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Advances in Noninvasive Cardiovascular Imaging: Implications for the Anesthesiologist

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DURING THE PAST DECADE, major advances in microelectronics have made it possible to acquire noninvasive diagnostic information in the form of remarkably revealing images of human anatomy and physiology, including even single subcellular processes. Patients and physicians benefit from these noninvasive methods because they offer more information and less risk to the patient than previous techniques. In this review, we summarize recent advances in echocardiography, cardiovascular nuclear medicine, and magnetic resonance imaging and spectroscopy, all of which have implications for the practice of anesthesiology.

Many anesthesiologists may be unfamiliar with all the clinical applications of these new techniques because the technology has developed so quickly. We have a fourfold purpose in preparing this review: (1) to enable anesthesiologists to better use information provided by imaging techniques to assess patient cardiovascular status; (2) to facilitate the appropriate initiation of these studies by consultant anesthesiologists; (3) to educate practitioners to more critically review new reports on these techniques; and (4) to provide guidelines by which to measure progress in noninvasive cardiovascular imaging.

Echocardiography

Piezoelectric crystals are the transducers and receivers of the sound waves used in echocardiographic studies. These quartz crystals vibrate when electrically stimulated to produce ultrasound—sound at frequencies above the level detectable by the human ear (>20,000 Hz). Conversely, when struck by ultrasound, the crystals produce an electrical signal. Typically, an echocardiographic study involves intermittent pulses of ultrasound at 2.5–5 MHz. When ultrasound strikes the interface of tissues of different densities—for example, the pericardium and the heart—a portion of the ultrasound is reflected. The greater the difference in densities, the greater the portion of ultrasound reflected. For example, air in the left ventricle (LV) reflects a much greater portion of the transmitted ultrasound than blood, and is translated as a brighter signal on the display screen. The longer the sound wave takes to bounce back to the transducer, the greater its distance from the transducer. This provides information on the location of the tissue. (Sound is assumed to travel at 1540 m/sec in all tissues of the body at 37° C.) No ionizing radiation of any type is used in echocardiography, and no adverse effects of ultrasound have ever been demonstrated in humans.

PRECORDIAL ECHOCARDIOGRAPHY

The first echocardiograms were single-plane views of cardiac structures traced on moving photosensitive paper, and were called motion or M-mode studies. Today, M-mode echocardiograms are still used for viewing rapidly moving structures, such as valve leaflets, because M-mode transducers can produce up to 1000 images/sec. However, M-mode echocardiograms reveal only a small portion of the heart at one time, making orientation and interpretation of spatial relationships difficult. By using multiple crystals (linear or phased array transducers) or rapidly moving a single crystal (mechanical transducer), multiple views can be obtained and collated into a two-dimensional (2-D) image. Although 2-D techniques produce only about 30 images/sec, definition in two dimensions provides an enormous advantage in recognizing anatomic and pathologic landmarks. Images are displayed in "real time" on a monitor screen or recorded on video tape for later review. Viewing them, one has the illusion that they are continuously moving, an effect similar to movies.

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More and more echocardiographic laboratories have been established in which patients are examined by specially skilled technicians, and recordings are interpreted promptly and consistently by echocardiographers. Patients may spend an hour in the "echo lab" and have preliminary results before they leave. Portable services are available for those patients who cannot be transported to the echo lab, but an adequate examination often requires that they be able to cooperate in breath holding and body positioning. The minimum examination consists of multiple cross-sectional views of the heart and great vessels from the parasternal (fig. 1), apical, subcostal, and suprasternal "windows."[1] The windows are the areas of the precordium through which the ultrasound beam can reach the heart without being reflected by overlying lung tissue. The goal of the examination is to map the internal and external anatomy and function of the heart, pericardium, and great vessels. The relative and absolute size of the chambers and vessels are noted, the extent and pattern of regional and global contraction estimated, and the anatomic or pathologic abnormalities delineated. A sample finding might be LV hypertrophy and depressed ejection fraction in a patient with long-standing hypertension.

As in other consultative services, patients are referred with brief histories and specific diagnostic questions requiring resolution. A sample referral may read: "The patient is a 19-year-old healthy male with prominent pulmonary vascular markings and right ventricular (RV) outflow tract demonstrated on his chest roentgenogram. Does he have an atrial septal defect?" To help confirm the presence of an intraatrial shunt, the echocardiographer performs a contrast study by injecting 3–5 ml of normal saline into a peripheral vein. The microbubbles contained in the saline form bright reflections in the right atrium, marking the flow of any blood across an intraatrial shunt. During this study, right atrial pressure may be transiently raised above left atrial pressure by a Valsalva maneuver, which will help push the contrast vehicle across the defect into the left atrium. The microbubbles are so small and in such low concentration that they pose no risk to the patient.

Elucidating the luminal size of coronary arteries is beyond the technology of current precordial echocardiographic systems. However, we can obtain important information on the presence and extent of ischemic heart disease. Since Tennant and Wiggers first described the association of segmental wall motion abnormalities (SWMA) and ischemia,[2] others have proven that ischemic segments of human and animal heart do not exhibit normal inward wall motion or thickening during systole.[3,4] In one dramatic application of 2-D echocardiography, Horowitz *et al.* correctly diagnosed 31 of 33 patients having acute myocardial infarctions by documenting SWMA: only 18 of the 33 had diagnostic electrocardiographic changes.[5] In a separate application of 2-D echocardiography, Kisslo *et al.* found 90% of the SWMAs documented by biplane angiography.[6]

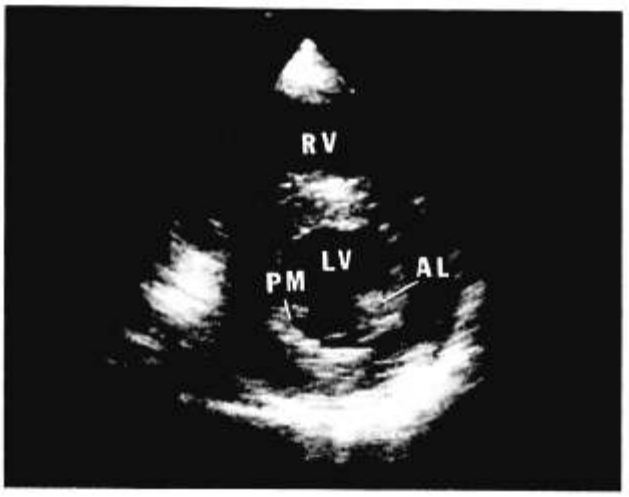

FIG. 1. A stop-action, short-axis echocardiogram of the left ventricle at the papillary muscles. This image was produced with a precordial transducer placed in the fourth intercostal space immediately to the left of the sternum. LV = left ventricle; RV = right ventricle; AL = anterolateral papillary muscle; PM = posteromedial papillary muscle.

