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THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN THE ASSESSMENT OF CARDIAC TUMORS: THE ADDED VALUE OF THE EXTRA DIMENSION

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Introduction

Echocardiography is the most frequently used imaging modality in the assessment of cardiac tumors. Historically, this evaluation had been based on the analysis of 2-dimensional (2D) echocardiographic sectors of the heart. The information obtained from orthogonal tomographic planes from several acoustic windows was used in an attempt to mentally reconstruct a model of how the tumor would actually look in 3 dimensions and how it would relate to its adjacent structures.

New technology using matrix-array-transducers has permitted the development of real-time three-dimensional echocardiography (RT3DE), bringing cardiac imaging to a new dimension. Now it is possible to capture and analyze the entire volume of a cardiac tumor in a single cardiac cycle. This new imaging modality provides valuable clinical information that empowers echocardiographers with new levels of confidence in the diagnosis of heart disease.[1]

This manuscript discusses the added value of this new technology in the echocardiographic assessment of cardiac tumors.

Echocardiographic Assessment of Cardiac Tumors

The complete echocardiographic evaluation of a cardiac tumor is summarized in Table 1. It starts with a thorough description of its location and relationship to adjacent structures. Tumors can be either intra- or extra-cardiac. The description should include the location and mechanism of implantation of the tumor to the heart (for instance, "pedunculated mass attached to the basal segment of the inferior wall through a long stalk"), the malignancy's route of access to the heart (such as superior or inferior vena cava, pulmonary veins, direct access through a wall), and whether or not the tumor is primarily attached to the heart (Figure 1).

The characterization of the shape, longest dimensions, and ideal volume of the mass is essential. A description of the hemodynamic consequences of the mass should also be reported. The echocardiographer should then integrate all the information to generate a differential diagnosis.

The anatomic assessment of the tumor should be complemented with an accurate calculation of cardiac chamber dimensions, left ventricular volumes and ejection fraction (EF).

Once all this information is taken in consideration, a decision can be made as to the most appropriate treatment for the patient (chemotherapy, immune therapy, radiation or surgery).

The 3D Examination

Three acquisition modes are used with RT3DE in the evaluation of cardiac tumors: full volume, live 3D and 3D zoom (a smaller, magnified pyramidal data at a higher resolution).[2]

Unlike the other modes, the full-volume (wide angle) acquisition usually requires electrocardiographic gating. Depending on the vendor and the resolution desired, the gating requires somewhere between 2 to 6 cardiac cycles, as the dataset is compiled by merging the

Table 1. Echocardiographic evaluation of cardiac masses

1. Characterization of the mass
a. Location: Intra- or extra-cardiac
b. Relationship with adjacent structures
c. Site and mechanism of implantation
d. Route of access to the heart
e. Shape, size and volume
f. Hemodynamic consequences
2. Differential diagnosis
a. Benign
1. Embryonic remnants
2. Normal variants (false chords, heavy trabeculation, accessory papillary muscles)
3. Thrombi (mural or associated with catheter or devices)
4. Benign cardiac tumors
5. Cardiomyopathy (apical HCM, noncompaction cardiomyopathy)
6. Vegetations
b. Malignant
1. Primary
2. Metastatic
3. Accurate estimation of LV volumes and ejection fraction
4. Therapeutic decision making

