Thallium-201 gated single-photon emission tomography for the assessment of left ventricular ejection fraction and regional wall motion abnormalities in comparison with two-dimensional echocardiography

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Received 20 February and in revised form 12 June 1999

Abstract. Simultaneous assessment of myocardial perfusion and function by gated single-photon emission tomography (GS) after a single tracer injection provides incremental information and is feasible with technetium-99m sestamibi. The present study validated the use of GS with thallium-201 for the assessment of left ventricular ejection fraction (LVEF) and regional wall motion by comparison with two-dimensional (2D) echocardiography (echo), which has not been done before**.** After injection of 111 MBq ^{201}Tl at peak bicycle exercise (*n*=55) or pharmacological stress (*n*=17), GS was acquired 15 (post stress) and 120 min post injection (rest) on a double-head camera. An automatic algorithm (QGS) was used for processing. Echo (Acuson Sequoia C256) was performed immediately after rest GS. LVEFs assessed by GS and echo were correlated. The overall and segmental sensitivity and specificity of GS for the detection of regional wall motion abnormalities (WMAs) were calculated, echo serving as the gold standard. Perfusion abnormalities were scored. The success rate of the automatic algorithm was 100%, and visually assessed image quality was good to excellent in 88% of cases. Post-stress and rest LVEF as assessed by GS were highly correlated (*r*=0.91). Good correlations were obtained between post-stress LVEF (GS) and rest LVEF (echo) and between rest LVEF (GS) and rest LVEF (echo) (*r*=0.76 and 0.86 respectively). In patients with a reduced LVEF of less than 50% (*n*=23), these correlations were even better (*r*=0.84 and 0.89 respectively). Regional wall motion abnormalities (WMAs) were identified by GS with high sensitivity and specificity (88%–100% and 82%–98% respectively) and were directly related to the extent and severity of stress as well as of resting perfusion defects. It is concluded that GS with ^{201}Tl is a feasible and reliable tool for the evaluation of patients with compromised left ventricular function in the context of coronary artery disease, and thus improves diagnosis and prognostic stratification. Regional WMAs were identified with high diagnostic accuracy and the method may prove helpful for the detection of myocardial viability.

Key words: Gated single-photon emission tomography – Thallium-201 – Wall motion – Left ventricular ejection fraction – Stunning

Eur J Nucl Med (1999) 26:1533–1540

Introduction

ECG-gated acquisition of myocardial perfusion single-photon emission tomography (GS-SPET) studies with technetium-99m sestamibi allows simultaneous assessment of perfusion and left ventricular function after a single tracer injection [1]. The advantage of this technique lies in the broad spectrum of information obtained, i. e. perfusion at time of peak exercise and rest, and both global and regional left ventricular function after stress and at rest [1–3]. Moreover, the assessment of regional wall motion and the thickening pattern allows viability studies to be performed [4, 5]. Artefacts are easier to detect by separate reading of the thickening pattern from end-diastolic and end-systolic frames [2, 3, 6, 7]. Inclusion of this information in the interpretation of perfusion studies increases specificity, as previously reported [3]. GS with ^{99m}Tc-sestamibi was introduced several years ago. It was initially based on manual [8] or semi-automatic processing [9, 10], which resulted in high observer variability [8]; however, a fully automated algorithm

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(QGS) was developed in 1995 [11]. GS with ^{99m}Tc-sestamibi has been validated against a variety of techniques, i.e. equilibrium blood pool studies [8] and contrast [9, 10] and first-pass [10, 11] ventriculography, as well as two-dimensional (2D)echocardiography [2]. However, despite its lower photon energy compared with ^{99m}Tc [12], thallium-201 remains the most widely used radiotracer for cardiac perfusion studies in the United States [13] and Europe, owing to its lower cost and the better possibility of myocardial viability assessment [14, 15]. Moreover, a combined stress and rest study can be performed after a single dose of ^{201}Tl. The question of whether GS can be performed equally well with this tracer has not yet been answered. Thus the purpose of the present study was to investigate the clinical feasibility of GS with ^{201}Tl for left ventricular ejection fraction (LVEF) and regional wall motion assessment by comparison with 2D echocardiography, which has not been done before.

Materials and methods

Study population. Seventy-nine patients (47 males and 32 females), aged 57±10.1 (30–78) years, referred for evaluation of coronary artery disease (CAD), were studied. Twenty-five patients (31.6%) had a history of prior myocardial infarction, and seven (8.9%) underwent coronary artery bypass grafting. Mean body surface was 1.82±0.15 m^2 (1.43–2.38 m^2), and the maximum heart rate at stress (n=72) was 130.2±21.5 (77–179).