Although focal myocarditis and certain rare infiltrative disorders and tumors of the myocardium also may produce SWMAs, these are much less common causes than ischemic heart disease. The presence of an akinetic (noncontracting) or dyskinetic (paradoxically moving) segment of the LV may indicate an old infarction.[7] However, the development of a new SWMA during examination, *e.g.*, during a stress test,[8] is likely to be caused by myocardial ischemia. Nearly all patients having transmural infarctions will have SWMAs.[9,10] The extent of the abnormalities detected by echocardiography correlates with overall ventricular function[11,12] and patient prognoses,[13,14] but usually results in overestimates of the extent of infarction.[15]

Two-dimensional echocardiography provides reliable estimates of ventricular filling and ejection,[16–18] wall thickness,[19] and mass.[20] Such quantitative data can be used to calculate end-diastolic volume, ejection fraction, systolic wall stress, and correlates of contractility, such as velocity of circumferential fiber shortening. Echocardiography is thus the premier clinical tool for assessment of ventricular function. However, no echocardiographic parameter is an ideal measure of ventricular function, because all available measures are critically dependent on cardiac loading conditions, valvular function and, often, heart rate. Newer indices of ventricular function are emerging which appear to be independent of loading conditions, but these require volume and intraventricular pressure

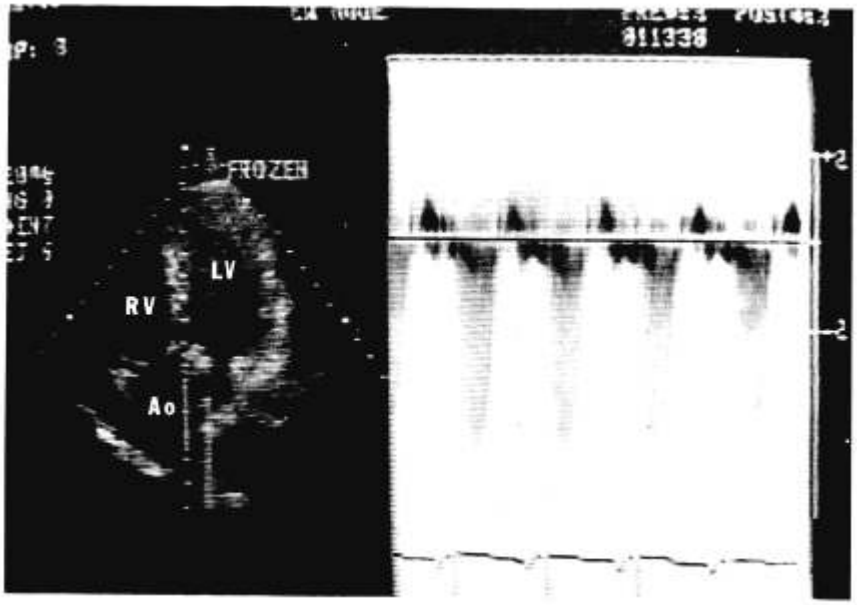

FIG. 2. To the left, a stop-action, long-axis echocardiogram of the left ventricle. This image was produced with a precordial transducer positioned over the apex impulse. The nearly verticle white line in the aorta (Ao) marks the location of the continuous wave (CW) ultrasound beam whose reflection is analysed for the Doppler effect. This beam is positioned through the aortic valve outflow. Just right of the CW marker, a second vertical white line is an artifact emanating from the lateral edge of the heavily calcified aortic valve. To the right, the CW Doppler signal is displayed as a graph of velocity *vs.* time. From the formula Gradient = $4V^2$, the maximum aortic gradient in this patient is estimated to be 71 mmHg where V is the maximum velocity (4.2 m/sec) shown in the graph. LV is left ventricle and RV right ventricle.

determinations, such as end-systolic pressure-volume indexes.[21,22]

Quantitative tools have been recently introduced to assess the Doppler shift while simultaneously producing 2-D echocardiograms. The Doppler shift is the apparent shift in frequency of a wave when the source of the wave (in this case, the reflected wave) is moving in relation to a stationary listener or observer. The classic example is the change in pitch of a train whistle as the train approaches and then passes the observer. When the ultrasound beam strikes a moving object, the reflected sound returns to the transducer with a slightly altered frequency. This shift in frequency is proportional to the speed of the object.[23] For example, cardiac output is accurately estimated by measuring flow velocity in the ascending aorta, mitral inflow, or left ventricular outflow areas.[24-26] Similarly, one might scan a sampling area just distal to a stenosed aortic or mitral valve until the maximum flow velocity is detected. Applying a modification of the Bernoulli formula will then allow calculation of the transvalvular pressure gradient and valve cross-sectional area (fig. 2).[27-30] In general, Doppler studies are highly reliable in quantitating valvular stenosis. They do not result in overestimates of the gradient, because the Doppler effect is maximum when blood flow is parallel to the direction of the ultrasound beam. An inexact alignment of the beam and blood flow results in underestimation of the peak velocity of flow. Regurgitant flow is reliably detected, but, as in angiography, its measurement is semiquantitative.[31-33]

The blood velocity information provided by Doppler is vital in the assessment of congenital heart disease. Gutgesell *et al.* performed 2-D echocardiographic studies without Doppler prior to cardiac catheterization in 128 pediatric patients.[34] The study was technically adequate for diagnostic evaluation of all but two patients, and 87% of the 259 congenital lesions were correctly identified. Only eight false positive diagnoses occurred. However, in 33 patients, the authors judged the errors in echocardiographic diagnosis to be of potential surgical importance. The most common lesions misdiagnosed were patent ductus arteriosus (21% missed) and pulmonic stenosis (23% missed and four false positives). Subsequent studies have demonstrated that a combined 2-D echocardiographic and Doppler technique can reliably diagnose patent ductus arteriosus and pulmonic stenosis.[35,36] However, the point-by-point search for maximum flow velocities is very time-consuming, and does not reveal the instantaneous distribution of flow velocities throughout the sector scan. Thus, color-coded Doppler flow imaging was developed. This new technology simultaneously presents real-time images of intracardiac blood flow and structure in two dimensions: continuous color maps of flow superimposed on monochromatic cross-sectional echocardiograms.[37] With "color" Doppler, the evaluation of valvular and congenital cardiac lesions should be easier and quicker,[38-40] making this technology particularly promising for intraoperative applications.

Noninvasive testing, including echocardiography, may provide sufficient data to eliminate presurgical assessment of certain valvular and congenital lesions by cardiac catheterization.[41-45] Echocardiographic study should also be considered when invasive intraoperative monitoring or prolonged intensive care may be likely because the extent of a patient's cardiac disease is uncertain. Conditions for which diagnosis by echocardiography might affect the degree of monitoring and choice of anesthetic technique

include pericardial tamponade, valvular heart diseases, hypertrophic and congestive cardiomyopathies, congenital heart diseases, and ischemic heart disease. Immediate qualitative assessment of the relative function of the two ventricles may be of value in the management of critically ill patients. Using 2-D echocardiography, D'Cruz *et al.* found that, after cardiac surgery, tamponade occurred with a small, often posterior, effusion which altered movement of the posterior wall of the left ventricle;[46] Jardin *et al.* demonstrated that positive end-expiratory pressure decreased cardiac output by displacing the intraventricular septum to the left.[47]

The echocardiogram should not be considered a standard screening device, and should never be used in lieu of history-taking and physical examination. However, when these preliminary efforts do not define a patient's cardiovascular status adequately, echocardiographic study should be considered before more invasive measures or major surgery are undertaken. Consider the following clinical scenario: an elderly patient with an unremarkable history and physical examination is scheduled for total hip arthroplasty. Q waves of questionable significance are noted on the ECG, but the patient admits of no angina and has little physical activity because of hip pain. The surgeon requests deliberate hypotension to minimize blood loss and facilitate surgery. Does the patient have significant coronary-artery disease, and should the anesthesiologist avoid deliberate hypotension? If the patient's echocardiogram reveals SWMAs, the overwhelming chances are that significant disease is present, and that overall LV function may be affected. If the echocardiogram is normal, significant coronary-artery disease may still be present, and other noninvasive measures which we will discuss can be used to confirm or deny this diagnosis.

