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# Dobutamine Thallium-201 Myocardial SPECT in Patients with Left Bundle Branch Block and Normal Coronary Arteries

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Dobutamine is a positive inotropic and chronotropic agent and is being widely used as a pharmacologic stress agent in patients unable to achieve maximal dynamic exercise test. The purpose of the current study was to document the dobutamine induced false-positive septal defect in terms of its frequency and extent on $^{201}$Tl myocardial SPECT in patients with left bundle branch block (LBBB). **Methods:** Twenty-five symptomatic patients with LBBB underwent dobutamine and redistribution $^{201}$Tl myocardial SPECT studies. Coronary angiographies were also performed. Only those patients with normal coronaries (n = 19) were included in the study. For each study, tomograms were divided into 19 segments, and each segment was analyzed qualitatively as to presence and type of perfusion defect (reversible or fixed). In addition, septal perfusion was scored in each patient (1 = markedly, 2 = moderately reduced, 3 = normal uptake). **Results:** Sixteen of 19 patients (84.21%) had false-positive septal reversible perfusion defect, and the remaining 3 had normal images. Perfusion defects were confined to only the septum in 5 of 16 patients (31.25%), whereas a greater proportion of patients had septal defect extending to the contiguous myocardial areas, mainly to the anterior wall. Five of 16 patients with false-positive defects had a septal perfusion score of 1, while the remaining 11 had a score of 2. **Conclusion:** Dobutamine myocardial scintigraphy in patients with LBBB was misleading for the diagnosis of coronary artery disease, since up to 84.21% of patients had false-positive septal perfusion defects.

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Dynamic exercise testing is the usual method of stress testing for myocardial perfusion scintigraphy. However, it is not ideal for detection of coronary artery disease in patients with left bundle branch block (LBBB) due to the high percentage of false-positive septal defects (*1–3*). For patients who are unable to exercise, alternative pharmacological stress agents to detect coronary artery disease have been developed. Dobutamine is one such agent with an accuracy and sensitivity similar to dynamic exercise or dipyridamole (*4–7*).

As a positive inotropic and chronotropic agent, dobutamine produces similar physiologic effects as exercise. Therefore, it is theoretically possible that dobutamine can induce false-positive septal abnormalities in patients with LBBB. This study was designed to determine the frequency of dobutamine-induced false-positive septal defects and the extent of such defects in patients with LBBB and normal coronary arteriograms.

## MATERIALS AND METHODS

### Patients

We studied 25 consecutive patients with LBBB and chest pain who were referred for dobutamine thallium myocardial perfusion scintigraphy followed by cardiac catheterization. Informed written

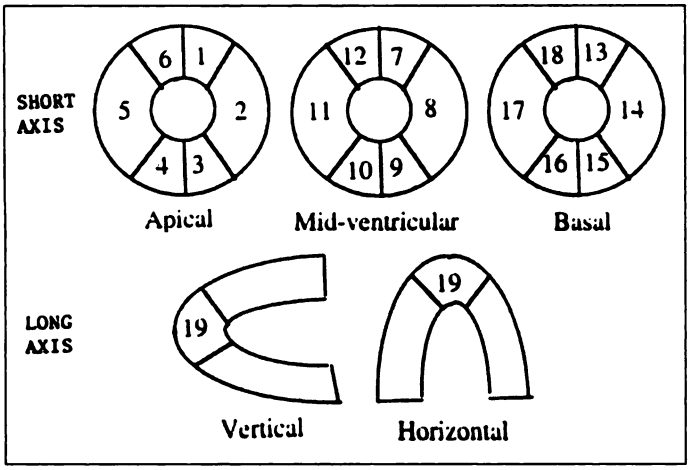


**FIGURE 1.** Myocardial segmentations used to indicate location of dobutamine SPECT $^{201}$Tl defects. Segments 1, 6, 7, 12, 13 and 18 are anterior; 5, 11, 17 are septal; 3, 4, 9, 10, 15 and 16 are inferior, 19 is apex.

consent was obtained from each patient. The interval between $^{201}$Tl SPECT and coronary angiography ranged between 3–38 days. Coronary angiography was performed using the Judkins technique, and a luminal narrowing greater than 50% was defined as a significant lesion. Nineteen patients had normal coronary arteries and the remaining six had significant coronary artery disease. To study the pure effect of underlying LBBB on dobutamine $^{201}$Tl SPECT, only patients with normal coronary arteries (n = 19; 14 women, 5 men; age range 32–70 yr) were included in the study. None of these patients participating in the study had heart failure, cardiomyopathy or valvular heart disease. All had normal left ventricular ejection fractions.

