aged 5 days to 15 years, left ventricular systolic dysfunction was found in 13 (57%) patients [12]. Diastolic dysfunction was found in 6/13 (45%) of those with systolic dysfunction and in 6/10 (60%) patients with normal systolic function. The incidence of left ventricular systolic dysfunction identified in this pediatric cohort was higher than that seen in the adult literature of 10–42%. The reason for this difference is unknown but may be related to the sensitivity of the young myocardium to the catecholamine storm that results from neurologic injury [12]. White et al. demonstrated that younger hearts exhibit an increased myocardial sensitivity to beta-agonist stimulation as well as higher beta-adrenergic receptor density compared to older hearts. These hearts are therefore vulnerable to a sudden increase in sympathetic activity [18]. In another pediatric study with 60 potential donors with brain death and at least one transthoracic echocardiogram, 23 (38%) were found to have cardiac dysfunction [13]. The proportion of procurement was significantly lower in the group with cardiac dysfunction (56.5% vs. 83.8%).

3. Serial Echocardiography in Donor Hearts

Systolic dysfunction evidenced early following brain death, may persuade medical personnel to decline an organ offered for transplantation. There are, however, dynamic changes in echocardiographic systolic function following brain death and as noted above, potential for improvement. The role for serial echocardiography is well supported by the literature. With appropriate “donor management” and time, greater than 50% of donors with global left ventricular dysfunction and/or regional wall motion abnormalities have been shown to improve enough to allow for organ procurement [9,10,19] with as high as 82% in the one pediatric study [13].

In a pilot study using the California Transplant Donor Network Database (CTDN), serial echocardiograms were completed on 16 patients with initial global or regional left ventricular dysfunction that were declined by the regional transplant centers [9]. After correction of loading and metabolic conditions with inotropic management and intravenous use of high-dose corticosteroids, a second echocardiogram was performed. Left ventricular ejection fraction improved between the first and second echocardiogram in 12 out of 16 patients with an average increase from 41 to 56%. There were no significant differences between groups who improved and those who did not other than a trend towards longer times from brain death to the initial and follow-up echocardiograms in those who improved. Twelve of the 16 donor hearts underwent transplantation with good recipient results including a 92% survival rate and mean left ventricular ejection fraction of 61%.

Aggressive treatment with hormonal therapy while obtaining serial echocardiograms in brain dead donors resulted in normalization of hemodynamic conditions including ejection fraction in 67% of cases in a single-center study [19]. Fifteen consecutive brain dead potential donors with hemodynamic instability were evaluated. Hormonal therapy with insulin, methylprednisolone, vasopressin and T3 was started as soon as possible and echocardiogram was obtained before brain death, within 6 h of brain death, at 24 h and within 48 h. Normalization of hemodynamic conditions with improvement in mean arterial pressure, cardiac index and ejection fraction was observed in 10/15 (67%) of patients. Two patients were found to have coronary artery stenosis on pre-transplant angiography; however, the other eight hearts were transplanted uneventfully without any signs of early graft failure and all eight patients alive at 6-month follow-up.

Prolonged donor management with serial echocardiogram resulted in transplantation of 52% of initially marginal donor hearts in a cross-sectional study using the Life Center Northwest organ database [10]. Cardiac dysfunction was present in 74/246 (30%) of patients on initial echocardiogram and among the patients receiving serial echocardiograms, 29 patients had cardiac dysfunction. After pharmalogic support for hypotension with inotropes and other medications such as levothyroxine, 15 (52%) of patients demonstrated resolved cardiac dysfunction over a mean time period of 20.3 h leading to organ procurement. Interestingly, potential donors with and without cardiac dysfunction differed significantly in several baseline characteristics including age. The group with cardiac dysfunction was significantly younger than the group without cardiac dysfunction, which supports the hypothesis mentioned above that the younger myocardium is more sensitive to the catecholamine storm.

Pediatric studies have shown similar outcomes with serial echocardiography. In the study discussed previously with 60 potential