SEMINARS IN
NEPHROLOGY

Continuous Monitoring of Left Ventricle Function by VEST in Hemodialyzed Patients

Vincenzo Cuccurullo,* Davide Stellato,† Pier Francesco Rambaldi,* Marco Spadafora,‡ Natale G. De Santo,† Massimo Cirillo,† and Luigi Mansi*

Cardiovascular disease is a major cause of morbidity and mortality in chronic kidney disease. Radionuclide-based methods can be used for analyses on the perfusion of coronary arteries and ventricular function. The present study reports the use of a new procedure for continuous measurements of left ventricle function during a dialytic session with the use of a recently developed portable gamma radiation detector (ventricular function study system). On average, left ventricle ejection fraction and stroke volume progressively and continuously decreased throughout the session (end session versus baseline: −13.8% for ejection fraction, −25.9% for stroke volume, $P < .02$). A biphasic response was found for heart rate: a transient modest decrease (at session midpoint, −4.2%) followed by an increase up to values higher than baseline (end session, +4.7%). Cardiac output decreased by 10.4% at session midpoint ($P = .023$ versus baseline) without further reduction in the following hours. Mean changes in systolic pressure paralleled data for cardiac output. Individual changes in indices of left ventricle function were scattered and strongly were correlated with thickness of interventricular septum and telediastolic left ventricular volume measured by standard echocardiogram in the interdialytic period ($R > .75$, $P < .05$). Data indicate that the ventricular function study system could be a powerful tool for characterization of the profile of left ventricular function in hemodialyzed patients.
Semin Nephrol 26:80-84

KEYWORDS CKD, VEST, nuclear medicine, hemodialysis left ventricle, ejection fraction radionuclide, end-stage renal disease

Cardiovascular disease is an important cause of morbidity and mortality in chronic kidney disease (CKD) because CKD patients have a high frequency of coronary artery disease, cerebrovascular disease, peripheral vascular disease, and heart failure regardless of the type of kidney disease.[1-3] The epidemics of cardiovascular disease in CKD appear to be caused by the combination of traditional cardiovascular risk factors (hypertension, hyperlipidemia, smoking, diabetes, and so forth) with CKD-related conditions (anemia, hypervolemia, secondary hyperparathyroidism, and so forth).[1-3] Radionuclide-based methods could play a role for the clinical evaluation of cardiac disease in CKD since they are without the contraindications typical of iodinated contrast media and are useful in early and late stages either of coronary artery disease and of heart failure.[4] The accuracy and prognostic power of these methods can be increased by stress tests that allow the evaluation of ischemia and ventricular dysfunction also under dynamic conditions.[5] The present study reports preliminary data on the use of a new procedure for analyses of left ventricle function changes in the course of a dialytic session.

Methods

The ventricular function study system (VEST, C-VEST system; Capintec Inc., Ramsey, NJ) is a technique for monitoring changes over time in the left ventricle volume and ejection fraction.[6,7] The instrument consists of 2 gamma radiation detectors mounted on a hard plastic garment coupled with an ambulatory electrocardiogram (ECG) recording system. The weight of the entire set (garment with detectors plus recorder) is approximately 3.0 kg. The main detector of the instrument is placed over the left ventricle, the second detec-

*Nuclear Medicine Unit, Second University of Naples, Naples, Italy.
†Nephrology Unit, Second University of Naples, Naples, Italy.
‡Nuclear Medicine Unit, A.O. "G. Moscati", Avellino, Italy Centro di Eccellenza Malattie Cardiovascolari, Seconda Università Napoli, Napoli, Italy.
Address reprint requests to Professor Luigi Mansi, Servizio di Medicina Nucleare, Seconda Università di Napoli, Piazza Miraglia, 2, 80138 Napoli, Italy. E-mail: luigi.mansi@unina2.it

 0270-9295/06/$-see front matter
doi:10.1016/j.semnephrol.2005.06.016

tor is placed over the right lung field. The left ventricle detector uses a 5.0-cm diameter sodium-iodide crystal with a parallel-hole high-sensitivity collimator interfaced by 2 photomultipliers for maximum sensitivity. The lung detector uses a cadmium telluride crystal with a flat-field collimator for minimum weight.[8-14]

