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Adenosine Thallium-201 Is Superior to Exercise Thallium-201 for Detecting Coronary Artery Disease in Patients With Left Bundle Branch Block

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Objectives. We sought to assess the comparative diagnostic accuracy of adenosine versus exercise in conjunction with thallium-201 scintigraphy for the detection and localization of coronary artery disease in patients with left bundle branch block on the rest electrocardiogram (ECG).

Background. Patients with left bundle branch block on the rest ECG frequently have artifactual reversible septal perfusion defects on exercise thallium-201 scintigraphy. Adenosine thallium scintigraphy is a theoretically attractive alternative in these patients.

Methods. One hundred seventy-three consecutive patients with left bundle branch block were evaluated with either exercise thallium ($n = 56$) or adenosine thallium ($n = 117$) scintigraphy. The tomographic thallium images were interpreted visually with adjunctive quantitative analysis. Follow-up cardiac catheterization was performed in 31 of the 56 patients in the exercise thallium group and 42 of the 117 patients in the adenosine thallium group.

Results. Minor subjective side effects were noted in most patients in the adenosine thallium group (86%); atrioventricular block occurred in seven patients (6%). The overall predictive accuracy was 93% in the adenosine thallium group and 68% in the exercise thallium group ($p = 0.01$). The combined specificity for the detection of disease in the coronary arteries subtending the septum (the left anterior descending and right coronary arteries) was only 42% with exercise thallium scintigraphy versus 82% with adenosine thallium scintigraphy ($p < 0.0002$).

Conclusions. Adenosine thallium imaging 1) was superior to exercise thallium imaging in the detection of coronary artery disease in patients with left bundle branch block; 2) obviated septal artifacts, thereby markedly improving the specificity in the left anterior descending and right coronary arteries; and 3) was safe in patients with left bundle branch block.

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The presence of left bundle branch block on an electrocardiogram (ECG) obtained at rest is commonly associated with coronary artery disease and nonischemic cardiomyopathies (1–3). Unfortunately, left bundle branch block precludes meaningful analysis of the ST segments during exercise stress testing (4) and confounds the interpretation of most of the more sophisticated noninvasive modalities for the detection of coronary artery disease. In patients with left bundle branch block, abnormal septal motion and left ventricular dyssynergy are present at rest and often worsen during exercise (5). Thus, exercise radionuclide ventriculography and exercise echocardiography may be misleading in these patients. Additionally, artifactual reversible septal perfusion defects have been reported to be a common problem with exercise thallium scintigraphy in patients with left bundle branch block and angiographically normal coronary arteries (6–10).

Pharmacologic coronary vasodilation with intravenous dipyridamole in conjunction with thallium-201 scintigraphy appears to result in improved specificity by obviating the septal artifacts commonly observed with exercise thallium scintigraphy in patients with left bundle branch block (11–13). More recently, adenosine has also been used as a pharmacologic adjunct to thallium imaging. Adenosine is a potent coronary vasodilator that can be used to assess coronary flow reserve (14–16). It has a direct mechanism of action with an ultrashort half-life of approximately 2 s, allowing for maximal coronary vasodilation with precise control. These characteristics make it an attractive alternative to dipyridamole for pharmacologic perfusion imaging. The purpose of the current study was to document the comparative diagnostic accuracy of adenosine versus exercise in conjunction with thallium-201 scintigraphy for the detection and localization of coronary artery disease in patients with left bundle branch block on the ECG at rest.

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Methods

Study patients. We studied 173 patients with left bundle branch block who had been referred to our nuclear cardiology laboratory for tomographic thallium-201 scintigraphy during the period August 1988 through February 1992. Of the 56 patients with left bundle branch block who underwent exercise thallium stress testing, 31 did so before March 1990, the date that the use of adenosine thallium scintigraphy was approved by the Institutional Review Board of our institution. The other 25 patients underwent exercise thallium scintigraphy after March 1990 but were not candidates for adenosine infusion.

Patients were excluded from receiving adenosine for the following reasons: 1) asthma or chronic obstructive pulmonary disease with bronchospasm requiring daily bronchodilators; 2) hemodynamic instability with significant hypertension (blood pressure >210/120 mm Hg) or hypotension (blood pressure <90/60 mm Hg) at rest; 3) second- or third-degree atrioventricular (AV) node block or symptomatic sick sinus syndrome without a permanent pacemaker; or 4) decompensated congestive heart failure. Patients were advised to avoid caffeine-containing beverages and food for the 12 h immediately preceding the test. Administration of dipyridamole, theophylline and pentoxifylline was discontinued for at least 24 h before testing.

