Subspecialty Clinics: Cardiology

Determination of Ventricular Ejection Fraction: A Comparison of Available Imaging Methods

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Knowledge of left ventricular ejection fraction has been shown to provide diagnostic and prognostic information in patients with known or suspected heart disease. In clinical practice, the ejection fraction can be determined by using one of the five currently available imaging techniques: contrast angiography, echocardiography, radionuclide techniques of blood pool and first pass imaging, electron beam computed tomography, and magnetic resonance imaging. In this review, we discuss the clinical application as well as the advantages and disadvantages of each of these methods as it relates to determination of ventricular ejection fraction.

(Mayo Clin Proc 1997;72:860-870)

EBCT = electron beam computed tomography; LAO = left anterior oblique; LVEDD = left ventricular end-diastolic diameter; LVESD = left ventricular end-systolic diameter; MRI = magnetic resonance imaging; MUGA = multiple gated acquisition; RAO = right anterior oblique; RVU = relative value unit; Tc = technetium

Measurement of left ventricular size and systolic function is commonplace in clinical practice. Knowledge of ejection fraction,[1] absolute ventricular volumes,[2,3] and site and extent of regional wall motion abnormalities provides substantial diagnostic and prognostic information for clinicians. Historically, both left and right ventricular ejection fractions were first examined by using direct contrast ventriculography. Later, first pass and blood pool measurements of right and left ventricular ejection fraction were added by using technetium (Tc) and nuclear medicine techniques. Early M-mode echocardiography provided a limited assessment of left ventricular ejection fraction, but the advent of two-dimensional echocardiography affords a ready method to assess size and function of both ventricles. Finally, within the past decade, electron beam computed tomography (EBCT) and magnetic resonance imaging (MRI) have emerged as true three- and four-dimensional methods for precise quantification of biventricular volumes and ejection fractions.

Today, in many medical centers, clinicians often have a choice of one or more of these five methods to determine ejection fraction. The general category of each technique is as follows: planar-projection imaging (single projection images of entire ventricular chamber [contrast angiography]), volumetric imaging (time-volumetric radionuclide activity), and tomographic imaging (echocardiography, EBCT, and MRI). The purposes of this article are to discuss these methods in detail and to define the applications and limitations of each modality.

LEFT VENTRICULAR (CONTRAST) ANGIOGRAPHY

Measurement of left ventricular volumes with left ventricular angiography was first described during the late 1950s[4] and was validated in the studies by Dodge and associates[5] and Arvidsson.[6] Left ventriculography, in conjunction with selective coronary angiography, is still widely used to assess left ventricular function and left ventricular volumes.

Technique.—Although left ventricular angiography has relied on cinefilm for image display (and off-line image processing), modern-day x-ray systems now allow immediate high-quality playback with on-line digital image processing and analyses.[7] During direct left ventriculography, a suitable angiographic catheter is placed retrogradely across the aortic valve and into the left ventricular cavity. In rare cases, ventriculography is performed transseptally; the atrial septum is crossed, and a catheter is advanced through the mitral valve and into the left ventricle. This transseptal approach is generally used only when the aortic valve cannot

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be crossed retrogradely—for example, in the presence of a mechanical prosthetic aortic valve—or for the assessment of severe aortic stenosis. Alternative but uncommon ventriculographic techniques include opacification of the ventricle in conjunction with angiography of the root of aorta when aortic regurgitation is severe, direct left atrial angiography, or imaging during the levophase of angiography of a pulmonary artery (main trunk). Digital subtraction techniques, which require less contrast administration, have also been described,[8] as has the use of videodensitometry.[9-11]

For optimal assessment of global and regional left ventricular function, biplane imaging of the left ventricle is desirable and is the "gold standard" at our institution. Calculation of ventricular volumes and ejection fraction has been validated, however, from both monoplane and biplane images.[12-15] With biplane imaging, the x-ray image intensifiers are positioned in a 30° right anterior oblique (RAO) and a 60° left anterior oblique (LAO) projection; angulation of the LAO view (20 to 30° cranial) may overcome the foreshortening of the left ventricle associated with this view. For imaging of the left ventricle, 20 to 50 mL of contrast medium (ionic or nonionic) is injected through the catheter with use of a standard powered injector at a rate of 8 to 15 mL/s. The precise volume and rate depend on the type of catheter and the size of the ventricle. For optimal opacification of the endocardial contours, adequate iodinated contrast medium must be delivered at a rate that provides filling of the entire ventricle without causing ventricular ectopic activity. Depending on the individual heart rate, three to six cycles of ventricular contractions are visualized with this technique.

Determination of left ventricular volumes depends on defining the endocardial contours of the left ventricular cavity at end-systole and end-diastole, suitable calibration, and assumptions about the shape of the left ventricle. Edge detection of the endocardial contours of the cavity involves either manual (that is, visual) or automated approaches. Manual techniques are relatively straightforward to perform but are tedious. In the future, particularly with the greater use of digital imaging techniques and replacement of cinefilm, automated edge detection algorithms will be prevalent. Calculation of absolute volumes necessitates calibration of the system. This can be accomplished by filming a centimeter-ruled grid at the same imaging plane as the heart; one must consider the magnification of the image (table height, image intensifier height, and magnification mode) and correct for pincushion distortion at the periphery of the image. Alternatively, a similarly positioned sphere of known diameter can also provide a convenient calibration tool. The accuracy of left ventricular volume determinations has been well validated in the past by direct comparisons with measured volumes of cadaver hearts[5,12] and in vivo stroke volume measurements in which Fick[6] or indicator-dilution[16] techniques were used.