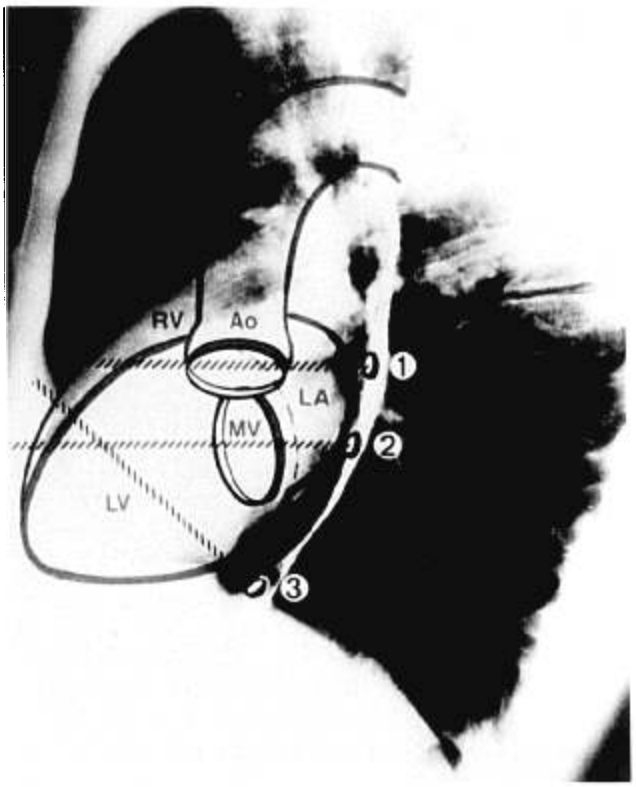

FIG. 3. A lateral chest x-ray during barium swallow. The superimposed drawings delineate the anatomic structures, some commonly used transducer positions (1, 2, and 3), and the corresponding imaging planes (hatched lines) of 2-D transesophageal echocardiography. LV = left ventricle; RV = right ventricle; MV = mitral valve; Ao = aorta; LA = left atrium. (Reproduced from Schlüter M, Hinrichs A, Their W, Kremer P, Schröder S, Cahalan MK, Hanrath P: Transesophageal two-dimensional echocardiography. Comparison of ultrasonic and anatomic sections. Am J Cardiol 53:1173–1178, 1984, with permission)

TRANSESOPHAGEAL ECHOCARDIOGRAPHY

With the introduction in West Germany of a phased array transducer which could be positioned in the esophagus, intraoperative 2-D echocardiography became a practical diagnostic tool for anesthesiologists (fig. 3).[48] At the University of California—San Francisco, we use a commercially available 3.5 MHz transducer system (Diasonics® Cardio-Imaging, Milpitas, CA) consisting of 32 piezoelectric elements mounted on the tip of a gastroscope. The transducer is 35 mm long, 15 mm wide, and 16 mm thick. An acoustical lens within the plastic mounting of the transducer focuses the ultrasound beam 2–15 cm in front of the array. With appropriate phasing of the elements by an ultrasonograph, a 90° sector for real-time imaging is obtained.

Once the transducer is inserted through the mouth and advanced approximately 35–40 cm, all four cardiac chambers can be viewed (fig. 4). The juxtaposition of the left ventricular outflow track, aortic valve, and mitral valve also can be observed. Advancing the transducer another 2–5 cm (and angling it forward) allows cross-sectional images of the left ventricle, including a short-axis view at the level of the papillary muscles (fig. 5). If the heart is not enlarged, a cross-sectional view of both ventricles can frequently be obtained. In studies of more than 800 patients, we have obtained high-resolution echocardiograms in 97% of our patients, with no complications. However, we do not perform transesophageal echocardiographic monitoring in patients with a history of swallowing complaints or esophageal disease. One published report describes two patients who suffered temporary unilateral vocal cord paralysis after transesophageal echocardiographic monitoring during "sitting" craniotomies.[49] Both of these patients were positioned with nearly full neck flexion. The authors of this report believe (personal com-

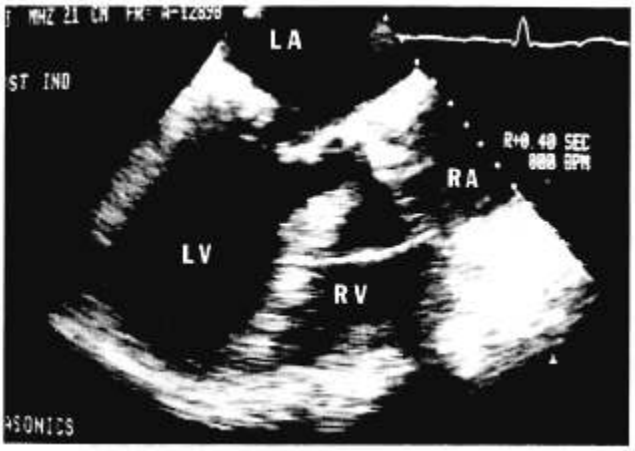

FIG. 4. A stop-action echocardiogram of multiple cardiac chambers. This image was produced with a transesophageal transducer inserted 30–35 cm from the incisors. LV = left ventricle; RV = right ventricle; LA = left atrium; RA = right atrium. The corresponding imaging plane in figure 3 is number 2.

munication) the recurrent laryngeal nerve was injured when the larynx, endotracheal tube, and shaft of the gastroscope were compressed between the chin and vertebral column. These authors now use a smaller gastroscope and have reported no further complications. The controls of the smaller gastroscope allow positioning of the transducer along only one axis, which is adequate for intraatrial air monitoring but occasionally inadequate for left ventricular monitoring.

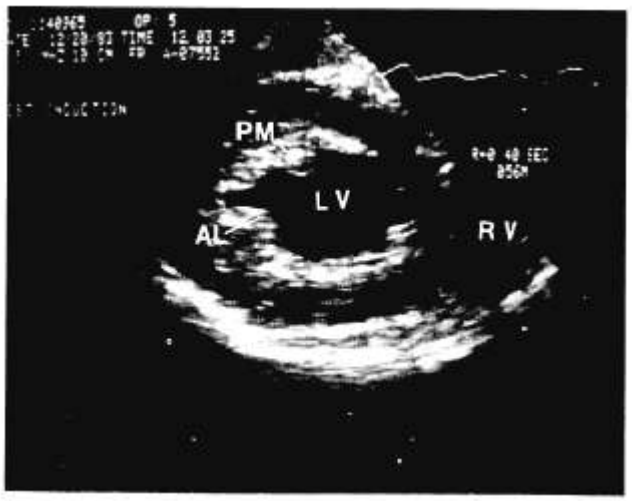

FIG. 5. A stop-action, short-axis echocardiogram of the left ventricle at the level of the papillary muscles. This image was produced with a transesophageal transducer inserted 35–40 cm from the incisors. LV = left ventricle; RV = right ventricle; AL = anterolateral papillary muscle; PM = posteromedial papillary muscle. The corresponding imaging plane in figure 3 is number 3.

In our experience, inserting and positioning the ultrasound transducer usually requires less than 60 s. We monitor the short-axis view of the left ventricle at the level of the papillary muscles (fig. 5), and have done so for up to 12 h. In approximately 8–10% of patients, this view cannot be obtained because of horizontal displacement of the heart by the contents of the abdomen. Other views, such as a four-chamber view, must then be monitored, but changes in left ventricular filling and segmental contraction are not as easily assessed. Quantitative estimates of left ventricular filling and ejection that are accurate to within 10% can be produced by the same observer, and estimates accurate to within 15% can be produced by different observers, using a computer-assisted video review system. However, such calculations are currently too time-consuming for use in the operating room.