The first step of the entire procedure was to perform an ECG gated radionuclide ventriculography after the administration of radiolabeled red blood cells (740 MBq of technetium-99 per month) with the patient in the supine position [multigated analysis (MUGA) study]. A left anterior oblique projection (best septal) was used for optimal separation of the 2 ventricles. Imaging data were obtained by a Siemens E-Cam gamma camera (Siemens, Erlangen, Germany) equipped with a low-energy collimator (64 $\times$ 64 matrix; 2.0 zoom; average number of beats, 900; 24 frames per cardiac cycle). After completion of the MUGA study, the VEST garment and the ECG electrodes were positioned accurately. The main detector of the garment over the left ventricle was placed under direct gamma camera visualization with the use of a target to focus the center of the left ventricle cavity. The second detector (right lung) was used for measurements of pulmonary background activity. Detectors and ECG leads were connected to a digital recorder adapted for data collection of both the time-activity curve and ECG data. The VEST study lasted for an entire 4-hour dialytic session. A final static scan was performed at the end of the procedure to control that the 2 detectors had been stable in the course of data collection. The entire procedure was validated in 20 patients undergoing analyses for coronary artery disease. Data collected by VEST for 6 to 10 hours during daily activities were compared with data collected by MUGA at the beginning and at the end of the procedure (not shown).

Data Analysis

Parameters related to left ventricle function in the MUGA study (defined as baseline) were computed starting from the global time-activity curve with the use of a single semiautomated method.[15] Intradialytic data collected by the VEST recorder were expressed as the percent change over baseline after correction for physical decay (calculated as per ^{99m}Tc half-life). The graphic and numeric data on left ventricle volume and ECG were analyzed automatically with manual editing. Data for single beats were excluded from analyses when the beat duration differed by 20% or more compared with the average calculated for the 4 previous beats. Cardiac output, stroke volume, and ejection fraction were the variables used for the present analyses focusing on 3 time points of the dialytic session (start, midpoint, and end). Data analysis was performed by 2 independent observers (V.C. and P.F.R.), who were blind to patient clinical information.

Patient Selection and Clinical Data

Patients were enrolled in the study after informed consent was obtained and on the basis of the following inclusion criteria: bicarbonate-hemodialysis for at least 6 months (3 session/wk), regular treatment with erythropoietin and antihypertensive drugs, absence of previous diagnosis of myocardial infarction, absence of intradialytic hypotension, and absence of clinical signs of heart failure. The Kt/V value was used as an index of dialysis adequacy. A standard echocardiogram was performed in the interdialytic period 1 week before the VEST study. Weight and blood pressure were monitored by automated procedures during the dialytic session in parallel with the VEST study.

Table 1 Descriptive Statistics

Men/women	4/3
Age, y	55.1 ± 11.2
Dialytic age, mo	19.7 ± 21.1 (range, 7–60)
Hemoglobin, g/dL	11.41 ± 1.98
On erythropoietin treatment (Epo)	7/7
Weight, kg	
Before hemodialysis	71.5 ± 10.0
After hemodialysis	69.0 ± 9.5
After minus before change	2.5 ± 0.8
Kt/V	1.34 ± 0.09
Systolic pressure, mm Hg	143.6 ± 22.1
Diastolic pressure, mm Hg	80.0 ± 11.6
On drug	7/7
Data at ECG	
Interventricular septum thickness, mm	12.7 ± 1.8
Left ventricle telediastolic diameter, mm	50.7 ± 8.0

Results

Table 1 reports descriptive data for the patients included in the study. Figure 1 shows the time course of mean values for cardiac output, ejection fraction, heart rate, and systolic blood pressure during the hemodialytic session. Cardiac output decreased by 10.4% at the midpoint of the session without further reduction in the following hours. Ejection fraction progressively and continuously decreased throughout the session down to a value 13.8% lower than baseline. A similar trend was found for stroke volume. A biphasic response was found for heart rate: a transient decrease at the midpoint of the session followed by an increase up to values higher than baseline. The changes in systolic pressure were similar to the changes in cardiac output with an initial decrease followed by a stable period. Changes in diastolic pressure were not significant (not shown).

Figure 2 shows the individual changes (end minus start) in cardiac output and ejection fraction. Individual data were scattered, ranging from negative values (decrease) to positive values (increase) for both indices of cardiac activity. Individual changes in cardiac output and ejection fraction measured by VEST were correlated strongly with thickness of the interventricular septum and left ventricle telediastolic volume measured by echocardiogram (Fig 3), not with dialysis-induced body weight change or other variables analyzed ($r < 0.3.$, $P > .5$).

