Advances In echocardiography: three dimensional echocardiography and contrast echocardiography

Okpara Ihunanya Chinyere
Cardiology Unit. Department of Internal Medicine. Benue State University Teaching Hospital, P.M.B 102131, Makurdi, Nigeria. E-mail Address:iokparajubilee@gmail.com, Phone No: 08037067040

Accepted 11 September 2013

Three dimensional echocardiography is a recent and advanced technique analysing the structures of the heart starting from bidimensional images obtained in three different planes (sagittal, frontal and transversal). Images are then processed by special to reproduce the real three dimensional structures of the heart. This technique by its two methods (transthoracic and transesophageal three dimensional echocardiography) allows an accurate view of the cardiac structures and helps to identify the most favourable type and timing of surgical treatment. Intravenous contrast is now available to improve image quality in those patients whose ultrasonographic evaluation was previously suboptimal. The use of contrast is indicated for left ventricular opacification and endocardial border delineation especially in obese patients and those with lung disease. Improvements in image quality with intravenous contrast agents can facilitate image acquisition and enhance delineation of regional wall abnormalities at the peak level of exercise during stress echocardiography. In addition, substantial research efforts are underway to use ultrasound contrast for assessment of myocardial perfusion.

Key words: Three dimensional echocardiography, transthoracic, transesophageal, intravenous contrast agents, left ventricular opacification.

INTRODUCTION

Recent advances in the field of echocardiography are targeted towards the improvement of image quality and diagnostic accuracy. Transthoracic echocardiography (echo) was initially the most frequently used non-invasive technique for the assessment of the cardiovascular system. This was done by M - mode evaluation and two dimensional (2D) echocardiography without intravenous (IV) contrast agents and later on in the 70's the Doppler echocardiography was introduced. These combined techniques were able to provide a good understanding of underlying pathology and pathophysiology of many cardiac diseases.

In the 20th Century, new developments began as ways were sought to improve on the above techniques. Newer techniques became necessary to improve image quality especially in obese patients and those with lung diseases. Three dimensional echocardiography (3D) and use of intravenous contrast agents were introduced to improve on image qualities. 3D echo is a recent and advanced method of analysing the structures of the heart starting from two dimensional images obtained in three different planes (sagittal, frontal and transversal). These images are then processed by special software to reproduce the real three dimensional structures of the heart (3D reconstruction) thereby improving image accuracy (Roldan and Vargas, 1968).

The ability to opacity vascular structures with intravenous contrast on echocardiograms has been recognised for over 40 years (Gramiak and Shah, 1968). Intravenous injection of ultrasound contrast agents has been documented to improve endocardial border delineation (Cohen et al., 1998). Contrast enhancement of the blood tissue boundary enables improved assessment of ventricular wall motion, wall thickness and delineation of cardiovascular structural abnormalities. Experimental results indicate that contrast has the potential to provide qualitative and quantitative assessment of myocardial perfusion and coronary blood flow (Perchett et al., 1995).

Over the years, new modalities have evolved in the area of contrast echocardiography, 3D echocardiography, tissue Doppler imaging (TDI) and speckle tracking echocardiography (STE) to evaluate parameters such as ventricular volume, myocardial velocity, regional strain and strain rate, mechanical dysynchrony, and ventricular twist and provide new insight into cardiovascular
morphology and ventricular function.

This review focuses primarily on developments in the field of contrast and 3D echocardiography and attempts to propose standards and recommendations for the appropriate application of these developments on the basis of published scientific evidence.

BACKGROUND

Three dimensional echocardiography

Three dimensional echocardiography can be done by two techniques: transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). 3D real time TTE is an acquisition method developed in 2003. The key element of this technique is an xMatrix transducer of 3000 active crystals (unlike the 128 crystals of a 2D classic transducer). This transducer is able to make bi-dimensional acquisition without changing the probe position and switching from 2D mode to 3D mode is made by pressing one button. Acquisition takes few seconds and it has a pyramidal form (pyramidal volume) (Nanda and Miller, 2006). Then, the image is post processed and the 3D image is obtained by choosing the three sectional planes (frontal, capital and transversal).

