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SHORT COMMUNICATION

Echocardiographic assessment of radial right ventricular function in heart transplant recipients

Marc Atzenhoefer[1], Arshad Jahangir[1,2], Abby Payne[1], Mohamed Hendawi[1], Omar Dakwar[3], Mahmoud Ali[1], Vinay Thohan[4] and Lakshmi Muthukumar[1]*

[1]*Aurora Cardiovascular and Thoracic Services, Aurora Sinai/Aurora St. Luke's Medical Centers, University of Wisconsin School of Medicine and Public Health, 2801 W. Kinnickinnic River Parkway, Ste. 880, Milwaukee, WI 53215, USA;* [2]*Center for Advanced Atrial Fibrillation Therapies, Advocate Aurora Health, Milwaukee, WI, USA;* [3]*Quality Management, Aurora St. Luke's Medical Center, Milwaukee, WI, USA; and* [4]*Mission Health System/HCA, Asheville, NC, USA*

Abstract

Aims Right ventricular (RV) allograft dysfunction is present in half of all heart transplant (HT) recipients. Non-invasive assessment of RV function in the setting of rejection is not well described. We outline an echocardiographic technique, short-axis fractional area change (SAXFAC), to evaluate RV function in the HT population and correlate this with the grade of pathologic rejection.

Methods and results We retrospectively reviewed the electronic medical records of 110 people who received a HT between 1 January 2015 and 29 February 2020 and had no evidence of rejection. One hundred eighty-two transthoracic echocardiograms (TTEs) completed up to 1 year from the date of transplantation were analysed for the target acoustic window, the parasternal mid-ventricular short-axis view. Sixty-one TTEs from 23 healthy transplants were deemed appropriate for SAXFAC determination. Thirty-three organ recipients with at least grade 1R allograft rejection were also identified, and their TTEs screened for SAXFAC analysis. Two expert readers independently calculated SAXFAC as follows: RV end-diastolic area minus end-systolic area divided by end-diastolic area. Using commercially available software (Epsilon, Ann Arbor, Michigan), we quantified RV radial strain, longitudinal strain, and apical fractional area change (FAC). Twenty-eight transplant recipients with grade 0R or 1R rejection and nine patients with clinically significant rejection completed the study analysis. SAXFAC demonstrated significant variability in the entire population with an inverse relationship to severity of allograft rejection ($P \leq 0.01$). Radial strain and FAC were also associated with clinically significant rejection ($P \leq 0.01$).

Conclusions Short-axis fractional area change is a simple two-dimensional technique to assess RV function in HT recipients and showed no significant inter-observer variability. In our small, single-centre, retrospective case series, lower SAXFAC values were associated with clinically significant allograft rejection. The small sample size and infrequent occurrence of rejection make our observations hypothesis-generating only. We advocate dedicated RV SAXFAC imaging planes be included when assessing allograft function.

Keywords Function; Heart transplant; Non-invasive; Rejection; Right ventricle

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**Correspondence to: Lakshmi Muthukumar, MD, Aurora Cardiovascular and Thoracic Services, Aurora St. Luke's Medical Center, 2801 W. Kinnickinnic River Parkway, Ste. 880, Milwaukee, WI 53215 USA Tel: +1 414-649-3909; Fax: +1 414-649-3578. Email: wi.publishing405@aah.org*

Background

Heart transplantation (HT) is the gold standard treatment in end-stage heart failure and provides a durable improvement in patient quality of life. Serial Doppler echocardiographic assessment of allograft function provides non-invasive assessment and typically focuses on the measurement of left ventricular (LV) cardiac structure, function, and haemodynamics. Most non-invasive echocardiographic parameters in the assessment of right ventricular (RV) function are longitudinal,[1] including tricuspid annular plane systolic excursion, S′ tissue velocity, free wall strain, global longitudinal strain, and apical fractional area change (FAC). Lakatos *et al*.[2] demonstrated how important radial contraction is in the function of the RV by assessing three-dimensional ejection fraction. Interrogating radial RV function is of particular importance in the transplant population given the immediate post-operative drop in longitudinal function and the inability of tricuspid annular plane systolic excursion and S′ to differentiate active RV contraction from the passive pull of the LV.[1,2] RV dysfunction has been independently associated with HT rejection, coronary allograft vasculopathy, and death.[3]

Aims

We sought to determine the feasibility of RV assessment with short-axis FAC (SAXFAC), which incorporates radial function, in HT patients with and without clinically relevant rejection.