Stress testing. Seventy-two patients underwent a GS myocardial perfusion study at stress and rest as part of nuclear cardiology routine. Beta-blocking agents and long-acting nitrates were withdrawn 48 and 24 h prior to testing, respectively. 111 MBq (3 mCi) ^{201}Tl was administered at peak bicycle exercise (n=55) or at maximal hyperaemia induced by dipyridamole (0.142 mg/kg per minute) (n=17). Exercise was continued at the same level for an additional 60 s. The endpoint was achievement of at least 85% of the predicted heart rate. Seven patients underwent only rest GS due to unstable angina. (2D) Echocardiography (echo) was performed immediately after rest GS by an experienced cardiologist. Informed consent was obtained from all patients.

Acquisition and processing of GS. Images were acquired on a dual-detector camera (ADAC, Vertex), equipped with a low-energy, general-purpose collimator, employing step by step detector rotation and 30 s of data collection per projection. A 20% window was centered over the 68–80 and 167 keV ^{201}Tl photopeaks. Attenuation correction was performed with a gadolinium-153 point source**.** Eight frames per cardiac cycle were utilized, and 100% of beats accepted [11]. The gated projection data sets were filtered with a two-dimensional Butterworth filter (order 10, critical frequency 0.33). Commercially available, automated software was employed (QGS) [11]. For perfusion assessment, the summed GS projection data sets were used, iteratively reconstructed employing Butterworth filtering (order 5, cut-off 0.5).

Acquisition of echocardiography. 2D echocardiographic analysis of regional and global left ventricular function was performed with a high-resolution ultrasound unit (Sequoia C256, Acuson Inc., Mountain View, Calif., USA), equipped with a 3.5-MHz transducer. Parasternal long and short axis as well as apical two- and four-chamber views were analysed by an experienced echocardiographer, blinded to scintigraphic data, and were used to assess regional wall motion and thickening of left ventricular segments and to measure LVEF.

Interpretation of perfusion images. Perfusion was assessed semi-quantitatively, based on apical, mid and basal short axis and vertical long axis tomograms, divided into 20 segments [16]. A five-point scoring system was employed (0 = normal tracer uptake, 1 = equivocal, 2 = mildly reduced, 3 = severely reduced, 4 = absent). Summed stress score (SSS) and summed rest score (SRS) were calculated as the sums of scores of the 20 segments in the stress and rest images, respectively. The sum of the differences between each of the 20 segments on stress and rest images was defined as summed difference score (SDS), representing ischaemia [16].

Image quality of GS. Images were assessed visually for contrast, background activity and brightness. When gating artefacts were present, studies were excluded. The automatic algorithm for myocardial edge detection dealt with severe perfusion defects (Fig. 1) by extracting count profiles from the non-threshold image and by employing the three-dimensional myocardial surface gradients at the border of perfusion defects. An asymmetric gaussian was fitted to each profile and inner and outer standard deviations (SDs) were measured. In the case of low perfusion along a profile, these SDs were combined with those of each of its four spatially neighbouring profiles [11]. Correct automatic border placement was confirmed visually.

LVEF measurement by GS and echocardiography. End-diastolic (EDV), end-systolic (ESV) volumes and LVEF were provided automatically by QGS [11]. (It should be mentioned here that while the validation of volumes was not the aim of the current study, validation of EDV and ESV versus 3D-echo is underway in this institution.) Echocardiographic LVEF calculation was performed according to Simpson's rule [17].

Detection of regional wall motion abnormalities (WMAs) by GS and echocardiography. Semi-quantitative assessment of regional wall motion in GS was made by an experienced observer, dividing the left ventricular myocardium into segments on the basis of apical, mid and basal short axis slices and a midventricular vertical long axis slice, as described elsewhere [18]. The segments were: anterior, anterolateral, inferolateral, inferior, inferoseptal, anteroseptal (apical, mid and basal regions), antero-apical and infero-apical. WMAs in GS and echo were scored using the same four-point scale: 0 = normal wall motion, 1 = mild to moderate hypokinesia, 2 = severe hypokinesia, 3 = akinesia or dyskinesia [13, 17]. Segmental sensitivity and specificity for detection of WMAs by GS were calculated by comparison with the corresponding echo segment. WMAs were allowed to differ by one point between echo and GS (between scores 1 and 3). Echo served as the gold standard and was based on the 16-segment model proposed by the American Society of Echocardiography [17]. The same definition was used for the anterior, inferior, antero-apical and infero-apical segments in echo and GS. Owing to a slightly differing definition between GS and echo for the remaining segments, they were correlated with each other: Anterolateral (GS) was regarded as equivalent to apicolateral and mid/basal anterior (echo), and inferolateral (GS) as equivalent to midposterior, midlateral and basolateral (echo). Inferoseptal (GS) was taken to correspond to basoseptal