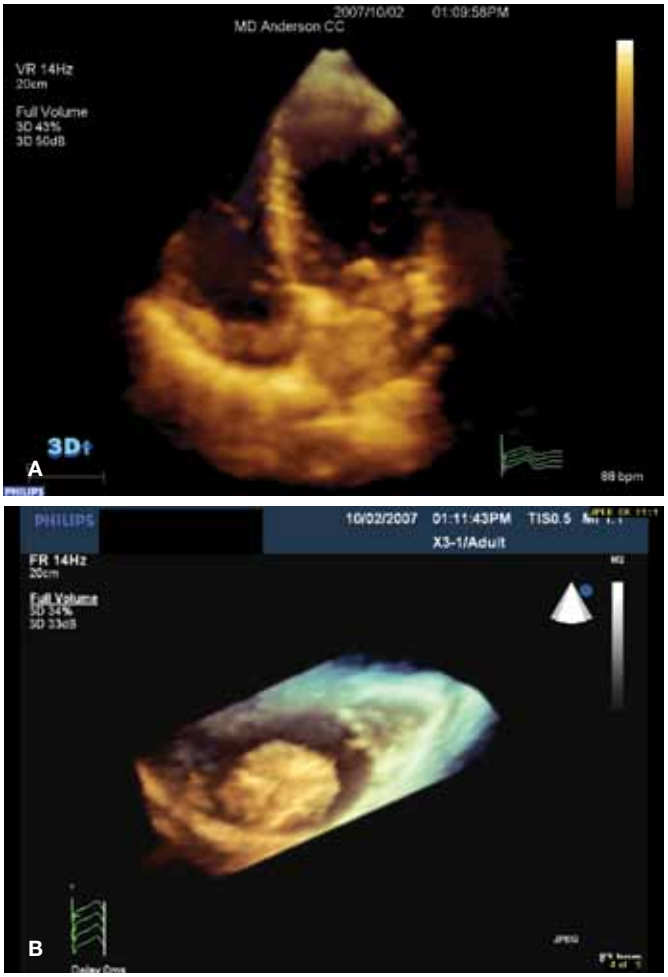

Figure 1. Full-volume acquisition (A) and cropped image (B) obtained from the apical 4-chamber view of a 22-year-old male with a recurrent metastatic osteosarcoma. The images show the tumor accessing the heart through the right upper pulmonary vein.

narrower pyramidal scans during the consecutive heartbeats. To minimize reconstruction artifacts, data should be acquired during suspended respiration. Full-volume acquisitions can be obtained from the parasternal, apical 4-chamber, apical 2-chamber, and sub-costal views. However, the availability of a larger amount of data in these big pyramids of information comes at the expense of lower image resolution. Hence, imaging with narrow angles (live 3D) is recommended if high-resolution images of the cardiac mass are desired.

Real Time 3D Evaluation of Cardiac Tumors

In our institution, the evaluation of a cardiac tumor using transthoracic RT3DE includes, at the minimum, performing a full-volume acquisition in the parasternal long axis and in the apical 4-chamber views. If the mass in question is located in the right atrium, a full-volume acquisition and live 3D images are obtained from a modified right ventricular inflow view and the subcostal window.

Live 3D images of the right parasternal and supraclavicular windows have been used in the echocardiographic assessment of thrombus in the innominate vein and the superior vena cava (SVC).[3] If the clinical question is not successfully answered by the transthoracic RT3DE, a real-time 3D matrix array transesophageal echocardiogram (3D-MTEE) is performed. In addition to the 2D images obtained following our lab protocol, a full-volume acquisition of the left ventricle (LV) is obtained. Depending upon the location of the mass in question, 3D-zoom images are captured from the mitral valve (MV), the tricuspid valve (TV), the left atrial appendage (LAA), the left upper pulmonary vein (LUPV), and the interatrial septum (IAS). Full-volume and live 3D acquisitions in the bicaval view are useful in characterizing masses in the SVC, inferior vena cava (IVC), inter-atrial septum, and right atrium.

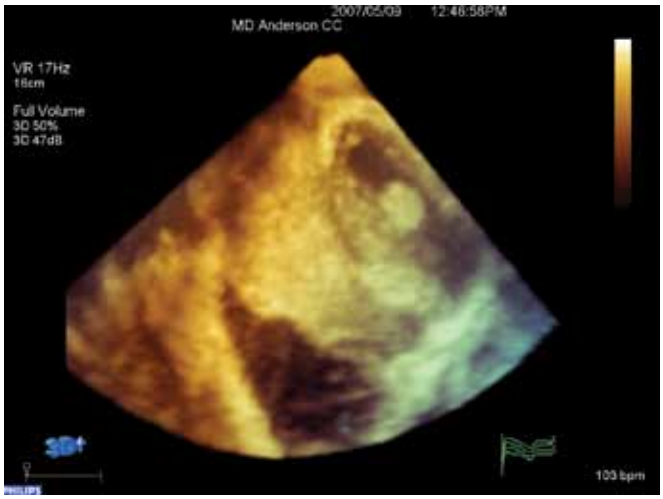

Figure 2. Full-volume acquisition obtained from the parasternal long axis view of a 35-year-old female with a primary cardiac sarcoma. There is evidence of a large exophytic mass originating from the base and mid segments of the inferolateral wall. An intracavitary mass is also visualized, originating from the mid segment of the inferior wall.

