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Reliability of echocardiographic measurements of left ventricular systolic function in potential pediatric heart transplant donors

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BACKGROUND: Echocardiogram reports, but not images, are usually available for the evaluation of potential donor hearts. To assess the reliability of local reports of potential pediatric heart donors, we compared echocardiographic measurements of left ventricular (LV) systolic function between local hospitals and a central echocardiography laboratory.

METHODS: We identified all potential donors aged <18 years managed by the California Transplant Donor Network from 2009 to 2013. Echocardiograms and reports were obtained from local hospitals. All studies were reviewed in a central laboratory by an experienced pediatric cardiologist blinded to local reports. Local and central measurements of fractional shortening (FS) were compared using the Bland-Altman method (mean difference ± 2 standard deviations). LV function was categorized based on FS as normal or mild, moderately, or severely depressed.

RESULTS: There were 70 studies from 59 donors with local and central measurements of FS. The mean difference between local and central FS was 3.9 ± 9.0. The limits of agreement ranged from –14.2 to 22. Twenty-five studies had discordant measurements of LV function, with 17 discordant by 1 category and 8 by 2 or more categories. Of 55 studies categorized as normal by local measurement, 6 were moderately to severely depressed by central review. Of 15 studies categorized as depressed by local measurement, 3 were normal by central review.

CONCLUSIONS: Local and central measurements of LV systolic function were discordant in 36% of studies. Given such discordance, efforts to obtain and view actual echocardiographic images should be part of the standard evaluation of potential pediatric heart donors.

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More than 500 children are added to the heart transplant waiting list in the United States each year, and nearly 20% will die while waiting for a suitable donor.[1,2] Identification of suitable donors includes evaluation of left ventricular (LV) systolic function in the donor heart, most commonly assessed by transthoracic echocardiography. In the United States, echocardiography is typically performed at local hospitals where donors have been admitted. Echocardiography reports are then sent to a centralized database for review by potential transplant recipient centers. Uploading and viewing of actual echocardiogram images is not routine. The reliability of local hospital reports of LV systolic function in pediatric donor hearts has not been systematically studied.

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Several studies in settings other than pediatric heart transplantation have examined the reliability of pediatric echocardiography performed at local sites and then reviewed in a central laboratory. Investigators of the Pediatric Pulmonary and Cardiac Complications of Vertically Transmitted HIV Infection (P2C2) study reported a mean difference in fractional shortening (FS) of –0.97 (95% confidence interval, –10.2 to 8.3) between measurements made at local clinical sites and in a central echocardiography laboratory.[3] Although the mean difference was not clinically significant, the confidence interval was notably wide. Similarly, Project HeartBeat!, a study of healthy children and adolescents, reported a significant difference in LV end-diastolic dimension (0.19 ± 0.97 mm, $p = 0.01$) between measurements made at local field centers and a central laboratory.[4]

On the basis of these studies, we hypothesized that among potential pediatric heart donors, there would be a significant difference in the echocardiographic measurements of LV systolic function between local hospitals and a central echocardiography laboratory. Our objectives were to compare local and central measurements of LV systolic function, characterized by FS, and to determine whether donor or imaging factors, such as donor size or time of echocardiogram, contributed to the discordance noted between local and central measurements.

Methods

The California Transplant Donor Network (CTDN) is the federally designated organ procurement organization for northern and central California and northern Nevada. We identified all potential heart transplant donors aged <18 years managed by CTDN from 2009 to 2013. Donor characteristics and echocardiogram results, including valvular insufficiency, wall motion abnormalities, FS, and ejection fraction (EF), were collected from reports submitted by local hospitals to CTDN. For donor hearts that were transplanted, outcome of transplant recipients was also obtained from CTDN. Actual echocardiographic images were obtained from local hospitals and loaded onto a secure server in a central pediatric echocardiography laboratory, with study identifiers removed. The Stanford University Institutional Review Board determined that this study did not require formal approval because the research did not involve living subjects.

