# Prognostic Value of Myocardial Perfusion Imaging with Exercise and/or Dipyridamole Hyperemia in Patients with Preexisting Left Bundle Branch Block

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The detection of myocardial ischemia in patients with preexisting left bundle branch block (LBBB) remains problematic. Pharmacologic hyperemia with dipyridamole is now used routinely in such patients for detection of significant coronary artery disease. Little data exists on the prognostic value of cardiac nuclear scintigraphy in patients with preexisting LBBB. The purpose of our study was to determine the prognostic value of cardiac nuclear scintigraphy in patients with preexisting LBBB. **Methods:** Ninety-six patients with preexisting LBBB underwent perfusion imaging between July 1987 and June 1995. Thirty-seven underwent planar $^{201}$Tl imaging, and 59 underwent SPECT sestamibi imaging. Images were interpreted by consensus of two experienced observers and classified as normal, abnormal low risk and abnormal high risk. Outcomes measured were survival, cardiac and noncardiac death. The final study group included 43 women and 53 men, aged 42–83 (mean 66 ± 9). Average follow-up was 3.4 ± 2.1 yr. **Results:** Of the 96 patients examined, 31 had normal scans, 39 had low-risk scans and 26 had high-risk scans. At the end of the study period, 27 patients with normal scans were still alive while 2 suffered cardiac death and 2 suffered noncardiac death. Of those with low-risk scans, 36 survived while 2 suffered cardiac death and 1 suffered noncardiac death. Finally, of those with high-risk scans, 17 survived while 8 suffered cardiac death and 1 suffered noncardiac death (chi-square test, $p = 0.020$). **Conclusion:** Dipyridamole imaging is an important prognostic tool for predicting future cardiac events in patients with preexisting LBBB and aids in their risk stratification for coronary artery disease.

**Key Words:** left bundle branch block; dipyridamole; prognosis; coronary artery disease

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The detection of myocardial ischemia secondary to significant coronary artery disease remains problematic in patients with preexisting left bundle branch block (LBBB). Exercise electrocardiography is nondiagnostic (*1*). Pharmacologic hyperemia with dipyridamole and $^{201}$Tl imaging is now used routinely in such patients for diagnostic purposes and appears to offer improved specificity over conventional exercise testing with $^{201}$Tl (*1–6*). Nuclear imaging with $^{99m}$Tc sestamibi and dipyridamole is now also used routinely in this population as it appears to offer similar, if not slightly improved, specificity over $^{201}$Tl imaging (*7–9*).

Although used for diagnostic purposes in LBBB, there is little data on the prognostic value of pharmacologic stress testing in such patients (*5*). In our study, we sought to confirm the hypothesis that the prognosis in patients with preexisting LBBB correlates with the size of reversible and irreversible perfusion defects on nuclear cardiac imaging with larger defects being associated with a poorer outcome. Dipyridamole imaging may provide a simple, reliable and noninvasive means of risk stratification as well as predicting future cardiac events and providing a documented rationale before proceeding with more invasive investigations.

## MATERIALS AND METHODS

### Patient Population

From July 1987 to June 1995, a total of 111 patients (43 women, 53 men; age range 42–83 yr; mean age 66 ± 9) with LBBB underwent nuclear cardiac imaging for assessment of real or potential ischemic heart disease. Of those patients, follow-up was possible in 96 (87%) who are included in this study. All patients were required to have complete and permanent LBBB as defined using standard electrocardiographic criteria. Exclusion criteria consisted of incomplete and pacemaker-related LBBB. All patients underwent diagnostic scintigraphy to assess coronary artery disease severity. Average follow-up was 3.4 ± 2.1 yr (range 0.5–8.6 yr). Charts of all patients were reviewed for assessment of baseline clinical characteristics (see Table 1) as well as outcome (survival, cardiac death, noncardiac death). Family physicians and patients were contacted directly when sufficient information was not available from the inpatient and outpatient charts.

### Dynamic Exercise Protocol

Using the Bruce or Naughton protocols, 34 patients completed symptom-limited dynamic exercise between 1987 and January 1992. At peak exercise near the end of the protocol, they were injected with $^{201}$Tl. Eight of these patients also received dipyridamole.

### Pharmacologic Stress Protocol

Beginning in February 1992, the remaining 62 patients underwent scintigraphic examination at rest using dipyridamole and sestamibi (*59*) or $^{201}$Tl (*3*). The protocol used for dipyridamole infusion has been described elsewhere (*2*).