In contrast, SWMAs can be detected by the anesthesiologist and are a reliable sign of intraoperative myocardial ischemia. In a recent study, we observed 50 patients at high risk for intraoperative myocardial ischemia while undergoing coronary-artery or major vascular surgery.[50] At predetermined intervals, we recorded echocardiograms and multilead ECGs, both of which were evaluated by "blinded" observers. All patients had postoperative ECGs and cardiac isoenzyme studies. Intraoperatively, six patients had ST-segment changes diagnostic of myocardial ischemia, while 24 had new SWMAs. No patient experienced an ST-segment change before or in the absence of a corresponding wall motion abnormality. In three of the six patients who experienced ST-segment change, the echocardiographic changes occurred minutes before the ECG change. Three of the 50 patients suffered intraoperative myocardial infarctions, and all three had an SWMA develop and persist in the corresponding area of myocardium. Only one of these patients had any intraoperative ST-segment change. Using similar techniques, Topol *et al.* found immediate improvement in systolic thickening of areas of dysfunctional myocardium with the increase in blood flow following successful coronary grafting.[51] However, detection of SWMAs may be influenced by artifact. For example, median sternotomy and pericardiotomy alter the translational and rotational motion of the heart within the chest, and thereby induce artifactual changes in ventricular septal endocardial motion. Consequently, a valid system for assessing SWMAs during cardiac surgery must compensate for this translational and rotational movement, and then evaluate both endocardial motion and segmental thickening.[52] Unfortunately, no currently available automated wall motion analysis system adequately manages these problems for transesophageal cross-sectional images.

Transesophageal echocardiography also can detect the small quantities of intravascular air which may enter the circulation. Moreover, 2-D transesophageal echocardi-

ography provides nearly ideal examination of the intratrial septum,[53] and, during contrast studies, can reliably diagnose atrial septal defects.[54] Two-dimensional transesophageal echocardiography is thus the first intraoperative monitor that can identify patients at risk of experiencing paradoxical emboli. Cucchiara *et al.* monitored 12 patients during suboccipital craniotomy in a sitting position using 2-D transesophageal echocardiography and precordial nonimaging Doppler.[49] All eight cases of Doppler-detected air were visualized by the transesophageal echocardiograms. In two of the cases, air was noted first on the echocardiogram. In two more cases, a questionable Doppler change was noted, and the presence of air was verified by the echocardiogram. For one severe episode of embolization, air could be seen crossing from the right to left atrium and passing to the left ventricle and aorta. The precordial Doppler monitor did not detect this event, because it does not image the heart, and, thus, can not localize an air embolism within the atria. A recent study in animals confirms that transesophageal echocardiography is more sensitive for detection of venous air embolism than monitoring the precordial Doppler, pulmonary artery pressure, end-tidal carbon dioxide concentration, or arterial oxygen tension.[55]

Clearly, 2-D echocardiography can be an essential tool for preoperative and postoperative diagnosis, and transesophageal echocardiography may be an important intraoperative monitor in the future. Despite the undisputed value of echocardiography in the evaluation of cardiac morphology, ventricular function, myocardial ischemia, and infarction, other significant diagnostic problems remain unsolvable with ultrasound techniques. In addition, inadequate images may be obtained from some patients, and reproducibility of quantitative findings is critically dependent on highly skilled operators. Finally, SWMAs are only indirect markers of myocardial perfusion, and can persist for prolonged periods in the absence of infarction. To address these limitations, we will review recent developments in cardiovascular nuclear medicine.

Cardiovascular Nuclear Medicine

Intravenously injected radioactive elements (radionuclides) circulate through or localize in the great vessels and heart and emit radiation detectable by a scintillation counter or camera, instruments similar to a Geiger counter. Because of their localizing properties and the character and brief duration of the radiation emitted, Technetium-99*m* (Tc-99*m*) and Thallium-201 (Tl-201) are the most commonly used radionuclides. The numbers 99 and 201 are atomic mass or isotope numbers, and equal the total number of protons and neutrons in the nucleus of these atoms. The letter *m* in Tc-99*m* identifies the high energy isomer of this isotope. Isomers are identical in all respects, except in the arrangement of the constituents of the nucleus. Tl is a member of periodic family III, trivalent cations like aluminum, but biologically resembles the alkaline cations, such as potassium. Tc is in periodic family VIIA, transitional metals such as manganese. Tl becomes an intracellular cation, indicating myocardial perfusion and viability,[56,57] while Tc can be coupled to a variety of carriers which will, in part, determine whether it remains intravascular or localizes in the myocardium.[58,59] When the radionuclide is contained in the intravascular space, the number of radioactive counts per unit of time directly over the heart can be related to the amount of blood in the heart. The difference in the counts between diastole and systole is related to stroke volume. Immediately after a bolus of tracer, radioactivity can be compared against time data by indicator-dilution principles to estimate cardiac output. Instead of a counter, a camera can record the pattern of the counts emitted from the radionuclide circulating through the heart, and thereby produce a radioangiogram. Data can be obtained immediately after injection on the first circulation of tracer through the heart (first-pass techniques), or after a larger dose of tracer following which the radionuclide is evenly distributed in the blood (equilibrium techniques). With either technique, the counts are recorded with (gated) or without (nongated) reference to the events of the cardiac cycle (usually the R wave of the ECG). Repetitive sampling at the same phases in successive cardiac cycles can be performed until the number of radioactive counts per unit of time is sufficient to produce images of the beating heart. Positioning the counter or camera appropriately is crucial if counts from surrounding organs are not to interfere. Although the dissemination of radioactivity inherent in all nuclear medicine studies is of concern, most of the techniques used involve the administration of less than 20 millicuries (mCi) of radioactivity, and, thus, are equivalent in dose to two standard abdominal roentgenograms. At this exposure (measured in millirads), nuclear medicine studies provide data on cardiovascular anatomy and function pertinent to all forms of heart disease. However, none of these studies is without inherent strengths and weaknesses, which must be appreciated if they are to be properly interpreted and exploited.

Cardiac Performance Studies

First-pass and equilibrium radioangiography are techniques ideally suited for quantitative evaluation of cardiac function. Usually, these studies are conducted in the nuclear medicine laboratory, but portable counters and cameras are available, and sometimes preferable. For a patient in the intensive care unit, a portable scintillation camera can be used to detect the first pass of Tc-99*m*-labeled (usually 8–20 mCi) albumin or red cells to estimate

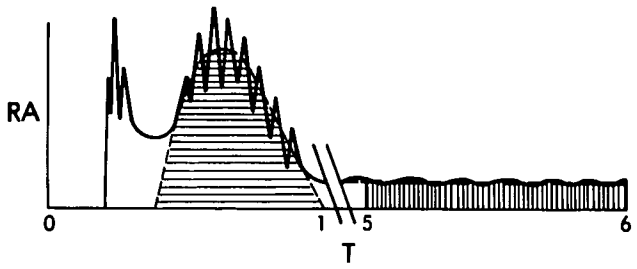

FIG. 6. First-pass evaluation of ventricular function. Diagrammed is the time (T) *vs.* radioactivity (RA) curve of an intravenous injection of a bolus of blood pool labeling agent. The probe or camera is sitting over the central circulation and initially sees a peak of RA as the bolus arrives in the right ventricle. The second, broader peak, represents bolus appearance in the left ventricle. Five to six minutes after injection, the injectate is at equilibrium, with each volume of blood having the same RA. Note the high frequency spikes superimposed on the low frequency data. These relate to systolic (valley) and diastolic (peak) volume. Knowing the background radioactivity level (easily measured), ejection fraction can be calculated. Knowing the injected dose, a blood specimen drawn at equilibrium will permit calculation of the absolute blood volume. The area under the equilibrium curve (vertical lines) can then be measured and used to calibrate the area under the left ventricular T *vs.* RA curve (horizontal lines) to determine left ventricular cardiac output in blood volumes/min. Ejection fraction, end-diastolic and end-systolic volume can also be calculated. (Reproduced from Botvinick EH, Glazer HB, Shosa DW: What is the reliability and the utility of scintigraphic methods for the assessment of ventricular function? Edited by S Rahimtoola, Cardiovascular Clinics 13:65, 1983, with permission).

cardiac output, stroke volume, right and left ventricular ejection fractions, end-diastolic volume (fig. 6), and the presence of left-to-right intracardiac shunt. This study requires only 5 min, and can be safely repeated many times, although the total daily administered dose should not exceed 35 mCi. Similar calculations can be made quickly, but less selectively, using equilibrium methods.

