Real-time 3D echocardiography:
an extra dimension in the echocardiographic diagnosis of congenital heart disease

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Real-time 3D echocardiography: an extra dimension in the echographic diagnosis of congenital heart disease

Real-time 3D echocardiografie: een extra dimensie in de echografische diagnose van aangeboren hartafwijkingen

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Annemien Elise van den Bosch

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Promotores:	Prof. dr. M.L. Simoons Prof. dr. A.J.J.C. Bogers
Copromotor:	Dr. F.J. Meijboom
Overige leden:	Prof. dr. ir. A.F.W. van der Steen Prof. dr. W.A. Helbing Prof. dr. L. Mertens

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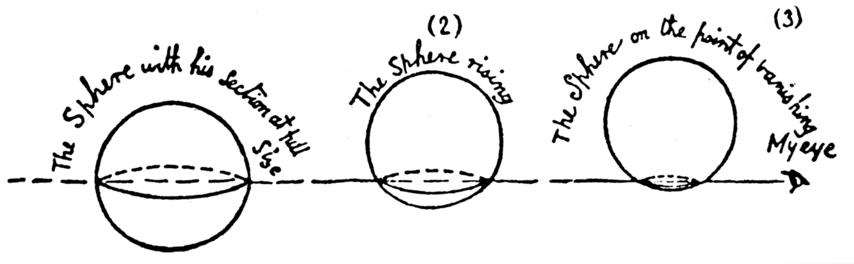
Aan Boudewijn en Mijntje
Aan mijn lieve ouders, Gerdien en Job



For a Square, it is truly impossible to appreciate the full reality of our 3-dimensional universe, called *Spaceland*.
To illustrate this deficiency, a Square watches a still pond being visite by a 3-dimensional being named a Sphere.
A Sphere goes down into the water and rises again before disappearing.
A Square can see only the part of the sphere intersecting his plane.
He sees only a succession of 2-dimensional circles changing size in time.

Flatland: A romance of many dimensions by Edwin A. Abbott (1884).

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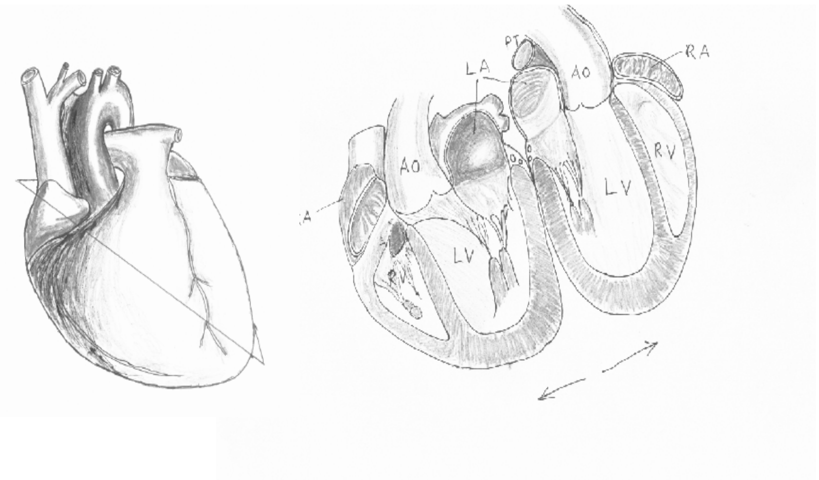
Chapter 1

Introduction



The incidence (approximately 1%) of congenital heart disease in the neonatal age has remained stable over the years, but the survival until adult age has increased dramatically in the past decades, as a result of the successes of cardiac surgery. [1, 2] Consequently, the number of patients with congenital cardiac malformations has increased to a substantial population of at least 25.000 patients in The Netherlands. This number is growing with approximately 5% per year and many of these patients have residual abnormalities, sometimes necessitating reoperation at adult age. [3, 4] Optimal pre-operative diagnostics, for a primary operation - often at infant age - or a reoperation often at adult age, contributes to better surgical results.

The non-invasive technique of echocardiography has acquired an increasingly important role in diagnostic and therapeutic management in congenital heart disease. An experienced (pediatric) cardiologist can diagnose most congenital heart malformations quickly and accurately with the help of the established echo modalities: M-mode, 2D echocardiography, pulsed- and continue wave and color Doppler. However, 2D echocardiography fails whenever detailed information about the spatial relationship of cardiac structures is necessary.

Three-dimensional echocardiography may contribute to this improvement of the diagnostic standards in this large population. Especially for complex intracardiac structures, such as abnormal atrioventricular valves or an abnormal left ventricular outflow tract, 3D echocardiography could yield valuable extra information (figure 1 and 2). Also the size, exact location and relation to adjacent structures of intracardiac shunts might be assessed more reliably. Better understanding of the intracardiac malformations will be helpful in the clinical decision making and planning of the surgical or catheter-interventional approach.

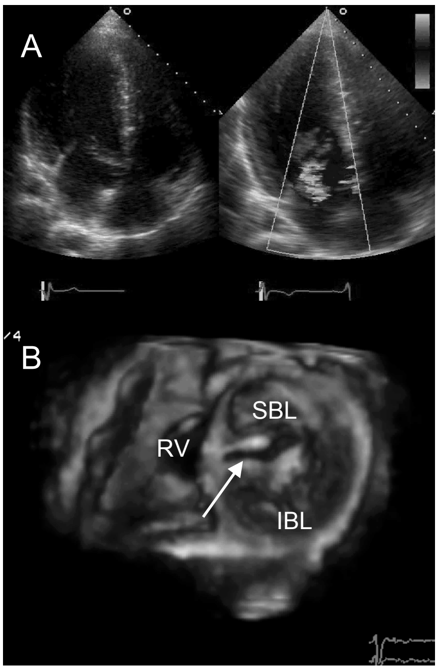


Fig.1.A.
Two-dimensional echocardiogram with and without color Doppler from an apical four chamber view showing left AV valve regurgitation in a patient with corrected partial atrioventricular septal defect.

B.Real-time 3D echocardiographic display of the left AV valve in diastolic frame, seen from a ventricular view. The anatomic substrate of the left AV valve regurgitation is clearly identifiable and is a result of the ‘cleft’ (arrow) between the two bridging leaflets. SBL = superior bridging leaflet; IBL = inferior bridging leaflet; RV = right ventricle.

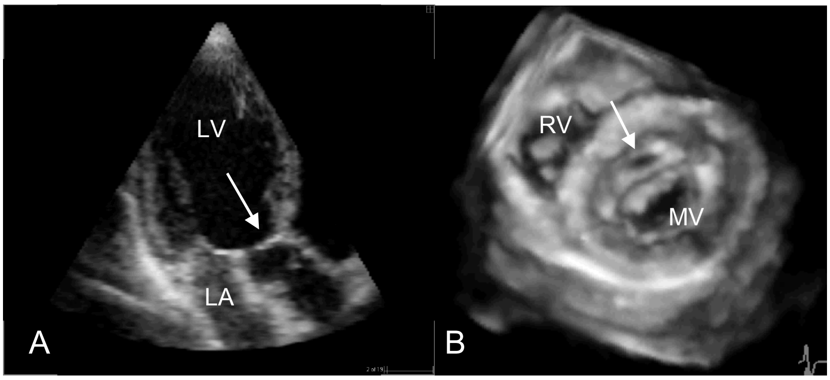


Fig. 2. A: Two-dimensional echocardiogram of severe subvalvular aortic stenosis (arrow). Note that the left ventricular outflow area cannot be measured.
B: Real-time 3D echocardiographic display of the left ventricular outflow tract seen from a ventricular view. The pinpoint opening (arrow) as a result of the subvalvular stenosis is demonstrated. MV = mitral valve; LV = left ventricle; LA = left atrium; RV = right ventricle

Three-dimensional echocardiography

Three-dimensional echocardiography has been advocated as the ultimate echocardiographic imaging modality since the start of the clinical application of echocardiography. Many innovative and quite elaborate echocardiographic technologies were developed to visualize and analyze the heart in a 3D format.
Over the years, a multitude of studies were published reporting the improved accuracy of 3D echocardiography over 2D imaging for important measurements and calculations, including determination of ventricular volumes, mass, and ejection fraction [(5-9)]. Equally important, 3D echocardiography allowed acquisition of complete digital data sets that could be rotated and analyzed in a myriad of specific cut planes and projections. This facilitated unique “en-face views” of congenital cardiac defects such as atrial and ventricular septal defects, and direct views of the semilunar and atrioventricular valves (figure 3)[(10-13)].
Yet, until recently and despite the recognized advances, 3D echocardiography was not easily applicable to the clinical arena. The acquisition phase was difficult and time-consuming. Furthermore, data acquisition required mandated additional personnel and time both rarely found in a clinical setting.
Three methods have been proposed for acquisition of 3D data: the positional locators (free-hand scanning), rotational systems and real-time volumetric scanning.
1) The freehand scanning devices allow free movement of the transducer at one acoustic window or at different acoustic windows. The limitation of this method is that the spaces between the sampled cross-sectional images are uneven and mistakes may result when interpolating big gaps between imaged planes. Furthermore, the reconstructed 3D images are static and lack tissue depiction [(14, 15)].
2) With the rotational systems, the transducer is rotated stepwise or continuously around its central axis, resulting in a conical volume dataset.

Different algorithms have been developed for computer-controlled sequential image collection of the heart. Unfortunately, the elaborate 3D echocardiographic machines were very cumbersome and expensive. The Erasmus University developed a fast continuous rotational transducer using a standard second-harmonic phased-array transducer and ultrasound system. The acquisition time is short (approximately 10s) making it possible to acquire all data during a single breath-hold and the echo machine is not very expensive. However, the fast rotating transducer is currently not commercial available. [16-18]

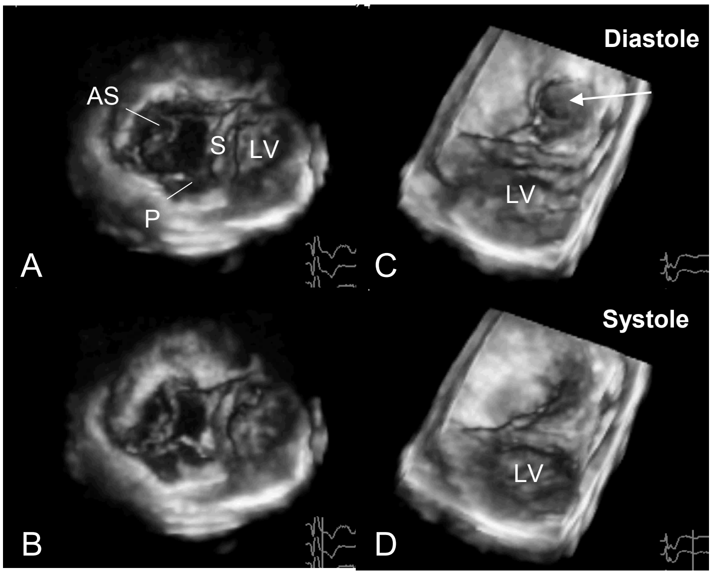


Fig. 3.
Real-time 3-dimensional echocardiographic display of Ebstein`s anomaly of the tricuspid valve, seen from a ventricular view.
A and B (diastole – systole) show the tricuspid valve ‘en face’ before valvuloplasty.
C and D show the tricuspid valve after Chauvaud valvuloplasty. Note that the tricuspid valve has become a monocusp (arrow).

3) Real-time 3D echocardiography (RT-3DE): the ideal method of 3D echocardiography is on-line acquisition of a 3D dataset without the need for ECG and respiratory gating avoiding spatial motion artifacts.
With the introduction of the matrix technology, first developed by Von Ramm et al. [19] at Duke University, a 3D data set can be acquired within a few seconds/heart cycles. The first system was a sparse matrix phased array transducer of 512 elements to scan a 60° × 60° pyramidal tissue volume using parallel processing technology. More recently, Philips Medical Systems has introduced its live 3D system using a matrix phased-array transducer with 3000 transmit-receive elements. In this transducer, multiple recordings are automatically performed to cover a 90° × 90° pyramidal tissue volume. Currently, it is possible to obtain a 3D data set of the heart within a few seconds, in which cross-sectional reconstructions as the “surgeon view” can be performed prior to surgery. This will enhance the ability to identify and pinpoint the exact locations of abnormalities. Having this information before the intracardiac operation, it may save significant time since the surgeon can limit the exploratory phase of the surgical procedure.

Outline of this thesis

The aim of the study that lead to this thesis was to assess the feasibility and clinical applicability of real-time 3D echocardiography in patients with congenital heart disease, and to determine whether 3D echocardiographic images would give a reliable reflection of the intracardiac anatomy in a wide variety of congenital heart defects.

Specifically the objectives of the present study are:

1) To evaluate the feasibility and clinical applicability of real-time 3D echocardiography for a variety congenital heart defects.
2) To assess whether real-time 3D echocardiographic images of structurally abnormal hearts give a reliable representation of these abnormalities. The surgeon's evaluation of this abnormality during operation will serve as a gold standard.
3) To evaluate the limitations and additional value of real-time 3D echocardiography images versus 2D echocardiography, stratified for adult or child, primary operation or reoperation and for the type of cardiac malformation that is investigated in the practical assessment of patients with congenital heart disease.
4) To evaluate real-time 3D echocardiographic assessment of left ventricular function and mass in congenital heart disease, compared with magnetic resonance imaging.

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Chapter 2

Three-dimensional echocardiography
Review

Minerva Cardioangiol

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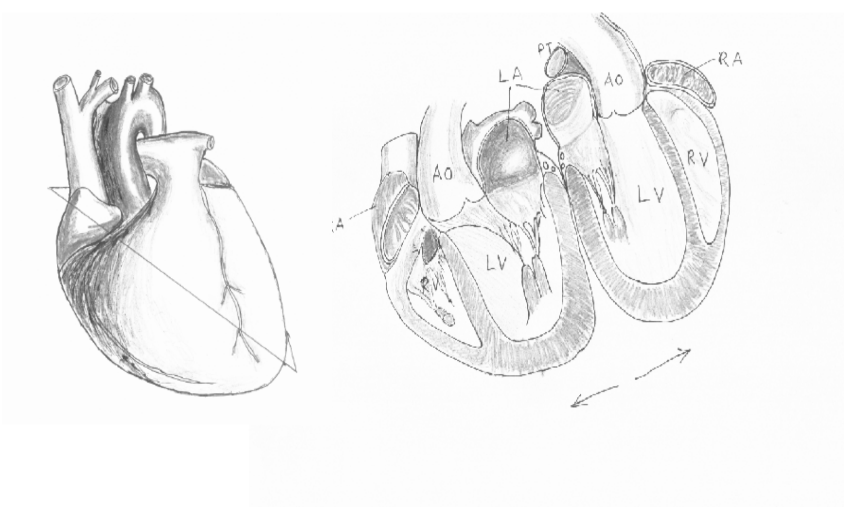
Annemien E. van den Bosch
Boudewijn J. Krenning
Jos R.T.C. Roelandt



Abstract

Three-dimensional echocardiography has been an important research goal ever since the introduction of two-dimensional echocardiography. Most approaches towards three-dimensional echocardiography were off-line and based on the sequential rotational scanning and acquisition of multiple cross-sectional images together with external or internal reference systems. These approaches were limited by long acquisition and analysis time in combination with poor image quality. Recently, improvements in the matrix array technology have significantly increased spatial and temporal resolution of second-generation real-time 3D transducers. Clinical use of modern 3D echocardiography is boosted by the marked reduction in acquisition time and the unique possibility of on-line rendering on the ultrasound system. The integration and future quantification of new parameters together with on-line review allows new insights into cardiac function, morphology and synchrony that offer great potentials in the evaluation of right and left global and regional function, diagnosis of small areas of ischemia, congenital and valvular heart disease and effects of biventricular pacing in dilated heart asynchrony. This report will review current and future applications of 3D data acquisition, emphasizing the real-time methods and clinical applications of the new matrix array transducer.

Introduction

The diagnosis of cardiac disease from multiple echocardiographic two-dimensional images requires a difficult mental conceptualization process that becomes further complicated by its dynamics. Objective three-dimensional images of the heart would greatly facilitate the diagnosis of unknown and complex pathology but its dynamic behavior places special demands on three-dimensional (3D) techniques. Therefore, not only the spatial distribution of cardiac structures but also their movement during the cardiac cycles is essential. Previous approaches to 3D echocardiography (3-DE) were off-line and based on sequential rotational scanning and acquisition of multiple cross-sectional images together with their spatial position using internal coordinate reference systems. These methods were hampered by long acquisition and analysis time in combination with limited image quality. Real-time 3D echocardiography (RT 3-DE), now allows to visualize the heart and its structure dynamics in a realistic fashion with instantaneous on-line volume-rendered reconstruction [(1-5)]. The availability of volumetric data sets allows retrieval of an infinite number of cardiac cross-sections. This capability provides an improved understanding of unpredictable morphology and decrease the variability in interpretation of complex pathology among investigators [(5-7)]. In particular, typical 3-DE parameters, such as ejection fraction, segmental wall function, LV shape and flow jets, become important diagnostic parameters based on 3-DE.

Real-time 3D echocardiography

Unlike 3D reconstruction techniques, real-time 3D echocardiography allows on-line acquisition of a volumetric data set without the need of reference system, ECG and respiratory gating to avoid spatial motion artefacts (table 1).

Table 1 Approaches to three-dimensional echocardiography

A.	Reconstruction techniques	
	(Spatial and temporal registration of 2-D images)	
	* External reference system (free-hand scanning)	
	-	Acoustic locator
	-	Electromagnetic locator
	* Internal reference system (predetermined transducer motion)	
	-	Linear movement
	-	Fan-like movement
	-	Rotational movement
B.	Real-time volumetric imaging	

Real-time 3D echocardiography was first based on novel matrix phased-array transducer technology in which the elements are arranged in a two dimensional grid.[8] The first system consisted of a sparse matrix phased array transducer of 512 elements to scan a 60° × 60° pyramidal volume using parallel processing technology. More recently, Philips Medical Systems has introduced the live 3D system using a matrix phased-array transducer with 3000 transmit-receive elements. In this transducer, multiple recordings are automatically performed, based on ECG gating, to cover the left ventricle in a full volume data set. This is especially useful in dilated ventricles because of the limited sector angle. The multi-directional beam steering capability enables visualization of two views of the heart simultaneously. Although experience remains limited, promising results have been reported.

Image rendering and analysis

To display the heart in three dimensions, reconstruction and display of 3D images from the processed 3D data sets is essential. The term rendering indicates the procedure whereby structures are reconstructed in the computed memory.[7] The volume-rendered 3D data set can be electronically segmented and sectioned. To display intracardiac structures, the heart can be opened by choosing a cutting plane and reconstruct the image beyond this plane as if the heart is cut open in surgery.[9] The display and analysis of size, shape and motion of cardiac structures from any desired perspective becomes possible and allows one to address any clinical question off-line without re-examination of the patient.

By manipulation of the cutting planes and rotation of the 3D image the ideal projection can be obtained.[10] Mitral and tricuspid valve can be viewed from above (electronically simulating atriotomy) or from below (as with ventriculotomy). Likewise, the aortic valve can be visualized from above with electronic aortotomy and from below looking through the left ventricular outflow tract. In the dynamic mode display, the opening and closing of the cardiac valves can be observed.
Interatrial and -ventricular septa can be examined `*en face*` with better perception of their spatial relationship with adjacent structures. Especially in patients with congenital heart disease, special structures can be identified by various display projections including unconventional views.
Wire-frame or surface-rendered reconstructions of selected structures are obtained from manually or electronically derived contours in cross-sectional images generated from the data set. This approach allows for the assessment of characteristics such as structure and shape and for improved quantification of left ventricular volume and function. [11]

Current applications

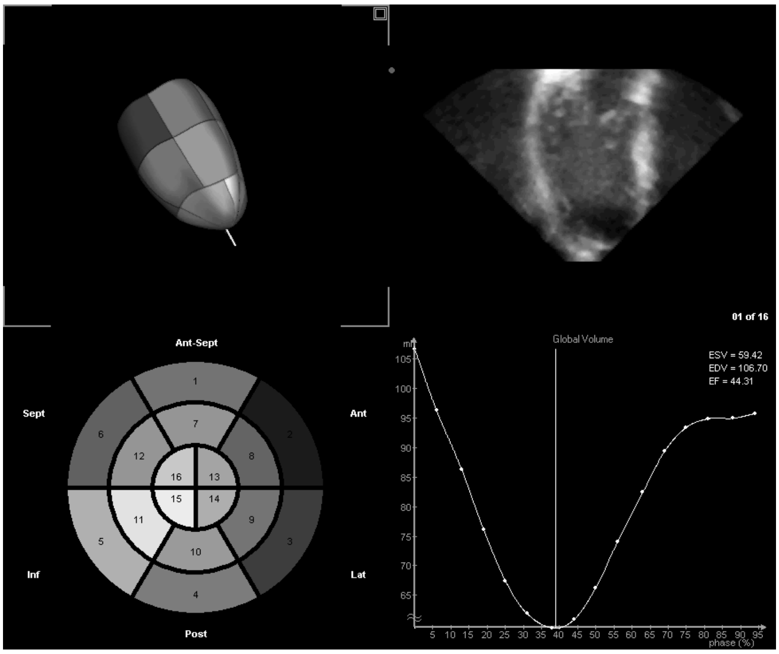
Most current applications of real-time 3D echocardiography are similar to those that have been evaluated with reconstruction 3D.[12]

LV analysis
The ability to accurately assess LV function is essential for patient management, prognosis and follow-up. A fast, practical and accurate method is a pre-requisite to obtain this important information. Although two-dimensional echocardiography (2-DE) is routinely used in clinical practice to obtain information on left ventricular dimension, wall thickness, and function, this technique relies on geometrical assumptions to provide quantitative parameters of left ventricular function. In order to avoid these geometrical constraints, 3D reconstruction of the left ventricular cavity have been performed using a variety of methods (figure 1).
Currently, data analysis and quantitative assessment is mostly performed on a computer with dedicated software (such as 4D LV analysis, TomTec GMBH, Munich, Germany or Qlab, Philips Medical systems, the Netherlands). Ventricular volumes are calculated using the disc summation method, which has been well validated in the past.
Semi-automatic border detection algorithm can be used to track endocardial borders throughout the cardiac cycle to obtain a dynamic display of the endocardial surface of the left ventricle, as well as instantaneous global and regional left ventricular volumes versus time curves (figure 2).

Fig.1

Display of a real-time 3D echocardiographic study of the left ventricle.

Fig.2



Semi-automatic border detection algorithm for LV volume and ejection fraction with 4D LV analysis software from TomTec Inc.. The semi-automatic segmentation of the left ventricle chamber (upper left), the extent and timing of left ventricular volume over time is demonstrated (lower right and left).

Several studies have shown that both 3D reconstruction and real-time 3-DE allow accurate calculation of left ventricular volume and ejection fraction.[13-16] Studies comparing real-time 3D echocardiographic studies with magnetic resonance imaging are shown in table 2.

Table 2 Volume and function measurement by real-time 3-DE in comparison with MRI

Author/ref.	Objects	N	r	SEE	Mean Diff ± SD
Jenkins et al.(13)	LV-EDV	50			−4 ± 29
	LV-ESV				−3 ± 18
	LV-EF				0 ± 7
Kuhl et al.(43)	LV-EDV	24	0.98		-13,6 ± 18,9
	LV-ESV		0.98		-12,8 ± 20,5
	LV-EF		0.98		0,9 ± 4,4
Shiota et al.(30)	LV-EDV	28	0.97	27 ml	-43 ± 65 ml
	LV-ESV		0.94	29ml	-37 ± 67 ml
	LV-EF		0.98	0.04%	0.001 ± 0.04%
Lee et al.(44)	LV-EDV	25	0.99	11.28ml	
	LV-ESV		0.99	10.21ml	
	LV-EF		0.92	0.06%	
Zeidan et al.(45)	LV-EDV	15			-6 ± 11 ml
	LV-ESV				-4 ± 9 ml
	LV-EF				2 ± 5%

3DE = three-dimensional echocardiography; MRI = magnetic resonance imaging; N = number of subjects; LV = left ventricle; r = correlation coefficient; SEE = standard error or regression; Diff. = difference; SD = standard differentiation; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction

The acquisition can be combined with the infusion of a contrast agent, particularly in patients with difficult acoustic window in whom it might be of benefit to improve the delineation of the endocardial contour.

RV analysis

The complex geometry of the right ventricle (RV) limits accurate assessment of right ventricular volume and function on conventional 2-DE.[17] The asymmetric shape of the RV, the limited number of well-defined landmarks and the position in relation to the usual acoustic windows limit the possibility for conventional 2-D assessments. Real-time 3D echocardiography permits to depict both the complete tricuspid valve as well as the complex shape of the right ventricle.[18] However, contrast enhancement is needed to improve the detection of the anterior RV wall since poor near field resolution significantly interferes with endocardial visualization in unenhanced 3D echo in many patients.[19] Assessment of RV volumes and function based on 3D echocardiography show better agreements with magnetic resonance imaging considered now as the reference standard than 2-DE.[20-24] However, even the full volume method is not sufficient to encompass the entire RV in many congenital dilated hearts.

Valve morphology and function

Three-dimensional echocardiography has already had an impact on both the diagnosis and treatment of mitral valve disorders.[5] Dynamic 3D reconstruction of mitral valve structure `*en face*` from either a left atrial or an LV perspective, including detailed visualization of the commissures, leaflet scallops, and fibrous trigones, are helpful in a comprehensive analysis of the underlying valve anomaly and preoperative assessment.

The quantitative analysis of three-dimensional echocardiography can be utilized for the volume and area quantification of the valve morphology and function, especially in mitral and aortic valve disease (figure 3).[25, 26]

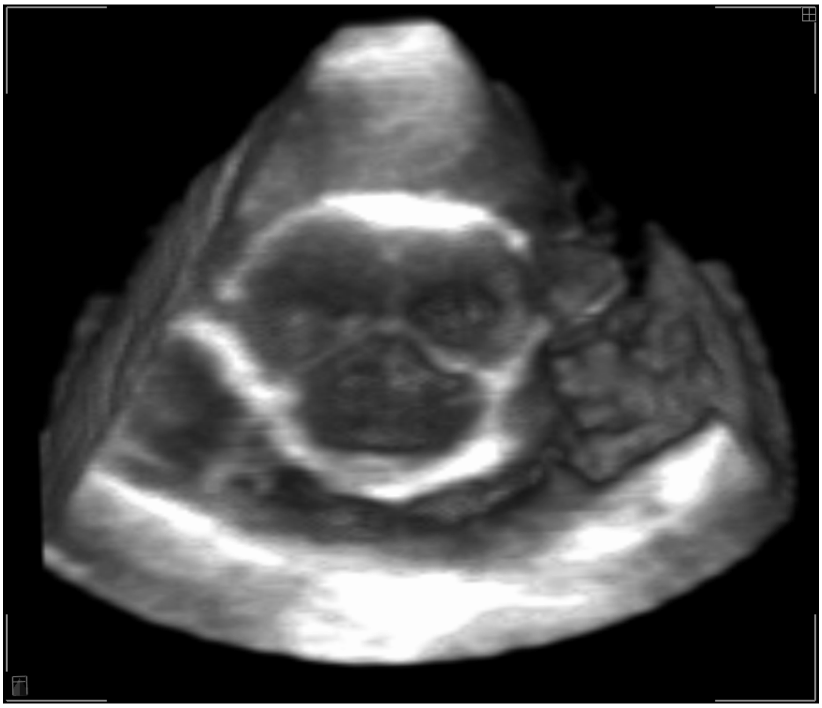


Fig. 3 Real-time 3-D echocardiographic image of the aortic valve. The aortic valve is visualized from above with electronic aortotomy.

In the assessment of valve incompetence, 3D reconstruction of color Doppler flow jets adds information to that available from 3D reconstructions of heart structures.[27] Clearly, real-time 3D echocardiography offers great advantage over reconstructive 3D by avoiding motion artefacts and more precise delineation of these delicate fast moving structures.

Methods for quantification of 3-DE color flow mapping have been described since the mid-1990s. The development of 3-DE grey-scale volume-rendered reconstructions raised the question of the possibility of reconstructing and quantifying color flow intracardiac jets and has been described recently. However, reliable quantification of 3-DE color flow jets, *in vivo*, remains investigational.[27-31]

Congenital heart disease

Conventional 2-DE is the most commonly used non-invasive diagnostic method for delineation of the presence and nature of congenital heart defects. Although the presence and anatomy of many congenital heart defects can be diagnosed readily by 2-DE, the anatomy is rarely displayed in views that are similar to the ones encountered during surgery. Especially, the 3D relationship of the cardiac structures in these complex hearts is hard to understand from conventional 2-D images.[32] The clinician must mentally integrate the sequentially obtained 2-D images to build up a 3D perception of the morphology, which is difficult in the presence of complex congenital defects.[33, 34] Display of images in a format closely resembling 3D reality clearly facilitates image interpretation and reduces interobserver variability of interpretation. The major advantage of real-time 3D echocardiography over 3D reconstruction is that imaging in small infants does not require sedation, which is necessary when acquisition time is prolonged.

The development of new techniques of atrial septal defect closure, including minimal-access surgery and percutaneous catheter closure, has increased the need for accurate assessment of not only defect size but also defect morphology and its spatial relations.[35] Studies in patients with atrioventricular septal defects have shown an incremental diagnostic value of 3D echocardiography in the assessment of dynamic morphology of such defects and in the accurate description of the mechanism of AV valve insufficiency after defect repair (figure 4).[36, 37] These findings are clinically important because, despite the improvement in surgical repair techniques. Early mortality and reoperation after repair of complex congenital heart malformations could be further reduced by more detailed preoperative patho-morphological information.

Future application

Stress echocardiography

Stress echocardiography is a clinical procedure to detect regional wall dysfunction induced by ischemia by comparing wall motion information in prestress and poststress ultrasound images. Good endocardial border delineation is essential and has been improved using harmonic imaging and contrast agents, but the time-consuming serial acquisition of identical 2-D imaging during different stress levels remains a significant limitation of conventional stress echo. Complete LV acquisition by 3-DE ensures detection of all wall motion abnormalities. The possibility to scan a full volume containing all LV wall segments during one breath hold has made this new technique suitable for stress echocardiography.[38, 39] Sensitivity and specificity will further improve by increasing image resolution and the use of contrast agents. RT-3DE could become a major application for global ventricular and regional wall function analysis in stress echocardiography.

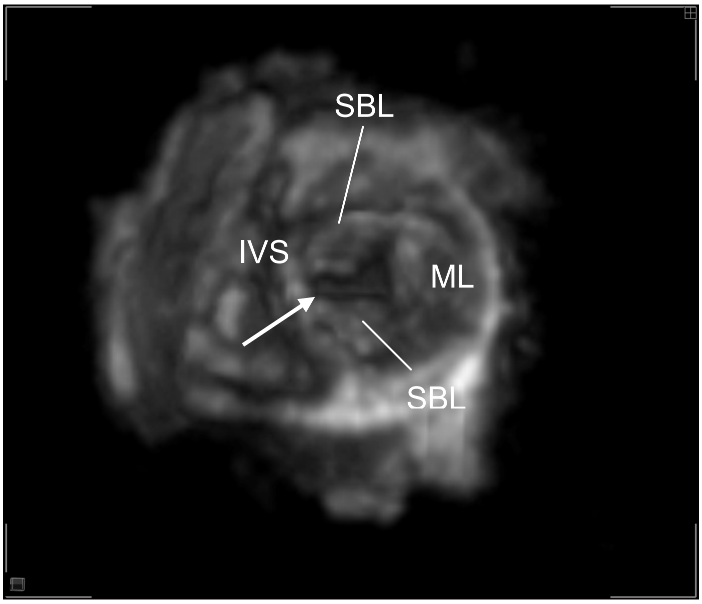
LV dyssynchrony and biventricular pacing

Echocardiography has an important role in the evaluation of patients with mechanical dyssynchrony before biventricular pacemaker implantation. Despite the promising results of cardiac resynchronization therapy (CRT) on acute hemodynamic performance and long-term functional status, the selection of suitable patients is still ill defined. Since real-time 3D echocardiography allows rapid and accurate evaluation of LV volumes and their changes in these patients, it has great potential for assessment of LV dyssynchrony before and during CRT.(40) Real-time 3-DE with appropriate software for segmental wall motion analysis allows to determine dyssynchrony between all segments.(41) Phase analysis of segmental volume-time curves based on 3D data demonstrates changes of regional myocardial motion and LV contraction pattern in a quantitative way.(42) However, defining and expressing the delay remains an important issue and there is a need for standardization.

Virtual reality in cardiac ultrasound

Three-dimensional echocardiography offers great potential for teaching and training, aiding in complex diagnostic situations and assisting in the planning of surgical procedures. Virtual reality models can assist in the interpretation of 3D presentations of the heart and can be useful as a permanent reference environment for diagnosis and assist in planning the surgical or catheter-interventional procedures. Utilizing a communication network, specialists can participate in training and even decision-making in remote areas in the future.

Fig.4



Real-time 3D echocardiographic image of the left-sided AV valve in a patient with atrioventricular septal defect. The AV valve is shown in a diastolic frame, seen from a ventricular view. The two bridging leaflets with the apparent \`cleft\` (arrow) is clearly identifiable. IVS = interventricular septum, IBL = inferior bridging leaflet, SBL = superior bridging leaflet, ML = mural leaflet.

Summary

Real-time 3D echocardiography provides the clinician with additional knowledge of cardiac disease and adds insights to the understanding of complex pathology. The availability and versatility in use of a 3-DE data set allows the cardiologist to retrieve an infinite number of different views after the examination procedure and to re-examine the patient after he has left the laboratory. More accurate and reproducible measurements, together with new physiologic parameters, such as wall motion phase analysis, LV curvature analysis for regional wall stress, flow jets and myocardial perfusion, will provide additional information and allow addressing of new clinical questions that are uniquely 3-DE (table 3). Further developments and improvements for widespread routine applications include faster acquisition, processing and reconstruction, improved image quality and easier approaches to quantitative analysis, e.g. by using more intelligent automated border detection algorithms. The perspective is that real-time 3-DE may eventually become the standard echocardiographic examination procedure.