Adenosine protocol. Adenosine was infused as a sterilized isotonic aqueous solution. The total dose was diluted in 30 ml of normal saline solution and infused at a constant rate of 140 μg/kg per min for 6 min. The infusion rate was titrated downward only in patients unable to tolerate the standard dose. Upward titration was not performed. A single intravenous port was used to infuse the adenosine and inject the thallium. At the 4-min mark of the adenosine infusion a weight-adjusted dose (range 2.5 to 4.0 mCi) of thallium-201 was injected as an intravenous bolus and flushed with 10 ml of normal saline solution through a Y connection at the far distal end of the tubing (near the venous entry site) to minimize inadvertent dead space bolus injection of adenosine. The adenosine infusion was then continued for an additional 2 min. Vital signs and 12-lead ECG tracings were obtained at baseline, after hyperventilation and at 1-min intervals during and for the 1st 6 min after the adenosine infusion. A second injection of 1.0 to 1.5 mCi of thallium was administered 3 h after stress testing and imaging was performed again 1 h later.

Exercise protocol. Exercise stress testing was performed in standard fashion using a Naughton or Bruce protocol. At peak exercise, thallium-201 was injected and the patients were encouraged to continue exercising for an additional 1 min. Beta-adrenergic blocking agents were withheld for 48 h and calcium channel antagonists for 24 h before exercise testing. The test was aborted without thallium injection if the patient was unable to reach [illegible]% of the age- and gender-adjusted maximal predicted hea[illegible]ate.

Thallium scintigraphy. Scintigraphic imaging was performed at 5 min after and again 3.5 to 5 h after the thallium-201 injection. Images were obtained using a large field of view rotating gamma camera (Siemens Orbiter-7500, Siemens Gammasonic), equipped with a low energy, all purpose collimator, interfaced to a computer (Siemens MicroDelta/MaxDelta). All patients underwent imaging in the supine position except during the 18-month period between January 1990 and September 1991 when men were imaged in the prone position.

Tomographic acquisition was begun as soon as possible after planar acquisitions and always within 12 to 18 min after discontinuation of the adenosine or exercise protocol. The imaging sequence consisted of 32 images obtained through a 180° arc with 40 stops/s on a 64 × 64 matrix. Anterior and 45° left anterior oblique planar images (650,000 counts each) were obtained immediately after the adenosine or exercise protocols, primarily to assess lung uptake of thallium and transient ischemic left ventricular dilation.

The tomographic data were used to reconstruct the left ventricle in the short-axis, horizontal long-axis and vertical long-axis orientations. The tomographic slices were ≈6.0-mm thick and were matched at stress and redistribution. The left ventricle was divided into 28 segments and scored as follows: 0 = normal uptake, 1 = mildly reduced uptake, 2 = moderately reduced uptake and 3 = severely reduced uptake. Myocardial perfusion on the tomographic images was quantified using two-dimensional polar plots representing the three-dimensional left ventricular structure. The quantitative polar map was divided into three regions corresponding to the typical anatomic distribution of the three major epicardial coronary arteries (17). The thresholds for abnormality on the polar plot were 12% in the left anterior descending and left circumflex arteries and 8% in the right coronary artery. The tomographic thallium studies were scored qualitatively by consensus of two expert observers, a nuclear cardiologist and a nuclear cardiology research technician. The scans were read prospectively without knowledge of clinical or coronary angiographic data. The planar and tomographic quantitative analyses were used to corroborate the qualitative, visual interpretation. A coronary artery territory was considered ischemic if a reversible defect (stress/redistribution scores of 3-0, 3-1, 2-0, 2-1) was noted with a reversible abnormality in the corresponding region on the quantitative polar plot.

The lung uptake of thallium was scored quantitatively. A lung/heart ratio was used, with abnormal lung uptake defined as a ratio of ≥0.52. Lung uptake of thallium was also scored qualitatively with normal lung uptake of thallium defined as no activity or trace thallium activity in the lungs on the planar anterior stress image. Abnormal lung uptake was defined as moderately or severely increased lung uptake during stress. Ventricular dilation was scored qualitatively as normal (absent or mild dilation during stress) or abnormal (moderate or severe transient dilation during stress).

