Nuclear Cardiology, Part II: Scintigraphic Evaluation of Cardiac Function

Anne-Sophie E. Hambÿe, Hendrik Everaert, Alex Maes, Lisbeth Mesotten, Johan Vandevivere, Luc Mortelmans and Philippe R. Franken

Nuclear Medicine, Middelheim Hospital, Antwerp; Nuclear Medicine, Free University of Brussels, Brussels; and Nuclear Medicine, Catholic University of Leuven, Leuven, Belgium

Objective: Different methods are currently available to assess cardiac function, especially left ventricular ejection fraction, using either planar or tomographic imaging, first-pass or equilibrium techniques, and blood-pool or myocardial perfusion agents. This is the second article of a four-part series on nuclear cardiology. In this article the authors review the most widely used radiopharmaceuticals and methodologies.
Key Words: cardiac function; radionuclide ventriculography; blood-pool imaging agents; left ventricular ejection fraction; gated myocardial SPECT

J Nucl Med Technol 1998; 26:72–79

Cardiac pump evaluation was once one of the most common tests in nuclear cardiology, showing a high reliability and reproducibility regardless of the method used and absolute ejection fraction (EF) value. With the development of echocardiography and other nonisotopic methods for EF measurement, however, the use of radionuclide ventriculography (RNV) in daily cardiological practice has decreased progressively over the past years, despite its accepted better reproducibility and superiority with regard to quantitation of ventricular function.

In this article, we first will review the most commonly used radiopharmaceuticals and acquisition techniques for measuring cardiac function. Then we will focus on the differences between the methods designed to assess right or left ventricular function and on the major clinical indications of both. Some functional parameters, such as regional EF, diastolic function analysis (1,2), shunt studies, calculation of absolute end diastolic and end systolic volumes (3,4) or continuous monitoring of the left ventricular function by means of a nonimaging detector (5), will not be discussed here because they are used less commonly in daily practice.

RADIOPHARMACEUTICALS

Using the first-pass technique, RNV can be obtained by monitoring the injection of a ^{99m}Tc-labeled radiopharmaceutical administered for any purpose. Technetium-99m-labeled DTPA, red blood cells or myocardial perfusion agents are the most frequently used. The former allow rapid renal clearance of the tracer and hence lower radiation exposure. The latter allow a simultaneous evaluation of myocardial perfusion and/or left ventricular ejection fraction (LVEF). For equilibrium RNV, ^{99m}Tc-pertechnetate-labeled autologous red blood cells (RBCs) or ^{99m}Tc-labeled human serum albumin (HSA) can be used.

Human Serum Albumin

Albumin presents some clear advantages over RBCs. It is readily available and easily labeled, avoids manipulation of blood samples, requires only a single injection, and shortens the delay between the tracer administration and the start of the acquisition. However, due to its relatively weak binding with the radionuclide and the resulting important and rapid extravascular diffusion, higher background activity is observed. This explains why HSA usually is not the agent of first choice (6). Recently a derivatized form of albumin (dimercaptopropionyl-HSA or DMP-HSA), available as a kit for ^{99m}Tc labeling, has been developed (7). In patients, it has demonstrated a stability and biodistribution very similar to RBCs (8). As this new agent is not yet commercialized, labeled RBCs remain the preferred radiopharmaceutical in many nuclear medicine departments despite their practical disadvantages.

Autologous Red Blood Cells

Three methods for RBC labeling are described, all of which are based on the same principles: intravenously injected pertechnetate passively diffuses into the RBC where, in the presence of reducing agents, it binds tightly to the hemoglobin and remains intracellular (9).

In Vivo Labeling. In vivo labeling is the easiest and quickest method, but several drugs and pathological conditions can interfere with the tagging and result in poor labeling efficiency (10). Using this technique, stannous agent, available as a kit, is

TABLE 1

TABLE 1
Acquisition Parameters for First-Pass (FPRNA) and Equilibrium Radionuclide Angiography (ERNA)

	FPRNA	ERNA
ECG gating	Yes	Yes
Injected activity (^{99m}Tc)	At least 740 MBq	370–740 MBq
Imaging mode	Frame List with subsequent conversion to 30 msec frames	Usually frame List mode if moderate arrhythmia
Number of frames per cardiac cycle	Depends on heart rate	16–32
Beat rejection window	Manual selection	10–15%
Matrix (20-cm field of view)	32 × 32	64 × 64
Collimator	Low-energy, high-sensitivity	Low-energy, high-resolution
Duration	±40-sec total 30 frames per sec for rest 40 frames per sec for stress	6.4 million counts per view or at least 10 min per view
Camera orientation	Anterior for left ventricle (apex beat = marker) 30° RAO for right ventricle	±45° LAO and 10° caudal tilt (best septal) + either anterior, or 45° LPO, or 20–30° RAO

intravenously injected at a dose of 10–20 µg/kg body weight. After 30 min tinning time, a second injection is performed with 555–740 MBq pertechnetate diluted in 1 ml saline solution, and acquisition may start about 10 min later. It is of crucial importance to use metal needles and separate injection sites for the two steps of the labeling (*10*).