Three dimensional TEE is performed with image acquisition in multiple 2D image plans and automatic rotational image acquisition on every 2 – 3 degrees from a complete 180 degrees rotation. For this, a special omniplane transducer and special echocardiographic software for the sequential image acquisition is needed. Bi-dimensional images are stored and then transferred to another computer where the reconstruction and 3D images are obtained.

Unfortunately, this method is time – consuming: image acquisition lasts for 10 – 25 minutes and post processing and three dimensional reconstruction takes another 45 – 60 minutes.

Transesophageal acquisition is more useful in emphysematous and obese patients and it is more likely to obtain more data of small cardiac structure which cannot be visualized with TTE.

Contrast echocardiography

Early contrast echocardiography by IV injection was used primarily to detect cardiac shunts or examine right heart structures. This was mainly because the micro bubbles included in the injectants to enhance their echogenicity which were small enough to pass through the microcirculation (red blood cell <8µm), dissolved rapidly in blood and lost their echogenicity. Early attempts to encapsulate the bubbles resulted in agents with improved stability but a size too large to traverse the pulmonary microvasculature.

The invasive administration of contrast agents directly into the central circulation or pericardial cavity was used to image the left ventricular (LV) cavity and the great vessels and to assist in determining needle location during pericardiocentesis. With the use of such approaches, numerous studies have validated the benefit of contrast echocardiography in the detection of atrial and ventricular septal defects, patent foramina ovale, congenital anomalies (Keber et al., 1974; Seward et al., 1977) and in the assessment of the placement of intrapericardial catheters (Callahan et al., 1985). Moreover, invasive assessment of myocardial perfusion has been achieved by direct injection of contrast agents into the heart or coronary arteries (Kaul et al., 1989; Tei et al., 1983; Kaul et al. 1984; Sabia et al., 1992; Ragosta et al., 1994).

Recently, new ultrasonic contrast agents have been developed, which are characterized by both smaller mean size and prolonged persistence. Various techniques are used to combine materials that control the bubble surface (“shells”) with gases that inhibit diffusion and bubble dissolution (e.g, perfluorocarbons). These new contrast agents can be visualized in the LV chamber and myocardium after IV injection.

Simultaneous with the emergence of novel agents, new ultrasound technologies have been developed to improve micro bubble detection. Enhancement of both the intensity and duration of the detection of micro bubbles has resulted from technologic advances exploiting the interactions that occur between micro bubbles and the incident ultrasound field (Villarraga et al., 1997; Wei et al., 1997). Some of these advances such as harmonic and pulse inversion imaging, have already been introduced into clinical echocardiographic practice, while others are in rapid evolution. Harmonic imaging (Wei et al., 1998; De Jong et al., 1991; Burns, 1996; Mulvagh et al., 1996) substantially enhances the detection of contrast within the cardiac chambers during clinical assessments (Al- Mansour et al., 2000; Allen et al., 1999), is commercially available and can readily be used in patients undergoing echocardiography.

New and evolving approaches to ultrasound delivery preferentially enhance the visualization of micro bubbles within the microcirculation of the myocardium (Porter and Xie, 1995; Powers et al., 1997; Hope Simpson et al., 1999). These emerging technologies have demonstrated investigational evidence for detection of myocardial perfusion with contrast echocardiography and are evolving in their design and application.

METHOD OF PERFORMING A CONTRAST STUDY

Bubbles in contrast agents are delicate and prone to destruction by physical pressure. Performing a contrast
study requires meticulous attention to the preparation and administration of the contrast agent to optimize desired effect. The agent should be prepared immediately before injection and vents used when withdrawing the agent into the syringe. Bubbles tend to float towards the surface and the contrast vial or syringe should be gently agitated each time fresh contrast administration is required. Injection through a small lumen catheter increases bubble destruction – a 20G or greater cannula should be used. Very small volumes of contrast are needed using second generation agents (< 1ml) and a flush is required. This is best done by using a three way tap, with contrast injected along the direct path to minimise bubble destruction, and saline flush injected into the right angle bend. Bubbles in agents currently available are buoyant and will tend to rise to the surface of the syringe. Purpose designed infusion pumps which agitate contrast continuously are in development but not yet widely available. Contrast should be injected immediately after preparation.