Table 3 Advantages of three-dimensional echocardiography

Decreases interpretation variability
Electronic cardiotomy and 'en face' views
Quantitation of (complex) volumes
New parameters (e.g. shape analysis)
Off-line (re) examination
Teleconsultation and tele-examination
Virtual reality

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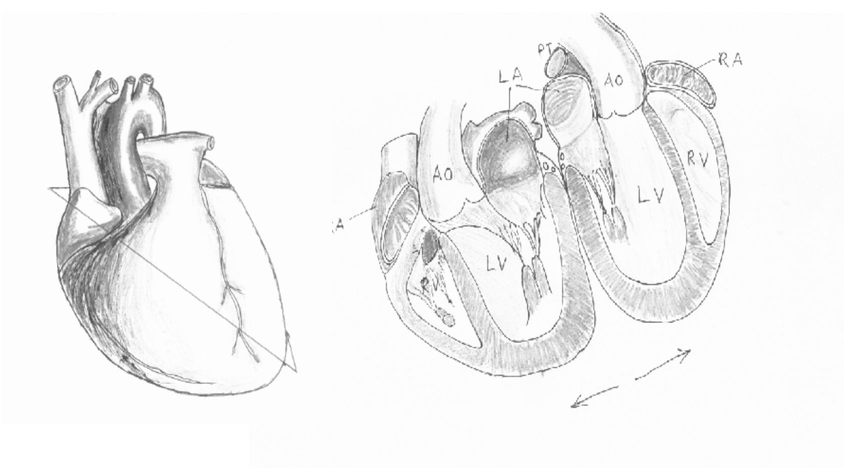
Chapter 3

How to perform a real-time transthoracic 3D echocardiographic examination of the heart;

experience of more than 400 real-time 3D echocardiographic studies

Annemien E. van den Bosch
Jackie S. McGhie
Folkert J. Meijboom



Introduction

Rapid advances have been made with real-time 3D echocardiography and will continue to evolve as this technology matures.[1-4] Over the past two years a total of 400 real-time 3D echocardiographic examinations were performed in our institution, two-thirds for congenital heart disease (adults and children) and one-third for the assessment of left ventricular function. Our experience has shown that there is a considerable learning curve for 3D echocardiographic data acquisition and analysis, even for those technicians and cardiologists who have worked with echocardiography for years. First, we assumed that one data set acquired from a single view, i.e. apical 4-chamber, would comprise all the necessary data to analyze the entire heart. This proved to be correct for left ventricular volumes, global and regional function, but thin structures as semilunar and atrioventricular valves were poorly defined or not captured in the 3D data set. These thin cardiac structures were not visualized probably as a result of the poor lateral resolution of the transducer. We experienced that for a good 3D image quality of these specific structures, the ultrasound beam must be perpendicular to the defined structure. This meant a refinement of our anatomical knowledge and moving away from the standard echo windows resulting in sometimes very unorthodox scanning planes. Even when technical issues relating to beam focusing and image quality were resolved, the direction of the ultrasound beam relative to the region of interest remained essential for the quality of the 3D image.[5, 6]

Three-dimensional echocardiography is not a magic tool, even with an optimal 2D image quality, 3D reconstructions can be disappointing. The limitations known of many ultrasound techniques are also true for 3D echocardiography. Extra-cardiac structures or cardiac structures hidden in part by lung tissue cannot be imaged. In addition ultrasound artefacts such as shadowing and reverberations are still there, along with near and far field penetration problems. New problems in 3D echocardiographic imaging were also encountered such as reduced resolution, a relatively low frame rate, limited frequency and a too large footprint for the intercostal space. The ongoing technical developments in 3D echocardiography will probably solve a lot of these problems in the near future.

The purpose of this paper is 1) to describe the technique of 3D imaging of the heart based on the author’s experience of more than 400 such examinations and 2) to describe the views most useful to examine specific cardiac structures in common pathologic conditions.

Ultrasound system

With the introduction of the matrix phased-array transducer technology, 3D echocardiography has become applicable in daily clinical practice allowing on-line acquisition and analysis. The transthoracic 3D images can be displayed in three different acquisition modes (figure 1): A) 3D echo mode display of a pyramidal volume (60° x 30°) in real-time without the need for respiratory gating; B) the magnified 3D echo mode in which a magnified view of a subsection of the pyramidal volume is displayed, and C) full volume 3D format that displays a large portion of the cardiac structures. The full volume data set is comprised of four wedges pyramids that are obtained over 4 to 8 consecutive cardiac cycles during breath hold with a stationary transducer position. The wedge pyramids are integrated to provide a full volume data set of 90° by 85°, to cover the entire left ventricle in a full volume data set. The multi-directional beam steering capability enables visualization of two views of the heart simultaneously. The first two 3D echo modes are predominantly used for orientation, to locate the area of interest and to have an idea of the 3D image quality. The full volume 3D mode is used to acquire a large portion of the heart, which can be analyzed immediately on the echo machine itself or in more detail with an off-line analysis system.

In pediatric echocardiography, the entire heart can often be visualized in one full volume data set. To create optimal 3D data sets for reconstruction, it is important to have a clear blood/structure definition with minimal noise. In our experience, with the gain and compression set around 50 (lower than normal) an optimal blood/structure definition can be obtained.

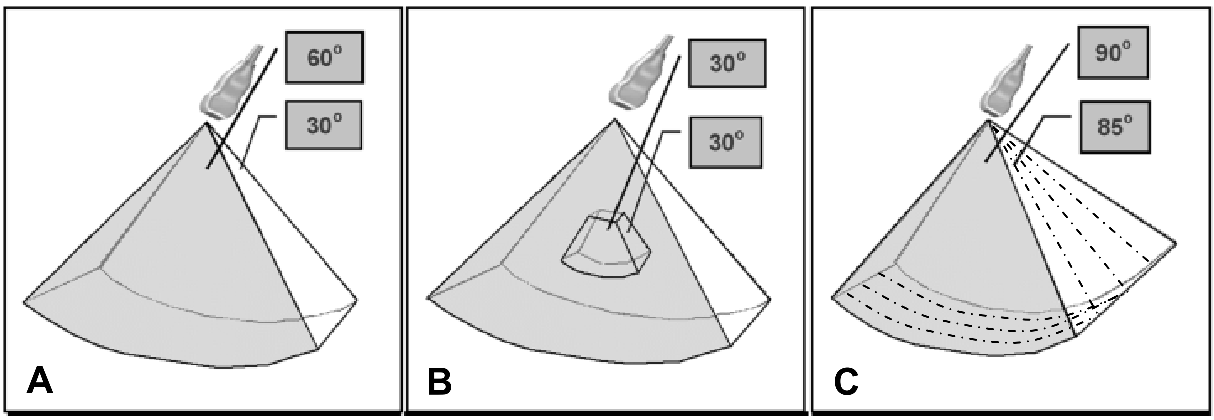


Fig. 1 Real-time 3D echocardiography with the X4 matrix transducer has three different acquisition modes: A) 3D echo mode display of a pyramidal volume (60° x 30°) in real-time; B) the magnified 3D echo mode in which a magnified view of a subsection of the pyramidal volume is displayed, and C) full volume 3D mode which consist of four wedges pyramids that are integrated to a data set of 90° by 85°, to cover the entire left ventricle (15).

Scanning procedure

Data acquisition in adults and children above the age of 4 years can be performed during a routine outpatient clinic visit. The 3D data acquisition in the neonates can only be performed in the outpatient's clinic if the child lies quiet, for example during feeding or sleep. Most of our 3D studies in neonates took place immediately before surgery, when they were under general anesthesia and on conventional mechanical ventilator. During the data acquisition, no breath hold or ventilation arrest was required. A 3D echocardiographic examination for LV function can be performed at the end of the routine 2D echocardiographic study. For more complex pathology or pre-operative 3D imaging a separate 3D echo appointment is advisable. The clinician or cardiac surgeon must give a clear definition of the region he is interested in, directing the echocardiographer to concentrate on that specific region in detail. Before acquiring a 3D full volume data set, the image is optimized in the biplane mode (two perpendicular 2D cross-sections are displayed). The region of interest must be located in the centre of both of these 2D images to ensure the best resolution and that the region of interest is entirely acquired in the 3D data set. In all patients, scanning technique was adjusted in such a way that the ultrasound beam was perpendicular to the region of interest. The standard echo transducer positions often do not fulfill this requirement and unorthodox transducer positions are necessary.

How to assess the region of interest with 3D echocardiography?

This section will describe the transducer position for each region of interest, which will generate the best possible 3D data set (figure 2 and 3, table 1).

Left ventricle

For quantative analyses of 3D LV data, second harmonics or contrast can be used to increase endocardial border detection. Only a clear-cut endocardial border will result in accurate LV analyses. It is highly desirable for certain applications such as automatic motion tracking, to remove artifacts and improve signal homogeneity within distinct anatomical tissues. The best position to obtain a 3D data set covering the entire left ventricle is the apical four-chamber view. The standard apical four-chamber view is obtained by orienting the plane of sound in a nearly coronal body plane through both ventricles and atria. Special attention is necessary to the correct alignment, because if the transducer is not positioned directly over the cardiac apex, the apex will not be included in the 3D full volume data set. Further LV analysis with manual or (semi)-automatic border detection software will become inaccurate and pathologic conditions involving the apex will not be detected.[7-12] The left ventricular cavity can be viewed from the left and right side as demonstrated in figure 4.

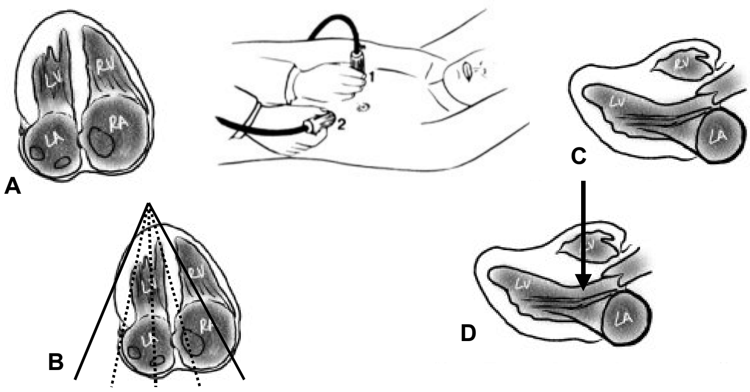


Fig.2
Two transducer positions for 3D echocardiography: 1) apical and 2) parasternal view obtained with the patients in the left lateral decubitus position. A and B are drawings of the apical view and shows in B that the left ventricle can be entirely included in the full volume (four wedges pyramids) 3D data set. C and D are drawings of the parasternal long-axis view and D shows that the ultrasound beam is perpendicular to the mitral valve anterior leaflet that results in the optimal 3D data set of this structure

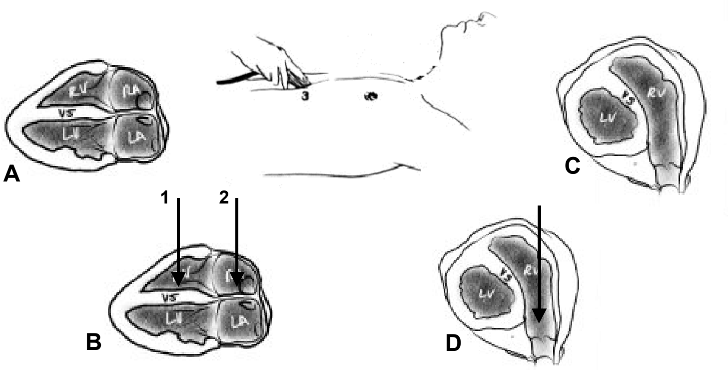


Fig.3
The subcostal view is obtained with the patients in the supine position. A and B are drawings of the subcostal 4-chamber view and B shows that in this position the ultrasound beam is perpendicular to the atrial (2) and ventricular (1) septum. C and D are drawings of the subcostal short-axis view that result in an excellent position, especially in children, to acquire a 3D data set of the pulmonary valve. D illustrates that the ultrasound beam is perpendicular to the pulmonary valve

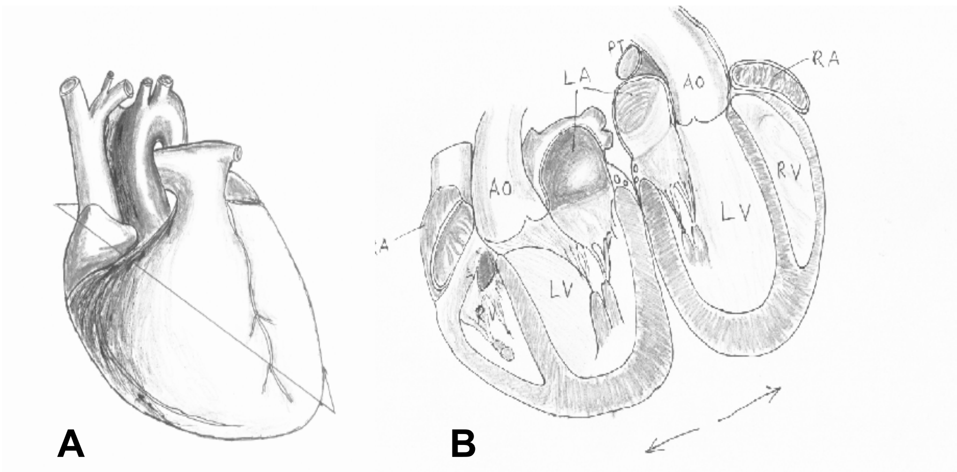


Fig 4

A: Drawing of the plane of section (long-axis).
B: View of the interior of the heart after section.

Right ventricle

Right ventricular dysfunction is a clinical problem that occurs frequently in the adult patients with congenital heart disease. The right ventricle (RV) has a complex shape and structure, prohibiting adequate RV volume and function assessment by 2D echocardiography. Real-time 3D echocardiography has the potential to encompass the entire right ventricle in one ultrasound dataset obtained from the apical 4-chamber position. The trabecularisation, inherent to any morphological RV, makes differentiation between RV cavity and RV wall sometimes difficult. Because of these trabecularisation and poor near field resolution of the transducer that significantly interferes with endocardial visualization contrast enhancement is needed to improve the detection of the anterior RV wall. In an optimal setting it is possible to encompass the entire RV in one full volume data set, but in our experience it is difficult to incorporate both RV inflow and outflow tract in one data set, especially when the RV is dilated.

Atria and atrial septum

To visualize the atrial septum, a subcostal examination provides the best 3D images. The transducer is placed in the midline of the patient and tilted superiorly so that it points towards the left supraclavicular fossa. The ultrasound beam is now perpendicular to the atrial septum. Interpretation and sizing of an atrial septal defect (ASD) must be done with great care as echo dropout may occur in the area of the fossa ovalis due to poor resolution. This can lead to an inaccurate description and size of the defect. Even when no ASD is present, dropout in the fossa ovalis area can be present giving a false positive diagnose.

Dropouts are more likely to be seen when the atrial septum is visualized from another location i.e. foreshortened 4-chamber view where the ultrasound beam is not fully perpendicular to the atrial septum.
By placing the transducer slightly more to the patient's right and pointed it towards the spine of the patient, a nice view of the ventricular septum can be acquired. This subcostal view is very rewarding in children, but frequently disappointing in adults, especially when they are obese. An other location of visualizing the atria and septum, also obtainable in adults and obese patients, is the foreshortened position.

A subcostal view, a foreshortened 4-chamber view and an apical 4-chamber view can be used for volume measurements of the atria. Experimental work has been done by Keller et al. focusing on quantification of left atrial (LA) volumes with 3D echocardiography compared with magnetic resonance imaging.(13) We don't have experience in this field yet.

Mitral valve
To assess the mitral valve, a subdivision in the region of interest was made: 1) anterior leaflet or 2) posterior leaflet with their chordal and papillary muscle attachments. The anterior leaflet appears longer and larger than the posterior leaflets and moves towards the ventricular septum. In the parasternal long-axis view, the mitral valve can be seen in the anterior-posterior direction, with excellent visualization of the anterior leaflet. The ultrasound beam is perpendicular to the anterior mitral valve leaflet. In some cases, it is necessary to move the transducer more inferiorly (about two intercostal paces) and angle it towards the left hip. This view is addressed, as a 'fore-shortened' view, and can also be very useful to obtain a good 3D data for visualizing of the anterior mitral valve leaflet. The posterior leaflet has a much smaller excursion compared to the anterior leaflet and moves in the opposite direction, making it more challenging to visualize. The parasternal, foreshortened or apical view can be used depending on its pathological condition.(14) In a dilated heart the apical view is excellent. Due to the dilatation the posterior leaflet is flattened and thus more perpendicular to the ultrasound beam.

Aortic valve
Examination of the aortic valve begins by viewing the 2D echocardiographic study to see the position and direction of opening of the valve. In the majority of the 3D reconstruction of the non-thickened aortic valve only the closure line is visible and not the leaflets. The resolution of the 3D transducer is not able to pick up these very thin leaflets, only when they co apt during diastole, the midline of the aortic root can be identified. However, thickened and calcified leaflets will be visualized. The best view to assess the aortic valve and also the most difficult to obtain is the high right parasternal region, usually from the first or second right intercostal space. From this position the ultrasound beam is almost perpendicular with the aortic valve and the best possible resolution is obtained.

Due to inadequate right parasternal imaging in the majority of our patients a high left parasternal approach appeared to give acceptable 3D data sets. The annulus, sinus of valsalva and sinus-tubular junction together with the orifices of both coronary arteries can be defined clearly. The apical view is also an option but because of the far field definition problems, our results using this technique are disappointing.

Pulmonary valve

The pulmonary valve can be visualized from two parasternal positions. The first positions is from the standard parasternal short-axis view with slight cranial and leftward angulations of the transducer. With this position at the level of the great arteries, the right ventricular outflow tract and pulmonary valve can be visualized. In our experience, we repositioned the transducer more inferiorly and laterally on the chest wall so that the pulmonary valve, pulmonary artery and branches are visualized directly beneath the transducer assuming a good position to obtain a 3D data set.

The second parasternal position is obtained when the transducer is angled from the standard parasternal long-axis view towards the patients left shoulder giving a long-axis view through the right ventricular outflow tract. Although the ultrasound beam is not fully perpendicular to the region of interest, it can be useful for assessing the pulmonary valve.

For the children, a subcostal scanning position is the ideal choice. In the parasternal short and long-axis views the near field and lateral resolution limits visualization of the thin structures in this region. So like the aortic valve, details of the pulmonary valve leaflets could not be visualized in the 3D data set but the diameter of the valve annulus and closing line can easily be assessed. Better visualization occurs when the valve is thickened or calcified as can be seen in pulmonary valve replacement by a homograft.

Tricuspid valve

When the transducer is angled from the standard parasternal long-axis view towards the patient's right hip, a parasternal long-axis view through the right ventricular inflow (right atrium, tricuspid valve and right ventricle) is obtained. For the acquisition of the 3D full volume data set, centre the TV so that in the two-perpendicular cross-sections visualizing of the anterior and septal leaflet, and the anterior and posterior or septal leaflet of the tricuspid valve are displayed in the two planes. In our experience, it is necessary to use more gain (approximately 60 – 70) than normal to acquire the tricuspid valve leaflets.

From an apical 4-chamber view, the TV can be visualized in relation to other intracardiac structures. Especially its position relative to the MV and AoV is very illuminating. Identification of 3 leaflets is almost always possible when the image quality is adequate. On 2D echo it is difficult to judge which leaflet is seen from a standard apical 4-chamber or parasternal short-axis.

Three-dimensional echocardiography allows unequivocal identification of the 3 TV leaflets, their exact attachment in the TV annulus and their relation with the interventricular septum. In case of a perimembranous ventricular septal defect (VSD) - sometimes referred to as a sub-tricuspid VSD - the relation of the VSD with the TV leaflets can be assessed.

Table 1

Transducer positions for optimal acquisition of 3D data set of different intracardiac structures.

Apical 4-Chamber position	Left ventricle
	Mitral valve posterior leaflet
Parasternal long-axis position	Mitral valve anterior leaflet
	Tricuspid valve
Parasternal short-axis position	Pulmonary valve
High right parasternal position	Aortic valve
Subcostal position	Left and right atria
	Atrial septum
	Ventricular septum

Comments

Real-time 3D echocardiography is an exciting development and has opened a new area in noninvasive cardiologic imaging. The detailed anatomic and functional information provided by this technique has been unavailable with the conventional 2D echocardiography, MRI or CT. In this paper, we have provided detailed information regarding the technique, how to obtain the best 3D image and assess various regions of interest of the heart by presenting a simple but unified concept of image orientation.

It should be noted that because of the different chest wall configurations and variability of size, shape and position of the heart in the chest, the above-described transducer positions must be modified accordingly in order to obtain the desired region of interest in an individual patient. It is expected that with a widespread use of this technique, further clinical applications will be developed.

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Chapter 4

Characterization of atrial septal defect assessed by real-time 3D echocardiography

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AE van den Bosch

DJ Ten Harkel

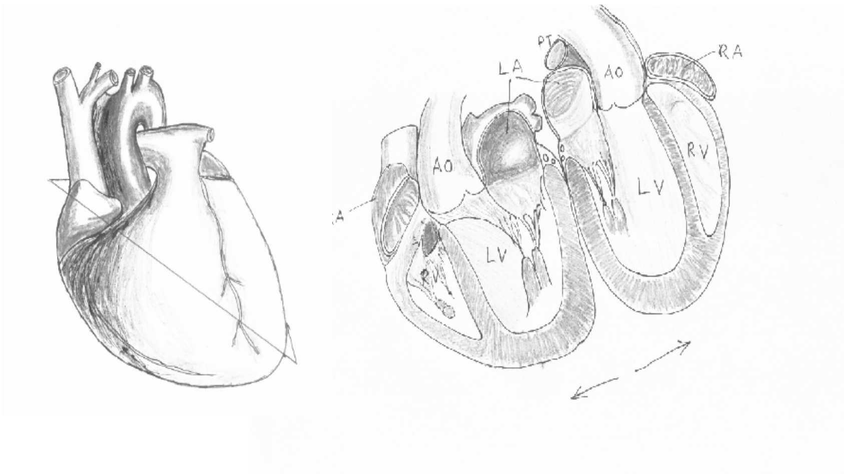
JS McGhie

JW Roos-Hesselink

ML Simoons

AJJC Bogers

FJ Meijboom



Summary

The aim of this study was to describe a quantitative evaluation by real-time 3D echocardiography (RT-3DE) of ASD and atrial septum that are important for patient selection for transcatheter closure, and to assess the reliability of RT-3DE findings compared with surgery.

Forty-five patients, who were scheduled for surgical or transcatheter closure of an ASD, were included in the study. In 43 (96%) patients, 3D reconstructions allowed optimal imaging of the ASD. The correlations between the ASD maximal diameter by RT-3DE and surgery or balloon sizing were excellent (r > 0.95). All surrounding rims of the atrial septum could be assessed on 3D reconstruction; except for the aortic rim a cross-sectional reconstruction was created mimicking the transesophageal echocardiographic cross-section (r > 0.92).

In conclusion, RT-3DE allows accurate determination of ASD localization, size and surrounding tissue of the atrial septum and might replace TEE for patient selection for surgical or transcatheter closure.

Introduction

In the past decade transcatheter closure of an atrial septal defect (ASD) has gradually become treatment of choice, as an alternative for surgery. However, not all ASDs can be closed with a transcatheter approach. If an ASD is too large, or the amount of circumferential tissue (‘rims’) is too small, the only treatment option is surgery. Adequate imaging of the essential anatomic features of the ASD is necessary for patient selection regarding transcatheter or surgical closure.[1-7] The role of two-dimensional transthoracic (TTE) and transesophageal echocardiography (TEE) is well established, although limitations, such as incomplete ASD measurements and poor delineation of tissue rim, have been emphasized frequently.[8-11] Imaging of an ASD with 2D echocardiography is, in clinical practice, based on a limited number of orthogonal planes through the heart from predefined transducer positions. This limited number of cutting planes can lead to an underestimation of ASD dimensions and surrounding rims, especially if the defect is asymmetrically in shape and not located centrally in the atrial septum. In theory, 3D echocardiography equals an always infinite number of 2D cutting planes integrated in one 3D data set, that allows an ‘en face’ view of the entire interatrial septum encompassing both atrial septum and surrounding rims during the cardiac cycle. This reduces the risk of missing relevant information when compared with 2D imaging, based on only limited number of scanning planes.[12-19] Using the new real-time 3D echocardiography (RT-3DE), we have tried to determine the anatomic characteristics of the secundum atrial septal defects (ASDs).

The purpose of the present study was (1) to describe a quantitative evaluation by RT-3DE of the various features of ASD and the atrial septum that are important for patient selection for transcatheter closure, and (2) to assess the reliability of the 3D echocardiographic findings compared with surgery.

Methods

From September 2004 to August 2005, all children and adults who were scheduled for surgical closure of an ASD, and all adult patients who underwent transcatheter closure of an ASD were included in the study. There were 45 patients (43% male), 24 children (mean age 2.9 ± 4.3 yrs) and 21 adults (mean age 47 ± 15 yrs). The indication for ASD closure was a left-to-right shunting resulting in a substantial right atrial and right ventricular overload. Adult patients with a maximal defect diameter of more than 30 mm were referred for surgical closure. Two-dimensional TEE was performed in adult patients deemed suitable candidates for transcatheter closure after TTE. Patients with a maximal ASD diameter > 30 mm measured with TEE or with insufficient rims were referred for surgery. Patients who were still considered good candidates for transcatheter closure after the TEE study were referred to the catherization laboratory. Patients with a patent foramen ovale were excluded.

Informed consent was obtained before the RT-3DE was performed. The hospital's institutional review board approved the study.

Two-dimensional Transthoracic Echocardiography (TTE) and transesophageal Echocardiography (TEE)

The echocardiographic studies were performed with the Philips Sonos 5500 and 7500-echo system (Philips Medical Systems, Andover, MA, USA). The transthoracic study was performed during an outpatient clinic consultation. Measurements of defect size and the maximal length of the interatrial septum were performed. For the TEE study, we used a standard multiplane TEE probe (Omni-probe, Philips Medical Systems). The TEE examination of the defect and surrounding rims was observed as previously described in detail.(20)

Real-time 3D echocardiography

Real-time 3D echocardiographic study was performed with a Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. After completion of the standard TTE examination, RT-3DE study was performed with a 2-4 MHz (X4) matrix transducer, in an end-expiratory breath-hold lasting 6 to 8 seconds. The RT-3DE study in infants and children under the age of 4 years took place immediately before surgery, when they were under general anesthesia. During data acquisition, no breath hold or ventilation arrest was performed in this pediatric population. The patients were on conventional mechanical ventilation (tidal volume 8 ml/kg body weight). Since the data were acquired during the time that the child was prepared for surgery, there was no prolongation of general anesthesia time.

The RT-3DE data were stored on a CD-ROM and transferred to a stand-alone TomTec workstation (TomTec, Munich, Germany) for off-line data analysis with TomTec Echoview 5.2® software. The 3D data set was cross-sectioned to show an \`en face\` anatomy of the ASD from the right and left atrium and a cross-sectional view for the aortic rim. The maximal ASD diameter was measured in the atrial diastolic phase. The surface area of the ASD was measured in atrial diastole and atrial systole. The percentual change in area during the cardiac cycle was calculated using the following formula: % change during cardiac cycle = (diastolic area – systolic area)/diastolic area x 100%. The cardiac phases were defined as immediately before the opening (atrial diastole) and closure (atrial systole) of the atrioventricular valve. An ASD consisting of multiple fenestrations was excluded from comparative measurements.

The minimal dimensions of the defects rims: antero-superior (distance from the aorta); antero-inferior rim (distance from the tricuspid valve); postero-superior rim (distance from the superior vena cava); postero-inferior rim (distance from the inferior vena cava); posterior rim (distance to the posterior wall) were assessed (figure 1). Any rim length ≤ 3 mm was considered absent.

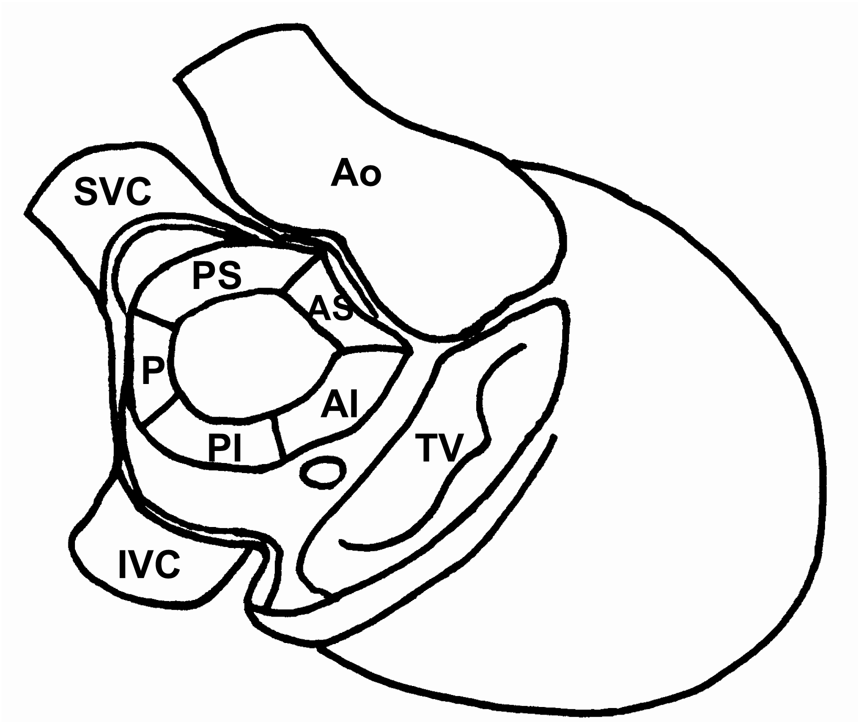


Fig. 1 Drawing of the `en face` right atrial septum surface of the heart with the right atrial free wall removed. The locations of the 5 measured atrial septal rims are shown: AS = antero-superior; AI = antero-inferior rim; PS = postero-superior rim; PI = postero-inferior rim; P = posterior rim. Ao = ascending aorta; SVC = superior vena cava; IVC = inferior vena cava.

In the patients who underwent transcatheter closure of the defect, a sizing balloon was inflated with diluted contrast under fluoroscopic and transesophageal echocardiographic guidance until the appearance of waisting (in a way similar to angioplasty) and disappearance of left-to-right shunt by transesophageal echocardiography (TEE). Once waisting was visible, a cine image was performed and the size of the waist was measured using the markers positioned in the balloon for calibration. This was considered to be the stretched diameter of the defect and compared with the 3D echocardiographic measurements. The patients who underwent surgical closure of the ASD, the surgical measurements performed during the intracardiac operation were utilized for comparison to the echocardiographic measurements.

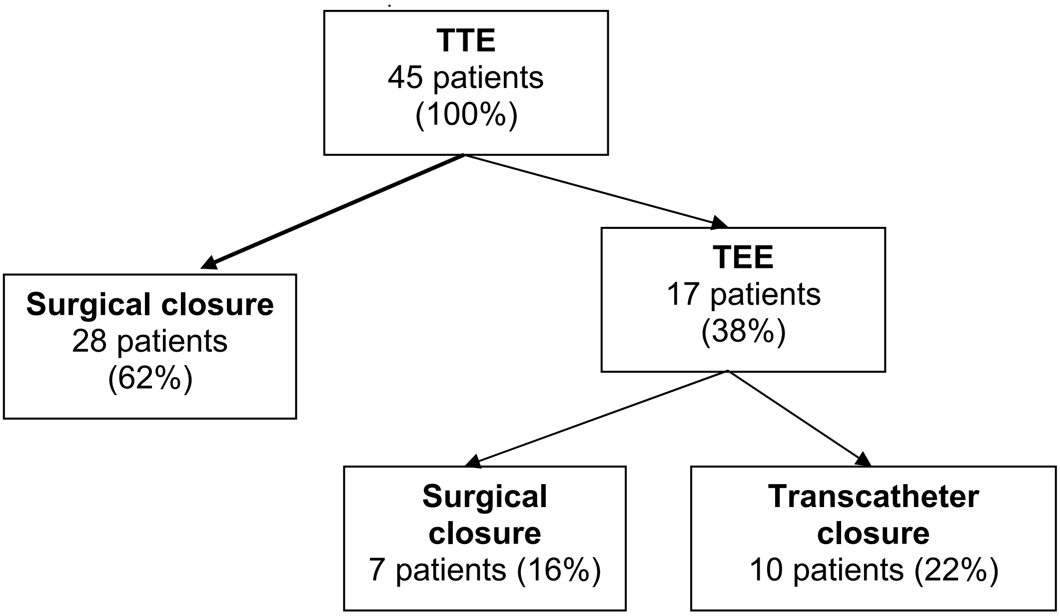
Statistical analysis

All values are expressed as means ± standard deviation (SD) when data were normally distributed. Data were tested for normality with the Kolmogorow-Smirnov test. The median and range are given when data were distributed asymmetrically.

The agreement between maximum diameter and minimal dimensions of the defects rims of the ASD by TTE, TEE, RT-3DE and surgery were compared by linear regression and by Bland-Altman analysis.[21] Limit of agreement is expressed as 2 SDs of the difference between two modalities. To determine whether the difference in the values was statistically significant, a paired t-test was performed. A p-value < .05 was considered statistically significant.

Results

Two-dimensional transthoracic echocardiography was performed in all patients (figure 2).



Flowchart of patient selection for transcatheter or surgical closure according to size and morphology of the ASDs. TTE = two-dimensional transthoracic echocardiography, TEE = two-dimensional transesophageal echocardiography.

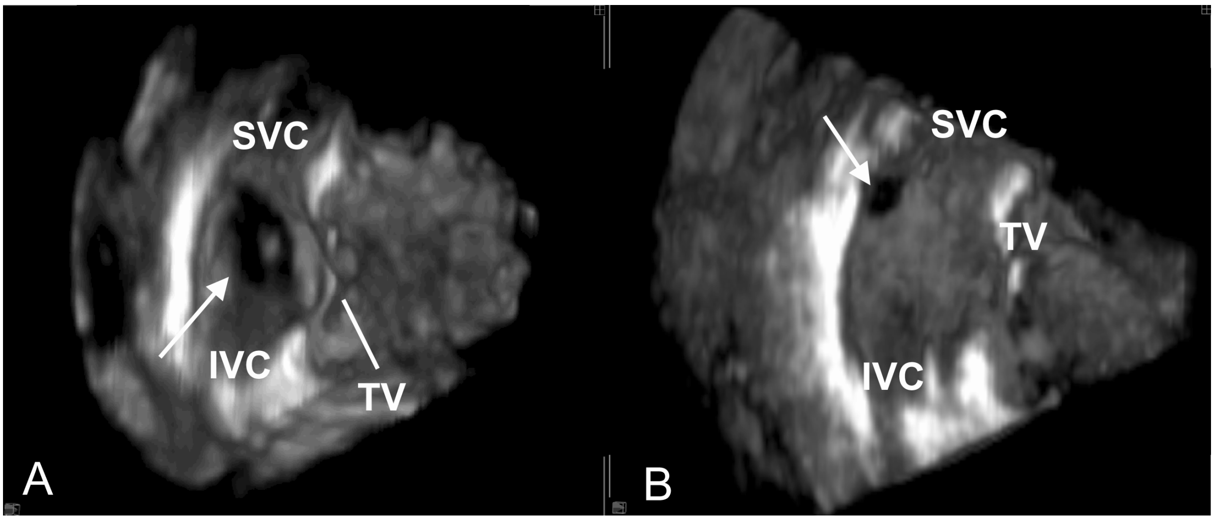
On the basis of the TTE data, 17 patients who appeared candidates for transcatheter closure underwent a TEE study. According to the TEE criteria, 7 patients had defects that were not suitable for transcatheter closure. Eventually, 10 of the 45 patients (22%) fulfilled the morphological criteria for transcatheter closure and 35 patients (78%) underwent surgical closure of the defect. In the 45 patients, 44 single ASDs were detected (39 secundum ASDs, 4 sinus venosus defects and one sinus coronarius defect) and one patient had multiple fenestrations.