In Vitro Labeling. With this method, the patient's blood is incubated first with stannous ion and then with ^{99m}Tc. This method gives the highest labeling efficiency but is quite time and labor consuming. Recently, a commercially available kit for in vitro labeling has been developed (UltraTag® RBC, Mallinckrodt, Inc., St. Louis, MO). This kit decreases the number of manipulations required and significantly facilitates the in vitro labeling of RBCs, but its high price could prevent its widespread use.

Modified In Vivo Labeling. Modified in vivo labeling is intermediate between the other two methods and might be a good alternative for RBC tagging. Stannous ion is intravenously injected at the same dose as for the in vivo technique and, after 15–30 min waiting time, 5 ml of the patient's blood is withdrawn into a syringe containing the pertechnetate and a small amount of acid citrate dextrose as an anticoagulant. After 10 min incubation at room temperature with gentle rotation of the syringe, the mixture can be reinjected and the acquisition started (*11*).

ACQUISITION METHODS

As already mentioned, two types of radionuclide ventriculography can be performed, both at rest and during exercise, allowing the measurement of either right or left EF. First-pass studies image the passage of a tracer injected as a bolus as it passes through the cardiac chambers, while equilibrium meth-

ods rely on the use of an intravasculary stable tracer imaged over several hundred heart beats.

First-Pass Radionuclide Angiography

First-pass radionuclide angiography (FPRNA) requires either a gamma camera with high counting rate capability or a multicrystal camera. Images are obtained during the first passage of the bolus through the cardiac chambers in either list or frame mode (this latter using a 32 × 32 matrix size for a 20-cm field of view) and a low-energy high-sensitivity collimator. The patient is positioned in the anterior projection unless the test is performed specifically for right ventricular ejection fraction (RVEF) assessment, and the location of the left ventricle is determined by clinical examination, using the apex beat as the marker. Acquisition lasts about 20–40 sec at a rate of 20–30 frames/sec depending on the heart rate (Table 1). A good quality bolus is a prerequisite for an adequate study. Therefore, an indwelling catheter (usually 18-gauge diameter) is placed in a large antecubital vein of the right arm (or less often in the external jugular vein) and connected to an extension tube of 3 ml volume filled with saline solution. Up to 800–1000 MBq activity, contained in a volume of less than 1 ml, is then introduced into the tube and immediately flushed in rapidly with at least 20 ml saline solution. The electrocardiographic (ECG) signal is used to gate the images. When injecting a ^{99m}Tc myocardial perfusion compound as the tracer, this technique allows the successive evaluation of myocardial function and perfusion with a single injection (*12,13*).

Equilibrium Radionuclide Angiography

In equilibrium radionuclide angiography (ERNA), the patient usually is positioned supine under the camera with the left arm above the head and with continous ECG-monitoring.

As data are gated to the R wave of the patient's ECG, a good signal is mandatory and some efforts must be made to obtain an optimal trigger before starting the test. Images usually are acquired in a 64 × 64 matrix size and a 16- to 32-frame/heart cycle protocol. The mean RR interval is measured for 1 min and a 10%-beat rejection window is set around this mean heart rhythm. A camera equipped with a low-energy, high-resolution or all-purpose collimator is placed in the left anterior oblique position (LAO), typically with a 45° oblique and 5–15° caudal tilt and the heart located centrally within the field of view. However, according to each individual patient's thoracic conformation, both LAO and caudal tilt angles can vary and one must use the screen persistent mode to search the optimal septal separation between both ventricles before starting the acquisition. Standard protocols include at least this "best septal view" image (allowing the analysis of the septal, posterolateral and inferoapical segments of the left ventricle and much of the right) and either a 20–30° right anterior oblique (RAO) or a 45° left posterior oblique (LPO) to evaluate the inferior, posterior, anterior and apical segments. Some nuclear medicine laboratories also acquire 0° anterior, left lateral or other complementary views.

Studies can be acquired in fixed presets of time, counts or heart beats. When using a time preset, at least 10 min must be acquired for each view, while a count density of more than 5–6 million counts is required for the count preset, and about 600–900 beats for the beat preset method (Table 1). At least 350 kcounts/frame must be obtained to ensure an adequate target-to-background ratio.

