

The Evolutionary Development of Echocardiography

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This article has Continuous Medical Education (CME) credit for Iranian physicians and paramedics. They may earn CME credit by reading this article and answering the questions on page 280.

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Abstract

Echocardiography is a non-invasive diagnostic technique which provides information on cardiac morphology, function, and hemodynamics. It is the most frequently used cardiovascular diagnostic test only after electrocardiography. In less than five decades, the evolution in this technique has made it the basic part of cardiovascular medicine. Herein, the evolution of various forms of echocardiography is briefly described.

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Introduction

Considerable changes have occurred in cardiovascular medicine with the help of echocardiography which is the most cardiovascular diagnostic test after electrocardiography. Echocardiography helps obtain information about cardiac morphology, function, and hemodynamics non-invasively. "In less than half a century, echocardiography has evolved as a mainstay technology of cardiovascular medicine".¹ "The first academic course on cardiac ultrasound, the first echocardiography textbook, and even the term 'echocardiography' were developed in the 1960s and 1970s".¹ Herein, we describe briefly the early evolution of echocardiography and the development of different kinds of echocardiography.

Early Evolution of Echocardiography

Echocardiography has had a dramatic improvement. "The origins of echocardiography date back to the discovery of piezoelectricity in 1880".^{2,3} Ultrasound waves are created by piezoelectric crystals inside the transducers.

The origins of clinical echocardiography date back to the 1950s and credited to Carl Helmuth Hertz and Inge Edler. During assessing patients with mitral stenosis using the time motion or M-mode approach, Edler, known as the 'Father of Echocardiography', identified a moving signal with cardiac motion.⁴ Then after, this technique was used for the evaluation of mitral stenosis. Their first paper entitled, 'The Use of Ultrasonic Reflectoscope for Continuous Movements of the Heart Wall' was published in 1954.⁵ In 1969, Edler introduced the combined use of Doppler and echocardiography as an approach to diagnose aortic and mitral regurgitation.⁶ Japanese investigators were the first to work on Doppler technology.^{7,8} For the first time the detection of pericardial effusion with ultrasound was reported by Harvey Feigenbaum and colleagues in 1965.⁹

The development of the M-mode technique for measuring left ventricular dimensions was introduced by Feigenbaum and Dodge In 1968.¹⁰ Eventually, echocardiography was recognized

as a perfect diagnostic technique, and after 1970, echocardiography were assigned in all annual meetings of the American College of Cardiology.¹¹ “The first academic course dedicated to cardiac ultrasound was learnt in Indianapolis in 1968 and the first book on echocardiography published in 1972”.¹²

Origin of Echocardiography

Eidler named the technique as ultrasound cardiography (UCG). However, because echoencephalography was the only popular examination for detecting echo from the midline of the brain to see its deviation by an intracranial space-occupying lesion,¹¹ the examination of the heart was named as echocardiography. In early years the abbreviation “echo” could not be used because of the inability to differentiate between echocardiography and echoencephalography. However, with the disappearance of echoencephalography as a diagnostic tool, finally echocardiography was agreed as the name for this procedure.¹ Currently, the abbreviation “echo” is used for echocardiography.

Development of Various Forms of Echocardiography

Obviously, there have been many important developments in the field of cardiac ultrasound. They are too numerous to explain in detail.

The first person who described transesophageal echocardiography (TEE) was an American.¹³ Japanese investigators also worked in this area, however, TEE was primarily developed in its

current state by European investigators,¹⁴ and became popular after the Europeans revealed how this approach could be clinically useful.¹⁵

Doppler has a similar story. The Japanese most unique contribution to this area was the development of color flow Doppler. Although, the first paper about color flow Doppler was credited by the University of Washington in Seattle.¹⁶ Then, Hatle,¹⁷ showed that using Doppler echocardiography, hemodynamic data could be determined correctly.

Contrast echocardiography began at the University of Rochester by Gramiak and Shah during an accidental observation with the creation of large clouds of echoes within the heart after the injection of indocyanine green dye.¹⁸ Contrast echocardiography has become an important diagnostic tool for the detection of left ventricular endocardial borders.¹⁹ The implication of contrast echocardiography for detecting right-to-left shunts was reported by the Mayo Clinic group.²⁰ Currently, there are commercial contrast agents which can pass through the pulmonary capillaries and are visible on the left side of the heart.²¹ Three-dimensional echocardiography, intracardiac echo, myocardial velocity imaging, and 2D strain imaging were developed sequentially.

Considerably increased applications of echocardiography along with the availability of portable machines, has made echocardiography even more noticeable in clinical practice.¹¹

M-Mode Echocardiography

M-mode echocardiography was the first developed form of cardiac ultrasound (figure 1), in which a single ultrasonic beam was directed

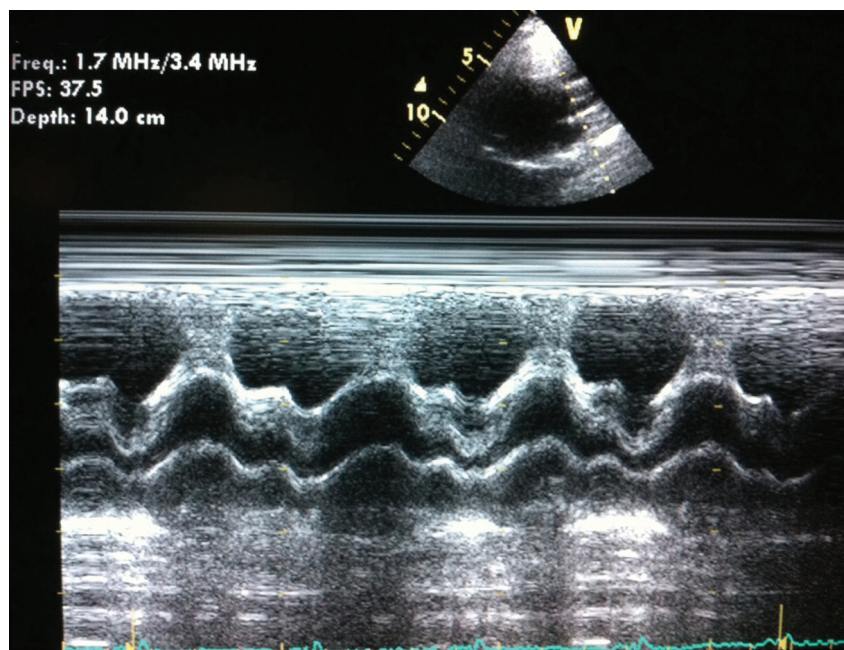


Figure 1: This figure shows M-mode echocardiogram of left atrium and aortic root.