Real-time 3D echocardiography

Three-dimensional echocardiographic reconstructions allowed optimal imaging of the ASD in 43 of the 45 patients (96%). In 2 patients (age 5 and 10 years) a poor acoustic window due to small intercostal space prohibited adequate 3D rendering. The mean acquisition time (total time for preparation – optimalization of setting and transducer position – and the acquisitions of all the 3D data sets) was 7 ± 3 minutes. Three views - two \`en face\` views from the right and left atrium and a cross-sectional view for the aortic rim determination - were reconstructed per patient (figure 3 and 4). Assessment of the ASD maximal diameter, area changes and rims by RT-3DE required approximately 20 minutes. The correlations between the ASD maximal diameter by TTE, RT-3DE and surgery are reported in table 1.

In 10 patients selected for device closure, RT-3DE was not feasible in one patient and another patient had multiple fenestrations. In the patients with circular ASD without fenestration (n=8) the correlation was r = 0.97 with a mean difference of 1.6 ± 1.1 mm.

Fig.3



A. Real-time 3D echocardiographic display of a right atrial \`en face\` view of a secundum ASD (arrow); B. Real-time 3D echocardiographic display of sinus venosus defect of the superior type (arrow), viewed from the right atrium. TV = tricuspid valve; SVC = superior vena cava; IVC = inferior vena cava.

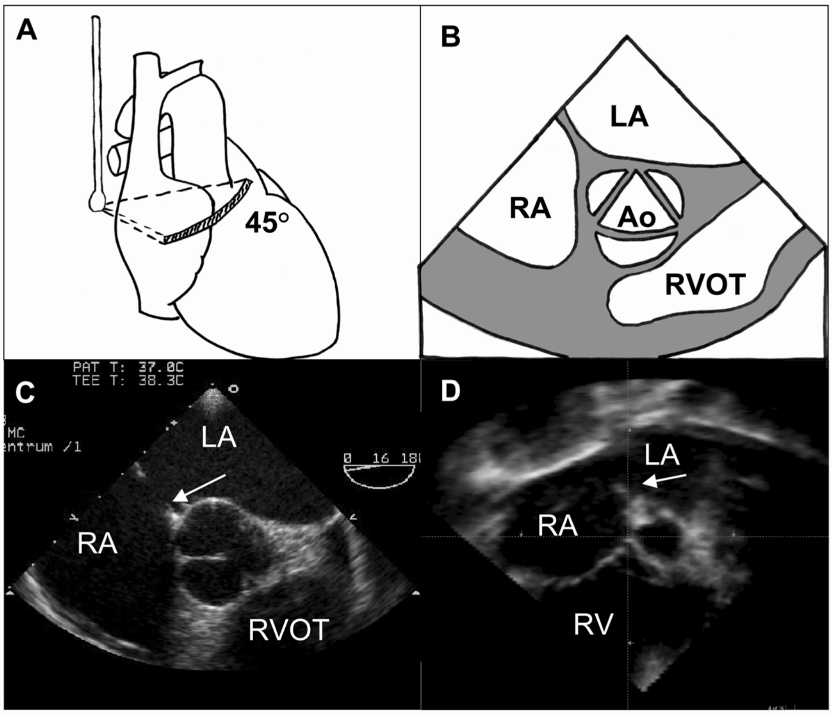
Table 1. Patients (n = 35) who underwent surgical closure of the defect.

Maximal ASD diameter measurements by two-dimensional transthoracic echocardiography, real-time 3D echocardiography and surgery.

	TTE (mm) (mean ± SD)	RT-3DE (mm) (mean ± SD)	Surgery (mm) (mean ± SD)	Mean of diff	Line of identity
Maximal diameter	16.7 ± 9	23.2 ± 15	24.1 ± 15		
TTE vs RT-3DE		p < 0.01		-7.4 ± 12	y = 0.51x + 5.1; r = 0.77
TTE vs Surgery		p < 0.01		-8.4 ± 12	y = 0.46x + 5.7; r = 0.75
RT-3DE vs Surgery			p = NS	-0.9 ± 4.9	y = 0.91x + 1.3; r = 0.95

TTE = two-dimensional transthoracic echocardiography; RT-3DE = real-time 3D echocardiography; Mean of diff = difference between two methods.

Fig.4



A. Illustration of the position of the transesophageal transducer to obtain a short-axis transesophageal view
B. Illustration of this short-axis transesophageal cut plane
C. A transesophageal echocardiographic image of the cut plane showing the aortic rim (arrow)
D. A transthoracic cross-sectional reconstruction from a 3D data set showing the aortic rim (arrow). LA = left atrium; RA = right atrium; RVOT = right ventricular outflow tract; RV = right ventricle.

Dynamic change in the atrial septal defect during the cardiac cycle

The end-diastolic area of the ASD ranged from 0.4 to 15.7 cm^2 and the end-systolic area from 0.2 to 6.4 cm^2. In 7 patients with small secundum ASD, the end-systolic area could not be assessed because the defect was too small. The mean relative area change, as a measure of ASD dynamics, was 51% ± 15% and varied markedly between the individual patients.

Surrounding tissue of atrial septal defect

In 25 of the 35 patients undergoing surgical closure of the ASD, surrounding tissue rims were assessed. In 4 patients, the surgeon assessed the localization and maximal diameter of the ASD but not the exactly length of the surrounding rims. In 6 other patients adequate measurements were not feasible on the 3D images. The correlation for the antero-inferior rim, postero-superior rim, postero-inferior rim and posterior rim assessed by RT-3DE and surgery are shown in table 2. The aortic rim could not be assessed on the `en face` reconstruction of the atrial septum, therefore a cross-sectional reconstruction from the 3D data set was created mimicking the TEE cross-section that allowed measurement of the aortic rim (figure 4).

In the 16 of the 17 patients undergoing TEE, the aortic rim was assessed and compared with RT-3DE measurements. In one patient cross-sectional reconstruction of the aortic rim was not feasible. The correlation for the antero-superior rim (distance from the aortic) measurements by TEE and RT-3DE are reported in table 2.

Table 2.Tissue rim measurements of the atrial septum defect.

RT-3DE vs Surgery (n = 25)	RT-3DE (mm)	Surgery (mm)	Mean of diff	Line of identity
Antero-inferior rim (length ≤ 3 mm in 4 patients)	14.9 ± 11.1	13.0 ± 6.1	-0.3 ± 3.9	y = 0.95x + 0.74; r = 0.91
Postero-superior rim (length ≤ 3 mm in 8 patients)	8.8 ± 5.0	10.4 ± 6.3	1.1 ± 4.2	y = 0.83x + 0.48; r = 0.88
Postero-inferior rim (length ≤ 3 mm in 10 patients)	13.2 ± 8.8	18.6 ± 11.7	4.5 ± 7.0	y = 0.57x + 0.95; r = 0.79
Posterior rim (length ≤ 3 mm in 10 patients)	7.3 ± 4.2	10.0 ± 6.1	1.8 ± 2.9	y = 0.64x + 0.49; r = 0.84
TEE vs RT-3DE (n = 16	TEE (mm)	RT-3DE (mm)	Mean of diff	Line of identity
Antero-superior rim	8.4 ± 5.2	9.2 ± 4.6	0.4 ± 2.2	y = 0.91x + 1.1; r = 0.92

TEE = two-dimensional transesophageal echocardiography; RT-3DE = real-time three-dimensional echocardiography; Mean diff = difference between two methods.

Discussion

Real-time 3D echocardiography can reliably assess the dimensions of a secundum ASD, its exact localization and extent of the surrounding tissue in a large majority of the patients. This study demonstrates the excellent correlation of RT-3DE findings compared with surgical and TEE measurements.

Until now, suitability for transcatheter closure of an ASD was evaluated by TTE and TEE.(22, 23) To select patients for transcatheter closure, 2 crucial parameters are acquired: the maximal diameter of the defect in order to choose a device with the appropriate size and the tissue rim dimensions around the defect to allow adequate anchorage of the device.(5, 24-26) As shown in this study, RT-3DE can provide this information. Moreover, it provides additional information on anatomical details and ASD area changes during the cardiac cycle. With the right atrial `en face` view, the entire circumference and tissue surrounding the defect can be visualized in one single view. The distance from the secundum ASD to the posterior wall, superior vena cava, tricuspid valve can be shown readily. However, the correlation between RT-3DE and surgical measurements regarding the distance of the ASD to the inferior vena cava was poor. Apparently this distance is difficult to assess with RT-3DE. A possible explanation is the relatively poor definition of the entrance of the inferior vena cava in the right atrium.

The `en face` view of the ASD as shown in several reports on 3D echocardiographic assessment of the ASD, allows delineation of most rims. However, the aortic rim is not discernible in this view.(12, 14, 17, 19, 24, 27-30)

For the assessment of the distance of the ASD to the aorta, a cross-sectional reconstruction comparable with the TEE image was necessary. In this cross-section, demonstrated in figure 4, the aortic rim was assessed easily and accurately in patients with an adequate transthoracic image quality. In our study, in whom 16 of the 17 patients underwent a TEE, a 3D transthoracic study alone provided all images and data that were required for clinical decision making, either transcatheter or surgical closure. Especially patients will appreciate that TEE is no longer necessary for a complete diagnosis. The advantages of RT-3DE together with the non-invasiveness and relatively short acquisition and analysis time, shows that transthoracic RT-3DE can replace TEE for the selection of patients for surgical or transcatheter closure in a large proportion of patients.

This study shows that RT-3DE provides important information concerning several aspects of the atrial septum. Unique imaging planes and projections can be generated from the 3D data set enhancing our understanding of the atrial septum, ASDs and successful device placement. Real-time 3D echocardiography will aid in the patient selection for transcatheter closure and may help in appropriate selection of type and size of the device.

Image resolution

Inherent to the physical properties of ultrasound, the best 3D images are obtained by positioning the ultrasound beam perpendicular to the atrial septum and locate the region of interest in the centre of the data set. All structures located in the far or near field of the ultrasound sector have an inferior spatial resolution compared with that in the centre of the image. In all patients, an attempt was made to utilize this window by a subcostal approach. In patients in whom the subcostal views were difficult to obtain (i.e. in obese patients), the best transducer position was the low parasternal four-chamber view. The resolution of the 3D data sets is reduced compared to 2D echocardiography. Very thin cardiac structures as foramen ovale can be difficult to visualize and dropout of thin structures are common. In our experience, the use of color Doppler together with positioning of the ultrasound beam perpendicular to the atrial septum can help differentiate between a real defect and a dropout. Therefore, we recommend obtaining a 3D data set with and without color Doppler in each patient.

Limitations

The RT-3DE reconstructions and measurements are performed off-line. The real-time 3D mode of the matrix transducer could not be used due to the limited angle sector (60° x 30°) that precluded assessment of the entire atrial septum. Therefore it is arguable whether the used technique is really `real-time` in the strictest sense.

Real-time 3D echocardiography can also be used in infants and neonates in the setting as described in this study, with children under general anesthesia. We did not investigate the clinical applicability of RT-3DE in children without sedation. It remains to be established whether the inability of a proper breath hold and a possible need for sedation will limit the application of these types of investigations in infants and young children in clinical practice.

Conclusion

Real-time 3D echocardiography provides us with unique imaging planes and projections of the atrial septum, and allows accurate determination of ASD localization, size and the extent of the surrounding tissue. The advantages of RT-3DE together with the non-invasiveness and relatively short acquisition and analysis time, shows that transthoracic RT-3DE can replace TEE for the selection of patients for surgical or transcatheter closure in a large proportion of patients.

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Chapter 5

Surgical validation of real-time transthoracic 3-D echocardiographic assessment of atrioventricular septal defects

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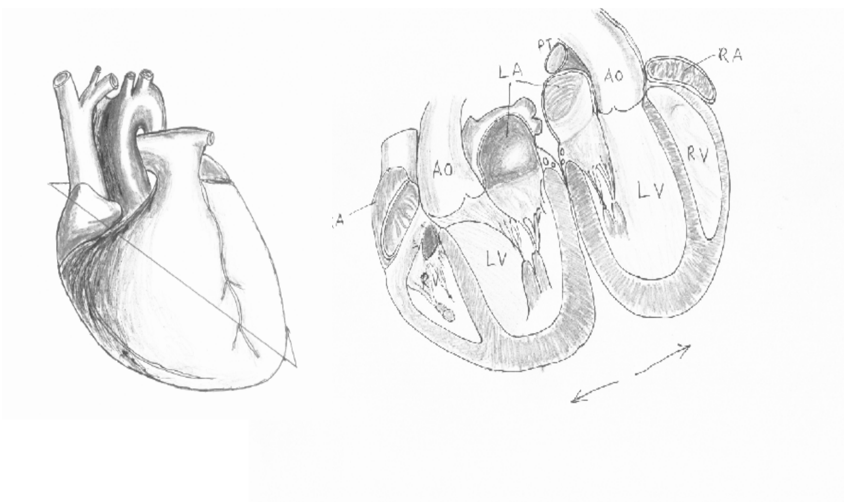
AE van den Bosch
DJ Ten Harkel
JS McGhie
JW Roos-Hesselink
ML Simoons
AJJC Bogers
FJ Meijboom



Abstract

Background
The purpose of this study was to evaluate the accuracy of AV valve morphology assessed by real-time transthoracic 3D echocardiography (RT-3DE) compared to surgical findings and to assess whether RT-3DE is applicable in clinical practice.

Methods
Between June 2004 to May 2005, 19 patients with an atrioventricular septal defect (AVSD) undergoing surgical treatment at our institution were enrolled in the study. RT-3DE was performed with Philips Sonos 7500 echo-system and off-line analysis with TomTec Echoview© software. The AVSD was assessed for the morphology of AV valve, with particularly interest to the superior and inferior bridging leaflets. 3D data were compared with measurements and descriptions acquired during the surgical procedure.

Results
Acquisition of RT-3DE datasets was feasible in all patients. Of the 19 patients, there were 11 infants (age < 1 year). The duration of 3D data acquisition was 12 ± 3 min for patients above 1 year and 4 ± 2 for infants. Reconstruction time was 22 ± 8 minutes. In all patients the AV valve orifice and RT-3DE observations of the superior and inferior bridging leaflets were all correctly identified by RT-3DE compared with the surgical findings.

Conclusion
Real-time transthoracic 3D echocardiography provides accurate assessment of AVSDs and correctly depicts the AV valve morphology. After a short learning curve, RT-3DE is easily applicable during daily clinical practice.

Introduction

Surgical repair of atrioventricular septal defects (AVSD) is directed to closure of the interatrial and interventricular communications and repair of the atrioventricular valves.[1, 2] The latter aspect is of major importance because valve incompetence after the procedure is the most important risk factor associated with late morbidity and mortality.[3-5] The anatomy of the atrioventricular valves is highly variable, both in size and number of the leaflets – most often 5, sometimes 4 or 6 leaflets – as well as in their papillary muscles and chordal attachment.[6] The exact morphology of the AV valve and the anatomic details determine whether or not a valve is amenable for surgical repair and to which extent the common AV valve can be reconstructed into two separate AV valves with an adequate function. Despite the acceptable diagnostic accuracy of the currently available standard 2D echocardiography, the information on AV valve morphology and mechanism of regurgitation often remains incomplete. [7, 8] Three-dimensional echocardiography provides a 3D data set, in which an infinite number of cutting planes can be retrieved, especially cutting planes that are impossible to obtain with 2D echocardiography. Experimental work has shown that `en face` 3D reconstruction of the AV valves can be created, which facilitates identification of all AV valve leaflets. Therefore, 3D echocardiography may provide additional information about AV valve morphology and the surrounding structures.[9, 10] Yet, it remains to be established, whether new real-time transthoracic 3D echocardiography (RT-3DE) with matrix technology provides reliable information and reflects the true anatomic AV valve orifice. The purpose of this study was to evaluate the accuracy of the AV valve morphology assessed by RT-3DE compared to surgical findings and to assess whether RT-3DE is applicable in clinical practise in patients with an AVSD.

Methods

Patient population

Between June 2004 to May 2005, 19 patients with an AVSD undergoing surgical treatment at our institution were enrolled in the study. Among the 19 patients, were 11 infants (age range 1 months to one year), 3 children (age 4, 6 and 16 years) and 5 adults (age range 21 – 65 years). In all patients the clinical diagnosis and the decision for surgery was based on standard 2D echocardiography and confirmed later by both 3D echocardiography and surgical findings. All patients and patients` parents or guardians were informed about the purpose of the study and gave informed consent to be enrolled in the study. The institutional review board approved the study.

Real-time transthoracic 3D echocardiography

The real-time 3D images were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. The X4 transducer has a frequency range from 2 – 4 MHz. For most patients, the real-time 3D mode was used for orientation and choosing the optimal window for full volume acquisition. The full volume 3D acquisition was done with ECG gating and in 7 patients above the age of 4 years an end-expiratory breath-hold lasting 6 to 8 seconds (depending on the heart rate) was performed. 3D data acquisition in these patients was performed within two weeks before surgery during an outpatient clinic consultation or on the day prior to the operation. 3D data acquisition in the infants took place immediately before surgery, when they were under general anesthesia. During data acquisition, no breath hold or ventilation arrest was performed. The patients were on conventional mechanical ventilation (tidal volume 8 ml/kg body weight). There was no prolongation of general anesthesia time, since the 3D data were acquired during the time that the child was prepared for surgery. The digital data was stored on CD-ROM and transferred to a separate workstation using TomTec Echoview 5.2 software (TomTec Inc., Munich, Germany) for off-line data analysis. Three-dimensional acquisition and reconstruction times were recorded in each patient. Acquisition time is defined as the total time for preparation – optimalization of setting and transducer position – and the acquisitions of all the 3D data sets. The mean reconstruction time is defined as the time for screening all the 3D data sets for image quality and whether of not the entire region of interest was present in the data set, and making the necessary cut-planes in the best 3D data set for off-line analyses.

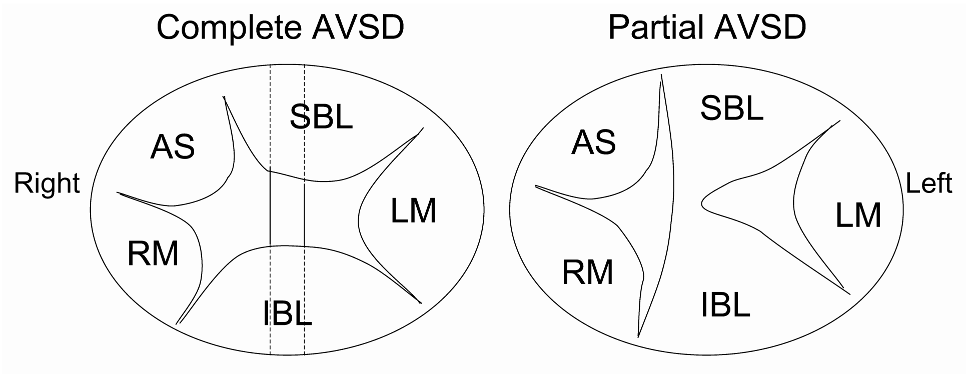
Image display and analysis

In each patient, several 3D reconstructions were carried out. For analysis of the AV valve, two opposite views were reconstructed. The `unroofed` view from the left atrium orientated toward the atrioventricular junction allowed the creation of a `surgical view` of the AV valve. Similar reconstruction, but orientated from the left ventricular apex toward the AV junction, allowed the assessment of the AV valve from below. For analysis of the atrial and/or ventricular septal defect, a cut plane was placed in the 3D data set through the right ventricle from apex to base, parallel to the ventricular septum, creating an `en face` view of the RV septal surface. By using this `en face` 3D reconstruction, also the superior and inferior bridging leaflets were identified, together with their attachments to the ventricular septum. The number, size and chordal attachment to the crest of the interventricular septum of AV valve leaflets were identified. The interatrial and/or interventricular communications were determined by measurements of maximal (= longitudinal diameter of the defect) diameter of the ASD and/or VSD. Two independent experienced observers (AvdB and JM), who were blinded to the results of the routine 2D echo study and the surgical report, analyzed all 3D data sets.

Morphologic description

The anatomic hallmarks of an AVSD are a common atrioventricular junction guarded by a common AV valve. A partial AVSD (formerly known as ostium primum atrial septal defect) was defined as a common AV valve that is divided into two orifices, whereas a complete AVSD was defined as a common valve guarding a common orifice. A partial AVSD has a connecting tongue of tissue between the superior and inferior leaflet (figure 1).[6, 11-15] The morphology of the superior leaflet was identified according to the Rastelli classification.[2, 12] The morphology of the inferior leaflet was distinguished into four patterns, related to its attachment to the crest of the ventricular septum. The inferior leaflet was 1) directly attached to the crest of the septum, 2) attached by a short membrane, 3) attached by multiple chordae and 4) attached by a few tiny chordae (virtually free floating).[16]

Fig. 1



Diagrammatic representation of the arrangement of the AV valve orifice as viewed from an apical position. (A) is a complete AVSD with a common AV valve guarding the common atrioventricular junction, (B) is a partial AVSD with a common atrioventricular junction that is divided into two orifices by a connecting tongue of tissue between the superior and inferior bridging leaflets. SBL = superior bridging leaflet; AS = anterior-superior leaflet; RM = right mural leaflet; IBL = inferior bridging leaflet; LM = left mural leaflet.

Surgical procedure and assessment of morphology

Surgical repair was performed on cardiopulmonary bypass through a right atriotomy. The surgeon, who was blinded for the 3D data, described and made a drawing of the anatomy of the AV valve, and measured the maximal diameter of the ASD and VSD. Using the surgical description as the gold standard, the accuracy of the echo assessment was determined.

Statistical analysis

All values are presented as means ± standard deviation (SD).

Results

Acquisition of RT-3DE datasets was feasible in all patients. The mean heart rate was 110 ± 19 bpm for children, and 73 ± 8 bpm for the adult patients during RT-3DE examination. Weight of the 11 infants (age < 1 year) was 5.0 ± 2.1 kg.

The time of 3D data acquisition was 12 ± 3 min for the patients above 4 years of age. For the infants the acquisition time was shorter, mean 4 ± 2 min. The total number of data sets acquired varied from 4 to 12 datasets per patient. Reconstruction time (mean 22 ± 8 minutes) varied considerably, depending on our learning curve and the complexity of the AVSD. In all children, a subcostal approach was the best approach to get an unobstructed acoustic window to create a 3D data set. For the adult patients an apical or foreshortened window was used to create a 3D data set.

Complete or partial atrioventricular septal defect

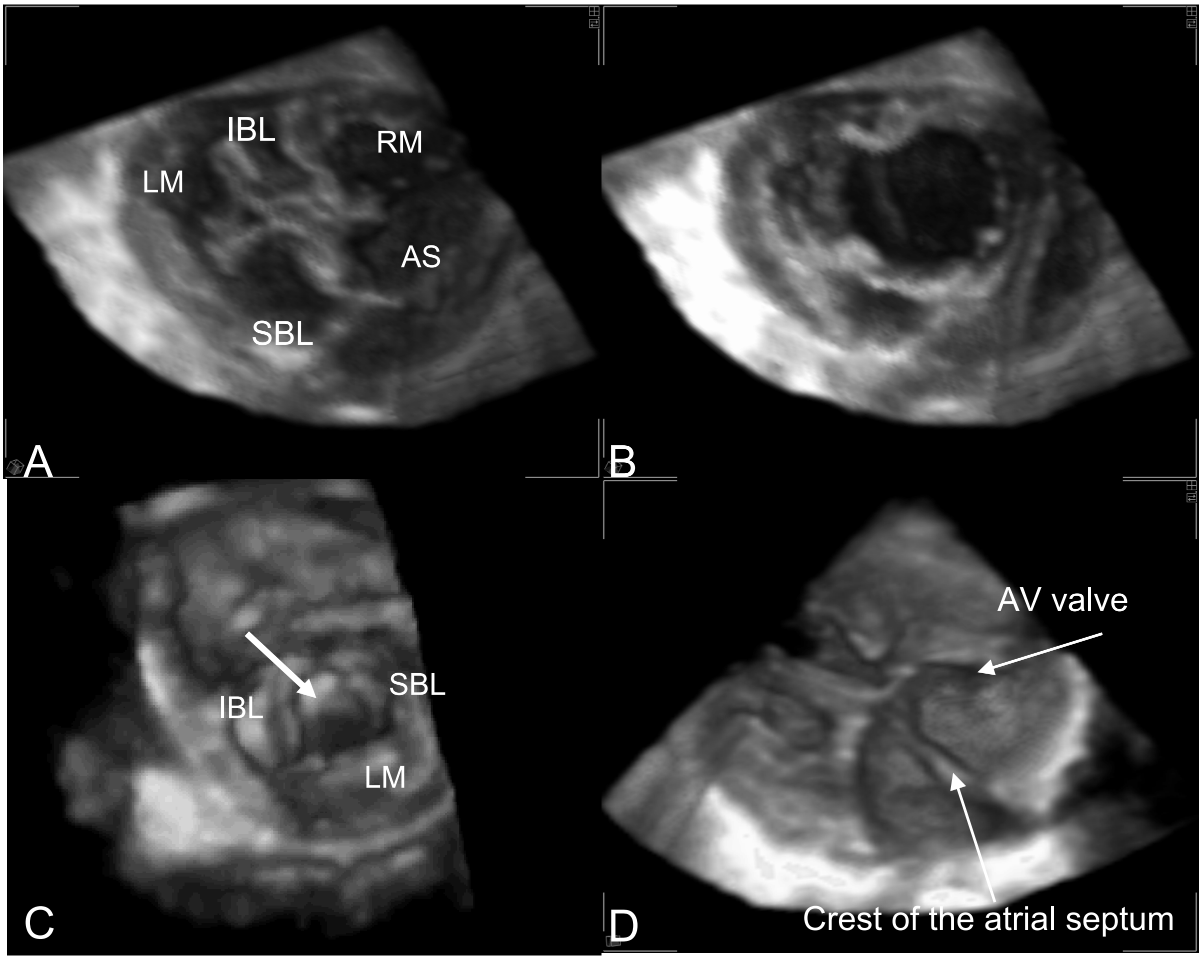
On the 3D reconstruction, 9 patients were assessed with a common AV orifice (complete AVSD) and 10 patients with divided AV orifices (partial AVSD). In all patients the AV valve orifice was correctly identified by RT-3DE compared with the surgical findings (Table 1)(Figure 2).

Table 1. Morphology of the AV valve in patients with an AVSD.

	Divided orifice (n = 10)	Common orifice (n = 9)		
	No	Rastelli classification		
		A	B	C
Inferior bridging leaflet				
1. Directly	6			
2. Membrane	4		1	
3. Multiple chordae		5		3
4. Few chordae			1	

Relation between the morphology of the superior bridging leaflet, classified according to the Rastelli classification, and the morphology of the inferior bridging leaflet as classified by its attachment to the crest of the ventricular septum.

Fig. 2



Real-time 3D echocardiographic display of a complete AVSD (A, B and D) and a partial AVSD (C). (A and B) show the closure and opening of the common AV valve in a patient with a complete AVSD. The 5 AV valve leaflets are clearly identified; SBL = superior bridging leaflet; AS = anterior-superior leaflet; RM = right mural leaflet; IBL = inferior bridging leaflet; LM = left mural leaflet. Figure C shows the commissure (arrow) between the superior and inferior bridging leaflets in a partial AVSD. Figure D shows the crest of the atrial septum and the chordal attachment of the AV valve leaflets to the interventricular septum.

Morphology of the AV valve leaflets

Of the 19 patients, it was possible to identify all AV valve leaflets on the `en face` 3D reconstructions (figure 2). In 18 patients, 5 AV valve leaflets were identified and in one patient only 4 AV valve leaflets. In this particular patient, the common AV valve consisted of a superior bridging leaflet, a right mural leaflet, an inferior bridging leaflet and a left mural leaflet. All these findings were confirmed during surgery.

In the 9 patients with a common AV valve orifice, the superior bridging leaflet was assessed according the Rastelli classification. RT-3DE showed in 6 patients that the superior leaflet had minimal bridging across the crest of the ventricular septum (Rastelli type A). In these hearts the medial papillary muscle supported the commissure between the bridging and the anterosuperior leaflets.

A multitude of additional chordae attached both leaflets. No patients showed intermediate bridging of the superior bridging leaflet (Rastelli type B). In the remaining 3 patients the superior bridging leaflet extended far into the right ventricle (Rastelli type C) (Table 1). In the 10 patients with divided AV orifices, the left AV valve has a commissure between the superior and inferior bridging leaflet The RT-3DE observations of the superior bridging leaflet were 100% accurate compared with the findings during surgery.

In all patients, it was feasible to assess the inferior bridging leaflet according to the attachment of the leaflet to the crest of the septum. The first type of the inferior leaflet was present in 6 patients. The anatomy was such that no interventricular communication was observed. The second type, in which a short membrane is attached to the leaflet, was identified in 5 patients. In one patient with a common orifice, the multiple chordae were fused together to a membrane. There were 7 patients with a type three inferior leaflet. In this situation a moderate to large interventricular communication, through interchordal space, was present. In the fourth type, one patient was identified. In this type, the inferior leaflet was virtually free floating, allowing a large ventricular septal defect. In all patients, the left and right mural leaflets were identified on the 3D reconstructions. The RT-3DE observations were 100% accurate compared with the findings at operation (Table 1).

Atrial and/or ventricular septal defect

Atrial septal defect was identified by RT-3DE in all of the 19 patients. In none of the patients the bridging leaflet attached to the atrial septum. There were 17 patients with an ASD > 15 mm and 2 patients with an ASD smaller than 15 mm (Table 2).

Table 2. Atrial and/or ventricular septal defect in patients with AVSD.

Divided orifice			Common orifice		
Defects	RT-3DE	(surgery)	Defects	RT-3DE	(surgery)
Large ASD, no VSD	10	(9)	Large ASD and VSD	4	(4)
Large ASD and VSD	0	(0)	Large ASD, small VSD	2	(3)
No ASD, large VSD	0	(0)	Large ASD, restrictive VSD	2	(2)
			Small ASD, Large VSD	1	(1)
			Small ASD and VSD	0	(0)

Accuracy of real-time 3D echocardiography in the detection of atrial septal defects (ASD) and ventricular septal defects (VSD) in 19 patients with an AVSD compared with surgical findings (between brackets). An ASD and/or VSD were considered small when the maximal diameter was ≤ 15 mm.

At surgery, a ventricular septal defect was present in 10 patients. In one patient with a divided AV valve orifice, RT-3DE could not depict the VSD (6 mm in diameter) that was located in the membrane attached to the crest of the septum. Maximal diameter of the VSD was 18 ± 6 mm and 19 ± 7 mm, respectively for RT-3DE and surgery.

In this small population (n = 10), there was a good correlation between the maximal diameters of the VSD measured by RT-3DE compared with the surgical findings ($r > 0.9$). In the remaining 9 patients with separate right and left AV valve orifices, the connecting tongue of tissue between the superior and inferior leaflets was closely attached to the ventricular septum, thus completely obliterating the ventricular component of the defect.

Discussion

This study demonstrates that real-time transthoracic 3D echocardiography is highly accurate for the assessment of AVSDs and correctly depicts the AV valve morphology. The ability of RT-3DE to accurately identify these anatomical features in adults and young children, allows a better preoperative planning of the surgical approach and an improved estimation of chances on a successful AV valve repair.

From a surgical viewpoint, one of the most essential anatomic questions about an AVSD is the AV valve morphology and the relation of the bridging leaflets with ventricular septum, both spatially (i.c. Rastelli classification) as well as anatomically (i.c. chordae attachment).[17, 18] The great advantage of RT-3DE is that a single `en face` view can be created in which the entire AV valve apparatus is visualized. With this `en face` 3D reconstruction, the common AV valve orifice or a divided AV valve orifice can be identified with 100% accuracy.

Morphology of AV valve leaflets

Real-time 3D echocardiography makes it possible to visualize all AV valve leaflets simultaneously and allows us to determine the morphology and size of the different leaflets. Exactly, this `en face` view of the AV valve leaflets is impossible to obtain with 2D echocardiography. The morphologic variability of the superior leaflet in hearts with an AVSD and a common orifice, as categorized by Rastelli and associates, and described so often in surgical reports, can now be fully visualized echocardiographically. Type A was seen in 6 patients, type C in 3 and no type B was observed. This study shows that we could correctly identify the variability of the superior bridging leaflet in all patients. This is of great importance, because many patients with a small bridging leaflet and large left mural leaflet have significant regurgitation at the zone of apposition between these leaflets that require surgical repair. [5, 18, 19]

The variability in morphology of the inferior leaflet has been described by several investigators.[16, 20-22] We used this classification because it gives information in terms of surgical implication. From a surgical point of view, it is essential whether or not an interventricular communication is present underneath the leaflet and, if so, whether or not the arrangement of the valve apparatus allows an interventricular patch to be placed underneath without specific precaution.

The inferior bridging leaflet was correctly identified from the RT-3DE reconstructions compared with surgical findings.

Atrial and/or ventricular septal defect

The `en face` 3D reconstruction of the primum ASD was feasible in all patients. The `en face` view of the RV septum, is a unique view of 3D echocardiography. It is impossible to obtain this image with 2D echocardiography, which is restricted by the number of cut planes. The `en face` view of the atrial- and ventricular septum, clearly outlined the component of the septal defect. It also showed both the bridging leaflets and identified the degree of their attachments to the crest of the ventricular septum. In the 9 patients with separate valvular orifices and no ventricular component, it showed close approximation of the bridging leaflets, by direct attachment or membrane, to the crest of the ventricular septum with complete obliteration of the ventricular component. In one patient, the small ventricular septal defect was not identified with RT-3DE. The defect was obliterated by multiple chordae and membrane attached to the crest of the septum. In this membrane, the surgeon found the small ventricular septal defect.

Clinical implications

This study shows that RT-3DE is feasible in not only adult patients, but also in the very small neonates and provides important morphological information. A more detailed preoperative patho-morphological information, appreciating the variability in morphology of the superior and inferior bridging leaflet, might lead to an improved `individualized ` planning of the operative procedure in patients with AVSD.[5, 16] In contrast to the earlier experimental 3-DE equipment, the current generation of real-time 3-DE provides adequate images with a short acquisition time and after a short learning curve an acceptable reconstruction time. The great advantage of RT-3DE is that once a complete 3-DE data set is stored an infinite number of different views can be retrieved anytime after the examination procedure, without the need to re-examine the patient for additional information.

Therefore, real-time 3D echocardiography is a simple and accurate diagnostic tool that can easily be used for adults and children in daily practice.

Limitations

To take advantage of the best spatial resolution settings in a 3D reconstruction, the `region of interest` needs to be located in the center of the ultrasound scan sector. All structures located in the far or near field of the ultrasound sector have an inferior spatial resolution compared with that in the centre of the image.