The geometric reference for the left ventricle is likened to a prolate spheroid[5]—an ellipsoid whose minor axes are equal (the two-dimensional projection image being a simple ellipse). For calculating ventricular volumes, the two methods that are considered accurate and generally used are the area-length method and Simpson's rule.

1. With the *area-length method (Dodge method)*,[5] the volume (V) of an ellipsoid is calculated as follows: $V = L \times M \times N \times \pi/6$. L is the semimajor (long) axis length of the cavity, and M and N are the semiminor transverse diameters measured from each of the biplane images. Measurements are usually performed directly on a computer screen. When only monoplane images are used, M and N are assumed to be the same, and because the area (A) of an ellipsoid is $A = \pi \times L/2 \times M/2$, the volume of the ellipsoid of revolution is $V = 8A^2/3\pi L$. Calculation can be made for both the global end-diastolic and end-systolic volumes.

2. With *Simpson's rule*,[5,6] volumes are calculated by dividing the biplane images into many equal segments, generally perpendicular to the longitudinal axis of the ventricle, and then adding them ("stack of coins"). In the past, this method was generally difficult to perform but is now easily performed with the availability of on-line digital imaging.

The calculated volumes from contrast angiographic studies consistently overestimate the true intracardiac volumes because the volume of the papillary muscles and trabeculae is not considered in the initial calculation.[5] Furthermore, despite the precision of the linear measurements, some estimation of the overall shape of the left ventricle is necessary. In order to overcome these problems, regression equations are used. The earliest validation studies were performed by using anteroposterior and lateral projections, and later studies that compared these to the more conventional oblique projections have shown excellent correlations.[17,18] A comparison of the anteroposterior projection to the RAO projection has documented that the latter actually yields slightly more precise volumes.[15] The correlation between monoplane and biplane methods is high, although the biplane approach is more precise; however, for practical purposes, the monoplane method is used in most laboratories, and it provides accurate volumes if corrected with a regression equation.[12-14] At our institution, calculation of ventricular volumes for clinical examinations relies only on the monoplane (RAO) method, although biplane imaging is routinely performed to complement a complete assessment of regional wall motion.

The stroke volume, the difference between end-diastolic and end-systolic volumes, divided by the end-diastolic volume times 100 yields the ejection fraction in percent. Cardiac output can also be estimated based on the calculated stroke volume and heart rate. The reproducibility of left ejection fraction measured by contrast angiography is excellent, with a mean interobserver difference of approximately 5%; however, serial ejection fraction determinations may vary by approximately 10%.[18-20]

Angiographic determination of left ventricular volumes and ejection fraction has been in use for more than 30 years. Its major drawback is that it is invasive. In the vast majority of patients, however, the risks associated with contrast ventriculography are minimal and can be minimized further by modifying the technique. In some very high-risk patients, alternative techniques should be considered. Left ventricular angiography performed in conjunction with coronary angiography or diagnostic cardiac catheterization (or both) represents a safe, accurate, and effective approach for assessment of left ventricular function. This is particularly important in the setting of acute myocardial infarction or unstable angina in which the planning of subsequent coronary interventions is facilitated by relating the coronary anatomy with the regional ventricular function.

Associated Risks and Adverse Effects.—After intraventricular injection of iodinated contrast media, most patients have a generalized sensation of warmth, which varies in intensity and lasts for 20 to 30 seconds. Ventricular ectopic beats may occur during the injection and are usually due to improper catheter placement or catheter "whip," when the rate of injection is too rapid. Such ectopic activity is rarely sustained but can make accurate calculation of ventricular volumes difficult. Serious complications can occur during ventriculography, including air embolism or thromboembolism, but with a meticulous technique, these events should be extremely rare. Careful use of pigtail catheters avoids the risks of intramyocardial staining with contrast medium and its consequences that occasionally occurred in the past when end-hole catheters were used.

Contrast agents include either ionic or nonionic iodinated compounds. Both are generally well tolerated, but hemodynamic changes with transient hypotension or bradycardia occur most frequently with ionic compounds. Nonionic contrast agents are much more expensive than ionic agents and thus should probably be reserved for patients with unstable angina or acute myocardial infarction, poor left ventricular function, hypotension, severe aortic stenosis, renal insufficiency (serum creatinine level higher than 2.5 mg/dL), or a history of severe contrast allergy. If the amount of contrast medium to be used is a concern, a smaller volume can be administered, and left ventricular opacification will be good if digital subtraction techniques are used.

