Thallium-201-Dipyridamole Imaging: Comparison Between a Standard Dose and a High Dose of Dipyridamole in the Detection of Coronary Artery Disease

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The purpose of this study was to compare two different doses of dipyridamole as a pharmacologic stress test for ^{201}Tl imaging. **Methods:** Twenty-four patients with significant coronary artery disease (15 had undergone a coronary angiogram and 9 had undergone a previous ^{201}Tl study with a significant lesion) were prospectively studied. Within 1 wk, all patients underwent two [201]T-dipyridamole myocardial planar studies, one using a standard dose (STD) and the other, a high dose (HIGH) of dipyridamole. The protocol order was randomly assigned. The STD protocol used a dose of 0.14 mg/kg/min for a duration of 4 min (0.56 mg/kg), and the HIGH protocol used a dose of 0.14 mg/kg min for a duration of 6 min (0.84 mg/kg). The ^{201}Tl was injected 3 min after the end of the dipyridamole infusion. Images, obtained 5 min and 4 hr later, were interpreted (divided into five segments each) by three blinded observers. **Results:** The STD protocol showed normal, ischemia and scar in 252, 91 and 17 segments, respectively. The HIGH protocol detected 232, 118 and 10 segments, respectively. A side-by-side evaluation was done to evaluate the defect extent subjectively, which was greater with HIGH in 14, equal in six and smaller in four patients. One or more side effects were seen in 14 patients with STD and in 19 with HIGH. Increased heart rate (8 bpm for STD and 19 bpm for HIGH, p < 0.001) was the only significant change seen in the hemodynamic parameters. **Conclusion:** This preliminary study indicates that a high dose of dipyridamole seems to be safe and can be helpful to increase the sensitivity of ^{201}Tl imaging.

Key Words: thallium-201; dipyridamole; coronary artery disease

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Thallium-201 myocardial perfusion imaging after dipyridamole-induced stress is a widely accepted procedure in the diagnosis and prognosis of coronary artery disease

(1-3). It represents a useful alternative to myocardial imaging after a stress test on a treadmill for patients who cannot achieve an adequate level of exercise because of musculoskeletal abnormalities, peripheral vascular disease, chronic lung disease or myocardial chronotropic pharmacologic treatment. The standard procedure usually consists of the injection, over 4 min, of a predetermined (according to body weight) dose of dipyridamole, followed by low-level exercise. The injection of ^{201}Tl is performed a few minutes after the end of the dipyridamole infusion. A dipyridamole dose of 0.56 mg/kg of body weight, up to a maximum of 50–60 mg is generally considered adequate for radionuclide imaging (1-7).

In echocardiography, a dipyridamole dose of up to 0.84 mg/kg of body weight, injected over 10 min, was proposed for the purpose of testing myocardial contractility under dipyridamole-induced stress (8-14). Even though some minor side effects have been reported in 65%–73% of patients (8,10), the procedure is usually well tolerated.

This prospective study was performed to evaluate the potential benefits of increasing the dipyridamole dose for ^{201}Tl myocardial perfusion imaging. A group of patients with coronary artery disease was submitted to two successive ^{201}Tl planar myocardial perfusion imaging studies, one with a standard dipyridamole dose of 0.56 mg/kg of body weight (over 4 min) and the other with an increased dose of 0.84 mg/kg of body weight (over 6 min).

MATERIALS AND METHODS

Patient Population

A total of 24 patients with either angiographically or scintigraphically documented coronary artery disease was included in this prospective study. Of this number, 15 patients underwent coronary angiography, either alone or in combination with ^{201}Tl myocardial imaging. The other nine patients were referred to this institution for investigation of chest pain and showed significant abnormalities on ^{201}Tl myocardial imaging with either exercise or dipyridamole-induced stress. These patients (20 men and 4 women) were aged between 36 and 81 yr (mean 61 ± 9.5 yr).

Patients with a known allergy to dipyridamole or aminophylline, unstable angina, severe arrhythmias, recent (less than 6 wk) myocardial infarction, overt congestive heart failure, significant valvular heart disease or severe pulmonary disease were excluded from the study. Written informed consent was obtained from each patient, and the protocol was approved by the ethics committee of this institution.

Cardiac Catheterization

Fifteen patients underwent coronary angiography and left ventriculography, using the Judkins technique, with multiple views of the right and left coronary arteries. Coronary angiograms were interpreted by two observers who did not know the results of the ^{201}Tl myocardial studies or stress tests. Significant coronary artery stenosis was defined as a 70% or greater reduction in the luminal diameter of one or more major coronary arteries. Both scans and angiography were performed within 1 mo in every patient.

