Use of Real-Time Three Dimensional Echocardiography with Semi-Automatic Endocardial Contour Detection for Prediction of Response to Cardiac Resynchronization Therapy in Patients with Heart Failure

THESIS

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) is an established therapy in heart failure. However, one third of patients are non-responders, accordingly, proper selection of CRT eligible patients are essential.

Aims: 1) To test their ability to predict response to CRT in patients with ischemic and non-ischemic cardiomyopathy. 2) To compare TomTec and QLAB software packages for the three-dimensional echocardiographic (3DE) assessment of left ventricular (LV) dyssynchrony.

Methods and results: A total of 140 heart failure patients with the LVEF ≤35% and 60 healthy volunteers underwent 3DE. A subgroup of 60 patients underwent CRT and were evaluated before and 6-12 months after implantation. The systolic dyssynchrony index (SDI) for all 16 LV segments was measured with both software packages and compared using Pearson's correlation and Bland–Altman analysis. Measurements of SDI were significantly higher using TomTec compared with QLAB in both patients (10.9 ± 3.8 vs. 9.7 ± 3.9, P<0.001) and healthy volunteers (4.1 ± 0.8 vs. 2.4 ± 1, P <0.001), with large biases and wide limits of agreement. A moderate correlation (r= 0.65, P <0.001) was observed between both software packages in patients while their inter-observer and intra-observer reliability were good. Of the 60 patients undergoing CRT, reverse remodeling as a measure of response was observed in 41 patients (68%). The optimal SDI cut-off value to predict response to CRT was higher for TomTec than for QLAB (8.8 vs.7.3%, P <0.001) and demonstrated better sensitivity and specificity (93 and 61%, respectively) compared with QLAB (88 and 33%, respectively). Response prediction in patients with non-ischemic cardiomyopathy was excellent with a sensitivity and specificity of 95 and 100% for TomTec and 70 and 83% for QLAB.

Conclusion: Dyssynchrony assessment with 3DE for the prediction of response to CRT seems particularly useful in patients with non-ischemic cardiomyopathy. Different 3DE software packages for the assessment of mechanical dyssynchrony should not be used interchangeably until better software standardization is achieved.

Keywords: • Three-dimensional echocardiography • Software packages • Dyssynchrony • Cardiac resynchronization therapy

Contents

Abbreviations

2DE	Two-dimensional echocardiography/ echocardiographic
3DE	Three-dimensional echocardiography/ echocardiographic
3D STE	Three-dimensional speckle tracking echocardiography
CMR	Cardiac magnetic resonance
CRT	Cardiac resynchronization therapy
CT	Computed tomography
EF	Ejection fraction
EDV	End-diastolic volume
ESV	End-systolic volume
IHD	Ischemic heart disease
LA	Left atrium/ Left atrial
LV	Left ventricle / Left ventricular
LV EDV	Left ventricular end-diastolic volume
LV ESV	Left ventricular end-systolic volume
MV	Mitral valve
RA	Right atrium/ Right atrial
RV	Right ventricle / Right ventricular
SDI	Systolic dyssynchrony index
TEE	Trans-esophageal echocardiography/ echocardiographic
TTE	Trans-thoracic echocardiography/ echocardiographic
TV	Tricuspid valve

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INTRODUCTION

Heart failure is an epidemically growing syndrome. Aging of the population, improved survival of patients with acute myocardial infarction, better medical management of left ventricular (LV) dysfunction and reduced mortality from other diseases are amongst the main reasons for the rapid increase in incidence of heart failure. Despite the major advances that have occurred in our understanding of the pathophysiological abnormalities, pharmacological, device and surgical therapies for this syndrome during the last decade, heart failure remains a major cause of morbidity and mortality worldwide.[1]

Left ventricular dyssynchrony pertains to a lack of proper coordination in the intra-ventricular electrical activation and subsequent mechanical contraction of the LV and has emerged as an important factor in the pathogenesis of heart failure. Its presence can significantly affect cardiac morphology and function, and may cause or worsen pre-existing heart failure. Cardiac resynchronization therapy (CRT) is an established therapy for patients with drug-refractory heart failure that specifically targets LV dyssynchrony and has been shown to improve LV function, survival, and quality of life.[2-4] Unfortunately, 30-40% of patients fail to improve after CRT and several studies have suggested that mechanical dyssynchrony might be a better predictor of response to CRT than the current selection criterion of prolonged QRS.[5,6]