toward the heart and reflected signals were displayed on an oscillograph.¹¹ Although the real anatomy of the heart could not be well visualized by M-mode echocardiography, it plays a specific role where precise measurements of cardiac time intervals (during systole and diastole) are necessary, and when rapidly moving targets (i.e. vegetation) have to be studied.^{11,22}

Two-Dimensional Echocardiography

The major advancement in echocardiography was the clinical application of two-dimensional echocardiography which helped provide real-time images of the heart.²³ When the ultrasound beam is swept back and forth through an arc, a two-dimensional image would be created.¹¹ Two-dimensional images were firstly reconstructed from M-mode tracings by Gramiak.²⁴ The popular real-time, two-dimensional scanner was developed by Bom,²⁵ and then, mechanical hand-held transducer device for two-dimensional scanning was developed by Griffith and Henry.²⁶ The first successful and standard commercial scanner was introduced by Eggleton and the Indiana group. "Since then real-time two-dimensional echocardiography has become the backbone of the current echocardiographic examination".¹¹

Doppler Echocardiography

Christian Doppler (an Austrian mathematician and physicist) was the first who examined the effect of the observer's motion relative to the source of an ultrasound wave, known as the Doppler effect.²⁷ Regardless of the development of Doppler echocardiography from the early 1950s, its clinical use was delayed until late 1970s.²⁸ Doppler was firstly used in 1969 to assess valvular regurgitation.⁶ After that Holen,²⁹ and Hatle,²⁰ showed that accurate hemodynamic data could be obtained using the Doppler technique.

The major discovery in Doppler ultrasound in 1970s was its success in quantifying pressure drops across valvular stenoses in terms of the simplified Bernoulli equation.^{29,30} In early 1970s aortic blood flow velocity was obtained by transesophageal Doppler,³¹ and in the late 1980s Doppler capabilities were added to transesophageal probes. In the early 1980s, color-flow imaging was developed based on the Doppler concept to visualize blood flow non-invasively.³² In 1982, Kitabatake and colleagues,³³ introduced pulsed-wave Doppler for recording transmitral blood flow velocities to assess left ventricle diastolic function. This method has been the main clinical modality for non-invasive assessment of diastolic filling patterns.

Stress Echocardiography

In 1970, left ventricular wall motion was analyzed at rest and during exercise in healthy individuals by ultrasound.³⁴ In 1973, M-mode echocardiography was used for the determination of left ventricular regional wall motion abnormalities (RWMA).³⁵ In the late 1970s, exercise stress combined with M-mode echocardiography was used for the detection of ischemia-induced wall motion abnormalities (WMA).³⁶ The introduction of 2D echocardiography led to specific interest in stress echocardiography. With technical evolution and development of digital echocardiography in the mid 1980s, which allowed digital recording of both rest and stress images and side-by-side comparison, stress echocardiography has become a routine clinical test.³⁷ Supine exercise, handgrips, upright bicycles and cold pressor tests were used in early studies.³⁸ But the great advance was the ability of recording stress-induced WMA during treadmill exercise. Subsequently pharmacological agents and cardiac pacing were also used to induce ischemic WMA.

Transesophageal Echocardiography

The first experimental probes with the potential utility for TEE were established in the 1970s.¹¹ TEE was first performed in 1980 by putting a two-dimensional transducer on a fiberoptic endoscope.³⁹ After that, a phased-array ultrasound transducer was attached to the tip of a flexible gastroscope by Hanrath and colleagues,⁴⁰ and TEE entered its modern era.¹¹ With early monoplane transesophageal probes, only transverse images via a limited field of view were obtainable. Better imaging of the heart was achieved after the development of smaller probes with biplane and particularly multiplane imaging capabilities. Therefore, the diagnostic field of TEE has increased greatly (figure 2).

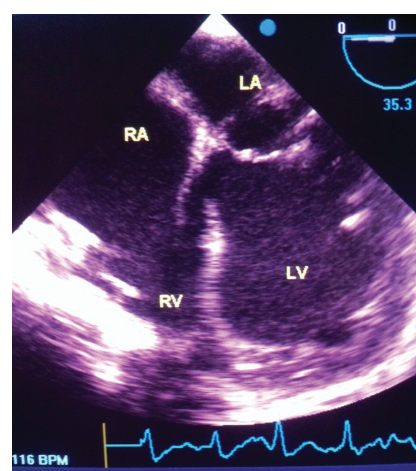


Figure 2: Transesophageal echocardiography (0 degree) shows a 4-chamber view at mid esophageal level. RA: right atrium, LA: left atrium, RV: right ventricle, LV: left ventricle

The semi-invasive nature of TEE allowed progressive uses in both inpatient and outpatient settings.

Intraoperative Echocardiography

Intraoperative echocardiography is being used by the epicardial and/or transesophageal approach. The first use of epicardial echocardiography using the M-mode technique was done in the operating theater to evaluate the results of open mitral commissurotomy in 1972.⁴¹ However, it was used routinely only after the widespread application of transesophageal echocardiography combined with color-flow imaging. "The ability to monitor cardiac performance led to the early acceptance of transesophageal echocardiography to monitor changes in ventricular function and hemodynamic measures during cardiac surgery".¹¹

Before cardiopulmonary bypass (CPB), it helps to establish the cardiac structural and functional abnormalities and to search for additional or sometimes neglected findings which may change the surgical plan in the operative room.⁴²⁻⁴⁴

After CPB, it provides assessment of the surgical results and even new abnormalities which may need second run. Furthermore operative complications would be reduced by intraoperative monitoring of LV function and detecting cardiovascular causes responsible for hemodynamic instability in the operating room which may cause difficulty to off pump.