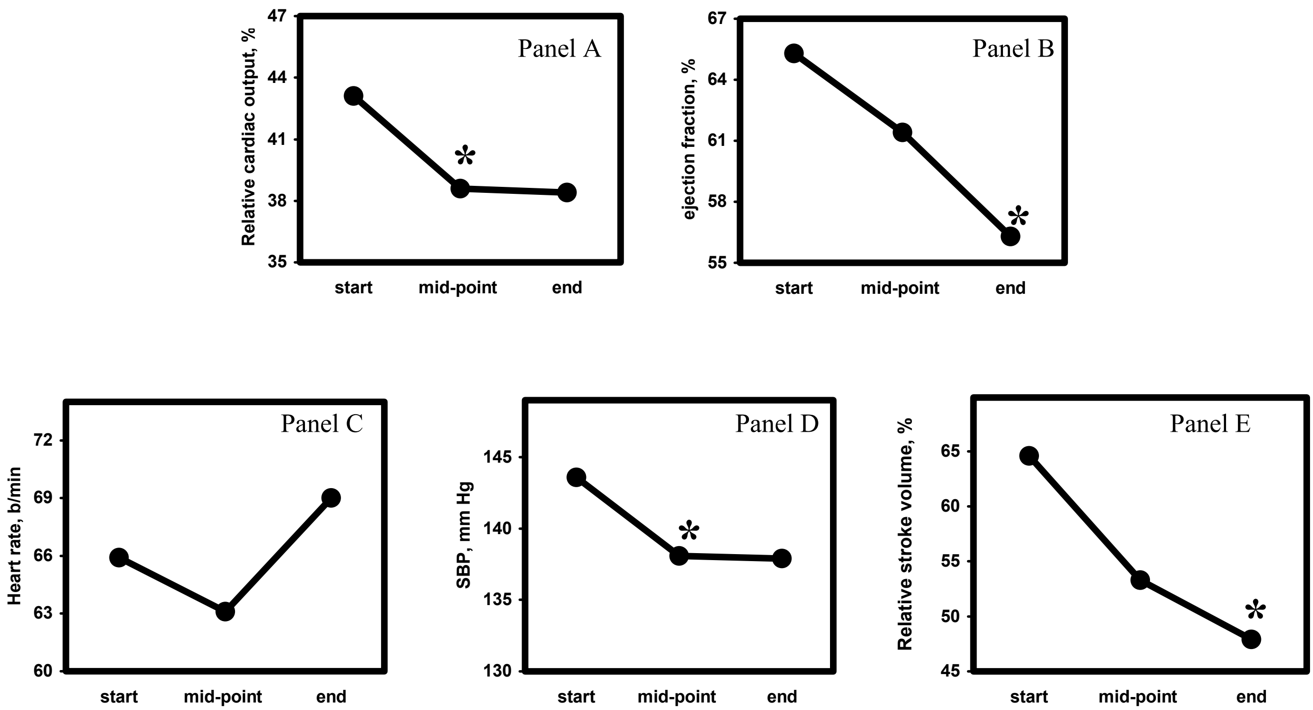

Figure 1 Time course of (A) cardiac output, (B) ejection fraction, (C) heart rate, (D) systolic pressure, (E) and stroke volume in the course of a hemodialytic session (means, $*P < .03$ by paired Student t test versus start).

Discussion

Probes and/or miniature detectors of gamma radiation derived from a conventional gamma camera have been investigated by several studies.[16,17] The VEST apparatus has been used to study indices of left ventricle function when changes are expected in a time period of hours.[18-20] Investigations have been performed at rest, during routine daily activity, during standardized physical activity, or other interventional tests focusing on myocardial ischemia, cardiac and noncardiac disorders, treatment with drugs, cold stimulation, tilt test, and angioplasty.[21-31] The use of VEST was proposed also for risk stratification in coronary artery disease.[32,33] Theoretically, information collected by VEST could be of help for the definition of the time course of the changes in left ventricle function associated with hemodialysis, a condition that is characterized by a very high frequency of various cardiac diseases.