Dipyridamole Infusion Protocol

Each patient underwent two ^{201}Tl dipyridamole myocardial studies, one with a standard dose (STD) of 0.56 mg/kg of dipyridamole and the other one with an increased dose (HIGH) of 0.84 mg/kg. In both studies, the rate of infusion of dipyridamole was 0.142 mg/kg/min. The duration of the infusion was 4 min for the STD study and 6 min consecutively for the HIGH study. The order of the two tests was randomly assigned, and the average time elapsed between them was 5.6 days (range 1–13 days).

For both studies, the procedure was as follows. Patients were instructed to withhold drugs containing methylxanthines for at least 48 hr prior to the test and to avoid tea, coffee, soft drinks, chocolate and foods containing caffeine for at least 24 hr prior to the test. They were instructed to fast, starting at midnight on the day of the test. The preparation was identical for both studies for all patients.

After the patients were placed in the supine position, an intravenous line with normal saline solution was inserted in an upper limb vein. A baseline electrocardiogram (ECG), heart rate and blood pressure were recorded. The dipyridamole infusion was then started and lasted either 4 min (STD protocol) or 6 min (HIGH protocol) at a rate of 0.142 mg/kg/min. During and after the dipyridamole infusion, ECG monitoring and vital signs were recorded every 60 sec. Side effects were monitored throughout the course of the study. After the dipyridamole infusion, the patient stood up and walked in place for 2 min. A dose of ^{201}Tl-labeled thallous chloride (2.0–3.0 mCi) was then injected as a bolus while the patients continued to walk for 2 min more, for a total of 4 min. Patients were then positioned under the scintillation camera for planar imaging. Aminophylline was readily available, and if necessary, patients were injected with 2 mg/kg intravenously of this drug to stop the action of dipyridamole and reverse any adverse side effects.

Data Acquisition

Two sets of planar images were obtained for each study using a scintillation camera with a small field of view and a low-energy all-purpose collimator. The photopeak was set at 80 keV by using a symmetric 20% window.

Each set consisted of analog images obtained with a preset-time acquisition of 8 min (350,000–450,000 counts) and of 128 × 128 pixels numeric images. A 45° left anterior oblique view was initially obtained, followed by an anterior and a left lateral view with the patients being placed in the right lateral decubitus position.

Acquisition of the first set of images started immediately after the end of low-level exercise (approximately 5–7 min after the ^{201}Tl injection). The second set (redistribution imaging) was obtained 4 hr after the ^{201}Tl injection. Between the two acquisitions, the patient was instructed to eat lightly if at all.

Data Analysis

Qualitative Analysis. In each of the three views, the myocardium was divided into five segments, for a total of 15 segments per study. Each study was submitted to a panel of three experienced observers in random order. The observers had no prior knowledge of the dipyridamole dose used (STD or HIGH), the results of previous tests (coronary angiogram or ^{201}Tl study), the ECG findings or the patient's history.

The observers were asked to interpret each segment as being either normal or presenting fixed or transient perfusion defects. For each study, the diagnosis was divided into three categories: normal, ischemic or scarred myocardium. Disagreements in interpretation were resolved by consensus.

At the end of this initial reading session, a second reading was performed. For each patient, the STD and the HIGH study findings were placed side by side for comparison. Without knowledge of the corresponding dipyridamole dose, the observers had to evaluate subjectively which of the two studies gave better diagnostic information or better subjective "diagnostic certainty."

Quantitative Analysis. Regions of interest of similar size and location for a given patient were drawn over normal myocardium, ischemic myocardial walls and lungs for both the STD and HIGH studies. Activity ratios of ischemic-to-normal myocardium and normal myocardium-to-lung were computed.

Statistical Analysis. All results are expressed as the mean ±1 s.d. Changes in activity ratios were evaluated using a paired Student's t-test. For each study, a variation in heart rate was defined as the heart rate measured at the end of the dipyridamole infusion minus the baseline heart rate. A variation in systolic blood pressure (SBP) was defined as SBP at end of the infusion minus the baseline SBP. A variation in the double product (DP, defined as heart rate multiplied by the SBP) was defined as the DP at the end of infusion minus the baseline DP. Comparisons between STD and HIGH protocols for these three parameters and for heart rate, SBP and DP, baseline and final, were made with Student's paired t-test.

Changes in segmental analysis and patient diagnosis were evaluated by applying chi-square analysis and kappa residual analysis over a contingency table.

RESULTS

Patient Population

A total of 15 of the 24 patients underwent coronary artery angiograms. All 15 (100%) were abnormal. Four of them (27%) showed single-vessel disease, eight (53%) showed double-vessel disease and three (20%) showed triple-vessel disease for a total of 29 diseased coronary vessels: 13 left anterior descending arteries, six circumflex and 10 right coronary arteries.