Cardiac wall motion is visualized with the first-pass technique, and the serial transit of radioactivity provides an excellent opportunity to image separately the structure and function of the right and left sides of the heart.[60,61] However, equilibrium techniques, which incorporate data from many cardiac cycles, produce superior images for quantitative assessment of global and regional left ventricular function.[62] Equilibrium radioangiography produces estimates of left ventricular end-diastolic filling and ejection fraction that correlate well with estimates from cineangiography, and that, unlike echocardiographic estimates of volume, do not rely on assumptions of ventricular geometry.[63,64] This technique requires 20 mCi of Tc-99*m*-labeled albumin or red blood cells, and allows both immediate and subsequent evaluation of ventricular function over a period of hours. Thus, equilibrium studies are ideally suited for serial assessment of acute drug or stress effects.[65] For example, in 50 patients with cardiogenic shock of unresolved etiology after cardiac surgery, Bateman *et al.* used equilibrium radioangiography to establish a diagnosis in 45 patients which resulted in a change in therapy for 21 of them.[66] Cardiac tamponade and regional and global ventricular dysfunction were clearly distinguishable in these 45 patients. Similarly, Hansen *et al.* used equilibrium radioangiograms to demonstrate that changes in pulmonary arterial wedge pressure following coronary bypass surgery correlate poorly with changes in left ventricular end-diastolic volume.[67]

Multiple projections of radioangiograms (each requiring 5–10 min of sampling) are necessary if the specialist in nuclear medicine is to evaluate segmental wall motion comprehensively during equilibrium studies. Using computer processing, the data obtained can provide information on almost any cardiac function of interest. For example, stroke volume "parametric" images may be produced by subtracting the end-systolic frame from the end-diastolic frame on a pixel(picture element)-by-pixel basis, resulting in a reflection of the volume ejected during a cardiac cycle.[68] Dividing the stroke volume image by the end-diastolic image will produce the ejection fraction image, a map of regional ejection of the left ventricle.[69] The simple fact that the radioactive counts in a region are proportional to the amount of tracer makes such data manipulation possible.

Radioangiographic evaluation of global and regional ventricular function is valuable for the diagnosis of coronary-artery disease. Findings considered diagnostic in an exercise radionuclide test include patient failure to increase left ventricular ejection by at least 5% and/or development of a segmental wall motion abnormality. The sensitivity of this technique is 75–85% and the specificity is 80–90%: both figures are somewhat superior to those of ECG stress testing.[70] However, because of its limited expense, the latter method is likely to remain the initial diagnostic screening test for patients suspected of having coronary-artery disease. The most efficient use of diagnostic resources for evaluating coronary-artery disease is currently under study.[71,72] Although a full discussion of the issues involved is beyond the scope of this review, a number of generally accepted tenets should be mentioned. First, no single diagnostic strategy is likely to work for all patient populations because the relative value of each test is dependent on the prevalence of coronary-artery disease and other complicating diseases (*i.e.*, valvular dysfunction or bundle branch block). Second, the testing strategy will depend on the diagnostic information required; for example, the extent of myocardium at risk for ischemia (of primary concern to the anesthesiologist, and discussed later in this review), the location of epicardial coronary obstructions (of primary concern to the cardiac surgeon), or prognosis with medical management (of primary concern to the medical specialist). Third, strategies will

change as new diagnostic tests are developed and the interpretation of existing tests is improved. For example, Wasserman *et al.* demonstrated that hypertensive patients without coronary-artery disease frequently display a falsely positive response on exercise radioangiography;[73] however, Poliner *et al.* used the same test and identified patients with coronary-artery disease by detecting alterations in diastolic filling rate with 98% sensitivity and 94% specificity.[74] As these diagnostic strategies continue to evolve, clear definition and communication of diagnostic and theraputic goals must become a priority among consultants.

In summary, first-pass and equilibrium radioangiography have distinct advantages and disadvantages for clinical application. First-pass techniques require less time and, thus, less patient cooperation. Assessment of individual cardiac chambers, especially the right ventricle, is better with first-pass techniques because of the temporal separation of the signal from each chamber. However, equilibrium studies are superior for evaluation of regional left ventricular performance, because data can be gathered from multiple cardiac cycles and camera angles. For the same reason, they are less likely than first-pass studies to be invalidated by transient dysrhythmias. Equilibrium studies also are more appropriate when serial evaluation of cardiac performance is required. Neither technique directly reveals myocardial perfusion. This is better accomplished with Tl imaging techniques.

Perfusion Scintigraphic Studies

Perfusion scintigraphic studies (in which radionuclide deposits in the myocardium) are now fundamental tools for the evaluation of ischemic heart disease. Tl-201 localizes in the myocardium because it appears to the heart to be potassium. Minimal amounts of Tl-201 localize in areas of diminished perfusion or in areas of scar. After injection of a 1–2 mCi dose, multiple views are completed in approximately 15–30 min. The perfusion defects or "cold spots" on the scans correspond to areas of the heart with relatively little or no perfusion. When this study is performed in conjunction with exercise testing, the perfusion defects resolving after cessation of exercise indicate viable areas of myocardium at risk for infarction, while fixed defects represent areas of necrosis or scar. Using data from multiple projections during stress perfusion scans, investigators have identified perfusion defect patterns which are 95% specific and 75–80% sensitive for three-vessel or left-main artery disease.[75] Overall, perfusion scintigraphic studies have a diagnostic sensitivity and specificity for the detection of ischemic heart disease in the range of 80–95% if they are quantitatively analysed and dynamic Tl washout is evaluated.[76,77]

One recent development extends perfusion scintigraphy to patients who cannot exercise. Administration of intravenous dipyridamole causes coronary vasodilation by increasing the circulating concentration of adenosine. In areas with fixed stenoses, flow cannot be augmented, and, thus, Tl-201 injected at the peak of the dipyridamole effect is distributed primarily in areas of myocardium served by relatively patent coronaries (fig. 7). This pharmacologic stress test is an appropriate measure for patients who cannot submit to exercise because of joint pain, claudication, or other conditions which prevent physical activity. Recall the clinical example discussed earlier in which deliberate hypotension was proposed. If the patient had an echocardiogram without SWMAs but reversible Tl perfusion defect(s) after dipyridamole injection, deliberate hypotension would be likely to induce myocardial ischemia and should, therefore, be avoided. Stressing a patient with dipyridamole is less likely to provoke ischemia than stress induced with exercise, but the sensitivity and specificity of these tests appear comparable.[78,79] Quantitative assessment of the perfusion Tl-201 scans produced in conjunction with exercise or dipyridamole injection permits estimates of the extent of coronary-artery disease and the amount of myocardium at risk for ischemia and infarction.[80–83]

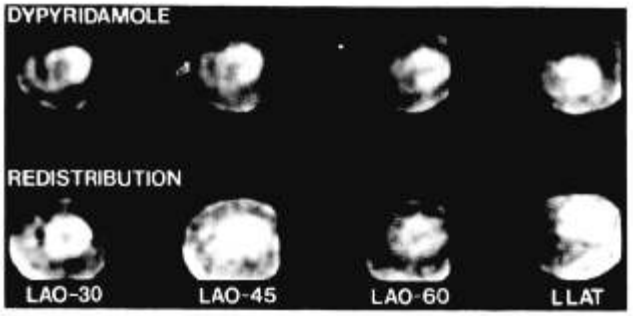

FIG. 7. Dypyridamole Tl-201 Imaging. Shown are images formed from a Tl-201 injection made during peak effect (above) of intravenous dypyridamole and 4 h later (below). LAO-30, 45, and 60 are 30°, 45°, and 60° left anterior oblique views and LLAT is the left lateral view. Note the large apical-septal defect which appears in all projections of the upper images, then disappears within 4 h (lower images). This is evidence of flow heterogeneity induced by the coronary dilating effects of dypyridamole. This redistribution pattern is strong evidence of significant coronary-artery disease without the use of dynamic stress.