### Dobutamine Infusion Protocol

Beta-blockers were discontinued for 48 hr before the dobutamine stress test. Dobutamine was infused starting from 10 μg/kg/min infusion rate to a maximum of 40 μg/kg/min. The dose was increased at 3-min intervals. The total infusion time was 12 min. ECG and blood pressure were recorded every minute during the infusion. Four millicuries (148 MBq) of $^{201}$Tl were injected 1 min before cessation of peak dose, or earlier if any significant adverse effect occurred, such as chest pain, dyspnea, significant ECG (any ST-segment elevation or depression more than 1 mm) or blood pressure changes (diastolic blood pressure >110 and systolic blood pressure >240 mmHg or a sudden decrease in systolic blood pressure ≥20 mmHg compared with baseline). Infusion was maintained for 1 min more. Atropine (up to a maximum of 1 mg) was added when 85% of age-predicted maximum heart rate had not been achieved 9 min into the study. A syringe pump was used for dobutamine infusion.

### Imaging Protocol

Data were acquired with a single-head gamma camera equipped with a LEAP collimator. Dobutamine $^{201}$Tl SPECT images were taken approximately 5–7 min after completion of infusion using a circular orbit starting from the 45° right anterior oblique to the 45° left posterior oblique projection. Sixty-four projections were obtained using a 64 × 64 matrix for 20 sec per frame. Imaging was performed using a 20% window centered on the 69–83 keV mercury x-rays. Four hours after $^{201}$Tl injection, the patients underwent the redistribution study. No attenuation correction was applied to the images. A Butterworth filter with a cutoff frequency of 0.35 cycles/cm was used for tomographic reconstruction, and transaxial tomographic slices were obtained. From the transaxial images, vertical and horizontal long-axis slices were generated. No reinjection study was performed.

### Image Interpretation

Two experienced nuclear physicians qualitatively interpreted the stress and redistribution $^{201}$Tl slices of each patient. To analyze the extent of the perfusion defect more precisely, tomograms were divided into 19 segments representative of apical, midventricular and basal cuts of the short-axis and midventricular horizontal and vertical long-axis (Fig. 1). The following two points were investigated on the tomographic images:

1. Presence or absence of perfusion defect in a segment and defect type (reversible or fixed). Presence of a reversible perfusion defect was decided when a defect on the stress study showed partial or complete redistribution on the redistribution study.
2. Septal perfusion score. The degree of septal perfusion compared to the maximal activity seen in the reference area, mainly the lateral myocardium, was determined visually and graded on a scale from 1 to 3 (1 = markedly, 2 = moderately reduced uptake, 3 = normal uptake).

Disagreements were resolved by consensus.

### Statistical Analysis

Hemodynamic parameters are presented as mean value ± s.d. Variables were compared using Student's t-test for paired data. A p value of ≤0.05 was considered statistically significant.

## RESULTS

### Changes in Hemodynamic Parameters During Dobutamine Infusion

At the peak dobutamine infusion rate, mean heart rate significantly increased compared to basal value (158.1 ± 13 $min^{-1}$ versus 79.4 ± 13.7 $min^{-1}$). The mean of maximal systolic blood pressure achieved during the infusion (146 ± 27.1 mmHg) was slightly but not significantly higher than that of the basal value (140 ± 19 mmHg, $p > 0.05$). Whereas, the decrease in diastolic blood pressure was significant (from 90 ± 10.6 to 83.9 ± 14.2 mmHg, $p < 0.05$). All patients, but one, achieved 85% of their age-predicted maximal heart rate during dobutamine infusion. Eight of 19 patients received 0.5 mg of atropine to reach target heart rate at 9 min during infusion.

### Side Effects of Dobutamine Infusion

Seven of 19 patients reported no side effects, while the remaining 12 patients reported various side effects. Two of the patients had a sudden decrease in systolic blood pressure accompanied by a decrease in diastolic blood pressure and heart rate that required premature termination of the dobutamine infusion at the dose of 30 μg/kg/min and atropine injection for recovery. Patients also reported the following symptoms: palpitation, n = 4; flushing, n =2; dyspnea, n = 3; headache, n = 2; chest discomfort, n = 2; dizziness, n = 5; nausea, n = 1. These symptoms were largely self-limited and no medication was applied to resolve such symptoms. Arrythmias were recorded on the ECGs of five patients (n = 4, occasional premature ventricular contraction and n = 1, ventricular tachycardia).

