

Prognostic Significance of Dipyridamole-Induced ST Depression in Patients with Normal ^{82}Rb PET Myocardial Perfusion Imaging

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Recent studies have shown that vasodilator-induced ischemic electrocardiographic (ECG) changes have incremental prognostic value over normal SPECT myocardial perfusion imaging (MPI) and identify patients at higher risk for cardiac events. The prognostic value of vasodilator-induced ischemic ECG changes in the setting of normal PET MPI has yet to be determined. We sought to determine the prognostic importance of dipyridamole-induced ischemic ECG changes in patients with normal ^{82}Rb PET myocardial perfusion images. **Methods:** Between 2000 and 2003, 2,029 consecutive patients undergoing dipyridamole stress ^{82}Rb PET at the University of Ottawa Heart Institute were evaluated. Patients with normal PET MPI and interpretable ECGs were enrolled. Electrocardiograms were assessed for ST depression or elevation and patients were categorized into those with and without dipyridamole-induced ischemic ECG changes. Images were graded using the 17-segment model. Follow-up information was obtained by telephone interview, from hospital records, or from treating physicians. All cardiac events (cardiac death, nonfatal myocardial infarction [MI], percutaneous coronary intervention, coronary artery bypass grafting, or angiography) were verified with hospital records. **Results:** Of the 629 enrolled patients with normal PET MPI, 72 patients had dipyridamole-induced ischemic ECG changes. There was no significant difference between the 2 groups in the combined endpoint (cardiac death, nonfatal MI, and revascularization) at follow-up (mean \pm SD, 27.1 ± 13 mo). There were no cardiac deaths in either group. One (1.4%) patient with ischemic ECG changes had a nonfatal MI (0.6% annual event rate). Two (2.8%) patients with ischemic ECG changes required revascularization compared with 11 (2.0%) in the nonischemic ECG group. **Conclusion:** Normal ^{82}Rb PET confers an excellent prognosis regardless of dipyridamole-induced ST depression.

Key Words: PET; dipyridamole; electrocardiogram; prognosis

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Dipyridamole- or adenosine-induced ischemic electrocardiographic (ECG) changes are specific for severe coronary artery disease (CAD) and predict adverse cardiac events (1–6). Previous studies have shown that normal SPECT myocardial perfusion imaging (MPI) confers an excellent prognosis with an annual cardiac event rate of $<1\%$ (7,8). However, 2 recent studies have demonstrated that patients with normal SPECT MPI but with vasodilator-induced ST depression have significantly increased cardiac events (9,10).

PET has very good diagnostic sensitivity and specificity (89% and 86%, respectively) for CAD (8) and may identify patients with abnormal perfusion not visually present with $^{99\text{m}}\text{Tc}$ SPECT MPI (11). It is unknown whether dipyridamole-induced ischemic ECG changes have incremental prognostic value in patients with normal ^{82}Rb PET MPI.

MATERIALS AND METHODS

Study Population

Reports of all consecutive patients at the University of Ottawa Heart Institute undergoing clinical dipyridamole stress ^{82}Rb PET MPI between January 2000 and September 2003 were reviewed. Patients over the age of 18 y and with “normal” ^{82}Rb PET MPI (as interpreted by a nuclear cardiologist) were eligible for inclusion. All eligible patients had their perfusion images reviewed by 2 experienced observers who were unaware of clinical data. Patients were enrolled if both observers agreed that the MPI was qualitatively normal. Disagreements in MPI interpretation were resolved by consensus.

Enrolled patients had their rest and stress ECGs reviewed by the same expert observers. Patients were excluded if the PET MPI was abnormal or if there was ECG evidence of a Wolf-Parkinson White pattern, a left bundle branch block, or a ventricular paced rhythm. For patients with more than one PET study, the date of the first normal dipyridamole ^{82}Rb PET MPI was used.

All patients gave informed consent to participate and the protocol was approved by the University of Ottawa Heart Human Research Ethics Board.