Finally, with left ventricular angiography, use of ionizing radiation is necessary, and thus the patient and the attending personnel are exposed to scattered radiation. Phantom studies from our laboratory[21] have shown that, during fluoroscopy, radiation exposure ("skin" entry) is approximately 1 rad/min (fluoroscopic exposure occurs for approximately 1 minute), whereas recording-acquisition (cine or digital) exposure is approximately 12 rad/min (total exposure, less than 10 seconds). These radiation doses relate to 30 frames per second and would be double for biplane acquisition. The individual exposure varies depending on the size of the patient and would be much higher for large patients. A careful fluoroscopic technique, which includes collimation of the x-ray beam and minimization of the patient-to-image intensifier height, should always be used. For a further reduction in the cumulative radiation dose, slower frame rates (7.5 or 15 frames per second), if available, can be used when catheters are being positioned.

ECHOCARDIOGRAPHY

Echocardiographic estimation of left ventricular ejection fraction is widely available. An appropriate and standardized imaging technique is essential and should provide multiple views when all possible acoustic windows are being used.[22] With this approach, each segment of the left ventricle can be visualized from multiple angles. These views must be orthogonal to the major and minor axes of the heart in order to avoid images that foreshorten the left ventricular chamber. The experience of the sonographer or physician is crucial for correct performance and interpretation of the echocardiographic images, inasmuch as the technique is highly operator-dependent. Ideally, the best approach for assessment of left ventricular function involves the physician directly supervising the sonographer and reviewing the images while the patient is still available for additional imaging. Although echocardiography is a real-time imaging technique, sufficient imaging time should be allowed for examination and recording of a large number of beats for analysis. For calculation of left ventricular ejection fraction, on-line software that uses several algorithms[23,24] is commonly available on modern two-dimensional echocardiographic equipment.

Visual Estimation of Ejection Fraction.—A visual estimation of ejection fraction is commonly determined in patients undergoing routine transthoracic echocardiography. The estimated ejection fraction is reported either as a number (often rounded) or as a range (for example, 50 to 55%). The general validity of this approach has been shown in a comparison with other techniques,[25-27] and this method avoids potential sources of error related to calculations that incorporate several semiquantitative measures, each of which has its own range of errors. Nonetheless, errors related to interobserver variability (which may be relatively high)[27] are a concern but are related to experience of the sonographer.

Another potential pitfall of visual estimation of ejection fraction is that the sonographer judges the area change of the tomographic image of the left ventricle on the screen and this is not absolutely the same as the true volumetric changes of the left ventricle during contraction. This source of error may be of minor clinical importance in patients with well-preserved left ventricular function but can be substantial in patients with reduced function. For example, an area change of 10% from diastole to systole can correspond to as much as a 19% volumetric change in global ejection fraction. Therefore, visual estimation of ejection fraction is not commonly used as the sole technique for assessing left ventricular function. In circumstances in which the quantitative assessment is technically difficult or flawed because of various technical factors, however, visual estimation of ejection fraction is clinically useful.

Quantification of Ejection Fraction.—Quantification or semiquantification of left ventricular ejection fraction is routinely performed by several two-dimensional echocardiographic techniques.

Measurement of Left Ventricular Diameters.—Mid-left ventricular end-diastolic and end-systolic diameters can be measured by using the M-mode[28] cursor, oriented by two-dimensional imaging, to ensure appropriate positioning of the line of measurement, generally at the mid-papillary muscle level from the short (transverse cardiac) axis image. The left ventricular end-diastolic diameter (LVEDD) is measured as coincident to the R wave of the electrocardiogram, and the left ventricular end-systolic diameter (LVESD) is measured at the maximal excursion of the septum during the cardiac cycle. The ejection fraction (EF) is calculated by using the square of these diameters: $EF (\%) = [(LVEDD)^2 - (LVESD)^2] \times 100/(LVEDD)^2$. A similar evaluation can be made by estimating the end-diastolic and end-systolic volumes provided by these diameters.[29] The method based on the squared diameters is clinically satisfactory but can be limited by the presence of regional wall motion abnormalities, especially at levels near the base and the apex of the left ventricle, and it implies certain a priori assumptions about overall left ventricular shape. Additionally, it does not incorporate changes in the long-axis length of the left ventricle during contraction, which can contribute to errors from this calculation, although a correction can be modeled into the original equation.[30] If the ultrasonic beam cannot be appropriately aligned, it is possible to measure (by using parasternal long-axis and apical four- and two-chamber views) a series of diameters directly from the two-dimensional images in diastole and systole to calculate the ejection fraction.[30]