The real-time 3D mode of the matrix transducer was only used for orientation and choosing the optimal window for full volume acquisition. Due to the limited angle sector (60° x 30°) of the real-time mode the entire region of interest could not be assessed. We acquired a full volume data set for which off-line reconstruction is still necessary and therefore it is arguable whether the used technique is really `real-time` in the strictest sense.
It is a great advantage that RT-3DE is applicable on neonates. However, the inability of a proper breath hold and the need for sedation will limit the clinical application of these types of investigations in young children.

Conclusion

This study demonstrates that real-time 3D echocardiography is highly accurate for the assessment of AVSDs and correctly depicts the AV valve morphology. After a short learning curve, RT-3DE is easily applicable in daily clinical practice. The ability of RT-3DE to accurately identify these anatomical features is most important for the clinical decision-making regarding its pre-operative planning.

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Supplementary data can be found at the site of International Journal of Cardiology

Chapter 6

Real-time transthoracic three-dimensional echocardiography provides additional information of left-sided AV valve morphology after AVSD repair

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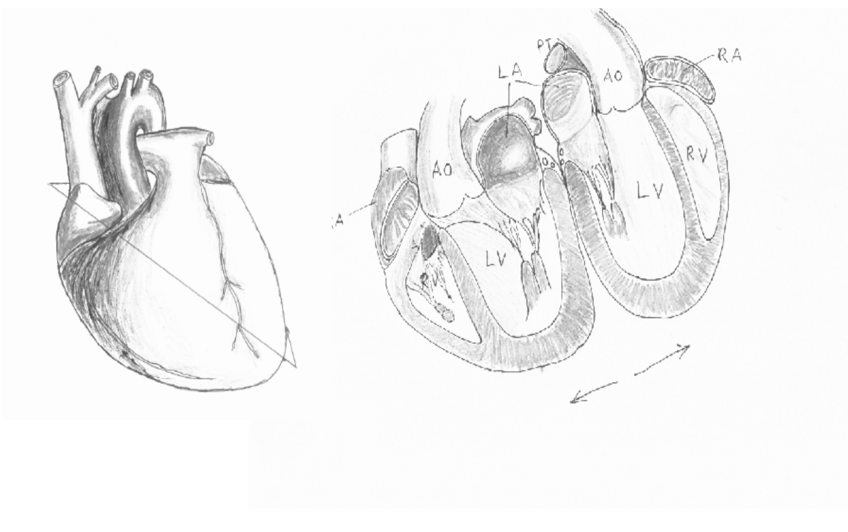
AE van den Bosch
VF van Dijk
JS McGhie
AJJC Bogers
JW Roos-Hesselink
ML Simoons
FJ Meijboom



Abstract

Aims

The purpose of this study was to assess the feasibility of real-time 3D echocardiography (RT-3DE) data acquisition in adult patients after atrioventricular septal defect (AVSD) repair and to evaluate whether RT-3DE has additional value over 2D echocardiography, regarding morphology and function of the left-sided AV valve (LAVV).

Methods

Twenty consecutive patients with surgically corrected partial or complete AVSD were enrolled in this study. The 3DE data sets were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA). Images were reviewed off-line with assistance of TomTec Echoview 5.2 software (TomTec Inc., Munich, Germany) by experienced observers. En face reconstructions, from, respectively, the ventricular and atrial view, were made to evaluate the LAVV morphology and motion.

Results

3DE reconstruction of the LAVV was feasible in 17 of 20 patients (85%). Mean time of 3DE acquisition was 9 ± 6 min. The quality of the 3DE images was optimal in 35%, good in 30%, sufficient in 20% and insufficient in 15%. Identification of the LAVV structures was importantly better facilitated from a ventricular view. Accurate identification of LAVV morphology was possible in all 17 patients (85%). Relationship of the LAVV and the abnormal position of the LVOT was easier to evaluate from the 3DE reconstructions than from 2D echo.

Conclusion

This study demonstrate that RT-3DE is feasible in daily practice and provides new insight into the dynamic morphology of the left-sided AV valve and LVOT anatomy after AVSD repair.

Introduction

Left-sided AV valve (LAVV) regurgitation is the major cause of late morbidity after surgical repair of atrioventricular septal defect (AVSD).[1, 2] Past studies have indicated that up to 40% of the patients ultimately require reoperation.[3-5] Detailed preoperative description of the valve malformation is essential in clinical decision making whether the valve is amenable for repair or that an artificial valve is unavoidable.[6]

Transthoracic and transesophageal two-dimensional (2D) echocardiography combined with color Doppler is the most commonly used non-invasive imaging tool for assessment of the LAVV. Despite its acceptable diagnostic accuracy, the information on LAVV morphology and mechanism of regurgitation remains incomplete. Recently, real-time transthoracic three-dimensional echocardiography has become available, permitting `en face` visualization of the LAVV and its relationship with surrounding structures.[7]

The purpose of this study was to assess the feasibility of real-time 3D echocardiography (RT-3DE) data acquisition, and to evaluate whether RT-3DE has additional value over 2D echocardiography, regarding morphology and function of the left-sided AV valve in adult patients after AVSD repair.

Methods

Patients

A cohort of 20 consecutive patients with surgically corrected partial (n = 14) or complete (n = 6) AVSD, seen in the outpatient clinic for adult congenital heart disease, underwent a 3D echocardiographic study after their scheduled routine 2D echocardiography. Partial AVSD, formerly known “ostium primum atrial septal defect”, was defined as shunting only at atrial level with separate valve orifices to the left and right ventricle. An AVSD was defined as complete in care of one large common valve guarding one common orifice. Mean age of the patients was 32 ± 14 years. Demographic data of the study population and details of the clinical presentation are summarized in table 1. All patients were in sinus rhythm. Informed consent was obtained from each patient after they were given a full explanation of the procedure.

Real-time 3D echocardiography

The real-time 3DE images were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. The transducer is a X4 matrix array with almost 3,000 active elements, connected to the ultrasound machine. In order to encompass the entire region of interest into the 3DE data set, a full volume scan was acquired.

For this purpose, a pyramidal volume of 90° x 85° is scanned, which is divided into four conical subvolumes of approximately 90° x 21° each. The acquisition was performed with ECG gating and in end-expiratory breath-hold lasting 6 to 8 seconds (depending on the heart rate). Breath hold is necessary to minimize the movement of the heart within the chest. 3D data sets were acquired from standard parasternal, apical and foreshortened windows. The digital data were stored on CD-ROM and transferred to a separate workstation for off-line data analysis.

Table 1. General data (presentation and morphologic features)

Number of Patients		20
Age (years)		32 ± 14
Male (%)		12 (60%)
Associated Syndrome or feature:		
- Down syndrome		1
- Noonan syndrome		1
Age at primary operation (median)		9.5 (range 0 to 62 years)
Type of LAVV repair at primary operation:		
- Direct suture of the commissure		18
- No LAVV repair		2
Reoperation for LAVV repair		8 (40%)
Residual lesions on 2-D color Doppler echocardiography:		
- LAVV regurgitation	Mild	4 (20%)
	Moderate	8 (40%)
	Severe	8 (40%)
- RAVV regurgitation	Mild	15 (40%)
	Moderate	3 (15%)
	Severe	2 (10%)

LAVV = left-sided atrioventricular valve, SC = direct suture of the cleft, RAVV = right-sided atrioventricular valve.

Image analysis

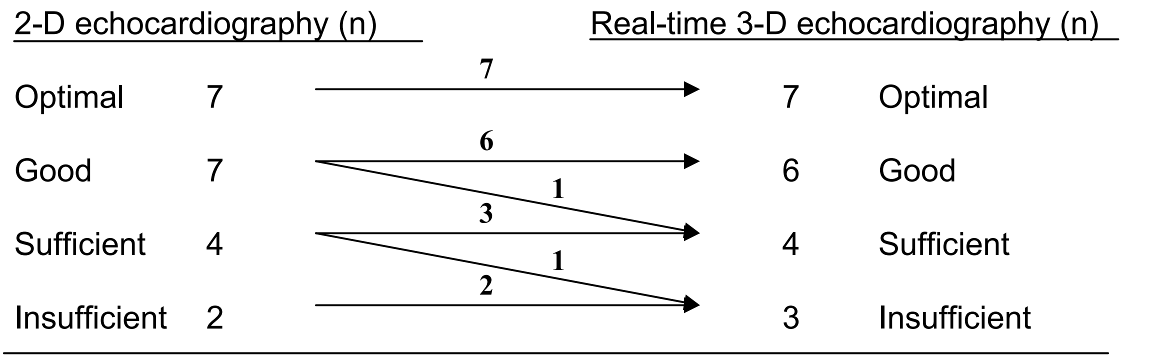
The 3DE data sets were analyzed off-line with assistance of TomTec Echoview 5.2 software (TomTec Inc., Munich, Germany). In each patient, several 3D reconstructions were carried out. For the analysis of the LAVV, two opposite views were reconstructed: 1) a view from the left atrium towards the atrioventricular junction, allowing a “surgical view” of the LAVV, and 2) a view from the left ventricular apex toward the LAVV. The 3D relationship of the LAVV and the surrounding structures was also assessed.

The quality of images of the 2D and RT-3DE images were assessed. The RT-3DE data set was judged on the basis of the absence of artefacts throughout the cardiac cycle and the possibility of correctly evaluating the reconstructed image was graded as: optimal (excellent quality without artefacts), good (sufficient or good quality without artefacts), sufficient (sufficient or good quality with artefacts), and insufficient (insufficient quality of cardiac imaging).

Results

Three-dimensional reconstruction of the LAVV was feasible in 17 of the 20 patients (85%). Two patients had poor acoustic windows due to severe obesity and one patient had persistent respiratory artefacts that precluded 3D rendering. Mean time necessary for 3D acquisition was 9 ± 6 min. The quality of the 3D images was optimal in 7 patients, good in 6 patients, sufficient in 4 patients and insufficient in 3 patients. The 3D images quality was associated with the 2D image quality as shown in figure 1. Analysis time of the 3D data sets varied considerably, depending on the complexity of the AVSD and our learning curve, and ranged from 15 minutes to 60 minutes.

Fig. 1 Quality of image from 2-D echocardiography compared with real-time 3-echocardiography



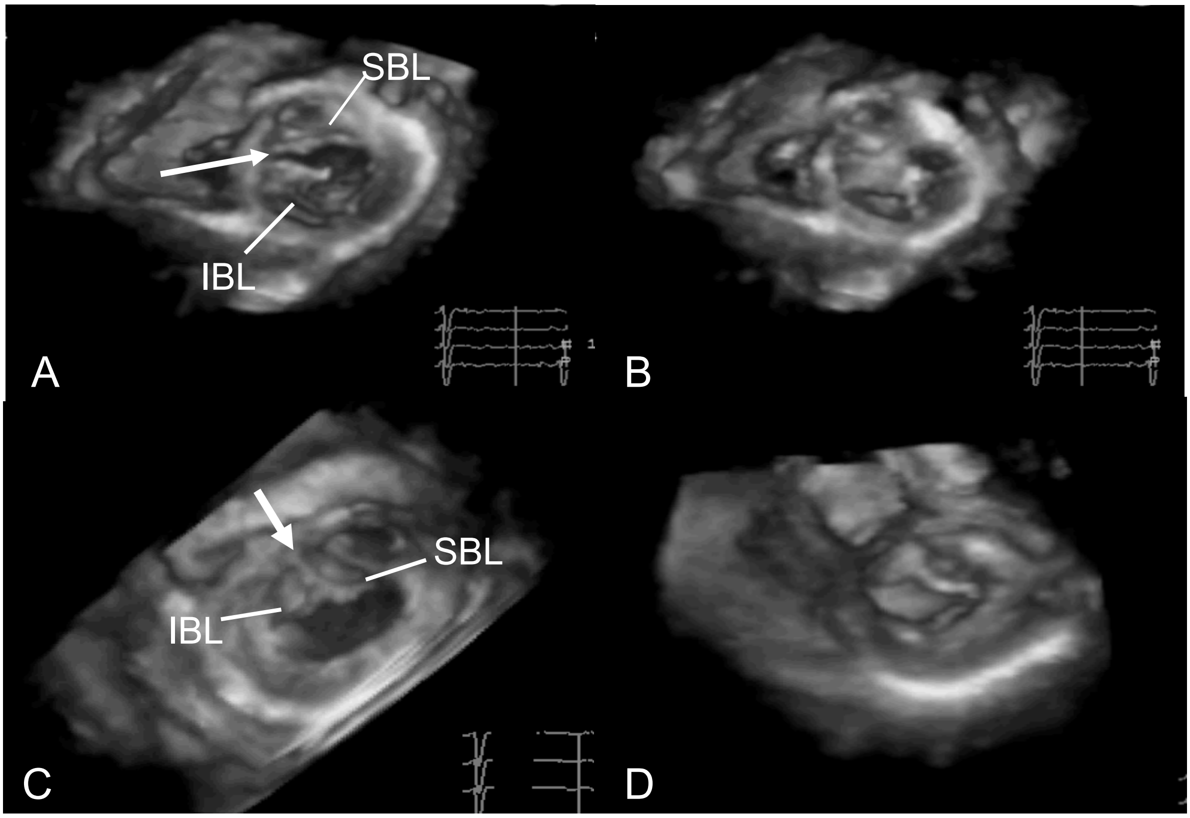
Left sided AV valve morphology

Four-chamber view reconstruction from the 3DE data sets was feasible in all 17 patients with sufficient image quality. The cut planes reconstructed from the 3DE data sets that visualized the LAVV \`en face\` from atrial and ventricular view could easily be reconstructed. The cut planes that visualized the LAVV from a ventricular view were most useful for the comprehensive assessment of dynamic valve morphology and motion, and the mechanism of the valve regurgitation. Figures 2a/b show the LAVV seen from a ventricular view. The zone of apposition (arrow in figure 2a) between the superior and inferior bridging leaflets is clearly identifiable.

Figure 2c shows the LAVV from a ventricular view of a patient who had a closure of the zone of apposition in the past. The white line (arrow in figure 2c) indicates the reconstructed line of the two bridging leaflets. Color Doppler reveals only a small regurgitation jet, originating at the site with the lateral left leaflet. This corresponds with the good closure of the LAVV in systole (figure 2d).

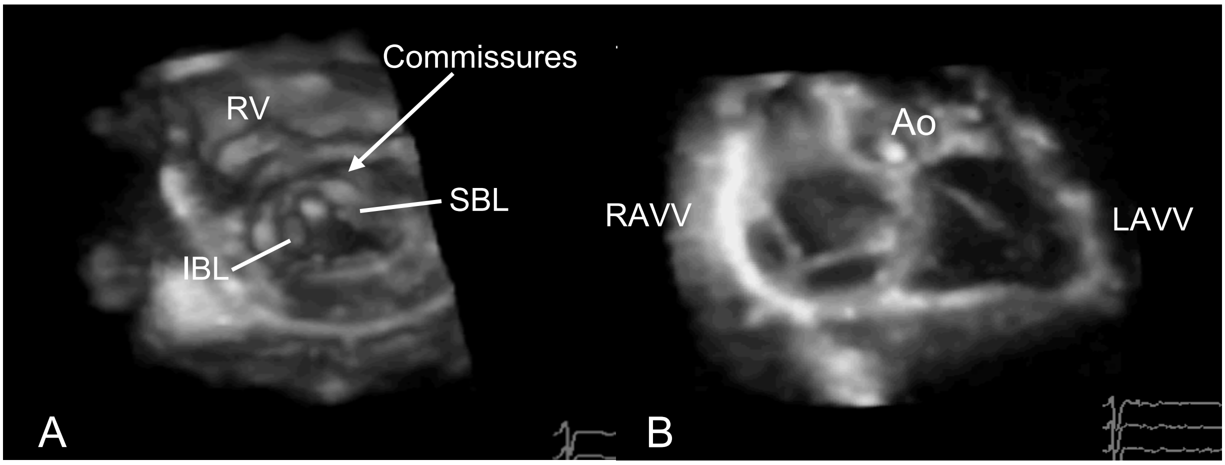
Figures 3a and 3b show the LAVV, seen from respectively the LV and LA. The ventricular view gives the most, and also clearest information of the LAVV morphology. When looking from a LA perspective, the AV valve anatomy is not always optimal, but the relation with the right-sided AV valve and aortic valve is better demonstrated. Especially, the unwedged position of the aorta between the atrioventricular valves is clearly visualized (14/20 patients).
The relation of the AV valves with the left ventricular outflow tract (LVOT) is demonstrated in figure 4. The LVOT makes a 90° corner with AV junction. The three successive images show the LAVV and LVOT from 3 different directions. In the last figure (4c), we look straight into the LVOT with the aortic valve lying behind.

Fig 2



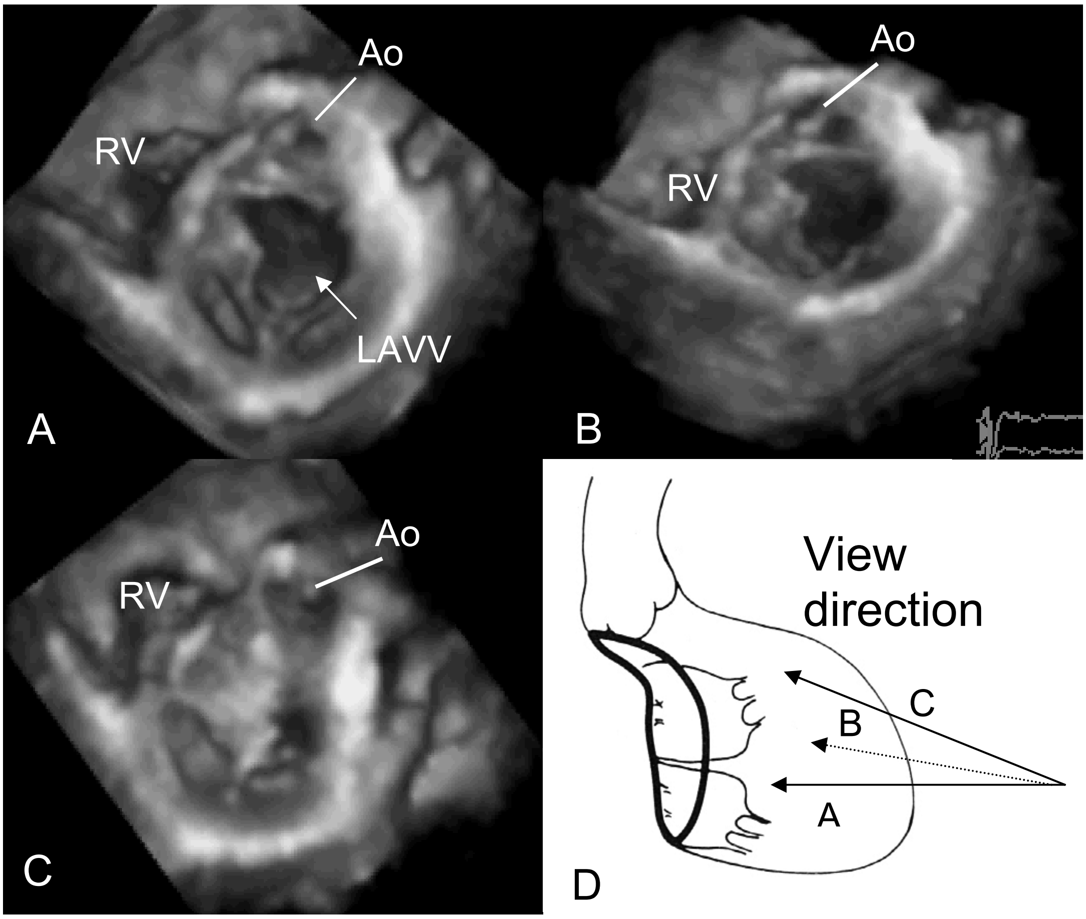
A and B show the LAVV in diastolic and systolic frame, seen from a ventricular view. The two bridging leaflets with the zone of apposition are clearly identifiable (arrow in A). C and D show the LAVV in diastolic and systolic frame from a patient who had a closure of the zone of apposition in the past. The white line over the AMVL indicates the closing line of the two bridging leaflets (arrow in C). SBL = Superior bridging leaflet, IBL = Inferior bridging leaflet.

Fig 3



A and B show the LAVV seen from respectively LV and LA. Note that the view from the LV gives the most information of the valve morphology. Looking from a LA view, the unwedged position of the aorta is visible. SBL = Superior bridging leaflet, IBL = Inferior bridging leaflet.

Fig 4



A, B and C show three successive images viewing the LAVV and LVOT from different directions as shown in the diagram D. This demonstrates the 90° corner between LAVV and the LVOT. In the last figure (C), we look straight into the LVOT with the aortic valve lying behind.

Discussion

This study demonstrates that real-time transthoracic 3D echocardiography is feasible and provides a better understanding of the dynamic morphology of LAVV and its relation with the surrounding structures in patients after AVSD repair compared to 2D echocardiography. Until now, the clinical usefulness of 3D echocardiography was hampered by long acquisition time and even longer off-line reconstruction of the 3D data set. With the current technique of RT-3DE, acquisition time is very short compared with 2D transthoracic studies. In our laboratory, the mean time of 2D echocardiographic studies for congenital heart disease is 25 minutes.

The quality of the 3D images was sufficient in 85%, but strongly related to the 2D image quality. If there is poor 2D image quality, RT-3DE image quality will certainly be poor or worse than the 2D quality. We found that `en face` reconstructions of the LAVV from a LA and a LV view were easy to perform in all patients with sufficient image quality. Clear anatomic reconstruction of the LAVV by selection of the optimum 2D cut plane for 3D reconstruction are experience related and require a learning curve.[8, 9] After the learning curve that is needed to find these new cut planes and how to interpret them, the extra information leads to a more complete delineation of the LAVV abnormality.

Additional value of 3D echocardiography

The reconstructions made from the 3D data sets were most useful in displaying the morphology of the AV valve(s) and closely resembled the actual anatomy of the heart. With the 3D reconstructions, we can display the AV valves as the anatomic diagrams of the AV valve malformations. The variability in morphology of the superior and inferior bridging leaflet that can be visualized 3D, together with the hemodynamic information of the 2D echocardiography leads to a better understanding of the complex anatomy in our patient population. Moreover, the 3D technique allows creating cut planes that are not obtainable with the conventional 2D transthoracic and transesophageal echocardiography. Now, we can evaluate the LAVV from numerous different angles. This provides completely new echo information that has not been available before.

We anticipated that the standard view for assessing the LAVV with this technique would be the LA view, as the surgeon sees it. However, in our experience the LA view is not always optimal. The principal reason for this was the presence of artefacts caused by poor far field resolution or reverberations in the left atrium from surrounding structures. In all but three patients we found that the LV view provided all the information required for clarification of LAVV morphology and function (figures 1 and 2).

With the 3D reconstructions, it was possible to assess the relation of the LAVV with the surrounding structures. This additional clinical value was demonstrated for the abnormal position of the aorta and narrowing LVOT. On 2D echocardiography, the characteristic `gooseneck` deformity or elongation of the LVOT is seen.[10]

Real-time 3D echocardiography gives more information about the relation of the AV valves with the LVOT and the possible LVOT obstruction as shown in figure 3. New reconstructions obtained using this technique of 3D, gives more precise information of the LVOT abnormality. This is essential for truly appreciating the postoperative result. Clinical decision-making will be substantially improved by comprehensive understanding of the interplay between valve morphology and function.

Limitations

Although, RT-3DE has great potential, it is still limited by less resolution when compared with 2D echocardiography. An additional limitation of the RT-3DE includes the limited size of the pyramidal volume of the data set and irregular heart rate for full volume 3D acquisition.

Conclusion

This study demonstrates that real-time 3-D echocardiography is feasible in daily practice and provides new insight into the dynamic morphology of the left-sided AV valve and LVOT anatomy after AVSD repair. We believe that this simple and reproducible method of analysis of the 3D dataset, combined with standard 2D assessment, allows better understanding of the interplay between left-sided AV valve morphology and function.

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Supplementary data can be found at the site of International Journal of Cardiology

Chapter 7

Feasibility and accuracy of real-time three-dimensional echocardiographic assessment of ventricular septal defects

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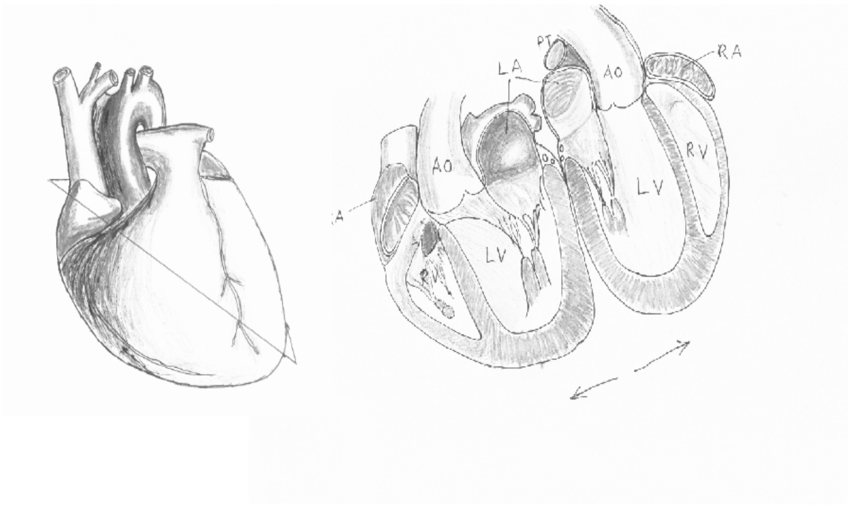
AE van den Bosch
DJ Ten Harkel
JS McGhie
JW Roos-Hesselink
ML Simoons
AJJC Bogers
FJ Meijboom



Summary

The aim of this study was to evaluate feasibility, accuracy and clinical applicability of real-time transthoracic 3D echocardiography (RT-3DE) in the determination of the position, size and shape of VSDs.

Thirty-four patients (age 2 month – 46 years), who were scheduled for surgical closure of a VSD, were enrolled in the study. VSD localization, shape and dimensions were assessed and compared with measurements performed by the surgeon.

Acquisition of RT-3DE datasets was feasible in 30/34 (88%) patients. Duration of 3D data acquisition was 6 ± 2 min. Reconstruction time was 23 ± 16 minutes. Localization and number of the VSD were determined correctly by RT-3DE in all patients. There was a good correlation for VSD measurements between RT-3DE and surgery (r = 0.95).

Real-time 3D echocardiography allows accurate determination of VSD size, shape and location. The short acquisition time and acceptable reconstruction time value this technique as clinical applicable.

Introduction

Echocardiographic assessment of a ventricular septal defect (VSD) is not merely describing the presence of a hole in the ventricular septum. The ideal evaluation should comprise a description of the exact localization of the defect, its size and relation to essential intracardiac landmarks, such as the tricuspid and aortic valve.[1-3]
Transthoracic two-dimensional echocardiography (2-DE) with color Doppler has been the standard method for diagnosing VSDs, and is essential for the clinical decision making regarding its management.[4, 5] However, the information that 2-DE can provide on the anatomic details is limited, mainly because the number of cutting planes of the heart is restricted.[5-8] Therefore, it is difficult to obtain a true spatial appreciation of a VSD. Theoretically, three-dimensional echocardiography (3-DE) should offer direct visualization of the VSD and its relation with the surrounding structures. So far, 3-DE has been hampered by the fact that no real-time technique was available. The very long acquisition and even longer off-line reconstruction time made the technique not applicable in clinical practice.[9] Moreover, the poor spatial resolution of 3-DE when compared with 2-DE, in combination with small hearts and high heart rates, inherent to the clinical presentation of most congenital cardiac defects in infancy and childhood, posed an insurmountable problem. The currently available real-time 3-D echocardiography (RT-3DE) using matrix transducer technology might overcome these problems.[10, 11]
The aim of this study was to evaluate the feasibility and accuracy of RT-3DE determining the position, size and shape of VSDs, compared with measurements and descriptions done by the surgeon during the surgical procedure and to assess whether RT-3DE is applicable in clinical practice.

Methods

Study population

Thirty-four patients, who were scheduled for surgical closure of a VSD at our institution, were enrolled in the study. Associated lesions included pulmonary stenosis in 13 patients (of which 9 patients had a tetralogy of Fallot) and atrial septal defect in 5 of the patients. Of the 34 patients, 26 patients were infants (age < 1 year), 6 patients were children (6.6 ± 5.5 years) and 2 were adults (age 25 and 46 years). All patients were in sinus rhythm.

Real-time transthoracic 3D echocardiography

The real-time 3D images were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. RT-3DE acquisition was done with ECG gating.

In all patients above the age of 4 years an end-expiratory breath-hold, lasting 6 to 8 seconds (depending on the heart rate), was performed for the creation of a full volume data set. The 3D data acquisition was performed within two weeks before surgery, during an outpatient clinic consultation. The 3D data acquisition in the infants and children under the age of 4 years took place immediately before surgery, when they were under general anesthesia. During data acquisition, no breath hold or ventilation arrest was performed. The patients were on conventional mechanical ventilation (tidal volume 8 ml/kg body weight). Since the data were acquired during the time that the child was prepared for surgery, there was no prolongation of general anesthesia time. The real-time 3D mode was used for orientation and to locate the ventricular septal defect in the center of the data set. The digital data were stored on CD-ROM and transferred to a stand-alone TomTec workstation (TomTec, Munich, Germany) for off-line data analysis, using TomTec Echoview 5.2® software.

Two-dimensional echocardiographic study was performed with the Philips Sonos 5500 and 7500 echo system (Philips Medical Systems, Andover, MA, USA) during a routinely outpatients clinic consultation.

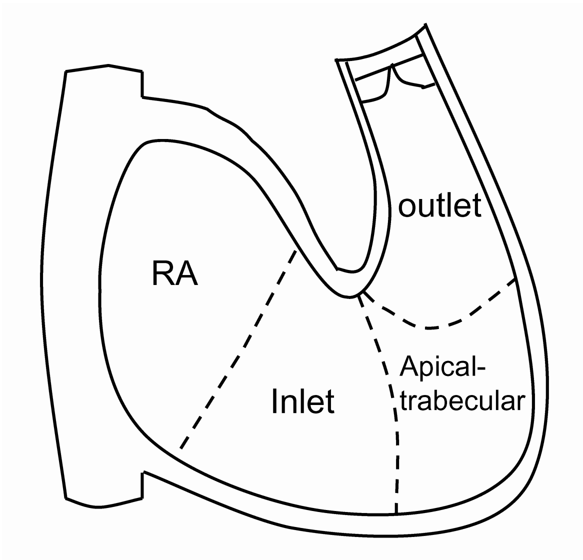
Image processing and analysis

In the 3D data set, a cut plane was placed through the left ventricle from apex to base, parallel to the ventricular septum, creating an `en face` view of the LV septal surface. The ventricular septum was viewed in a similar way from the right ventricle (RV), placing a cut plane through the RV from apex to base. Two independent experienced observers (AvdB and JM), who were (apart from the diagnosis VSD) blinded to the results of the routine 2D echo study and the surgical report, analyzed all 3D data sets.

The 2D echocardiographic images were viewed retrospectively (AvdB and DH). The position and maximal diameter of the VSD were assessed and compared with surgical and RT-3DE findings.

On the 3D images, the position and shape of the VSD and the observations relating to the surrounding structures were assessed. The classification of Soto and Anderson was used for the description of the position of the VSD (figure 1).[12, 13]

Fig 1



Diagrammatic representation of the right ventricle divided into three components: Inlet, apical-trabecular and outlet.

The dimensions of the VSD on the 3D images – measured in two directions – were assessed in end-diastole and end-systole (figure 5b). Measurements were obtained from `en face` LV and `en face` RV view. The relative changes in VSD area throughout the cardiac cycle are presented as end-systole area divided by end-diastole VSD area. Three-dimensional acquisition and reconstruction times were recorded in each patient. Reconstruction time was defined as the time used to create the optimal 3D cut planes in the 3D full volume data set and the complete assessment of VSD morphology, including measurements.

Surgical procedure and assessment of morphology

Surgical repair was performed, using cardiopulmonary bypass, through a right atriotomy. VSD measurements were made, in a flaccid heart after cold cardioplegia (St. Thomas solution) from a RV view after transtricuspid exposure of the defect. The surgeon, who was blinded for the 3D data, described and measured the VSD. Using the surgical description as the gold standard, the accuracy of each type of echo assessment was determined.

Statistical analysis

All values were expressed as means ± standard deviation (SD). The relations between diameters derived from RT-3DE and surgical procedure, and interobserver variability were analyzed by linear regression and Bland-Altman analysis.[14] For the latter, the 3D VSD measurements from the two observers were averaged. To determine whether the difference in the values between RT-3DE and surgical measurements was statistically significant, a paired t-test was performed.

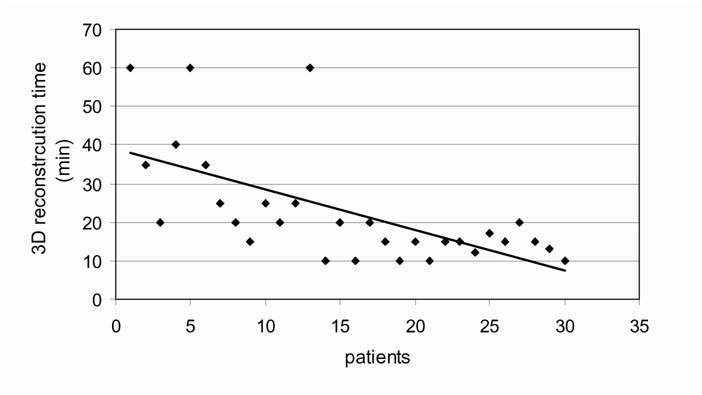
Limit of agreement is expressed as 2 SDs of the difference of the RT-3DE and surgery. A p-value less than .05 was considered significant.

Results

Acquisition of RT-3DE datasets was feasible in 30 of the 34 (88%) patients. Two patients (age 2.5 and 15 years) had poor acoustic windows and two patients (age 2 months and 1 year) had persistent respiratory artefacts that precluded adequate 3D rendering. The mean heart rate was 119 ± 14 bpm for infants and children, and 65 and 70 bpm for the adult patients during RT-3DE examination. The weight of the 26 infants (age < 1 year) was 5.8 ± 2.9 kg.

The time of 3D data acquisition was 6 ± 2 min, for the infants the acquisition time was shorter (mean 3 ± 1.5 min). The mean reconstruction time was 23 ± 14 minutes, but becomes significantly shorter during the study. The learning curve is demonstrated in figure 2.

Fig 2



Learning curve of the 3D reconstruction time of the 30 consecutive patients.

In all infants and children a subcostal approach was the best approach to get an unobstructed acoustic window to create a 3D data set. For our adult patients, a foreshortened or parasternal approach was used to create a full volume 3D data set.