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Dipyridamole Stress ^{82}Rb PET

Rest Image Acquisition. Patients abstained from caffeine, xanthine derivatives, and atrioventricular nodal blocking drugs for ≥ 12 h and fasted (except for medications) for ≥ 6 h before the study. Each patient was positioned in the Siemens/CTI ECAT ART whole-body scanner equipped with 24 detector rings, allowing the acquisition of 47 contiguous transaxial slices (12). A 4-min ^{137}Cs transmission scan was acquired to confirm proper patient positioning and for attenuation correction (13,14). After the transmission scan, 5–15 MBq/kg of ^{82}Rb were infused over 30 s at rest followed by saline flush (1 min) using a custom infusion system (15). Approximately 2.5 min after tracer infusion, a static emission scan was acquired for 7.5 min.

Dipyridamole Stress Image Acquisition. Dipyridamole was administered intravenously (0.14 mg/kg/min for 5 min). Eight minutes after initiation of dipyridamole infusion, 5–15 MBq/kg ^{82}Rb were administered and static uptake images were acquired as described. Aminophylline (2 mg/kg) was infused 12 min after initiation of dipyridamole infusion. After dipyridamole stress imaging, a 4-min transmission scan was acquired for attenuation correction of the stress data (16).

Transaxial images were reconstructed using filtered back-projection with an 18-mm Hann window of the ramp filter, then reoriented into short-axis sections, and displayed in a standard format (8).

Image Interpretation

All PET images were reviewed by 2 experienced observers. Visual analysis of myocardial perfusion used a 17-segment model and a 5-point grading system (0 = normal radiotracer uptake, 1 = mildly reduced, 2 = moderately reduced, 3 = severely reduced, and 4 = absence of radiotracer uptake) (17). The sum stress score (SSS), sum rest score (SRS), and sum difference score (SDS) were calculated.

ECG Interpretation

All ECGs were interpreted using the recommended criteria from the American College of Cardiology and American Heart Association practice guidelines for exercise testing (18). Ischemic ST depression was defined as horizontal or downsloping ST depression of ≥ 1.0 mm at the J point that was sustained for 80 ms or upsloping ST depression of ≥ 1.5 mm at 80 ms beyond the J point. ST elevation was present if ≥ 1.0 mm was present at the J point and was sustained for ≥ 60 ms. Disagreements were resolved by consensus.

Patient Follow-Up

Patient follow-up was performed through telephone interviews, hospital records, local death records, and referring physicians. Information collected included cardiac death, nonfatal myocardial infarction (MI), revascularization (coronary artery bypass grafting [CABG], and percutaneous coronary intervention [PCI]), and coronary angiography. All data were confirmed with hospital records.

Statistical Analysis

Continuous measures are presented as mean \pm SD. The Wilcoxon signed rank test was used to test univariate relationships between continuous measures and ECG groups. Categorical measures are presented as counts with percentages. The Fisher exact test was used to test univariate relationships between categorical measures and ECG groups. Survival estimates were described with Kaplan–Meier curves and compared with the log-rank test. All

tests used $P < 0.05$ for the critical value of statistical significance. Analyses were performed using SAS version 8.02.

RESULTS

Between January 2000 and September 2003, 2,029 patients had dipyridamole stress ^{82}Rb PET MPI at the University of Ottawa Heart Institute. A total of 93 patients were excluded for a left bundle branch block or paced rhythm (90 patients), age < 18 y (2 patients), and a Wolf–Parkinson–White pattern (1 patient). Of the remaining 1,936 patients, 694 had a normal myocardial perfusion scan, of which 74 patients had ischemic ECG changes and 620 patients did not. Total follow-up was 90.6% with 65 patients refusing the study or lacking follow-up information. Thus, the study was comprised of 629 patients (with follow-up data): 72 (11.4%) patients had ischemic ECG changes and 557 patients had no ischemic ECG changes. Two of 65 patients without follow-up data had ischemic ECG changes and the remaining 63 patients had no ischemic ECG changes.

The baseline characteristics of the patients with and without dipyridamole-induced ischemic ECG changes were compared (Table 1). Dipyridamole-induced ECG changes were more commonly seen in women (83% and 70%; $P < 0.03$) but there was no significant difference in the other baseline characteristics.