The preliminary data of the present study indicate that VEST could be a powerful tool for investigations of cardiac activity in hemodialysis. Data show that the average trend in the course of hemodialysis is a reduction of cardiac output as expected in the course of a progressive and large reduction of the plasma volume. Changes in heart rate were biphasic, with an initial decrease followed by a later increase. The late heart rate increase likely could reflect an activation of the sympathetic tone that contributes to maintain the stability of cardiac output and systolic blood pressure in the second half of the dialytic session despite the progressive decrease in plasma volume and ejection fraction. Analyses of the individual data indicated a large interindividual variability in the intradialytic changes of indices measured by VEST. Changes of cardiac output ranged from a large

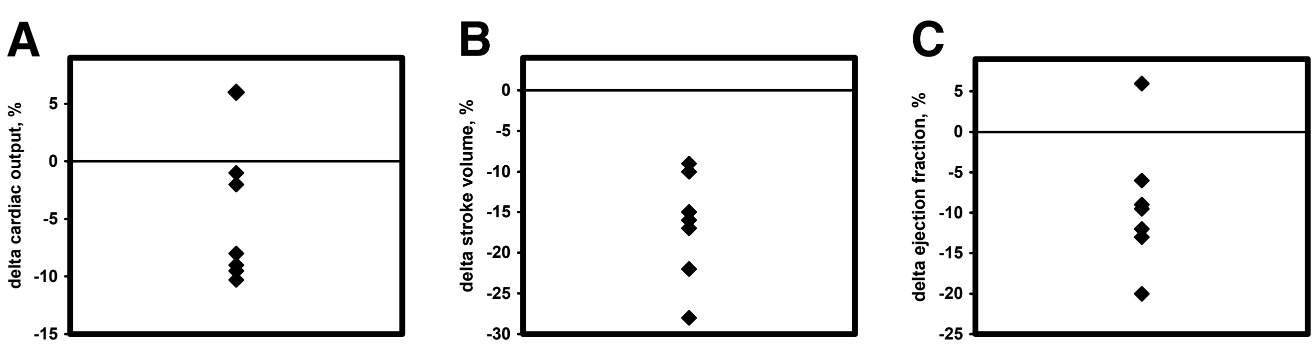

Figure 2 Individual changes (end session value minus start session value) in (A) cardiac output, (B) stroke volume, and (C) ejection fraction.

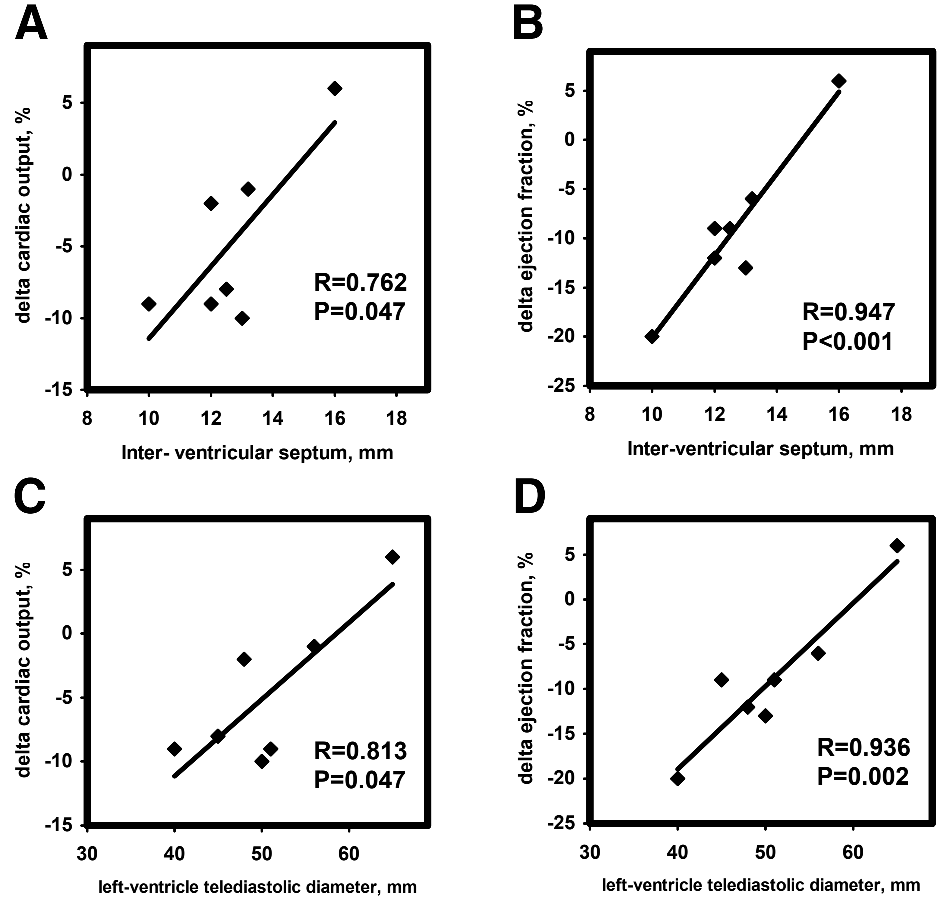

Figure 3 Correlation between changes in (A, C) cardiac output and (B, D) ejection fraction as measured by VEST with (A, B) interventricular septum thickness and (C, D) left-ventricle telediastolic volume.