Coronary angiography. Cardiac catheterization with coronary angiography was performed for clinical indications in

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Table 1. Demographics

	Adenosine (n = 117)	Exercise (n = 56)	p Value
Age (yr)			
Mean	68 ± 7	67 ± 7	NS
Range	44–86	44–82	NS
Men	78 (67)	41 (73)	NS
Women	39 (33)	15 (27)	NS
Prior infarct	49 (42)	30 (54)	NS
Prior CABG	38 (32)	7 (13)	0.004
Age ≥70 yr	56 (48)	22 (39)	NS

Unless otherwise indicated, data are presented as mean value ± SD or number (%) of patients. CABG = coronary artery bypass grafting.

Table 3. Exercise Versus Adenosine for Localization of Coronary Artery Disease With Thallium Imaging

	LAD	RCA	LCx
Sensitivity (%)			
Exercise	73 (11 of 15)	81 (13 of 16)	75 (9 of 12)
Adenosine	96 (23 of 24)	100 (10 of 10)	76 (16 of 21)
Specificity (%)			
Exercise	44 (7 of 16)	40 (6 of 15)*	84 (16 of 19)
Adenosine	72 (13 of 18)	88 (28 of 32)	100 (19 of 19)

*$p < 0.001$. Data in parentheses indicate number of patients. LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; RCA = right coronary artery.

73 (42%) of the 173 patients. Angiographic interpretation was performed by experienced invasive cardiologists, who were unaware of the findings on thallium scintigraphy. Significant coronary artery disease was defined as a visually determined relative lumen diameter stenosis ≥70% in a major epicardial coronary artery or branch (excluding far distal lesions located within the final 1.0 cm of the vessel).

Statistical analyses. Data were presented as mean value ± SD. Sensitivity, specificity and positive and negative predictive values and predictive accuracy were calculated using standard definitions. Categoric variables were compared using chi-square analysis or a Fisher exact test. A p value ≤ 0.05 was considered statistically significant.

Results

The study groups were similar with respect to most of the pertinent patient descriptors (Table 1). A greater proportion of the patients in the adenosine group had previously undergone bypass graft surgery. During the adenosine infusion, mean heart rate increased 11 ± 14 beats/min over baseline. Systolic blood pressure decreased by 4 ± 16 mm Hg. Subjective symptoms were noted in 86% of the patients who underwent adenosine thallium imaging (Table 2). These symptoms were largely benign and self-limited. Chest pain occurred in 45 patients (38%) and two or more symptoms were noted in 66 patients (56%). The only serious side effect noted during adenosine infusion in the current study was AV block. Seven patients were noted to have AV block, including two with Wenckebach (Mobitz type I block), three with Mobitz type II second-degree AV block, and two with third-degree AV block. Six of the seven patients with AV block were asymptomatic. Transient loss of consciousness was noted in one patient with complete heart block during a 4.2-s pause. The mean duration of the AV block was 2.1 ± 1.4 s. The adenosine infusion rate was reduced in five of the seven patients with AV block. All of the episodes were transient and no patient required hospitalization or cardiac pacing.

Table 2. Symptoms During Adenosine Infusion in 117 Patients*

	Patients	
	No.	%
Dyspnea	58	50
Flushing	52	44
Chest discomfort†	45	38
Headache	12	10
Light-headedness	11	9
Atrioventricular block	7	6
Nausea	4	3

*Eighty-six percent of patients experienced at least one symptom. †Typically described as tightness, heaviness or pressure in the chest or neck, or both.

Fifty-five of the 56 patients who underwent exercise thallium stress testing achieved at least 75% of their age- and gender-adjusted estimated maximal peak heart rate. The exercise stress test was limited by angina in 20 patients (36%) and dyspnea in 32 patients (57%). The ECG was read as nondiagnostic because of the underlying intraventricular conduction defect with baseline repolarization abnormalities in all 173 patients with left bundle branch block in the study.

