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# Diagnostic and prognostic value of gated myocardial perfusion single-photon emission computed tomography in low-risk patients with left bundle-branch block

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***Background*** **The abnormal left ventricular activation pattern in patients with a left bundle-branch block (LBBB) frequently induces myocardial perfusion defects, decreasing the specificity of noninvasive coronary-risk stratification with stress testing. We assessed the diagnostic and prognostic impact of gated single-photon emission computed tomography (SPECT) in low-risk patients with LBBB.**

***Methods*** **A total of 114 patients underwent dual-day protocol Tc-99m sestamibi gated SPECT and were divided into two subsets: without LBBB (group 1, $n=57$) and with LBBB (group 2, $n=57$). Sixty-eight (60%) patients had negative coronary angiography and 46 (40%) were at a low risk for coronary artery disease. The variables incorporating the extent and severity of perfusion defects were calculated: summed stress score, summed rest score and summed difference score, end-diastolic volume (EDV), end-systolic volume (ESV), and left ventricular ejection fraction. The mean variations in EDV and ESV were computed as follows: rest volume − poststress volume. Cardiac events were classified as major and minor.**

***Results*** **Gated SPECT was positive in eight (14%) patients of group 1 and 33 (58%) patients of group 2 ($P<0.001$). The summed stress score was significantly higher in group 2 than in group 1 ($4.7\pm4.8$ vs. $0.9\pm1.8$, $P<0.001$); similarly, EDV and ESV were significantly higher in LBBB patients ($P<0.05$ in both). The mean variation in EDV was −2.21 ml for group 1 and 1.32 ml for group 2 ($P<0.05$). After a mean follow-up period of $32\pm19$ months, cardiac events occurred in 22 (23%) patients, six of group 1 and 16 of group 2 (12 vs. 35%, $P<0.01$).**

***Conclusion*** **Functional and perfusion parameters obtained by gated SPECT are different between patients with and without LBBB. In LBBB patients, the decrease in EDV between rest and poststress could be considered an early marker of diastolic dysfunction that might anticipate left ventricular ejection fraction reduction and may have an impact on prognosis.** ***Nucl Med Commun*** **33:491–497**


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**Keywords: coronary artery disease, left bundle-branch block, myocardial perfusion imaging, prognosis**

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## Introduction

Complete left bundle-branch block (LBBB) is a common ECG disorder that is often associated with coronary artery disease (CAD) [1]. Epidemiological and clinical observations have demonstrated that patients with LBBB have a worse cardiovascular prognosis compared with patients with a normal QRS complex, when clinically overt heart disease is present [2]. Thus, it is useful to establish whether patients with LBBB also have CAD. The traditional exercise myocardial perfusion scintigraphy may have limited value in patients with LBBB because of the high percentage of false-positive anteroseptal and septal perfusion defects induced by the abnormal left ventricular (LV) activation pattern [3–8]. Alternative approaches, including the use of coronary vasodilators (i.e. dipyridamole and adenosine) as stress agents and the application of different interpretation criteria, have reduced but not eliminated the incidence of false-positive results [9]. The introduction of gated single-photon emission computed tomography (SPECT) has allowed the evaluation of myocardial perfusion and function in one study, thus increasing diagnostic accuracy and prognostic value over perfusion data alone. Sharir *et al.* [10] showed that poststress LV ejection fraction (LVEF) and end-systolic volume (ESV) were independent predictors of total coronary events and had incremental value over perfusion data. According to their criteria, the aim of our study was to verify whether

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functional data provided by gated SPECT were able to provide diagnostic and prognostic information in low-risk patients with LBBB.