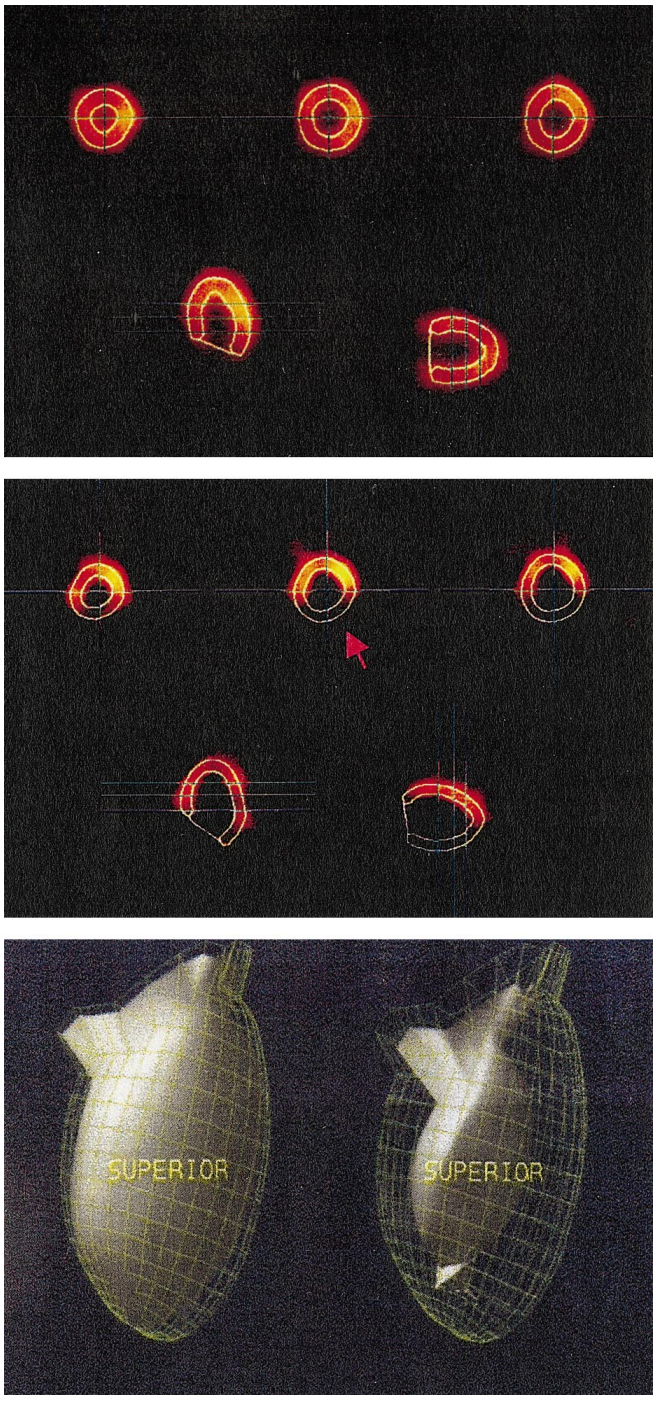

Fig. 1. *Upper and middle panels*: Endo- and epicardial borders drawn by QGS on apical, mid and basal short axis and vertical long axis slices. Systolic inward movement of borders can be viewed in cine mode. For visual analysis of regional WMAs, images can be displayed either with or without overlayed contours. *Upper panel*: normal perfusion. *Middle panel*: perfusion defect in inferior wall. *Lower panel*: 3D display of inward movement of the left ventricle from end-diastole (left) to end-systole (right)

and midinferior (echo) (right coronary artery territory), and anteroseptal (GS) (left anterior descending artery territory) was considered equivalent to apico- and midseptal (echo). For calculation of overall sensitivity and specificity of GS and evaluation of frequency of WMAs, a GS study was considered normal if the sum of the WMAs of all eight segments was ≤1 (a score of 1 was therefore allowed in one of the segments).

Definition of "stunned" myocardium. In this study the definition of stunned myocardium was based on the presence of transient WMAs post stress in patients with reversible perfusion defects (SDS>4), which improved by ≥2 points at rest [4].

Statistical analysis. Values were expressed as mean ± SD. The unpaired Student's *t*-test was used to assess continuous LVEF variables, and the chi-square test for categorical variables. Linear regression analysis was performed for correlation between GS and echo. A probability value of 0.05 was considered statistically significant.

