Abstract. Acceptance of technetium-99m sestamibi as a tracer of myocardial viability is growing, particularly when nitrate-enhanced imaging is used. However, few data are available on the ability of 99mTc-sestamibi to predict the evolution of global left ventricular ejection fraction (EF). The aim of this study was to examine the ability of resting and nitrate 99mTc-sestamibi single-photon emission tomography (SPET) to predict EF changes after revascularisation in patients who have chronic coronary artery disease with left ventricular dysfunction. Using baseline resting and nitrate 99mTc-sestamibi SPET, we studied 61 patients scheduled for revascularisation because of left ventricular dysfunction. EF was estimated using two-dimensional echocardiography before and after the intervention. A post-revascularisation improvement of ≥5 EF units was defined as significant. Using a 13-segment model, 99mTc-sestamibi activity was quantified and the nitrate-induced activity changes calculated. Three different criteria for detecting viability (defined as post-revascularisation reversible dysfunction) in asynergic segments were compared: (1) resting 99mTc-sestamibi activity ≥60%; (2) nitrate 99mTc-sestamibi activity ≥65%; and (3) nitrate-induced increase >+10% or nitrate-induced increase ≤+10% and nitrate activity ≥65%. EF increased significantly in 32 patients. The number of viable asynergic segments was significantly higher in these patients than in the remaining 29 subjects, and the difference was greater (P<0.0005). There was a significant relationship between EF changes and number of viable asynergic segments: Spearman R=0.38, P<0.005 using baseline; Spearman R=0.39, P<0.002 using nitrate activity; and Spearman R=0.55, P<0.000005 using definition (3). According to receiver operating characteristic (ROC) curve analysis, this last criterion achieved the best results (81% sensitivity, 69% specificity and 75% accuracy), with an area under the ROC curve of 0.838; this area was significantly larger than when using either baseline (0.744, P<0.02) or nitrate activity (0.747, P<0.005). 99mTc-sestamibi SPET appears able to predict the evolution of global left ventricular EF after revascularisation, thereby confirming the value of 99mTc-sestamibi as a tracer of myocardial viability. The combination of baseline resting and nitrate imaging seems to significantly improve the diagnostic accuracy of 99mTc-sestamibi SPET for this particular purpose.

Keywords: Ejection fraction – Nitrates – Revascularisation – Technetium-99m sestamibi – Viability


Introduction

Technetium-99m sestamibi is an established myocardial perfusion tracer for the diagnosis of coronary artery disease and risk stratification, but its value for the detection of myocardial viability has been disputed. In spite of favourable experimental results [1, 2, 3], early clinical studies suggested that 99mTc-sestamibi imaging underes-
timates viable myocardium compared with other methods such as thallium-201 perfusion scintigraphy or positron emission tomography [4, 5]. Later reports, however, demonstrated a good relationship between myocardial viability and $^{99m}$Tc-sestamibi uptake [6, 7, 8]. Most importantly, it was found that $^{99m}$Tc-sestamibi single-photon emission tomography (SPET) had good ability to predict functional recovery of asynergic segments after coronary revascularisation [9, 10]. A further increase in $^{99m}$Tc-sestamibi diagnostic reliability was achieved by performing nitrate-enhanced imaging [11, 12, 13, 14, 15]. Although the evolution of regional function is the most frequently used reference standard for evaluating viability detection methods, improvement in global left ventricular function is probably the most important clinical goal of coronary revascularisation [16]. Good diagnostic accuracy for the prediction of improvement in global left ventricular function has been demonstrated for positron emission tomography [17, 18, 19], $^{201}$TI imaging [20, 21] and dobutamine echocardiography [19, 20, 22, 23], but virtually no data are available for $^{99m}$Tc-sestamibi SPET. The aim of this study was to evaluate the ability of $^{99m}$Tc-sestamibi SPET to predict changes in global left ventricular function after coronary revascularisation, and in addition to examine the possible contribution of nitrate-enhanced imaging in this respect.