### Scintigraphy

In patients who underwent $^{201}$Tl scans after exercise and/or dipyridamole hyperemia, 85–111 MBq $^{201}$Tl-chloride was injected. Ten min later, multiple planar images were obtained of 10 min duration each using a small field-of-view camera. Three to 4 hr later, redistribution images were obtained in matched view.

Technetium-labeled images were obtained with patients receiving 555 MBq technetium-labeled sestamibi after dipyridamole hyperemia. One hr later, a 20-min perfusion image was obtained using a multiheaded tomographic camera. Rest images were obtained 1 hr following another 555 MBq technetium-labeled sestamibi injection on a subsequent day. Tomographic images were then reconstructed by filtered backprojection, offset corrected and displayed in view slices representing the short axis, vertical long axis and horizontal axis. Images were interpreted by consensus by two experienced practitioners with full knowledge of the stress

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**TABLE 1**
Baseline Characteristics of 96 Patients

| Variable | Alive (n = 80) | Decreased (n = 16) | p value |
|---|---|---|---|
| Age > 70 | 28 (35%) | 11 (69%) | 0.048 |
| Male sex | 48 (60%) | 5 (31%) | 0.14 |
| Cerebrovascular disease | 6 (8%) | 3 (19%) | 0.18 |
| Known coronary disease | 50 (63%) | 12 (75%) | 0.90 |
| Prior myocardial infarct | 33 (41%) | 6 (38%) | 0.17 |
| History of angina | 42 (35%) | 9 (56%) | 0.38 |
| History of congestive heart failure | 22 (28%) | 11 (69%) | 0.0015 |
| Hypertension | 4 (5%) | 3 (19%) | * |
| Prior CABG | 17 (21%) | 4 (25%) | 0.91 |
| Prior PTCA | 17 (21%) | 1 (6%) | * |
| Peripheral vascular disease | 8 (10%) | 1 (6%) | * |
| Diabetes mellitus | 17 (21%) | 2 (13%) | * |
| COPD | 4 (5%) | 1 (6%) | * |
| Renal failure | 2 (3%) | 1 (6%) | 0.43 |

*Sample size too small for statistical interpretation.
CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; PTCA = percutaneous transluminal coronary angioplasty.

electrocardiographic, hyperemic and clinical data. Images were classified as normal when neither fixed nor reversible defects were observed. Abnormal, low-risk scans consisted of the presence of a fixed defect, without additional reversible defects, or reversible defects involving only one or two cardiac segments in a single coronary artery distribution.

High-risk scans were defined by a fixed defect involving three or more cardiac segments and also showing reversible defects in a separate coronary distribution or any scan showing a reversible defect involving four or more cardiac segments in one or more vascular distributions (*10*).

### Statistical Analysis

Analysis was performed using a standard statistical package. The relationship of outcome (death) to scan results was evaluated by chi-square analysis. The relative importance of clinical characteristics to survival was assessed by multivariate analysis using multiple logistic regression.

## RESULTS

Baseline characteristics are noted in Table 1. There was no significant difference in clinical characteristics between patients whether alive or deceased. Age over 70 was more common in the group of deceased patients, 69% versus 29%, respectively, of those still alive ($p = 0.048$). Congestive heart failure was also more common in the group of deceased patients, 69% versus 23%, respectively, ($p = 0.0015$).

Outcome results are noted in Table 2. Among the 31 patients who had normal myocardial perfusion scans, 27 were still alive while 2 patients suffered cardiac deaths, and 2 suffered noncardiac deaths. Thirty-nine patients had low-risk scans, of which 36 were alive, 2 had suffered cardiac deaths and 1 suffered a noncardiac death. Twenty-six patients had high-risk scans, of which 17 survived, 8 suffered cardiac deaths and 2 suffered noncardiac deaths. These results were statistically significant with a chi-square test p value of 0.020.

**TABLE 2**
Results of Scintigraphy

| Scan result | Survival | Cardiac death | Noncardiac death |
|---|---|---|---|
| Normal scan (n = 31) | 27 (87%) | 2 (7%) | 2 (7%) |
| Low-risk scan (n = 39) | 36 (92%) | 2 (5%) | 1 (3%) |
| High-risk scan (n = 26) | 17 (65%) | 8 (31%) | 1 (4%) |

Chi-square p value = 0.020.

In this population, concurrent investigation is common. Cardiac catheterization was performed in 29 patients consequent to the scan (mean 229 ± 353 days), and 10 had cardiac catheterization less than 1 yr prior. Coronary angioplasty was performed in 10 patients subsequent to the test (mean 352 ± 582 days), and another 4 had percutaneous transluminal coronary angioplasty less than 1 yr prior. Finally, 9 patients had undergone surgical revascularization after the scan (mean 419 ± 581 days) with another 3 having had surgery less than 1 yr prior.