Methods

We performed a retrospective analysis of patients at our institution who had HT between January 2015 and February 2020. This study complied with the Declaration of Helsinki and was approved by the local institutional review board. Due to the retrospective nature of the study, patient consent was not required. A total of 143 HT recipients who had routine echocardiograms and endomyocardial biopsies performed on the same day at regular intervals, per protocol, were identified. Echo contrast was routinely used. In the apical view, contrast is not validated in the assessment of RV function and was not used. As determined by an expert reader, 37 of the 143 patients had the target acoustic window: the parasternal mid-ventricular short-axis view. A major obstacle in recruitment was that the RV is often overlooked in regular echocardiographic assessment. Our target acoustic window was not systematically obtained; the retrospective study included those in which such assessment could be made. To be considered for analysis, the echocardiograms must have had the RV captured in the short axis at the mid-ventricular level, sufficient acoustic quality to undergo post hoc analysis with commercially available software (Epsilon, Ann Arbor, Michigan), and multiple studies from the same patient meeting criteria over the period of interest. Analysis of RV radial strain, longitudinal strain, and FAC was subsequently performed. Due to thin RV walls in the short-axis view, speckle tracking in the analysis of RV radial strain was technically challenging. Inability to acquire these data resulted in many studies being excluded from further analysis. Of the 148 studies imported to Epsilon, 61 studies from 23 healthy HT recipients were completely analysed. These same studies were independently assessed by two expert readers for SAXFAC by measuring the RV end-diastolic area minus end-systolic area divided by end-diastolic area [*Figure 1(A)*]. Inter-observer variability was assessed by comparing the SAXFAC determinations of the expert readers, who were blinded to each other's assessments. During the same investigation period, 33 HT recipients with at least grade 1R allograft rejection were identified for similar analysis. Retrospectively, only 14 patient echocardiograms had sufficient RV image quality to undergo analysis [*Figure 1(B)*].