Results

The automatic program was executed successfully on all post-stress (*n*=72) and rest (*n*=79) studies, yielding a success rate of 100%. No manual readjustment of myocardial contours was required even when severe perfusion defects were present (Fig. 1), defined by an SSS >13 for the post-stress (*n*=11), and an SRS ≥4 for the rest images (*n*=25). Forty patients (50.6%) had a normal perfusion scan, defined by an SSS <4 [16]. Visually determined image quality for post-stress studies (*n*=72) was excellent in 21 cases (29.2%), good in 39 (54.2%) and poor in 12 (16.6%), while for rest studies (*n*=79) it was excellent in 19 (24%), good in 51 (64.5%) and poor in 9 (11.4%).

Table 1. Left ventricular ejection fraction and end-diastolic and end-systolic volumes calculated by GS post stress and at rest, and by echo

	GS post stress (*n*=72)	GS rest (*n*=79)	Echo rest (*n*=79)
LVEF (%)	57.6±14.5* (21–86)	55.4±13.7** (18–86)	54.15±13.2 (20–88)
EDV (ml)	89.4±41.6 (29–268)	93.5±46.8** (26–300)	
ESV (ml)	44.5±33.9 (5–198)	48.9±37.8** (4–248)	

Data are expressed as mean ± SD (range)
GS, Gated SPET; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; Echo, 2D echocardiography
*NS versus Echo rest
**NS versus GS post stress

Left ventricular ejection fraction

LVEFs calculated by GS post stress and at rest and the corresponding data obtained by echo are summarized in Table 1. In addition, end-diastolic and end-systolic volumes (EDV and ESV, respectively) are presented.

Relationship between GS LVEF post stress and at rest (Table 1, Fig. 2). Post-stress LVEF was slightly but not significantly higher than rest LVEF (Table 1). This difference proved to be more marked in a subgroup of healthy subjects with a normal perfusion scan (SSS <4) and an LVEF >50% (*n*=34): GS LVEF values post stress and at rest for this group were 70±7.5 and 66±7.9, respectively (*P*=NS), the higher post-stress LVEF value being due to the contractile behaviour of the left ventricle after stress. Overall correlation between GS LVEF values post-stress and at rest was close for all patients over a wide range, as demonstrated in Fig. 2.

Relationship between GS LVEF and echo LVEF (Figs. 3, 4). The good correlation obtained between GS LVEF post stress and echo LVEF at rest for all patients, and for a subgroup of patients with reduced LVEF, is presented in Fig. 3. As is further demonstrated by Fig. 4, GS LVEF at rest correlated more closely with echo LVEF than did GS LVEF post stress. The right panels of Figs. 3 and 4 show that the correlation between echo LVEF and GS LVEF post stress and at rest was particularly close for patients with reduced left ventricular function.

When correlation was evaluated according to the stress protocol employed, post-stress GS LVEF after bicycle exercise demonstrated a weaker correlation with echo than did post-stress GS LVEF after pharmacological stress (Table 2). It was further noted that the maximal heart rate was significantly higher following exercise (*n*=55) than after pharmacological stress (*n*=17)

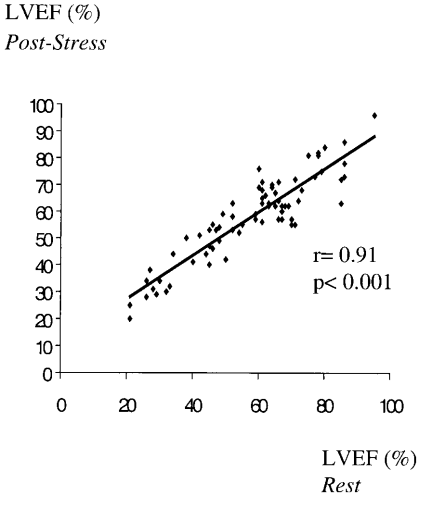

Fig. 2. Correlation between post-stress and rest LVEF measured by GS (*n*=72)

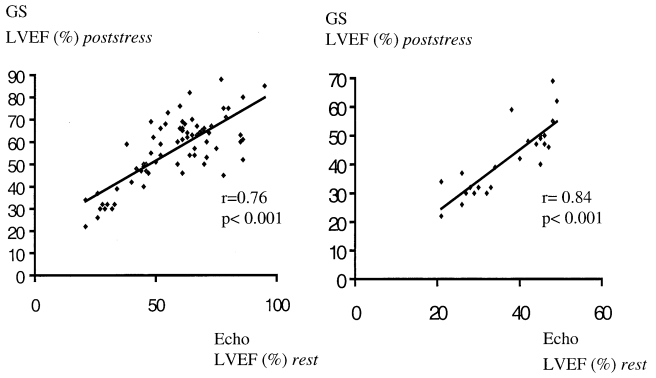

Fig. 3. Correlation between post-stress LVEF assessed by GS and rest LVEF assessed by echo. The *left panel* shows the correlation for all patients (*n*=72). The *right panel* shows the correlation for only those patients with an ejection fraction of <50% (*n*=24). *GS*, Gated SPET; *LVEF*, left ventricular ejection fraction; *echo*, 2D echocardiography