Frame Mode Acquisition. Frame mode acquisition is the most commonly applied technique. The acquisition data are directly visualized on the computer screen. A regular heart rate is necessary in this acquisition mode to obtain an adequate evaluation of LVEF and to obtain reproducible diastolic parameters.

List Mode Acquisition. Moderate to severe arrhythmias are a problem for RNV, as the duration of the cardiac cycle becomes irregular. List mode acquisition can be used to overcome this problem. With this method, the x-y coordinates of each scintillation event are stored sequentially in the computer's memory, together with the ECG signal and time markers. No image is visualized on the screen during the acquisition. This technique requires a large amount of computer storage and processing is time consuming.

Tomographic ERNA

Until now most reports on ERNA studies used planar imaging techniques. However, as the number of multiheaded gamma cameras and computer capabilities have increased tremendously over the past few years, tomographic (SPECT) imaging has gained more popularity. Tomographic imaging is especially popular in postmyocardial infarction studies (*14*), for calculating ventricular volumes (which is expected to be easier and at least as reproducible and accurate as the volume calculation by means of planar methods) and assessing right ventricular function. As with planar imaging, the patient's heart rate is first sampled to define the mean RR interval. About 50 beats falling within a range of 10%–15% of this mean heart rate are required for each tomographic angle. Due to the large computer memory necessary and low-counting statistics per image, no more than 16 frames per heart cycle can be acquired. Acquisition occurs usually with 3–4° steps over a body-contoured 180° anterior orbit from 45° RAO to 45° LPO. However, with a three-detector or 180°-opposed two-detector system, 360° acquisition is recommended.

Stress Radionuclide Ventriculography

Assessing both global and regional function at exercise is an important diagnostic and prognostic tool in patients with coronary artery disease (CAD) or nonischemic cardiomyopathies (CMP). Supine or upright bicycle stress testing is more suitable than the treadmill for stress RNV since it minimizes movement and motion-induced artifacts. However, image blurring is frequently observed, especially when the patient is exercising maximally.

FPRNA. Using a ^{99m}Tc myocardial perfusion compound as a tracer, successive evaluation of the functional response of the left ventricle and of the perfusion status at peak exercise can be obtained by coupling an FPRNA study to myocardial perfusion imaging (*12*). This is particularly indicated in patients with suspected or known CAD. Motion artifacts and mispositioning of the left ventricle are the major problems encountered with this technique which requires highly trained technologists to succeed. The test is performed under continuous ECG and blood pressure monitoring, according to the local standard protocol applied for exercise stress testing. Endpoints are: maximal heart rate, significant ECG changes or angina, exhaustion, hypotension, significant arrhythmia or dyspnea. Camera position and acquisition parameters are the same as for the resting method, with a rate of 40 frames per sec.

Stress Planar ERNA. This method is indicated more for evaluating nonischemic CMP and is technically easier to perform. After injection of a blood-pool imaging agent (usually RBC), the patient is placed on the bicycle using the best septal LAO view. First a resting ERNA is acquired using the same frame rate and acquisition time that will be used for the exercise (commonly 16–32 frames/beat during 2 min). Exercise is then started under continuous ECG and blood pressure monitoring at a workload of 25–30 W, and increased by 25–30 W every 3–5 min. At each stage, at least 1 min is allowed for the heart rate to stabilize and images are acquired during the last 2 min. Endpoints are the same as for the standard exercise stress testing. It is important that the patient maintains the peak workload for a minimum of 3 min to allow adequate imaging. During the recovery phase, 2-min images are acquired every 3 min over 8–10 min.

DATA PROCESSING

Images are processed to generate parametric data and to calculate global and, eventually, regional EF. Spatial and/or temporal smoothing are applied to reduce inherent statistical errors. The spatial smoothing corrects each pixel within a frame to average counts from the surrounding pixels, while the

temporal smoothing averages the pixel counts between different frames.

Evaluation of Global EF Value

End diastolic (ED) and end systolic (ES) ventricular edges can be drawn either manually or automatically. Fully or semi-automatic (where only the ED edge is manually drawn) processing programs can be used only for LVEF calculation and are not suitable for RVEF assessment. Furthermore, they require good count statistics and are less reliable and reproducible than the full-manual processing program in case of poor delineation between ventricular and surrounding structures. However, this latter requires well-trained nuclear cardiology technologists. Indeed, although functional images can be used as an aid to draw the ED edge, the ES border is more complicated to delineate since it can be drawn only on the real original systolic frame. In our experience, a reproducible LVEF value can be obtained with either processing program in 90%–95% of cases, while only full-manual processing is reliable in the remaining cases, with a mean interobserver variability of less than 1% (8). Usually the first image is taken as the end diastolic image and the frame with the lowest ventricular counts is taken as the end systolic image. Background correction is mandatory because up to 50% of the total ventricular counts originate from tissues lying behind or in front of the heart. A small crescent moon-shaped area (2–3 pixels wide and 90°-angle long) is commonly placed 1 pixel away from the ventricle at end systole, assuming that its count density reasonably approximates the extracardiac background activity. After substraction of the background activity, EF (%) is calculated as: (ED counts − ES counts)/ED counts. This makes use of the direct relationship between the ventricular activity and its volume.