## DISCUSSION

Dipyridamole imaging has been shown to be useful in preoperative cardiac risk assessment (*11–21*). Dipyridamole $^{201}$Tl scintigraphy also has significant prognostic value in patients with known or suspected coronary artery disease by predicting future cardiac events (*11, 22–27*). The prognostic use of nuclear scintigraphy in patients with preexisting LBBB, however, has received little attention. In this population, nuclear imaging has focused primarily on diagnostic accuracy as a means of detecting ischemic heart disease. This was first done using exercise $^{201}$Tl imaging, which has been plagued by relatively low specificity for anteroseptal perfusion defects (*1, 28–32*). Postulated mechanisms for these false-positive perfusion defects include enhanced constriction of septal vessels similar to that caused by myocardial bridge, reduced diastolic time for adequate septal perfusion and heterogeneous increase in coronary flow demand in exercising patients (*1–6, 28–32*). Nuclear imaging with dipyridamole is now routinely used instead because it appears to offer improved specificity (*1–6*). The use of $^{99m}$Tc sestamibi has become an attractive alternative to $^{201}$Tl in this population as it appears to provide similar, if not slightly improved, specificity in preliminary studies (*7–9*) along with other technical advantages over $^{201}$Tl (*34, 35*).

In the non-LBBB population, sestamibi imaging using either dynamic or pharmacologic stress protocols has been used to determine the presence and extent of coronary artery disease with very similar results to those seen with $^{201}$Tl imaging (*36–38*).

The prognostic value of sestamibi myocardial perfusion imaging only has recently become established (*34, 39, 40*). Stratmann (*34, 39, 40*) has examined this issue in three separate patient populations with and without the use of dipyridamole. The results indicate that sestamibi is an important prognostic tool for patients with medically treated unstable angina, as well as those with stable angina, with or without the use of dipyridamole. These results are comparable to those seen with $^{201}$Tl imaging (*22–27*).

Krishnan et al. (*5*) were the first to consider the prognostic role of dipyridamole-$^{201}$Tl imaging in patients with LBBB in addition to examining its diagnostic accuracy. In their study of 69 patients followed for a 4-yr period, patients with extensive scintigraphic defects were more likely to be hospitalized for chest pain and underwent more revascularization procedures, which made prognostic interpretation more difficult. Those with relatively low-risk scans were treated medically and achieved a benign outcome with a death rate of only 2.5% per year, which is similar to that seen in asymptomatic individuals with risk factors for ischemic heart disease (*5, 33*).

Our study findings are in agreement with those of Krishnan et

al. (5) with respect to the prognostic value of myocardial imaging in patients with preexisting LBBB. Indeed, cardiac mortality in the group with normal or low-risk scans was approximately 1.8% per year indicating a relatively benign outcome for such patients. In contrast, patients with high-risk scans were subject to a significantly higher risk of cardiac death despite intervention in some of them (9.9% per year versus 1.8% per year; chi-square test p-value = 0.020). Unlike Krishnan's study, however, our study was not concerned with determining which patients in the high-risk group underwent angiography with or without some form of revascularization procedure. The clinical complexity of having diagnostic and therapeutic procedures done both pre- and postscan, as well as multiple procedures being done in some patients, makes statistical analysis of this aspect impossible given the small numbers in the subgroups. Again, despite intervention in some patients, there was still an overall higher risk of death. Further study is indicated to determine the effectiveness of revascularization procedures in this patient population.

## CONCLUSION

Our study has the advantages and disadvantages of any retrospective study. Disadvantages include the lack of control over specific variables as well as difficulties with complete data collection and potentially biased recall. Myocardial perfusion imaging is an important diagnostic tool in patients with preexisting LBBB and symptoms and signs of coronary artery disease. Although scan artifacts have been reported in our group of patients, these can be reduced in frequency by appropriate imaging procedures. Although these scan artifacts may cause confusion when diagnosing coronary artery disease, their prognostic importance is small compared to a high-risk scan and is indistinguishable from a normal study. A high-risk scan appears to be an important prognostic tool for predicting future cardiac events in this patient population and aids in their risk stratification. Dipyridamole $^{201}$Tl scintigraphy as used in this patient population does not weaken this prognostic tool. Further studies are required to more clearly identify the role of myocardial perfusion imaging in the risk stratification of patients with preexisting LBBB. Such studies should be prospective and assess the efficacy of medical and nonmedical management of patients considered high risk.

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