decrease to a sizeable increase, in contrast with the relatively homogenous decrease in body fluids secondary to hemodialysis. Data from a standard ECG were strong predictors of the findings of VEST. Patients with echocardiographic measures close to the normal range experienced a progressive decrease in cardiac output during hemodialysis. In contrast, patients with septal hypertrophy and left ventricle dilation experienced no change or a slight increase in cardiac output.

Data interpretation must be cautious because of the low number of patients in the present study. Nevertheless, an intriguing possibility raised by the present data are that hemodialyzed patients are extremely sensitive to the preload conditions for their hemodynamic equilibrium. In the presence of left ventricle function that is normal or slightly altered, the extracellular volume expansion that is proper for the predialytic phase could be a factor favoring cardiac performance. Therefore, under these conditions, the rapid depletion of the extracellular fluid volume induced by hemodialysis could decrease the cardiac performance via decreases in venous return and filling pressure. In other words, the hemodialytic session could unmask a diastolic impairment previously counterbalanced by the volume overload and could imply a decrease in cardiac output and ejection fraction caused by the reduced stroke volume. In the second half of the hemodialytic session the increasing heart rate could permit maintenance of a relatively stable cardiac output despite the continuously decreasing stroke volume. The opposite would occur in the presence of left ventricle function that was altered more severely. In this condition, cardiac output does not decrease in the course of the hemodialytic session, perhaps because the predialytic expansion of the extracellular volume is one of the factors contributing to low cardiac performance.

In summary, this study indicates that VEST could be an important tool for the definition of the pattern of left ventricular function in hemodialyzed patients. Data in a small group of patients without clinically overt heart disease show that the changes of cardiac performance in the course of a dialytic sessions are not the same in all patients. The average trend is a decrease, but there are cases with opposite changes (ie, with an intradialytic increase in cardiac performance) irrespective of changes in body weight and blood pressure. The precise definition of left ventricle function during hemodialysis and of its determinants might be relevant to the treatment and control of epidemics of cardiovascular mortality in hemodialysis.

References

1. Foley RN, Parfrey PS, Sarnak MJ: Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 32:112-119, 1998
2. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification.