Functional Images

Based on a mathematical technique, called Fourier analysis, applied to the time-activity curve generated from the different frames constituting the cardiac cycle, functional images are dynamic parameters illustrating the magnitude and synchronism of the cardiac contraction by means of a color-coded display. The time-activity curve, considered approximately equivalent to a symmetrical cosine curve, is characterized by its amplitude and the phase angle. The amplitude image represents the magnitude of the contraction and is used to determine the regional contractility status (ranging from normal to akinetic). The phase angle, expressed in degrees over the RR interval, images the timing of the peak contraction and is useful in identifying delays in regional contraction, such as in dyskinesia (aneurysm) or some conduction disturbances.

First-Pass Radionuclide Angiography

Before processing the data, the bolus quality must be checked by drawing a region of interest (ROI) over the superior vena cava. A mean transit time of less than 1.5–3 sec duration is considered adequate. As the transit time through the right lung and pulmonary circulation also may influence the EF measurement, an ROI is drawn over the right lung at a

distance from the left ventricle. Normal pulmonary transit time amounts to less than 8 sec. When bolus quality is considered good, a representative image of the cardiac cycle is created by summing a selected series of images from several heart cycles, corresponding to the washout phase of the ventricle to minimize the residual lung activity. Usually about 6–10 cardiac cycles are summed. After spatial and temporal smoothing, images are expanded into a 64 × 64 matrix size, if necessary, to improve the accuracy of delineation of the ventricular edges, before ED, ES and functional images are generated and regional and global EF can be calculated. A full manual processing is mainly used, and special care must be taken in determining the valve plane. Therefore, the functional amplitude image may be an important aid, the valve plane corresponding to a hypoamplitude zone in which the "vascular" border indicates the ED border of the ventricle, and the "ventricular" border indicates its ES border. For the background substraction, a horseshoe-shaped ROI usually is used.

Equilibrium Radionuclide Angiography

Frame Mode Acquisition. When the data have been acquired by frame mode, the images are scaled to the pixel with the highest activity and displayed in a color scale depending on the counts in each pixel. After spatial and/or temporal smoothing, the EF can be calculated, functional images generated and regional wall motion qualitatively analyzed using an endless cine loop display.

List Mode Acquisition. Using list mode acquisition, a histogram of the cardiac cycle length is generated after completion of the acquisition. Beats with a similar RR interval are selected manually and added to create an image representative of the mean cardiac cycle from which EF and functional images can be obtained as described above.

Stress ERNA. In stress ERNA, the images are processed in the same way as for resting data. However, a full manual or at least semiautomatic protocol is recommended since the count statistics are not as high as with a standard ERNA acquisition. Motion correction is sometimes necessary. Both global EF value and regional wall motion are analyzed at each stage.

Tomographic ERNA. Images are reprojected and reoriented, as usual, to obtain the three orthogonal projections (short axis, vertical and horizontal long axis). For EF calculation, a method has been described recently, generating a reprojected vertical long-axis "best septal" SPECT image by summing the counts in the different short-axis slices from back to front for each time point (15). As activity arising from outside the heart can be masked easily, a background correction is superfluous.

RIGHT VENTRICULAR FUNCTION

Radiopharmaceuticals

In addition to the previously mentioned tracers, intravenously administered inert gases, such as [81m]Kr or ^{133}Xe, have been proposed to overcome the difficulty encountered in separating the right ventricle from the other superimposed cardiac structures (16,17). However, since [81m]Kr is not available in all nuclear medicine departments and the use of ^{133}Xe requires a