Rest and Dipyridamole Stress ^{82}Rb PET

Patients with ischemic ECGs had higher heart rates and blood pressures at rest and with stress (Table 2). However,

TABLE 1
Patient Demographics

Characteristic	Ischemic ECG (n = 72)	Nonischemic ECG (n = 557)	P value
Age (y)	61 \pm 11	59 \pm 11	NS
Female	60 (83)	391 (70)	<0.03
BMI (kg/m ²)	27 \pm 5	29 \pm 7	NS
Cardiac risk factors			
Smoker	7 (10)	89 (16)	NS
Hypertension	44 (61)	276 (50)	NS
Diabetes	14 (20)	71 (13)	NS
Dyslipidemia	42 (58)	307 (55)	NS
Family history of CAD	35 (49)	265 (48)	NS
Cardiac medications			
Aspirin	37 (52)	247 (44)	NS
β -Blocker	25 (35)	179 (32)	NS
HMG-CoA reductase	34 (49)	212 (38)	NS
ACE-I	21 (30)	132 (24)	NS
Past medical history			
MI	7 (10)	52 (9)	NS
PCI	6 (8)	70 (13)	NS
CABG	2 (3)	18 (3)	NS
Coronary angiography	25 (35)	134 (24)	NS

NS = not significant; BMI = body mass index; HMG-CoA reductase = statin; ACE-I = angiotensin-converting enzyme inhibitor. Values in parentheses are percentages.

TABLE 2
Rest and Dipyridamole Stress ^{82}Rb PET in Patients With and Without Ischemic ECG Changes

Parameter	Ischemic ECG (<i>n</i> = 72)	Nonischemic ECG (<i>n</i> = 557)	<i>P</i> value
Resting heart rate (bpm)	73 ± 13	66 ± 11	<0.001
Resting blood pressure (mm Hg)			
Systolic	147 ± 20	140 ± 22	0.01
Diastolic	79 ± 11	76 ± 13	0.01
Peak stress heart rate (bpm)	99 ± 16	85 ± 14	<0.001
Peak stress blood pressure (mm Hg)			
Systolic	150 ± 24	138 ± 22	<0.001
Diastolic	78 ± 20	73 ± 14	NS
Rate × pressure product			
Rest	10,717 ± 2,545	9,278 ± 2,246	<0.001
Stress	14,916 ± 3,564	11,722 ± 2,774	<0.001
Persantine-induced chest pain*	39 (54)	230 (41)	<0.05
Stress ECG			
ST depression*	72 (100)	0	<0.001
Leads with ST depression	3.6 ± 1.9	0	<0.001
Maximum ST depression (mm)	1.3 ± 0.4	0	<0.001
MPI			
SSS	0.15 ± 0.53	0.19 ± 0.49	NS
SRS	0.32 ± 0.73	0.7 ± 1.58	<0.03
SDS	0.10 ± 0.31	0.07 ± 0.23	NS

*Values in parentheses are percentages.
bpm = beats per minute; NS = not significant.

there was no significant difference in the SSS, SRS, and SDS between the 2 groups (Table 2). All patients with dipyridamole-induced ischemic ECG changes had horizontal or downsloping ST depression. None of the patients had abnormal upsloping ST depression, ST elevation, or arrhythmia with dipyridamole stress. Of the 72 patients with dipyridamole-induced ST depression, 29 (40%) patients had ST depression of 1.0 mm, 34 (47%) patients had ST depression of 1.1–1.9 mm, and 9 (13%) patients had ST depression of ≥2.0 mm. Fifty-seven (79%) patients had ST depression in multiple leads.

Cardiac Events

During the mean follow-up duration of 27.1 ± 13.0 mo, there were no cardiac deaths and only 1 nonfatal MI. The total event rate for cardiac death and nonfatal MI in our patient population (normal ^{82}Rb PET MPI) was 0.2%. There was no significant difference in the incidence of cardiac death, nonfatal MI, revascularization, or coronary angiography between the 2 groups (Table 3). In the ischemic ECG group, 1 (1.4%) patient had a nonfatal MI and 2 (2.8%) patients required revascularization. In the nonischemic ECG group, there were no cardiac deaths or nonfatal MIs. Eleven

TABLE 3
Cardiac Events

Parameter	Ischemic ECG (<i>n</i> = 72)	Nonischemic ECG (<i>n</i> = 557)	<i>P</i> value
Mean follow-up (mo)	26.3 ± 11.0	27.2 ± 13.3	NS
Cardiac death	0	0	NS
Nonfatal MI	1 (1.4)	0	NS
Revascularization	2 (2.8)	11 (2.0)	NS
PCI	1 (1.4)	8 (1.4)	NS
CABG	1 (1.4)	3 (0.5)	NS
Coronary angiography	3 (4.2)	22 (4.0)	NS
Cardiac death and nonfatal MI	1 (1.4)	0	NS
Cardiac death, nonfatal MI, or revascularization	3 (4.2)	11 (2.0)	NS

NS = not significant.
Values in parentheses are percentages.