Measurement of Left Ventricular Volumes.—Left ventricular volumes can be measured with two-dimensional echocardiography by imaging the apical views (four- and two-chamber) and using the area-length method[24] (similar to that used for contrast angiography) or modified Simpson's rule. The ejection fraction is the ratio of the stroke volume and the end-diastolic volume. The clinical utilization of these techniques is limited, not by the current equipment that provides high-resolution imaging but by the difficulty in consistently identifying and then measuring the entire endocardial left ventricular contour with a planimeter. Structures such as the papillary muscles and ventricular trabeculations must be carefully separated from the true left ventricular endocardial contour to avoid errors in determining the left ventricular volumes. Straightforward visual identification of the endocardium may not be possible in all positions, especially in the lateral (peripheral) sections of the ultrasonic images ("side lobe artifacts"); however, some ultrasound devices offer the ability to adjust the lateral gain compensation to improve lateral image border definition. These distortions tend to decrease the size of the cavity artifactually.[31] Therefore, a useful approach is to judge the relationship of the endocardial surface with the position of the epicardial surface and the known thickness of the ventricular wall judged at the base of the heart. The technique of tracing the left ventricular contour for the measurement of left ventricular volumes is associated with a pronounced "learning phase." During the learning phase, it is useful for the sonographer to corroborate the stroke volume obtained with this technique with an independent factor—the left ventricular stroke volume measured by Doppler velocimetry[32]—to ensure the accuracy of the method. The reproducibility of left ventricular volume estimates with use of transthoracic echocardiography was low during the early 1980s[33] but has improved considerably,[34,35] and now ejection fraction can be measured even when regional wall motion abnormalities are present.[36] Recently introduced methods such as B-mode color imaging[37] and contrast enhancement of the left ventricular cavity with sonicated albumin or, in the future, newer intravenously administered contrast agents may be useful, especially in difficult cases.

All methods of measurement or estimation of ejection fraction with use of echocardiography have ranges of error or variation. Of importance, the range of error must be decreased by combining various methods and maintaining quality control. Therefore, our practice (in most cases) is to combine, within the echocardiographic examination, the qualitative results of the visually estimated ejection fraction with the calculated ejection fraction to provide a result with a limited range of error. Although the reliability of the measurement of ejection fraction by echocardiography has been confirmed, ongoing quality control is essential. A review of results based on comparisons with other methods performed within a short interval (such as left ventricular angiography or radionuclide angiography) and a detailed review of the discrepant cases are necessary to analyze potential causes of systematic errors.

New Techniques.—Some echocardiography vendors now provide automatic border detection by using information derived from back-scattered ultrasonography.[38] The advantage of such algorithms is in providing a real-time recognition of the left ventricular endocardial border and thus allowing beat-by-beat calculation of ejection fraction, albeit based on a single two-dimensional area and only in one projection. The limitations of this method include the algorithm recognizing trabeculation and papillary muscles as part of the left ventricular wall (these structures must not be included as part of the volumetric analyses previously discussed) and gain dependence of border placement (especially in the lateral portions of the image).[39] Although several studies[38,40] have suggested that this technique is appropriate for the measurement of ejection fraction, consensus regarding its broad clinical use is not widespread. Three- and four-dimensional ultrasound imaging is making great strides toward clinical applicability,[41] and preliminary studies for the quantification of left ventricular volume and ejection fraction are encouraging.[42,43] Transesophageal echocardiography provides excellent images of the left ventricle[44] and can be used to measure ejection fraction.[45,46]

RADIONUCLIDE ANGIOGRAPHY

Radionuclide angiography, a volumetric technique, provides a reliable and quantitative measurement of left ventricular ejection fraction. It is obtained without assumptions about left ventricular geometry and is highly reproducible during serial measurements. This technique contrasts with conventional angiography (ventriculography), a planar-projection method, and two-dimensional echocardiography (despite multilevel tomographic data), both of which require some assumptions about overall left ventricular geometry to calculate ejection fraction.

For radionuclide angiography, a small field-of-view Anger gamma camera with a single sodium iodide crystal is used to acquire the data. A lead collimator is needed to "stratify" the gamma rays from the tracer radionuclide (^{99m}Tc) to allow only parallel rays to interact with the camera crystal. A high sensitivity collimator increases the count rate but decreases the spatial resolution of the image. This is needed for exercise studies in which less time is available to acquire data. For resting studies (when more time is available for imaging), a medium sensitivity collimator is desirable, and spatial resolution is improved. The system is operated by a standardized microcomputer.

Radionuclide angiography can be divided into first pass and equilibrium ("blood pool" or multiple gated acquisition [MUGA]) studies.

First Pass Radionuclide Angiography.—First pass radionuclide angiography measures cardiac performance by using a multicrystal camera that detects count activity from the initial transit of ^{99m}Tc pertechnetate or a ^{99m}Tc-labeled myocardial perfusion agent (such as sestamibi) through the heart chambers. Because the half-life of Tc-based perfusion agents is sufficiently long and redistribution is minimal, perfusion imaging can be delayed, if necessary, for up to 6 hours after completion of the first pass measurements.

The radionuclide is injected as a bolus into a moderate-sized peripheral vein (such as the medial antecubital), followed by a saline flush; it passes through the right atrium and right ventricle, enters the lungs and then the left atrium and left ventricle. When one tracks the bolus into the left side of the heart and uses appropriate camera positioning, overlapping count activity from the right ventricle does not usually interfere with first pass imaging of the left ventricle. The study is gated to the electrocardiogram, and 20 to 100 frames are obtained per R-R interval. Approximately 5 heart beats are averaged to increase overall count density and the reliability of the ejection fraction calculation. Because count averaging is used, ectopic activity and atrial fibrillation adversely affect the accuracy of the measurement. The greatest activity recorded during each heart beat represents end-diastole, and the smallest amount represents end-systole. The difference between end-diastolic and end-systolic counts represents the stroke volume. Stroke volume is divided by the end-diastolic counts to obtain ejection fraction (that is, EF (%) = [diastolic counts – systolic counts]/[total diastolic counts] x 100).