Three dimensional echocardiography: current indications

The clinical indications for use of 3D echocardiography include:

1. Valvular heart disease
2. Congenital Heart disease
3. Hypertensive heart disease
4. Cardiomyopathies
5. Intracardiac masses
6. Pericardial diseases etc.

Assessment of vascular morphology and pathology

Valvular heart disease is a very common pathology and often requires surgical treatment. Actual diagnostic methods allow making a precise and early diagnosis of these diseases, before irreversible destruction of the leaflets and make possible interventional or surgical valvular repair. Therefore, echocardiography is the ‘gold standard’ diagnostic method in valvular heart disease.

3D echocardiography allows the surgeon to view on the computer the valvular morphology either from the atrium (surgical perspective), or from the ventricle (ventriculotomy perspective), making his decision easier. In many countries, there is a special interest in the assessment of mitral valvulopathy with 3D echo. In 1996, at Mainz University, Kupferwasser et al. (1996), one of the pioneers of this technique, used 3D TEE for the evaluation of mitral stenosis. The result proved the superiority of this method compared to classic 2D transthoracic and transesophageal echocardiography especially in patients with severe aortic regurgitation or massive aortic calcification.

Veiga (1999) from University of Medicine from Lisbon successfully used the same method for the assessment of mitral valve morphology and interatrial septum (Veiga et al., 1999).

In 2003, Qin et al. published an interesting paper which cleared up the importance of the mechanism of ischemic mitral regurgitation using 3D transesophageal echocardiography, with direct results in subsequent treatment approach. Around the same time, Lange et al. (2002) from echocardiography department in Brisbane, Australia, have quantified by 3D echocardiography the severity of mitral regurgitation by calculating mitral regurgitant orifice area on virtually reconstructed valve. This method was then generally accepted and now it is the most accurate technique for the assessment of mitral regurgitation severity.

The most important role of 3D echocardiography in mitral valve disease is morphology information in mitral valve prolapse (Macnab et al., 2004; Hirata et al., 2008). In 2004, it was possible to reconstruct and calculate precisely mitral regurgitant volume with the same accuracy as MRI (Albers et al., 2004). This was really necessary and helpful in eccentric jets where 2D both transthoracic and transesophageal echo had many limits.

The ability of 3D echocardiography to calculate eccentric jets helped determine which patient needed cardiac surgery and those to be treated medically. 3D echo is also more accurate than 2D echo in aortic valve evaluation (aortic valve area) and tricuspid regurgitation (Goland et al., 2007; Handke et al., 2003; Shiota et al., 2002; Anwar et al., 2008; Nucifora et al., 2007).

Congenital heart disease assessment

The most used technique in congenital heart disease is 2D echocardiography with good results and accurate diagnosis, although the correct anatomy, compatible with intraoperative aspect is rarely obtained. In contrast, 3D echocardiography images are much close to intraoperative aspects (Chan et al., 2004).

The great evolvement of new percutaneous technique for atrial and ventricular septal defect closure needed also a new imaging method for a better analysis of this pathology (Acar et al., 2002; Miller et al., 2003; Marx and Sherwood, 2002). The use of 3D echocardiography clearly decreased early postoperative mortality and number of re-interventions after complex surgery for congenital heart disease.