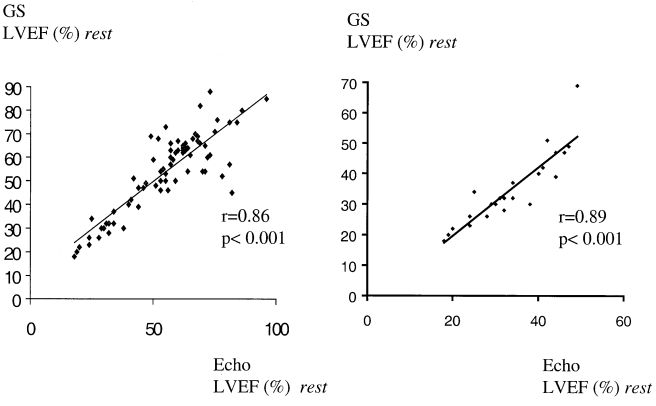

Fig. 4. Correlation between rest LVEF assessed by GS and rest LVEF assessed by echo. The *left panel* shows the correlation for all patients (*n*=79). The *right panel* shows the correlation for only those patients with an ejection fraction of <50% (*n*=23). (Same abbreviations as in Fig. 3)

Table 2. Correlation between ^{201}Tl GS LVEF and echo LVEF for different patient subgroups

	GS LVEF post stress	GS LVEF rest
Bicycle exercise (*n*=55)	*r*=0.68	*r*=0.85
Dipyridamole (*n*=17)	*r*=0.89	*r*=0.86
Males (*n*=47)	*r*=0.85 (*n*=41)	*r*=0.93 (*n*=47)
Females (*n*=32)	*r*=0.66 (*n*=31)	*r*=0.68 (*n*=32)
No WMAs[a]	–	*r*=0.82
Severe WMAs[b]	–	*r*=0.87
SSS >13 (*n*=11)	*r*=0.75	–
SRS ≥4 (*n*=25)	–	*r*=0.83

GS, Gated SPET; LVEF, left ventricular ejection fraction; SSS, summed stress score; SRS, summed rest score
[a]Score 0 or 1 in 1 segment
[b]Score 2 or 3 in ≥1 segment

(134.7±16 and 99.3±10.3, respectively; $P<0.001$), which may explain the weaker LVEF correlation after exercise.

Relationship between GS and echo LVEF in males versus females (Table 2). As further demonstrated, the correlation between GS LVEF and echo LVEF was weaker for women than for men.

Relationship between GS and echo LVEF in patients with severe perfusion defects (Table 2). The correlation between echo and GS LVEF was close in the case of severe stress perfusion defects (SSS>13), measured from stress images, as well as in the case of fixed perfusion defects, calculated from rest images (SRS>4).

Relation between GS and echo LVEF in patients with or without severe WMAs (Table 2). The correlation between echo and GS LVEF at rest was good for both patient groups, although it was particularly close in patients with severe regional WMAs.

Regional wall motion abnormalities

WMAs were identified by GS with a high overall sensitivity (28/29) and specificity (43/59) (96.5% and 84% respectively). Segmental sensitivity and specificity are displayed in Table 3: Sensitivity was particularly high for the apex and the anterolateral segment and lowest for the inferolateral segment. Specificity exceeded 90% in all but the inferoseptal segment. A case example of a patient with antero-apical akinesia is presented in Fig. 5.

Relationship between WMAs at rest and the pattern of perfusion defects. As shown by Fig. 6, the frequency of WMAs at rest GS was significantly and directly related to both the SSS, assessed from the stress perfusion image, and the SRS, characterizing fixed defects and determined from the rest image; however, the frequency of WMAs proved to be highest in regions with fixed perfusion defects. No significant linear relationship was found between frequency of WMAs at rest and reversible ischaemia, represented by the SDS: WMAs were observed in 37.7% (20/53) of patients with an SDS of <4, 54.5% (6/11) with an SDS of 4–8 and 37.5% (3/8) with an SDS of 9–13 (SDS<4 vs 9–13: NS).