TABLE 2
Major Indications of Radionuclide Ventriculography

Left ventricle	Right ventricle

Normal values: > 50% (FPRNA)
 > 50% (ERNA)
 • Diagnosis of extent and severity of coronary artery disease (ERNA, FPRNA, exercise RNV, gSPECT)
 • Prognosis after acute myocardial infarction (ERNA, FPRNA, exercise RNV, gSPECT)
 • Diagnosis of nonischemic cardiomyopathy (exercise ERNA)
 • Therapeutic monitoring (rest ERNA):
   • During cardiotoxic chemotherapy
   • After revascularization (bypass surgery or angioplasty)
   • Drug efficacy for treatment of cardiomyopathy or heart failure
 • Risk stratification before major nonvascular or peripheral vascular surgery (ERNA, FPRNA, exercise RNV)
 • Evaluation of cardiac function in patients with impaired renal function (ERNA, FPRNA, exercise RNV)
 • Cardiac shunts (FPRNA)
 • Functional significance of small vessel disease (exercise RNV)
 • Valvular heart disease (ERNA)
	Normal value: > 40%
	 • Prognosis after right ventricle acute myocardial infarction
	 • Diagnosis of right ventricle failure (cor pulmonale) especially in patients with chronic lung disease
	 • Therapeutic monitoring
	   • After revascularization (bypass surgery or angioplasty)
	   • Drug efficacy for treatment of cardiomyopathy or heart failure
	 • Valvular disease
	 • Cardiac shunts

ERNA = equilibrium radionuclide angiography; FPRNA = first-pass radionuclide angiography; RNV = radionuclide ventriculography; gSPECT = gated myocardial perfusion tomography

closed breathing circuit to avoid room contamination, an alternative aproach for RVEF calculation using ^{99m}Tc-macro aggregates (MAA) has been proposed (18). Combining the advantages of good RV delineation offered by ^{81m}Kr with the availability of ^{99m}Tc, this method has demonstrated an excellent correlation with the RVEF calculated with ^{81m}Kr and constitutes a good approach for estimating RVEF in daily practice.

Acquisition and Processing

FPRNA. The camera is placed in 30° RAO projection. Using the R wave of the ECG for triggering, data from several heart cycles are summed, smoothed and expanded into a 64 × 64 matrix size before ED and ES contours of the right ventricle can be drawn. With this approach, no significant overlap is noted between the right ventricle and other structures.

ERNA. As FPRNA is a rather complicated technique, assessment of RVEF is more commonly obtained from the standard gated planar ERNA in 45°LAO projection by using manual processing. The major technical limitation of this technique is the determination of tricuspid and pulmonic valve planes. Phase and amplitude images can be used to locate these valve planes. However, right atrial and ventricular overlap is unavoidable in many patients. Therefore, despite a correlation coefficient between FPRNA and ERNA of 0.85 (19), RVEF measured by ERNA is usually lower.

Normal Values

Regardless of the method used, a global RVEF of less than 40% must be considered abnormal.

Clinical Applications

Calculation of the RVEF can be useful in certain clinical settings, such as cor pulmonale due to pulmonary disease, especially chronic obstructive lung disease (Table 2). It also is useful for evaluating the functional significance of right ventricular myocardial infarction, congestive heart failure, valvular disease or atrial septal defects on right ventricular function (19).

LEFT VENTRICULAR FUNCTION

Radiopharmaceuticals

In addition to ^{99m}Tc-HSA and RBCs, as well as the promising ^{99m}Tc-DMP-HSA (8), technetium-labeled myocardial perfusion tracers that allow the evaluation of LVEF and perfusion with a single injection now are used frequently.

Methodology

Planar ERNA, and to a lesser degree FPRNA, both at rest and at peak exercise, was popular until the 1990s. With the development of multiheaded gamma cameras, powerful computers and dedicated software, the use of SPECT to assess LV function has gained interest in the nuclear medicine community. SPECT has become one of the state-of-the-art investigations of nuclear cardiology. In this setting, tomographic ERNA is one possible technique for measuring LVEF and regional motion. However, gated myocardial perfusion SPECT is more prevalent and is applied widely in patients referred for myocardial perfusion imaging. For LVEF evaluation with gated ERNA SPECT, acquisition and processing occur as described previously (Table 1).
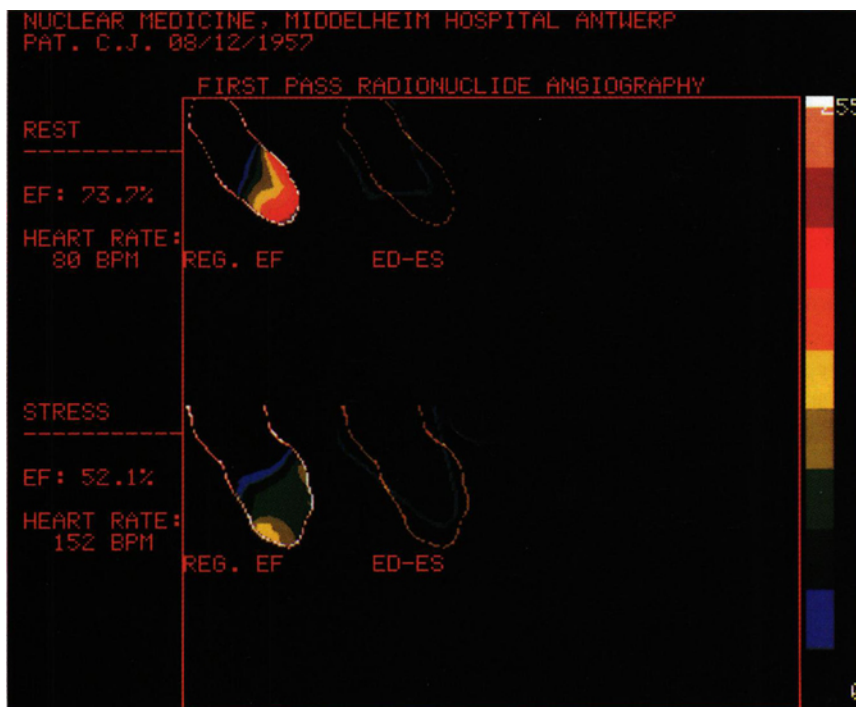
FIGURE 1. Resting (top) and peak-exercise (bottom) left ventricular function assessed by FPRNA in a 40-yr-old man with chest pain. Regional EF (Reg EF) is represented by means of color-coded semiannular bands on the left, and superimposed end diastolic and end systolic (ED-ES) manually drawn contours on the right. The distance between ED and ES contours illustrates the systolic thickening of the LV. The resting study demonstrates completely normal EF and contractility. At peak exercise, a severe drop in global and regional EF is observed, and regional wall-motion abnormalities appear as represented by the lesser systolic thickening in a large part of the LV. The coronary angiogram revealed a severe single-vessel disease of the left anterior descending artery.