Cardiac catheterization was performed for clinical reasons in 31 (55%) of the 56 patients who underwent exercise thallium scintigraphy and 42 (36%) of the 117 patients who underwent adenosine thallium scintigraphy ($p = 0.01$). The mean interval from thallium stress testing to cardiac catheterization was 9 ± 8 days in the exercise thallium group versus 7 ± 5 days in the adenosine thallium group (p = NS). The overall predictive accuracy for the detection of significant coronary artery disease was 68% in the exercise thallium group and 93% in the adenosine thallium group ($p = 0.01$). Sensitivity for the exercise and adenosine thallium groups was 86% and 97%, respectively (p = NS); specificity was 13% and 67%, respectively (p = NS). The two thallium tests were also compared with respect to their ability to localize ischemia to specific coronary vascular distributions (Table 3). The combined specificity for the detection of coronary artery disease in the left anterior descending and right coronary arteries with exercise thallium scintigraphy was 42% compared with 82% specificity with adenosine thallium scintigraphy ($p < 0.0002$). Artifactual reversible septal perfusion defects (with angiographically normal left anterior descending and right coronary arteries, Fig. 1) were

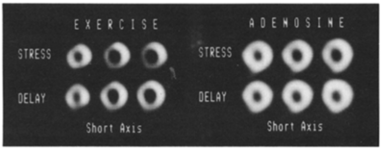

Figure 1. Artifactual reversible septal perfusion defect present on exercise but not adenosine thallium scintigraphy in a patient with angiographically documented normal coronary arteries. Images displayed are stress and reinjection short-axis midventricular tomographic slices.

observed more frequently in the exercise thallium group (35%) than in the adenosine thallium group (5%, p = 0.001). Exercise and adenosine thallium stress testing appeared to be equally accurate with respect to ability to localize disease to the left circumflex system.

Patients with normal adenosine thallium scintigraphy were followed up clinically to assess the prognostic utility of the study in this subgroup. The mean follow-up period was 13 ± 6 months. Cardiac events were defined as unstable angina, myocardial infarction, need for revascularization procedures or death. No cardiac events occurred in the 29 patients with normal adenosine thallium studies during the 13-month mean follow-up period.

The accuracy of exercise and adenosine thallium scintigraphy was analyzed in the subgroup of patients without symptoms or a previous cardiac history (except for left bundle branch block on the ECG). Specificity was 100% in the four patients who constituted the adenosine portion of this subgroup compared with 17% in the 12 who constituted the exercise portion. Thus, specificity was also improved in this subgroup of patients without a previous cardiac history when they were studied with adenosine rather than exercise thallium scintigraphy.

Transient ventricular dilation and lung uptake of thallium. Transient ischemic ventricular dilation and increased lung uptake of thallium were markers for significant coronary artery disease in both the exercise and adenosine thallium groups. Transient ischemic ventricular dilation occurred in 23 patients (20%) in the adenosine thallium group and 10 patients (18%) in the exercise thallium group (p = NS). High grade coronary artery disease (≥70% stenosis) was seen in 9 of the 10 patients with transient ischemic dilation during adenosine infusion who had undergone coronary angiography and in 7 of the 8 patients in the exercise thallium group (p = NS). Increased lung uptake of thallium was noted in 33 patients (28%) in the adenosine thallium group and 26 patients (46%) in the exercise thallium group (p = 0.02). Significant coronary disease was seen in 14 of the 15 patients with abnormal lung uptake in the adenosine thallium group and in 11 of the 14 patients with abnormal lung uptake in the exercise thallium group (p = NS). Thus, transient ischemic ventricular dilation and abnormal lung uptake of thallium were relatively specific but insensitive markers for the detection of significant myocardial ischemia for both the adenosine and exercise thallium tests.

Discussion

The findings of the current study document a clear superiority of adenosine over exercise in conjunction with thallium-201 scintigraphy for the detection and localization of coronary artery disease in patients with left bundle branch block. Reversible septal perfusion defects on exercise thallium-201 imaging have been demonstrated in ≈80% of patients with left bundle branch block and normal coronary arteries (6–10). These artifactual septal defects are seen much less commonly with adenosine imaging, thereby markedly improving the specificity of the test in the coronary arteries subtending the septum (the left anterior descending and right coronary arteries). Similar findings have been described previously in two small series using dipyridamole thallium scintigraphy (11,12).