When compared with patients with no history of myocardial infarction, patients who have had a previous infarction are five- to 100-fold more likely to have another infarction during or after surgery.[84] Within the population at risk are individuals with and without significant coronary obstructions serving viable myocardium. This is crucial information for the preoperative evaluation of patients considered for coronary surgery[85] and other major procedures with high risk of perioperative infarction.

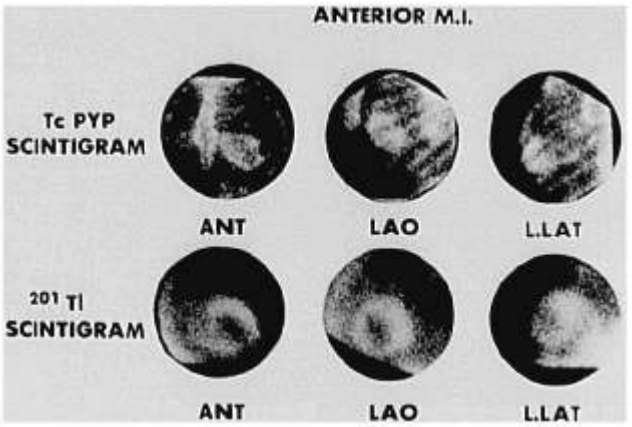

FIG. 8. Tc-pyrophosphate infarct imaging. Shown are ^{99m}Tc-pyrophosphate (TcPYP) (above) and Tl^{201} rest scintigrams (below) in anterior (ANT), left anterior oblique (LAO) and left lateral projections (L.LAT). Note the "hot spot" to the left of the sternum and anterior in the chest in the TcPYP images. This "hot spot" represents uptake of TcPYP by an acute anterior myocardial infarction, and corresponds to the "cold spot" or perfusion defect on the Tl-201 images. While these findings are consistent with infarction and are extremely sensitive to acute infarction, they are not specific, and may be seen with severe ischemia. (Reproduced from Botvinick EH, Shames DM: Nuclear Cardiology—Clinical Applications. Baltimore, Williams and Wilkins, 1979, with permission).

Boucher *et al.* identified patients at risk by preoperative dipyridamole-thallium imaging.[86] They studied 54 patients with ischemic heart disease who were scheduled for peripheral vascular surgery. All eight patients who had a postoperative cardiac event (unstable angina or myocardial infarction) were among the 16 patients who revealed reversible Tl perfusion defects preoperatively. No other customary preoperative clinical index, including age, history of previous myocardial infarction, or angina, predicted which patient would have postoperative cardiac events, as well as dipyridamole-thallium imaging. No patient with a normal Tl scan or a fixed defect had a significant cardiac event.

In summary, both radioangiography and perfusion scintigraphy can provide essential data in the evaluation of patients with suspected coronary-artery disease. These studies should be considered whenever a patient at high risk (*e.g.*, an elderly patient with typical chest pain) has a negative ECG stress test or a patient at low risk (*e.g.*, a young patient without typical chest pain) has a positive or equivocal test. Tl perfusion imaging has the unique capacity to measure the functional or physiologic severity of coronary-artery disease and amount of viable myocardium at risk for ischemia. However, to distinguish recent from remote infarction or to estimate the size of acute infarction, other techniques must be considered.

Myocardial Infarct Imaging

Both Tl-201 and Tc-99*m* pyrophosphate (PYP) studies are important supplementary tools for the diagnosis of acute myocardial infarction (fig. 8). The former is a highly sensitive yet nonspecific diagnostic method. The latter is highly specific and sensitive for transmural and large subendocardial infarctions.[87] Localization of Tc-99*m* PYP in the myocardium is directly proportional to the degree of tissue damage and the residual blood flow to the area. These facts partially explain why the peak intensity of the Tc-99*m* image does not occur until 48 h after infarction, and why most of the radionuclide accumulates in the periphery of the infarct.[88,89] After 7 days, most infarcts cannot be identified with this technique.[90] Although transmural right ventricular infarction is reliably detected,[91] subendocardial infarction is not.[92–94] Recent studies indicate that single-photon emission computed tomography (see below) using Tc-99*m*-PYP may increase sensitivity for small infarctions including nontransmural events.[95] Tomography is the technique of spatially encoding images, such that data from superimposed structures (the heart and vertebrae in a standard chest roentgenogram) can be viewed in cross-section. The size of the myocardial "hot spot" on the TcPYP scan and the fixed defect on the Tl-201 scan indicate the extent of myocardial necrosis and are important prognostic signs.[96–99] Tl imaging has somewhat greater prognostic value, because it reveals areas at risk for infarction and those already infarcted. TcPYP imaging is particularly useful when the established and extremely sensitive methods of acute infarct diagnosis (cardiac isoenzymes and ST-segment/Q wave analysis) are unavailable or uninterpretable because of prior infarction, ECG conduction abnormalities, recent surgery,[100] or defibrillation.[101] Other radionuclides less often used are gallium-67, Tc-99*m* tetracycline, and Tc-99*m* imidodiphosphonate.

Nuclear medicine techniques have been used in the operating room for research purposes,[102–104] but not for routine care of patients. However, because decreased reinfarction rates are associated with intensive perioperative care,[105] and because intraoperative myocardial ischemia is associated with postoperative infarction,[106] scintigraphic methods may become more common preoperative tools. Tl-201 perfusion studies in conjunction with exercise or dipyridamole administration might identify which high-risk patients will benefit from invasive intraoperative monitoring and longer periods of postoperative intensive care. Patients with previous infarctions, good exercise tolerance, and no reversible coronary perfusion defects, probably have little risk for reinfarction. However, patients with minimal angina and no previous infarctions who reveal a triple-vessel or left-main pattern

on perfusion study are probably at very high risk for perioperative myocardial infarctions. Before such patients undergo major surgery, coronary catheterization, angioplasty, or coronary bypass grafting should be considered.[107,108]

Although the radionuclide techniques discussed above may accurately characterize the cause and effect of myocardial infarction, they do not provide direct information on myocardial metabolism, an essential variable in the determination of cell survival. Positron-emission tomography (PET) and single photon-emission computed tomography (SPECT) are newer techniques capable of imaging ventricular function, perfusion, infarction, and myocardial metabolism. The latter technique refers to the method of acquiring tomographic images from standard (*i.e.*, Tl and Tc) gamma-emitting radionuclides. The former refers to the use of positron-emitting substances which simultaneously release photons in opposite directions, and thereby facilitate the spatial encoding necessary for tomography. Radionuclides of carbon, nitrogen, and oxygen are positron emitters with sufficiently short half-lives that allow them to be safely administered in amino acids, drugs, or other substrates. With PET, intrinsic labels can be attached to myocardial metabolic processes. With SPECT, an extrinsic (photon-emitting) label must be attached to a substrate. Although the clinical impact of these techniques is not yet well defined,[109] some applications seem to hold particular promise for surgical patients with coronary-artery disease. Brunken *et al.* demonstrated with PET that viable myocardium may exist within areas of the heart having chronic electrocardiographic Q wave infarctions.[110] Only relatively short exposures (radionuclides with half-lives of a few hours) to the high energies of positron emission are safe for clinical use. Recently, an alternative method for study of myocardial function and metabolism without the hazard of ionizing radiation has emerged: magnetic resonance imaging and spectroscopy.