The central echocardiography laboratory is located in a pediatric heart center that performs more than 10,000 echocardiograms and an average of 17 transplants per year.[5] An experienced pediatric cardiologist (S.T.) with training in pediatric echocardiography, blinded to local reports, reviewed all echocardiograms. All measurements were made at end-systole and end-diastole. The LV end-systolic dimension (LVESD) and end-diastolic dimension (LVEDD) was obtained at the level of the papillary muscle from M-mode or 2-dimensional images (depending on image quality). LV endocardial areas in systole (LVAS) and diastole (LVAD) were measured in the parasternal short-axis view at the level of the papillary muscles. LV endocardial lengths in systole (LVLS) and diastole (LVLD) were measured from the 4-chamber view in the plane of the mitral valve annulus. Wall motion abnormalities, intracardiac anomalies, and presence and degree of valvular regurgitation were noted. Before FS and EF were calculated, a qualitative assessment of LV systolic function was assigned. FS was calculated as: [(LVEDD – LVESD)/LVEDD] × 100. EF was calculated by the 5/6 area-length method as: 5/6 × [(LVAD × LVLD) – (LVAS × LVLS)]/(LVAD × LVLD) × 100.[6,7] Categories of LV function based on FS and EF were assigned according to guidelines from the American Society of Echocardiography as normal (FS ≥ 28 and EF ≥ 55), mildly depressed (FS = 22–27 and EF = 45–54), moderately depressed (FS = 17–21 and EF = 30–44), or severely depressed (FS ≤ 16 and EF < 30).[8]

The date and time of each study was noted. Business hours were defined as Monday to Friday, 8:00 A.M. to 5:00 P.M. Characteristics of local hospitals were obtained from the American Hospital Association's Hospital Database, a Web-based database that serves as a primary reference for the Centers for Disease Control and Prevention and also Medicare and Medicaid Services.[9] Certifications of local physicians interpreting the echocardiograms were verified with the American Board of Pediatrics[10] and American Board of Internal Medicine.[11] Physicians were classified as pediatric or adult cardiologists, or unknown.

To assess intraobserver variability in the central laboratory, the primary reader (S.T.) read 10 randomly selected studies twice in a blinded manner. To assess interobserver variability, a second experienced pediatric cardiologist (D.R.) read another 10 randomly selected studies that had also been read by the primary reader (ST.). To ensure that our assessment of variability included studies with decreased LV function, 3 from each group of 10 studies were selected from studies with local FS <24.

Variables are described as mean ± standard deviation and median (range). Concordances between local and central FS and EF were compared using the Bland-Altman method. Mean differences were calculated as local measurements minus central measurements. Limits of agreement were calculated as ± 2 standard deviations.[12] Intraclass correlation coefficients (ICC) were calculated for intraobserver and interobserver variability within the central laboratory. Student's paired *t*-test was used for comparisons between local and central measurements and between studies with depressed vs normal function. Wilcoxon rank sum tests and analysis of variance were used in the analysis by donor and imaging characteristics, and *p*-values of ≤0.05 were considered significant. Statistical analysis was performed using STATA/IC 13 software (StataCorp LP, College Station, TX).

Data were collected and managed using the Research Electronic Data Capture (REDCap) electronic data tool hosted at the Stanford Center for Clinical Informatics. REDCap is a secure, Web-based application designed to support data capture for research studies.[13]

Results

Between 2009 and 2013, 85 potential pediatric heart donors were managed by CTDN. One donor had a study that the local hospital could not locate. We obtained 100 echocardiographic studies on 84 donors from 32 local hospitals. Studies for 8 donors were in a format incompatible with the central server. The remaining 92 studies from 76 donors were reviewed in the central laboratory.

Characteristics of the potential donors are reported in Table 1. The median age was 14 years (range, 7 days–17 years). Head trauma was the most common cause of brain death (53%), followed by anoxia (37%). Seventy-six percent of potential donor hearts were transplanted. Two