Ventricular septal defect localization

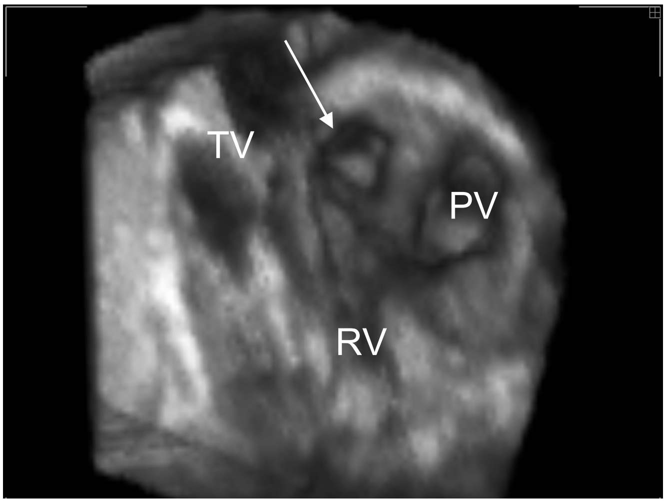
In the 30 patients, 30 VSDs were detected with RT-3DE: 29 perimembraneus VSD, and one doubly committed subarterial VSD. In 11 patients the perimembranous VSD extended into the inlet septum, in 16 patients into the outlet septum and in 2 patients the VSD extended both into the inlet and outlet septum. In our study population, no muscular VSD was encountered. There was a 100% sensitivity and specificity regarding localization and number of the VSD determined by RT-3DE compared to surgical findings.

In 4 patients the localization of the VSD determined on 2-D echocardiography was not assessed correctly. In these patients the VSD extended to the inlet part of the interventricular septum, which was not visible and could not be retrieved from the stored 2D data set.

Ventricular septal defect viewed from the right ventricle

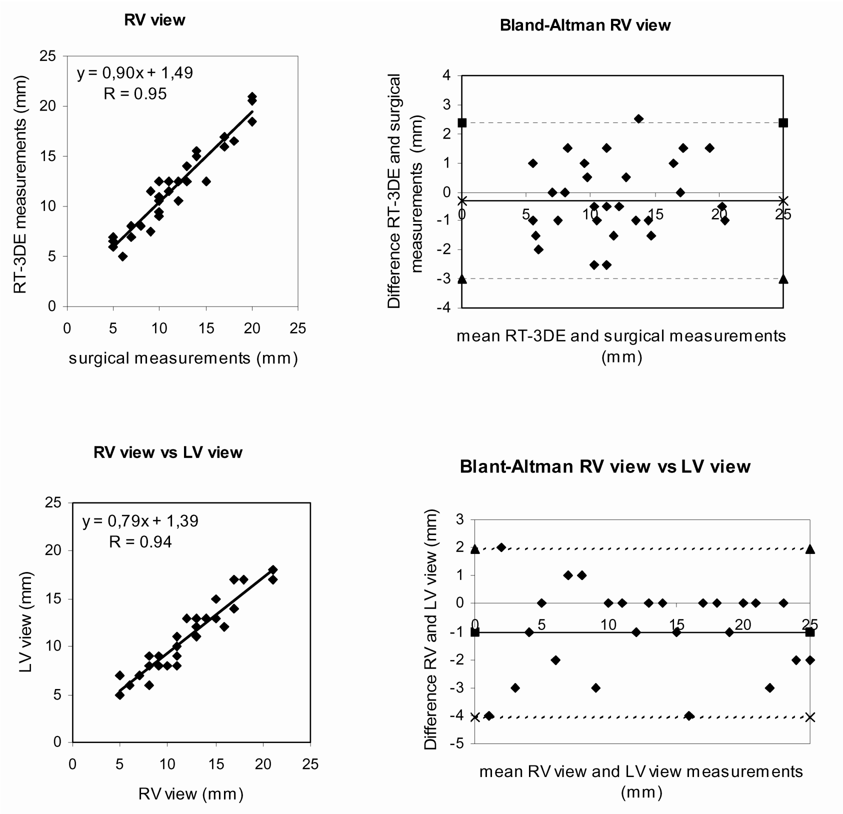
In the 30 patients, it was possible to reconstruct a right ventricular `en face` view of the VSD. The free wall of the RV was removed from 3D data set to visualize the right side of the ventricular septum (figure 3). In 10 patients the VSD was completely or partly covered by the anterior-superior or septal leaflet of the tricuspid valve. By digitally cutting the tricuspid valve from the 3D data set, the entire VSD was visualized. Maximum VSD diameter was 11.9 ± 4.2 mm (range 5 to 21 mm) and 11.6 ± 4.5 mm (range 5 to 20 mm), for respectively RT-3DE and surgery (P = NS). Minimum VSD diameter was 7.8 ± 3.6 mm (range 2 to 18 mm) and 9.6 ± 4.5 (range 3 to 20), for respectively RT-3DE and surgery (P = 0.04). The correlation between RT-3DE and surgery for the maximum VSD diameter was r = 0.95 (y = 0.90x + 1.49; SEE = 1.3 mm) with a mean difference of –0.3 ± 2.7 mm (figure 4). Correlation observed for the minimum VSD diameter between RT-3DE and surgery was r = 0.66. There was a weak correlation between the maximal 2D and the maximal 3D diameter of the VSD (r = 0.57), and between maximal 2D diameter and surgical findings (r = 0.66).

Fig 3



Real-time 3D echocardiographic display of perimembranous VSD (arrow), viewed from right ventricular surface of the interventricular septum. A part of the tricuspid valve is digitally cut away from the 3D data set to disclose the entire VSD. RV: right ventricle; TV: tricuspid valve; PV: pulmonary valve.

Fig 4



Linear regression plots and Bland-Altman plots for maximal diameter of the VSD from `en face` RV as assessed with real-time three-dimensional echocardiography (RT-3DE) compared with surgical measurements as the reference standard (two upper panels). Linear regression plots and Bland-Altman plots for the `en face` RV view and LV view for VSD measurements (two lower panels).

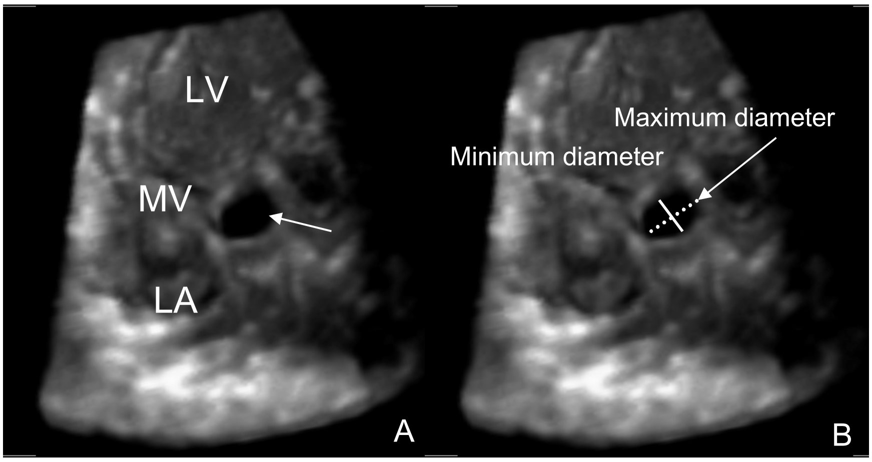
Ventricular septal defect viewed from the left ventricle

In all RT-3DE studies, an optimal 3D LV `en face` view was reconstructed and the position, shape and size of the defect could be assessed (figure 5). Linear regression and agreement plots for maximal VSD diameter measurements from a LV view and a RV view are shown in figure 4. The limits of agreement analysis demonstrated a mean difference of –1.0 ± 3.0 mm.

Relative change of VSD area during the cardiac cycle

The end-diastolic area of the VSD ranged from 30 to 590 mm^2 and the end-systolic area from 10 to 360 mm^2. The mean relative area change, as a measure of VSD dynamics, was 0.53 ± 0.12 (range 0.33 – 0.80) and varied markedly between the individual patients.

Fig 5

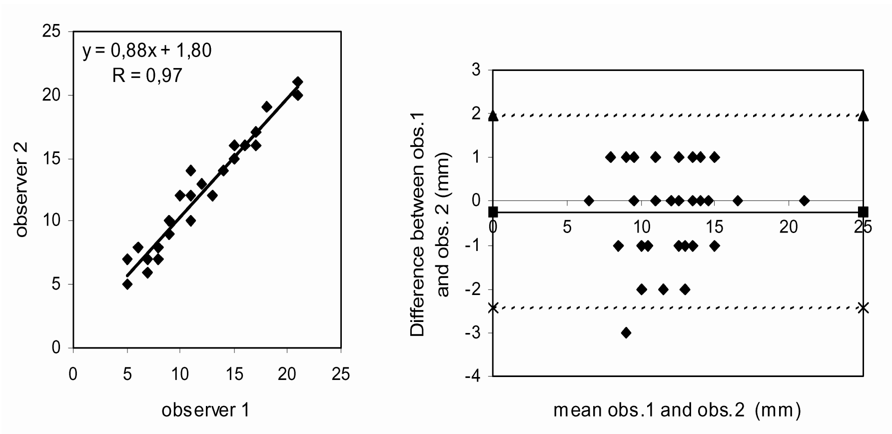


Real-time 3D echocardiographic display of a typical perimembranous ventricular septal defect (arrow 5a), viewed from left ventricular surface of the interventricular septum. Figure 5b shows the minimum and maximum diameter of the VSD when the VSD has the maximum area in the cardiac cycle. LV: left ventricle; LA: left atrium; MV: mitral valve.

Interobserver variability

The measurements performed by the two observers did not differ significantly. The results for interobserver variability showed a good correlation for the VSD measurements (r = 0.97; y = 0.88x + 1.80; SEE = 1.1 mm) with a mean difference of –0.2 ± 2.2 mm (figure 6).

Fig.6



Interobserver variability for VSD measurements obtained with real-time 3D echocardiography

Discussion

This study demonstrates that real-time 3D echocardiography of VSDs for quantitative analysis is feasible, and accurately depicts the position, dimension and shape of various types of VSDs.

Two-dimensional echocardiography and Doppler color flow mapping have proven to be valuable for diagnosis and monitoring of VSDs.[15, 16] However, the limited ability of 2D images to visualize the entire shape and contours of the VSD prohibits an accurate quantification as shown in our results[7, 8] Real-time 3D echocardiographic imaging provides an undisputed presentation of defect's morphology and spatial orientation.

A great advantage of 3D echocardiography is the possibility to create an `en face` view of the VSD from the RV. This unique view allows us to identify the specific features from the RV and to differentiate the anatomy of the various defects. Exactly this important RV `en face` view of the interventricular septum is impossible to obtain with 2D echocardiography. Since a VSD is surgically closed through a right atrial (or RV) approach, surgeons make comparative measurements from the right side.[17] To simulate that methodology, we created RV cut planes through the 3D dataset. However, as in a real `surgeon's view`, VSDs are often hidden or difficult to visualize from a RV view. Especially the perimembranous VSDs were frequently obscured by overlying tissue of the tricuspid valve.[18] In this study, we demonstrate that it is possible to disclose the entire VSD by digitally cutting away a part of the tricuspid valve from the 3D data set.[19] Therefore, it was possible to provide a clear assessment of the VSD to the cardiac surgeon about the dimension, shape and relation of the defect to various RV septal structures. An excellent correlation was observed between the maximal VSD diameter measurements obtained by RT-3DE looking from a RV view compared to the surgical findings. The morphological information from RT-3DE can be used on top of the hemodynamic measurements derived from 2D echocardiography.

An important finding of our study is that a VSD increases and decreases considerable in size during the cardiac cycle (mean area change 0.53 ± 0.12). Comparing the dynamic area changes of the VSD with the area changes of atrial septal defects described in the literature, the changes of the VSD area are less striking but still statistically significantly.[20-22] Although, this finding needs further investigation and validation, its clinical relevance might lie in the recently introduced catheter-based techniques for device-closure of VSDs. This requires a specific patient selection, based on a minimum weight of the patient (depending on the size of the recurrently available delivery systems), exact position of the VSD, its maximal area and relation to the surrounding cardiac structures. RT-3DE with the ability of unique 3D displays, is probably of great use in the selection of eligible patients.[23-25]

The minimum diameter of the VSD in end-diastole by RT-3DE is significantly smaller than the surgically measured minimum diameter.

Although we cannot substantiate this, we assume that this is due to the fact that VSD measurements on the 3D reconstructions were performed on a beating heart with normal muscle tone, while the VSD measurements by the surgeon, who were performed in a flaccid heart in diastolic arrest.

In contrast to the earlier experimental 3-DE equipment, the current generation of real-time 3-DE provides adequate images with a short acquisition time and acceptable reconstruction time. After a short learning curve (figure 2), the time for a complete RT-3DE study is comparable with that of a 2-DE study. Another great advantage of RT-3DE is that once a complete 3-DE data set is stored an infinite number of different views can be retrieved anytime after the examination procedure, without the need to re-examine the patient after he/she has left the laboratory.

Limitations

Twelve per cent of the real-time transthoracic 3-D echocardiographic studies were not suitable for analysis because of motion artefacts or poor spatial resolution. Further improvement of the image resolution is required, particularly for neonates and small children, where near field resolution is of utmost importance. The real-time 3D mode of the matrix transducer was only used for orientation and choosing the optimal window for full volume acquisition. Due to the limited angle sector (60° x 30°) of the real-time mode, the entire region of interest could not be assessed. Therefore, we acquired a full volume data set and off-line reconstruction is still necessary.

All children under age of 4 years, including infants and neonates, were studied under general anesthesia. The outcomes of this study cannot be extrapolated to the use of RT-3DE in clinical practice for the study of children without anesthesia or sedation.

Conclusion

This study shows that real-time 3D echocardiography is not only feasible for quantitative assessment of VSDs with accurate determination of VSD size and localization, but that it is also applicable in daily practice because of the short acquisition and reconstruction time. The use of RT-3DE gives a better understanding of the exact anatomy and size of the defect, which may lead to a further optimalization of the planning of surgical or catheter-interventional procedures in patients with a VSD.

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Chapter 8

Real-Time transthoracic three-dimensional echocardiographic assessment of left ventricular volume and ejection fraction in congenital heart disease

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AE van den Bosch

D Robbers-Visser

BJ Krenning

MM Voormolen

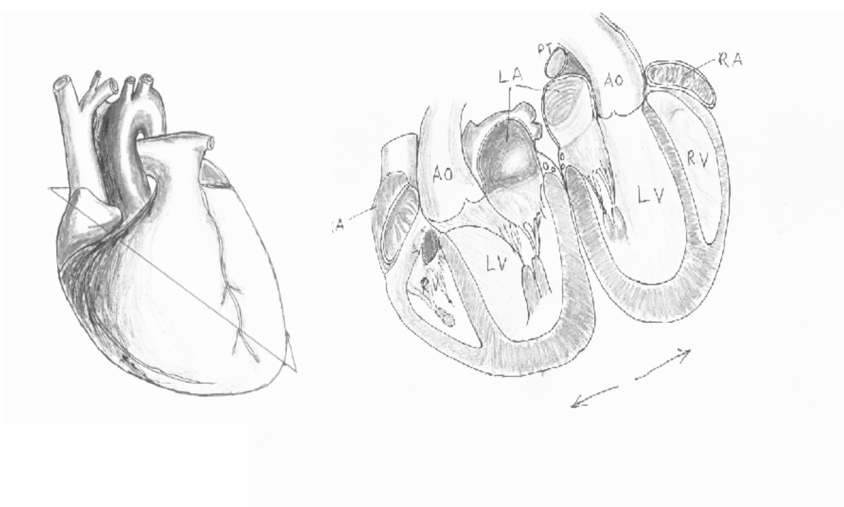
JS McGhie

WA Helbing

JW Roos-Hesselink

ML Simoons

FJ Meijboom



Summary

The purpose of this study was to assess: 1) the feasibility of real-time 3D echocardiography (RT-3DE) data acquisition, and 2) volumes and function of the abnormal left ventricle (LV) in adult patients with congenital heart disease (CHD), compared with MRI data. Thirty-two patients (59% male) with CHD were evaluated on the same day by MRI and RT-3DE. Acquisition of RT-3DE data sets was feasible in 29 of the 32 (91%) patients. The time of 3D data acquisition was 4 ± 2 min and LV analysis 17 ± 5 minutes per patient for manual border tracing. A good correlation was observed between RT-3DE with manual border detection and MRI for LV-EDV (r = 0.97), LV-ESV (r = 0.98) and LV-EF (r = 0.94).

RT-3DE is feasible for volumetric analysis of the abnormal left ventricle allowing accurate determination of LV volume and EF compared with MRI in adult patients with CHD.

Introduction

Reliable determination of left ventricular (LV) volume and function is important for prognosis, guiding therapy and follow-up in patients with congenital heart disease.[1] Currently, magnetic resonance imaging (MRI) is considered to be the gold standard for quantification of LV volumes and mass.[2-4] However, this technique is costly, not widely available and not applicable in patients with arrhythmias and pacemakers, who constitute an increasing proportion of the adult patients with congenital heart disease. Therefore, other quantitative methods have been proposed. In patients with congenital heart disease two-dimensional echocardiography assessment of LV function is limited because of the abnormally shaped left ventricle.[5-10] Real-time three-dimensional echocardiography assessment of the LV function has proven to be highly accurate when compared with MRI in patients with structurally normal hearts.[11] So far, this method has not been investigated for the abnormally shaped left ventricle as seen in patients with congenital heart disease.
The purpose of this study is to assess in adult patients with congenital heart disease, the feasibility of real-time 3D echocardiography (RT-3DE) data acquisition, and the volume and function of the abnormally shaped left ventricle, comparing the results to those obtained by MRI.

Methods

Study population

Thirty-two consecutive patients (59% male), who were scheduled for routine magnetic resonance imaging examination, were included into the study. The mean age was 31 ± 9 years (range 19 – 51 yrs). All patients distorted LV geometry originating from the congenital heart malformation itself and as a result of dilated or high-pressured right ventricle. In 13 patients with surgical corrected tetralogy of Fallot, LV geometry was abnormal throughout the cardiac cycle due to flattening of interventricular septum and abnormal septal motion.[12] In 7 patients with transposition of the great arteries with Mustard repair and in one patient with congenital corrected transposition of the great arteries, the LV was squashed and banana-shaped behind the high-pressure RV. Also in 7 patients with right ventricular outflow tract obstruction after homograft insertion, the LV was squashed due to the high-pressure RV. The LV was grossly dilated in 2 patients with congenital aortic valve stenosis after Ross procedure and in one patient with partial atrioventricular septal defect, due to severe left-sided AV valve regurgitation. In a patient with Ebstein`s anomaly, the abnormal LV geometry was a result of the unbalanced septal motion. All patients were in sinus rhythm. The MRI and RT-3DE study were both completed within two hours to ensure comparable hemodynamic conditions between the examinations. All patients gave informed consent.

Real-time three-dimensional echocardiography

RT-3DE was performed using a commercially available X4 matrix transducer connected to a RT-3D system (Sonos 7500, Philips medical systems, Andover, MA). In order to encompass the complete LV into the 3D dataset, a full volume scan has to be acquired. For this purpose a pyramidal volume of 93° x 84° which is divided into four conical subvolumes, is scanned. Acquisition of the subvolumes is steered electronically by the ultrasound system while the transducer is kept in a stable position. The patient is placed in a left decubital supine position and the scanning procedure was optimized in order to obtain the entire LV in the full volume data set. The acquisition is triggered to the R-wave of the electrocardiogram of every heartbeat to allow acquisition of a full cardiac cycle for each subvolume. In order to accomplish correct spatial registration of each subvolume, the acquisition is performed in an end-expiratory breath-hold lasting 6 to 8 seconds. The majority of the 3D acquisitions (90%) were acquired in the fundamental imaging mode. The 3D dataset is stored on CD-ROM and transferred to a separate workstation for off-line data analysis.

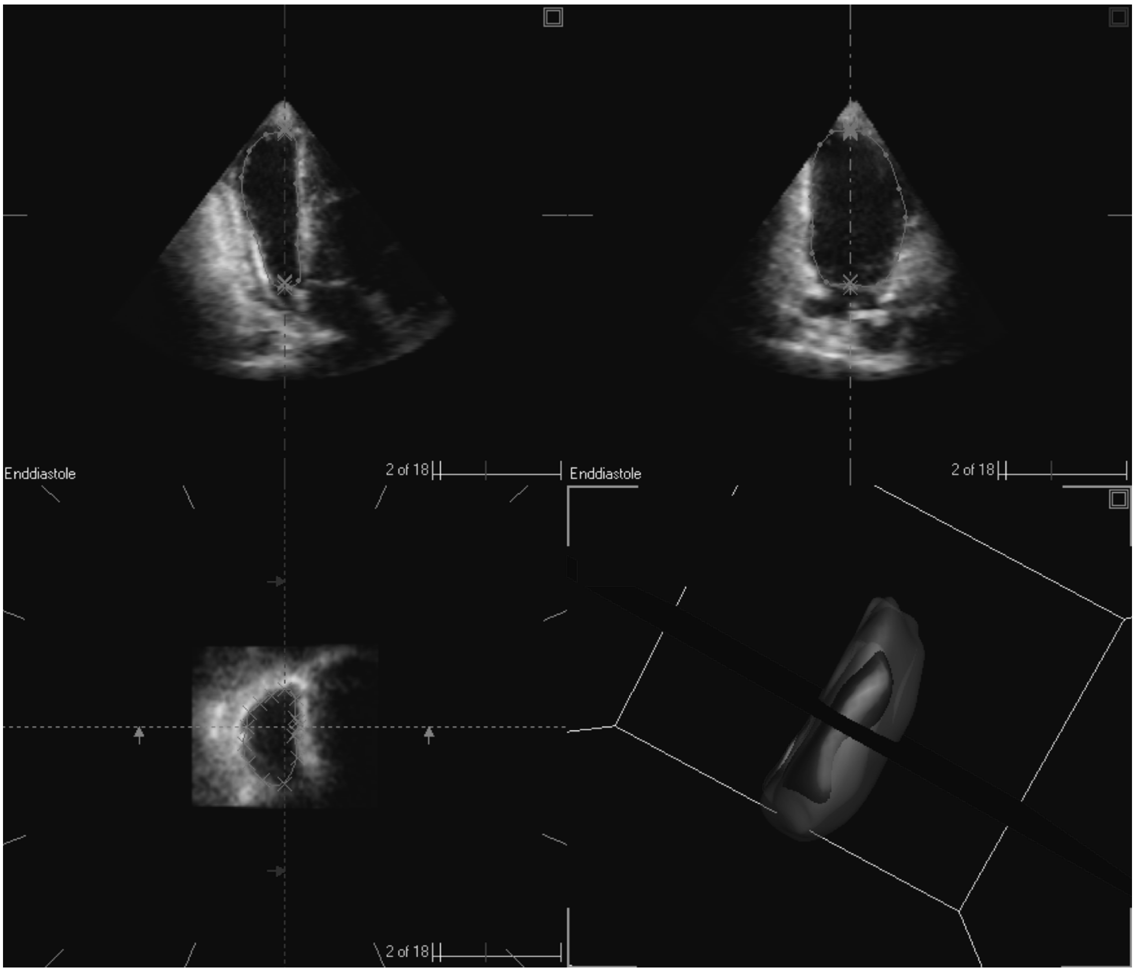
Data analysis

The 3D data set is analyzed off-line using dedicated analysis software packages (TomTec© 4D LV analysis 1.2 and Echoview© software 5.2, TomTec, Inc., Munich, Germany). In each data set end-systolic and end-diastolic frames were identified. The image before closure of the mitral valve was selected as end-diastole and the image before closure of the aortic valve was selected as end-systole. Around a user-defined LV long axis, the software generated 8 uniformly spaced apical images 22.5° apart for each volume. The systolic and diastolic images were manually traced (figure 1). Left ventricular trabeculation and papillary muscles were included within the traced area. Subsequently, end-systolic (LV-ESV) and end-diastolic volumes (LV-EDV) were calculated by the system using the "Rotaplane" algorithm.[13] Ejection fraction (LV-EF) was calculated as: (EDV – ESV)/EDV x 100%. All manual tracings were performed by two independent investigators and blinded for the MRI results. Intra- and interobserver variability for RT-3DE measurements were determined.

The second measurement of LV volume was performed with semi-automatic border detection software (TomTec© 4D analysis 1.2). Frames for LV-EDV and LV-ESV measurements were identified as written above. Contour tracing was performed on 8 different cross-sections with automatic border detection. After identification of the apex and mitral annulus on each cross-section, a pre-configured ellipse was fitted to the endocardial borders of each frame. After completion of the endocardial border tracing, the program performed a dynamic surface rendered endocardial reconstruction of the LV. Left ventricular end-diastolic volume, LV-ESV and LV-EF are calculated applying Gaussian quadrature formulas.[14]

In the 7 patients with transposition of the great arteries and the patient with congenital corrected transposition of the great arteries, the anatomical LV that is often banana-shaped and functions as a subpulmonary ventricle, was assessed for LV volumes and EF.

Fig 1



Example of manual border tracing in a patient with transposition of the great arteries corrected using the Mustard method. Note the abnormal axis and banana shape of the ventricle that differs extremely from the normal left ventricle.

Magnetic Resonance Imaging and analysis

Studies were performed with a 1.5 T magnetic resonance imaging system (General Electric, Milwaukee WI, USA; Signa 1.5 T MRI) equipped with a 4-element torso coil. A cardiac triggered steady state free precession sequence (FIESTA; TR and TE of 3.5 and 1.3 ms respectively, flip angle of 45 degrees) was used for quantitative analysis. During a breath-hold of 6 - 8 seconds, 11 to 13 cine short-axis series (slice thickness 10 mm, gap 0 mm) were acquired. Additional imaging parameters: field of view of 320 to 380 mm and a matrix of 160 x 128. Quantitative analysis was performed using standardized software (MassPlus, Medis Inc. Leiden, NL).

With this software endocardial contours were manually traced on all end-diastolic and systolic images to calculate the LV volumes and EF using Simpson's rule.

Statistical analysis

All values were expressed as means ± standard deviation (SD). A linear regression analysis was performed for the comparison of LV volumes and EF obtained by RT-3DE and MRI and for the results by two independent observers. Interobserver variability was expressed relative to the average volume + 2 SD by Bland-Altman analysis.[15] Similarly, this was performed for analysis of the agreement of RT-3DE with MRI. For the latter, the 3D LV volume and EF estimations from the two observers was averaged. To determine whether the differences in values between the two methods are statistically significant, a paired t-test was performed. A p-value less than .05 was considered significant.

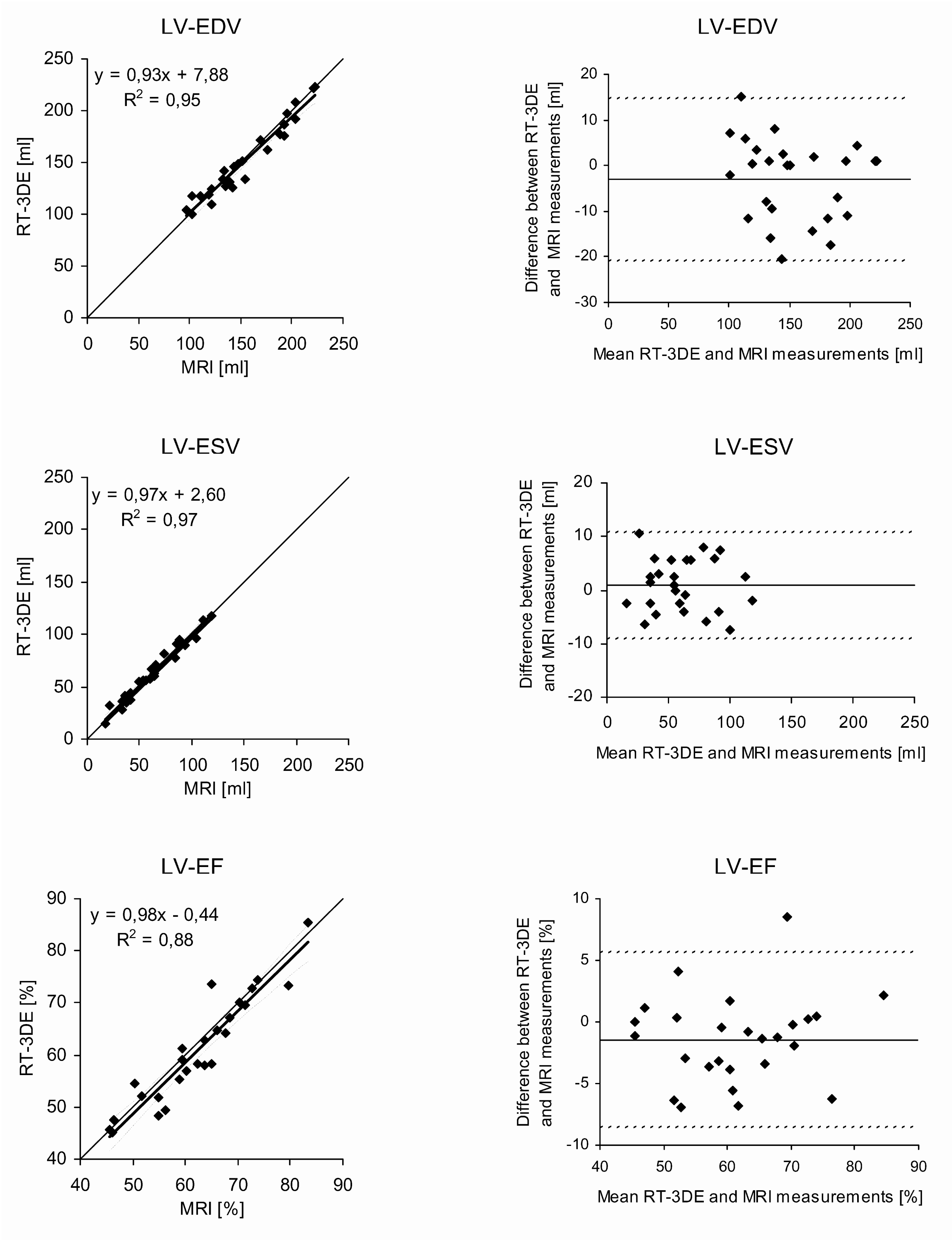
Results

Acquisition of RT-3DE data sets was feasible in 29 of the 32 (91%) patients. One patient had poor acoustic windows due to severe obesity and 2 patients had persistent respiratory artefacts that precluded adequate 3D rendering. MRI was feasible in 29 patients; 3 patients (not the same patients in which RT-3DE was not successful) had claustrophobia or artefacts that prohibited complete analysis. The mean heart rate was 68 ± 8 bpm during echocardiographic examination and 66 ± 9 bpm during MRI. The time needed for 3D data acquisition was 4 ± 2 minutes. Off-line image processing and tracing required approximately 17 ± 5 minutes for manual border tracing and 6 ± 2 minutes for automatic border tracing for each patient. MRI data acquisition and analysis could be performed within 45 minutes.

LV volume comparison of RT-3DE with manual border tracing and MRI

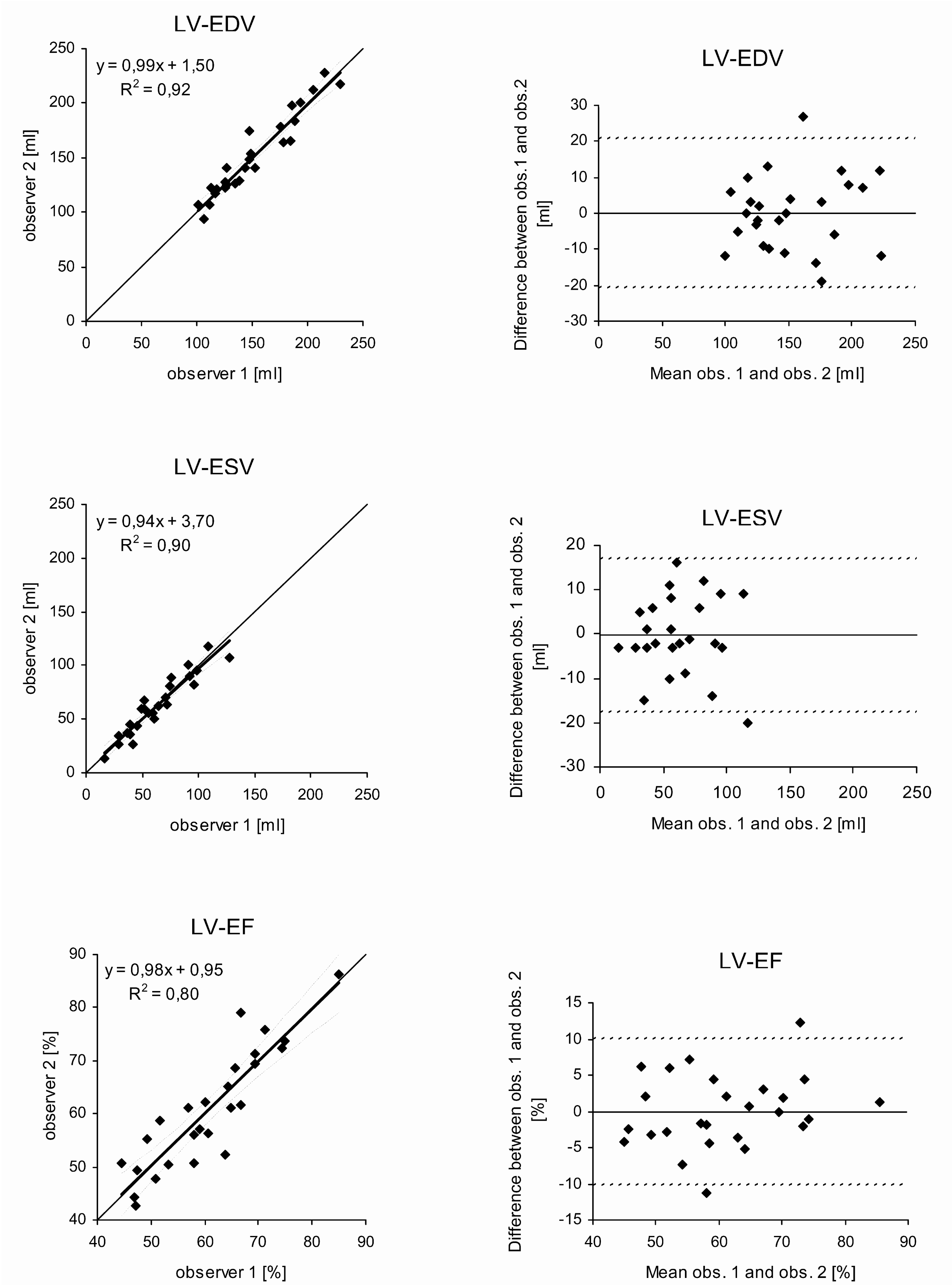
Mean LV-EDVs were 155 ± 38 ml and 151 ± 36 ml (P = NS), for respectively MRI and RT-3DE. Mean LV-ESVs were 62 ± 27 ml and 61 ± 27 ml (P = NS), for respectively MRI and RT-3DE. Linear regression and agreement plots for LV-EDV, LV-ESV and LV-EF from RT-3DE with manual border tracing and MRI as function of average measurements are shown in figure 2. A good correlation was observed between RT-3DE and MRI for both LV-EDV ($r = 0.97$; $y = 0.93x + 7.88$; SEE = 8.7 mL) and LV-ESV ($r = 0.98$; $y = 0.97x + 2.6$; SEE = 5.0 mL). The limits of agreement analysis demonstrated a mean difference of –2.9 ± 12.0 mL for LV-EDV and 0.9 ± 9.9 mL for LV-ESV. A good correlation was also observed for calculated LV-EF ($r = 0.94$; $y = 0.98x + 0.44$; SEE = 3.6%), with a mean difference of –1.4 ± 7.2%.