Equilibrium Radionuclide Angiography.—In an effort to enhance count activity and reliability of ejection fraction measurements, an equilibrium (blood pool) radionuclide angiographic method was developed. With this method, ^{99m}Tc pertechnetate is mixed with the patient's blood, either in vivo, by injecting the agent into a vein, or in vitro, by mixing it in a syringe. Tin, a reducing agent, is added to enhance transit of the ^{99m}Tc pertechnetate into the erythrocytes. Acquisition of the data is gated to the electrocardiogram and continues until a prespecified number of counts have been obtained. A high spatial resolution ejection fraction measurement is obtained with 5 to 10 million counts in 30 to 60 frames. In contrast with first pass acquisition, however, the left ventricle must be carefully separated from the other cardiac chambers, especially the right ventricle and left atrium, to prevent overlap of count activity and diminished accuracy of the ejection fraction measurement. Thus, the camera is positioned to facilitate maximal septal separation between the right and left ventricular chambers. A "routine view" for quantification of the left ventricular ejection fraction by equilibrium imaging is approximately a 45° LAO projection (with or without some cranial tilt); thus, imaging of the interventricular septum is perpendicular to the plane of the face of the gamma camera. In studies comparing the measurement of ejection fraction with radionuclide angiography and contrast angiography, a close correlation has been shown. Despite pronounced interindividual variability due to differences in body size, body habitus, and subsequent tissue attenuation, serial studies in the same patient have a high degree of reproducibility.

Both qualitative and quantitative assessments of regional wall motion are possible with radionuclide angiography; however, most assessments are done qualitatively by visually grading the degree of wall motion impairment, from mildly hypokinetic to dyskinetic. A regional ejection fraction, although less commonly performed, can be determined and provides a quantitative assessment of regional endocardial motion.

Although radionuclide angiography can measure left ventricular volume and cardiac output, it is not widely used for this purpose. Several methods have been tried, and the most useful is based on count rate from the background-corrected left ventricle in comparison with activity in a known volume of the patient's blood. Attenuation correction is necessary and depends on the distance from the surface of the chest wall to the center of the left ventricle. Considerable effort is needed to obtain a reliable volume measurement and probably contributes to the underuse of this method.

Limitations.—The radionuclide technique has four major limitations. (1) Erythrocytes may not tag appropriately with ^{99m}Tc pertechnetate (an uncommon occurrence), and thus overall count activity is reduced during an equilibrium study. (2) Measurement of ejection fraction with the first pass method may be unreliable because of an inadequate bolus injection and "stretching out" of the radionuclide as it passes through the heart, an outcome that contributes to a reduction in count activity; this problem can be compounded by poor plane separation of the right and left ventricle. (3) If other cardiac chambers overlap the left ventricle, the count activity from these chambers will be included in the calculation of the ejection fraction, and thus an erroneous measurement is obtained, resulting in an artificial lowering of the ejection fraction. (4) Arrhythmias including ectopic beats and atrial fibrillation produce R-R variability, and count activity varies from beat to beat; thus, the accuracy of ejection fraction measurements is limited.

ELECTRON BEAM COMPUTED TOMOGRAPHY

EBCT, also called ultrafast or cine-CT, was designed by Boyd[47] and is manufactured by Imatron, Inc. (South San Francisco, California). Quantitative determination of ejection fraction by EBCT is predicated on precise measurement of end-diastolic and end-systolic volumes of the left and right ventricular chambers. The entire ventricular cavity is imaged in 12 cardiac cycles (left ventricle, 8; right ventricle, 4 more), at least from end-diastole through end-systole; polytomographic, high spatial resolution images are obtained. A conventional Simpson's rule algorithm is then used to avoid any assumptions about ventricular conformation.

Routinely, one of two polytomographic views of the heart is appropriate for quantification of left and right ventricular ejection fraction. (1) A "short-axis" view (or transverse cardiac axis analogous to that obtained by using two-dimensional echocardiography) is obtained by "slewing" the scanning table clockwise (to the patient's right) by 15 to 25° and using an upright cranial tilt of 15 to 20° (additional cranial tilt is often provided by having the patient rest on a 10 to 15° standardized wedge pillow). (2) With a long-axis view, which is analogous to the "modified" four-chamber view in echocardiography (similar to the RAO contrast ventriculogram), the scanning table is maximally rotated (about 25°) counterclockwise (to the patient's left) without cranial tilt.

Because the CT densities of the myocardium and blood are similar, intravenous administration of iodinated contrast medium is necessary to facilitate selective opacification of the ventricular chambers during scanning. Sixty to 100 mL of nonionic contrast medium administered in a peripheral vein at a rate of 3 to 4 mL/s is necessary. One 8- to 12-level scan is usually sufficient for visualizing the entire extent of the heart, from the left ventricular apex through the right ventricular outflow tract. Images are obtained at a spatial resolution of 0.97 mm^2/pixel (360 x 360 matrix and a 350-cm field of view) with a slice thickness of 8 mm.