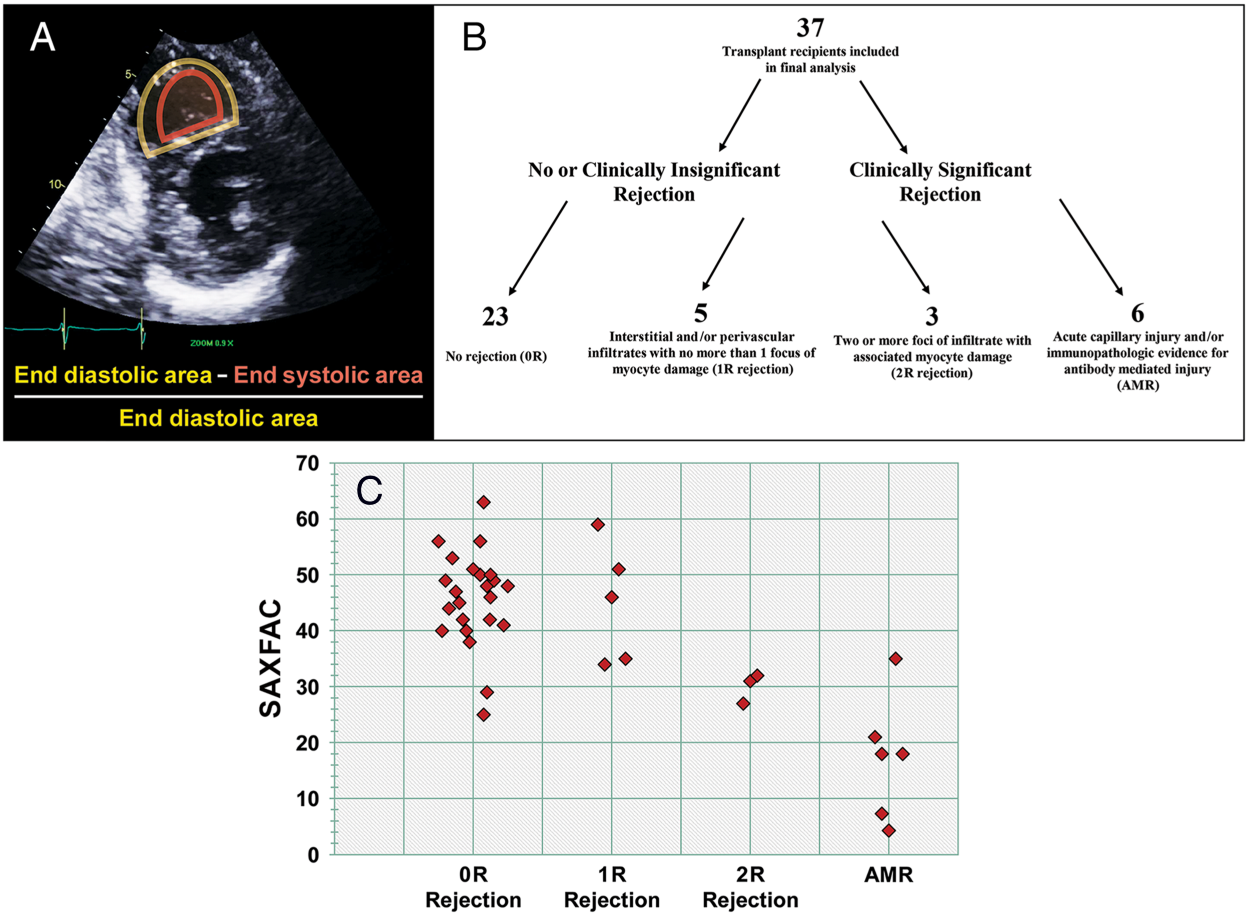
Results

The final cohort comprised 37 patients who were able to undergo complete analysis for RV function by SAXFAC, longitudinal strain, radial strain, and FAC [*Figure 1(B)*]. Standard echocardiographic interrogation of the HT recipient does not focus on RV radial function. Inter-observer variability in the assessment of SAXFAC demonstrated reproducibility as statistically significant differences between readers' assessments were not detected. Average SAXFAC values were lower in those patients with clinically significant rejection, as defined by pathologic grade 2R or antibody-mediated rejection (AMR) on biopsy, than in healthy transplants [*Figure 1(C)*, 32% vs. 46%, $P = 0.01$]. Presence of transplant heart coronary artery disease was associated with rejection (80% vs. 43.5%, $P = 0.04$). Rejection occurred more frequently in younger patients (average age 49 years old vs. 57 years old, $P = 0.02$). Sex, body mass index, diabetes, history of smoking, hypertension, and obstructive sleep apnoea were evenly distributed between the two groups. Due to the small sample size and non-normal distribution, Kruskal–Wallis tests were conducted. SAXFAC readily identified clinically significant rejection when compared with healthy transplants ($P \leq 0.01$). Similarly, radial strain and apical FAC were able to differentiate between clinically significant rejection and healthy transplant echocardiograms ($P \leq 0.01$). Longitudinal strain did not differ between cohorts ($P = 0.82$). LV function on routine transthoracic echocardiography was normal at the time of incidentally discovered clinically significant rejection in five out of nine patients. A drop in LV function was observed in three patients. One of the patients' LV function was depressed 6 months prior to the rejection episode and remained unchanged at the time of rejection. However, a decrease in RV SAXFAC was noted at the time of rejection in all nine patients with clinically significant rejection compared with 6 months prior. This suggests that RV SAXFAC may be a more sensitive indicator of rejection.

Discussion

Prior investigations describing the complex nature of RV structure and function suggest that longitudinal echocardiographic assessment does not completely assess the RV of the HT patient. Previous studies have correlated RV FAC with

Figure 1 Short-axis fractional area change (SAXFAC). (A) Right ventricular short-axis fractional area change as measured by the parasternal mid-ventricular short-axis window. (B) Patient recruitment. Retrospective chart review between January 2015 and February 2020 yielded 37 patients whose echocardiograms underwent full analysis. (C) Short-axis fractional area change (%) of heart transplants categorized by type and severity of rejection. AMR, acute humoral/antibody-mediated rejection.



magnetic resonance imaging among HT recipients.[4] However, abnormal longitudinal parameters, present up to 1 year post-HT,[5] do not allow differentiation of HT rejection. Our data support the finding that measures of RV radial function may indeed provide a more sensitive non-invasive marker of RV function.[3] Importantly, SAXFAC image acquisition and quality parasternal mid-ventricular short-axis windows resulted in a small final sample size for assessment in each of the two groups, which may have led to selection bias and limited generalizability. Obtaining the short axis of the RV is inherently difficult because of RV geometry. Oblique cuts are possible. However, when it is obtained, SAXFAC can be assessed reliably. Alternative measurement modalities include magnetic resonance imaging FAC, which is expensive and time consuming. A possible method to mitigate short-axis obliquity is to obtain three levels of windows (base, mid, and apex).

A prospective study with focused image acquisitions including the SAXFAC window would address some of these concerns.

Of the patients studied, 27% of patients had the appropriate window to assess the RV SAXFAC despite adequate LV functional assessment. Efforts should be made to improve RV interrogation in the short axis to better evaluate radial RV function.

Conclusions

Short-axis fractional area change clearly identified HT patients who were incidentally found to be undergoing clinically significant rejection in our small cohort. The complex nature of RV structure and function suggests that longitudinal non-invasive assessments alone are insufficient. We suggest that RV radial and circumferential function be assessed after HT with SAXFAC and radial strain methodologies. Further prospective research is needed to determine the clinical significance of SAXFAC and radial function in acute and chronic rejection within the HT population.

Conflict of interest

Marc Atzenhoefer, Arshad Jahangir, Abby Payne, Mohamed Hendawi, Omar Dakwar, Mahmoud Ali, Vinay Thohan, and Lakshmi Muthukumar declare that they have no conflict of interest.

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Author contributions

All authors approved the final manuscript. Atzenhoefer—conception and design of the study, acquisition of data, analysis and interpretation of data, drafting of article; Payne—data acquisition, critical review of the manuscript; Hendawi—data acquisition, critical review of the manuscript; Dakwar—data analysis, critical review of the manuscript; Ali—critical revision of the article for important intellectual content; Thohan—critical revision of the article for important intellectual content; Jahangir—critical revision of the article for important intellectual content; Muthukumar—conception and design of the study, critical revision of the article for important intellectual content.

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