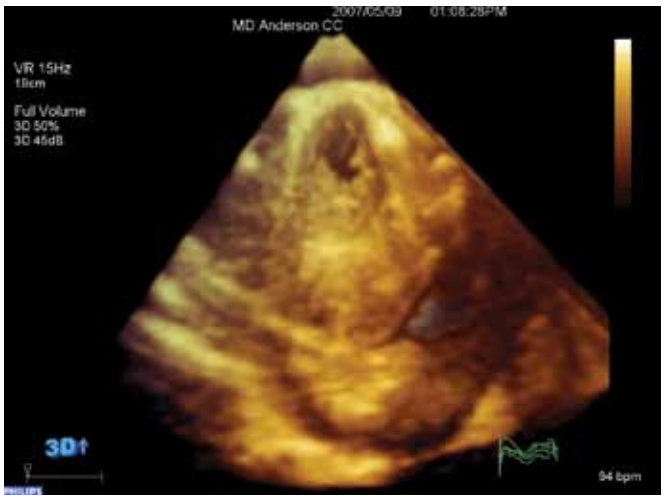

Figure 3. Cropping of a full-volume acquisition obtained from the apical 4-chamber view of the patient with primary cardiac sarcoma mentioned in Figure 2. The tumor originates from the inferior, inferolateral and anterolateral walls of the LV. A large pleural effusion is seen with large amounts of echodense material visualized floating in the space.

Differential Diagnosis

The differential diagnosis of intracardiac masses includes tumors (benign, malignant or metastatic), normal structures or their variants, embryonic remnants, thrombi, masses associated with the presence of cardiomyopathy (apical hypertrophic cardiomyopathy, noncompaction cardiomyopathy and hypereosinophilic syndrome) and masses, or complications associated with device implantation (Table 1).

Primary tumors are far less common than metastatic tumors in the heart, occurring in at least 7 out of 10,000 people (Figure 2).[4] Benign primary cardiac tumors occur more frequently than malignant ones. The most common cardiac tumor is a myxoma. In a large, single-institution series of primary cardiac tumors at the University of Minnesota, 42% were cardiac myxomas and 16% were malignant tumors (sarcomas).[5]

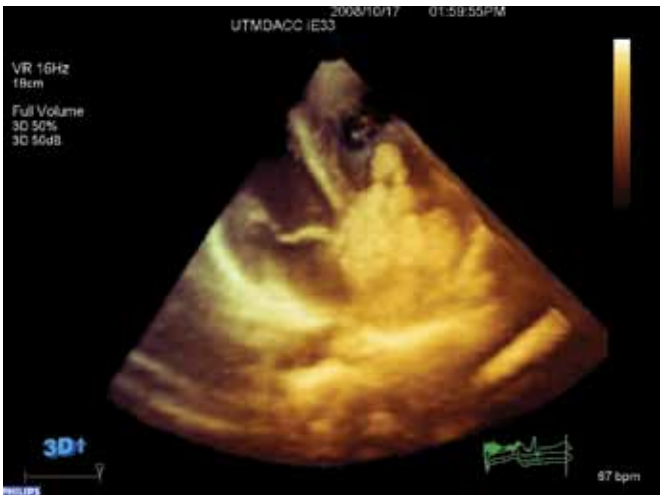

Figure 4. Full-volume acquisition obtained from a modified right ventricular inflow view of a 31-year-old patient with hepatocellular carcinoma. The mass accesses the heart through the IVC. The mass prolapses into the right ventricle through the tricuspid valve.

Added Value of RT3D Echocardiography in the Assessment of Intra-Cardiac Benign, Malignant, and Metastatic Cardiac Tumors

Unlimited slicing and cropping

Once a full-volume 3D data set is acquired, it can be sliced and cropped in many different ways. This allows manipulation of images in space, obtaining views and planes, and aligning structures in ways that were impossible to get with 2D imaging.

This feature is particularly useful in the way in which echocardiography is practiced in the United States, where images are captured by a sonographer and interpreted later by a physician. The availability of the full-volume acquisition allows the echocardiographer to slice and crop the heart in as many ways as required to obtain a comprehensive tomographic evaluation of the mass (Figure 3). The full volume allows for a detailed description of the location, shape, attaching interface and relationship to adjacent structures of the cardiac mass (Figure 4). In addition, it is well known that 2D echocardiography is very operator dependant. RT3DE, on the other hand, permits acquisition of the cardiac mass images with less dependence on the operator's

skill level. It is also important to realize that the availability of all of the information in just one capture can significantly reduce the time needed to fully characterize the cardiac tumor.