### Scintigraphic Findings

The scintigraphic findings are summarized in Table 1. Dobutamine $^{201}$Tl scintigrams revealed that 16 of 19 patients (84.21%) had a septal defect (with or without extension to the contiguous myocardial segments), and the remaining 3 had normal myocardial perfusion. All perfusion defects were reversible.Various patterns of perfusion defects in terms extent of defects were revealed:

1. Defect limited to septal area only (n = 5).

**TABLE 1**
Scintigraphic and Angiographic Data of Patients with LBBB

| Patient no | Age (yr) | Sex | % Achieved heart rate ($min^{-1}$)* | Scintigraphy: Area of perfusion detect | Scintigraphy: Septal perfusion score | Cardiac catheterization: Coronaries | Cardiac catheterization: EF (%) |
|---|---|---|---|---|---|---|---|
| 1 | 45 | M | 92 | Segments 5, 11, 17 | 2 | RCA 40% | 65 |
| 2 | 65 | F | 90 | Segments 10, 11, 16, 17 | 1 | Normal | 60 |
| 3 | 64 | F | 90 | Segments 5, 11, 17 | 2 | Normal | 68 |
| 4 | 56 | M | 89 | None | 3 | Normal | 58 |
| 5 | 61 | F | 100 | Segments 5, 11, 12, 17, 18 | 1 | Normal | 67 |
| 6 | 61 | F | 97 | Segments 5, 11, 17 | 2 | Normal | 65 |
| 7 | 58 | M | 99 | Segments 11, 12, 17, 18 | 2 | Normal | 65 |
| 8 | 53 | F | 90 | None | 3 | Normal | 55 |
| 9 | 62 | F | 100 | Segments 5, 11, 17 | 2 | Normal | 72 |
| 10 | 32 | F | 100 | Segments 5, 6, 11, 12, 17, 18, 19 | 2 | Normal | 50 |
| 11 | 57 | F | 98 | Segments 5, 11, 12, 17, 18 | 2 | Normal | 60 |
| 12 | 55 | F | 90 | Segments 5, 11, 12, 17, 18 | 1 | Normal | 69 |
| 13 | 70 | F | 100 | Segments 6, 11, 17, 18 | 2 | Normal | 60 |
| 14 | 65 | F | 100 | None | 3 | Normal | 54 |
| 15 | 60 | F | 100 | Segments 4, 10, 11, 12, 16, 17, 18, 19 | 2 | Normal | 72 |
| 16 | 35 | M | 97 | Segments 11, 17 | 2 | Normal | 51 |
| 17 | 57 | F | 80 | Segments 5, 11, 12, 17, 18 | 2 | Normal | 63 |
| 18 | 61 | F | 94 | Segments 5, 11, 12, 17, 18 | 1 | Normal | 58 |
| 19 | 60 | M | 100 | Segments 5, 6, 10, 11, 12, 16, 17, 18, 19 | 1 | Normal | 66 |

* Percentage of maximum age-prdicted heart rate.

2. Septal defect extending to contiguous anterior segment (n = 7).
3. Septal defect extending to contiguous inferior segments (n = 1).
4. Septal defect extending to contiguous anterior and apical segments (n = 1).

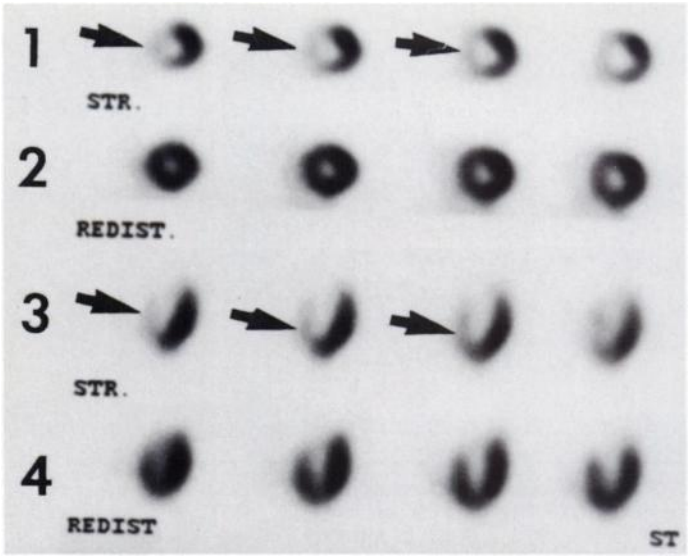


**FIGURE 2.** Short-axis and horizontal long-axis (rows 1 and 3, respectively) dobutamine $^{201}$Tl and corresponding redistribution tomograms (rows 2 and 4) in a 55-yr-old woman (Patient 12) with LBBB and normal coronary arteriograms. A reversible septal is seen extending to contiguous anterior regions (arrows).

5. Septal defect with extension to contiguous anterior, inferior and apical segments (n = 2).

Five of 16 patients (31.25%) with false-positive septal defects (whether or not there was extension to other areas) had a severity score of 1 (markedly reduced), while 11 had a score of 2 (moderately reduced). A representive case with marked false-positive septal defect is seen in Figure 2.