Hemodynamic Parameters

Table 1 summarizes the results of hemodynamic parameters and their difference for both STD and HIGH studies. There was no significant difference in baseline heart rate, SBP or DP between the STD and HIGH protocols. At the

TABLE 1
Hemodynamic Parameters: Comparison Between Standard and Increased Doses of Dipyridamole

	STD	HIGH	p value
Heart rate (bpm) (baseline)	72 ± 11	68 ± 12	NS
Blood pressure (mmHg) (baseline)	150 ± 25	149 ± 21	NS
Double product (baseline)	10,900 ± 2800	10,300 ± 2800	NS
Heart rate (final)	80 ± 12	87 ± 14	0.002
Blood pressure (final)	138 ± 22	132 ± 16	0.08
Double product (final)	11,100 ± 2700	11,600 ± 2800	NS
Heart rate (variation)	7.8 ± 7.2	18 ± 12	<0.001
Blood pressure (variation)	−12 ± 11	−16 ± 14	NS
Double product (variation)	200 ± 1500	1350 ± 2300	0.05

NS = not significant; STD = standard-dose protocol; HIGH = high-dose protocol.

end of dipyridamole infusion, the heart rate was 80 ± 12 bpm for the STD study and 87 ± 14 bpm for the HIGH study. The variation in heart rate was 8 ± 7 bpm for the STD and 18 ± 12 bpm for the HIGH (p < 0.001).

At the end of infusion, the SBP was 138 ± 22 mmHg and 132 ± 16 mmHg for the STD and HIGH protocols, respectively. The variation in blood pressure was −12 ± 11 mmHg (STD) and −16 ± 14 mmHg (HIGH). The DP was 11,100 ± 2700 (STD) and 11,600 ± 2800 (HIGH). These differences are not statistically significant (Table 1). DP variation was marginally significant (200 ± 1500, p = 0.05).

Side Effects

After infusion of the STD dipyridamole dose, 14 patients (58%) showed at least one side effect. This number went up to 19 (79%) after the HIGH dose (Table 2). The most frequently encountered side effect was chest pain, which occurred in nine patients (38%) during the STD study and 14 patients (58%) during the HIGH study. Other reported side effects were nausea, dizziness, flushing or sensation of heat, headache and fatigue.

At the end of the low-level exercise period during the STD protocol, 15 patients of 23 (65%) showed no ST segment depression, seven patients (30%) showed a 1-mm ST segment depression and one patient (5%) showed a 2-mm ST segment depression. For one patient, the ECG was not available. At the end of the low-level exercise period for the HIGH study, eight patients of 24 (34%) showed no ST segment depression, 10 patients (43%) showed a 1-mm ST segment depression and six patients (23%) showed a 2-mm or more ST segment depression.

Chi-square analysis showed that only the raise in frequency for ST segment depression was significant (p = 0.01). The difference in frequency for all other side effects was not significant.

Fourteen patients (58%) reported at least one side effect during the STD study (Table 3). Eleven of them (78%) noted that they were more intense during the HIGH study, and two (15%) judged that they were of comparable intensity. One patient reported slight and transient chest pain during the STD study but no side effects at all during the HIGH study. Six patients (25%) experienced side effects during the HIGH study only, and four patients (16%) reported no side effects at all. During the STD study, six patients (25%) received aminophylline for chest pain; 10 patients (42%) were so treated during the HIGH study. Of those 10 patients, five had also received aminophylline during the STD protocol, and the other five were injected with aminophylline during the HIGH protocol only. One
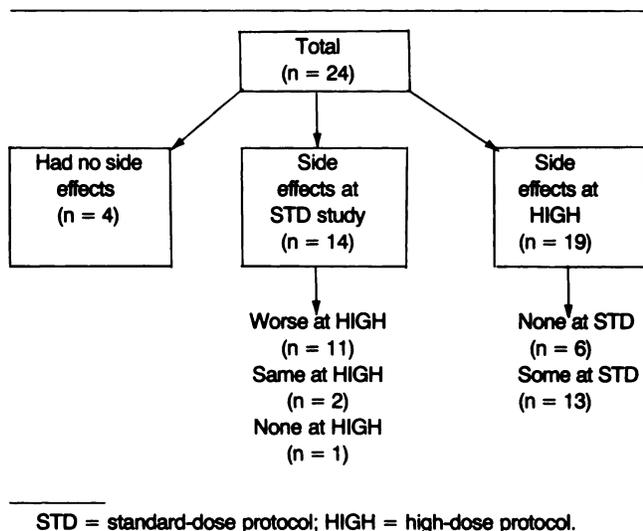
TABLE 2
Frequency of Side Effects for Standard and High-Dose Protocols*

	STD	HIGH	Chi-square	p value
Headache	17% (4)	21% (5)	0.14	NS
Dizziness	13% (3)	25% (6)	1.2	NS
Flushing	4% (1)	13% (3)	1.0	NS
Nausea	0% (0)	4% (1)	1.0	NS
Fatigue	0% (0)	4% (1)	1.0	NS
Dyspnea	0% (0)	4% (1)	2.1	NS
Chest pain	38% (9)	58% (14)	0.0	NS
Hypotension	0% (0)	0% (0)	0.0	NS
Any symptom	58% (14)	79% (19)	2.4	NS

*Numbers in parentheses represent absolute number of patients.
STD = standard-dose protocol; HIGH = high-dose protocol; NS = not significant.

