Measurement of cardiac output by real-time 3D echocardiography in patients undergoing assessment for cardiac transplantation

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Aims Heart transplant assessment includes cardiac output calculation by right heart catheterisation. Real-time 3D echocardiography (RT-3DE), unlike 2D echocardiography, can measure stroke volume without inaccurate geometrical assumptions. The purpose of this study was to assess the feasibility and accuracy of non-invasive RT-3DE cardiac output calculation.

Methods and results Forty consecutive patients referred for transplant assessment underwent transthoracic RT-3DE. Full volume 3DE data sets were acquired from apical views with the iE33 ultrasound system (Philips Ultrasound, Bothell, USA). Four patients were excluded due to poor image quality. The remaining 36 patients had end-diastolic (LV EDV) and end-systolic (LV ESV) left ventricular volumes manually traced, using endocardial detection software. Cardiac output was subsequently calculated: \[ \text{Cardiac output} = \frac{(LV EDV - LV ESV) \times \text{heart rate}}{\text{C}_2} \] Thermodilution derived cardiac outputs, under the same haemodynamic conditions, were used as reference for comparison. There was close correlation between RT-3DE and catheter derived cardiac outputs \((r = 0.91, y = 0.86x + 0.45, \text{SEE} 0.39 \text{ L/min}, \text{mean difference} \text{ from reference} -0.06 \text{ L/min}, \text{SD} 0.40 \text{ L/min})\). RT-3DE data analysis took 3 min per case.

Conclusion This study shows RT-3DE is an accurate method for calculating cardiac output. In patients requiring serial evaluation of cardiac function, this non-invasive test may be preferable to invasive right heart catheterisation.

KEYWORDS Real-time 3D echocardiography; Cardiac output; Cardiac transplant assessment

Introduction

Accurate evaluation of left ventricular (LV) size and function is important in guiding patient treatment decisions and prognosis. Assessment using both M mode and two-dimensional (2D) echocardiography make geometric assumptions about the LV.¹,² M mode calculations assume the LV is a prolate ellipse whereas two-dimensional echocardiography uses the method of discs (Simpson’s rule) and assumes the LV is a series of cylinders. This leads to inaccuracies in measurements, especially in diseased and dilated ventricles, that preclude the use of these techniques to accurately follow up patients or guide management.

The ‘gold standard’ non-invasive technique for the reproducible quantification of LV size and function is cardiac magnetic resonance (CMR) imaging. However, CMR is expensive, not widely available and cannot be used in patients treated for heart failure with implantable devices. Recent advances in real-time three-dimensional echocardiography (RT-3DE), have bridged the gap, offering highly accurate (compared to CMR) analysis of LV size and function at the bedside.³–⁶ RT-3DE avoids geometrical assumptions about the shape of the left ventricle⁷ and image manipulation can minimise underestimations of LV size due to foreshortening. Semi-automated endocardial detection software creates a mathematical model or ‘cast’ of the LV, improving the accuracy of volume calculation enabling serial measurements of stroke volume and cardiac output.

Currently patients referred for cardiac transplant assessment at our institution are investigated with right heart catheterisation to calculate their cardiac output by the thermodilution method. In addition, other important haemodynamic variables that influence patient selection for cardiac transplantation, such as pulmonary artery pressure and pulmonary vascular resistance, are also...
measured. Serial right heart catheterisation to document changes in haemodynamic indices and guide management is not uncommon. However, the thermodilution method is an invasive procedure and not without risk.8

We hypothesised that the assessment of cardiac output using RT-3DE would produce comparable values to those provided by the thermodilution, but without the associated risk. The objective of the study was to compare cardiac output measurements between RT-3DE and thermodilution, to determine the feasibility and accuracy of RT-3DE cardiac output assessment in a busy echocardiography department.

Methods

Study population
Forty consecutive patients referred for cardiac transplant assessment to our institution from July to December 2005 (24 men; mean age 48 ± 9 years; 24 ischaemic cardiomyopathies, 10 idiopathic dilated cardiomyopathies) underwent clinical assessment with real-time 3D echocardiography and right heart catheterization, under steady state haemodynamic conditions, on the same day. Full informed consent was gained in accordance with local ethical guidelines.

Real-time 3D echocardiography
Full volume 3DE data sets were acquired from apical views with the iE33 ultrasound system (Philips Ultrasound, Bothell, USA), during a single breath hold. The depth was optimised to ensure that the left ventricle filled the entire pyramidal volume and the data sets manipulated manually so that the orthogonal images of the left ventricle were not foreshortened (Figure 1). The left ventricular end diastolic volume (LVEDV) was defined as occurring on the R wave of the QRS complex. Maximal volume was verified by scrolling through temporally adjacent acquired images. Left ventricular volume measurements were performed at the bedside. Endocardial markers were placed manually on either side of the mitral annulus in 2 orthogonal views and at the apex, and semi-automated endocardial border detection software then traced the endocardium and calculated the volume automatically. The endocardial detection accuracy was checked and optimised manually. This was repeated for left ventricular end systolic volume (LVESV) defined as the frame before mitral valve leaflet opening. Cardiac output was subsequently calculated: \[ \text{CO} = \frac{(\text{LVEDV} - \text{LVESV}) \times \text{heart rate}}{2} \].