In hemodynamically unstable patients the cause of hemodynamic compromise can be determined and intraoperative complications would be identified. Importantly, before leaving the operating room the adequacy of valve repairs (or replacements) and surgical correction of congenital defects can be evaluated.⁴⁵⁻⁴⁷ The value of intraoperative TEE is particularly well established in patients undergoing mitral valve repair.⁴⁸⁻⁵⁰

In 1999, the guidelines for the performance of a comprehensive intraoperative multiplane TEE examination were published by the American Society of Echocardiography and Society of Cardiovascular Anesthesiologists.⁵¹

Currently, intra-operative TEE (IOTEE) is requested for all patients undergoing all valve repair, patients with aortic valve disease requiring valve replacement (for evaluation of mitral regurgitation), myomectomy in patients with hypertrophic cardiomyopathy (HCM), cardiac mass removal, repair of intracardiac shunts including atrial and ventricular septal defects, and all patients with congenital heart disease.^{41,42}

Contrast Echocardiography

There are several clinical implications for

contrast echocardiography. It is especially useful for evaluating intracardiac shunts.⁵² Initially, it was done by injecting agitated saline through a peripheral vein. But inability to control the intensity of the contrast effect was the major problem of this technique. This problem was solved by the development of stable contrast agents that were suitable for opacifying the right-sided cardiac chambers and evaluating the intracardiac shunts.⁵³ Subsequently, several studies,^{53,54} showed that intravenous left heart contrast agents improve left ventricular endocardial border definition, besides the image quality in patients with poor image views (figure 3). In ischemic heart disease, myocardial perfusion could be investigated using intravenous contrast agents.

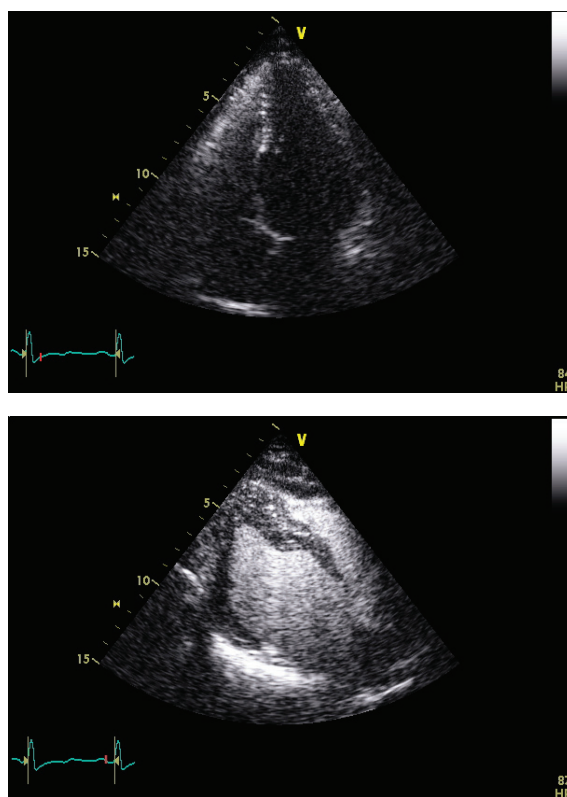


Figure 3: This figure shows contrast echocardiography in a patient with poor image quality (upper panel) showed marked apical hypertrophy and spade-like LV cavity (lower panel).

Epicardial Echocardiography

Sometimes TEE images may be suboptimal or there may be contraindications to TEE. By placing a high frequency ultrasound probe in a sterile sheath, the heart can be imaged from the epicardial surface.

Three-Dimensional Echocardiography

The idea of three-dimensional (3D) echocardiography began to develop in the 1960s. However, the first three-dimensional scans of the

heart were reported in 1974.⁵⁵

The earliest 3D echocardiograms were obtained using the reconstruction technique.^{47,56} With this technique ECG gated images are obtained from varying transducer locations of definite position. Using different software programs, each image is located into its proper three dimensional spatial positions in cardiac cycle; and then using specific image processing techniques the structure can be reconstructed as a 3D object. Then the surfaces and volumes are displayed. Developing complex transthoracic transducer enabled us to acquire 3D volume data sets in real time or near real time.

The 3D technique has changed rapidly, and currently different types of real-time 3D imaging are available. In current real-time 3D systems, matrix array transducers with 3000-4000 elements have been used.

Since cardiac structures could be shown closely to their real forms using 3D echocardiography, it is helpful particularly in complex congenital heart disease (figure 4).

The accuracy, feasibility, and value of 3D echocardiography also have been demonstrated in the operating room.⁵⁷ In addition, the use of contrast 3D echocardiography has several advantages to improve left ventricular volumes quantification.⁵⁸ The clinical applications of 3D echocardiography are expanding rapidly, but quantitative measurements of LV volumes, RWMA, congenital heart disease, valvular disease (figure 4), and evaluation of ventricular dyssynchrony are the most common indications of real-time 3D echocardiography.

The advantages of 3D echocardiography over 2D echocardiography include improvements in visualization of complex shapes and relations between cardiac structures, calculation of cardiac

volumes, mass, and function, imagination of color Doppler flow fields, and assessment of valvular abnormalities and dysfunctions.

Tissue Doppler Imaging (TDI) and Strain and Strain Rate Imaging (SRI)

The Doppler technique is used to measure myocardial velocities because of different signal amplitudes and Doppler frequencies between the blood and myocardium. The myocardial motion speed is much lower than that of the blood; however, the amplitude of myocardial signals is much higher than those for the blood. These differences allow the separation of myocardial velocities from blood flow velocities by filters, which reject echo signals originating from the blood pool. Velocities can be recorded using color Doppler or pulsed wave Doppler.