Normal Values

Planar ERNA. Normal values depend on the technique used but the lowest normal LVEF is usually about 55% for planar ERNA and 50% for FPRNA. At peak exercise, an increase of at least 5% above the resting value is expected, although failure to fulfill this criterion must not be systematically considered diagnostic of cardiac disease. Indeed, failure to increase with at least 5% or even drop in EF at exercise without underlying cardiac pathology can be observed in elderly patients (20), individuals with a high resting EF or undertrained individuals, and women (21).

Tomographic ERNA. Compared to planar ERNA, tomographic ERNA has shown a good correlation with the LVEF value (r = 0.89) despite a significantly higher absolute EF with SPECT (by a factor 1.4), probably due to the influence of the left atrium in the ventricular activity in the planar images (15).

Clinical Applications

Using radionuclide functional testing (Table 2), LVEF is the most frequently used parameter to characterize cardiac performance, particularly in patients with suspected or known CAD (Fig. 1). It has demonstrated its additional diagnostic value compared with ECG and clinics with regard to the presence and severity of CAD (22,23). It also has highly significant prognostic value after acute myocardial infarction, with an LVEF of less than 40% being one of the strongest predictors of poor short- and long-term outcome (23,24). Assessing cardiac performance is not limited to CAD and can be useful in a wide variety of other clinical circumstances, such as diagnosing CMP, stratifying risk before surgery (especially major nonvascular or peripheral vascular surgery), monitoring therapy in patients under medical treatment for cardiac failure, following up patients treated with cardiotoxic drugs for cancer,

evaluating the efficacy of coronary revascularization after bypass grafting or angioplasty in patients with ischemic ventricular dysfunction, assessing cardiac function before transplantation or in patients with renal failure (in whom impaired renal function precludes contrast ventriculography), diagnosing and quantifying cardiac shunts, or evaluating the clinical significance of angiographically-demonstrated coronary stenoses or small-vessel disease (encountered in diabetes mellitus, connective tissue diseases or some types of familial dyslipidemias) on exercise cardiac function.

Gated Myocardial Perfusion SPECT

Gated myocardial perfusion SPECT (gSPECT) allows the simultaneous (instead of successive, as with FPRNA) evaluation of LV function and perfusion with a single test, without significantly increasing the acquisition duration, radiation burden or cost for the patient or the health insurance carrier (25–27). Gated SPECT has gained preference over the past few years and currently should be recommended for all patients submitted for myocardial perfusion study. However, due to the delay between tracer administration and the start of the acquisition with ^{99m}Tc-perfusion agents, LVEF measured by gSPECT after a stress test does not really reflect the stress LV function (28), and can thus not replace FPRNA when an accurate evaluation of the exercise EF value is required.