Fig 2



Linear regression plots and Bland-Altman plots for end-diastolic volume (LV-EDV), end-systolic volume (LV-ESV), and ejection fraction (LV-EF), as assessed with real-time three-dimensional echocardiography (RT-3DE) with manual border tracing, compared with magnetic resonance imaging (MRI) as the reference standard.

Figure 3



Linear regression plots and Bland-Altman plots for end-diastolic volume (LV-EDV), end-systolic volume (LV-ESV), and ejection fraction (LV-EF), as assessed by two independent observers with real-time three-dimensional echocardiography (RT-3DE) and manual border tracing.

LV volume comparison of RT-3DE with automatic border detection and MRI
Correlation coefficients and limits of agreement between RT-3DE with automatic border tracing and MRI were observed for LV-EDV (r = 0.79; y = 0.94x - 15.4; SEE = 28.1 mL), LV-ESV (r = 0.83; y = 0.78x + 12.2; SEE 14.9 mL) and LV-EF(r = 0.54; y = 0.60x + 17.5; SEE = 9.5%).

Intra- and interobserver variability
Results of the interobserver variability for manual border detection are shown in figure 3. No significant difference was present between the two observers. The results for intra-observer variability show also a good correlation for both LV-EDV (r = 0.96, y = 0.99x + 1.5; SEE = 10.6 mL) and LV-ESV (r = 0.95, y = 0.94x + 3.7; SEE = 5.1 mL). Also the correlation for calculated LV-EF (r = 0.89, y = 0.98x + 1.0; SEE = 5.1%), with a mean difference of 0.0 ± 10.1%.

Discussion

The results of this study indicate that RT-3DE data acquisition of the abnormally shaped LV for volumetric analysis is feasible in patients with congenital heart disease. There is a good agreement between RT-3DE using manual border tracing and MRI for the assessment of LV volume and function. Furthermore, the intra- and interobserver variability was very limited. This implies that this technique is largely operator-independent and can be used in clinical practice.

Until now, 3D echocardiography was hampered by long acquisition and analysis time in combination with poor image quality. The introduction of the RT-3DE has permitted faster acquisition of the 3D data set with improved image quality. In this study we show that in 90% of the patients an adequate 3D volumetric analysis of the LV could be performed. This is equal to the 90% feasibility of the MRI studies. The duration of a complete RT-3DE study was much shorter, compared with MRI data acquisition and analysis. Because of comparable feasibility and reliability in combination with a shorter acquisition and reconstruction time, RT-3DE potentially provides convenient, mobile and comprehensive evaluation of LV function in adult patients with congenital heart disease.

Accurate determination of LV volume and EF is a major goal in non-invasive cardiology for assessing patients with a variety of cardiac malformations.[2,3,16-21] Especially in the adult patients with congenital heart disease, LV geometry is distorted due to the congenital heart malformation itself and as a result of a dilated or high-pressured right ventricle. We found in a group of patients with a wide range of LV shape and volume, a strong overall correlation between RT-3DE and MRI measurements. The results of the present study demonstrate that RT-3DE, in combination with manual border tracing, is feasible and accurate for the assessment of LV volume and function in patients with congenital heart disease.

This is the first study using the commercial available 3D matrix transducer for the assessment of LV volume and function in congenital heart disease. The results of our study are in agreement with the results of previous studies using different 3D echocardiographic methods in patients with congenital heart disease.[9,22,23] However, RT-3DE assessment of LV volumes is no longer a research tool, but can be used in clinical practice.

In contrast to the excellent correlation of the RT-3DE in combination with manual border tracing, the correlation with the automatic border detection was poor. The main reason for this finding may be explained by differences in the applied tracing technique. The TomTec© LV analysis software uses an algorithm that fits the geometrics of structurally normal hearts. The axis and shape of the LV in patients with congenital heart disease may differ considerably from the normal hearts. This suggests that the TomTec© LV analysis software is not suitable for this specific patient population.

Study Limitations

In order to acquire a full-volume dataset, four high-resolution subvolumes need to be acquired over consecutive heartbeats in a short breath-hold. Patients with arrhythmia or severe dyspnoea, who are incapable of breath holding, cannot be investigated using this technique. However, this applies also for MRI.

The RT-3DE system has a limited angle for full volume acquisition; this may cause inaccurate measurements of LV volume when the entire LV cannot be included in the pyramidal volume.

This study is performed in the adult population with congenital heart disease. The results cannot be extrapolated to the children's population with congenital heart disease: inability of a proper breath hold and the need for sedation will limit the clinical application of these types of investigations in young children.

Conclusion

Real-time 3D echocardiography is feasible in adult patients with congenital heart disease for volumetric analysis of the abnormal LV and allows accurate determination of its volume and EF compared with MRI. Real-time 3D echocardiography may potentially provide convenient, mobile and comprehensive evaluation of left ventricular function in patients with congenital heart disease.

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Chapter 9

Comparison of real-time three-dimensional echocardiography to magnetic resonance imaging for assessment of left ventricular mass

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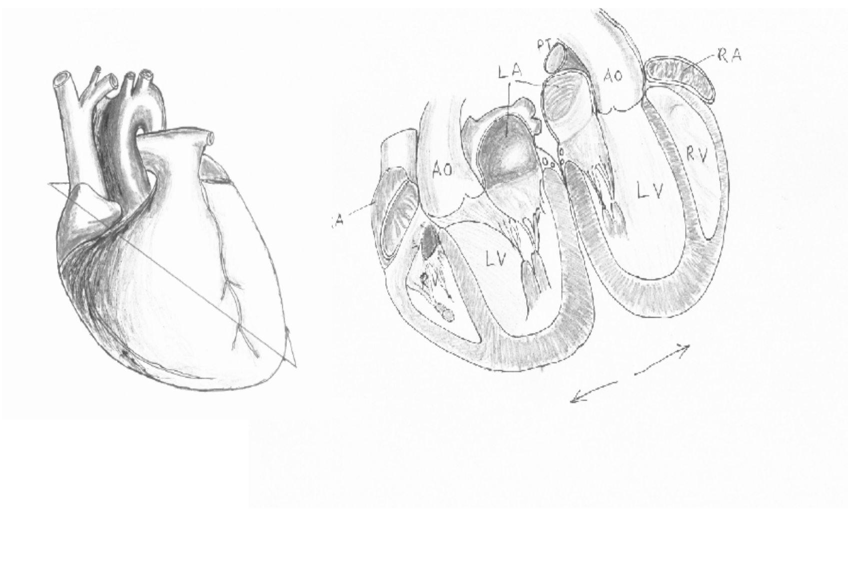
AE van den Bosch
D Robbers-Visser
BJ Krenning
JS McGhie
WA Helbing
FJ Meijboom
JW Roos-Hesselink



Abstract

This is the first study to assess the feasibility and accuracy of real-time 3D echocardiography (RT-3DE) for the measurements of LV mass in patients with congenital heart disease (CHD) compared with magnetic resonance imaging (MRI). Twenty patients (60% male) with CHD were evaluated by MRI and RT-3DE on the same day. Mean age was 29 ± 8 years (range 19 – 49 years). RT-3DE was performed with Philips Sonos 7500 echo system and LV mass analyses with assistance of TomTec software. The results for LV mass obtained by manual tracing were compared with Signa 1.5 T MRI data. Acquisition of RT-3DE data sets was feasible in all 20 patients. Nine patients (45%) had good, 5 patients (25%) moderate and 6 patients (30%) poor image quality of the 3D data set. Time of 3D data acquisition was 4 ± 2 minutes. Off-line image processing and tracing required approximately 11 ± 3 minutes. A very good correlation was observed between RT-3DE data with sufficient image quality and MRI (r = 0.98; y = 0.96x + 4.1; SEE = 9.8 g), with a mean difference of 2.0 ± 20 g. Interobserver agreement was excellent (r = 0.99; y=0.97x + 3.81) with a mean difference of -1 ± 11 g. In conclusion, assessment of LV mass from RT-3DE data is feasible in patients with congenital heart disease. The mass of the abnormally shaped left ventricle can be determined with high accuracy and low interobserver variability in patients with good or moderate echo image quality.

Introduction

Left ventricular (LV) hypertrophy has been identified as a strong and independent predictor of adverse cardiac events even in patients without associated cardiovascular disease.[1-3] This important clinical variable has been subject to extensive scientific investigation.[4] The conventional 2D and M-mode echocardiography is the imaging modality most commonly used to assess LV wall mass. However, these methods are based on geometric assumptions that ignore possible abnormal ventricular shape and variability in the distribution of LV mass. An accurate, easily reproducible means for quantification of ventricular mass is desirable. The introduction of the real-time 3D echocardiography (RT-3DE) offers a promising new approach for more accurate determination of LV mass. Analysis by 3D echocardiography requires no geometric assumption and has been shown to be an accurate method for the determination of LV mass for structural normal heart.[5-10] So far, this method has not been investigated for the abnormally shaped left ventricle and this is the first study to assess the role of RT-3DE for the measuring of LV mass in patients with congenital heart disease (CHD), comparing it with magnetic resonance imaging (MRI).

Methods

Twenty consecutive patients (60% male) with CHD, referred for a clinical MRI study, were evaluated by both MRI and RT-3DE. The mean age of the patients at the time of the study was 29 ± 8 years (range 19 – 49 y). The diagnosis of the 20 patients was tetralogy of Fallot after surgical repair in 8 patients, pulmonary stenosis in 6 patients, transposition of the great arteries corrected with a Mustard procedure (in which the anatomical right ventricle functions as systemic ventricle) in 3 patients, congenital aortic stenosis in 2 patients and one patients had Ebstein`s anomaly. All patients were in sinus rhythm. The MRI and RT-3DE study were completed both within two hours in each patient to ensure comparable hemodynamic conditions between the examinations. All patients gave informed consent.

Magnetic Resonance Imaging and analysis
All patients were studied with a 1.5 T MRI system (General Electric, Milwaukee WI, USA; Signa 1.5 T MRI) equipped with a 4-element torso coil. For quantitative analysis 11 to 13 cine short-axis series (slice thickness 10 mm, gap 0 mm) covering the heart from base to apex were acquired, using a breath-hold cardiac triggered steady state free precession sequence (FIESTA; TR and TE of 3.5 and 1.3 ms respectively, flip angle of 45 degrees). Additional imaging parameters: field of view of 320 to 380 mm (75 % rectangular) and a matrix of 160 x 128. Quantitative analysis was performed using standardized software (MassPlus, Medis Inc. Leiden, NL).

With this software endocardial and epicardial contours were manually traced on all end-diastolic images to calculate the LV mass, while including the papillary muscles in the LV cavity. LV mass was calculated as the difference of volumes multiplied by density of myocardium (1.05 g/ml).[11-13]

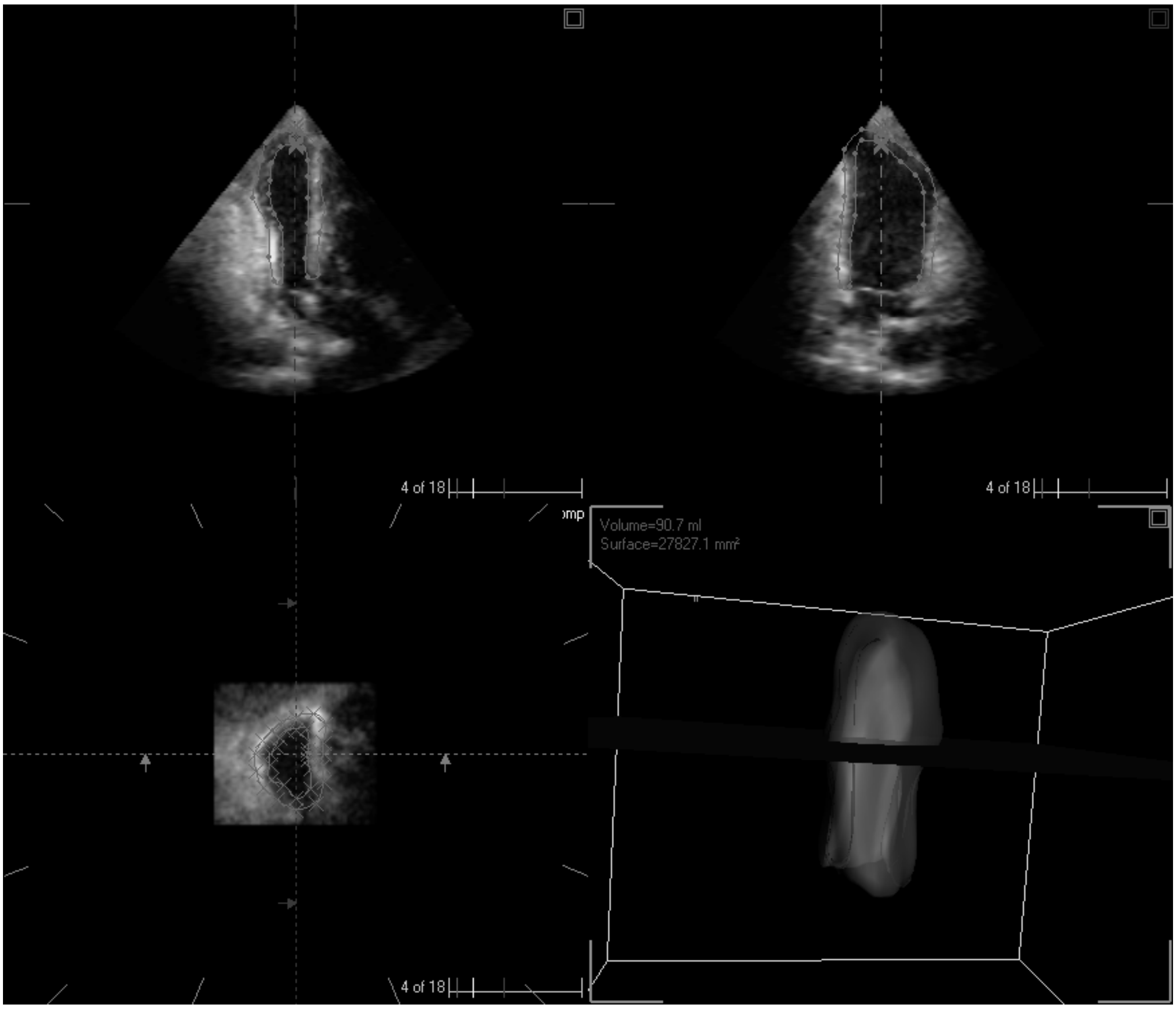
Real-time three-dimensional echocardiography

Data acquisition was performed by using a X4 matrix transducer connected to a RT-3D system (Sonos 7500, Philips medical systems, Andover, MA). In order to encompass the complete LV into the 3D dataset, a full volume scan was acquired. For this purpose, a pyramidal volume of 90° x 85° is scanned, which is divided into four conical subvolumes. Acquisition of the subvolumes is steered electronically by the ultrasound system while the transducer is kept in a stable position. The acquisition is triggered to the R-wave of the electrocardiogram of every heartbeat to allow acquisition of a full cardiac cycle for each subvolume. In order to accomplish correct spatial registration of each subvolume, the acquisition is performed in an end-expiratory breath-hold lasting 6 to 8 seconds (depending on the heart rate). The 3D dataset is stored on CD-ROM and transferred to a separate workstation for off-line data analysis.

Data analysis

The quality of RT-3DE data set was graded on the basis of acceptable image quality of the 17-left ventricle segments model, as good (0 to 2 segment not visible), moderate (3 to 4 segments not visible) and poor (≥ 5 segments not visible). The 3D data set is analyzed off-line with assistance of TomTec Echoview© software 5.2 (TomTec, Inc., Munich, Germany). We selected the anatomically correct 2- and 4-chamber views with the largest long-axis dimension. Around this user-defined LV long axis, the software generated 8 uniformly spaced apical images 22.5° apart for each LV mass calculation. In each view, epicardial and endocardial contours, including the papillary muscles in the LV cavity, were traced manually at end diastole (figure 1). The traced contours were then used to calculate a myocardial volume. This volume was multiplied by the specific mass of myocardial tissue (1.05 g/mol). Two independent investigators who were blinded for the MRI results performed all manual tracings. The repeated measurements by two observers were used to evaluate the interobserver variability. In the 3 patients with transposition of the great arteries corrected using the Mustard procedure, the anatomical LV was assessed for LV mass calculation.

Fig. 1



Example of 3D echocardiographic tracing of the LV mass in a patient with transposition of the great arteries corrected using the Mustard procedure. Note the abnormal axis and banana shape of the ventricle that differs extremely from the normal left ventricle.

M-mode measurements

M-mode imaging was performed from a parasternal long axis position using a standard transthoracic transducer. Measurements of the septal wall thickness (SWT), posterior wall thickness (PWT) and LV internal diameter (LVID) were performed according to the recommendations of the American Society of Echocardiography at the beginning of end-diastole.[14] LV mass was calculated according to the cube formula using the correction described by Devereux *et al.*[15]

LV mass (g) = $0.8[1.04\{(IVS+LVID+PWT)^3-LVID^3\}]+0.6$

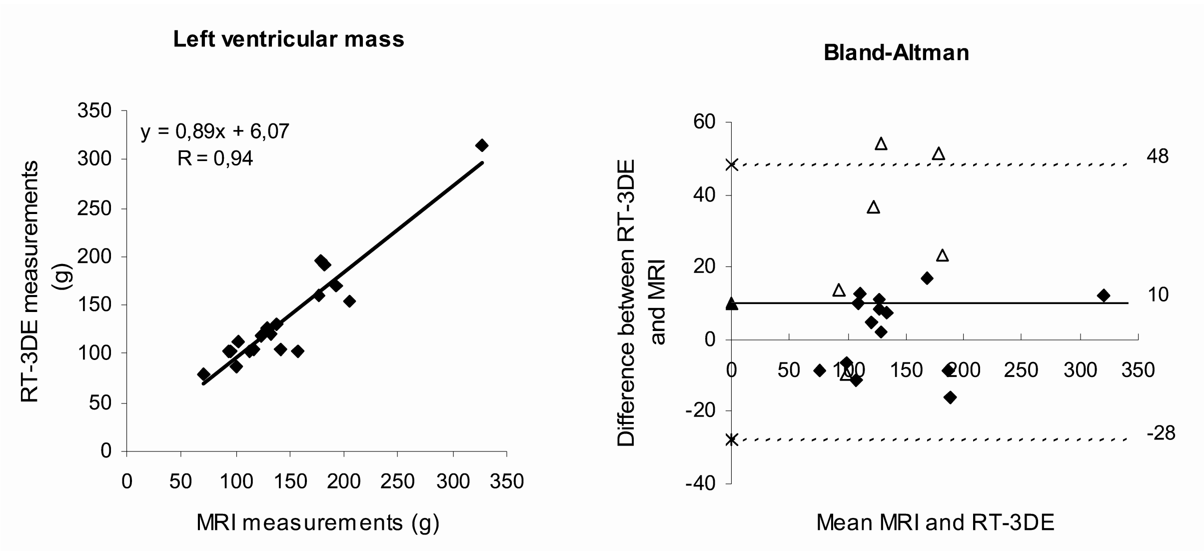
Statistical analysis

All values were expressed as means ± standard deviation (SD). A linear regression analysis was performed for the comparison of LV mass obtained by M-mode, RT-3DE and MRI and the results by two independent observers. Interobserver variability was expressed relative to the average volume + 2 SD by Bland-Altman analysis.[16] Similarly, this was performed for analysis of the agreement of M-mode with RT-3DE and MRI as for RT-3DE with MRI. For the latter, the 3D mass estimations from the two observers are averaged. To determine whether the differences in values between the two methods are statistically significant, a paired t-test was performed. A p-value less than .05 was considered significant.

Results

Acquisition of RT-3DE data sets was feasible in all 20 patients. None of the patients was excluded from the study because of inadequate 3-DE image quality or other reasons. Nine patients (45%) had good, 5 patients (25%) moderate and in 6 patients (30%) the image quality of the 3D data set was poor. The mean heart rate was 68 ± 7.7 bpm during 3D echocardiographic examination and 70 ± 7.4 bpm during MRI (p = NS). The time of 3D data acquisition was 4 ± 2 min. Off-line image processing and tracing required approximately 10 ± 2.4 minutes for patients with good to moderate image quality and 13 ± 1.8 minutes for patients with poor image quality (P > 0.05). MRI data acquisition and analysis could be performed within 45 minutes.

Fig 2



Linear regression plots and Bland-Altman plots for LV mass assessed with real-time 3D echocardiography (RT-3DE) compared with magnetic resonance imaging (MRI) as the reference standard in patients with CHD. △ represent the patients with poor 3D image quality; ◆ represent the patients with good to moderate 3D image quality.

Comparison of LV mass between RT-3DE and MRI

LV mass in end-diastole was 145 ± 55 g and 135 ± 52 g (p = NS), for respectively the MRI and RT-3DE. Linear regression and agreement plots for LV mass from RT-3DE and MRI as function of average measurements are shown in figure 2. A correlation was observed for LV mass calculation between RT-3DE and MRI (r = 0.94; y = 0.89x + 6.1; SEE = 18.8 g) with a mean difference of 10 ± 38 g.

Left ventricular mass of patients with good to moderate 3D image quality

The LV mass measurement of the 14 patients (70%) with good to moderate 3D image quality was 144 ± 59 g and 143 ± 58 g (p = NS), for respectively MRI and RT-3DE. A good correlation was observed between RT-3DE and MRI (r = 0.98; y = 0.96x + 4.1; SEE = 9.5 g) with a mean difference of 2.0 ± 20 g. A poor correlation was observed for LV mass calculation in patients with poor image quality (r = 0.86; y = 0.62x + 28.1; SEE = 18.9 g) with a mean of difference of 28 ± 45 g.

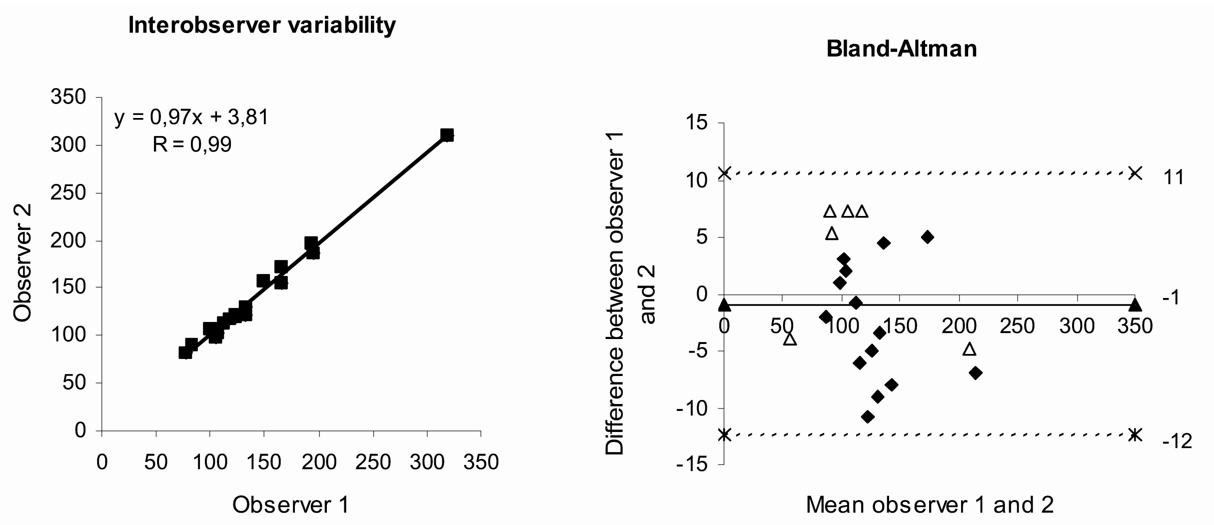
M-mode measurements (n = 20)

Mean LV mass calculation with M-mode was 168 ± 70 g. A poor correlation was observed for LV mass calculation between M-mode and RT-3DE (r = 0.42), as between M-Mode and MRI (r = 0.38) in these patients with abnormally shaped ventricles.

Interobserver variability

Results of the interobserver variability for LV mass are shown in figure 3. No significant difference was present between the two observers. The limits of agreement analysis for interobserver variability demonstrated a mean difference of -1 ± 11 g for LV mass.

Fig 3



Linear regression plots and Bland-Altman plots for LV mass assessed by two independent observers with real-time three-dimensional echocardiography (RT-3DE). △ represent the patients with poor 3D image quality; ◆ represent the patients with good to moderate 3D image quality.

Discussion

This study demonstrates our initial experience with real-time 3D echocardiography for determination of LV mass in patients with abnormally shaped left ventricles. The results show that LV mass measurements from RT-3DE data can be achieved with high accuracy and low interobserver variability in patients with good and moderate echo image quality. Good image quality RT-3DE data sets obtained with the commercially available equipment provided images with sufficient detail to allow easy off-line analysis.

Several studies have demonstrated that elevated LV mass, as defined by echocardiography, is associated with adverse prognostics and useful for risk stratification and follow-up in the general population as in CHD population.[1,17-19] For example in patients with tetralogy of Fallot and congenital aortic stenosis, LV function and mass are independent predictors for mortality and morbidity.[19-23] This is also true in planning palliation by the Fontan procedure. Numerous studies have demonstrated the significant impact of ventricular pump function and mass-to-volume ratio on immediate postoperative outcome and long-term prognosis.[24,25]

In the presented study, all patients had distortion of the LV geometry originated from the congenital heart malformation itself or as a result of a dilated right ventricle. Geometric assumptions about the shape of the left ventricle and image plane positioning errors are believed to be the most important limited factors for reliable M-mode measurements. This explains the high variability between M-mode and 3D imaging techniques for LV mass calculation.[8,26-29] Our results confirm this high variability and show a poor correlation between M-mode and RT-3DE or MRI for the abnormally shaped ventricles. Accordingly, 3D echocardiography proves to be an attractive alternative to MRI for accurate evaluation of LV mass, which can be measured directly from the 3D data set without geometrical assumptions and modeling.

Nowadays, real-time 3D echocardiography has a short acquisition time and analysis time, which makes it applicable in daily clinical practice and as our results show, it is highly accurate in patients with a variety of LV shape and good to moderate image quality. Furthermore, RT-3DE is cheap, easy to assess and less time consuming than other 3D imaging modalities such as MRI and computer tomography.

Poor 3D echo imaging quality, 30% in this study, has a direct effect on the reliability of the measurements. The same accounts for the patients with dilated left ventricles, the entire epicardial surface may be difficult to trace and require extrapolation of a part of the epicardial volume tracings by the observer. Therefore, we may not extrapolate our findings to patients with for example a dilated cardiomyopathy. Furthermore, in order to acquire a full-volume dataset, four high-resolution subvolumes need to be acquired over consecutive heartbeats in a short breath-hold. Patients with arrhythmia or severe dyspnoe, who are incapable of breath holding, cannot be readily investigated using this technique.

However, this applies for MRI also. MR sequence settings used were standard settings as routinely applied in clinical practice, allowing limited breath hold times. This resulted in a spatial resolution between 1.9 x 1.9 and 2.2 x 2.2 mm, which is adequate for clinical purposes.

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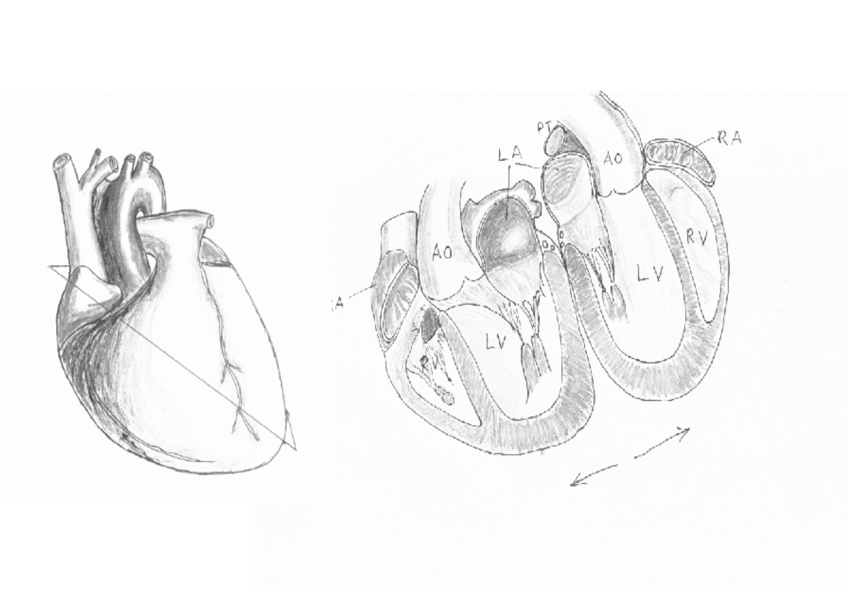
Chapter 10

Validation of real-time transthoracic 3D echocardiography in children with congenital heart disease

Submitted

AE van den Bosch
DJ Ten Harkel
JS. McGhie
JW Roos-Hesselink
AJJC Bogers
WA Helbing
FJ Meijboom



Abstract

Aims
Assessment of feasibility, accuracy and applicability in clinical practice of real-time three-dimensional echocardiography (RT-3DE) in children with congenital heart defects.

Methods and results
From September 2004 to June 2005, 100 consecutive children (57 infants, 43 children > 1 year of age), who were scheduled for corrective intracardiac surgery, were enrolled in this study. RT-3DE was performed with Philips Sonos 7500 echo-system and analyzed off-line with TomTec Echoview© software. Quantitative and qualitative assessments of the region of interest were performed on the 3D reconstruction, comparing these results with the anatomic findings and measurements performed during intracardiac surgery. Acquisition of RT-3DE datasets was feasible in 92 of the 100 (92%) patients and acquisition time was 6 ± 3 minutes. The overall quantitative analyses showed an excellent correlation (r > 0.90) between RT-3De and surgery. Also the qualitative analyses were accurate when compared with surgical findings, in all patients in which RT-3DE was feasible.

Conclusion
This study shows that RT-3DE can be used in the clinical practice for the assessment of intracardiac anatomy in children with congenital heart disease. The information derived from the 3D reconstructions can be taken into consideration in the preoperative planning and management regarding interventional or surgical therapy.

Introduction

In a short time, real-time 3D echocardiography (RT-3DE) has developed into a clinically useful tool for the assessment of left ventricular (LV) volumes and function. [1-5] Recent experimental work has demonstrated that the current RT-3DE technique is also very promising for the assessment of intracardiac anatomy, not in the least because of its potential to present structural abnormalities in novel views.[6-11] The intracardiac anatomy is especially interesting in structural heart disease, of which congenital heart disease is the main contributor. Congenital heart disease often presents at neonatal or infant age, where accurate morphological and hemodynamic assessment is required as the basis of medical and/or surgical management. The question is whether the current commercially available RT-3DE transducer is applicable in daily clinical practice in the pediatric population.

The RT-3DE transducer is not primarily developed for pediatric cardiology as is evident from the low frequency (2 – 4 MHz) of the transducer and large footprint. Such low frequency is essential for use in the adult patients, but in conventional phased array transducers, it does not allow sufficient resolution of images in small pediatric patients. A larger footprint could be a problem when the transducer is placed in the narrow intercostal spaces of infants and young children.

We evaluated the feasibility, accuracy and possibility for clinical application of RT-3DE in children. Hundred children with a variety of congenital heart defects were imaged by RT-3DE comparing the results to the anatomic findings at intracardiac surgery.

Methods

Study population

From September 2004 to June 2005, 100 children (47% male) with congenital heart disease, who were scheduled for corrective intracardiac surgery in our institute, were enrolled in this study. Of the 100 patients, 57 were infants (mean age 3.6 ± 2.4 months, body weight 5.1 ± 3.0 kg) and 43 were children over the age of 1 year (mean age 6.7 ± 4.5 years, body weight 22 ± 13 kg). Patients were excluded from the study if they were hemodynamically unstable, or acutely ill. The patient's characteristics are shown in table 1.

The study was explained to the patients and/or their parents who gave informed consent to be enrolled in the study. The institutional review board approved the study.

Table 1. Patient characteristics

Diagnosis	N	Region of interest	Age	Range	BW (Kg)	Range
ASD II	11	ASD	4.5 y	(8m – 15y)	16	(6.2-54)
VSD	23	VSD	4.8 m	(1.5m - 15y)	5.2	(2.4 – 31)
ASD and VSD	9	ASD / VSD	3.0 m	(1.2m –1y)	4.7	(3 – 7.7)
AVSD	17	AVSD	4.8 m	(1.2m – 16 y)	5.1)	(3.1 – 49)
ToF	11	VSD / RVOT	3.6 m	(1.5m – 15y)	5.2	(2.4 – 31
Fontan	7	LVOT	3 y	(2wk – 9y)	14	(2.6 – 30)
AoS (subv/val)	6	LVOT	7 y	(8m – 12y)	24	(9 – 34)
VSD with AoS	3	VSD / LVOT	3.5 y	(3y – 16y)	15	(12 – 60)
VSD with PS	3	VSD / RVOT	10 m	(3m – 9y)	5.1	(4.6 – 32)
TGA	3	LVOT / ASD	2 wk	(1.5wk – 3wk)	3.5	(3.5 – 4.4)
PS	4	RVOT	12 y	(6m – 14y)	37.5	(2.8 – 53)
MV pathology	2	Inflow MV	10 m	(2.4 m, 1.5y)	5.7	(3.5, 7.8)
Ebstein`s	1	Inflow TV	7 y	7 y	24	24

Age and Body weight (BW) are expressed as median and range, y = years; m = months. ASD II = secundum atrial septal defect; VSD = ventricular septal defect; AVSD = atrioventricular septal defect; ToF = tetralogy of Fallot; AoS = valvular of subvalvular aortic stenosis; TGA = transposition of the great arteries; PS = pulmonary stenosis; MV = mitral valve; LVOT = left ventricular outflow tract; RVOT = right ventricular outflow tract; TV = tricuspid valve

Three-dimensional echocardiographic data acquisition

The real-time transthoracic 3D images were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. The full matrix array (X4) transducer has several modes of data acquisition: 1) narrow angle acquisition which consist of 60° x 30° pyramidal volumes, displayed in a volume rendered manner. This is an actual real-time mode without the need for respiratory gating; 2) the `zoom mode` which allows a magnified view of a subsection of the pyramidal volume; and 3) wide angle acquisition which is used to collect a full volume data set of the heart. In this acquisition mode, four wedges are obtained over 8 consecutive cardiac cycles with ECG gating. The full matrix array (X4) transducer has a frequency range of 2-4 MHz.