Adenosine and left bundle branch block. As experience accumulates, adenosine is proving to be a highly useful pharmacologic adjunct to perfusion imaging. With infusion rates between 100 and 140 μg/kg per min, the coronary blood flow velocity increases to ≈4.4 times baseline (14–16). Adenosine is equivalent to papaverine in its ability to induce maximal coronary arteriolar vasodilation and increase coronary blood flow. Because adenosine can reliably unmask coronary flow reserve, it is highly accurate in identifying hemodynamically significant coronary artery disease (17–21). Intravenous adenosine infusion as a pharmacologic stress has been proved to be safe in several large series. The major problem encountered in the current series and in most previous adenosine thallium series was heart block (18–25). Second- or third-degree heart block was noted in 6% of our patients with left bundle branch block. This prevalence is similar to the 5% prevalence of AV block noted in a meta-analysis of nearly 1,500 patients without left bundle branch block (18). Adenosine induces AV block through a direct action on the AV node (26,27). Thus, it is not surprising that the infra-HS disease in patients with left bundle branch block does not predispose these patients to AV block during adenosine infusion.

Although the incidence of side effects with adenosine was high, chest pain and dyspnea accounted for the majority of the complaints. Furthermore, chest pain (36%) and dyspnea (57%) were equally as common in the patients who underwent exercise testing. Serious sequelae from the adenosine infusion were not observed in any of the 117 patients who received the agent.

Etiology of septal artifacts. The etiology of the relative septal hypoperfusion noted during exercise in patients with left bundle branch block remains unknown, although two plausible hypotheses have been offered. In patients with left bundle branch block, septal depolarization occurs at the

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very end of systole. The regional myocardial compressive effects may restrict blood flow during early diastole, when most perfusion normally occurs. As the heart rate increases and diastole shortens, the relative septal hypoperfusion becomes more apparent. Alternatively, with greatly delayed septal activation, the myocardium in this region encounters a decreased afterload relative to that of other left ventricular segments during exercise. This may result in a relative reduction in blood flow to the septum during exercise as a result of coronary autoregulatory mechanisms. The results from two reports using a canine model of left bundle branch block support the former explanation (9,28). These studies found that septal intramyocardial pressure was increased during diastole in dogs with left bundle branch block and resulted in relative hypoperfusion, without true ischemia, in the septum. The rate-related relative septal hypoperfusion noted during exercise would not be expected to be a major problem with adenosine thallium imaging. Although the specificity of thallium imaging in patients with left bundle branch block is improved by using adenosine rather than exercise as the stressor, false positive tests continued to be an occasional problem, especially in the territory perfused by the left anterior descending coronary artery where the specificity was 72%. This finding is perhaps due to the mean increase in heart rate of 11 beats/min during adenosine infusion, even though this increase is lower than the increase noted during exercise (58 ± 18 beats/min increase). One of the two patients with a false positive adenosine thallium test was noted to have a reversible septal defect. That patient's heart rate increased to a greater degree than that of any of the patients with normal adenosine thallium studies (from 61 beats/min at rest to 85 beats/min during the infusion). The other patient with a false positive study was noted to have a "patchy" reversible defect in the left anterior descending coronary artery territory and idiopathic cardiomyopathy was subsequently diagnosed.

Matzer and colleagues (29) have reported an interpretation technique whereby the presence of a reversible apical perfusion defect, in addition to the septal abnormality, is required for the diagnosis of left anterior descending ischemia on exercise thallium tomographic imaging in patients with left bundle branch block. This technique appeared to improve the specificity of exercise thallium imaging in the left anterior descending coronary artery territory. The application of these principles to the occasional patient with left bundle branch block and equivocal septal defects despite adenosine thallium imaging might help to further improve the specificity of the adenosine thallium study.

Need for cardiac catheterization. Adenosine thallium scintigraphy reduced the cardiac catheterization rate by 19% (from 55% in the exercise group to 36% in the adenosine group) in this series of patients with left bundle branch block. The incidence of artifactual reversible septal perfusion defects in the exercise thallium group was 35%. Thus, the increased rate of catheterization in those patients who underwent exercise thallium scintigraphy could be accounted for entirely by the occurrence of septal artifacts. From these data, it is apparent that the continued use of exercise as an adjunct to thallium scintigraphy in this subset of patients not only will compromise diagnostic accuracy but also may expose the patients to unnecessary risk and expense.