Transient WMAs post stress for the detection of stunned myocardium (Table 4). "Stunning" was evaluated in all patients who underwent a stress followed by a rest ^{201}Tl GS perfusion study (n=72). By this approach, a certain time course of perfusion and function after stress could be observed, fitting the pattern of restored perfusion in conjunction with a transient contractile dysfunction that has been described for this special condition [23]: Nine out of 19 (47.4%) patients with severe reversible perfusion defects (SDS ≥4) showed severe hypokinesia (score

Table 3. Sensitivity and specificity of ^{201}Tl GS for the detection of regional WMAs (n=79)

Segments[a]	Sensitivity (%)	Specificity (%)	TP/TN/FP/FN
Anterior	94.1	93.5	16/58/4/1
Anterolateral	100	97	13/64/2/0
Inferolateral	88.2	95.2	15/59/3/2
Inferior	95.6	94.6	22/53/3/1
Inferoseptal	91.6	81.8	22/45/10/2
Anteroseptal	95.2	91.3	20/53/5/1
Infero-apical	100	98.5	13/65/1/0
Antero-apical	100	94.1	11/64/4/0

WMAs, Wall motion abnormalities; GS, gated SPET, TP, true-positive; TN, true-negative; FP, false-positive; FN, false-negative
[a]Apical, mid and basal region (except infero- and antero-apical) GS segments were adjusted to corresponding segments in echocardiography (see Materials and methods). Echo was used as the gold standard

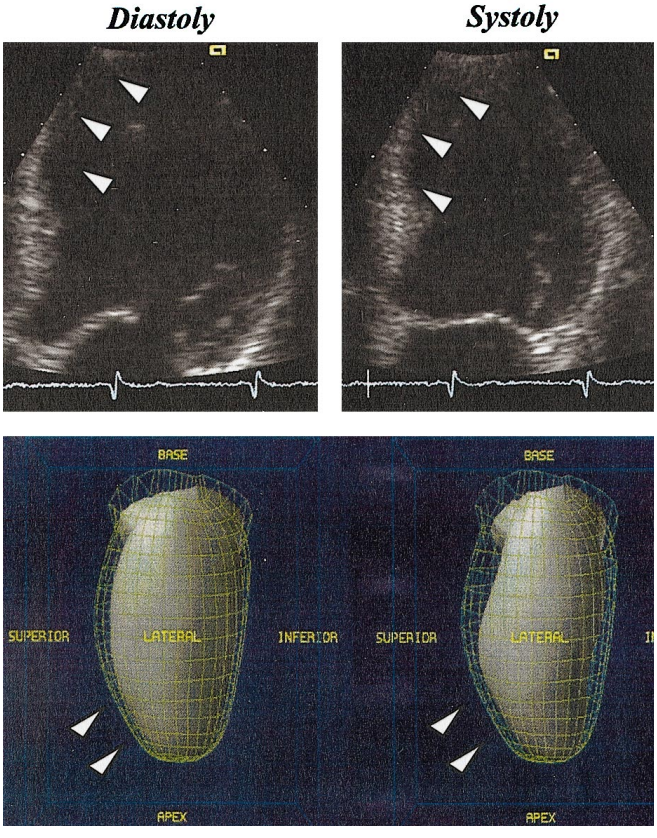

Fig. 5. Case example: Patient with akinesia of the antero-apical segment. No wall thickening is seen from diastole (*upper left panel*) to systole (*upper right panel*) in echo. There is no significant inward movement of the antero-apical segment from diastole (*lower left panel*) to end-systole (*lower right panel*) in 3D display of ^{201}Tl GS

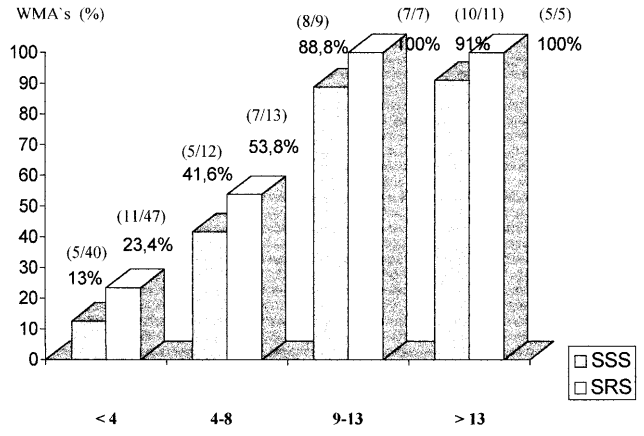

Fig. 6. Relationship between perfusion abnormalities at stress (SSS) and rest (SRS) and the frequency of WMAs on ^{201}Tl rest GS. Summed perfusion scores (SSS and SRS) are expressed on the x-axis, and the percentage of patients with WMAs on the y-axis. *SSS*, Summed stress score; *SRS*, summed rest score; *WMAs*, wall motion abnormalities. SSS: <4 vs 4–8 and 4–8 vs 9–13 and <4 vs >13*: P*<0.01. SRS: <4 vs 4–8 and 4–8 vs 9–13 and <4 vs >13: *P*<0.01. SRS and SSS: 9–13 vs >13: *P*=NS