## DISCUSSION

A high percentage of false-positive septal defects is a well-known phenomenon on exercise $^{201}$Tl myocardial perfusion scintigraphy in patients with LBBB (*1–3*). The etiology of such false-positive perfusion defects remains unknown, although some hypotheses have been offered (*1,2,8*). Hirzel et al. (*1*) reported on 19 patients with anteroseptal defects in whom coronary angiography was performed and found that left anterior coronary artery disease was present in only 21% of the patients, leaving 79% with normal perfusion to the septum. DePuey et al. (*2*) reported that 9/10 patients (90%) with LBBB had false-positive septal perfusion defects, indicating that in the presence of LBBB, exercise $^{201}$Tl SPECT was indeterminate for coronary artery disease. Moreover, at higher peak heart rates (>170 bpm) septal abnormalities were most marked. However, in another study performed in a large population of unselected patients, the authors reported that only 14% of patients with LBBB had septal defects on exercise $^{201}$Tl planar images, concluding that exercise $^{201}$Tl imaging remains a useful procedure for evaluating patients with complete LBBB (*9*).

Dobutamine as a positive inotropic and chronotropic agent produces physiologic effects similar to exercise. Therefore, it is logical that dobutamine can induce false-positive septal abnormalities in patients with LBBB. Reports on dobutamine-induced false-positive septal perfusion abnormalities are rather limited. So far, only three patients with LBBB who underwent

dobutamine $^{201}$Tl myocardial scintigraphy have been reported (*10,11*). In one of these patients, planar myocardial scintigraphy was performed, which revealed false-positive septal and periapical perfusion defects. The authors noted that SPECT might reveal more extensive and marked defects (*10*). In the other two patients with LBBB and normal coronary arteriograms, SPECT myocardial scintigrams demonstrated septal defects. There were no detailed data on the extent and severity of perfusion defects (*11*). To investigate such defects in terms of their frequency, location and severity, this study was performed, and dobutamine myocardial $^{201}$Tl SPECT studies of 19 patients with LBBB and normal coronary arteriograms were evaluated. The location of perfusion defects was studied in detail by analysis of the myocardium segmentally. A high percentage (84.12%) of false-positive septal defects was found in our patients, which raises concern over the usefulness of dobutamine $^{201}$Tl imaging in patients with LBBB when diagnosing coronary artery disease. Since none of the 19 patients studied had any associated disease that could cause perfusion defects such as cardiomyopathies or valve disease, all septal perfusion defects were attributed to the presence of LBBB. It is of interest that not all patients with LBBB exhibited abnormal septal perfusion; this might be secondary to the existence of different behaviors in LBBB situations. In 16 patients with false-positive septal abnormalities, all defects were not present on the redistribution studies, indicating that LBBB-induced functional septal ischemia was reversible.

There are contradictory results about the relationship between the level of heart rate achieved and the development of false-positive perfusion defects on exercise $^{201}$Tl myocardial images in patients with LBBB. Jazmati et al. (*9*) claimed that the level of exercise achieved played no role in the development of septal defects. In contrast, some other investigators reported that at higher peak heart rates septal abnormalities were most marked (*2,12*). In our study, all patients but one reached ≥85% of age-predicted heart rate. Moreover, although they reached a similar extent of heart rate, the severity score of perfusion defects was not always marked (Table 1). It is also interesting that there were three patients with normal septal perfusion, although they achieved at least ≥85% of their maximal predicted heart rate (Patients 4, 8, 14).

The use of atropine with dobutamine is not routinely done with perfusion imaging. It was shown that an addition of up to 1 mg of atropine to dobutamine stress echocardiography in patients whose test results were negative and who did not achieve 85% predicted maximal heart rate during dobutamine infusion alone increased the sensitivity of the test for detection of coronary artery disease without loss of specificity (*13*). There are some other authors who use atropine during dobutamine myocardial scintigraphy to augment the heart rate, reasoning that the higher the heart rate achieved, the more chance there is for myocardial ischemia (*7*). Therefore, atropine injection was also used in eight of our patients when they did not achieve 85% predicted maximal heart rate.

Dipyridamole or adenosine has been suggested to be the best alternative when diagnosing coronary artery disease in patients with LBBB since they induce only a slight increase in heart rate but do not cause some impairment of septal blood flow. However, false-positive results have been reported (*14,15*).

### Study Limitations

Assessment of the overall sensitivity of dobutamine $^{201}$Tl imaging was not the intent of this study. Our purpose was to reveal the frequency of septal false-positive perfusion defects in the presence of LBBB. Therefore, this study was confined to only those patients with angiographically normal coronary arteries. Moreover, sensitivity of dobutamine myocardial scintigraphy has been well established in previous reports (*4–7*). Our patient population was small, but patients with LBBB and normal coronary arteries are not always easy to find.

## CONCLUSION

These data demonstrate that dobutamine is not a suitable pharmacological stress test when diagnosing coronary artery disease with myocardial perfusion scintigraphy in patients with LBBB, since up to 84.21% of patients have false-positive septal perfusion defects.

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