(2.0%) patients required revascularization. There was no significant difference in the composite endpoint (cardiac death, nonfatal MI, and revascularization) between the 2 groups (4.2% and 2.0%; $P = \text{NS}$) (Fig. 1). Patients with ischemic ECG changes had an annual event rate of 0.6% for cardiac death and nonfatal MI and 1.9% annual event rate for cardiac death, nonfatal MI, and revascularization. Cardiac events in the ischemic ECG group were not predicted by the severity of ST depression or the number of leads with ST depression.

DISCUSSION

These data demonstrate that normal ^{82}Rb PET MPI portends a good prognosis irrespective of dipyridamole-induced ECG changes. Patients with dipyridamole-induced ischemic ECG changes and a normal ^{82}Rb PET MPI have a low annual event rate for cardiac death, nonfatal MI, or revascularization.

Exercise-induced ST depression has a specificity of 77% for significant CAD (19). Clinicians often disregard exercise-induced ST depression if SPECT MPI is normal. However, it has been demonstrated that vasodilator-induced ST depression is 91% specific for reversible perfusion defects (6). Until recently, the clinical significance of vasodilator-induced ST depression and normal SPECT MPI was unclear.

Overall, patients with normal SPECT MPI have an annual mortality rate of <1% (7,20–22). Patients with normal adenosine SPECT have a slightly higher annual cardiac event rate (0.7%) compared with those patients undergoing exercise stress (0.4%) (7). However, patients with normal SPECT MPI but with vasodilator-induced ST depression had an approximately 5% annual rate for cardiac death and nonfatal MI (9). A similar study by Abbott et al. confirmed a high cardiac death and nonfatal MI rate in patients with ischemic ECGs (10.6%) compared with controls (1.5%) at 29 ± 12 mo follow-up (10). In the same study, the cardiac

death, nonfatal MI, and revascularization rate was 24.2% compared with 4.0% in the control group.

Our study demonstrates patients with normal ^{82}Rb PET have good prognosis regardless of ECG changes. Studies evaluating the overall prognostic value of PET are limited. Marwick et al. noted that defect severity with PET was related to outcome (23). Preliminary data from our group support these findings (24). The current study extends these observations to the ECG changes in a population of patients with normal PET perfusion. The incremental value of the ECG observed in SPECT studies is not observed with negative (or “low-risk”) PET MPI.

Dipyridamole-Induced ST Depression

The enrollment of patients with “false-positive” vasodilator-induced ST depression may dilute the “true-positive” patients at higher risk for cardiac events. A higher incidence of false-positive stress-induced ECG changes may occur in women and in patients with hypertension.

It is accepted that women are more likely to have false-positive ST depression with exercise stress. Our results and those of Klodas et al. suggest that women were more likely to develop dipyridamole-induced ECG changes (9). The mechanism by which exercise induces ST depression in women is unknown but may be due to a greater catecholamine release (25), hormonal differences, or microvascular dysfunction (26). A similar mechanism with vasodilator stress may increase the prevalence of false-positive ST depression in women.

Our patients with ischemic ECG changes had higher heart rates and blood pressure at rest and with stress (Table 2). It has been hypothesized that heart rate, hypertension, and left ventricular hypertrophy may play a role in vasodilator-induced ECG changes (10,27–29). These findings may also account for false-positive ST depression.

Comparison with Previous Studies Using SPECT MPI

Klodas et al. (9) and Abbott et al. (10) have each performed similar studies with SPECT MPI. Both groups demonstrated that vasodilator-induced ischemic ECG changes had incremental prognostic value over normal SPECT MPI. In spite of our patient population being similar to those of these previous studies (Table 4), our event rates appear much lower (Table 5).