Evaluation of the size of the cardiac mass

Echocardiography is the method of choice to establish the diagnosis and prognosis of cardiac masses, whether they are thrombi, vegetations or tumors.[6] Maximum diameter measurements from 2D echocardiography are routinely used to determine mass size. The size of an intracardiac mass has important clinical implications in predicting embolic events, congestive heart failure, and death, and as an efficacy assessment after treatment (anticoagulation, antibiotics and chemotherapy).[6]

However, most masses are irregularly shaped, making it difficult to accurately image or select the largest diameter. Nanda et al. reported that 2D measurements from a transthoracic or a transesophageal study underestimates the true maximum diameter of irregularly shaped structures.[7] In the case of cardiac masses, this can lead to a misrepresentation of the patient's prognosis. RT3DE images the entire volume of a mass, which allows for accurate measurements in multiple planes. Asch et al. conducted a study testing the hypothesis that measurements of the maximum diameter of a mass by RT3DE are larger than those obtained by 2D. He reported that 2D transthoracic and 2D transesophageal consistently underestimated the maximum diameter by 24.6% (P<0.001) and 19.8% (P=0.01), respectively, as compared to RT3DE. The measurements were fast and with excellent intraobserver and interobserver variability (better than 2D echocardiography). The authors suggested that RT3DE may be the technique of choice for the noninvasive evaluation of intracardiac mass size.[6]

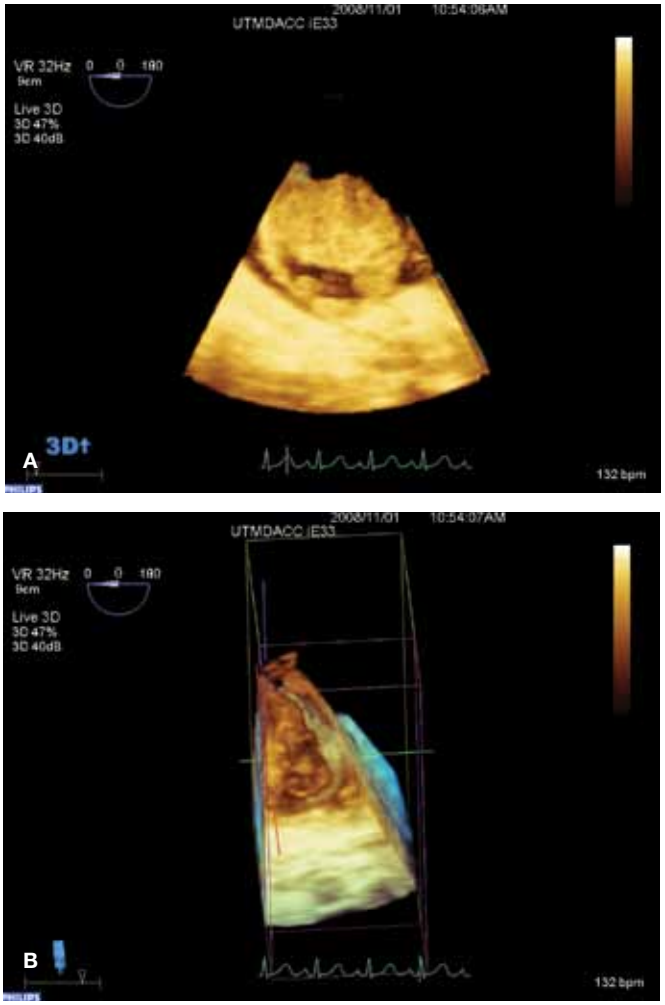

Figure 5. (A and B) Orthogonal views from live 3D-MTEE obtained at 0 degrees from a 61-year-old male with a metastatic thymoma. The mass appears homogenously echodense in frame A. When the mass is cropped from the orthogonal plane, it appears to have a cystic component as well.

Evaluating the composition of the tumor

One of the critical aspects of characterizing a cardiac tumor is the evaluation of its composition (Figure 5). Mehmood et al. demonstrated in a preliminary study the superiority of live 3D over 2D transthoracic echocardiography (2D-TTE) in assessing left atrial (LA) tumors in patients with myxomas and hemangiomas. Because of the unique ability of live RT3DE to systematically section and view the contents of an intracardiac mass, LA myxomas in the patients studied could be more confidently diagnosed by noting isolated echolucent areas consistent with hemorrhage/necrosis in the tumor mass. In patients with hemangiomas, live RT3DE showed much more extensive and closely packed echolucencies with little solid tissue, as compared to a myxoma consistent with a highly vascularized tumor.[8] Other studies have demonstrated that RT3DE provides a more comprehensive assessment of the inner structure of the mass that correlates better with pathologic findings (necrosis, hemorrhage, cystic areas or fibrotic bands).[9, 10]

Unparalleled level of anatomic detail

Recent advances in ultrasound transducer technology have lead to the miniaturization of matrix array transducers, allowing their incorporation into the tip of an esophageal probe and, in turn, the ability to perform 3D-MTEE.