## Materials and methods

### Patients

We searched our database for patients with a complete LBBB pattern on the resting electrocardiogram and low coronary risk who were referred for myocardial gated SPECT between September 2002 and May 2009 (group 2; $n = 57$). We then selected as controls 57 patients without LBBB consecutively referred to our service in the same period (group 1). Of the 114 patients, 68 (60%) had documented negative coronary angiography and 46 (40%) were at a low risk for CAD. The mean age of patients in group 1 was $63 \pm 10$ years, as compared with $65 \pm 10$ years in group 2. Fifty-eight patients were investigated for chest pain, 33 for dyspnea without chest pain, whereas 23 were asymptomatic. Of the latter group, 12 patients underwent myocardial SPECT for risk stratification for proposed noncardiac surgery and 11 were diabetic patients with two or more coronary risk factors and abnormal resting ECG. The pretest likelihood of CAD was calculated by CADENZA software (San Rafael, California, USA) to categorize patients into different risk subsets [11]. CADENZA is a computer software designed to analyze demographic and clinical variables as aggregate descriptors of proven prognostic importance on the basis of Bayesian analysis of the following patient data: age, sex, presenting symptoms, blood pressure, smoking history, serum cholesterol, glucose intolerance, family history of CAD, rest ECG abnormalities, and the results of exercise ECG stress testing (heart rate, blood pressure, duration, magnitude and slope of ST segment changes, and exertional hypotension). For patients undergoing dipyridamole stress, pretest likelihood of CAD does not include the results of ECG stress testing. According to the pretest of CAD, patients with a likelihood score less than 0.15 were considered at low risk, and were thus included in the analysis [12]. All patients underwent a transthoracic Doppler echocardiogram, and those with clinically significant valvular disease or dilated cardiomyopathy were excluded from the analysis. The demographic and clinical characteristics of patients in both groups are shown in Table 1. The research was carried out according to the Declaration of Helsinki (2000) of the World Medical Association. At the time of SPECT imaging, all patients gave their informed consent both for the exam and for the subsequent follow-up: this is a routine practice at our center. Because of the retrospective nature of the study, neither the Institutional Review Board nor the local ethical committee was involved.

**Table 1 Demographic and clinical characteristics**

| | Group 1 ($n=57$) | Group 2 ($n=57$) | *P*-value |
|---|---|---|---|
| Age (years) | 63 ± 10 | 65 ± 10 | 0.26 |
| Male sex (*n*, %) | 32 (56) | 30 (53) | 0.70 |
| Diabetes (*n*, %) | 22 (39) | 39 (68) | <0.05 |
| Hypertension (*n*, %) | 40 (70) | 37 (65) | 0.23 |
| Dyslipidemia (*n*, %) | 25 (44) | 35 (62) | <0.05 |
| History of smoking (*n*, %) | 7 (30) | 14 (25) | 0.99 |
| Family history of CAD (*n*, %) | 21 (37) | 22 (39) | 0.60 |
| Chest pain (*n*, %) | 28 (49) | 30 (52) | 0.71 |
| Dyspnea (*n*, %) | 16 (28) | 17 (30) | 0.83 |
| No symptoms (*n*, %) | 13 (23) | 10 (18) | 0.48 |
| Exercise test (*n*, %) | 38 (67) | 15 (26) | <0.001 |
| Dipyridamole test (*n*, %) | 19 (33) | 42 (74) | <0.001 |

Values are expressed as mean ± SD.
CAD, coronary artery disease.

### Definition

LBBB was defined as QRS duration of at least 120 ms, the presence of notched R waves in the lateral precordial leads (V5–V6) and leads I and VL, small or absent initial R waves in the right precordial leads (V1 and V2) followed by deep S waves, absent septal waves in left-sided leads, and a prolonged intrinsicoid deflection ( > 60 ms) in V5 and V6. Hypertension was defined as present if patients were on antihypertensive medication, had a history of hypertension, or had evidence of hypertension (blood pressure > 130/85 mmHg). Dyslipidemia was defined by history or recent cholesterol level of at least the 90th percentile for age and sex.

### Stress study protocol

Beta-blocking medications and calcium antagonists were withheld for 48 h and long-acting nitrates for 12 h before testing. For the dipyridamole stress test, patients were instructed not to consume products containing caffeine for 24 h before the test. For patients undergoing the exercise test, symptom-limited treadmill standardized protocols were performed, with monitoring of heart rate and rhythm, blood pressure, and electrocardiography. Test endpoints were physical exhaustion, horizontal or downsloping ST-segment depression of greater than 2 mm, ST-segment elevation of greater than 1 mm, moderate to severe angina, systolic blood pressure decrease of greater than 20 mmHg, blood pressure greater than 230/120 mmHg, dizziness, or clinically important cardiac arrhythmia. Dipyridamole was infused at a dose of 0.56 mg/kg intravenously over 4 min. At peak exercise, or 2 min after the completion of dipyridamole infusion, a bolus of 740 MBq of technetium-99m sestamibi was injected intravenously. Patients continued the physical exercise for an additional 60 s after tracer injection. For both types of stress, heart rate, blood pressure, and 12-lead electrocardiographic data were recorded at rest, at the end of each stress stage, at peak stress, and in the delay phases at rest. Maximal degree of ST-segment change at 80 ms after the J-point of the electrocardiogram was measured and assessed as horizontal, downsloping, or upsloping. After dipyridamole infusion, in the event of chest pain or other symptoms, or after significant ST depression, a dose between 75 and 125 mg of aminophylline was administered intravenously. Gated SPECT was performed 30–45 min after tracer injection for stress study. A separate-day stress–rest protocol was used;

therefore, the rest of the study was performed the next day, injecting 740 MBq of technetium-99m sestamibi and beginning the acquisition after 45–60 min of tracer administration.