Magnetic Resonance Imaging

Magnetic resonance imaging is the epitome of applied, high-technology medicine. It is by far the most complex, expensive, and potentially revealing imaging technique yet introduced. Unlike echocardiography (which relies on the difference between tissue densities) and radionuclide studies (which rely on differences in radioisotope flow through or uptake by tissues), magnetic resonance imaging can use multiple variations in tissue characteristics to construct images. To understand the applications of magnetic resonance imaging, we must first review some of the basic principles of this technology and the new lexicon it brings to medicine.[111]

Atomic nuclei are composed of protons and neutrons. Any nucleus possessing an odd number of either of these subatomic particles will have a magnetic moment which makes the nucleus behave somewhat like a tiny bar magnet or compass needle. An applied magnetic field will tend to align the nuclear magnetic moments, just as the earth's magnetic field aligns compass needles toward the north pole. At any particular magnetic field strength, a phenomenon known as nuclear magnetic resonance allows one to change the alignment of "compass needles" for a particular type of nucleus. The change is effected by introducing a small pulse of electromagnetic energy at a radiofrequency (rf), the resonance frequency, which is precisely 4.257 MHz/kilogauss for protons, 4.007 MHz/kilogauss for fluorine, and 1.724 MHz/kilogauss for phosphorous. The magnitude of nuclear magnetization, which can be determined from the response to the rf pulse, will depend on the number of nuclei (spin density) in the substance being sampled. After the rf pulse, perturbed nuclei "relax" back into original alignment. This relaxation period is characterized by T_1 and T_2, the time constants for the recovery of longitudinal and transverse magnetization. Thus, in order to completely characterize a substance with magnetic resonance, all four parameters (T_1, T_2, resonance frequency, and spin density) must be quantified. Most clinical magnetic resonance imaging is currently based on detecting the protons that are in H_2O and the methylene groups in lipids. The resonance frequency of these two classes of protons differs by only 3.15 parts per million. Although water at a 55 molar concentration forms the most abundant peak, a substantial contribution to the image comes from the protons in fat. Very recent engineering techniques have allowed chemical shift imaging,[112,113] in which only water or only lipids are visible. It is also possible to reconstruct images using the detection of fluorine in fluorinated hydrocarbons and volatile anesthetics.[114]

Nuclear magnetic resonance spectroscopy, which is concerned with the dependence of signal amplitude as a function of resonance frequency, was first used 40 years ago for nonbiologic studies;[115–117] application to living tissues has been possible for little more than a decade.[118] Advances in computer technology have permitted elaborate control of rf transmissions and of the processing of the detected signals, making nuclear magnetic resonance imaging possible.[119] NMR spectroscopy and imaging are commonly referred to by radiologists as MRS (magnetic resonance spectroscopy) and MRI (magnetic resonance imaging). MRI signals are detected using high frequency electronic transmitters and detectors (operating in the range 6–85 MHz), large computers, and a powerful magnetic field, typically 0.15–2.0 Tesla (the earth's magnetic field is 0.5×10^{-4} Tesla). Most MRI magnetic fields are produced by large solenoidal superconducting magnets which have almost no electrical resistance, because they

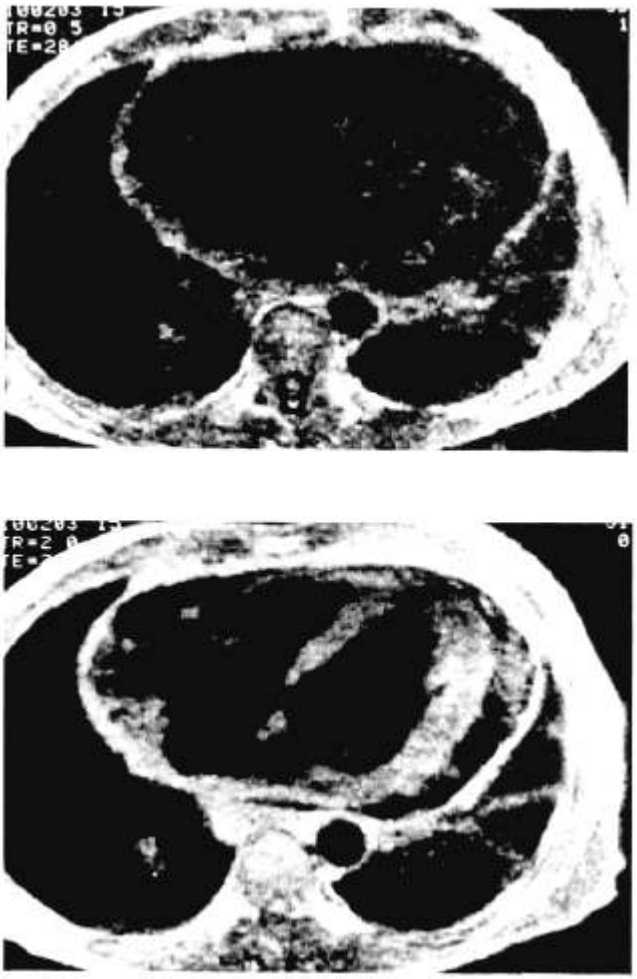

FIG. 9. Gated magnetic resonance imaging. Shown are ungated (above) and gated (below) magnetic resonance images in a patient with chronic pericarditis, pleuritis, and pericardial effusion. Little of the cardiac anatomy can be seen in the ungated image, but with gating, all of the pertinent anatomy becomes evident. Note particularly the high intensity material in the pericardial sac, which may be evidence of exudate, and the linear streaks related to probable pericardial and pleural adhesions. The pleura is also thickened. (Reproduced from Lanzer P, Ortendahl DA, Botvinick EH, Higgins CB: Cardiac imaging by magnetic resonance, Cardiac Imaging and Image Processing. Edited by Collins, Steve M. and Skorton, David J., New York, McGraw-Hill Book Co., 1986, with permission).

operate at the temperature of liquid helium. Systems designed for clinical use typically occupy a large isolated room, and consist of a console of computer and electronic equipment, and a superconducting cylindrical magnet which is approximately 2 meters in diameter with a hollow horizontal bore to accommodate the patient. Spatial information is obtained in MRI by altering (or exciting) the nuclear magnetization in regions of space where either static or oscillating magnetic field gradients are superimposed upon the uniform magnetic field of the superconducting magnet. These gradients are used to uniquely assign or "tag" the resonance frequency of the water proton to a particular location within the magnet.[120] Because hundreds of acquisitions are necessary to construct an image, and because there must be some waiting time between acquisitions (typically tenths of a second), it takes from 5–30 min to obtain data for a standard MRI image. Different rf pulsing and detection combinations (*e.g.*, "saturation recovery," "inversion recovery," and "spin-echo" pulse sequencing) have been developed for high-contrast spatial definition, tissue characterization, and definitions of T_1 and T_2. As a result, MRI imaging will permit not only visualization of subdural hematomas invisible on CT scan, but also an estimate of the time of hemorrhage derived from determination of T_1 and T_2.[121] Special techniques (called "echo-planar imaging") have been developed at a few institutions to enhance the detected MRI signal by 30–50-fold, leading to "real-time" MRI cinema based on two images per second.[122]

Movement of tissues and blood affects the magnetic resonance image. A tissue sample (*e.g.*, blood in an aortic cross-section) can be excited by an rf pulse and exit the MRI detection volume before the signal of resonance excitation can be recorded. This is why magnetic resonance images have "blank" regions within patent vessels, and why no contrast material is needed to define the edge of a vessel. For cardiac studies in which the tissue being studied is in constant motion, scans are gated to the cardiac cycle. This ameliorates the loss or gain in signal to some degree, and permits good contrast resolution of cardiac structures with excellent spatial resolution without the use of contrast material (fig. 9).