Because the cardiac catheterization rate was relatively low, the problem of underdiagnosis of coronary artery disease with adenosine thallium scintigraphy was not definitely excluded by this trial. However, none of the 29 patients with normal adenosine thallium study results experienced a cardiac event during follow-up. Previous investigations (19–22,30,31) have shown concordantly high sensitivity levels with adenosine perfusion scintigraphy. Adenosine thallium scintigraphy also improves the specificity of the test in patients without cardiac symptoms or a previous cardiac history. It is this subgroup of patients with left bundle branch block that has previously been among the most problematic for exercise thallium imaging. In these low risk patients, adenosine thallium imaging should obviate the need for unnecessary invasive evaluation.

Dipyridamole and left bundle branch block. Intravenous dipyridamole thallium scintigraphy has also been shown to improve diagnostic accuracy in patients with left bundle branch block over that obtained with exercise thallium imaging. Burns and colleagues (11) studied 10 patients with both exercise and dipyridamole thallium single-photon emission computed tomographic (SPECT) imaging. The specificity for the detection of left anterior descending coronary artery disease was 33% and 100% during exercise and dipyridamole thallium imaging, respectively. Rockett and coworkers (12) evaluated 19 patients with left bundle branch block using dipyridamole SPECT thallium scintigraphy and reported a low incidence of false positive septal perfusion defects. Intravenous dipyridamole induces marked coronary arteriolar vasodilation and increases coronary blood flow by reducing uptake and blocking degradation of endogenous adenosine. Because adenosine and dipyridamole share this final common pathway, it is not surprising that both of these agents appear to enhance the diagnostic accuracy of thallium scintigraphy in patients with left bundle branch block. A study (30) comparing these two agents in 15 patients who underwent pharmacologic stress scintigraphy (not necessarily for left bundle branch block) was recently reported. Adenosine and dipyridamole produced highly concordant diagnostic accuracies in that study. Transient minor side effects were seen more often in adenosine-treated patients, but serious adverse effects, such as hypotension and ischemia, occurred more frequently and persisted longer in the dipyridamole group. In a large series (32), intravenous dipyridamole has been shown to result on rare occasions in myocardial infarction and even death. These effects may prove to be less of a problem with adenosine because of its shorter duration of action and intrinsic cardioprotective effects (33). Further studies comparing adenosine and dipyridamole will be required to establish the relative safety and efficacy of the two agents in patients with and without left bundle branch block.

Limitations of the study. More than half of the patients who underwent exercise thallium scintigraphy in the current study were enrolled during the 20 months preceding the initiation of adenosine thallium scintigraphy at our institution. Once adenosine was available, we began to routinely use this agent for pharmacologic perfusion imaging in patients with left bundle branch block. Thus, there was a temporal dispersion in the enrollment of these two groups of patients and they do not truly represent concurrent cohorts. Throughout the course of the study, the imaging equipment and protocols in our nuclear laboratory did not change significantly, except for the use of prone imaging (34) in men during an 18-month period. Because of the temporal dispersion in the enrollment of the two groups, a higher proportion of patients in the adenosine thallium group (49%) than in the exercise thallium group (16%) underwent imaging in the prone position. However, the predictive accuracy of adenosine thallium scintigraphy was similar in patients who underwent imaging in the supine (86%) and prone (96%) positions (p = NS). Furthermore, the combined specificity of adenosine thallium imaging in the coronary arteries subtending the system (the left anterior descending and right coronary arteries) was 80% using supine positioning and 85% using prone positioning, compared with 42% for exercise thallium scintigraphy.

The patients referred to the cardiac catheterization laboratory represent a very select subgroup chosen on the basis of their abnormal thallium results. A higher percentage of patients in the exercise thallium group than in the adenosine thallium group were referred for cardiac catheterization. This finding undoubtedly reflects the higher incidence of artifactual (false positive) septal defects seen with exercise thallium than with adenosine thallium scintigraphy. This referral bias probably accounts for the relatively small proportion of patients judged to have normal coronary arteries on subsequent angiography. The true specificity of the diagnostic modalities remains somewhat uncertain because of this limitation. The angiographic data were analyzed by visual interpretation without adjunctive quantitative techniques. This method has been shown to be suboptimal and renders the coronary angiographic data less reliable.