The difference between our study and the previous SPECT studies may be attributable to the overall improved sensitivity of PET (8). Go et al. have previously demonstrated that ^{82}Rb PET is more sensitive than ^{201}Tl SPECT (93% and 76%) for the detection of CAD (11). Another possible explanation is that PET may have accuracy superior to that of $^{99\text{m}}\text{Tc}$ SPECT in patients with small hearts. It has been previously demonstrated that the diagnostic accuracy of SPECT may be reduced in women and in patients with small hearts due to γ -camera resolution (30,31). Our study, as well as those of Klodas et al. (9) and Abbott et al. (10), demonstrated that ischemic ECGs and normal MPI occurred more commonly in women. In our study, an anal-

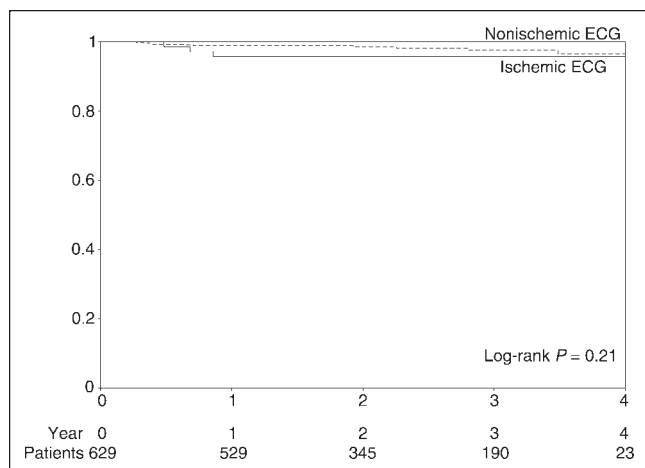


FIGURE 1. Kaplan-Meier survival curve for cardiac death, nonfatal MI, and revascularization.

TABLE 4
Baseline Characteristics of Patients with
Vasodilator-Induced ST Depression

	Chow et al. (this study)	Klodos et al. (9)	Abbott et al. (10)
Vasodilator-induced ST depression	PET (n = 72)	SPECT (n = 49)	SPECT (n = 66)
Age (y)	61 ± 11.0	67 ± 10	64.8 ± 15.3
Female (%)	83	88	82
β-Blocker (%)	35	24	
CAD (%)	30		30
MI (%)	10	2.0	
Revascularization (%)	9.7	10.2	
Dyslipidemia (%)	58	55	42
Hypertension (%)	61	57	77
Diabetes (%)	20	14	32
Smoker (%)	10	33	29

ysis of body mass index was performed and no significant difference was found between the 2 groups. However, further analysis revealed that our patients with ischemic ECGs had a smaller mean body surface area (1.8 ± 0.2 vs. 1.9 ± 0.3 m²; $P < 0.01$) and were shorter (162.2 ± 8.3 vs. 166.0 ± 10.0 cm; $P < 0.01$). The results of the current study may suggest that the diagnostic accuracy in patients with small hearts is maintained by PET.

The higher cardiac event rates seen in patients with vasodilator-induced ST depression and normal SPECT MPI may be attributable to triple-vessel disease or balanced ischemia. However, in our study, all 3 patients with ischemic ECG changes and cardiac events underwent coronary angiography and only 1 patient (with previous CABG) had significant triple-vessel disease.

Limitations

This was a single-center retrospective study and was subject to selection bias. The 2 previous SPECT studies by Klodos et al. (9) and Abbott et al. (10) were also retrospective studies of similar design and would potentially have been subject to similar bias.

It is difficult to make direct comparisons between our study and the 2 previous SPECT studies because there may be significant differences in patient populations. Studies have demonstrated that patients undergoing pharmacologic stress have a higher mortality than those who undergo exercise stress MPI (7). Previous vasodilator SPECT MPI studies may have enrolled higher risk patients because lower risk patients underwent exercise stress SPECT MPI.

Since all PET patients underwent dipyridamole stress (without the option of exercise stress), it is possible that our PET population was of lower risk than those in the vasodilator SPECT studies. We do not believe that this is the case. At our institution, PET patients are almost exclusively referred by cardiologists, who typically see a higher risk patient population. It is also possible that PET MPI was performed in patients with an “equivocal” SPECT MPI. Women with a breast attenuation artifact on SPECT were referred for PET, thus accounting for the higher prevalence of women with normal PET MPI. Our population, compared with that of the 2 previous SPECT studies, shared a similar prevalence of CAD, MI, and revascularization.