### Single-photon emission computed tomography imaging

Gated SPECT acquisitions were performed using a dual-head rotating gamma camera (E.CAM; Siemens Medical Systems, Hoffman Estates, Illinois, USA) equipped with a low-energy, high-resolution collimator and connected to a dedicated computer system. No attenuation or scatter correction was used. A total of 64 projections of 30-s duration were acquired over a 180° arc from the 45° right anterior oblique to the 45° left posterior position. For Tc-99m sestamibi, a 15–20% window centered at the 140 keV peak was used, and images were obtained in supine positions. Gated SPECT was performed obtaining 16 frames/cycle. Images were acquired using a $64 \times 64$ image matrix. All studies were processed with a nine-order Butterworth filter at a cutoff frequency of 0.32 cycles per pixel or 0.26 cycles per pixel. All images were subjected to quality-control measures, including cinematic display for assessment of patient motion and corrections for field nonuniformity and center of rotation. The reconstructed data were projected as tomographic slices in short-axis and vertical/horizontal long-axis views.

### Analysis and interpretation of single-photon emission computed tomography imaging

A quantitative analysis of relative perfusion distribution in 17 myocardial segments was carried out in accordance with the American Heart Association [13]. Each segment was scored using a five-point scoring system (0 = normal, 1 = mild, 2 = moderate, 3 = severe reduction, and 4 = apparent absence of detectable tracer uptake). A commercially available software program (Cedars-Sinai Medical Center, Los Angeles, California, USA) was used to automatically calculate the variables incorporating both the extent and the severity of perfusion defects such as summed stress score (SSS), summed rest score, and summed difference score (SDS) [14,15]; further, parameters such as LVEF, end-diastolic volume (EDV), ESV, summed wall motion score, and summed wall thickening score were calculated for the analysis of LV function. SSS of less than 3 was defined as a normal scan, SSS of at least 3 but up to 10 as a mild–moderately abnormal scan; and SSS of greater than 10 as a severely abnormal scan [16]. Patients with an abnormal scan were considered to have no ischemia with an SDS of less than 2, mild–moderate ischemia with an SDS of 2–6, and severe ischemia with an SDS of at least 7 [17]. The variations in ventricular volumes (EDV and ESV) were analyzed according to the following formulas: EDV rest – EDV poststress and ESV rest – ESV poststress.

### Follow-up

Data were collected by scripted telephone interviews by a researcher blinded to the patient's test results and then confirmed by the revision of medical archives. For the outcome end point, all patients were contacted for a follow-up at least 18 months after SPECT examinations. Cardiac events were defined as major (cardiac death and nonfatal myocardial infarction) and minor (late revascularization procedure performed $> 3$ months from SPECT imaging and hospitalization for cardiac causes). Patients who underwent early revascularization procedures ($\leq 3$ months after SPECT imaging) were censored. Cardiac death was confirmed by review of the death certificate, hospital chart, or physician's records. Cardiac biomarkers and electrocardiographic changes documented myocardial infarction.

### Statistical analysis

Continuous variables were expressed as mean ± SD and categorical data as percentage. Differences between groups were assessed by the unpaired Student *t*-test and by the $\chi^2$-test with Yates correction, as appropriate. Survival curves were constructed using the Kaplan–Meier method to account for censored survival times and were compared with the log rank test. Cochran–Mantel–Haenszel analysis was used to compare the cardiac events between group 1 and group 2. A *P*-value of less than 0.05 was considered significant. Statistical analyses were performed using SPSS (SPSS Inc., Advanced Models 15.0, Chicago, Illinois, USA).