Sugeng et al. recently published the initial experience of her group using 3D-MTEE. They tested the feasibility and clinical utility of this new technology in the imaging of different cardiac structures, including mitral, aortic, and tricuspid valves, interatrial septum, LA appendage, and pulmonic veins. The percentage of

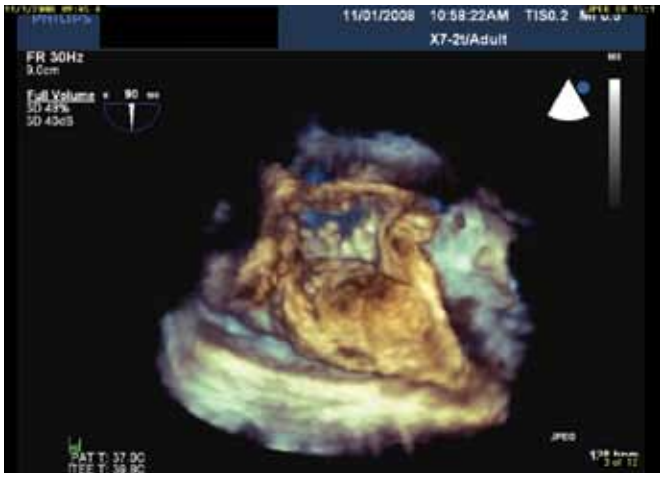

Figure 6. Cropped full-volume acquisition obtained from a 3D-MTEE at 90 degrees from the patient with metastatic thymoma mentioned in Figure 5. The tumor completely obliterates the superior vena cava (SVC) and extends through the right atrium into the tricuspid valve annulus. Please note the mass is heterogeneous. The mass appears uniformly echodense in the SVC and at the cavo-atrial junction, and appears cystic as it gets close to the tricuspid valve annulus.

patients in whom each cardiac structure was assigned an optimal score of 2 was 85%–91% of all scallops for both mitral valve leaflets, 84% of the interatrial septum, 86% of the left atrial appendage, and 77% of the left ventricular endocardium.[11]

One of the biggest limitations of assessing cardiac masses with 2D echocardiography is the possibility of actually "missing" the mass during the evaluation. As mentioned before, orthogonal planes are used to evaluate cardiac masses; if the mass happens to be anatomically located in an area between the imaging planes, it would not become apparent during the examination.

3D-MTEE has allowed us to acquire and analyze the full volume of 3-dimensional structures with a new level of unparalleled anatomic detail (Figure 6). We are now able to really understand the 3D nature of the left atrial appendage and its unique anatomic relationship with the ridge and the left upper pulmonary vein. With this new technology, we are also able to visualize the foramen ovale of the interatrial septum from the left or the right atrium, taking advantage of its posterior anatomic location.

Evaluation of associated abnormalities

Real-time 3D echocardiography can also enhance the ability of the echocardiographer to detect associated abnormalities and conditions that predispose to the development of a mass, such as an LV apical aneurysm or rheumatic mitral valve disease.[12-15]

Added value in the evaluation of embryonic remnants and normal variants

Normal cardiac structures (moderator band or false chords) or their variants (accessory papillary muscles) can be confused with cardiac tumors in a 2D-TTE. In addressing these questions, we find it useful to obtain a full-volume acquisition and crop the structure to understand its 3D relationship. We also receive frequent referrals to our laboratory to characterize masses in the right atrium, where the differential diagnosis includes a normal structure (prominent IVC ridge or a crista terminalis), embryonic remnants (prominent eustachian valve or a Chiari network), a thrombus, a tumor or a tumor-thrombus arising from the IVC.[16-18] The ability