### Materials and methods

#### Patient population.

The study population was selected from among all those patients who underwent $^{99m}$Tc-sestamibi SPET for the detection of myocardial viability in our laboratory. Inclusion criteria were: (a) diagnosis of chronic coronary artery disease confirmed by coronary angiography, (b) known left ventricular dysfunction with ejection fraction (EF) $<50\%$, (c) presence of clear regional wall motion abnormality in at least one coronary artery territory, (d) an already scheduled revascularisation procedure and (e) willingness to participate in the study. Exclusion criteria were: (a) recent (<3 months) myocardial infarction or unstable angina, (b) heart disease other than coronary artery disease and (c) a history of prior revascularisation procedures. Of the potentially eligible patients, 22 were excluded after initial enrolment because the revascularisation procedure was incomplete. The final study cohort comprised 61 patients (54 men and 7 women, mean age 60.7±11 years, range 30–77).

#### Study protocol.

All patients underwent baseline resting and nitrate-enhanced $^{99m}$Tc-sestamibi SPET. A few days before or after the scintigraphic studies and under stable clinical conditions, global left ventricular EF was assessed by two-dimensional echocardiography. The subsequent revascularisation procedure involved all stenotic vessels. At least 3 months later, a follow-up control using two-dimensional echocardiography was performed to assess the changes in global left ventricular EF. The Ethics Committees of our institutions approved the study protocol and informed consent was obtained from each patient.

#### Functional evaluation.

Both echocardiographic studies were collected at rest with the patient in the left lateral decubitus position using commercially available echocardiographic equipment (SSD-870, Aloka, Tokyo, Japan or Sonos 2000, Hewlett Packard, Palo Alto, Calif.) with 2.5- to 3.5-MHz transducers. Multiple imaging sections were obtained for each study and recorded on videotape. All studies were analysed off-line by two experienced observers who were blinded to the clinical, angiographic and scintigraphic data and to the acquisition sequence. For wall motion analysis, the left ventricle was divided into 13 segments [11], and wall motion and thickening of each segment were scored as follows: 1=normal, 2=hypokinesia, 3=akinesia, 4=dyskinesia [11]. Discrepancies were resolved by consensus. For calculation of the left ventricular EF, the biplane Simpson’s method as recommended by the American Society of Echocardiography was applied on three consecutive cardiac cycles examined with the apical four-chamber view, and the mean of the three measured values was used [24]. Improvement in global left ventricular EF after revascularisation was arbitrarily defined as an increase ≥5 EF units in the follow-up control compared with the baseline value [23].

#### $^{99m}$Tc-sestamibi SPET.

The protocol included two separate studies, one after tracer injection at rest and the other after tracer administration during nitrate infusion, as previously described [10]. The $^{99m}$Tc-sestamibi dose was 740–925 MBq (20–25 mCi) in both instances. For the nitrate study, patients received 10 mg of isosorbide dinitrate in 100 ml of isotonic saline solution administered over 20 min. $^{99m}$Tc-sestamibi was injected after 15 min of infusion or earlier if either a decrease of ≥20 mmHg in systolic blood pressure or a systolic blood pressure <90 mmHg was registered [10]. Tomographic projections were collected approximately 1 h later using either a single-head (Axial SP4, Elscint, Haifa, Israel) or a dual-head (Vertex, ADAC, Milpitas, Calif.) large-field-of-view tomographic gamma camera equipped with ultra-high-resolution collimators, and with a 20% window centered on the 140-keV photopeak of $^{99m}$Tc. Image reconstruction was performed using filtered back-projection, without attenuation or scatter correction, and the slices were re-aligned along the heart axis. For the quantitative evaluation of SPET images, the short-axis slices from the first with apical activity to the last with activity at the base were used. Their count profiles were generated by computer software and plotted onto a two-dimensional volume-weighted polar map, which was then divided into 13 segments, matching the echocardiographic ones [15]. Using an automated procedure, segment tracer activity was calculated as the total of the counts of the pixels included within the segment divided by the pixel number. The segment with maximal activity was then normalised to 100 and the activity of the other segments was expressed as a percentage thereof [15].

#### Criteria for myocardial viability.

The assessment of viability was restricted to the segments with resting wall motion abnormality (scores 2–4) as determined by two-dimensional echocardiography. Three different criteria were used to define the likelihood that a segment would be viable, i.e. display functional recovery following revascularisation. The first criterion was based on the baseline activity level, and reversible dysfunction was defined as likely in asynergic segments with a $^{99m}$Tc-sestamibi activity value ≥60% [9]. According to the second criterion, reversible dysfunction was regarded as likely in asynergic segments with nitrate activity ≥65% [15]. The third criterion was based on the nitrate-induced activity changes [15, 25]. Functional recovery was considered likely in asynergic segments with a nitrate-induced increase in ac-