## Results

### Patient characteristics

Many clinical and demographic characteristics were similar in groups 1 and 2 (Table 1). The prevalence of diabetes and dyslipidemia was higher in group 2 than in group 1 (68 vs. 39% and 62 vs. 44%; $P < 0.05$, respectively). Furthermore, most patients in group 1 performed physical exercise (67%); many patients with LBBB underwent a dipyridamole stress test (74%), thus reducing the incidence of false-positive results on SPECT imaging.

### Left bundle-branch block and single-photon emission computed tomography results

The scintigraphic findings in both groups are shown in Table 2. Thirty-three patients with LBBB showed positive SPECT findings, whereas only eight patients of

**Table 2** Scintigraphic parameters

| | Group 1 ($n=57$) | Group 2 ($n=57$) | *P*-value |
|---|---|---|---|
| Negative SPECT (*n*, %) | 49 (86) | 24 (42) | <0.001 |
| Positive SPECT (*n*, %) | 8 (14) | 33 (58) | <0.001 |
| SSS | 0.9 ± 1.8 | 4.7 ± 4.8 | <0.001 |
| SRS | 0.2 ± 0.5 | 2.8 ± 3.5 | <0.001 |
| SDS | 0.8 ± 1.8 | 1.8 ± 2.6 | <0.01 |

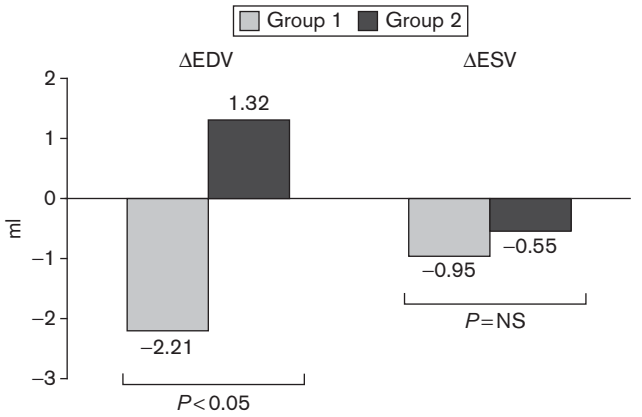
Values are expressed as mean ± SD.
SDS, summed difference score; SPECT, single-photon emission computed tomography; SRS, summed rest score; SSS, summed stress score.

**Table 3 Gated SPECT parameters ($n=96$ patients)**

| | Group 1 ($n=43$) | Group 2 ($n=53$) | $P$-value |
|---|---|---|---|
| SWMS rest | 5.6 ± 9.0 | 11.7 ± 13.1 | <0.05 |
| SWTS rest | 3.7 ± 6.6 | 7.2 ± 9.0 | <0.05 |
| EDV rest (ml) | 75.7 ± 27.1 | 98.2 ± 51.1 | <0.05 |
| ESV rest (ml) | 31.6 ± 20.7 | 49.0 ± 44.4 | <0.05 |
| LVEF rest (%) | 53.5 ± 10.8 | 51.3 ± 14.20 | NS |
| SWMS stress | 4.8 ± 8.2 | 13.1 ± 12.5 | <0.001 |
| SWTS stress | 3.3 ± 6.2 | 7.8 ± 9.1 | <0.005 |
| EDV stress (ml) | 78 ± 27.2 | 96.9 ± 54.7 | <0.05 |
| ESV stress (ml) | 32.6 ± 20.7 | 49.5 ± 46.8 | <0.05 |
| LVEF stress (%) | 53.8 ± 9.9 | 50.4 ± 13.9 | NS |

Values are expressed as mean ± SD.
EDV, end-diastolic volume; ESV, end-systolic volume; LVEF, left ventricular ejection fraction; SPECT, single-photon emission computed tomography; SWMS, summed wall motion score; SWTS, summed wall thickening score.

**Fig. 1**




EDV and ESV variations between group 1 and group 2. EDV, end-diastolic volume; ESV, end-systolic volume.

group 1 had a positive nuclear scan (58 vs. 14%, $P < 0.001$). The extent and severity of perfusion defects (SSS) were significantly higher in group 2 than group 1 ($4.7 \pm 4.8$ vs. $0.9 \pm 1.8$, $P < 0.001$). Among patients with LBBB and those with positive SPECT findings ($n = 33$), 28 (84%) had a mild–moderate abnormal scan, whereas five (15%) showed severe perfusion defects. Furthermore, in 12 patients (36%), the perfusion defects were related to abnormal electrical activation (septal and anteroseptal regions), whereas 21 patients (64%) had abnormal myocardial perfusion outside these regions. In particular, one in the anterolateral wall, one in the apex and inferior wall, two in the apex and lateral wall, eight in the inferior wall, one in the inferior and inferoseptal walls, three in the inferolateral wall, two in the inferoseptal wall, and three in the lateral wall.