For each individual patient a region of interest was defined. The region of interest is a part of the intracardiac anatomy that was inspected by the surgeon as a part of the surgical procedure. To evaluate different cardiac malformations, a list was made of the regions of interest for the most common congenital heart malformations: atrial septal defect (ASD), ventricular septal defect (VSD), atrioventricular septal defect (AVSD), left ventricular outflow tract obstruction (LVOTO), right ventricular outflow tract obstruction (RVOTO), mitral valve (MV) and tricuspid valve (TV) abnormalities. In some patients, more than one region of interest could be evaluated.

The 3D data acquisition in the infants and children under the age of 4 years took place immediately before surgery with the patients under general anesthesia. During the data acquisition, no breath hold or ventilation arrest was performed.

The patients were on conventional mechanical ventilation (tidal volume 8 ml/kg body weight). Since the data were acquired during the time that the child was prepared for surgery, there was no prolongation of total anesthesia time.
In all patients over 4 years of age (N = 24) a 3D data acquisition was performed without sedation, two weeks before surgery, during an outpatient clinic consultation.

Three-dimensional echocardiographic data analysis
The RT-3DE data were stored on a CD-ROM and transferred to a stand-alone TomTec workstation (TomTec, Munich, Germany) for off-line data analysis with TomTec Echoview 5.2® software. Three-dimensional reconstructions, focused on the region of interest, were analyzed and interpreted off-line by two independent observers (AvdB and JM) unaware of the 2D echocardiographic findings. Acquisition time was defined as the total time for preparation – optimalization of setting and transducer position – and the acquisitions of all the 3D data sets. The mean reconstruction time was defined as the time for screening all the 3D data sets for image quality and whether of not the entire region of interest was present in the data set, and making the necessary cut-planes in the best 3D data set for off-line analyses.

Qualitative analysis
The intracardiac structures were analyzed by making cut planes through the 3D data set in order to get an optimal visualization of the region of interest. These cut planes can be made at any desirable angle. The images were rotated in space to visualize the intra-cardiac structures from different sides.
For analysis of the atrial and/or ventricular septal defect, a cut plane was placed in the 3D data set through the LV and RV from apex to base, parallel to the ventricular septum, creating an \`en face\` view of the septal surface. For analysis of the AV valves (AVSD, MV and/or TV pathology), two opposite views were reconstructed. The \`unroofed\` view from the left atrium orientated toward the atrioventricular junction creating a \`surgical view\` of the AV valve. Similar reconstruction, but orientated from the LV apex toward the AV junction, allowed the assessment of the AV valve from below. The number, size and chordal attachment of the AV valve leaflets, especially to the crest of the interventricular septum were identified. In cases of LVOT or RVOT obstruction, the outflow tract was assessed from long axis and short axis cut planes at different angles and distances, from below and above the obstruction. The morphology of the sub- or valvular obstruction, its extension and relation to the aortic or pulmonary valve were assessed. The aortic and pulmonary valves were evaluated for the number of cusps and the fusion of the commissures.

Quantitative analysis

Quantitative analysis was performed for measurements of distance and diameters. Septal defects – ASD, VSD and AVSD – were assessed for the maximal diameter and compared with surgical measurements. Also the shape and number of defects were determined. In LVOT, RVOT, MV and TV abnormalities the maximal annulus diameter was measured on 3D image.

Surgical procedure and assessment of morphology

The surgeon was blinded for the RT-3DE study to avoid bias in the surgical report. Measurements and descriptions were obtained, in the flaccid heart after cold cardioplegia (St. Thomas solution). Using the surgical description as the gold standard, the accuracy of each type of echo assessment was determined.

Statistical analysis

All values are expressed as means ± standard deviation (SD) when data were normally distributed. Data were tested for normality with the Kolmogorow-Smirnov test. The median and range are given when data were distributed asymmetrically. The relations between diameters derived from RT-3DE and surgical procedure, and interobserver variability were analyzed by linear regression and Bland-Altman analysis [12]. Limit of agreement is expressed as 2 SDs of the difference between RT-3DE and surgery. To determine whether the difference in the values between RT-3DE and surgical measurements was statistically significant, a paired t-test was performed. A p-value less than .05 was considered significant.

Results

Different regions of interest were selected according to the specific congenital defects. Acquisition of RT-3DE datasets was feasible in 92 of the 100 (92%) patients. There were 4 patients with poor acoustic windows (age 1, 2, 3 and 3 years) and 4 patients (age 6, 7, 7 and 10 months) with persistent respiratory artefacts that precluded adequate 3D rendering. The time of 3D data acquisition was 6 ± 3 minutes. In all infants and young children the subcostal view was found to be the best approach giving an unobstructed acoustic window for creating an adequate 3D data set for any of the defined region of interest. This window was sufficient to enclose the entire heart including the region of interest in one data set. For the children above the age of 4 years, the transducer position was adjusted in order to have the ultrasound beam perpendicular to the region of interest resulting in some unorthodox transducer positions. The overall reconstruction time becomes significantly shorter during the study (figure 1). Figure 1 also demonstrates that patients with simple congenital heart diseases, including ASD, VSD and AVSD, have a shorter analysis time than patients with complex lesions.

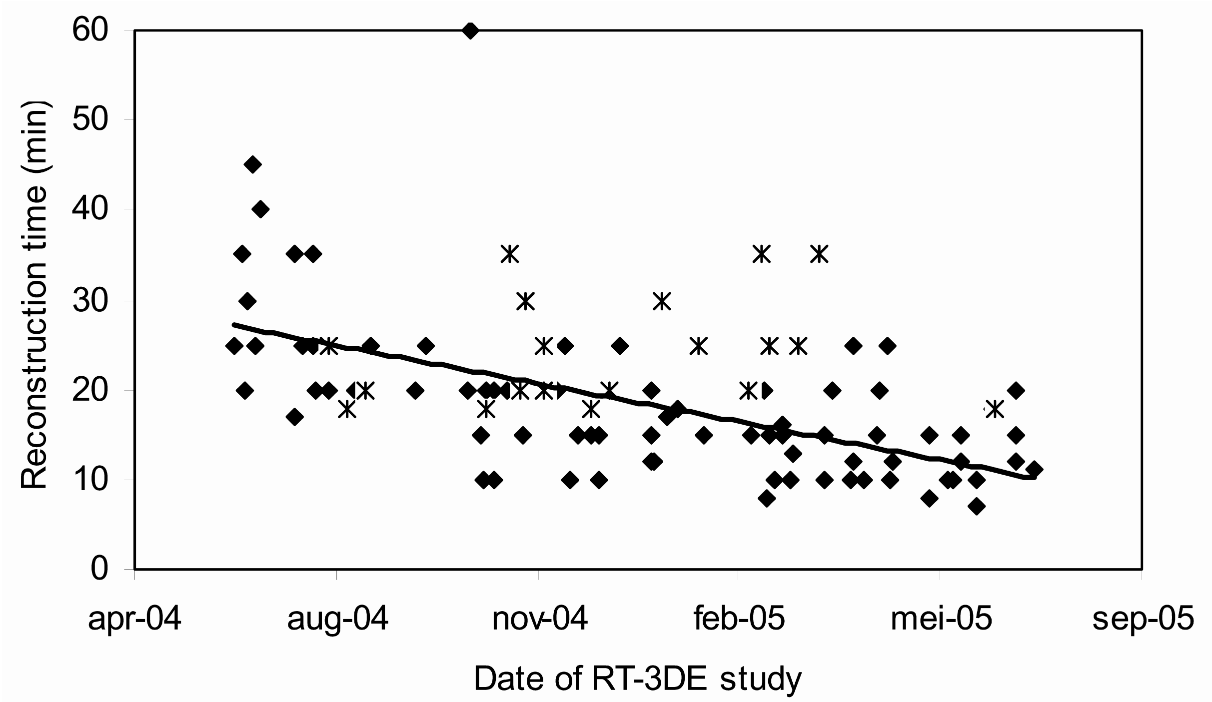


Figure 1. represents our learning curve for 3D reconstruction during the study. ◆ = patients with simple congenital heart disease (including atrial septal defect, ventricular septal defect and atrioventricular defect); ✳ = patients with complex congenital heart disease (including all other congenital heart malformations).

Region of interest

Atrial septal defects

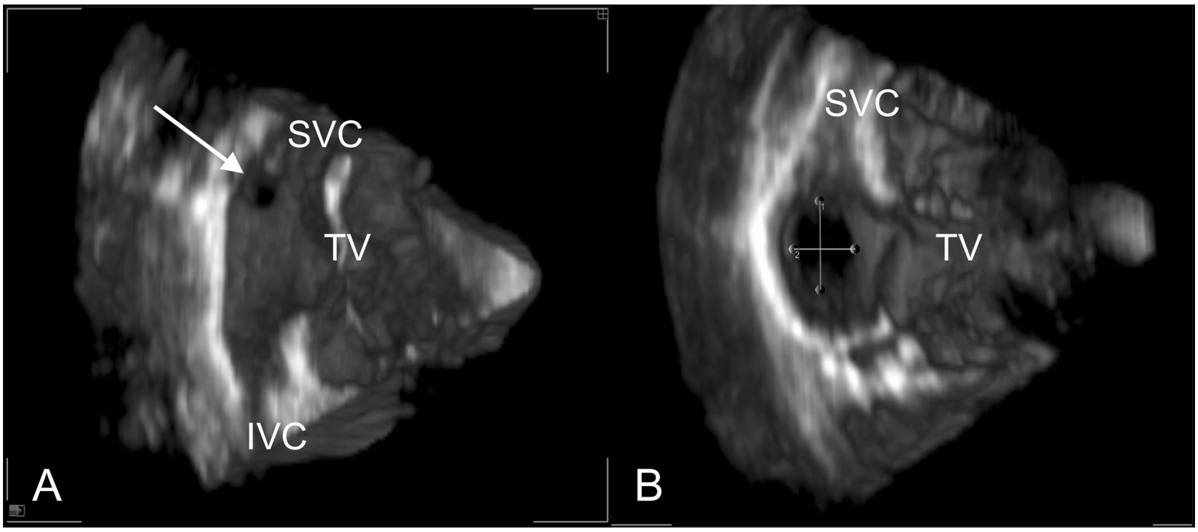
RT-3DE acquisition was feasible in 20 of the 21 (95%) patients. Real-time 3D echocardiographic evaluation of 17 secundum ASDs and 3 sinus venosus defects provided unique enface views of the defect from the right atrial (RA) as well as the left atrial (LA) sides and its spatial orientation (figure 2). The mean reconstruction time was 15 ± 4 minutes, but became significantly shorter during the course of the study as experience improved. Maximum ASD diameter was 17 ± 11 mm by RT-3DE and 18 ± 11 mm by surgery (P = 0.1). Minimum ASD diameter was 11 ± 5 mm by RT-3DE and 11 ± 6 mm by surgery (P = 0.3). The correlation between RT-3DE and surgery for the maximum ASD diameter was r = 0.97 (y = 0.93x + 0.29; SEE = 2.6 mm) with a mean difference of 1.0 ± 5.0 mm.

Ventricular septal defects

RT-3DE acquisition was feasible in 40 of the 45 (89 %) patients (23 patients with isolated VSD, 9 patients with ASD and VSD, and 13 patients with VSD and PS/AoS or ToF).

In all patients, the free wall of the RV was digitally resected from the 3D data set to visualize the right side of the ventricular septum (surgical view). The mean reconstruction time was 17 ± 10 minutes. Maximum VSD diameter was 11.5 ± 3.7 mm and 11.9 ± 4.6 mm, for respectively RT-3DE and surgery ($P = 0.3$). Minimum VSD diameter was 6.9 ± 2.9 mm and 9.6 ± 4.3, for respectively RT-3DE and surgery ($P < 0.001$). The correlation between RT-3DE and surgery for the maximum VSD diameter was $r = 0.94$ ($y = 0.84x + 1.79$; SEE = 1.5 mm) with a mean difference of 0.1 ± 2.8 mm. The measurements performed by the two observers did not differ significantly. The interobserver variability showed a good correlation for the VSD measurements ($r = 0.93$; $y = 0.97x + 0.31$) with a mean difference of 0.4 ± 1.5 mm.

Fig 2

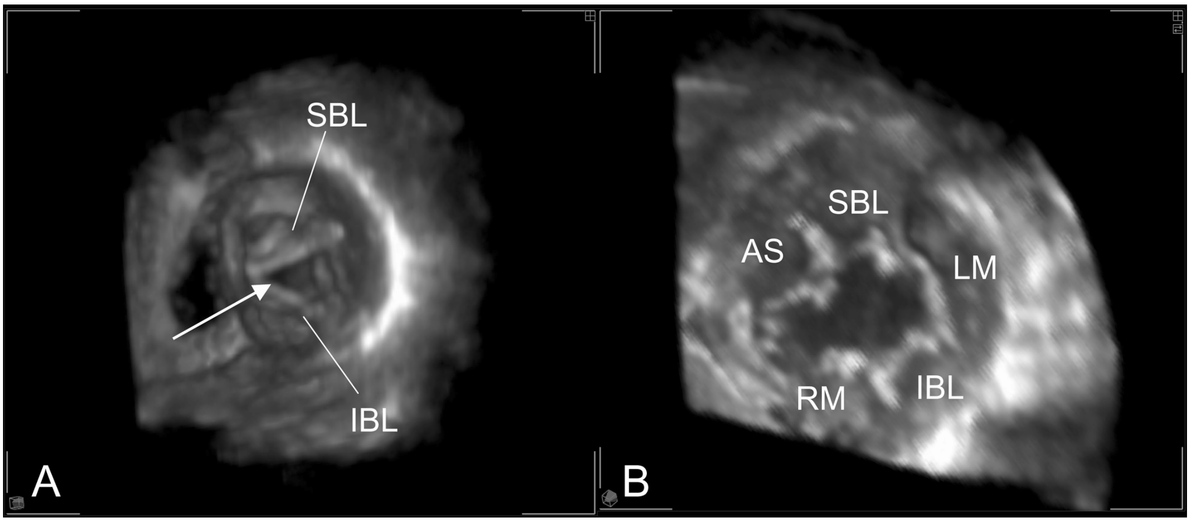


Real-time 3D echocardiographic display of sinus venosus defect of the superior vena cava type (A, arrow), viewed from right atrial surface in a patient of 5 years old. Figure B shows the diameter measurement of a secundum atrial septal defect. TV: tricuspid valve; SVC: superior vena cava; IVC: inferior vena cava.

Atrioventricular defects

RT-3DE acquisition was feasible in all 17 patients (10 patients with a common AV orifice (complete AVSD), 7 patients with divided AV orifices (partial AVSD)). In all 17 patients, the AV valve leaflets were assessed correctly compared with the surgical findings. In 16 patients, 5 AV valve leaflets were identified and one patient had 4 AV valve leaflets (figure 3). The superior bridging leaflet was assessed on the RT-3DE image according to the Rastelli classification: 7 patients with Rastelli type A and 3 patients with Rastelli type C. The RT-3DE observations of the superior bridging leaflet were accurate compared with the findings during surgery.

Fig 3



Real-time 3D echocardiographic display of a partial (A) and complete AVSD (B) in respectively a patients of 3 years and 1 month old. Figure A shows the commissure (arrow) between the superior (SBL) and inferior bridging leaflets (IBL) in a partial AVSD, viewed from the LV apex. Figure B shows the opening of the common AV valve in a patient with a complete AVSD. The 5 AV valve leaflets are clearly identified; AS = antero-superior leaflet; RM = right mural leaflet; LM = left mural leaflet.

Left ventricular outflow tract and/or aortic valve pathology

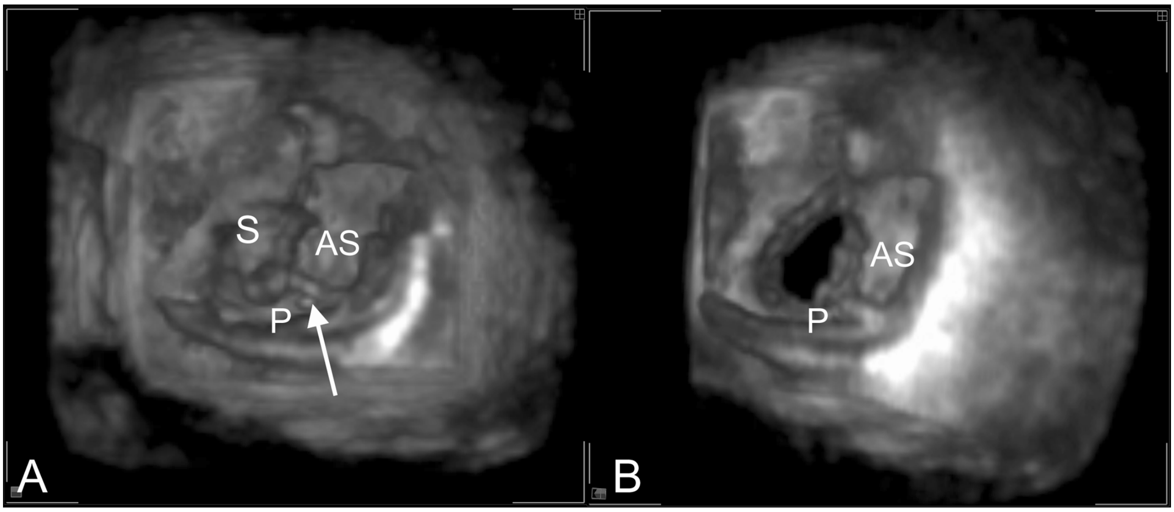
In 12 of the 13 (92%) patients a reconstruction of this region of interest was performed. In 5 patients, a subvalvular stenosis was assessed by 3D reconstruction looking from the LV up to the LVOT. The diameter of the LVOT was reduced for 25 – 50% in 4 patients by a fibrous crescent or ring; in one patient the obstruction was almost 90%. The distance from the base of the obstruction to the aortic valve was 9 ± 1.3 mm. These findings were confirmed by surgery. In 3 patients, severe aortic regurgitation was present and one patient had severe aortic stenosis. In the 3D reconstruction of aortic valve, the closure line was clearly visible, but often not the separate cups. In the 3 patients with transposition of the great arteries, the parallel arrangements of the great arteries and spatial relations could simultaneously be visualized. The LVOT obstruction and arrangement of the great arteries were correctly assessed by RT-3DE compared with surgery.

Right ventricular outflow tract defect and/or pulmonary valve pathology

Three-dimensional reconstructions of the RVOT were performed in 10 patients with subvalvular obstruction. Infundibular hypertrophy was present in 9 patients and one patient had pulmonary atresia. The smallest RVOT diameter was 6.4 ± 1.1 mm and 5.6 ± 1.5 mm, for respectively RT-3DE and surgery (P = 0.2). The pulmonary valve was assessed in 17 of the 20 (85%) patients. The closure line of the pulmonary valve was visible, but not the pulmonary valve cusps. The maximal pulmonary valve annulus was 8 ± 5 mm and 8 ± 5 mm, for respectively RT-3DE and surgery (P = 0.2).

Mitral or tricuspid valve pathology
Tricuspid or mitral valve was evaluated in 7 patients (3 patients with hypoplastic LV, two patients with mitral valve stenosis and regurgitation, one patients with Ebstein`s anomaly and one patients with double outlet RV). Real-time 3D echocardiography provided 'en face' view of all leaflets at any point in cardiac cycle by single acquisition (figure 4). The TV and MV annulus could be measured in all 7 patients.

Fig. 4



Real-time 3D echocardiographic display of a patient with single ventricle anatomy viewed from the apex. Figure A and B show an en face view of an open and closed of the tricuspid valve (TV). The arrow points out the fusion between the anterior-superior (AS) and posterior (P) leaflets of the tricuspid valve. S: septal leaflet of the tricuspid valve.

Discussion

This study demonstrates that RT-3DE is feasible in infants and children, with the current commercially system and accurately depicts the intracardiac morphology of congenital heart malformations. Acquisition time is short and reconstruction time is, after a brief learning curve, acceptable. This implies that RT-3DE is no longer a research tool, but can be used in the daily clinical practice of pediatric cardiology.

At this moment, 2D echocardiography is the most commonly used non-invasive diagnostic method for analysis of congenital heart defects. However, when information about the spatial relationship of the cardiac structures is necessary, 2D echocardiography has its obvious shortcomings as it rarely displays the anatomy in views that are similar to the ones encountered during surgery. It can only provide (multiple) 2D imaging planes, which requires a difficult mental conceptualization process of the viewer to create a 3D image of the intracardiac anatomy.

In this study, we were able to diagnose the cardiac malformation in (92%) patients with the RT-3DE technique providing us with depth perception of cardiac structures; now really showing their relation with surrounding structures and generating `en face` views such as the surgical views.

For example, RT-3DE can delineate atrial- and ventricular septal defects for localization, size and relation to relevant structures during the cardiac cycle. [8,13,14] With the development of new techniques for septal defect closure, the need for accurate assessment of not only defect size but also defect morphology and its spatial relations increases. [15,16] This unique presentation of the intracardiac anatomy, validated in this study, is the main advantage of RT-3DE over the consisting 1-D and 2-D mode.

A great advantage of RT-3DE is the applicability in infants and young children. The inability of a proper breath hold and use of sedation in young children could limit the clinical application. However, sedation is often used when performing 2D echocardiograms in infants and children younger than 3 years to limit motion artifacts and to ensure a complete echocardiographic examination.[17,18] We expect that sedation is not necessary in peacefully lying neonates and young children, for example during feeding or sleep, because RT-3DE acquisition time is very short.

A learning period was necessary before it was possible to obtain adequate 3D data sets. We assumed that one 3D data set acquired from one view, would comprise all data and that it would be possible to analyze the entire heart. But it appeared impossible to visualize all intracardiac structures with the same optimal image quality in one data set.[19,20] The reduced lateral resolution, far and near field problems of the matrix transducer hampers the image quality of structures in these part of the 3D data set. To ensure good image quality, we adjusted our scanning technique in such a way that the ultrasound beam was always perpendicular on the region of interest and that this region of interest was in the centre of the 3D data set. For infants and young children the best approach was the subcostal view, however for children above 4 years of age standard transducer positions required adjustment, resulting in unorthodox scanning planes.

The highest frequency transducer currently available is 2 – 4 MHz, which in a conventional 2D transducer precludes good image resolution in small pediatric patients. Despite this low frequency, we were able to obtain adequate 3D data set and found that the resolution was adequate. Even small intracardiac structures as chordae and papillary muscles could be visualized. An explanation for the relatively good lateral resolution could be the large number of crystals in the matrix transducer. The crystals are parallel processed allowing a significant increase in the ratio of transmitted to received ultrasound signals. The currently available matrix transducer has a relative large footprint that prohibits undistributed echo window in the small intercostals space of infants and young children. In our experience, the optimal acoustic window in neonates and small children is the subcostal view, making the drawback of large footprint less relevant.

We believe that with further refinement of the 3D matrix technology, such as the development of a high frequency transducer and smaller footprint, 3D echocardiography is likely to play a valuable role in the analysis of congenital heart disease and could aid in the choice in the preoperative planning by providing undisputed presentation of defect's morphology and spatial orientation on top of the conventional 2D echocardiography.

Limitations of real-time 3D echocardiography

Although RT-3DE has great potential, it is still limited by less resolution then 2D echocardiography. Very thin cardiac structures as aortic and pulmonary leaflets are difficult to visualize, even with optimal gain settings, and dropouts in the 3D data set are common. An additional limitation of the RT-3DE is the limited size of the pyramidal volume of the data set and irregular heart rate for full volume 3D acquisition that can prolong acquisition time and degrade the quality of the 3D image. Three-dimensional data acquisition in the infants and children under the age of 4 years was performed under general anesthesia. Therefore, the outcomes of this study cannot directly be extrapolated to the use of RT-3DE in clinical practice for the study of young children without sedation.

Conclusion

Real-time 3D echocardiography has great potential in the assessment of intracardiac anatomy, so important in congenital heart disease. This study shows that, despite the shortcoming of the currently commercially available RT-3DE equipment in terms of limited image resolution and large footprint of the transducer, RT-3DE can be used in the clinical practice for the assessment of intracardiac anatomy in infants and children with congenital heart disease. The information derived from the 3D reconstructions can be taken into consideration in the preoperative planning and management regarding interventional or surgical therapy.

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Chapter 11

Dynamic 3D echocardiography in virtual reality

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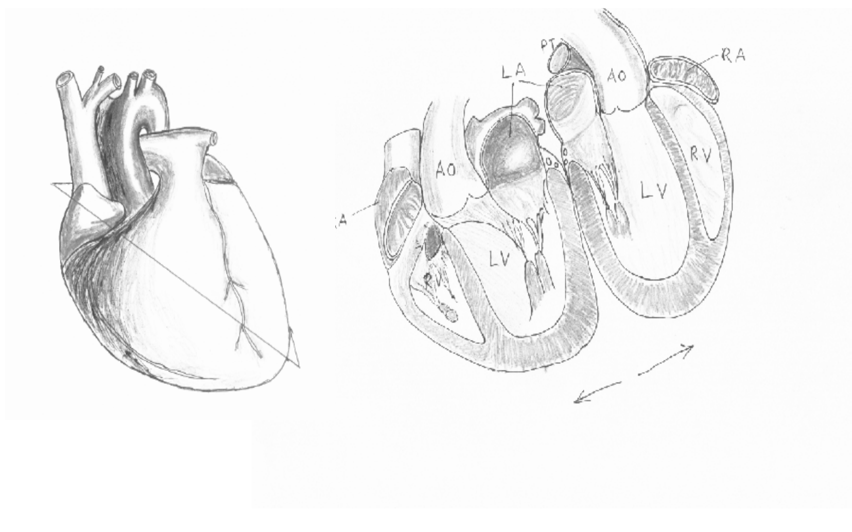
AE van den Bosch
AHJ Koning
FJ Meijboom
JS McGhie
ML Simoons
PJ van der Spek
AJJC Bogers



Abstract

Background

This pilot study was performed to evaluate whether virtual reality is applicable for three-dimensional echocardiography and if three-dimensional echocardiographic `holograms` have the potential to become a clinically useful tool.

Methods

Three-dimensional echocardiographic data sets from 2 normal subjects and from 4 patients with a mitral valve pathological condition were included in the study. The three-dimensional data sets were acquired with the Philips Sonos 7500 echo-system and transferred to the BARCO (Barco N.V., Kortrijk, Belgium) I-space. Ten independent observers assessed the 6 three-dimensional data sets with and without mitral valve pathology. After 10 minutes' instruction in the I-Space, all of the observers could use the virtual pointer that is necessary to create cut planes in the hologram.

Results

The 10 independent observers correctly assessed the normal and pathological mitral valve in the holograms (analysis time approximately 10 minutes).

Conclusion

This report shows that dynamic holographic imaging of three-dimensional echocardiographic data is feasible. However, the applicability and use-fullness of this technology in clinical practice is still limited.

Introduction

Evaluation of intracardiac anatomy from multiple two-dimensional echocardiographic images requires a mental conceptualization process that is complicated by cardiac dynamics.[1-3] Currently, real-time 3D echocardiographic images of the heart do no longer demand this difficult and individually variable conceptualization processes, by offering an equivocal presentation of cardiac anatomy throughout the cardiac cycle. However, the full 3D potential of these imaging modalities cannot be appreciated, since the 3D data are presented on a flat 2D screen. Virtual dynamic systems, known as virtual reality, can assist with the interpretation of 3D data of the heart in space and makes it possible to `dive` into the 3D model of the heart.[4-8] This study is an attempt in the technological process of the future to evaluate whether virtual reality is feasible for 3D echocardiography and if 3D echocardiographic images in a virtual reality can advance to a clinically useful tool.

Methods

Data sets from normal subjects and from patients with mitral valve disease, referred for a diagnostic echocardiogram, were selected with the aim of gathering a representative series of mitral valve pathological conditions with sufficient image quality. For this feasibility study, we selected 3D data sets of clinical conditions which have advantage of 3D perspective: (1) two patients with a normal mitral valve, (2) a patient with a mitral valve prolaps of the P2 segment of the posterior leaflet, (3) a patient with mitral valve stenosis, (4) a patient with hypertrophic obstructive cardiomyopathy and systolic anterior motion of the mitral valve, and (5) a patient with an atrioventricular septal defect (AVSD) where there is a commissure present between the superior and inferior bridging leaflets. Ten observers (5 cardiologist, 3 cardiologist-in-training and 2 cardiothoracic surgeons), who were blinded for the type of mitral valve morphology, were instructed to assess mitral valve anatomy/pathology and function.

Three-dimensional echocardiographic data acquisition

The 3D data sets were acquired with the Philips Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA) equipped with a 3D data acquisition software package. Real-time 3D echocardiographic (RT-3DE) acquisition was done with ECG gating and in an end-expiratory breath-hold, lasting 6 to 8 seconds (depending on the heart rate). The 3D image data was stored on CD-ROM in DICOM 3.0 format and transferred to the computer (SGI Onyx4 Ultimate Vision, Silicon Graphics, Inc., Mountain View, CA, USA) driving the I-space.

Visualization in a virtual reality environment

The BARCO (Barco N.V., Kortrijk, Belgium) I-space installed at the ErasmusMC, is a so-called four-walled CAVE(tm)-like virtual reality system (figure 1). In the I-space researchers are surrounded by computer-generated stereo images, which are projected by 4 high quality DLP-projectors on three walls and the floor of a small "room". The virtual reality system has a resolution of 1280 by 1024 pixels per projector. This is comparable to or greater than the resolution of the CRT monitors and LCD flat panels used in ultrasound systems and with workstations. The CAVORE (CAve VOlume REnderer) volume rendering application is used to investigate 3D ultrasound images during the cardiac cycle.[9] In the I-space, this result in an animated "hologram" of the dataset being visualized, floating in space in front of the viewers. The viewers wear a pair of lightweight glasses with polarizing lenses that allows seeing the hologram with depth. Interaction with this "hologram" is by means of a virtual pointer and makes it possible to assess the interior of the heart.

The observers were instructed to create several cut plane in the hologram. For the analysis of the mitral valve, two opposite views were reconstructed: 1) a view from the left atrium towards the atrioventricular junction, allowing a “surgical view” of the mitral valve, and 2) a view from the left ventricular apex toward the mitral valve. The observers were asked to assess in theses views, the anterior and posterior leaflets, and subvalvular apparatus for possible pathology.

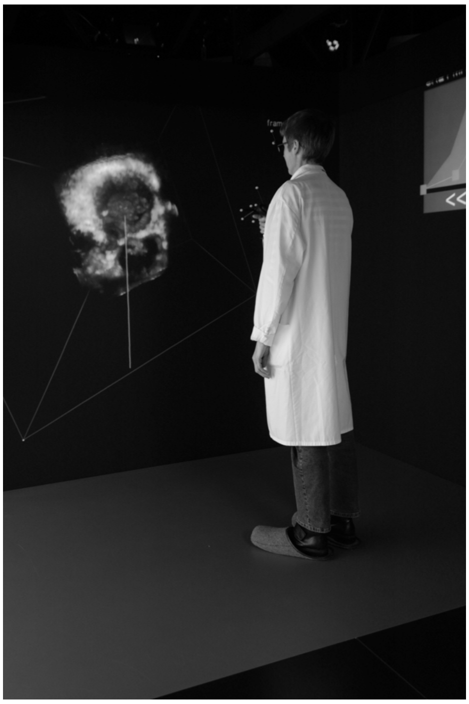
Fig 1

An impression of a 6-walled I-space virtual reality system (image courtesy of Barco N.V.).
The I-space installed at the Erasmus is a 4-walled system, without ceiling and sliding back wall.

Results

The 3D data sets of the 6 patients with normal or abnormal mitral valve anatomy were transformed to 3D holographic heart models. Once the transformation method had been developed, the time required to create a hologram from the 3D data set varied from 1 to 3 minutes. Figure 2 demonstrates the reviewer inside the I-space creating the necessary cut planes in a hologram. After 10 minutes instruction in the I-Space, all observers could use the virtual pointer and make the necessary cut planes. The 10 independent observers correctly assessed the normal and pathological mitral valve in holograms with analysis time of approximately 10 minutes for each study.

Fig 2



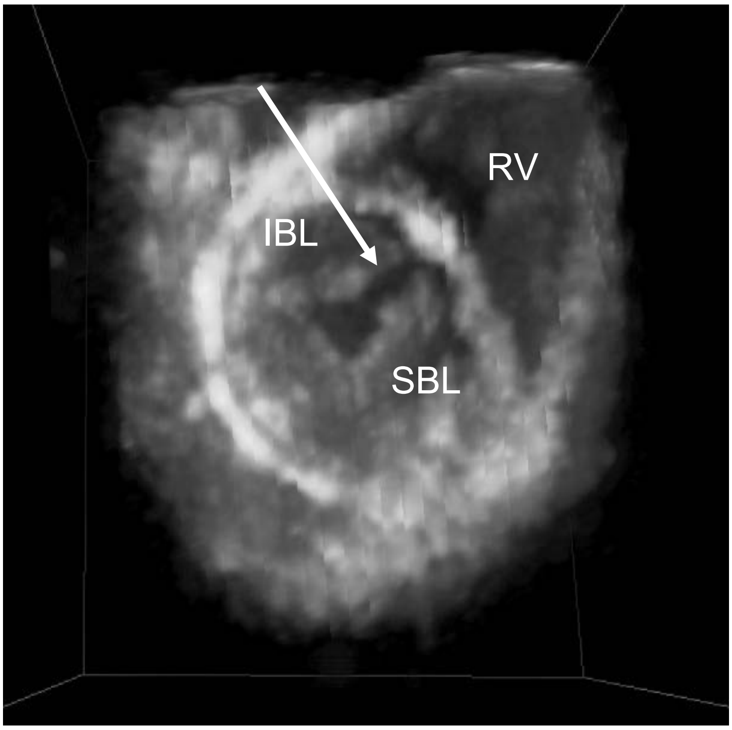
This figure shows a researcher in the I-Space, looking at the 3D hologram wearing a lightweight pair of glasses with polarizing lenses.
Within the I-space the head and hand movements of the viewer is being tracking by four infrared cameras, allowing a natural interaction with the images that are displayed.

Visualization of the mitral valve in virtual reality

In the generated 3D hologram of a normal mitral valve, the mitral valve is best visualized from the apex of the left ventricle (LV) looking upwards to the crux of the heart. The anatomy of the mitral valve can clearly be discerned. Mitral valve motion becomes more apparent when the hologram is tilted up or down and can be stopped in any desired phase of the cardiac cycle. In the patient with localized prolaps of the posterior leaflet, this prolaps was best seen when looking down from the left atrium towards the mitral valve. In early systole, the mitral valve closes and the localized prolaps of the posterior mitral valve leaflet starts to become visible. With the time progression during systole, the extent of the prolaps is seen to increase to its maximum late in systole.