Experimental studies[48] have shown an excellent correlation between the left ventricular stroke volume measured by aortic electromagnetic flow probes and thermodilution (r = 0.99, slope = 1.01), under a wide variety of loading conditions and alterations in regional wall motion. Both intraobserver and interobserver variability for all cardiac variables measured (end-diastolic volumes, end-systolic volumes, stroke volumes, ejection fraction, and muscle mass) are negligible (less than 3%). Quantification of right ventricular function has been documented by using EBCT,[49] in which determinations of global ejection fraction and comparison of stroke volume with that of the left ventricle may be clinically pertinent.

With EBCT, the total scanning time is approximately 8 to 12 cardiac cycles (at heart rates up to 120 beats/min). Fifteen minutes are needed for positioning of the patient, placement of the intravenous access, determination of the circulation time, and obtaining "scout images" for subsequent computer-controlled scanning. Thus, a total of 20 to 25 minutes are needed to perform a complete study of right and left ventricular volumes and function.

Qualitative Assessment.—Image reconstruction is about 1 second per tomogram. A qualitative (visual) assessment of ejection fraction and regional wall motion can then be made by using methods similar to those described for two-dimensional echocardiography. The inherent advantage of EBCT for this purpose (as with MRI, which is subsequently discussed) is that multiple, parallel tomographic levels are available for review, from the base of the heart through the ventricular apex.

Quantitative Assessment.—For quantification of the ejection fraction, the endocardial borders of the end-diastolic and end-systolic frames from each tomographic level are inscribed with use of software supplied by the manufacturer. Individual tomographic volumes are determined, and the global ventricular end-diastolic and end-systolic volumes are determined by using a modified Simpson's rule.[49] The ejection fraction of both the left and right ventricles is determined by taking the global stroke volume of the respective chambers and dividing by their respective end-diastolic volumes. Left ventricular muscle mass is routinely quantified when both ventricles are assessed. Because images are acquired from the left ventricular apex through the base, qualitative and quantitative assessments of regional ventricular wall motion, wall thicknesses, and systolic thickening are available.[50] The unique image representation of EBCT allows determination of cardiac structure independent of geometric or kinetic assumptions; the negligible intraobserver and interobserver variability and the precision of the measurements make it well suited for serial studies of the heart. In more than 90% of patients, an excellent scan can be obtained, with appropriate opacification of all cardiac cavities for visualization and evaluation of cardiac parameters. Tomographic imaging of the chest with EBCT (as with MRI) facilitates definition of the atria, gross valvular malformations, pericardium, mediastinum, and pulmonary parenchyma.

Limitations.—The two major drawbacks of EBCT for determination of cardiac anatomy and function are radiation exposure and use of iodinated contrast media. In EBCT studies of ventricular function, radiation exposure occurs. Gonadal exposure (unlike radionuclide methods) is nil due to the focused electron beam and x-ray collimation. Skin entrance exposure is approximately 12 rad/s when scanning posteriorly and 2 rad/s when scanning anteriorly because the beam enters over a 210° angle from the spine, not a 360° exposure as with routine CT of the body. The total mean radiation dose for a ventricular function study is about 5 rad (slightly less than that for a standard CT of the chest). The use of a nonionic contrast agent abolishes the interference of dye with cardiac function, as has been described with ionic contrast agents.[48] Patients with proven severe contrast allergy and pronounced renal failure (creatinine level greater than 2.5 mg/dL) should not undergo EBCT for calculation of the ejection fraction. In patients with mild contrast sensitivity, a corticosteroid preparation and proper hydration may be necessary before they undergo EBCT cardiac scanning. Another limitation is that an EBCT scan is computer controlled, and electrocardiographic triggering is necessary for scan initiation and appropriate timing between scans. Thus, a regular rhythm is needed for appropriate scanning sequences (either sinus or paced rhythm). Frequent extra systoles or atrial fibrillation (or both) with substantially varying R-R intervals will result in inaccurate scanning sequences (for example, end-diastolic frame is not the first frame of the cardiac cycle sequence), and imaging may not span the entire cardiac cycle. Finally, EBCT scanning is currently available only at a few major medical centers throughout the United States, Europe, and Asia.

MAGNETIC RESONANCE IMAGING

The earliest method of determining left ventricular function with MRI was to obtain a single end-diastolic and end-systolic spin echo image in the short axis and then calculate the ejection fraction in a manner similar to that described when two-dimensional echocardiography is used.[51] Because MRI is a tomographic technique with a slice thickness of about 1 cm, this approach was useful only in patients with global left ventricular dysfunction. A second approach was to obtain an end-systolic and end-diastolic image in the longitudinal axis of the left ventricle parallel to the septum and then calculate the ejection fraction.[52] This simulated the RAO single plane angiographic view. This approach, however, was unreliable in patients with regional wall motion abnormalities. A more dependable method of measuring ejection fraction in patients with coronary artery disease was to obtain multiple short-axis spin echo images that spanned the left ventricle from the apex to the base.[53] By stacking the images with use of a Simpson's rule algorithm, volumes and ejection fraction are readily measured. Data are obtained, however, during at least 128 heart beats, and a limitation of the spin echo pulse sequence is the lengthy time needed for acquisition—about 2 minutes for each image. At least 20 minutes is needed to obtain end-systolic and end-diastolic images at five levels in the short axis of the left ventricle. Difficulty in accurately selecting end-systole without an endless-loop display of ventricular contraction is a major limitation.