Left ventricle assessment

Precise evaluation of left ventricular (LV) function and
Figure 1. Example of three dimensional (3D) left ventricular volumes generated by post-processing of a real-time 3D data set, acquired in a heart failure patient scheduled for cardiac resynchronization therapy.

morphology is essential for management of the cardiac patient. 2D echocardiography has many limits because it does not take into account the ventricular geometry and heart rotational movement. These limits were overcome with the new software for 3D analysis which allowed the assessment of global and segmental left ventricular motility and contractility. With all these techniques, with or without contrast echocardiography, it is possible to measure precisely left ventricular volumes and ejection fraction (Jenkins et al., 2004; Fei et al., 2004; Arai et al., 2004; Krenning et al., 2003).

Also, it permits more accurate evaluation of intraventricular dissynchrony and response of biventricular pacing (Marsan et al., 2008; Kapetanakis et al., 2005). Left ventricular mass can be correctly measured for the prognosis and diagnosis of hypertensive heart disease and hypertrophic cardiomyopathy (Chan et al., 2004; Miller et al., 2003). An example of 3D echocardiogram of LV volumes is shown in figure 1.

**Intracardiac masses assessment**

Although there are no clear data regarding the exact number of cases of intracardiac masses, 3D echocardiography was reported to contribute to early and correct diagnosis. It was useful in the determination of implant site of myxomas, extension of cardiac humours, vegetation, diameters.

**CONTRAST ECHOCARDIOGRAPHY: CURRENT INDICATIONS**

In the United States and Europe, the food and drug administration (FDA) and European Union, respectively have approved several echocardiographic contrast agents for the following indications:

1. Left ventricular cavity opacification and enhancement of endocardial border definition
2. Stress echocardiography
3. Doppler enhancement needed to evaluate diastolic and valvular function.

Thus contrast enhancement may be used in the following clinical conditions:

a) Congenital heart disease (atrial and ventricular septal defects)
b) Coronary artery disease
c) Valvular heart disease
d) Hypertensive heart disease

e) Pericardiocentesis (to show location of needle) etc

Enhancement of endocardial border definition

Contrast opacification of left heart structures after IV injection has now been achieved with several micro bubble agents. Sonicated human serum albumin (albunex) was the initial agent approved for this application. Multicenter data established the ability of an IV albunex injection to enhance the echocardiographic diagnosis of LV size and function (Feinstein et al., 1990).

Unfortunately, the consistency with which diagnostic studies could be obtained with this study was disappointing, mainly because of the fragility and short duration of the effect of the air containing micro bubbles. Newer contrast agents containing low solubility gases and/or surface stabilizing shells have been shown to achieve studies of diagnostic quality more reliably. In a multicentre study of more than 200 patients in whom LV opacification was produced by a commercially available agent (optision), the degree of LV opacification, the number and length of LV endocardial border segment visualized, and the duration of contrast enhancement achieved were significantly superior to that resulting from Albunex (Cohen et al., 1998).

The patient contact was selected on the basis of suboptimal baseline echocardiograms with nonvisualization of at least 2 to 6 segments of the apical 4 chamber view. Contrast administration in these patients converted a nondiagnostic study to a diagnostic echocardiogram in 75% of those examined. This added ability in image quality resulted in a greater ability to answer the primary referred question in as many as 50% of patients (Shaw et al., 1998).

In terms of physician assessment, diagnostic information (i.e., added value) increased from 35% to 40% with the use of contrast echocardiography in patients selected for suboptimal image quality (Shaw et al., 1998). Similar findings have been observed after LV opacification produced by IV injections of investigational contrast agents (Grayburn et al., 1998; Kitzman et al., 1998). Administration of an IV contrast agent has also been shown to enable more accurate assessment of LV volume and ejection fraction in human beings, and is most useful in subjects with two or more adjacent endocardial segments not seen at baseline (Hundley et al., 1998).

It has also been demonstrated clinically that with the use of contrast, harmonic imaging produces improvements over fundamental imaging in LV opacification, endocardial border definition, and reviewer confidence in the assessment of systolic function (Al-Mansour et al., 1998). An example of left ventricular myocardial contrast echocardiography for opacification of the LV is shown in figure 2.