Myocardial velocity imaging was first introduced in the early 1990s,^{59,60} and is now well established for quantifying the LV systolic and diastolic function. Myocardial motion can be imaged in real time as color-coded velocities superimposed on a 2D gray scale image. The frame rate for 2D color Doppler is between 80-200 frames per second, depending on the sector width, and is usually set higher than for the simultaneous gray scale images. The myocardial velocities can be analyzed offline though (figure 5).

Tissue Doppler velocity imaging can be applied clinically to diagnose myocardial ischemia, to evaluate patients with diastolic dysfunction and select patients for cardiac resynchronization therapy by assessment of ventricular dyssynchrony (figure 6).

Speckle Tracking Echocardiography (STE)

Non-Doppler 2D strain imaging is a newer technique for measuring strain and strain rate

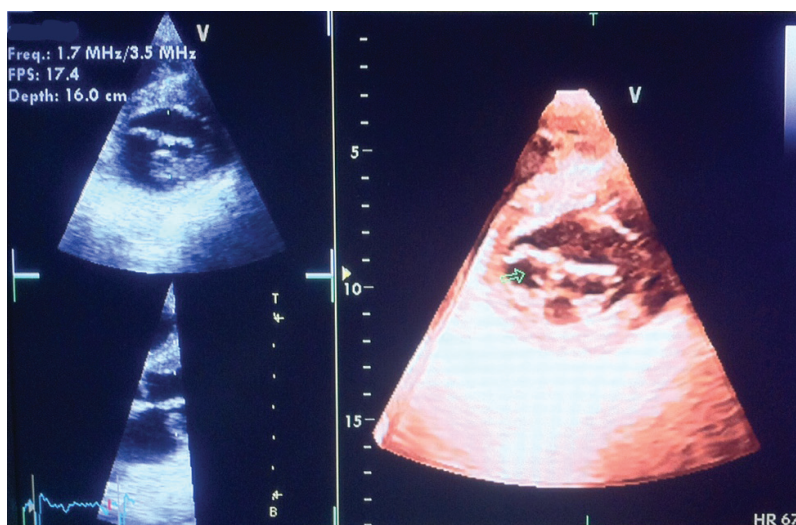


Figure 4: This figure shows transverse view at the level of the mitral valve from the parasternal short axis using full-volume 3D imaging in a patient with prolapse of posterior leaflet and ruptured chordae (arrow).

values. It analyzes motion by tracking natural acoustic markers (speckles) in 2D gray scale images. The speckles are produced by interference of ultrasound beams in the myocardium,^{61,62} and act as natural acoustic markers, which can be tracked frame by frame.

STE automatically measures the distance

between speckles; therefore, strain measurement is possible in an angle-independent method. Measurements from multiple regions can be done simultaneously within an image plane (figure 7). Doppler-based strain measures velocities from a fixed point to a reference point (e.i. external probe). On the contrary, STE measures the

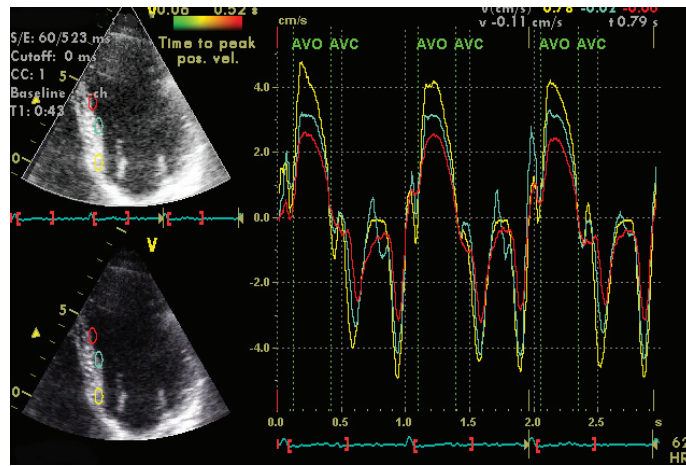


Figure 5: This figure shows offline analyses of tissue Doppler imaging from apical 4-chamber view at basal, middle and apical segments of interventricular septum in a healthy individual.

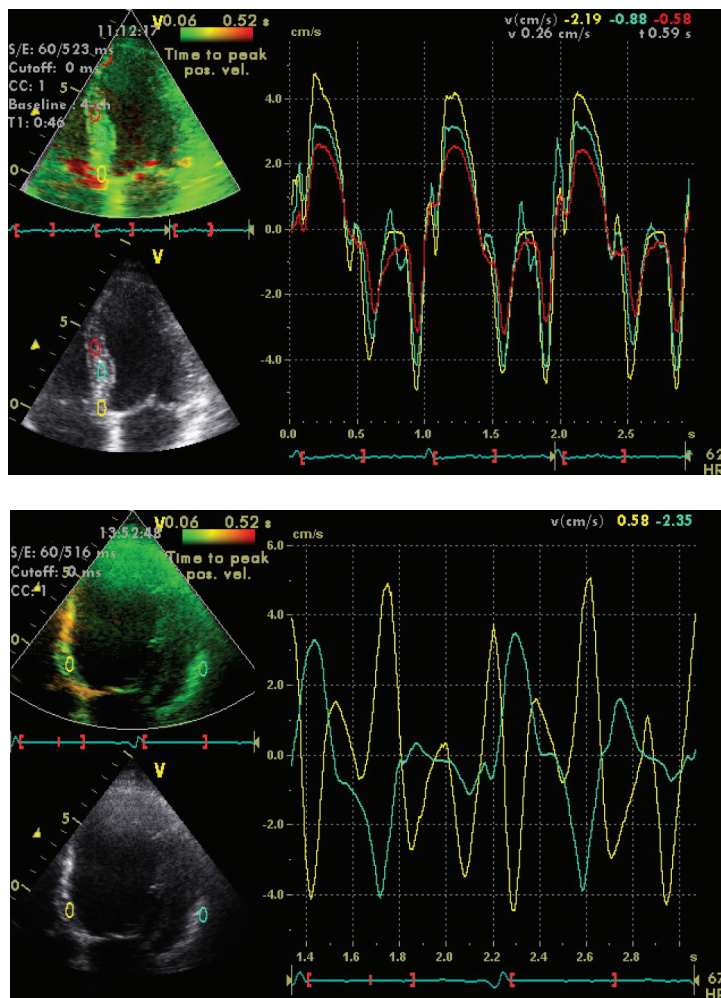


Figure 6: This figure shows the assessment of left ventricular dyssynchrony by tissue Doppler imaging from apical 4-chamber view in a normal patient (right panel) versus a patient with LBBB (left panel). Dyssynchrony was defined as maximal differences in time-to-peak regional velocity in septal versus lateral wall. LBBB: left bundle branch block.