In order to avoid unnecessary pacemaker implantation in patients who subsequently do not respond to this invasive and expensive therapy, a need to establish novel selection criteria focusing on mechanical dyssynchrony that might be a better predictor of response to CRT than QRS width is warranted.[7,8] Consequently, echocardiography emerged as a promising technique for assessment of mechanical dyssynchrony and many single center studies indeed demonstrated encouraging results for prediction of response to CRT with both traditional and tissue Doppler derived parameters of LV dyssynchrony. However, this initial enthusiasm was tempered by the results of the multicenter PROSPECT trial, which reported modest sensitivity and specificity of all studied two-dimensional dyssynchrony parameters and concluded that none should be recommended to improve patient selection for CRT beyond current guidelines.[9]

Three-dimensional echocardiography (3DE) has been shown to be more accurate and reliable than two-dimensional echocardiography in the quantification of LV volumes and ejection fraction (EF) in comparison to cardiac magnetic resonance as the reference technique.[10-12] In addition, with the abilities of 3DE to assess all the myocardial segments simultaneously in three dimensions without assumption, 3DE may provide a complete evaluation of intra-ventricular mechanical dyssynchrony by examining the composite effect of radial, longitudinal and circumferential dyssynchrony for more adequate measurement of LV mechanical dyssynchrony and ultimately, better prediction of response to CRT. Concurrently, the use of 3DE for dyssynchrony assessment gained increasing attention as a growing number of studies demonstrated its added value for prediction of response to CRT. The 3DE-derived systolic dyssynchrony index (SDI) has been proved to be a feasible and reliable parameter of LV mechanical dyssynchrony, which may have additional value to current selection criteria for an accurate prediction of response to CRT.[13,14] Currently, there are different 3DE quantitative software packages that quantify LV volumes and function, including dyssynchrony. The comparability of these software for the quantification of LV volumes and EF was found to be clinically acceptable in both adult and paediatric populations.[15,16] However, a recent meta-analysis on the assessment of LV dyssynchrony with 3DE demonstrated that different software packages provide different SDI values.[13] Distinguishing normal from pathological mechanical dyssynchrony values and establishing a generally usable cut-off value for the prediction of response to CRT may be hampered if measurements by different software packages are not comparable.

AIM OF THE WORK

1) To compare TomTec (four-dimensional LV analysis, Research Arena 3.0, TomTec, Munich, Delaware) and QLAB (3DQ Advanced, QLAB 7 or 8, Philips, The Netherlands) software packages for the three-dimensional echocardiographic (3DE) assessment of left ventricular (LV) dyssynchrony in a prospective manner.

2) To test their ability to predict response to cardiac resynchronization therapy (CRT) in patients with ischemic and non-ischemic cardiomyopathy.

Technique And Clinical Applications Of Three-Dimensional Echocardiography

Echocardiography is the most clinically used diagnostic imaging modality in cardiac practice today, and with good reason. In addition to its non invasive nature and time- and cost-efficiency, its bedside availability in the clinic, emergency ward and operating room is a major advantage. Furthermore, its uncomplicated use in children, pregnant women, and those with implanted pacemakers or defibrillators has set it apart from other closely competing imaging modalities such as cardiovascular computed tomography (CT) and cardiac magnetic resonance (CMR).

However, both M-mode and two dimensional echocardiography (2DE) have their own limitations, mainly the inherent 2D nature, their quantitative measurements derived from assumptions of symmetrical cardiac structures' geometry that is unreliable, especially when cardiac champers are dilated, aneurysmatic or with regional wall motion abnormalities. These assumptions as well as the inadvertent use of foreshortened views, and the conscious decision of many cardiologists to rely on visual estimates of cardiac size and function despite the inherent subjectivity in interpreting 2D data, probably account for the relative inaccuracy and poor reproducibility of these techniques. As important diagnostic, prognostic and therapeutic decisions rest upon this analysis, it is paramount that inter-observer and intra-observer variability are reduced by developing and utilizing accurate and reproducible echocardiographic quantification methods.

A significant development in this regard has been the introduction of 3DE. Although the technology had a slow initial development with