Stress echocardiography

Accurate assessment of global or regional LV systolic performance is essential to the evaluation of coronary artery disease. Because the criteria for ischemia are based on the detection of contractile dysfunction in any myocardial segment, complete visualization of all LV walls is necessary to document or exclude abnormalities confidently.

Two dimensional stress echocardiography has shown high sensitivity and specificity in the detailed evaluation of regional wall motion, cavity size, LV function at rest and peak stress induced by either exercise or pharmacologic means (Pellikka et al., 1995). Stress echocardiography has also been shown to predict cardiovascular outcome in patients with normal (McCully et al., 1998) and abnormal results (Chuah et al., 1998).

However, interpretation of stress echocardiograms is qualitative, and multiple factors may produce suboptimal image quality and decreased endocardial border definition, leading to diminished diagnostic accuracy. Impaired transmission of sound energy caused by body habitus and/or lung disease, as well as the challenges imposed by excessive cardiac motion resulting from hyperventilation and tachycardia, can result in nondiagnostic images in 30% of patients (Marwick et al., 1992).

Investigations that used the earliest IV contrast agents found incremental improvement in the reproducibility of stress echocardiography by producing greater than 80% improvement in endocardial border definition (Crouse et al., 1993). Improved reproducibility in the quantitative analysis off LV function both at rest and during stress has also been reported (Leischik et al., 1997).

Doppler enhancement

Recordings of blood flow velocity by echocardiographic Doppler methods have long been applied to estimating intracardiac pressures and transvalvular gradients. Contrast enhancement produced by hand agitation of the saline solution has traditionally been used for enhancement of right sided Doppler flow velocity signals (Hagler et al., 1987). This technique has been limited to the non-invasive assessment of pulmonary artery systolic pressure analysis of tricuspid regurgitant signals.

The advent of contrast agents capable of traversing the pulmonary vasculature enables clinical application of the contrast enhanced Doppler technique to the assessment of left sided valvular lesions (Terasawa et al., 1992). Amplification of Doppler signals has been shown to be of great value in aortic stenosis, which poses a frequent
challenge in the obtainment of representative peak velocities across the stenosed valve. In one clinical study, contrast enhanced Doppler recordings across stenotic aortic valves produced clear spectral signals in 9 of 10 patients in whom they could not be recorded otherwise, and the gradients calculated from these signals correlated with those of catheterization (Nakatanis et al., 1992). Transmitral and pulmonary venous flow velocities can also be enhanced by contrast agents, permitting more complex diastolic function assessments, especially in patients with faint signals and in those with mitral inflow patterns suggestive of pseudo normalization. It is very important to adjust gain settings and use only small amounts of contrast when assessing Doppler spectral profiles to avoid over estimation of spectral velocities caused by the blooming effect (Forsberg et al., 1994).

Colour flow Doppler enhancement has also been demonstrated with transpulmonary contrast agents, but clinical application of these observations is yet evolving.

CONCLUSION AND RECOMMENDATIONS

Contrast echocardiography is recommended for use in patients with suboptimal two dimensional or Doppler echocardiograms. Such patients are usually obese or emphysematous. In this subgroup the use of contrast echocardiogram for improvement of suboptimal rest and stress echocardiography is strongly validated. This enhancement definition has enabled assessment of cardiac structure and function, as well as diagnostic feasibility and accuracy. The combination of IV contrast with harmonic stress echocardiography is a powerful tool for improved wall motion analysis through enhanced image quality, routinely permitting evaluation of patients with suboptimal images.

Other future potential application of contrast echocardiography including assessment of endothelial function and targeted delivery of diagnostic and therapeutic agents are areas of intensive investigative research that do not currently have established clinical application.

Three dimensional echocardiography allows an accurate view of the cardiac structures in terms of valvular aspect, size and shape of inter-atrial defect, intracardiac masses and prosthetic valves.

It is recommended for use in identification of the most favourable type and timing of surgical treatment for
valvular heart disease. It assesses transvalvular jets by their velocity more accurately than 2D echocardiography and brings more data about left ventricular mechanical activity, geometric pattern and systolic function.

REFERENCES