distance between two points within a definite region of the myocardium. Moreover, speckle tracking provides a direct measure of strain, whereas tissue Doppler imaging (TDI) calculates strain by integrating SR.

However, the most important advantages of STE are its independency to ultrasound angle and of translational motion of heart in chest.⁶³⁻⁶⁵ So, circumferential and radial strains from the LV short axis, and longitudinal strain from apical myocardial regions would be measurable. Promisingly, the capability to measure LV rotation and torsion is accessible by STE.^{64,66} Although for measurement of peak velocities and SRs higher frame rates are needed, optimal frame rates are about 80 frames per second. The clinical applications of STE are the evaluation of regional ventricular and atrial myocardial function and assessment of atrial and ventricular dyssynchrony.

Velocity vector imaging (VVI) is a novel imaging technique that calculates and displays regional motions from routine 2D gray scale echo images in terms of velocity and direction. In brief, the VVI technique uses the combination of speckle tracking, mitral annulus motion and tissue blood border detection.⁶⁷

Intracardiac Echocardiography

Recently, catheter based probes with Doppler capabilities have been introduced in clinical practice.⁶⁸ The beneficial role of transcatheter intracardiac echocardiography (ICE) is guiding trans-catheter interventions, particularly atrial septal defect device closure. It is also useful in electrophysiology procedures, such as pulmonary veins ablation for atrial fibrillation, detection of

pulmonary vein stenosis and guiding of multisite pacing catheters.

Role of Echocardiography in the New Era of Medical Cost Containment

“The rapid development of echocardiography is a typical ‘good news/bad news’ scenario”.¹ “The bad news is that the examination is quite advanced, and physicians must work hard to continue to date to provide state-of-the-art examinations. There is a learning curve for every new echocardiographic application. Physicians must spend sufficient long time and effort for being expert in these new techniques”.¹

In the new era of cost containment, because of lower cost and the potential to provide definite information, comprehensive and appropriate echocardiography is mandatory. Doing such studies should eliminate further need for more expensive and potentially harmful examinations in the majority of patients and should have a big influence on cost-effectiveness of patients’ care.

Conclusion

Echocardiography is an essential part of practice in cardiology. Such as other technologies, this technology has many pros and cons. The major disadvantage is its need for a learning curve for providing quantitative examinations and interpretations. Its principal advantage is its outstanding versatile technology. Properly performed examinations in the right patient for the right reason, would be highly cost-effective.

Conflict of Interest: None declared

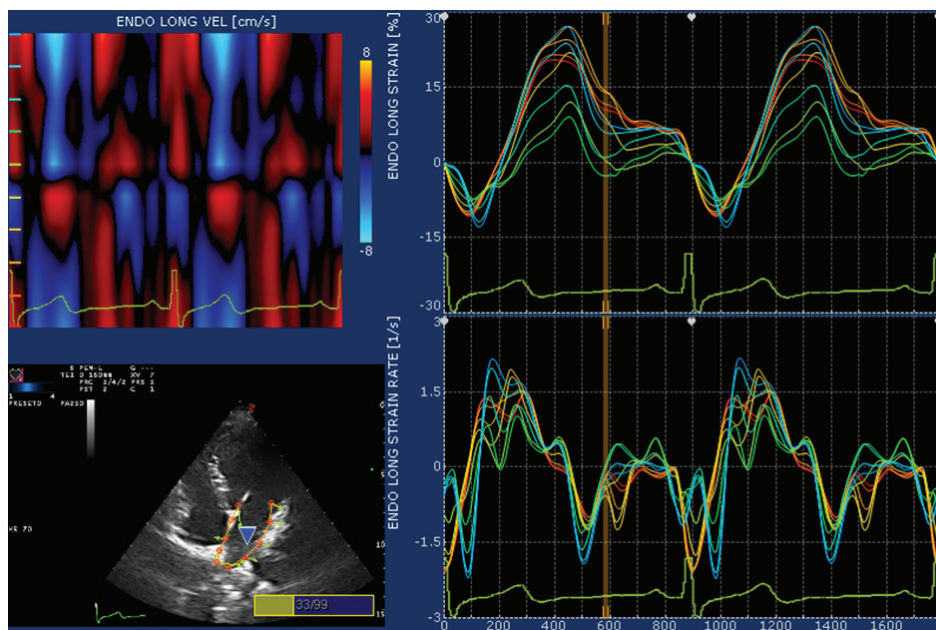


Figure 7: This figure shows the assessment of left atrial (LA) strain and strain rate by velocity vector imaging. Maximal strain was measured at left ventricular (LV) systole while strain rate was measured at early LV filling.