SSS in patients with and without anteroseptal and septal (LBBB related) perfusion defects was $5.7 \pm 2.8$ and $10.4 \pm 5.2$, respectively ($P < 0.005$). The presence of reversible defects was demonstrated in eight (100%) and 22 (66%) patients for group 1 and group 2, respectively ($P < 0.005$). The SDS value was higher in group 2 than in group 1 ($1.8 \pm 2.6$ vs. $0.8 \pm 1.8$, $P < 0.05$); in particular, the extension of reversible perfusion defects in the LBBB group was mild–moderate in 18 (82%) patients and severe in four (18%) patients.

### Left bundle-branch block and gated single-photon emission computed tomography

Gated SPECT was carried out in 96 (84%) patients. LV functional parameters are depicted in Table 3. As shown, most of the measures were significantly different in the two groups (all $P < 0.05$). Of note, poststress and rest EDV and ESV were larger in patients with LBBB; in particular, the difference was more relevant at rest ($P < 0.05$). In group 2, patients with mild–moderate perfusion defects on SPECT ($n = 28$) showed higher poststress and rest EDV than patients with a negative SPECT ($110 \pm 63$ vs. $76 \pm 31$ and $112 \pm 57$ vs. $57 \pm 10$, respectively, $P < 0.05$ in both). The mean variation in EDV was $-2.21$ ml for group 1 and 1.32 ml for group 2 ($P < 0.05$), whereas the variation in ESV was $-0.95$ ml and $-0.55-$ ml, respectively ($P =$ NS; Fig. 1).

### Left bundle-branch block, single-photon emission computed tomography, and prognosis

During follow-up ($32 \pm 19$ months, complete in 84% of the patients), 22 cardiac events occurred (2.3% cumulative event rate). There were four major cardiac events (cardiac death in two patients and nonfatal myocardial infarction in two patients) and 18 minor cardiac events (two late revascularization procedures, eight hospitalizations for chest pain, and eight hospitalizations for dyspnea). The event rate was significantly higher in group 2 than in group 1 (27 vs. 73%, $P < 0.01$). Cumulative event-free survival was lower in the LBBB group than in control patients (18 vs. 78%, $P < 0.05$), being significantly lower in patients with positive SPECT findings (Fig. 2). In LBBB patients, the cardiac-event rate showed a proportional increase on the basis of the severity and extension of perfusion defects (SSS < 3: 29%, 3–10: 36%, and SSS > 10: 67%).

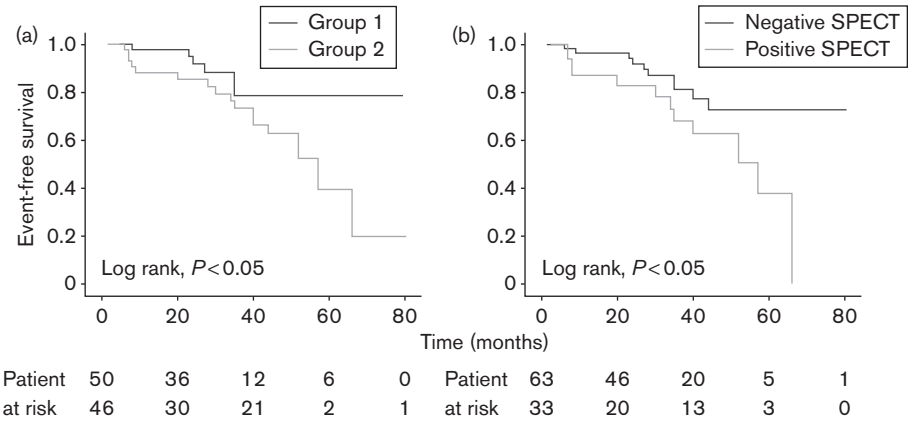
The Cochran–Mantel–Haenzsel analysis indicated a significant difference between group 1 and group 2; the value of the odds ratio was 3.91 (confidence interval 95%, $P < 0.05$). A detailed description of the SPECT results and cardiac events is shown in Table 4.