Methodology. After injecting a myocardial perfusion tracer, each cardiac cycle is divided into eight or 16 image sets with each set corresponding to a specific interval of the cycle. (The tracer is usually labeled with ^{99m}Tc, although some authors have demonstrated recently that accurate functional measurements can be obtained with gSPECT even when ^{201}Tl was used

(29).) Acquisition is started then using the parameters commonly applied to a myocardial perfusion study. With ^{99m}Tc-labeled compounds, the use of all-purpose instead of high-resolution collimators might be recommended to improve the count statistics. After measuring the mean heart rate of the patient, a mean RR interval is calculated and a beat rejection window is set around this mean value. Frequently, however, all beats are accepted or each frame is acquired during a fixed period of time. Afterwards images are processed in the same way as ungated images, but usually with a lower cutoff value for the filtering. The three standard orthogonal tomograms are then obtained from the transversal slices after reorientation according to the long axis of the LV. The LVEF is calculated from the ED and ES volumes measured by commercially available software programs based on either automatic or manual methods for edge detection (30–32). In addition to calculating global LVEF, other functional regional parameters such as wall motion and thickening also can be generated from the gated images (27,33), using the quantified systolic increase in count density as an indirect hallmark of wall thickening (34), and the visually assessed inward motion of the ventricular walls during the cardiac cycle on an endless cine loop display to evaluate wall motion.

Clinical Applications. By allowing the measurement of LVEF, gSPECT yields information about myocardial function when evaluating cardiac perfusion status. Assessing wall thickening and motion has been shown to increase both the sensitivity and specificity of myocardial perfusion imaging by differentiating fixed perfusion defects due to attenuation artifacts from those due to myocardial infarction (35), and identifying regions with decreased wall motion despite preserved perfusion (myocardial stunning). Its possible role in identifying residual viable myocardium in patients with known infarction, although strongly suggested by some authors (28), remains a matter of discussion and is under investigation currently.

CONCLUSION

Gated myocardial perfusion SPECT is one of the most recent developments in the functional evaluation of myocardial performance. It allows simultaneous assessment of global and regional left ventricular function, and myocardial perfusion. Equilibrium or first-pass radionuclide angiography maintain important roles in the diagnostic arsenal of nuclear cardiology for patients in whom a perfusion study is unnecessary. This is true particularly in the follow-up of patients treated with cardiotoxic drugs, patients under medical treatment for cardiac failure, and when the measurement of cardiac function at stress or when right ventricular ejection fraction is needed.

ACKNOWLEDGMENTS

REFERENCES

1. Lee KJ, Southee AE, Bautovich GJ, et al. Normalised radionuclide measures of left ventricular diastolic function. *Eur J Nucl Med* 1989;15:123–127.
2. Miller TR, Grossman SJ, Schectman KB, et al. Left ventricular diastolic filling and its association with age. *Am J Cardiol* 1986;58:531–535.
3. Clements IP, Brown ML, Smith HC. Radionuclide measurement of left ventricular volume. *Mayo Clin Proc* 1981;56:733–739.
4. Dehmer GJ, Lewis SE, Hillis LD, et al. Nongeometric determination of left ventricular volumes from equilibrium blood-pool scans. *Am J Cardiol* 1980; 45:293–300.
5. Breisblatt WM. Continuous radionuclide monitoring of left ventricular function: has the time come? *J Nucl Med* 1991;32:44–47.
6. Thrall JH, Freitas JE, Swanson D, et al. Clinical comparison of cardiac blood-pool visualization with technetium-99m red blood cells labeled in vivo and with technetium-99m human serum albumin. *J Nucl Med* 1978;19:796–803.
7. Verbeke KA, Vanbilloen HP, De Roo MJ, Verbruggen AM. Technetium-99m mercaptoalbumin as a potential substitute for technetium-99m labelled red blood cells. *Eur J Nucl Med* 1993;20:473–482.
8. Hambye AS, Verbeke KA, Vandermeiren RP, et al. Comparison of modified technetium-99m albumin and technetium-99m red blood cells for equilibrium ventriculography. *J Nucl Med* 1997;38:1521–1528.
9. Srivastava SC, Chervu LR. Radionuclide-labeled red blood cells: current status and future prospects. *Semin Nucl Med* 1984;14:68–82.
10. Hambye AS, Vandermeiren R, Vervaet A, Vandevivere J. Failure to label red blood cells adequately in daily practice using an in vivo method: methodological and clinical considerations. *Eur J Nucl Med* 1995;22:61–67.
11. Strauss HW, Griffeth LK, Shahrokh FD, et al. Cardiovascular system. In: Bernier DR, Christian PE, Langan JK, eds. *Nuclear medicine technology and techniques*, 3rd ed. St. Louis: Mosby-Year Book; 1994:279–284.
12. Port SC. The first-pass ventricular function study: why now? *J Nucl Med* 1994;35:1301–1302.
13. Baillet GY, Mena IG, Kuperus JH, et al. Simultaneous technetium-99m MIBI angiography and myocardial perfusion imaging. *J Nucl Med* 1989;30: 38–44.
14. Corbett JR, Jansen DE, Lewis SE, et al. Tomographic gated blood pool radionuclide ventriculography: analysis of wall motion and left ventricular volumes in patients with coronary artery disease. *J Am Coll Cardiol* 1985;6: 349–358.
15. Bartlett ML, Srinivasan G, Barker WC, et al. Left ventricular ejection fraction: comparison of results from planar and SPECT gated blood-pool studies. *J Nucl Med* 1996;37:1795–1799.
16. Ham HR, Franken PR, Georges B, et al. Evaluation of the accuracy of steady-state krypton-81m method for calculating right ventricular ejection/fraction. *J Nucl Med* 1986;27:593–601.
17. Martin W, Tweddel AC, McGhie I, Hutton I. Gated xenon scans for right ventricular function. *J Nucl Med* 1986;27:609–615.
18. Ham HR, Mols P, Froideville JL, Bourgeois P. Estimation of right ventricular ejection fraction by means of ^{99}Tc^m-macroaggregates. *Nucl Med Commun* 1992;13:738–743.
19. Schulman DS. Assessment of the right ventricle with radionuclide techniques. *J Nucl Cardiol* 1996;3:253–264.
20. Franken PR, Vervaet A, Ranquin R, et al. Improvement in the efficacy of exercise first-pass radionuclide angiocardiography in detecting coronary artery disease and the effect of the patient age. *Eur Heart J* 1992;13:1189–1194.