More recently, development of the gradient echo pulse sequence allows 15 to 30 images to be obtained in a single acquisition gated to the R wave of the electrocardiogram. This is then displayed as an endless-loop cine of ventricular contraction, allowing better depiction of end-systole. More frames will be obtained at a longer R-R interval. In contrast to the spin echo pulse sequence, gradient echo is highly sensitive to laminar blood flow and is associated with an increase in MR signal. With improved natural contrast between the myocardium and blood pool, the endocardium can be accurately identified. For calculation of global function, multiple levels of the ventricle must be imaged. An application of gradient echo imaging during pharmacologic stress has been described.[54]

The time needed to measure left ventricular ejection fraction can be shortened by obtaining two orthogonal gradient echo images and using an angiographic area-length method to calculate volumes. A longitudinal-axis image parallel to the septum (RAO equivalent) and a midventricular short-axis image are obtained, and volumes are calculated by using the Sandler-Dodge biplane method. The results correlate well with those of contrast angiography, although end-diastolic volume is consistently smaller with MRI, resulting in slightly lower ejection fractions. Of importance, the MRI biplane method may disregard regional wall motion abnormalities present outside the tomographic imaging plane. This limitation does not occur with contrast angiography because it is a projection imaging technique, and the entire ventricle is included in the analysis.

The development of a breath-hold MRI technique that allows acquisition of 20 to 30 images per cardiac cycle in 15 to 20 seconds represents a major advance in cardiac MRI. With repeated breath-holds, endless loop, short-axis displays of the left ventricle are obtained at multiple levels. Each endless loop display uses images that are 1 cm thick and, if obtained contiguously, would require about 10 breath-hold acquisitions to image a normal heart completely. A Simpson's rule algorithm is used to calculate volumes and ejection fraction. Although this method has not yet been correlated with established imaging techniques, it seems to represent the most accurate method to assess cardiac volumes and ejection fraction by MRI.

Cardiac measurements by MRI are made off-line. The ejection fraction can be calculated if the patient is undergoing routine cardiac MRI for some other reason, and an additional 10 minutes is needed if appropriate hardware and software from the manufacturer are in place. In order to shorten this portion of the study, the number of breath-hold acquisitions can be reduced by increasing the spacing between the tomographic slices that span the left ventricle. A qualitative estimate of ejection fraction can also be made by viewing single, short-axis, endless-loop scans obtained at the apex, midventricle, and base. Quantitative methods to determine ejection fraction are possible by using approaches similar to those discussed for EBCT. Calculation of right ventricular volumes and ejection fraction is also possible with MRI; however, due to the crescent shape of the right ventricle, the only practical method of assessing ejection fraction is by using a Simpson's rule algorithm and stacking of the MRI images (as is done with EBCT).

An advantage of MRI over radionuclide ventriculography and contrast angiography is its ability to measure regional wall thickening. In addition, left ventricular volumes can be measured without correcting for tissue attenuation or concern about overlap from surrounding structures, such as the left atrium and right ventricle. Because ionizing radiation is not a concern with MRI, this technique is appropriate for serial studies. The use of contrast medium (as needed with EBCT and traditional angiography) may not be desirable if the patient has renal failure or has had a reaction to contrast medium. In comparison with echocardiography, MRI has a larger window of view, and the entire heart is readily imaged. Overlying structures such as the lungs do not interfere with MRI.

The disadvantages associated with MRI in the measurement of volume and function include the occurrence of claustrophobia in 5 to 10% of patients and the degradation of image quality in 10 to 20% because of motion, mainly due to cardiac contraction and respiration. The development of motion-insensitive pulse sequences has been helpful, and new software continues to address this problem. All tomographic imaging methods are associated with inaccuracy due to rotational and translational motion as well as shortening of the ventricle during contraction. Although MRI is usually available in moderate to large medical centers and as stand-alone units in some areas, not all MRI units can perform cardiac studies without access to appropriate imaging sequences and imaging and analysis software. Thus, although MRI is much more available than EBCT throughout the United States, many centers may be unable to perform routine cardiac functional imaging.

COSTS ASSOCIATED WITH DETERMINATION OF EJECTION FRACTION

The procedural fees and costs for obtaining measurements of left ventricular ejection fraction vary considerably throughout the United States. Perhaps a more universal method to measure "costs" is to define the reimbursement based on the relative value unit (RVU). The RVU is a national standard of work effort or work value established by the Health Care Financing Administration in conjunction with the American Medical Association and is applicable for most CPT (Current Procedural Terminology) codes. It generally consists of three measurements—physician work effort, practice expense, and malpractice risk. These charges are usually applicable at most medical institutions throughout the United States for the measurement of left ventricular ejection fraction (Table 1).