Table 4. Stunned myocardium: transient WMAs poststress in patients with severe reversible perfusion defects (9/19; SDS≥4)

Post stress		Rest		SDS
WMAs[a,b]	LVEF (%)	WMAs[a]	LVEF (%)	
3	34	1	44	14
3	21	0	25	12
2	38	0	50	5
2	48	0	49	7
3	61	1	71	4
3	32	0	30	5
3	49	0	59	16
2	27	0	38	13
2	28	0	31	8
	Mean: 37.5±10.1		*Mean:* 44.1±11.6*	

SDS, Summed difference score; WMAs, wall motion abnormalities; GS, gated SPET; LVEF, left ventricular ejection fraction
**P*=0.3 vs post-stress LVEF
[a]Localization of post-stress WMAs: inferior/inferolateral (*n*=6), apical (*n*=2) and anterolateral (*n*=1)
[b]WMA score: 0 = normal; 1 = mild to moderate hypokinesia; 2 = severe hypokinesia; 3 = akinesia

≥2) at post-stress GS (within the area of the perfusion defect). In all nine patients (100%) WMAs improved by ≥2 points at rest, as shown in Table 4. In addition, global post-stress LVEF was lower than the rest LVEF in this group (Table 4).

Discussion

Validation of ^{201}Tl GS

The success rate of QGS, primarily designed for ^{99m}Tc-sestamibi GS [11], was 100% for post-stress and rest ^{201}Tl GS perfusion studies after a single tracer injection at the time of stress. The high accuracy for myocardial edge detection was based on the algorithm's features of not using thresholding and of employing a 3D model of the left ventricle [11]. Reliability of the algorithm in the presence of perfusion abnormalities was further confirmed by the good correlation obtained between GS and echo LVEF even when severe perfusion defects were present, in either the post-stress (SSS ≥13) or rest (SRS >4) images (Table 2). The visually assessed good quality of the GS images may also have been due to the fact that we used a longer acquisition time for ^{201}Tl GS than is commonly employed for ^{99m}Tc-sestamibi GS [11,19], and seems comparable to that reported for ^{99m}Tc-sestamibi GS [13,19]. We conclude that ^{201}Tl is as well suited as ^{99m}Tc-sestamibi for GS studies despite its lower photon energy.

Left ventricular function assessment

Few reports are available on ^{201}Tl GS in the literature. Those that have been published have compared LVEF [19] or WMAs [13] assessed by rest ^{201}Tl GS with the results of post-stress ^{99m}Tc-sestamibi GS, i.e. no technique other than post-stress ^{99m}Tc-sestamibi GS has been used for the validation of ^{201}Tl GS. Thus the aim of this study was to prove the value of ^{201}Tl GS by means of validation against echocardiography (echo), the most frequently used diagnostic technique in cardiac routine for the evaluation of ventricular function.

We obtained a good correlation between echo LVEF and GS LVEF both post stress and at rest; however, closer correlation was observed with GS LVEF at rest. This observation can be attributed to the following causes:

First, echo was performed immediately after completion of the rest GS study, whereas there was an interval of 2 h between post-stress GS and echo. As LVEF is easily influenced by changes in sympathovagal tone and autonomic nervous system stimulation [20,21], it is of importance that both methods for LVEF assessment be performed within as short an interval as possible.

The second reason for the better correlation between the rest GS LVEF and echo LVEF is that exactly the same condition applied for both measurements, i.e. a "real" rest state, whereas this was not completely true for GS LVEF obtained post stress, especially after bicycle exercise: The heart rate had not dropped to its baseline level 15 min after exercise, and contractility and thus LVEF still remained physiologically increased. This phenomenon, however, is less likely to occur after pharma-

cological stress, owing to a smaller increase in heart rate [22]; thus LVEF after pharmacological stress is more similar to rest LVEF. This could also be demonstrated in this study by the good correlation obtained between echo and GS post-stress LVEF after dipyridamole, along with the weaker correlation after exercise (Table 2).

Another bias may be produced by "stunning" in severely ischaemic patients [23]; this has to be taken into account when comparing post-stress with rest LVEF, as the post-stress LVEF may be decreased and thus lower than LVEF at rest.