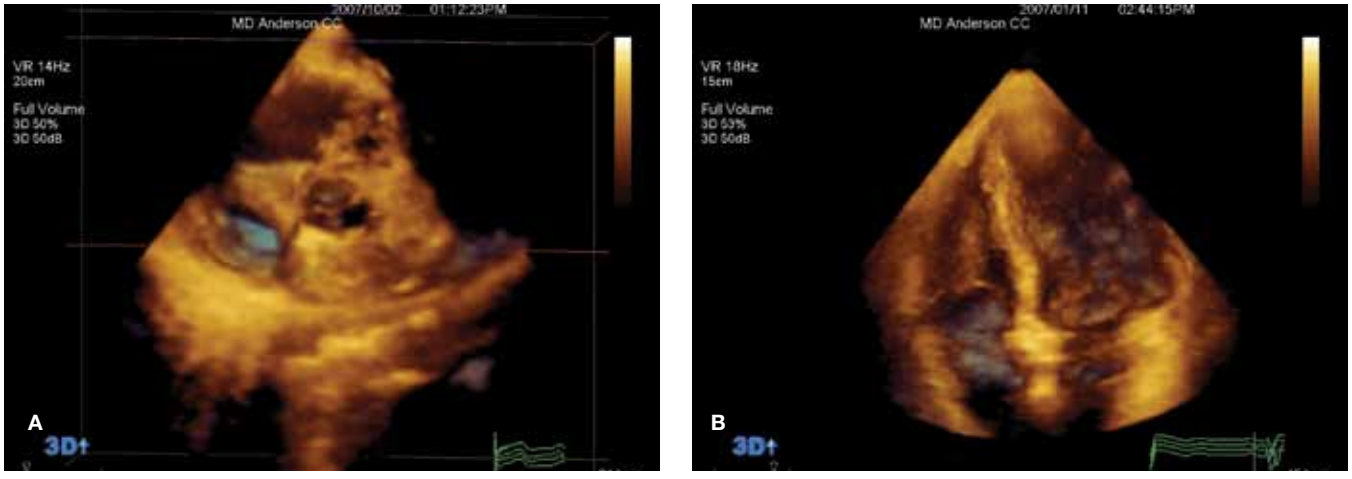

Figure 7. (A) Full-volume acquisition obtained from the short axis view of the patient with osteosarcoma shown in Figures 2 and 3. The mass was not amenable for surgical resection as it involved the aortic root. (B) Full-volume acquisition obtained from the apical 4-chamber view of a 60-year-old male with metastatic squamous cell carcinoma of the penis. The mass was not thought to involve the tricuspid valve after 2D-TTE evaluation; however, follow-up RT3DE revealed involvement of the tricuspid valve.

to use the live-3D mode to see these 3D structures in motion has in many instances allowed us to answer questions without conducting more invasive tests such as a 3D-MTEE.

Surgical planning

Muller et al. conducted a study evaluating the value of 3D-MTEE as an adjunct to conventional 2D imaging in preoperative evaluation of cardiac masses. In 37% of the patients, 3D-MTEE revealed 1 or more items of additional information regarding type and site of attachment, surface features, and spatial relationship to surrounding structures. They estimated that in at least 18% of all intracardiac masses, 3D-MTEE can be expected to deliver supplementary information. In 6 of their patients, the additional findings led to decisions deviating from those made on the basis of 2D-TEE. The authors concluded that the information revealed by 3D imaging facilitated therapeutic decision-making, especially the choice of an optimal surgical access prior to removing the intracardiac mass (Figure 7).[19]

Sugeng et al. demonstrated that 3D-MTEE consistently provided excellent quality, volume-rendered images of mitral valve components, including anterior and posterior leaflets as well as the annulus and subvalvular structures. This finding suggests that 3D-MTEE may become one of the modalities of choice to assess this valve during preoperative planning of mitral valve surgery, including the resection of tumors from the valve.[11, 20] Le Tourneau et al. reported on the use of live 3D-MTEE in assessing tumors of the aortic valve (papillary fibroelastomas). In their opinion, the use of this technology improved their operative planning.[21] However, the visualization of the aortic valve by 3D-MTEE appeared to be more challenging, as it is an anteriorly located cardiac structure; optimal visualization of the aorta from both the aorta and the LV perspectives was possible only in 18%–22% of the patients.[11] 3D-MTEE has also been used to assess neoplasms of the pulmonic valve.[22]

Visualization of the true apex and calculation of LV volumes and ejection fraction

Besides a thorough evaluation of cardiac tumors and their hemodynamic consequences, it is essential to be accurate in the reporting of LV ejection fraction. The mainstay in the treatment of cardiac sarcomas continues to be anthracycline-based regimens, which are known to cause cardiac toxicity in the form of systolic dysfunction. Hence, the accurate calculation of volumes and ejection fraction is essential in the initial and follow-up evaluations of these patients.

A variety of methods are available for calculation of EF using 2D echocardiography. Unfortunately, they all have 2 big limitations: they are based on geometrical models that have not considered the architecture of an abnormal sick heart, and they are strongly affected by foreshortening of the LV cavity by the tomographic plane of the 2D image. RT3DE has emerged as a solution to these problems. The ability to capture a full-volume acquisition of the LV allows for accurate identification of the true apex of the heart. An algorithm based on the detection of the endocardial border in turn allows for direct quantification of LV volumes without multiplane tracing or geometric modeling.