TABLE 3
Side Effect Intensity, According to Dose

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                    ┌──────────────┐
                    │    Total     │
                    │   (n = 24)   │
                    └──────────────┘
          ┌────────────────┼────────────────┐
┌──────────────┐   ┌──────────────┐   ┌──────────────┐
│ Had no side  │   │     Side     │   │     Side     │
│   effects    │   │  effects at  │   │  effects at  │
│   (n = 4)    │   │   STD study  │   │     HIGH     │
│              │   │   (n = 14)   │   │   (n = 19)   │
└──────────────┘   └──────────────┘   └──────────────┘
                          │                  │
                   Worse at HIGH       None at STD
                     (n = 11)            (n = 6)
                   Same at HIGH        Some at STD
                     (n = 2)            (n = 13)
                   None at HIGH
                     (n = 1)
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STD = standard-dose protocol; HIGH = high-dose protocol.

patient received aminophylline during the STD protocol but not during the HIGH one. In all cases, the relief of the side effects was complete and occurred within 5 min.

Qualitative Analysis

Segmental Comparison. Table 4 summarizes the comparison between STD and HIGH protocol for the segmental analysis. The STD study showed that 252 segments (70%) were classified as normal, 91 (25%) were classified as presenting reversible defects and 17 (5%) were classified as presenting fixed defects compared with 232 normal (64%), 118 reversible (33%) and 10 fixed defects (3%) on the HIGH study. The segmental agreement was 80%, and the kappa value was 0.58 for a total of 360 segments.

Reversible segments were seen in 91 cases for the STD study and in 118 cases for the HIGH protocol. Forty-nine segments that were classified either as normal (37 segments) or as fixed (12 segments) during STD were classified as reversible during HIGH, and 22 segments considered reversible during STD were classified either as normal (17 segments) or as fixed (5 segments) after HIGH (Figs. 1–2). This resulted in an 8% decrease in the number of normal segments (232 during HIGH instead of 252) and a 42%

TABLE 4
Segmental Analysis: Comparison Between Two Dipyridamole Protocols*

High	STD		
	Normal	Ischemia	Scar
Normal	215	17	0
Ischemia	37	69	12
Scar	0	5	5

*Segmental agreement = 80% (289/360 segments).
STD = standard-dose protocol; HIGH = high-dose protocol.

decrease in the number of fixed defects (10 during HIGH instead of 17 during STD).

Chi-square analysis showed that the proportion of normal, reversible and fixed segments was significantly different for the two tests at the level p = 0.05 (chi-square = 6.13, degrees of freedom [df] = 2). Furthermore, an analysis of normalized residuals showed that the difference in the two tests was caused mainly by a significantly higher proportion of reversible segments in HIGH (32.8% of all segments) than in STD (25.3% of all segments).

Patient Diagnosis. Following the STD study, five patients (21%) were considered to be normal; 18 (75%), to have ischemia; and one (4%), to have scar without ischemia. After the HIGH study, four patients (17%) were considered to be normal; 20 (83%), to have ischemia; and none, to have scar without ischemia. As shown in Table 5, in two patients (8%), the diagnosis was changed to ischemia after the HIGH test. One of them was classified as normal after the STD study, and the other one had fixed defects. These differences in diagnosis are not significant (p = 0.1, chi-square = 1.21, df = 2). The percentage of diagnostic agreement between the two protocols was 92%, and the kappa value was 0.76.

Sensitivity for Coronary Artery Disease Detection

For the 15 patients who had undergone coronary angiograms, the results of ^{201}Tl myocardial imaging were compared with those of the coronary artery angiograms. The sensitivity for coronary artery disease detection of STD protocol was 80% (12 of 15), and the sensitivity of the HIGH study was 87% (13 of 15). This yielded a chi-square value of 0.25 (df = 1, not significant).

Diagnostic Certainty

The blinded observers were asked to compare subjectively the diagnostic certainty (taking into consideration both defect extent and severity) of the STD and HIGH studies placed side by side for each patients. In 14 patients (58%), the HIGH protocol was judged to be better than the STD; the inverse was true in four (17%) patients. Both protocols gave similar results in the remaining six patients (25%).

Quantitative Analysis

Nine patients were excluded from the quantitative analysis of the activity ratio: four of them had entirely normal myocardium on both studies, three of them had partially reversible lesions on both studies and two of them had incomplete quantitative data because of technical problems. The 15 patients thus remaining had reversible defects (interpreted as purely ischemic lesions) on at least one study.