Our sample size, though larger than that of similar previous SPECT studies, was small and was not adequately powered to assess a statistically significant difference between the 2 groups. Our event rate in the ischemic ECG group was very small and no definitive conclusions can be made regarding the effects of hypertension or sex. However, we can conclude that normal PET (regardless of ECG changes) confers a good prognosis.

The annual rate for cardiac death, nonfatal MI, and revascularization in patients with ischemic ECGs (1.9%) appears higher than that of patients without ECG changes (0.9%), but this difference was not statistically significant. There were very few cardiac deaths and nonfatal MIs in our study, but it is possible that a difference does exist between the 2 groups. To detect a statistically significant difference between the 2 groups, a sample size of >4,000 patients (with normal MPI and interpretable ECGs) would be required. On the basis of our results, 11,350 patients would have to undergo dipyridamole ⁸²Rb PET MPI before normal PET MPI could be achieved in 4,000 patients.

Sixty-five (9.4%) patients refused to participate in the study or were lost to follow-up. The baseline characteristics of the patients without follow-up were compared with those with follow-up information (Tables 6 and 7). Patients without follow-up were younger, more commonly men, and less likely to be dyslipidemic.

Although 9.4% of patients refused or were lost to follow-up, we were able to obtain follow-up in 97.3% of patients with ischemic ECG changes; therefore, we do not believe that we have significantly underestimated the risk in this population. Follow-up in the nonischemic ECG group was lower (88.7%) and could result in either an underestimation or an overestimation of the true cardiac event rate. Marwick et al. studied the incremental value of ⁸²Rb PET and deter-

TABLE 5
Cardiac Events in Patients with Vasodilator-Induced ST Depression and Normal MPI

Annual event rate	Chow et al. (this study) PET	Klodos et al. (9) SPECT	Abbott et al. (10) SPECT
Cardiac death and nonfatal MI (%)	0.6	5	4.0
Cardiac death, nonfatal MI, and revascularization (%)	1.9	9	7.0

TABLE 6
Patient Demographics: Patients Lost to Follow-Up or Refused to Participate in Study

Characteristic	Patients with follow-up (n = 629)	Patients without follow-up (n = 65)	P value
Age (y)	59 ± 11	56 ± 12	<0.03
Female	451 (72)	38 (58)	<0.05
BMI (kg/m ²)	29 ± 7	29 ± 7	NS
Cardiac risk factors			
Smoker	96 (15)	8 (12)	NS
Hypertension	320 (51)	27 (42)	NS
Diabetes	85 (14)	12 (18)	NS
Dyslipidemia	349 (56)	25 (38)	<0.03
Family history of CAD	300 (48)	27 (42)	NS
Cardiac medications			
Aspirin	284 (45)	27 (42)	NS
β-Blocker	204 (33)	20 (31)	NS
HMG-CoA reductase	247 (39)	18 (28)	NS
ACE-I	153 (24)	9 (14)	NS
Past medical history			
MI	59 (9)	8 (12)	NS
PCI	76 (12)	5 (8)	NS
CABG	20 (3)	1 (2)	NS
Coronary angiography	159 (25)	16 (25)	NS

BMI = body mass index; NS = not significant; HMG-CoA reductase = statin; ACE-I = angiotensin-converting enzyme inhibitor. Values in parentheses are percentages.

mined that normal ⁸²Rb PET had an annual mortality rate of 0.9% (24). This mortality rate in Marwick's study was higher than that of our study and, since each event was confirmed with hospital records, we do not believe that the cardiac events have been overestimated. If our study has underestimated the cardiac events in the nonischemic ECG group, the difference in cardiac event rates between the

ischemic and nonischemic ECG groups would have been smaller and less significant.