References

- 1 Feigenbaum H. Evolution of echocardiography. *Circulation*. 1996;93:1321-7. doi: 10.1161/01.CIR.93.7.1321. PubMed PMID: 8641018.
- 2 Curie P, Curie J. Development, par pression de l'électricité polaire dans les cristaux hémédres à faces inclinées. *Comptes Rendus*. 1880;91:291-5.
- 3 Curie P, Curie J. Lois du dégagement de l'électricité par pression, dans la tourmaline. *Comptes Rendus*. 1881;92:186-8.
- 4 Fraser AG. Inge Edler and the origins of clinical echocardiography. *Eur J Echocardiogr*. 2001;2:3-5. doi: 10.1053/euje.2001.0082. PubMed PMID: 12071146.
- 5 Edler I, Hertz CH. The use of ultrasonic reflectoscope for the continuous recording of the movements of heart walls. 1954. 2004;24:118-36. PubMed PMID: 15165281
- 6 Lindstrom K, Edler I. Ultrasonic Doppler technique used in heart disease: clinical application. *Ultrasono Graphia Medica*. 1969;3:455-61.
- 7 Satomura S, Matsubara S, Yoshioka M. A new method of mechanical vibration and its applications. *Mem Inst Sci Ind Res*. 1955;13:125.
- 8 Yoshida T, Mori M, Nimura Y, Okimura M, Hikita G, Nakanishi K. Study of examining the heart with ultrasonics; IV: clinical applications. *Jpn Circ J*. 1954;20:228.
- 9 Feigenbaum H, Waldhausen JA, Hyde LP. Ultrasound Diagnosis of Pericardial Effusion. *JAMA*. 1965;191:711-4. doi: 10.1001/jama.1965.03080090025006. PubMed PMID: 14245510.
- 10 Feigenbaum H, Popp RL, Wolfe SB, Troy BL, Pombo JF, Haine CL, et al. Ultrasound measurements of the left ventricle. A correlative study with angiocardiology. *Arch Intern Med*. 1972;129:461-7. doi: 10.1001/archinte.129.3.461. PubMed PMID: 5017683.
- 11 Gowda RM, Khan IA, Vasavada BC, Sacchi TJ, Patel R. History of the evolution of echocardiography. *Int J Cardiol*. 2004;97:1-6. doi: 10.1016/j.ijcard.2003.07.018. PubMed PMID: 15336798.
- 12 Feigenbaum H. *Echocardiography*. Philadelphia: Lea & Febiger; 1972.
- 13 Frazin L, Talano JV, Stephanides L, Loeb HS, Kopel L, Gunnar RM. Esophageal echocardiography. *Circulation*. 1976;54:102-8. doi: 10.1161/01.CIR.54.1.102. PubMed PMID: 1277411.
- 14 Hisanaga K, Hisanaga A, Nagata K, Ichie Y. Transesophageal cross-sectional echocardiography. *Am Heart J*. 1980;100:605-9. doi: 10.1016/0002-8703(80)90223-9. PubMed PMID: 7446358.
- 15 Schluter M, Henrath P. Transesophageal echocardiography: potential advantages and initial clinical results. *Practical Cardiol*. 1983;9:149.
- 16 Brandestini MA, Eyer MK, Stevenson JG. M/Q-mode echocardiography: the synthesis of conventional echo with digital multigate Doppler. In: Lancee CT, ed. *Echocardiography*. The Hague, Netherlands: Martinus-Nijhoff; 1979.
- 17 Hatle L, Angelsen BA, Tromsdal A. Non-invasive assessment of aortic stenosis by Doppler ultrasound. *Br Heart J*. 1980;43:284-92. doi: 10.1136/hrt.43.3.284. PubMed PMID: 7437175; PubMed Central PMCID: PMC482277.
- 18 Gramiak R, Shah PM, Kramer DH. Ultrasound cardiography: contrast studies in anatomy and function. *Radiology*. 1969;92:939-48. PubMed PMID: 5771834.
- 19 Feigenbaum H, Stone JM, Lee DA, Nasser WK, Chang S. Identification of ultrasound echoes from the left ventricle by use of intracardiac injections of indocyanine green. *Circulation*. 1970;41:615-21. doi: 10.1161/01.CIR.41.4.615. PubMed PMID: 4245151.
- 20 Seward JB, Tajik AJ, Spangler JG, Ritter DG. Echocardiographic contrast studies: initial experience. *Mayo Clin Proc*. 1975;50:163-92. PubMed PMID: 1123933.
- 21 Feinstein SB, Cheirif J, Ten Cate FJ, Silverman PR, Heidenreich PA, Dick C, et al. Safety and efficacy of a new transpulmonary ultrasound contrast agent: initial multicenter clinical results. *J Am Coll Cardiol*. 1990;16:316-24. doi: 10.1016/0735-1097(90)90580-I. PubMed PMID: 2197312.
- 22 Dillon JC, Feigenbaum H, Konecke LL, Davis RH, Chang S. Echocardiographic manifestations of valvular vegetations. *Am Heart J*. 1973;86:698-704. doi: 10.1016/0002-8703(73)90350-5. PubMed PMID: 4743337.
- 23 Tajik AJ, Seward JB, Hagler DJ, Mair DD, Lie JT. Two-dimensional real-time ultrasonic imaging of the heart and great vessels. Technique, image orientation, structure identification, and validation. *Mayo Clin Proc*. 1978;53:271-303. PubMed PMID: 642598.
- 24 Gramiak R, Waag RC, Simon W. Ciné ultrasound cardiography. *Radiology*. 1973;107:175-80. PubMed PMID: 4689427.
- 25 Bom N, Lancée CT, Honkoop J, Hugenholtz PG. Ultrasonic viewer for cross-sectional analyses of moving cardiac structures. *Biomed Eng*. 1971;6:500-3. PubMed PMID: 5133281.
- 26 Griffith JM, Henry WL. A sector scanner for