Jacobs et al. compared 2D and 3D echocardiography against cardiac magnetic resonance imaging (CMR) in their ability to accurately calculate end diastolic volume, end systolic volume and ejection fraction. RT3DE measurements correlated highly with similar measurements by CMR (r = 0.96, 0.97, and 0.93 for EDV, ESV, and EF respectively).[23] The small underestimation of volumes, as compared to CMR, will hopefully be reduced as we gain experience with this new technique and learn to trace the endocardium underneath the trabeculations and not on top of them.[1]

More recently, contrast has been used to enhance RT3DE images. Contrast enhancement was found not only to improve the accuracy and reproducibility of LV volume measurements in patients with poor image quality, but also to enhance the assessment of regional wall motion from RT3DE datasets. The authors found that, with the use of selective dual triggering to minimize bubble destruction by ultrasound energy, contrast enhancement increased the accuracy of RT3DE-based analysis of regional LV function against CMR reference, and its reproducibility to levels similar to those noted in patients with optimal imaging quality.[24] The improved accuracy and reproducibility of RT3DE-based LV volumes and EF measurements are of vital importance to patients with cardiac tumors, since clinical decision-making relies completely in this measurement. In the study mentioned above by Jacobs, there was evidence of a wider limit of agreement for EDV, ESV, and EF (29 mL, 24 mL, and 9.5%) for 2D-TTE, as compared to RT3DE (17mL, 16 mL and 6.4%).[23] This means that when using 2D-TTE echocardiography, the ejection fraction can be potentially miscalculated by 9.5 points.

In our institution, anthracyclines are discontinued if patients have a symptomatic drop of more than 5% of their ejection fraction below 50% or an asymptomatic drop of more than 10% of their initial EF. The miscalculation of the ejection fraction by 2D-TTE can lead to the decision by the oncologist to erroneously stop the anthracycline-based regimen, due to concern for a toxic-

ity that is actually not occurring and is solely the result of the inherent limitations of the technology used.

Conclusions

Real-time 3D transthoracic and transophageal echocardiography have greatly improved the echocardiographic detection and evaluation of cardiac masses and tumors. A detailed characterization of the mass size, composition, location and relationship to adjacent structures, in conjunction with an accurate assessment of LV volumes and ejection fraction, empowers the echocardiographer with a new level of confidence in the diagnosis and surgical planning of the patient with a cardiac mass.