In most patients, performance of contrast ventriculography during selective coronary angiography increases the

Table 1.—**Relative Value Units for Measurement of Left Ventricular Ejection Fraction as a Function of Imaging**

Imaging modality	Relative value unit
Contrast angiography	55
Two-dimensional echocardiography	
Limited study	5.82
Extended study	13.5
Radionuclide angiography	
First pass	6.79
Blood pool (ejection fraction only)	7.08
Blood pool	10.59
Magnetic resonance imaging	13.78
Electron beam computed tomography	9.04

procedure time and radiation exposure only minimally; additional risk is also minimal. Radionuclide angiography can be done as a first pass technique, generally during a myocardial perfusion study, by using an agent such as sestamibi. MUGA examinations can be done as "ejection fraction" only and are generally less costly than a complete study, which includes a qualitative assessment of regional wall motion. The cost of echocardiography expressed in RVU (for an extended study) may be more than that for some other techniques for measurement of the ejection fraction; however, ejection fraction is only a part of the reported results, and other important information is provided, such as estimation of left ventricular mass, interpretation of regional wall motion, diastolic function, estimates of pulmonary systolic pressures, and valvular function. Although information is available for the RVUs for performance of MRI and EBCT of the heart, it is extrapolated from the cost figures for the more general examinations of the heart, chest, and thorax and may be subject to further modifications as these procedures become more commonplace. Routine MRI and EBCT scans of the left ventricle also include views of all the cardiac chambers and the proximal coronary arteries, as well as the pericardium, mediastinum, chest, and lung fields.

RECOMMENDATIONS

Each of the methods available for determination of ventricular ejection fraction and assessment of cardiac systolic function has distinct advantages and disadvantages. In this review, we attempted to present the technical and practical aspects of determination of left (and, when possible, right) ventricular function in clinical practice. The imaging method that the clinician chooses should depend on the clinical situation and the local availability of a specific technique.

Numerous attributes could be used to define the ideal method to assess ventricular ejection fraction. The ideal technique should provide images that can be unequivocally interpreted with minimal intraobserver and interobserver variability. The imaging method should not interfere with the biologic function itself, and risk to the patient should be minimal. Serial studies should be feasible in order to assess possible changes due to disease processes. Finally, the disease process itself should not interfere with the measurement of the ejection fraction. Unfortunately, none of the currently available imaging techniques discussed herein fulfill all these requirements. Additionally, in deciding which technique to use, the clinician should understand the general methods (planar projection, volumetric, and tomographic) and the potential limitations in a specific patient with respect to dependence (contrast angiography and echocardiography) or independence (radionuclide angiography, EBCT, and MRI) of measures on assumptions of global ventricular geometry.

Thus, despite the acknowledged importance of ventricular ejection fraction, the clinician is faced with decisions about the most efficient, accurate, and safe means to assess a patient's heart under a specific set of clinical circumstances. A comparison of the five available techniques for determining other potentially important clinical measures of cardiac function is presented in Table 2.

In patients in whom valvular function is uncertain, two-dimensional echocardiography is the method of choice. In patients with poor acoustic windows, commonly because of obesity or advanced emphysema, quantitative measures of ejection fraction may be difficult, but qualitative estimates are generally considered adequate.

For the resting ejection fraction, MUGA is the least costly of all the discussed methods, is reliable, and is appropriate for serial measurements. The first pass left ventricular ejection fraction using Tc sestamibi has limited validation but is a valuable adjunct to the assessment of patients undergoing stress perfusion imaging.

Direct left ventriculography performed during the course of elective or urgent coronary angiography is safe, adds little to the overall contrast media "dye" load, and is most appropriate under such circumstances, unless a prior measurement of ejection fraction has been made by using an alternative method.

Finally, when absolute measures of left and right ventricular volumes and ejection fraction are needed, MRI and especially EBCT are the most quantitative and reproducible methods. In patients undergoing studies because of congenital heart disease (MRI, EBCT), assessment before lung transplantation (MRI, EBCT), or coronary artery calcification (EBCT), ventricular volumes and global and regional function can be determined at the same time.

Table 2.—**Comparison of Imaging Modalities in Determining Cardiac Function***

Method	LVEF	RV function	LV mass	RWMA
Contrast angiography	Yes	No	No	Yes
Two-dimensional echocardiography	Yes	Yes	Yes	Yes
Radionuclide angiography				
First pass	Yes	Yes (quantitative†)	No	No
Blood pool	Yes	No	No	Yes
Magnetic resonance imaging	Yes	Yes (quantitative†)	Yes	Yes
Electron beam computed tomography	Yes	Yes (quantitative†)	Yes	Yes

*LVEF = left ventricular ejection fraction; LV = left ventricular; RV = right ventricular; RWMA = regional wall motion abnormality.

†Absolute measurements of global ventricular volumes possible to facilitate determination of ejection fraction.

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