- real time two-dimensional echocardiography. *Circulation*. 1974;49:1147-52. doi: 10.1161/01.CIR.49.6.1147. PubMed PMID: 4831657.
- 27 Doppler C. Uber das farbige Licht der Doppelsterne und einiger anderer Gestirne des Himmels. *Adhandlungen der Koniglich-Bohmischen Gesellschaft der Wissenschaften*. 1842;2:465-83.
 - 28 Baker DW, Rubenstein SA, Lorch GS. Pulsed Doppler echocardiography: principles and applications. *Am J Med*. 1977;63:69-80. doi: 10.1016/0002-9343(77)90119-X. PubMed PMID: 879197.
 - 29 Holen J, Simonsen S. Determination of pressure gradient in mitral stenosis with Doppler echocardiography. *Br Heart J*. 1979;41:529-35. doi: 10.1136/hrt.41.5.529. PubMed PMID: 465223; PubMed Central PMCID: PMC482066.
 - 30 Holen J, Aaslid R, Landmark K, Simonsen S. Determination of pressure gradient in mitral stenosis with a non-invasive ultrasound Doppler technique. *Acta Med Scand*. 1976;19:455-60.
 - 31 Side CD, Gosling RG. Non-surgical assessment of cardiac function. *Nature*. 1971;232:335-6. doi: 10.1038/232335a0. PubMed PMID: 5094838.
 - 32 Omoto R, Kasai C. Physics and instrumentation of Doppler color flow mapping. *Echocardiography*. 1987;4:467-83. doi: 10.1111/j.1540-8175.1987.tb01361.x.
 - 33 Kitabatake A, Inoue M, Asao M, Tanouchi J, Masuyama T, Abe H, et al. Transmitral blood flow reflecting diastolic behavior of the left ventricle in health and disease--a study by pulsed Doppler technique. *Jpn Circ J*. 1982;46:92-102. doi: 10.1253/jcj.46.92. PubMed PMID: 6948118.
 - 34 Kraunz RF, Kennedy JW. Ultrasonic determination of left ventricular wall motion in normal man. Studies at rest and after exercise. *Am Heart J*. 1970;79:36-43. PubMed PMID: 5410280.
 - 35 Jacobs JJ, Feigenbaum H, Corya BC, Phillips JF. Detection of left ventricular asynergy by echocardiography. *Circulation*. 1973;48:263-71. doi: 10.1161/01.CIR.48.2.263. PubMed PMID: 4726206.
 - 36 Mason SJ, Weiss JL, Weisfeldt ML, Garrison JB, Fortuin NJ. Exercise echocardiography: detection of wall motion abnormalities during ischemia. *Circulation*. 1979;59:50-9. doi: 10.1161/01.CIR.59.1.50. PubMed PMID: 758124.
 - 37 Armstrong WF, O'Donnell J, Dillon JC, McHenry PL, Morris SN, Feigenbaum H. Complementary value of two-dimensional exercise echocardiography to routine treadmill exercise testing. *Ann Intern Med*. 1986;105:829-35. PubMed PMID: 3777710.
 - 38 Feigenbaum H. The evolution of stress echocardiography. *Cardiol Clin*. 1999;17:443-6. doi: 10.1016/S0733-8651(05)70089-8. PubMed PMID: 10453291.
 - 39 Hisanaga K, Hisanaga A, Nagata K, Ichie Y. Transesophageal cross-sectional echocardiography. *Am Heart J*. 1980;100:605-9. doi: 10.1016/0002-8703(80)90223-9. PubMed PMID: 7446358.
 - 40 Hanrath P, Kremer P, Langenstein BA, Matsumoto M, Bleifeld W. Transesophageal echocardiography. A new method for dynamic ventricle function analysis. *Dtsch Med Wochenschr*. 1981;106:523-5. PubMed PMID: 7215178.
 - 41 Johnson ML, Holmes JH, Spangler RD, Paton BC. Usefulness of echocardiography in patients undergoing mitral valve surgery. *J Thorac Cardiovasc Surg*. 1972;64:922-34. PubMed PMID: 4636009.
 - 42 Practice guidelines for perioperative transesophageal echocardiography. A report by the American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. *Anesthesiology*. 1996;84:986-1006. PubMed PMID: 8638856.
 - 43 Kolev N, Brase R, Swanevelder J, Oppizzi M, Riesgo MJ, van der Maaten JM, et al. The influence of transoesophageal echocardiography on intra-operative decision making. A European multicentre study. *European Perioperative TOE Research Group. Anaesthesia*. 1998;53:767-73. PubMed PMID: 9797521.
 - 44 Katsnelson Y, Raman J, Katsnelson F, Mor-Avi V, Heller LB, Jayakar D, et al. Current state of intraoperative echocardiography. *Echocardiography*. 2003;20:771-80. doi: 10.1111/j.0742-2822.2003.03038.x. PubMed PMID: 14641385.
 - 45 Randolph GR, Hagler DJ, Connolly HM, Dearani JA, Puga FJ, Danielson GK, et al. Intraoperative transesophageal echocardiography during surgery for congenital heart defects. *J Thorac Cardiovasc Surg*. 2002;124:1176-82. doi: 10.1067/mtc.2002.125816. PubMed PMID: 12447184.
 - 46 Shapira Y, Vaturi M, Weisenberg DE, Raanani E, Sahar G, Snir E, et al. Impact of intraoperative transesophageal echocardiography in patients undergoing valve replacement. *Ann Thorac Surg*. 2004;78:579-83. doi: 10.1016/j.athoracsur.2004.02.075. PubMed PMID:

- 15276525.
- 47 Ommen SR, Park SH, Click RL, Freeman WK, Schaff HV, Tajik AJ. Impact of intraoperative transesophageal echocardiography in the surgical management of hypertrophic cardiomyopathy. *Am J Cardiol.* 2002;90:1022-4. doi: 10.1016/S0002-9149(02)02694-2. PubMed PMID: 12398979.
 - 48 Saiki Y, Kasegawa H, Kawase M, Osada H, Ootaki E. Intraoperative TEE during mitral valve repair: does it predict early and late postoperative mitral valve dysfunction? *Ann Thorac Surg.* 1998;66:1277-81. doi: 10.1016/S0003-4975(98)00756-5. PubMed PMID: 9800820.
 - 49 Freeman WK, Schaff HV, Khandheria BK, Oh JK, Orszulak TA, Abel MD, et al. Intraoperative evaluation of mitral valve regurgitation and repair by transesophageal echocardiography: incidence and significance of systolic anterior motion. *J Am Coll Cardiol.* 1992;20:599-609. doi: 10.1016/0735-1097(92)90014-E. PubMed PMID: 1512339.
 - 50 Agricola E, Oppizzi M, Maisano F, Bove T, De Bonis M, Toracca L, et al. Detection of mechanisms of immediate failure by transesophageal echocardiography in quadrangular resection mitral valve repair technique for severe mitral regurgitation. *Am J Cardiol.* 2003;91:175-9. doi: 10.1016/S0002-9149(02)03105-3. PubMed PMID: 12521630.
 - 51 Shanewise JS, Cheung AT, Aronson S, Stewart WJ, Weiss RL, Mark JB, et al. ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination: recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography. *J Am Soc Echocardiogr.* 1999;12:884-900. PubMed PMID: 10511663.
 - 52 Hartnell GG. Developments in echocardiography. *Radiol Clin North Am.* 1994;32:461-75. PubMed PMID: 8184024.
 - 53 Fritzsche T, Scharl M, Siegert J. Preclinical and clinical results with an ultrasonic contrast agent. *Invest Radiol.* 1988;23:S302-5. doi: 10.1097/00004424-198809001-00067. PubMed PMID: 3058634.
 - 54 Esmaeilzadeh M, Taghavi S, Bassiri HA. Contrast Echocardiography for Diagnosis of Apical Hypertrophic Cardiomyopathy. *Iranian Heart Journal.* 2010;11:37-9.
 - 55 Dekker DL, Piziali RL, Dong E Jr. A system for ultrasonically imaging the human heart in three dimensions. *Comput Biomed Res.* 1974;7:544-53. doi: 10.1016/0010-4809(74)90031-7. PubMed PMID: 4457270.
 - 56 Moritz WE, Shreve PL. A microprocessor-based spatial locating system for use with diagnostic ultrasound. *Proc IEEE.* 1976;64:966-74. doi: 10.1109/PROC.1976.10250.
 - 57 Abraham TP, Warner JG Jr, Kon ND, Lantz PE, Fowle KM, Brooker RF, et al. Feasibility, accuracy, and incremental value of intraoperative three-dimensional transesophageal echocardiography in valve surgery. *Am J Cardiol.* 1997;80:1577-82. doi: 10.1016/S0002-9149(97)00783-2. PubMed PMID: 9416939.
 - 58 Yao J, Takeuchi M, Teupe C, Sheahan M, Connolly R, Walovitch RC, et al. Evaluation of a new ultrasound contrast agent (AI-700) using two-dimensional and three-dimensional imaging during acute ischemia. *J Am Soc Echocardiogr.* 2002;15:686-94. doi: 10.1067/mje.2002.119114. PubMed PMID: 12094166.
 - 59 McDicken WN, Sutherland GR, Moran CM, Gordon LN. Colour Doppler velocity imaging of the myocardium. *Ultrasound Med Biol.* 1992;18:651-4. doi: 10.1016/0301-5629(92)90080-T. PubMed PMID: 1413277.
 - 60 Sutherland GR, Stewart MJ, Groundstroem KW, Moran CM, Fleming A, Guell-Peris FJ, et al. Color Doppler myocardial imaging: a new technique for the assessment of myocardial function. *J Am Soc Echocardiogr.* 1994;7:441-58. PubMed PMID: 7986541.
 - 61 Smith SW, Trahey GE, Hubbard SM, Wagner RF. Properties of acoustical speckle in the presence of phase aberration. Part II: Correlation lengths. *Ultrason Imaging.* 1988;10:29-51. doi: 10.1016/0161-7346(88)90064-8. PubMed PMID: 3291367.
 - 62 Bohs LN, Trahey GE. A novel method for angle independent ultrasonic imaging of blood flow and tissue motion. *IEEE Trans Biomed Eng.* 1991;38:280-6. doi: 10.1109/10.133210. PubMed PMID: 2066142.
 - 63 Behar V, Adam D, Lysyansky P, Friedman Z. The combined effect of nonlinear filtration and window size on the accuracy of tissue displacement estimation using detected echo signals. *Ultrasonics.* 2004;41:743-53. doi: 10.1016/j.ultras.2003.09.003. PubMed PMID: 14996535.
 - 64 Notomi Y, Lysyansky P, Setser RM, Shiota T, Popović ZB, Martin-Miklović MG, et al. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. *J Am Coll Cardiol.* 2005;45:2034-41. doi: 10.1016/j.jacc.2005.02.082. PubMed PMID: 15963406.

- 65 Amundsen BH, Helle-Valle T, Edvardsen T, Torp H, Crosby J, Lyseggen E, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: validation against sonomicrometry and tagged magnetic resonance imaging. *J Am Coll Cardiol*. 2006;47:789-93. PubMed PMID: 16487846.
- 66 Helle-Valle T, Crosby J, Edvardsen T, Lyseggen E, Amundsen BH, Smith HJ, et al. New noninvasive method for assessment of left ventricular rotation: speckle tracking echocardiography. *Circulation*. 2005;112:3149-56. doi: 10.1161/CIRCULATIONAHA.104.531558. PubMed PMID: 16286606.
- 67 Bussadori C, Moreo A, Di Donato M, De Chiara B, Negura D, Dall'Aglio E, et al. A new 2D-based method for myocardial velocity strain and strain rate quantification in a normal adult and paediatric population: assessment of reference values. *Cardiovasc Ultrasound*. 2009;7:8. doi: 10.1186/1476-7120-7-8. PubMed PMID: 19216782; PubMed PMCID: PMC2657114.
- 68 Schwartz SL, Gillam LD, Weintraub AR, Sanzobrin BW, Hirst JA, Hsu TL, et al. Intracardiac echocardiography in humans using a small-sized (6F), low frequency (12.5 MHz) ultrasound catheter. Methods, imaging planes and clinical experience. *J Am Coll Cardiol*. 1993;21:189-98. doi: 10.1016/0735-1097(93)90736-K. PubMed PMID: 8417061.