The additional structures of the mitral valve apparatus (chordae, papillary muscles and valve leaflets) were visualized and identified by all observers. In figure 3, the left-sided atrioventricular (AV) valve of a heart with an atrioventricular septal defect is displayed, visualized from the apex of the LV. All observers correctly identified the commissure between the superior and inferior bridging leaflets.

Fig 3



A 3D hologram of a patient with an atrioventricular septal defect is seen from a ventricular view.
The arrow points out the commissure between the superior (SBL) and inferior bridging leaflets (IBL) (RV = right ventricle).

Discussion

This report presents a novel approach for visualization of dynamic 3D echocardiographic data, known as virtual reality. The 3D echocardiographic data sets generated by a commercial available echo machine can be visualized as a dynamic hologram inside the I-Space. Until now, the 3D echocardiographic reconstructions could only be seen on a 2D screen, but virtual reality makes it possible to `dive` into the actual 3D anatomy of the heart. We show that professionals, familiar with intracardiac anatomy, can learn how to handle the technique and cut through these holograms within 10 minutes. Subsequently, they were all able to correctly diagnose the intracardiac anatomy or pathology of the mitral valve. At the moment, I-Space technology is only available in a few dedicated research centers throughout the world. Therefore, the combination of the 3D echocardiography and virtual reality is very uncommon and the applicability and usefulness in clinical practice is still limited. However, in our opinion, it has potential and one can think of possible applications in the future.
Virtual reality provides a unique resource for education of intracardiac anatomy in general and/or specific cardiac structures.

Especially for all professionals for whom detailed knowledge of the intracardiac anatomy is essential, virtual reality might lead to a better understanding of the intracardiac anatomy. With the growth of minimal invasive cardiac surgery and interventional procedures, the interest for simulation of the heart hologram as a training tool has increased. We believe that dynamic 3D echocardiography in virtual reality has the potential for wider applicability in providing a preview of real intracardiac anatomy. With the I-Space technology, the complex anatomy, pathology and dynamic changes of the heart are appropriately visualized in a virtual heart model, which increases the accessibility and availability of virtual reality for clinical practice. In order to be integrated into clinical practice, this application should be able to run on smaller virtual reality systems, either based on a single projection surface, or on a monitor (CRT or LCD).

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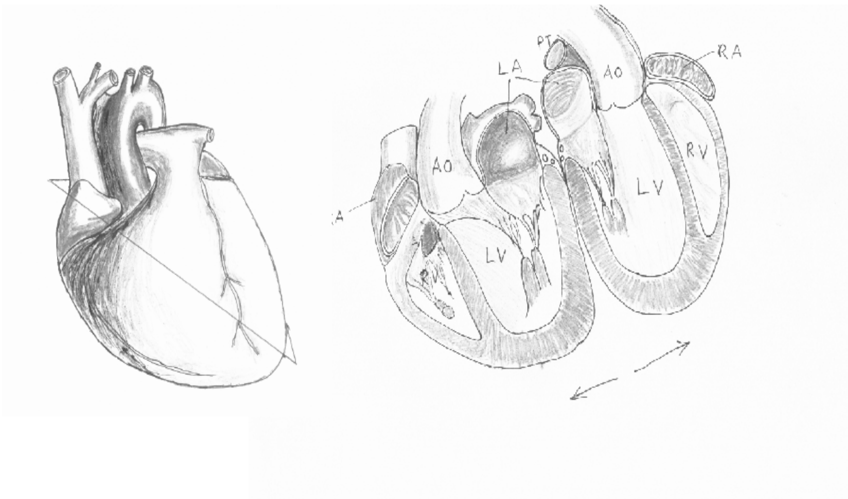
Chapter 12

Discussion, conclusions and perspectives

Discussie, conclusies en perspectieven



What have we learned and what shall it bring us?

Many years of 3D echocardiographic studies in experimental settings showed that the 3D technique was promising regarding imaging of intracardiac structures. However, its use in clinical practice was very limited. There were no commercially available 3D echo machines and the 3D technique was not real-time due to limited calculation power of the available computer processors making both acquisition and off-line analysis time extremely long.

Three years ago, the first commercially available echo machine with real-time 3D technology was introduced. Philips Medical Systems developed a matrix phased array transducer with a frequency of 2 to 4 MHz, targeted at the assessment of global and regional left ventricular function.

The currently used low-frequency transducers for 2D imaging have an image resolution which is generally regarded as too low to be used for detailed analysis of delicate intracardiac structures. Therefore, these transducers are not useful in pediatric cardiology, for the analysis of congenital structural heart disease. In adults with congenital heart disease, a low-frequency transducer is sometimes required in order to get sufficient tissue penetration of the ultrasound waves – a low frequency ultrasound wave has more ‘power’ than a high frequency wave – but the results of the analysis of delicate intracardiac structures is often disappointing. With these potential limitations in mind, we evaluated the usefulness of the available low-frequency – 2 to 4 MHz – 3D transducer for the analysis of structural heart disease, both in children and in adults. The outcome is presented in chapters 3 to 11.

The conclusion is that despite a still not optimal resolution, the 2 - 4 MHz transducer of the used echo machine, a Philips Sonos 7500, provides images that allow analysis of most details of the intracardiac anatomy, even in small infants. Delicate structures as atrioventricular valves, papillary muscles and even chordae can be assessed. However, very thin structures, such as semilunar valves and the fossa ovalis membrane, are often difficult to visualize and dropout of thin structures are common. The combination of limited lateral resolution, inherent to the ultrasound technique and the low frequency of the reflected ultrasound waves are responsible for this. Assuming that most details could be visualized, we have tried to validate the 3D images of intracardiac anatomy by comparing the 3D echocardiographic data with descriptions and measurements of the anatomy made by the cardiac surgeon during the operation. The correlations that we found were, without exception, very good. Therefore, we conclude that 3D echocardiography gives a reliable representation of the intracardiac anatomy.

After concluding that the 3D images really represented the intracardiac anatomy, we have looked at the value of 3D echocardiography, compared with the conventional 2D technique. We have learned that the acquisition of a good 3D data set is different, and consequently initially more difficult, than that of a complete 2D data set. The mainstay of 2D echocardiography is the acquisition of images from a limited number of fixed echo-windows, preferably in a fixed sequence.

After these images are acquired, each viewer can create his or her own virtual image of the intracardiac anatomy based on these 2D images. The integrity of these individually imagined 3D reconstructions cannot be controlled; therefore a huge interobserver variability of the appreciation of the anatomy, especially about the spatial relation between anatomical structures visualized in different 2D imaging planes, can develop.

One of the most important advantages of 3D echocardiography is that it eliminates this interobserver variability: the anatomy is shown as it really is, in 3D, including visualizing the spatial relations between anatomical structures.

However, before a 3D data set produces this desired bonus, one has to learn how to acquire and analyze the 3D data set. This means realizing, before scanning, what the regions of interest is and look for the optimal scanning plane in which this structure is best depicted. Realizing the limitations of ultrasound – a limited lateral resolution and loss of far field information – the best 3D data set is created by directing the ultrasound beam perpendicular to the defined structure, between 5 and 15 centimeters from the echo transducer. This is not by definition achieved by scanning from one of the conventional echo windows making 3D acquisition more difficult than the standard 2D echocardiographic acquisition. The result is that so-far unused and unconventional scanning planes are sometimes necessary in order to get an optimal 3D data set.

Furthermore, the understanding and analysis of 3D images can also be problematic. It was our experience that cardiac surgeons had less (or no) problems in the interpretation of 3D echo data than cardiologists and sonographers. After a learning curve of ‘thinking in 3D instead of 2D’, all cardiologists, pediatric cardiologist and sonographers who were involved in the project appreciated the 3D images and had the opinion that it contributed to their understanding of the intracardiac anatomy. Even professionals who had over 20 years of experience in echo of congenital heart disease expressed that 3D echocardiography had changed their appreciation of some cardiac abnormalities and that the depth of understanding had increased in several occasions.

Professionals without previous experience in 2D echocardiography seemed to learn the 3D images easier than people with 2D experience. This finding – the increase understanding of intracardiac anatomy due to 3D echocardiography – cannot be quantified and is therefore not measurable, but is a very important message that we have learned from the study.

This thesis is focused on the quantifiable aspects of 3D echocardiography, especially the validation by surgical descriptions and measurements, and whether or not the current technique is applicable in clinical practice. We have shown that there is a learning curve, but that it is relative short. For all studies the acquisition and analysis time was recorded.

Initially, data acquisition took at least 15 minutes and analysis of a 3D data set to a level that the primary questions could be answered was about one hour. A simple lesion was easier to evaluate and took less time than a complex case. After a few months (approximately 50 studies), acquisition time was down to 5 - 10 minutes and analysis time, once again depending on the complexity of the lesion, down to 10 - 20 minutes.

However, 3D echocardiography does not replace a 2D echocardiographic study. The better image resolution – both spatial and temporal – of 2D echocardiography, the integrated Doppler interrogation – pulsed wave, continuous wave and color Doppler – will probably guarantee a future role of 2D in echocardiographic imaging. With the current status of the 3D echocardiographic technique, it is our opinion that 3D echocardiography already deserves a place in the morphological analysis of the heart.

Training is another area where 3D echocardiography will realize significant improvements. Two-dimensional echocardiography requires a steep learning curve, which made training time-consuming and expensive, since it required visualizing the heart three-dimensionally in 2D cross-sections in order to understand the results. Real-time 3D echocardiography provides the ability to quickly view the heart as it really is, instantaneously, in 3D. This might reduce this learning curve substantially, reducing training costs and time.

It will be a step forward if we can teach professionals to start thinking ‘3D’. This will be easier for the next generation that has not the ‘ballast’ of 2D anatomy of the heart, but also the current generation of cardiologists and sonographers can, like we could, learn 3D echo. They will learn that it really adds a dimension in the understanding of congenital heart disease.

The current situation has some parallels with the introduction of 2D echocardiography after M-mode had been the standard for 10 years or more. The people experienced in M-mode had less use of it than people who were new in the field, but within a few years 2D echocardiography had become the standard imaging modality. M-mode remained to have a role in ultrasound diagnosis because of its superb temporal resolution (and to a lesser the degree the very good spatial resolution). We think that 2D will remain to play an important role in cardiac ultrasound, but that 3D echo will become the most widely used modality.

Before this becomes true, the 3D technique will have to develop further. Better image resolution is the first step. The first high frequency (4 - 8 MHz) transducer is expected to be released in spring 2006. With the advances of the transducer technology, not only resolution counts, but also the physical properties of the crystals used for emission and reception of the ultrasound waves. One of the technical innovations of the current platform is a parallel orientation of the crystals, instead of a random orientation.

This has lead to a better ratio of transmitted versus received ultrasound waves and might explain why the 3D 2-4 MHz transducer allows visualization of delicate structures which are poorly visualized with the conventional 2D 2 - 4 MHz transducers.

A second step is the possibility to have a real-time full-volume data set. The need to register several consecutive heartbeats will disappear and image artefacts, due to movements of the heart within the chest (respiration) will be reduced or eliminated. An increase of sector width will be useful to encompass the entire heart. Especially in case of a dilated heart, when analysis of cardiac function and morphology is of extra importance, a real-time wide sector will offer on-line, bedside assessment of ventricular function. We expect that with the speed of the development of calculation power by microprocessors, a real-time wide-angle 3D image will be available within a few years.

Evidently, not only the technical developments will decide in which extent 3D echocardiography will be introduced in clinical practice. As stated earlier, the speed in which ‘3D thinking’ can be taught in the clinical field is very important. It is our impression that the current technological innovations go faster than the clinical field can handle. Unlike the time that 2D echocardiography became available to clinicians – the clinicians had years to get used to this technique – the rate of progression of the technique is nowadays so fast that it has become almost an enemy of itself: why start with 3D echocardiography now, while we know that it will be more sophisticated, faster and probably cheaper within a few years? This question is far from being answered. It might explain - next to economics - the relatively scarce use of 3D echocardiography in clinical practice throughout Europe and the USA until now.

From the economic point of view: a cost-effectiveness study to compare conventional techniques for assessment of left ventricular function with the 3D echocardiography alternative will probably demonstrate that 3D is the cheaper technique. This would probably enhance the speed of introduction of 3D echocardiography in clinical practice.

Five to 10 years down the road, as more technologic advances continue to develop real-time 3D echocardiography; it will be used in guiding treatment of structural and congenital heart disease. Real-time 3D echocardiography is a significant new advancement in ultrasound that is changing the way in which cardiology is practiced from the clinic all the way to the operating room or catheterization laboratory.

Wat hebben we geleerd en wat zal het ons brengen?

Vele jaren van 3D echo studies in de experimentele fase hebben aangetoond dat 3D echo in potentie een veelbelovende techniek is om de intracardiale structuren in beeld te brengen. Echter, tot nu toe was het gebruik van 3D echo in de dagelijkse praktijk zeer beperkt: er was geen commercieel beschikbare 3D echo machine en de 3D techniek was niet ` real-time` door het beperkte vermogen van de beschikbare computerprocessoren. Dit resulteerde in een lange acquisitie en een nog veel langere offline analyse tijd.

Drie jaar geleden werd de eerste commercieel beschikbare echo machine met `real-time` 3D technologie geïntroduceerd. Philips Medical Systems ontwikkelde een matrix phased array transducer met een frequentie van 2 tot 4 MHZ, primair ter beoordeling van globale en regionale linker ventrikelfunctie.

Voor een goede beeldvorming van delicate intra cardiale structuren wordt veelal aangenomen dat een hogere resolutie nodig is dan de 2 – 4 MHZ van de huidige 3D transducer. Deze transducers leken daarom in eerste instantie niet erg geschikt voor analyse van aangeboren hartafwijkingen, vooral niet als dit zich presenteerde op de kinderleeftijd. Bij volwassenen met een aangeboren hartafwijking, is een laagfrequentie transducer soms nodig om voldoende weefselpenetratie van de ultrageluidsgolven te krijgen – laagfrequent ultrageluidgolf heeft meer weefsel penetratie dan een hoogfrequente golf – maar de resultaten wat betreft resolutie om intracardiale structuren te analyseren, is regelmatig teleurstellend. Omdat 3D analyse juist voor structurele hartafwijkingen, zoals aangeboren hartafwijkingen, veel potentiële meerwaarde heeft, hebben we er voor gekozen, ondanks bovengenoemde beperkingen de bruikbaarheid van de beschikbare laagfrequentie (2 tot 4 MHz) 3D transducer te evalueren voor de analyse van structurele hartafwijkingen, zowel bij kinderen als bij volwassenen. De resultaten zijn gepresenteerd in de hoofdstukken 3 tot 11.

De conclusie is dat ondanks een niet optimale resolutie, de 2 – 4 MHz transducer van de gebruikte echomachine, Philips Sonos 7500, voor 3D beelden zorgt die de meeste details van de intracardiale anatomie zichtbaar maakt, zelfs bij zuigelingen. Delicate structuren zoals atrioventriculaire kleppen, papillair spieren en zelfs chordea kunnen worden beoordeeld. Echter, heel dunne structuren, zoals de semi-lunair kleppen en het fossa ovalis membraan, zijn moeilijk in beeld te krijgen en `drop-out` van deze structuren komt regelmatig voor. Dit is het resultaat van de beperkte laterale resolutie, inherent aan de ultrageluidstechniek. Nadat we geconstateerd hadden dat de meeste details toch konden worden gevisualiseerd, hebben we getracht om de 3D echobeelden van de intracardiale anatomie te valideren door deze te vergelijken met de beschrijving en meting van de hartchirurg tijdens operatie. De correlatie tussen 3D echobeelden en chirurgische beschrijving die wij hebben gevonden was, zonder uitzondering, erg goed.

Daarom, concluderen wij dat 3D echocardiografie een betrouwbare weergave geeft van de intracardiale anatomie.

Na dit te hebben geconcludeerd, hebben we gekeken naar de verschillen tussen 3D echocardiografie en conventionele 2D echocardiografie. Gedurende deze studies hebben we geleerd dat de acquisitie van een goede 3D data set anders is, en als gevolg hiervan in het begin moeilijker, dan acquisitie van een complete 2D studie. Het voornaamste van 2D echocardiografie is de acquisitie van beelden van een beperkt aantal vaste echo-windows, bij voorkeur in een vaste volgorde. Aan de hand van deze 2D beelden kan elke beoordelaar zijn of haar eigen virtuele reconstructie maken van de intracardiale anatomie. De integratie van de verschillende 2D doorsneden tot een 3D beeltenis kan niet gecontroleerd worden en zou kunnen leiden tot interobserver variabiliteit van de beschouwde anatomie. Eén van de meest belangrijke voordelen van 3D echocardiografie is dat het deze interobserver variabiliteit elimineert; de anatomie wordt weergegeven zoals het echt is, in 3D, inclusief de ruimtelijke relatie tussen de anatomische structuren.

Voordat een 3D data set deze wenselijke informatie levert, moet men eerst leren hoe zo`n 3D data set wordt verkregen en geanalyseerd. Dit betekent, dat vóór het scannen, moet worden bepaald wat het gebied is, waarin men is geïnteresseerd en welke optimale scanning positie dit gebied het beste weergeeft. Realiserend de limitaties van ultrageluid – een beperkte laterale resolutie en het verlies van informatie van diep gelegen structuren – kan de beste 3D data set worden verkregen door de ultrageluidbundel loodrecht op het gebied waarin men geïnteresseerd is te plaatsen, tussen de 5 en 15 centimeter van de transducer. Dit is niet altijd te bereiken door te scannen van conventionele 2D echo posities. Dit maakt 3D acquisitie aanvankelijk moeilijker dan de standaard 2D echo acquisitie. Het resultaat is dat ongebruikelijke en onconventionele scanning posities soms nodig zijn om een optimale 3D data set te verkrijgen. Echter, onze ervaring leert dat na een relatief korte leercurve een acquisitie van een goed bruikbare 3D dataset nog hooguit 5 minuten kost.

Los van de 3D acquisitie die aanvankelijk moeilijker is dan van 2D echo, kan de analyse en het begrijpen van de 3D beelden ook tot problemen lijden. Het was onze ervaring dat thoraxchirurgen minder moeite hadden met de interpretatie van de 3D echo data dan de cardiologen en echografisten. Na een leercurve van ‘denken in 3D, in plaats van 2D’, konden alle cardiologen, kindercardiologen en echografisten die bij dit project betrokken waren de 3D beelden waarderen en begrijpen. Zelfs professionals die meer dan 20 jaar echo ervaring hadden met aangeboren hartafwijkingen benadrukten dat 3D echocardiografie in sommige gevallen had geleid tot een beter begrip en een andere interpretatie van de anatomie

Mensen, zonder voorafgaande kennis van 2D echocardiografie, lijken de 3D beelden makkelijker te begrijpen dan diegenen met jarenlange ervaring in en kennis van 2D echocardiografie.

Deze bevinding – het beter begrijpen van de intracardiale anatomie door 3D echo – kan niet worden gekwantificeerd en is daarom niet meetbaar, maar is wel een zeer belangrijke boodschap van deze studie.

Dit proefschrift richt zich op het kwantitatieve aspect van 3D echocardiografie, vooral het valideren van 3D echo met de chirurgische beschrijvingen en metingen, en de toepasbaarheid van deze techniek in de dagelijkse praktijk. We hebben laten zien dat er een leercurve is, maar deze is relatief kort. Voor alle studies is de acquisitie en analyse tijd bijgehouden. Aanvankelijk nam data acquisitie minstens 15 minuten in beslag en de analyse tijd was ongeveer 1 uur om de primaire vraag te kunnen beantwoorden. De complexiteit van de casus bepaalde in grote mate de analysetijd. Na een aantal maanden (ongeveer 50 3D echo`s later), was de acquisitietijd gereduceerd tot 5 - 10 minuten en de analysetijd, vooral afhankelijk van de complexiteit van de hartafwijking, was gereduceerd tot 10 - 20 minuten. Het is duidelijk dat met de huidige stand van techniek 3D echocardiografie 2D echocardiografie niet vervangt. De betere beeldresolutie – zowel spatieel als temporeel – van 2D echo, de integratie met Doppler – pulsed wave, continuous wave en kleuren Doppler – garanderen de rol van 2D echo in de komende jaren. Met de huidige status van de 3D echocardiografische techniek, zijn wij van mening dat 3D echocardiografie al wel een plaats verdient in de morfologische analyse van het hart, naast voornoemde echotechnieken

Training is een ander gebied waar 3D echo mogelijk een belangrijke verbetering kan bewerkstelligen. Tweedimensionale echocardiografie heeft een vrij lange leercurve. Voor een goed begrip van de anatomie moet uit multiple 2D doorsneden een eigen 3D reconstructie worden opgebouwd om de resultaten te kunnen beoordelen. Real-time 3D echocardiografie levert ons direct een beeld van het hart zoals het in de werkelijkheid is, in 3D. Dit zou de leercurve substantieel kunnen reduceren, wat trainingskosten en -tijd zal verminderen.

Het zal een stap vooruit zijn als we professionals kunnen leren om 3D te denken. Voor de volgende generatie zal het veel makkelijker zijn om 3D echo te begrijpen, omdat zij de ballast van de 2D anatomie van het hart niet hebben. Maar het is onze overtuiging dat ook de huidige cardiologen en echografisten, die wel die “ballast” hebben en het veel moeilijker zullen leren, zullen inzien dat 3D een extra dimensie geeft in de begripsvorming rondom aangeboren hartafwijkingen.

De huidige situatie in de echocardiografie heeft enkele parallellen met de introductie van 2D echo nadat M-mode voor meer dan 10 jaar de standaard was geweest. Degenen met veel M-mode ervaring hadden minder baat bij deze nieuwe techniek dan degenen die nieuw in het veld waren en toch is binnen enkele jaren 2D echocardiografie de standaard beeldvormingtechniek geworden.

M-mode is hiermee niet verdwenen, het blijft een belangrijke rol spelen in de echocardiografische diagnostiek vanwege zijn uitstekende temporele resolutie (en ook goede spatiele resolutie). Wij denken dat 2D een belangrijke rol blijft spelen, maar dat 3D echo in de toekomst de meeste gebruikte beeldvormingtechniek zal worden.

Voordat dit de werkelijkheid is, zal de 3D echo techniek werden ontwikkeld moeten worden.

De eerste stap moet de verbetering van de beeldkwaliteit zijn. De eerste hoogfrequentie (4 – 8 MHz) transducer zal, naar verwachting, in het voorjaar 2006 worden geïntroduceerd. Met de ontwikkeling van de transducer technologie, is niet alleen resolutie belangrijk, maar ook de fysische kenmerken van de kristallen die ultrageluid uitzenden en ontvangen. Een van de huidige technische innovaties is de parallel georiënteerde positie van de kristallen in plaats van een willekeurige rangschikking. Dit heeft geleid tot een betere ratio van uitzendend versus ontvangend ultrageluid en zou kunnen verklaren waarom de 3D (2-4 MHz) transducer dunne structuren wel redelijk goed kan weergeven terwijl de conventionele 2D (2-4 MHz) transducer dat maar matig kan.

De tweede stap moet een vergroting van de full-volume data set in real-time zijn. Het opnemen van een full-volume 3D data set geschiedt nu door meerdere op een volgende hartslagen te registreren en aan elkaar te zetten, waarbij de kans op artefacten ontstaat. Met een real-time full-volume data set zullen deze artefacten kunnen worden vermeden. Het vergroten van de opname sector is noodzakelijk om het gehele hart in de data set te vangen. Maar ook voor patiënten met gedilateerde harten, waar analyse van hartfunctie en morfologie van essentieel belang is, is een brede ‘real-time’ sector noodzakelijk om real-time en aan het bed de ventrikelfunctie beoordelen. Dit geldt zowel voor de linker als rechterventrikel. Het ligt in de lijn der verwachting dat met de huidige technologische ontwikkelingen, een ‘real-time’ 3D full-volume data set binnen enkele jaren beschikbaar is.

De technische ontwikkelingen zullen niet alleen de introductie van 3D echocardiografie in de dagelijkse praktijk bepalen. Zoals eerder beschreven, is de ontwikkeling in welke mate ‘3D denken’ kan worden geleerd in de klinische praktijk net zo belangrijk. De indruk bestaat dat de huidige technologische innovaties sneller gaan dan clinici kunnen bijhouden. Dit in tegenstelling tot de introductie van 2D echocardiografie. De technische ontwikkelingen gaan nu zo snel dat het bijna een vijand van zichzelf gaat worden. Vele in het veld vragen zich af: “Waarom zou ik nu met 3D echo beginnen, terwijl er binnen een (paar) jaar een veel snellere en goedkoper 3D techniek beschikbaar zal zijn?” Deze vraag is nu nog verre van beantwoord. Een mogelijke verklaring – naast economische redenen – is dat de 3D echo relatief weinig in de dagelijkse praktijk gebruikt wordt, zowel in Europa als de USA. Een kosteneffectiviteit studie, waarbij conventionele technieken voor de beoordeling van de linker ventrikelfunctie worden vergeleken met 3D echocardiografie, zou waarschijnlijk aantonen dat 3D echo goedkoper is.

Een dergelijke studie is nog niet verricht, maar zou de introductie van 3D echo in de dagelijkse praktijk zeker versnellen.

Wij verwachten dat binnen vijf tot 10 jaar, 3D echocardiografie verder ontwikkeld is en als belangrijkste echocardiografische methode voor diagnostiek van structurele en aangeboren hartafwijkingen aangewezen is. Real-time 3D echocardiografie zal een significant nieuwe vooruitgang in de echocardiografie blijken te zijn en zal de weg die de praktiserende cardioloog bewandeld van de kliniek naar de operatiekamer of catheterisatiekamer duidelijk veranderen.

Summary

This thesis investigates the role that real-time 3D echocardiography might play in the analysis of structural heart disease. The 3D echocardiographic assessment of patients with a variety of congenital heart disease is described, with specific focus on description and measurement of intracardiac anatomy and functional assessment.

In **chapter 1**, the outline of the thesis is given. This thesis focuses on the feasibility and clinical applicability of real-time 3D echocardiography in daily patient care for congenital heart disease and whether 3D echocardiographic images give a reliable reflection of the intracardiac anatomy in a wide variety of congenital heart defects.

Chapter 2 provides an overview of the current status of 3D echocardiography, with emphasis on the use of the real-time mode, the technical possibilities of the new matrix array transducer and its current and future applications. Three-dimensional echocardiography has been an important research goal for many years. Since the introduction of 2D echocardiography, it has been “a quest for the holy grail” to create a real and real-time 3D image of the heart. However, most approaches towards 3D echocardiography were off-line and based on the sequential rotational scanning and acquisition of multiple cross-sectional images. Despite temping results, long acquisition and analysis time in combination with poor image quality hampered their introduction in clinical practice. The current commercially available matrix array technology has overcome a large part of the technical problems: spatial and temporal resolution is significantly increased. The marked reduction in acquisition time and the unique possibility of on-line rendering on the ultrasound system boosted clinical use of 3D echocardiography. The integration and future quantification of new parameters together with on-line review allows new insights into cardiac function, morphology and synchrony that offer great potentials in the evaluation of right and left global and regional ventricular function, diagnosis of small areas of ischemia, congenital and valvular heart disease and effects of biventricular pacing in dilated heart asynchrony.

In **chapter 3**, a detailed description is given regarding the technique, how to acquire the best 3D echocardiographic images and how to assess various regions of interest of the heart by presenting a simple but unified concept of image orientation. On the basis of > 400 real-time 3D echocardiographic examinations, we learned that there was a considerable learning curve for both 3D echocardiographic data acquisition and analyses. This was true even for echo technician or cardiologist who have worked with echocardiography for many years.

Chapter 4 presents a quantitative evaluation by real-time 3D echocardiography of the various features of an atrial septal defect (ASD) and the atrial septum that are important for patient selection for transcatheter closure.

The 3D echocardiographic reconstruction provides us with unique projections of the atrial septum and a myriad of specific cut planes allowing accurate determination of ASD localization, size and the extent of the surrounding tissue. These advantages of real-time 3D echocardiography, together with the non-invasiveness and relatively short acquisition and analysis time, as shown in this study, make that real-time transthoracic 3D echocardiography can replace transesophageal echocardiography for the selection of patients for surgical or transcatheter closure in a large proportion of patients.

In **chapter 5**, RT-3DE is validated for the assessment of AV valve morphology by comparing 3D echocardiographic data with surgical findings. It also addresses the issue whether RT-3DE is applicable in clinical practice in patients with an atrioventricular septal defect and whether it has additional value on top of the hemodynamic measurements derived from 2D echocardiography. The most important finding in this study is the view of the entire AV valve apparatus in one single 3D `en face` reconstruction. The results show that real-time 3D echocardiography is accurate for the assessment of atrioventricular septal defects and correctly depicts the AV valve morphology. The ability of RT-3DE to accurately identify these anatomical features in adults and young children, might allow a better preoperative planning of the surgical approach and an improved estimation of chances on a successful AV valve repair.

Chapter 6 demonstrates the clinical application of real-time 3D echocardiography in patients with atrioventricular septal defect. New insights were obtained into the dynamic morphology of the left-sided AV valve and left ventricular outflow tract anatomy after AVSD repair. The simple and reproducible method of analysis of the 3D echocardiographic dataset, on top of the standard 2D echocardiographic assessment, allows better understanding of the interplay between left-sided AV valve morphology and function.

Chapter 7 focuses on the quantitative assessment of ventricular septal defects (VSDs) by RT-3DE. Real-time 3D echocardiographic imaging provides an undisputed presentation of ventricular septal defect morphology and spatial orientation. A great advantage of 3D echocardiography is the possibility to create an `en face` view of the VSD, both from the left and right ventricular (RV) side which is impossible to obtain with 2D echocardiography. Since a VSD is surgically closed through a right atrial (or RV) approach, it is now possible to provide a clear assessment of the VSD to the cardiac surgeon about the dimension, shape and relation of the defect to various RV septal structures. An excellent correlation was observed between for VSDs measurements obtained by RT-3DE looking from a RV view compared to the surgical findings.

The morphological information from 3D echocardiography can be used on top of the hemodynamic measurements derived from 2D echocardiography, and may lead to a further optimalization of the planning of surgical or catheter-interventional procedures in patients with a VSD.

In **chapter 8***,* the first study using the second-generation 3D matrix transducer for the assessment of left ventricular (LV) volume and function in congenital heart disease is described. In patients with congenital heart disease, the reliability of 2D echocardiographic assessment of LV function is limited because the used Simpson's method requires a round, concentrically contracting LV to produce reliable results, which in congenital heart disease the LV is often abnormally shaped and asymmetrical. A 3D imaging modality can solve the problem of the LV geometry, it does not rely on assumptions but actually depicts the LV shape. This study shows a good agreement between RT-3DE using manual border tracing and MRI for the assessment of LV volume and function. Furthermore, the intra- and interobserver variability was very limited. This implies that this technique is largely operator-independent and can be used in clinical practice. Real-time 3D echocardiography may potentially provide convenient, bedside and comprehensive evaluation of cardiac function in patients with congenital heart disease.

Chapter 9 focuses on the use of RT-3DE for the assessment of LV mass in congenital heart disease. It has been demonstrated that elevated LV mass, as defined by echocardiography, is associated with adverse prognosis and is useful for risk stratification and follow-up in the general population as in the congenital heart disease population. In the presented study, all patients had distortion of the LV geometry originated from the congenital heart malformation itself or as a result of a dilated right ventricle. Geometric assumptions about the shape of the left ventricle and image plane positioning errors are believed to be the most important limited factors for reliable M-mode measurements. Our initial experience with RT-3DE for determination of LV mass in patients with abnormally shaped left ventricles showed high accuracy and low interobserver variability in patients with good and moderate echo image quality. But only good image quality RT-3DE data sets obtained with the commercially available equipment provided images with sufficient detail to allow easy off-line analysis.

In **chapter 10**, the feasibility, accuracy and clinical applicability of RT-3DE in a pediatric population were evaluated by studying 100 children with a variety of congenital heart defects. Despite the shortcoming of the current commercially available RT-3DE equipment for children in terms of limited image resolution and large footprint of the transducer, both qualitative and quantative analysis of 3D data sets were evaluated by surgical measurements and descriptions. We concluded that RT-3DE can be used in the clinical practice for the assessment of intracardiac anatomy in infants and children with congenital heart disease.

The information derived from the 3D reconstructions can be taken into consideration in the preoperative planning and management regarding interventional or surgical therapy: Real-time 3D echocardiography is no longer a research tool, but can be used in daily clinical practice in pediatric cardiology.

Chapter 11 presents a novel approach for visualization of dynamic 3D echocardiographic data, known as virtual reality. The 3D echocardiographic data sets generated by a commercial available echo machine can be visualized as a dynamic hologram inside the virtual reality system, I-Space. Until now, the 3D echocardiographic reconstructions could only be seen on a flat screen, but virtual reality makes it possible to `dive` into the actual 3D anatomy of the heart. We show that professionals, familiar with intracardiac anatomy, can learn how to handle the technique and cut through these holograms within 10 minutes. All appreciated the real 3D presentation of the 3D data and realized once more that one of the important shortcomings of the current marketed 3D systems is the fact that 3D data are displayed on a 2D computer screen. The shortcoming of the I-Space technology is that it is very expensive and the size of the I-Space very large. As in many computer-dependent technological breakthroughs in the past, miniaturizing the systems and make these systems much cheaper, will be necessary to implement it in clinical practice.

Chapter 12 provides an overall discussion regarding 3D echocardiography

Dankwoord

Een dankwoord suggereert meestal de afsluiting van een onderzoeksperiode. Wat mij betreft is dit proefschrift echter een begin en een stimulans om 3D echocardiografie verder te ontwikkelen en te introduceren in onze cardiologische praktijk. Ik heb met ontzettend veel plezier aan dit proefschrift gewerkt. De intensieve samenwerking tussen de verschillende vakgebieden, cardiologie, thoraxchirurgie en kindercardiologie, heeft ertoe geleid dat dit onderzoek in een betrekkelijk korte tijd heeft kunnen plaatsvinden. Ik kijk er dan ook naar uit om deze samenwerking de komende jaren voort te zetten.

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Curriculum Vitae

Annemien Elise van den Bosch was born April 10, 1976 in Rotterdam, the Netherlands. She graduated in 1994 at the Montessori Lyceum Rotterdam: gymnasium certificate. From 1994 to 2000 she studied Medicine at the Erasmus University of Rotterdam and received her pre-medicine degree (‘doctoraalexamen’) in September 1998. During her study she completed an internship at the Great Ormond Hospital for sick children, London, UK and performed research in the field of cardio-thoracic surgery and pediatric cardiology. In December 2000, she obtained her Medical Degree (cum laude) at the Erasmus University of Rotterdam.
As part of the training in cardiology she worked and studied internal medicine from January 2003 to June 2004 at the Ikazia Hospital in Rotterdam
In June 2004 she started working as a research fellow for the Department Cardiology at the Thoraxcenter of Erasmus MC in Rotterdam and could further explore her interest in congenital heart disease.
After receiving her PhD she will continue her training in cardiology with a special interest in congenital heart disease at the Erasmus MC in Rotterdam.
The author of this thesis lives together with Boudewijn Krenning and they have one daughter, Mijntje (2005).