Measurement of catheter derived cardiac output
Patients underwent right heart catheterisation via the internal jugular vein and had their cardiac output derived by thermodilution.9 A thermistor-tipped catheter (Swan-Ganz) was inserted into the pulmonary artery and 0.5 ml of saline cooled to 4°C was injected into the right atrium from a proximal catheter port. The thermodilution profile at the catheter tip was computed to derive cardiac output, using the Baxter Vigilance Monitor (Baxter Healthcare Corporation, Irvine, CA). A mean of three readings was recorded.

Statistical analysis
Correlations were performed between RT-3DE and thermodilution derived cardiac output measurements, and agreement was
expressed according to the method of Bland and Altman.\textsuperscript{10,11} Interobserver and intra-observer variability of RT-3DE was performed by two experienced echocardiographers in 10 patients and was expressed as mean difference $\pm$ standard deviation.

**Results**

Of the 40 patients studied, 4 patients were excluded either due to a poor echocardiographic window or because the left ventricle, despite the use of a stand-off, could not be accommodated within the pyramidal volume. The remaining 36 patients studied demonstrated a close correlation between RT-3DE and catheter derived cardiac outputs ($r = 0.91$, $y = 0.86x + 0.45$, standard estimate error was 0.39 L/min). Mean difference from reference was $-0.06$ L/min and the standard deviation was 0.40 L/min (Figures 2 and 3). The Bland–Altman plot showed that as the cardiac output increased, the difference between the two methods remained constant. The inter-observer and intra-observer variability was 0.17 $\pm$ 0.09 L/min and 0.23 $\pm$ 0.09 L/min respectively.

Acquisition of RT-3DE data and analysis took, on average, 3 min per patient. It was well tolerated with no adverse events or complications.

**Discussion**

The results of this study demonstrate that cardiac output derived by RT-3DE produces comparable results to cardiac output values calculated by thermommodation, in patients undergoing transplant assessment, due to a variety of cardiac pathologies. This technique is feasible in 90% of patients attending for cardiac transplant assessment and is quick and easy to perform.

Prior to the advent of RT-3DE, echocardiographic assessment of LV volumes made geometric assumptions that were least likely to hold true in diseased asymmetrical ventricles, where there may be regional wall motion abnormalities. This leads to wide variances in volumes when compared to other imaging modalities.\textsuperscript{12} RT-3DE avoids geometric assumptions about the shape of the LV by tracking the endocardial border of the LV throughout the cardiac cycle.\textsuperscript{7,13} It is also possible to manipulate the images and optimize the plane in which the left ventricle is ‘cut’, ensuring that the LV is not foreshortened prior to the analysis of LV volume, which can lead to underestimations. RT-3DE has been validated against the non-invasive ‘gold standard’ of cardiac magnetic resonance imaging.\textsuperscript{1–6} However, RT-3DE is more accessible and is significantly cheaper.

This study has validated the use of RT-3DE to calculate cardiac output, when compared with thermodilution derived cardiac outputs, in patients undergoing cardiac transplant assessment. There was close correlation between the RT-3DE and thermodilution cardiac output values. In addition, the intra and inter-observer variability was low enabling this technique to be used to monitor the clinical progress of these patients.

The bolus thermodilution technique has been well validated,\textsuperscript{9,14,15} is widely used clinically and has been accepted as the invasive ‘gold standard’ to measure cardiac output, by a number of other investigators. The risks of right heart catheterization remain significant, even though they are low with experienced operators.\textsuperscript{16,17} The improved safety from non-invasive measurement of cardiac output and patient comfort are clear advantages in favour of RT-3DE. Furthermore, acquisitions of RT-3DE images are readily performed in conjunction with 2D echocardiography, providing further cardiac morphological detail.

**RT-3DE limitations**

The RT-3DE assessment was limited to cardiac output measurement and gives no indication of other haemodynamic variables, such as pulmonary vascular resistance, that are important in selecting patients that might benefit from cardiac transplantation. However, non-invasive Doppler derived parameters, such as the pulmonary flow acceleration time, have been shown to correlate with pulmonary pressure and pulmonary vascular resistance,\textsuperscript{18} and could, in theory, be used to monitor changes in pulmonary vascular resistance in patients with chronic heart failure.

RT-3DE was also unable to obtain a sufficient echocardiographic window to accommodate dilated left ventricle within the imaging pyramidal volume in 10% of patients attending for transplant assessment. Inaccuracies in the measurement of cardiac output with RT-3DE can also occur if there is significant valvular regurgitation.

Therefore, RT-3DE does not make right heart catheterisation in chronic heart failure patients obsolete. However, when these patients undergoing transplant assessment require serial cardiac output monitoring, then RT-3DE is an accurate, quick and safe method of determining cardiac output and, if used in combination with Doppler measurement of pulmonary haemodynamics, may obviate the need for right heart catheterization on every occasion.
Study limitations

Although patients were analysed using both techniques in quick succession to minimise any haemodynamic variation, cardiac output assessment was not made simultaneously. This may have led to a difference in cardiac output measurements between the two techniques. Variability can also occur in both the acquisition and analysis of data. Errors in acquisition were minimised by following standard guidelines and by ensuring the same investigator performed all the data acquisitions and analyses for each technique. The inter- and intra-observer variability was acceptable.

Conclusion

These data suggest that cardiac output can be accurately and reproducibly measured by RT-3DE in patients undergoing transplant assessment, when compared to right heart catheter derived cardiac output measurements by thermodilution. Non-invasive measurement of the cardiac output with RT-3DE may be preferable to repeated invasive right heart catheterisation to monitor clinical progress in these patients.

References