Of note was the particularly close correlation between LVEFs assessed by GS and echo in patients with reduced global left ventricular function (Figs. 3 and 4, right panels). Normal LVEFs (>50%), however, showed marked scatter in our study, with a slight tendency towards overestimation. This may have been due to worse resolution and a higher rate of scatter in ^{201}Tl images as compared with ^{99m}Tc-sestamibi images [11], which may lead to "disappearance" of the ventricular cavity in end-systole, especially in hyperkinetic or very small ventricles, as mentioned previously [13,19]. Myocardial walls have been reported to appear thicker and the cavity smaller with ^{201}Tl GS as compared with ^{99m}Tc-sestamibi GS [19]. As the detection of compromised left ventricular function has a greater clinical impact than whether a "normal" LVEF produces a particular value of 60% or 80%, this inaccuracy may be neglected. Since females tend to have smaller hearts in general, the aforementioned factors may also have contributed to the weaker correlation between GS and echo LVEF for women in this study. Similar results have been reported previously [19]. It should be mentioned in this context that, owing to geometric proportions, echo LVEF measurements may be more difficult to perform in women.

Regional WMAs

High segmental agreement between WMAs detected by ^{201}Tl and ^{99m}Tc-sestamibi GS has been reported previously [13]. To our knowledge, no study has attempted to define the clinical value of assessment of WMAs with ^{201}Tl GS by comparing this method with echo, which can be regarded as the gold standard for regional wall motion assessment in clinical routine [24,25]. Our results clearly demonstrate that identification of regional WMAs by ^{201}Tl GS is possible with high sensitivity (88%–100%) and specificity (82%–98%).

Correlation of WMAs at rest with SSS and SRS. It is demonstrated by Fig. 6 that particularly patients with fixed perfusion defects after prior myocardial infarction, characterized by a high SRS, presented with a high percentage of WMAs in these areas, i.e. every single patient with an SRS of more than 9 in our study showed WMAs in the underperfused regions. The slightly lower percentage of WMAs in patients with a high SSS, compared to the percentage with a high SRS, can be explained by the fact that some of the defects contributing to the initial SSS on the stress images showed reversibility over the course of time. Reversible perfusion defects, however, do not generally produce WMAs, except for the special condition of "stunning".

Stunned myocardium: detection of a specific time pattern of perfusion and function by ^{201}Tl GS? "Stunning" has been characterized as a reversible contractile dysfunction despite restored blood flow [23], this dysfunction leading to transient WMAs after stress (with a duration ranging from 30 min to 2 h) [23]. The mechanisms responsible for this phenomenon, however, are not entirely known. Hypotheses are based on the assumption of damage caused by free radicals during reperfusion, and the loss of sensitivity of contractile filaments to Ca^{2+}[23]. The possible contribution of GS with ^{99m}Tc-sestamibi in the assessment of viability is controversial [4,26], and the role of ^{201}Tl GS is unknown, having been assessed in only a single case report [27]. As we performed GS with ^{201}Tl at two different times, i.e. post stress and at rest, in the same patient, we had a unique opportunity to assess myocardial "stunning".

Transient WMAs after stress, which improved or resolved completely at rest, were detected in half of the patients (47%) with severe reversible ischaemia. We therefore concluded that ^{201}Tl GS is able to contribute to the detection of stunned myocardium by demonstrating a characteristic time pattern of perfusion and regional function post stress and at rest in a subgroup of patients with severe reversible perfusion defects. We further proved that "stunning" may impair not only regional, but also global function after stress (Table 4). These observations are consistent with the theoretical concept established for "stunning" [23], and confirm a recent, preliminary report on viability assessment with ^{99m}Tc-sestamibi GS [4]. Thus, nuclear testing with ^{201}Tl GS seems to be an appropriate and very promising approach with which to tackle the problem of viability.

WMA and LVEF assessment at post stress or at rest?

We conclude that both assessments at post stress and at rest yield important but slightly different information. In patients with prior myocardial infarction, WMAs in regions with fixed perfusion defects, as well as LVEF, should be determined in order to obtain information on the remaining regional and global function, and therefore on prognosis. This information, however, may be extracted from a single rest GS study. In addition, rest images facilitate differentiation between artefact and scar, thus reducing the number of false-positives. For the detection of stunned myocardium, however, a combined post-stress and rest study is preferable, owing to the characteristic pattern observed in this condition.

Conclusion

GS with ^{201}Tl is easy to perform and is a reliable tool for the assessment of LVEF and regional WMAs. The diagnosis and prognostic stratification of patients with CAD can be improved by the additional information obtained on LVEF and regional WMAs during ^{201}Tl myocardial perfusion studies.

The assessment of WMAs by a combined post-stress and rest GS study with ^{201}Tl seems to be a suitable method for the detection of viable myocardium. However, larger studies are required to support this hypothesis.

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