The activity ratio values of ischemic-to-normal myocardium and normal myocardium-to-lung are listed in Table 6. The ischemic-to-normal myocardium activity ratio in the immediate set was 0.79 ± 0.8 for STD study and 0.74 ± 0.9 for HIGH study.
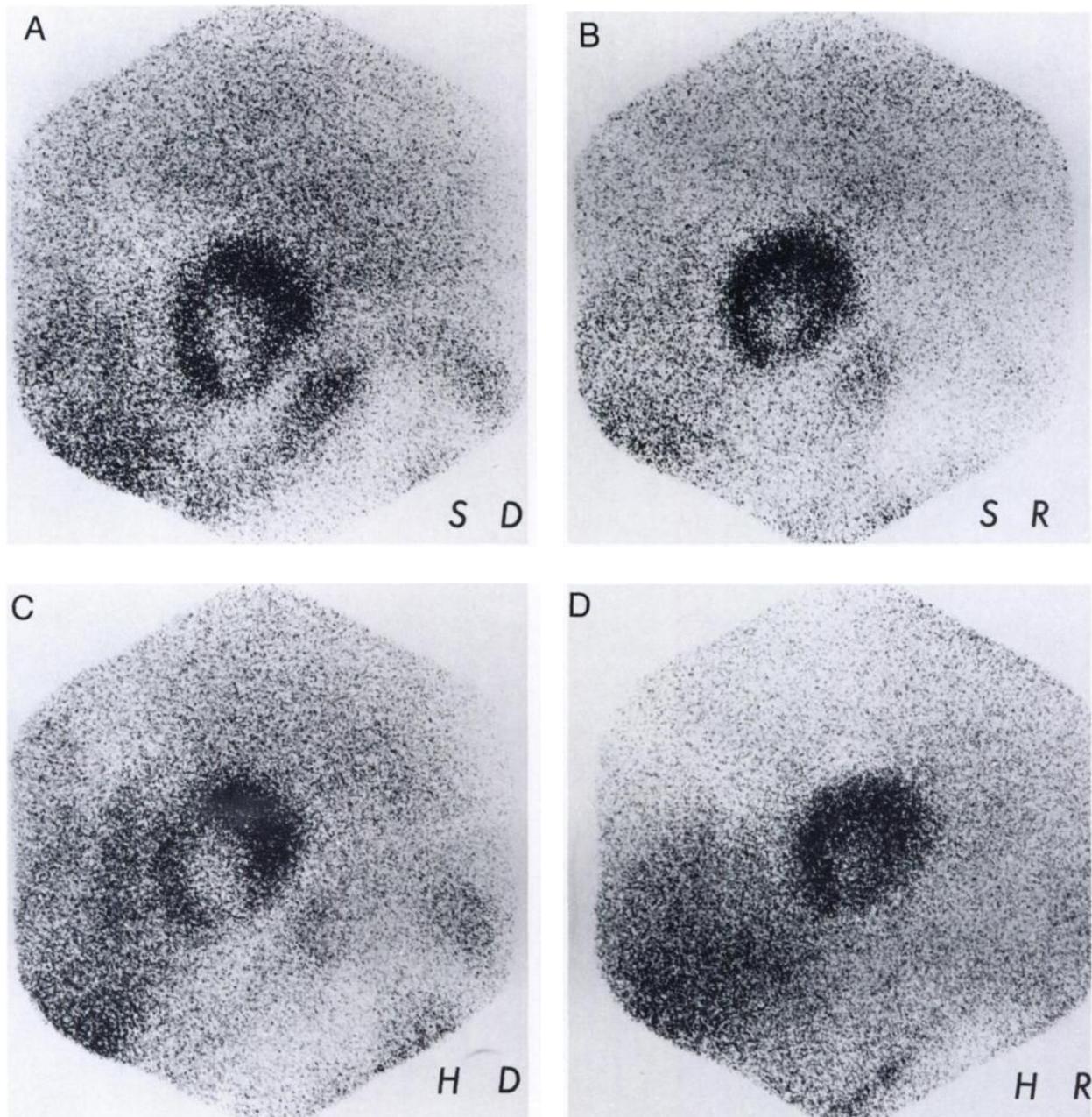
FIGURE 1. Studies of ^{201}Tl (45° left anterior oblique views) in a patient with significant stenosis of the left anterior descending and right coronary arteries and a previous inferolateral infarction. The study performed with a standard (S) dose of dipyridamole shows a partially reversible inferolateral defect; the study with the high dose (H) of dipyridamole shows a septal ischemic defect better which is accompanying the partially reversible inferolateral lesion D = immediate postdipyridamole imaging; R = redistribution. There is transient dilation of the left ventricle.

The normal myocardium-to-lung activity ratios in the immediate sets was 2.27 ± 0.33 for the STD study and 2.36 ± 0.35 for the HIGH study. The decrease in ischemic-to-normal myocardium activity ratio with the HIGH dose was highly significant (by paired Student's t-test, p < 0.01). The normal myocardium-to-lung activity ratio was also significantly higher with HIGH than with STD dose (by paired Student's t-test, p = 0.06).