References

1. Mor-Avi V, Sugeng L, Lang RM. Real-time 3-dimensional echocardiography: an integral component of the routine echocardiographic examination in adult patients? Circulation. 2009 Jan 20;119(2):314-29.
2. Hung J, Lang R, Flachskampf F, Shernan SK, McCulloch ML, Adams DB, Thomas J, Vannan M, Ryan T; ASE. 3D echocardiography: a review of the current status and future directions. J Am Soc Echocardiogr. 2007 Mar;20(3):213-33.
3. Upendram S, Nanda NC, Vengala S, Patel V, Mehmood F, Dod H, Bodiwala K, Frans E. Live three-dimensional transthoracic echocardiographic assessment of thrombus in the innominate veins and superior vena cava utilizing right parasternal and supraclavicular approaches. Echocardiography. 2005 May;22(5):445-9.
4. Reynen K. Cardiac myxomas. N Engl J Med. 1995 Dec 14;333(24):1610-7.
5. Molina JE, Edwards JE, Ward HB. Primary cardiac tumors: experience at the University of Minnesota. Thorac Cardiovasc Surg. 1990 Aug;38 Suppl 2:183-91.
6. Asch FM, Bieganski SP, Panza JA, Weissman NJ. Real-time 3-dimensional echocardiography evaluation of intracardiac masses. Echocardiography. 2006 Mar;23(3):218-24.
7. Nanda NC, Abd El-Rahman SM, Khatri G, Agrawal G, El-Sayed AA, Hassanian HA, Kamran M, Kirklin J, McGiffin DC, Holman WL, Pacifico AD. Incremental value of three-dimensional echocardiography over transesophageal multiplane 2-dimensional echocardiography in qualitative and quantitative assessment of cardiac masses and defects. Echocardiography. 1995;12:619-28.
8. Mehmood F, Nanda NC, Vengala S, Winokur TS, Dod HS, Frans E, Patel V, Bodiwala K, Upendram S, Kirklin JK, McGiffin DC, Pacifico AD. Live three-dimensional transthoracic echocardiographic assessment of left atrial tumors. Echocardiography. 2005 Feb;22(2):137-43.
9. Pothineni KR, Nanda NC, Burri MV, Bell WC, Post JD. Live/real time three-dimensional transthoracic echocardiographic description of chordoma metastatic to the heart. Echocardiography. 2008 Apr;25(4):440-2.
10. Suwanjutah T, Singh H, Plaisance BR, Hameed O, Nanda NC. Live/real time three-dimensional transthoracic echocardiographic findings in primary left atrial leiomyosarcoma. Echocardiography. 2008 Mar;25(3):337-9.
11. Sugeng L, Shernan SK, Salgo IS, Weinert L, Shook D, Raman J, Jeevanandam V, Dupont F, Settlemier S, Savord B, Fox J, Mor-Avi V, Lang RM. Live 3-dimensional transesophageal echocardiography initial experience using the fully-sampled matrix array probe. J Am Coll Cardiol. 2008 Aug 5;52(6):446-9.
12. Stewart JA, Silimperi D, Harris P, Wise NK, Fraker TD Jr, Kisslo JA. Echocardiographic documentation of vegetative lesions in infective endocarditis: clinical implications. Circulation. 1980 Feb;61(2):374-80.
13. Zamorano J, Cordeiro P, Sugeng L, Perez de Isla L, Weinert L, Macaya C, Rodríguez E, Lang RM. Real-time three-dimensional echocardiography for rheumatic mitral valve stenosis evaluation: an accurate and novel approach. J Am Coll Cardiol. 2004 Jun 2;43(11):2091-6.
14. Zamorano J, Perez de Isla L, Sugeng L, Cordeiro P, Rodrigo JL, Almeria C, Weinert L, Feldman T, Macaya C, Lang RM, Hernandez Antolin R. Non-invasive assessment of mitral valve area during percutaneous balloon mitral valvuloplasty: role of real-time 3D echocardiography. Eur Heart J. 2004 Dec;25(23):2086-91.
15. Monaghan MJ. Role of real time 3D echocardiography in evaluating the left ventricle. Heart. 2006 Jan;92(1):131-6.
16. Pothineni KR, Nanda NC, Burri MV, Singh A, Panwar SR, Gandhari S. Live/real time three-dimensional transthoracic echocardiographic visualization of Chiari network. Echocardiography. 2007 Oct;24(9):995-7.
17. McKay T, Thomas L. Prominent crista terminalis and Eustachian ridge in the right atrium: Two dimensional (2D) and three dimensional (3D) imaging. Eur J Echocardiogr. 2007 Aug;8(4):288-91.
18. Roldán FJ, Vargas-Barrón J, Vázquez-Antona C, Castellanos LM, Erdmenger-Orellana J, Romero-Cárdenas A, Martínez-Ríos MA. Three-dimensional transesophageal echocardiography of the atrial septal defects. Cardiovasc Ultrasound. 2008 Jul 18;6:38.

19. Muller S, Feuchtner G, Bonatti J, Müller L, Laufer G, Hiemetzberger R, Pachinger O, Barbieri V, Bartel T. Value of transesophageal 3D echocardiography as an adjunct to conventional 2D imaging in preoperative evaluation of cardiac masses. Echocardiography. 2008 Jul;25(6):624-31.
20. Handke M, Schöchlin A, Schafer DM, Beyersdorf F, Geibel A. Myxoma of the mitral valve: diagnosis by 2-dimensional and 3-dimensional echocardiography. J Am Soc Echocardiogr. 1999 Sep;12(9):773-6.
21. Le Tourneau T, Pouwels S, Gal B, Vincentelli A, Polge AS, Fayad G, Maréchaux S, Ennezat PV, Jegou B, Deklunder G. Assessment of papillary fibroelastomas with live three-dimensional transthoracic echocardiography. Echocardiography. 2008 May;25(5):489-95.
22. Singh A, Miller AP, Nanda NC, Rajdev S, Mehmood F, Duncan K. Papillary fibroelastoma of the pulmonary valve: assessment by live/real time three-dimensional transthoracic echocardiography. Echocardiography. 2006 Nov;23(10):880-3.
23. Jacobs LD, Salgo IS, Goonewardena S, Weinert L, Coon P, Bardo D, Gerard O, Allain P, Zamorano JL, de Isla LP, Mor-Avi V, Lang RM. Rapid online quantification of left ventricular volume from real-time three-dimensional echocardiographic data. Eur Heart J. 2006 Feb;27(4):460-8.
24. Corsi C, Coon P, Goonewardena S, Weinert L, Sugeng L, Polonsky TS, Veronesi F, Caiani EG, Lamberti C, Bardo D, Lang RM, Mor-Avi V. Quantification of regional left ventricular wall motion from real-time 3-dimensional echocardiography in patients with poor acoustic windows: effects of contrast enhancement tested against cardiac magnetic resonance. J Am Soc Echocardiogr. 2006 Jul;19(7):886-93.