Guideline 15. Association of Chronic kidney Disease with cardiovascular Disease. Am J Kidney Dis 39:S204-S205, 2002 (suppl 1)
3. Sarnak MJ, Levey AS, Schoolwerth AC, et al: Kidney disease as a risk factor for development of cardiovascular disease—a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Circulation 108:2154-2169, 2003
4. Meller J, Sahlmann CO, Becker W: Nuclear medicine studies in the dialysis patient. Semin Dial 15:269-276, 2002
5. Clark AN, Beller GA: The present role of nuclear cardiology in clinical practice. Q J Nucl Med Mol Imaging 49:43-58, 2005
6. Flotats A: Current status and future of continuous radionuclide left ventricular function monitoring. Nucl Med Commun 23:421-427, 2002
7. Zaret BL, Jain D: Continuous monitoring of left ventricular function with miniaturized nonimaging detectors, in Zaret BL, Beller GA (eds): Nuclear Cardiology: State of the Art and Future Directions. St. Louis, Mosby Year Book, 1993, pp 137-145
8. Harrison KS, Liu X, Han S, et al. Evaluation of a miniature CdTe detector for monitoring left ventricular function. Eur J Nucl Med 7:204-206, 1982
9. Suzuki Y, Ide M, Murakami T: Radionuclide cardiac monitoring system using dual cadmium telluride (CdTe) detectors: Specifications and some clinical applications. Nucl Med Commun 8:431-440, 1987
10. Wagner HN, Wake R, Nickoloff E, et al: The nuclear stethoscope: A simple device for generation of left ventricular volume curves. Am J Cardiol 38:747-750, 1976
11. Berger HJ, Zaret BL: Beat-to-beat left ventricular performance assessed from equilibrium cardiac blood pool using a computerized nuclear probe. Circulation 67:133-136, 1981
12. Hoffer PB, Berger HJ, Steidley J, et al: A miniature cadmium telluride detector module for continuous monitoring of left ventricular function. Radiology 138:477-481, 1981
13. Lahiri A, Crawley JCW, Jones RI, et al: A non-invasive technique for continuous monitoring of left ventricular function using a new solid state mercuric iodide radiation detector. Clin Sci 66:551-556, 1984
14. Wilson RA, Sullivan PJ, Moore RH: An ambulatory ventricular function monitor: Validation and preliminary clinical results. Am J Cardiol 52: 601-606, 1983
15. Flotats A, Serra-Grima R, Camacho V, et al: Left ventricular end-diastolic volume is decreased at maximal exercise in athletes with marked repolarisation abnormalities: A continuous radionuclide monitoring study. Eur J Nucl Med Mol Imaging 32:203-210, 2005
16. Yang LD, Bairey MN, Berman DS, et al: Accuracy and reproducibility of left ventricular ejection fraction measurements using an ambulatory radionuclide left ventricular function monitor. J Nucl Med 32:796-802, 1991
17. Pace L, Cuocolo A, Nappi A, et al: Accuracy and repeatability of left ventricular systolic and diastolic function measurements using an ambulatory radionuclide monitor. Eur J Nucl Med 19:800-806, 1992
18. Imbriaco M, Cuocolo A, Pace L: Repeatability of hemodynamic responses to cardiac stimulations by ambulatory monitoring of left ventricular function. J Nucl Biol Med 37:238-244, 1993
19. Bairey N, Yang LD, Berman DS, et al: Comparison of physiological ejection fraction responses to activities of daily living: Implications for clinical testing. J Am Coll Cardiol 16:847-854, 1990
20. McCarthy DM, Makler PT: Accuracy of left ventricular ejection fraction using the nuclear stethoscope in left ventricular aneurysm. Am J Cardiol 55:177-180, 1985
21. Hartmann A, Maul FD, Zimny M: Impairment of left ventricular function during coronary angioplastic evaluated with a nonimaging scintillation probe. Am J Cardiol 68:598-602, 1991
22. Kayden DA, Remetz MS, Cabin HS: Validation of continuous radionuclide left ventricular function monitoring in detecting silent myocardial ischemia during balloon angioplasty of the left anterior descending artery. Am J Cardiol 67:1339-1343, 1991
23. Wolz DE, Flores AR, Grandis DJ, et al: Abnormal left ventricular ejection fraction response to mental stress and exercise in cardiomyopathy. J Nucl Cardiol 2:144-150, 1995
24. Mizuno H, Yanagisawa A, Shigeyama T: Continuous ambulatory radionuclide monitoring of left ventricular function: Effect of body position during ergometer exercise. J Nucl Med 38:1669-1672, 1997
25. Legault S, Langer A, Armstrong PW, et al: Usefulness of ischemic response to mental stress in predicting silent myocardial ischemia during ambulatory monitoring. Circulation 75:1007-1011, 1995
26. Burg MM, Jain D, Soufer R, et al: Role of behavioral and psychological factors in mental stress induced silent left ventricular dysfunction in coronary artery disease. J Am Coll Cardiol 22:440-448, 1993
27. Nappi A, Cuocolo A, Imbriaco M, et al: Ambulatory monitoring of left ventricular function: Walk and bicycle exercise in congestive heart failure. J Nucl Med 38:453-498, 1997
28. Volpe M, Rao MAE, Cuocolo A, et al: Radionuclide monitoring of cardiac adaptation to volume loading in patients with dilated cardiomyopathy and mild heart failure: Effects of angiotensin-converting enzyme inhibition. Circulation 92:2511-2518, 1995
29. Mortelmans L, Vanhecke W, Mertens D: Assessment of the optimal atrioventricular delay in dual chamber-paced patients by a portable scintillation probe. J Nucl Cardiol 3:321-326, 1996
30. Imbriaco M, Cuocolo A, Pace L, et al: Ambulatory monitoring of left ventricular function during cardiopulmonary exercise tests in normal sedentary subjects. J Nucl Med 36:564-568, 1995
31. Aksut SV, Pancholy S, Johnson J: Comparison of left ventricular performance in healthy young women and men during exercise. J Nucl Cardiol 3:415-421, 1996
32. Cohn PF: Myocardial dysfunction in silent myocardial ischemia as demonstrated by ambulatory radionuclide left ventricular function studies. Cardiol Clin 10:473-478, 1992
33. Breisblatt WM, Wolf CJ, McElhinny B, et al: Comparison of ambulatory left ventricular ejection fraction and blood pressure in systemic hypertension in patients with and without increased left ventricular mass. Am J Cardiol 67:597-603, 1991