Some investigators (24) have suggested that the side effects related to intravenous adenosine infusion are exacerbated by the use of a single intravenous port for injection of both adenosine and thallium (as a result of the displacement of a column of adenosine in the intravenous tubing or arm vein, or both, into the central circulation). The incidence of serious side effects in the current study (6% incidence of AV block) is similar to that reported in previously published adenosine thallium series (18–23). Furthermore, in the current study, the AV block occurred at a mean of 2.4 min into the adenosine infusion, and well before the thallium was injected in all but one patient (in whom the AV block developed at 4 min 12 s). The added patient discomfort and the time delay involved with the placement of a second intravenous port does not appear to be warranted on the basis of these findings. Finally, the conclusions in the current study were based on results obtained with tomographic thallium imaging. Thus, these findings should not be generalized to planar thallium scintigraphy.

Conclusions. Adenosine infusion was superior to exercise in conjunction with thallium scintigraphy for the detection and localization of coronary artery disease in this series of 173 patients with left bundle branch block. Adenosine appeared to obviate septal artifacts and resulted in improved specificity in the left anterior descending and right coronary arteries. These findings suggest that pharmacologic stress perfusion imaging with adenosine should be strongly considered as a preferred noninvasive diagnostic modality for suspected coronary artery disease in patients with left bundle branch block.

References

1. Lev M, Unger PN, Rosen KM, Bharati S. The anatomic base of the electrocardiographic abnormality of left bundle branch block. Adv Cardiol 1975;14:16–24.
2. Herbert WH. Left bundle branch block and coronary artery disease. J Electrocardiol 1975;8:317–24.
3. Brake CM. Complete left bundle branch block and asymptomatic airmen. Aerosp Med 1969;40:781–2.
4. Surawicz B, Saito S. Exercise testing for detection of myocardial ischemia in patients with abnormal electrocardiogram at rest. Am J Cardiol 1978;41:943–51.
5. Bramlet DA, Morris KG, Coleman RE, Albert D, Cobb FR. Effects of rate-dependent left bundle branch block on global and regional left ventricular function. Circulation 1983;67:1059–65.
6. DePuey EG, Guertler-Krawczynska E, Robbins WL. Thallium-201 SPECT in coronary artery disease patients with left bundle branch block. J Nucl Med 1988;29:1479–85.
7. Braat SH, Brugada P, Bar FW, Gorgels AP, Wellens HJJ. Thallium-201 exercise scintigraphy and left bundle branch block. Am J Cardiol 1985;55:224–6.
8. Marin HE, Rodriguez PL, Castro BJM, Pey IJ, Asin CE. Thallium-201 exercise scintigraphy in patients having complete left bundle branch block with normal coronary arteries. Int J Cardiol 1987;16:43–6.
9. Hirzel HO, Senn M, Nuesch K, et al. Thallium-201 scintigraphy in complete left bundle branch block. Am J Cardiol 1984;53:764–9.
10. Huerta EM, Padial LR, Beiras JMC, et al. Thallium-201 exercise scintigraphy in patients having complete left bundle branch block with normal coronary arteries. Int J Cardiol 1987;16:43–6.
11. Burns RJ, Galligan L, Wright LM, Lawand S, Burke RJ, Gladstone PJ. Improved specificity of myocardial thallium-201 single-photon emission computed tomography in patients with left bundle branch block by dipyridamole. Am J Cardiol 1991;68:504–8.
12. Rockett JF, Wood WC, Moinuddin M, Loveless V, Parrish B. Intravenous dipyridamole thallium-201 SPECT imaging in patients with left bundle branch block. Clin Nucl Med 1990;15:401–7.
13. Bateman TM, O'Keefe JH Jr. Pharmacological (stress) perfusion scintigraphy: methods, advantages, and applications. Am J Card Imaging 1992;6:3–15.
14. Kern MJ, Deligonul U, Tatineni S, Serota H, Aguirre F, Hilton TC. Intravenous adenosine: continuous infusion and low dose bolus administration for determination of coronary vasodilator reserve in patients with and without coronary artery disease. J Am Coll Cardiol:18:718–29.
15. Wilson RF, Wyche K, Christensen BV, Zimmer S, Laxson DD. Effects of adenosine on human coronary arterial circulation. Circulation 1990;82:1595–606.
16. Rossen JD, Quillen JE, Lopez AG, Stenberg RG, Talman CL, Winniford

MD. Comparison of coronary vasodilation with intravenous dipyridamole and adenosine. J Am Coll Cardiol 1991;18:485–91.