DISCUSSION

The coronary dilatory activity of dipyridamole has been known for more than 30 yr (15,16). Fifteen years ago, Gould (17) demonstrated that the detection of a significantly diminished flow reserve in a stenosed coronary vessel was feasible by using an intravenous injection of dipyridamole and ^{201}Tl and external imaging of regional myocardial perfusion. Furthermore, he determined the ap-

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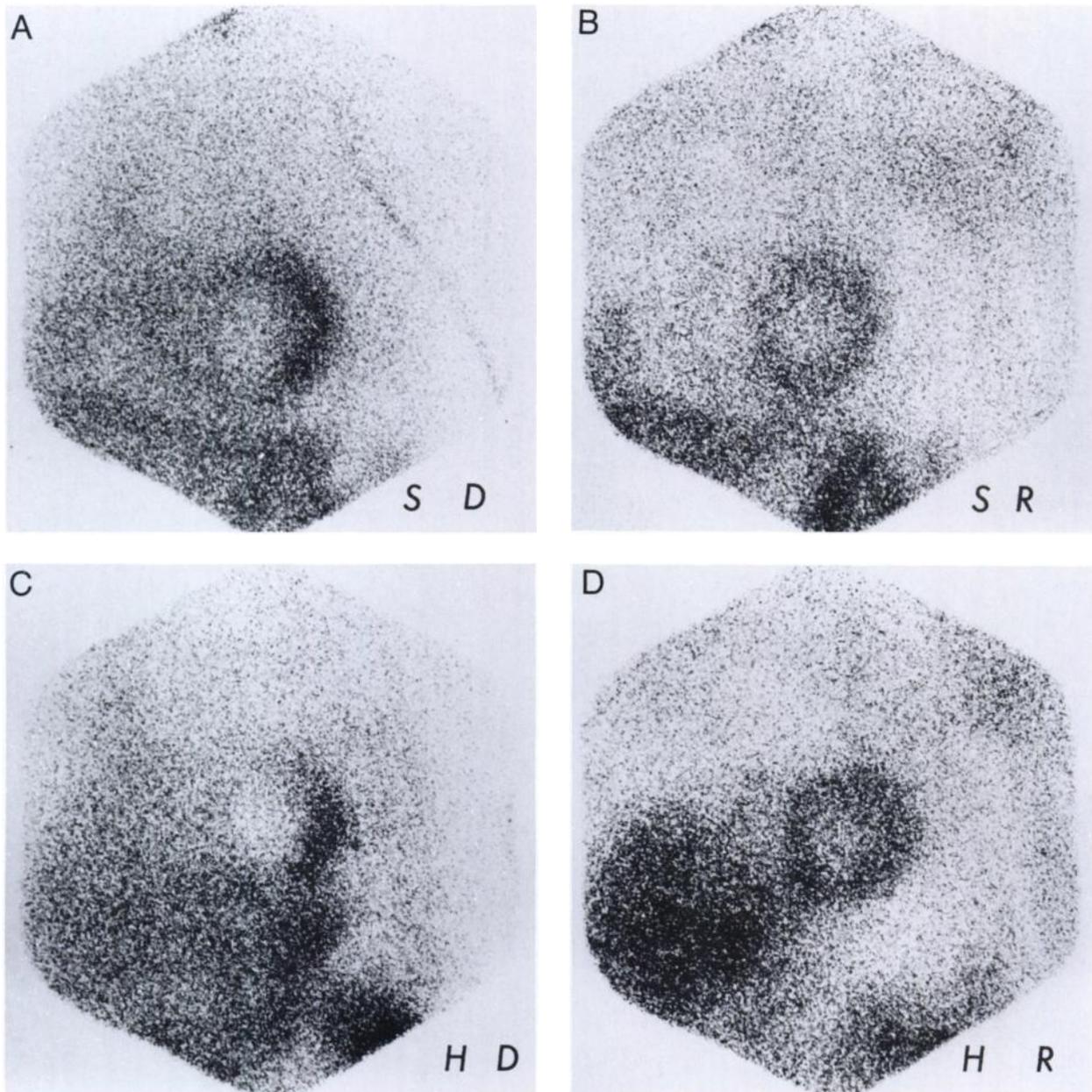
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FIGURE 2. In these 45° left anterior oblique views in a patient with a 95% stenosis of the left anterior descending artery, the study performed with a higher dose of dipyridamole shows a relatively more intense anteroseptal ischemic defect than that with the standard dose of dipyridamole. S = standard dose of dipyridamole; H = high dose of dipyridamole; D = immediate postdipyridamole imaging; R = redistribution.

propriate dipyridamole dosage to use. In the dog, he established that an infusion of 0.142 mg/kg/min for 4 min increased coronary blood flow to 95% maximal vasodilation, the latter being arbitrarily defined as the flow observed after a mechanical coronary occlusion of a 10-sec duration. It is noteworthy that the proposed dose was the maximal dose tested, except for a 0.68-mg/kg bolus injection, which produced even further vasodilation.