21. Gibbons RJ. Rest and exercise radionuclide angiography for diagnosis in chronic ischemic heart disease. *Circulation* 1991;84:93–99.

22. Borges-Neto S, Coleman RE, Potts JM, Jones RH. Combined exercise radionuclide angiocardiography and single photon emission CT perfusion studies for assessment of coronary artery disease. *Semin Nucl Med* 1991;21:223–229.

23. Bonow RO. Prognostic assessment in coronary artery disease: role of radionuclide angiography. *J Nucl Cardiol* 1994;1:280–291.

24. Lee KL, Pryor DB, Pieper KS, et al. Prognostic value of radionuclide angiography in medically treated patients with coronary artery disease. A comparison with clinical and catheterization variables. *Circulation* 1990;82: 1705–1717.

25. Mannting F, Morgan-Mannting MG. Gated SPECT with technetium-99m-sestamibi for assessment of myocardial perfusion abnormalities. *J Nucl Med* 1993;34:601–608.

26. Avery PG, Hudson NM, Hubner PJ. Gated technetium-99m methoxy-isobutylisonitrile perfusion imaging. *Int J Cardiol* 1992;35:227–234.

27. Marcassa C, Marzullo P, Parodi O, et al. A new method for noninvasive quantitation of segmental myocardial wall thickening using technetium-99m 2-methoxy-isobutyl-isonitrile scintigraphy–results in normal subjects. *J Nucl Med* 1990;31:173–177.

28. Chua T, Kiat H, Germano G, et al. Gated technetium-99m-sestamibi for simultaneous assessment of stress myocardial perfusion, postexercise regional ventricular function and myocardial viability. Correlation with echocardiography and rest thallium-201 scintigraphy. *J Am Coll Cardiol* 1994;23: 1107–1114.

29. Germano G, Erel J, Kiat H, et al. Quantitative LVEF and qualitative regional function from gated thallium-201 perfusion SPECT. *J Nucl Med* 1997;38:749–754.

30. Germano G, Kiat H, Kavanagh PB, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 1995;36:2138–2147.

31. Everaert H, Franken PR, Flamen P, et al. Left ventricular ejection fraction from gated SPET myocardial perfusion studies: a method based on the radial distribution of count density across the myocardial wall. *Eur J Nucl Med* 1996;23:1628–1633.

32. Hambÿe AS, Dobbeleir A, Vervaet A, Chi-Chou H. Can we rely on technetium-99m-sestamibi gated tomographic myocardial perfusion imaging to quantify left ventricular function? A comparative study with classical isotopic techniques for the measurement of ejection fraction. *Nucl Med Commun* 1997;18:751–760.

33. Goris ML, Thompson C, Malone LJ, Franken PR. Modelling the integration of myocardial regional perfusion and function. *Nucl Med Commun* 1994;15: 9–20.

34. Fukuchi K, Uehara T, Morozumi T, et al. Quantification of systolic count increase in technetium-99m-MIBI gated myocardial SPECT. *J Nucl Med* 1997;38:1067–1073.

35. DePuey EG, Rozanski A. Using gated technetium-99m-sestamibi SPECT to characterize fixed myocardial defects as infarct or artifact. *J Nucl Med* 1995;36:952–955.