Our study population did not undergo SPECT MPI but we did compare our patient population with the patient population of the 2 previous SPECT studies (9,10) and they appeared similar. Though the results are hypothesis generating, this study raises that possibility of PET MPI being

TABLE 7
Rest and Dipyridamole Stress ⁸²Rb PET in Patients With and Without Follow-Up

Parameter	Patients with follow-up (n = 629)	Patients without follow-up (n = 65)	P value
Resting heart rate (bpm)	67 ± 12	68 ± 12	NS
Resting blood pressure (mm Hg)			
Systolic	141 ± 22	144 ± 24	NS
Diastolic	76 ± 13	78 ± 12	NS
Peak stress heart rate (bpm)	86 ± 15	85 ± 15	NS
Peak stress blood pressure (mm Hg)			
Systolic	140 ± 23	141 ± 24	NS
Diastolic	73 ± 15	74 ± 12	NS
Rate · pressure product			
Rest	9,443 ± 2,325	9,749 ± 2,219	NS
Stress	12,087 ± 3,047	11,926 ± 2,688	NS
Dipyridamole-induced chest pain*	269 (43)	23 (35)	NS
MPI			
SSS	0.19 ± 0.49	0.22 ± 0.46	NS
SRS	0.65 ± 1.50	0.72 ± 1.20	NS
SDS	0.08 ± 0.24	0.05 ± 0.19	NS

*Values in parentheses are percentages.
bpm = beats per minute; NS = not significant.

used to further risk stratify patients with normal SPECT but with vasodilator-induced ST depression (Table 4). Future studies are required to confirm our findings. A prospective study enrolling patients with vasodilator-induced ST depression and normal ^{99m}Tc SPECT MPI who undergo further risk stratification with ^{82}Rb PET may confirm our results.

CONCLUSION

The excellent prognosis of normal ^{82}Rb PET is maintained regardless of dipyridamole-induced ST depression.