Clinical and research applications for MRI are increasing rapidly. Studies in animals confirm that magnetic imaging can detect myocardial infarction as an area of increased signal within four hours of occlusion of the coronary artery.[123,124] In humans, acute myocardial infarctions have been imaged within 5–12 days following the onset of symptoms,[125] and, in patients with chronic ischemic heart disease, postinfarctional thinning, aneurysms, and mural thrombi are visible.[126] Earlier detection may require contrast substances (paramagnetic nuclei) which collect in the area of ischemia/infarction. Higgins *et al.* studied 22 patients with a variety of congenital cardiac defects, and successfully imaged 11 of 11 defects of the great vessels, 6 of 6 atrial septal defects, and 10 of 11 ventricular septal defects. All complex anomalies were clearly delineated.[127] MRI also may make it possible to assess the success of palliative procedures.[128]

Because MRI can distinguish among fat, vessels, and tumor in the mediastinum,[129] the use of other invasive diagnostic procedures prior to thoracotomy may be avoidable. Inflammatory changes of the pericardium also are easily detected. However, calcium deposits cannot be

visualized, and images from the lungs are generally of low resolution because of low signal strength and movement during breathing. Consequently, for cardiovascular diagnosis, the combination of echocardiographic and radionuclide studies currently surpasses the sensitivity and specificity of MRI, although there are other diagnostic areas for which MRI may be beneficial to the practice of anesthesia.

The presence of bone does not complicate MRI as it does CT imaging. The bones of the arms are invisible with MRI, and structures within the cranium, spinal column, and pelvis can be detected with high contrast. MRI is also highly sensitive for the detection of central nervous system and spinal cord disease processes, because tumors, infarction, hemorrhage, and demyelination result in prolonged T_2.[130,131] Remarkable images of spinal disk disorders can be produced because MRI usually differentiates between nucleus pulposus and annulus fibrosis. Gross anatomic changes such as herniation can be detected, as well as more subtle, degenerative changes occurring in the absence of root compression.[132]

Advances in MRI techniques have encouraged efforts to image nuclei other than hydrogen. Initial experiments in animals indicate that acute tissue injury may be identified earlier with ^{23}Na-MRI than with ^{1}H-MRI, because large increases in intracellar sodium occur quickly after disruption of the active processes which maintain the normal transcellular sodium gradient.[133-135] In addition, "frequency shift reageants" are now under development for ^{23}Na-MRI, which shift the resonance frequency of extracellular but not intracellular sodium. Thus, ^{23}Na-MRI may provide important new insights into our understanding of cellular injury.

We have pointed out that, in MRI, spatial information is derived from data obtained with the use of magnetic field gradients. Because NMR resonance frequencies are proportional to magnetic field strength, gradients result in the same nuclear moment having a different resonance frequency at different spatial locations in the magnet. When magnetic resonance spectroscopy (MRS) is performed, the gradients are turned off, and the frequency dependence of the NMR signal intensity is examined in a selected region of homogenenous applied magnetic field strength. Several resonance peaks can be present in the frequency spectrum for a particular nucleus, because the local molecular environment may slightly shield the nucleus from the applied magnetic field. For example, proton NMR spectra will have separate resonance peaks for the protons in water molecules, lactate molecules, and amino acid molecules. ^{1}H, ^{13}C, ^{31}P, ^{23}Na, ^{39}K, and ^{19}F can all be studied *in vivo* with MRS. Significant advances in our knowledge of physiology will emerge from these studies. For example, ^{31}P MRS can quantify the levels of high-energy compounds inside living cells. Since the position of the inorganic orthophosphate peak is *p*H-dependent, proper analysis of the spectra allows estimation of intracellular *p*H. The pathophysiologic mechanisms resulting from myocardial ischemia have already been studied.[136-140] MRS also will provide a new method for investigating the effects of various substrates and drugs on the processes associated with ischemia. Clinical studies of human infants are underway to elucidate patterns of brain injury and recovery following neonatal asphyxia.[141] Laboratory studies of animals using MRS have demonstrated the effects of anesthetics on the high-energy compounds during hypoxemia and ischemia.[142] Nonradioactive, naturally abundant ^{13}C nuclei also can be studied, and thus fundamental biochemical reactions can be followed noninvasively *in vivo* from one organ to another. ^{19}F studies should enable us to understand better the metabolism and pharmacokinetics of inhaled anesthetics.[143]

MRI and MRS do not require the use of ionizing radiation or radioactive materials. Furthermore, no direct harm to patients or staff has ever resulted from the magnetic fields or the low-power radio wave exposure now used in clinical imaging. Use of a large applied magnetic field, however, does introduce questions of safety. Magnetic metal objects, including needles, laryngoscopes, and oxygen cylinders, can be drawn into the large magnets with projectile force. Patients with metallic implants (*e.g.*, aneurysm clips, hip joints, heart valves, and pacemakers) may be exposed to life-threatening risks if allowed near an MRI magnetic field. Certain alloys are sufficiently nonmagnetic that their presence in the magnet can be safely allowed. Thus, each case must be evaluated for potential risk when equipment and/or patients with metallic implants are allowed in the magnet area. Strict environmental standards must therefore be enforced at MRI imaging sites, and appropriate preparations made for monitoring patients requiring sedation, anesthesia, or resuscitation.[144]

Summary

We have presented a review of recent advances in medical imaging which are relevant to the practice of anesthesia and associated research. The appropriate interpretation and use of the information derived from these noninvasive technologies can prevent unnecessary morbidity and mortality. Echocardiography remains the most advanced tool for noninvasive cardiac imaging because of its applicability for most cardiac disorders and its exquisite spatial resolution. Two-dimensional systems produce real time, dynamic, qualitative assessments of cardiac chamber morphology, size, thickness, and performance. The development of transesophageal echocardiography has brought this imaging power into the operating room for use by anesthesiologists. Recently developed quanti-

tative and color-coded Doppler techniques will reveal intracardiac flow patterns and their alterations by anesthetics and surgery. These advantages are partially offset by inherent difficulties in quantifying echocardiographic data, and the need for highly trained operators for image reproduction.

Nuclear cardiology and echocardiology are highly complementary. The scintigraphic methods identify myocardium at risk for infarction, confirm infarction when present, and produce quantitative, highly reproducible estimates of ventricular filling and performance. Time required to obtain data can be very brief for first-pass techniques, and these data are ideally suited for computer processing. Equilibrium studies require a larger dose of radioactive material, but provide excellent assessment of segmental wall motion. Preoperative studies with dipyridamole and Tl can indicate the patients truly at high risk for perioperative myocardial infarction. Monitoring and intensive care efforts may be better allocated with this information.

No new technology in the past decade has stirred as much interest among clinicians as magnetic resonance imaging. Like echocardiography, it uses no ionizing radiation and is entirely noninvasive. But, unlike other imaging techniques, it utilizes multiple tissue characteristics to provide quick, highly resolved, tomographic images. Since bone is invisible to the magnetic resonance scanner, tissues inside bony structures are often best revealed with MRI. Nonimaging studies, *i.e.*, spectroscopic data not spatially encoded, may prove to be the most important research currently underway in this field. *In vivo* estimates of intracellular functions, enzyme kinetics, and drug kinetics and metabolism are already in progress. The effects of anesthetic in the central nervous system and other organs may be explored in ways previously not possible.

Clearly, these highly sophisticated imaging techniques come to us at significant cost. However, we predict that they will prevail in today's atmosphere of cost containment, because of the speed, safety, and accuracy with which they function. They are the images of things to come.

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