17. Maddahi J, Van Train K, Prigent F, et al. Quantitative single photon emission computerized thallium-201 tomography for evaluation of coronary artery disease: optimization and prospective validation of a new technique. J Am Coll Cardiol 1989;14:1689–99.
18. O'Keefe JH Jr, Bateman TM, Silvestri R, Barnhart C. Safety and diagnostic accuracy of adenosine thallium-201 scintigraphy in patients unable to exercise and those with left bundle branch block. Am Heart J 1992;124:614–21.
19. Nishimura S, Mahmarian JJ, Boyce TM, Verani MS. Quantitative thallium-201 single-photon emission computed tomography during maximal pharmacologic coronary vasodilation with adenosine for assessing coronary artery disease. J Am Coll Cardiol 1991:18:736–45.
20. Nguyen T, Heo J, Ogilby JD, Iskandrian AS. Single photon emission computed tomography with thallium-201 during adenosine-induced coronary hyperemia: correlation with coronary arteriography, exercise thallium imaging and two-dimensional echocardiography. J Am Coll Cardiol 1990;16:1375–83.
21. Coyne EP, Belvedere DA, Vande Streck PR, Weiland FL, Evans RB, Spaccavento LJ. Thallium-201 scintigraphy after intravenous infusion of adenosine compared with exercise thallium testing in the diagnosis of coronary artery disease. J Am Coll Cardiol 1991;17:1289–94.
22. Verani MS, Mahmarian JJ, Hixson JB, Boyce TM, Staudacher RA. Diagnosis of coronary artery disease by controlled coronary vasodilation with adenosine and thallium-201 scintigraphy in patients unable to exercise. Circulation 1990;82:80–7.
23. Abreu A, Mahmarian JJ, Nishimura S, Boyce TM, Verani MS. Tolerance and safety of pharmacologic coronary vasodilation with adenosine in association with thallium-201 scintigraphy in patients with suspected coronary artery disease. J Am Coll Cardiol 1991;18:730–5.
24. Cave V, Heo J, Cassel D, Iskandrian B, Iskandrian AS. Side effects during adenosine thallium imaging using single or double port infusion protocols (abstr). J Am Coll Cardiol 1991:19(suppl A):312A.
25. Nguyen T, Heo J, Paugh B, Iskandrian A. Atrioventricular block during adenosine-thallium imaging (abstr). Circulation 1990;82(suppl III):III-731.
26. Belardinelli L, Linden J, Berne RM. The cardiac effects of adenosine. Prog Cardiovasc Dis 1989;32:73–97.
27. DiMarco JP, Sellers TD, Berne RM, West FA, Belardinelli L. Adenosine: electrophysiologic effects and therapeutic use for terminating paroxysmal supraventricular tachycardia. Circulation 1989;68:1254–63.
28. Ono S, Nohara R, Kambara H, Okuda K, Kawai C. Regional myocardial perfusion and glucose metabolism in experimental left bundle branch block. Circulation 1992;85:1125–31.
29. Matzer L, Kiat H, Friedman JD, Van Train K, Maddahi J, Berman DS. A new approach to the assessment of tomographic thallium-201 scintigraphy in patients with left bundle branch block. J Am Coll Cardiol 1991;17:1309–17.
30. Vermeersch P, Verzijlbergen F, Cramer M-J, Ascoop C. Intravenous adenosine versus intravenous high dose dipyridamole, both in combination with low level exercise, in the same patients using technetium-99m SESTAMIBI SPECT myocardial perfusion imaging (abstr). J Am Coll Cardiol 1992;19(suppl A):311A.
31. Nishimura S, Mahmarian JJ, Boyce TM, Verani MS. Equivalence between adenosine and exercise thallium-201 myocardial tomography. A multicenter, prospective, crossover trial. J Am Coll Cardiol 1992;20:265–75.
32. Ranhosky A, Kempthorne-Rawson J, for the Intravenous Dipyridamole Thallium Imaging Study Group. The safety of intravenous dipyridamole thallium myocardial perfusion imaging. Circulation 1990;81:1205–9.
33. Ely SW, Berne RM. Protective effects of adenosine in myocardial ischemia. Circulation 1992;85:893–904.
34. Kiat H, Van Train KF, Friedman JD, et al. Quantitative stress-redistribution thallium-201 SPECT using prone imaging: methodologic development and validation. J Nucl Med 1992;33:1509–15.