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REFERENCES

- Hendel RC, Whitfield SS, Villegas BJ, Cutler BS, Leppo JA. Prediction of late cardiac events by dipyridamole thallium imaging in patients undergoing elective vascular surgery. *Am J Cardiol.* 1992;70:1243–1249.
- Lette J, Bertrand C, Gossard D, et al. Long-term risk stratification with dipyridamole imaging. *Am Heart J.* 1995;129:880–886.
- Iskandrian AS, Heo J, Lemlek J, et al. Identification of high-risk patients with left main and three-vessel coronary artery disease by adenosine-single photon emission computed tomographic thallium imaging. *Am Heart J.* 1993;125:1130–1135.
- Hart CYT, Miller TD, Hodge DO, Gibbons RJ. Specificity of the stress electrocardiogram during adenosine myocardial perfusion imaging in patients taking digoxin. *Am Heart J.* 2000;140:937–940.
- Ho KT, Miller TD, Christian TF, Hodge DO, Gibbons RJ. Prediction of severe coronary artery disease and long-term outcome in patients undergoing vasodilator SPECT. *J Nucl Cardiol.* 2001;8:438–444.
- Marshall ES, Raichlen JS, Kim SM, et al. Prognostic significance of ST-segment depression during adenosine perfusion imaging. *Am Heart J.* 1995;130:58–66.
- Hachamovitch R, Hayes S, Friedman JD, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: what is the warranty period of a normal scan? *J Am Coll Cardiol.* 2003;41:1329–1340.
- Klocke FJ, Baird MG, Lorell BH, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging: executive summary. *J Am Coll Cardiol.* 2003;42:1318–1333.
- Klodos E, Miller TD, Christian TF, Hodge DO, Gibbons RJ. Prognostic significance of ischemic electrocardiographic changes during vasodilator stress testing in patients with normal SPECT images. *J Nucl Cardiol.* 2003;10:4–8.
- Abbott B, Afshar M, Berger A, Wackers F. Prognostic significance of ischemic electrocardiographic changes during adenosine infusion in patients with normal myocardial perfusion imaging. *J Nucl Cardiol.* 2003;10:9–16.
- Go RT, Marwick TH, MacIntyre WJ, et al. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the diagnosis of coronary artery disease. *J Nucl Med.* 1990;31:1899–1905.
- Bailey DL, Young H, Bloomfield PM, et al. ECAT ART: a continuously rotating PET camera—performance characteristics, initial clinical studies, and installation consideration in a nuclear medicine department. *Eur J Nucl Med.* 1997;24:6–15.
- Xu EZ, Mullani NA, Gould KL, Anderson WL. A segmented attenuation correction for PET. *J Nucl Med.* 1991;32:161–165.
- deKemp RA, Jones WF, Nahmias C, Beanlands RS. Design and performance of 3D single photon transmission measurement on a positron tomograph with continuously rotating detectors. In: Grangeat P, Amans JL, eds. *Three-Dimensional Image Reconstruction in Radiology and Nuclear Medicine. Part 4: PET Quantitation and Reconstruction.* Dordrecht, The Netherlands: Kluwer Academic Publishers; 1996:245–254.
- Epstein J, Benelfassi A, Beanlands RSB, deKemp RAR. A ^{82}Rb infusion system for quantitative perfusion imaging with 3D PET. *Appl Radiat Isot.* 2004;60:921–927.
- Watson CC, Schaefer A, Luk WK, Kirsch CM. Clinical evaluation of single-photon attenuation correction for 3D whole-body PET. *IEEE Trans Nucl Sci.* 1999;46:1024–1031.
- Hachamovitch R, Berman DS, Shaw LJ, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. *Circulation.* 1998;97:535–543.
- Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation.* 2001;104:1694–1740.
- Gianrossi R, Detrano R, Mulvihill D, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease: a meta-analysis. *Circulation.* 1989;80:87–98.
- Gibbons RJ, Hodge DO, Berman DS, et al. Long-term outcome of patients with intermediate-risk exercise electrocardiograms who do not have myocardial perfusion defects on radionuclide imaging. *Circulation.* 1999;100:2140–2145.
- Galassi AR, Azzarelli S, Tomaselli A, et al. Incremental prognostic value of technetium-99m-tetrofosmin exercise myocardial perfusion imaging for predicting outcomes in patients with suspected or known coronary artery disease. *Am J Cardiol.* 2001;88:101–106.
- Vanzetto G, Ormezzano O, Fagret D, Comet M, Denis B, Machecourt J. Long-term additive prognostic value of thallium-201 myocardial perfusion imaging over clinical and exercise stress test in low to intermediate risk patients: study in 1137 patients with 6-year follow-up. *Circulation.* 1999;100:1521–1527.
- Marwick TH, Shan K, Patel S, Go RT, Lauer MS. Incremental value of rubidium-82 positron emission tomography for prognostic assessment of known or suspected coronary artery disease. *Am J Cardiol.* 1997;80:865–870.
- Yoshinaga K, Chow BJW, deKemp R, et al. Prognostic value of rubidium-82 perfusion positron emission tomography: preliminary results from the consecutive 153 patients [abstract]. *J Am Coll Cardiol.* 2004;43(suppl A):338A.
- Clark PI, Glasser SP, Lyman GH, Krug-Fite J, Root A. Relation of results of exercise stress tests in young women to phases of the menstrual cycle. *Am J Cardiol.* 1988;61:197–199.
- Gibbons RJ, Balady GJ, Bricker TJ, et al. ACC/AHA 2002 guideline update for exercise testing: summary article—A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *J Am Coll Cardiol.* 2002;40:1531–1540.
- Marshall ES, Raichlen JS, Tighe DA, Paul JJ, Breuninger KM, Chung E. ST-segment depression during adenosine infusion as a predictor of myocardial ischemia. *Am Heart J.* 1994;127:305–311.
- Villanueva FS, Smith WH, Watson DD, Beller GA. ST-segment depression during dipyridamole infusion, and its clinical, scintigraphic and hemodynamic correlates. *Am J Cardiol.* 1992;69:445–448.
- Chambers CE, Brown KA. Dipyridamole-induced ST segment depression during thallium-201 imaging in patients with coronary artery disease: angiographic and hemodynamic determinants. *J Am Coll Cardiol.* 1998;12:37–41.
- Hansen CL, Crabbe D, Rubin S. Lower diagnostic accuracy or thallium-201 SPECT myocardial perfusion imaging in women: an effect of smaller chamber size. *J Am Coll Cardiol.* 1996;28:1214–1219.
- Taillefer R, DePuey EG, Udelson JE, Beller GA, Benjamin EJ, Gagnon A. Comparison between the end-diastolic images and the summed images of gated ^{99m}Tc -sestamibi SPECT perfusion study in detection of coronary artery disease in women. *J Nucl Cardiol.* 1999;6:169–176.