In another publication, Gould et al. (18) studied the effect of a dipyridamole injection in humans for the purpose of ^{201}Tl myocardial perfusion imaging. They did not measure the actual coronary flow response to the injected

dipyridamole. Although independent studies measured the increase in coronary blood flow to an average of four times the baseline (19,20), it was not established that this was the maximum flow response achievable in humans. Rather, many consider that the usual dose of 0.57 mg/kg represents the minimal dose that produces consistently good results and thus can be considered the best compromise between the quality of imaging and the severity of side effects (18). Even though several investigators reported significant side effects with increased dipyridamole doses, aminophylline was not used in many of these studies (18,21,22). Furthermore, Rossen et al. (22), with the help of intracoronary

TABLE 5
Patient Diagnosis: Comparison between Two Dipyridamole Protocols*

High	STD		
	Normal	Ischemia	Scar
Normal	4	0	0
Ischemia	1	18	1
Scar	0	0	0

*Diagnostic agreement = 92% (22/24 patients).
STD = standard-dose protocol; HIGH = high-dose protocol.

Doppler catheters, found a number of patients with submaximal coronary dilation after a standard dipyridamole dose of 0.57 mg/kg. Several of these subjects, who had a depressed flow response after a standard dose of 0.57 mg/kg, exhibited a further increase in coronary flow after an additional dipyridamole infusion of 0.28 mg/kg. Other investigators reported similar results (23–25). Rossen et al. (22) concluded that further investigations of the efficacy and safety of larger doses of dipyridamole were desirable.

Regarding the safety of an increased dipyridamole dose, some data are already available. Picano et al. (8–14) performed more than 1200 stress echocardiographies using 0.84 mg/kg of dipyridamole. Approximately two-thirds of patients experienced some minor side effects (headache, flushing or nausea) but no severe or aminophylline-resistant side effects. Osterprey et al. (26) reported on a series of 500 patients studied with a dose of 0.75 mg/kg administered in 10 min. They observed no significant complications.

Theoretically, a higher dose of dipyridamole is desirable to produce better diagnostic information. Because it is a rather specific coronary vasodilator, an increased dipyridamole dose should result in a higher ratio of coronary over total systemic flow, therefore, increasing the myocardial uptake of ^{201}Tl and the myocardial-to-background activity ratio. Increased vasodilation of the coronary bed should also increase the ratio of perfusion between the normal vascular bed and the poststenotic bed, presenting a decreased coronary flow reserve. Increasing this perfusion ratio is especially important with agents such as ^{201}Tl, which have a decreased extraction efficiency at a high flow

TABLE 6
Quantitative Analysis: Ischemic-to-Normal Myocardium and Normal Myocardium-to-Lung Activity Ratio

	STD	HIGH	p value
I/N Immediate	0.79 ± 0.08	0.74 ± 0.09	0.008
N/L Immediate	2.3 ± 0.33	2.4 ± 0.35	0.06

I/N = ischemic-to-normal myocardium; N/L = normal myocardium-to-lung; STD = standard-dose protocol; HIGH = high-dose protocol.

rate, and causes the activity ratio to be less than the perfusion ratio between two myocardial regions.

In the present study, a more important variation in heart rate and blood pressure was observed with a HIGH dose than with the STD dose. Others reported similar results (24). Interestingly, the variations observed in the current study were significant for heart rate and DP only. It is possible that the lack of a significant difference in blood pressure was caused by the sample size.

Except for ST segment depression, no side effect was significantly more frequent after the HIGH dose than after the STD. In at least two other publications, the use of 0.84 mg/kg of dipyridamole was associated with a frequency of side effects comparable to what was observed in the current study. Picano et al. (14), in studies of echocardiography with dipyridamole, reported that about two-thirds of 1200 patients experienced some minor side effects (headache, flushing or nausea). Furthermore, no occurrence of severe or aminophylline-resistant side effects was reported, which was consistent with the present experience. However, five cases of hypotension/bradycardia were reported in the earlier study. Masini et al. (10) reported that 24 of 39 women (62%) with coronary artery disease showed ST segment depression. This was found in 67% of the 24 patients in the current study. They also reported that 30 of 39 women (77%) with coronary artery disease experienced some chest pain. The same was observed in 58% of the current 24 patients. In both of these studies, a total dose of 0.84 mg/kg of body weight of dipyridamole was administered to the patient over a period of 10 min; an initial perfusion rate of 0.56 mg/kg was used for the first 4 min, followed by 4 min without the infusion and then a second injection of 0.28 mg/kg over 2 min. Sensitivity was not significantly improved by increasing the dipyridamole dose in this study (from 80% after STD to 87% after HIGH). Sensitivity figures reported in the recent literature range from 67%–93% for dipyridamole doses of 0.56 mg/kg (1–3, 27–33).

The quantitative analysis of digital images yielded results consistent with the theoretic predictions, i.e., a decreased activity ratio of ischemic-to-normal myocardium (I/N) and increased normal myocardium-to-lung (N/L) activity ratio. As previously mentioned, these did not result in any significant increase in the sensitivity of the test. Albro et al. (29) previously reported that increase of N/L ratio was not related to an increase in sensitivity. Nevertheless, the improvement in both ratios resulted in an improvement of the quality of the images and the diagnostic certainty. A decrease in the I/N myocardial activity ratio caused the ischemic lesions to be more prominent, resulting in improved observer's diagnostic confidence, and this should also improve intra- and interobserver variability.

Another desirable effect of the HIGH dipyridamole dose was an improvement in the detectability of ischemic lesions. It was shown that as much as 44%–49% of the observed fixed defects represent ischemic lesions, instead of scars (30–32). A number of solutions have been pro-

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posed, such as acquisition of delayed 24-hr images, with or without a second injection of ^{201}Tl, in the hope of observing delayed redistribution. A 42% decrease was observed in the number of fixed defects during the HIGH protocol compared with the STD protocol. One possible explanation of this observation could be that the increased dose of dipyridamole resulted in a more important vasodilation in normal segments, which in turn, would cause a higher initial uptake but also more rapid clearance during the myocardial washout phase. Higher uptake would result in higher contrast between the normal and ischemic myocardium on the immediate images. A more rapid washout would cause a higher difference in the activity ratio between the immediate and delayed images, resulting in a more detectable redistribution.

Alternatively, enhanced vasodilation in a normal bed and the steal phenomenon could lead to more important ischemia in periinfarcted myocardial regions and more frequent detection of viable underperfused myocardium by increasing the contrast between normal and ischemic but viable myocardium.

Study Limitations

As previously mentioned, the size of the sample in this preliminary study was insufficient to draw conclusions about the significance of some results. For instance, the observed difference variation in blood pressure and the observed frequency of side effects was not significant.

There was a sampling bias, with 58% of the subjects having undergone a coronary angiogram prior to enrollment and all others having a previously abnormal ^{201}Tl myocardial perfusion test result. Therefore, it was not possible to obtain data on the specificity of the test. Data on the predictive value of a positive or a negative test finding, if they were available, could not be extrapolated to the general population.

Activity ratios were obtained from two separate acquisition sessions. Therefore, the comparison between ratios obtained from the STD and HIGH protocols were limited by variability in the repositioning of the subjects, especially with planar imaging.

The presented data were obtained by planar acquisition with ^{201}Tl on a limited number of patients. Further studies will be necessary to increase the number of patients and also to investigate other agents and tomographic acquisitions.

CONCLUSION

Despite these limitations, the higher dose of dipyridamole of 0.84 mg/kg offered the advantage of better image quality. Normal-to-abnormal myocardium and target-to-background activity ratios were improved. The observer's diagnostic confidence was enhanced. The detectability of ischemic and scarred tissue was improved. The safety of the test was unhampered despite a mild increase in the frequency of side effects.

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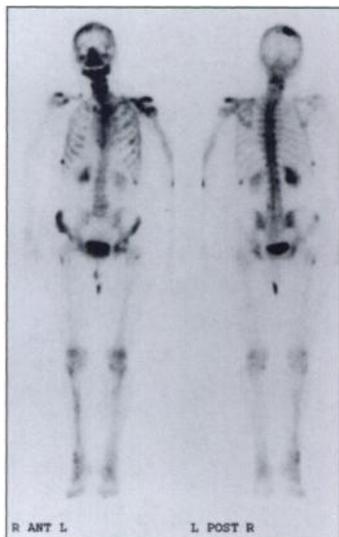
FIGURE 1.

FIRST IMPRESSIONS

Dislocated Shoulder

PURPOSE

A 64-yr-old woman with a history of breast cancer and known bone metastases was referred for a follow-up bone scan because of persistent left shoulder pain of 4 wk duration. Planar whole-body images show multiple sites of skeletal metastases, including the glenoid of the left scapula (Fig. 1). The unexpected finding is left shoulder dislocation, which accounts for the patient's new symptoms. This was also evident but not previously identified on a routine follow-up chest x-ray obtained a month prior to the bone scan (Fig. 2). The spot views (Fig. 3) show the shoulder separation, rib and scapular metastases. This case illustrates the merit and need for thorough bone scan evaluation to identify clinically unsuspected findings.

TRACER
Technetium-99m-MDP

ROUTE OF ADMINISTRATION
Intravenous

IMAGING TIME AFTER INJECTION
Three hours

INSTRUMENTATION
Dual-head Genesys (ADAC) gamma camera

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FIGURE 2.

FIGURE 3.