## Discussion

### Single-photon emission computed tomography imaging and left bundle-branch block

The diagnosis of myocardial ischemia in the presence of coexisting LBBB by baseline ST–T changes in rest and treadmill exercise ECG is complicated. In addition, the accuracy of other commonly used noninvasive techniques such as stress echocardiography and myocardial SPECT is confounded by the heterogeneous effects of LBBB on myocardial perfusion. Gated SPECT, including cardiac wall

**Fig. 2**




(a) Cumulative event-free survival curves in both groups. (b) Cumulative event-free survival curves on the basis of SPECT findings for the entire patient population. SPECT, single-photon emission computed tomography.

**Table 4 Events and SPECT results in the two groups ($n=96$ patients)**

| | Event | | No event | |
|---|---|---|---|---|
| | Group 1 ($n=6$) | Group 2 ($n=16$) | Group 1 ($n=44$) | Group 2 ($n=30$) |
| SPECT negative ($n$, %) | 4 (77) | 6 (38) | 38 (86) | 15 (50) |
| SPECT positive ($n$, %) | 2 (23) | 10 (62) | 6 (14) | 15 (50) |
| SSS | 1.1 ± 1.8 | 5.3 ± 4.7 | 1.0 ± 1.9 | 3.4 ± 4.1 |
| SRS | 0.14 ± 0.3 | 3.8 ± 4.2 | 0.17 ± 0.51 | 1.8 ± 1.9 |
| SDS | 0.9 ± 1.7 | 1.4 ± 1.6 | 0.9 ± 1.9 | 1.5 ± 2.9 |
| EDV poststress (ml) | 86.7 ± 25.3 | 113.7 ± 80.7 | 78.1 ± 28.6 | 88.1 ± 46.1 |
| ESV poststress (ml) | 36.1 ± 16.0 | 62.4 ± 71.9 | 32.9 ± 22.2 | 44.7 ± 38.1 |
| EDV rest (ml) | 89.0 ± 23.0 | 111.1 ± 70.0 | 75.0 ± 28.7 | 90.2 ± 45.2 |
| ESV rest (ml) | 35.7 ± 13.7 | 59.2 ± 63.3 | 31.9 ± 22.5 | 43.9 ± 37.9 |
| EF poststress (%) | 50.8 ± 5.4 | 47.7 ± 13.9 | 53.6 ± 10.6 | 50.9 ± 13.4 |
| EF rest (%) | 51.6 ± 4.3 | 48.7 ± 13.9 | 52.8 ± 11.2 | 52.1 ± 13.2 |
| Major events ($n$, %) | 2 (23) | 2 (12) | – | – |
| Minor events ($n$, %) | 4 (77) | 14 (88) | – | – |

Continuous values are expressed as mean ± SD.
EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; SDS, summed difference score; SPECT, single-photon emission computed tomography; SRS, summed rest score; SSS, summed stress score.

motion and perfusion data, could improve the diagnostic and prognostic value of myocardial scintigraphy in LBBB patients. In our study, we compared 114 low-risk patients divided into two groups, with and without LBBB. Both groups had similar demographic and clinical characteristics, except for a higher prevalence of diabetes and dyslipidemia in LBBB patients (39 vs. 68% and 44 vs. 62% for the control and the LBBB group, respectively; $P < 0.05$ in both). We found that myocardial perfusion defects on SPECT imaging were significantly different between the two groups, being greater in patients with LBBB. In this latter group, only 36% had an abnormal scan related to septal or anteroseptal segments, whereas 64% showed an abnormal myocardial perfusion outside these areas. Various mechanisms have been proposed to explain false-positive myocardial perfusion defects in LBBB patients. Among these are the following: (a) reduction of myocardial blood flow within the interventricular septum as a result of the delayed septal contraction, (b) septal fibrosis and small-vessel disease associated with fibrodegenerative changes, which may cause both the conduction abnormality and the exercise perfusion defect, (c) camera-field non-uniformity, (d) patients' movement during imaging, and (e) partial-volume effects [9,18].

Nevertheless, among 21 patients with perfusion defects not related to LBBB, 16 (76%) had mild–moderate (SSS 3–10) and five (24%) had severe perfusion defects (SSS > 10). These data are in accordance with other published reports [19–22].

### Gated single-photon emission computed tomography and left bundle-branch block

Bavelaar-Croon *et al.* [23] demonstrated that patients with LBBB and without previous myocardial infarction had higher average EDV and ESV, and significantly decreased

LV function as compared with controls. In our study, we found a significant difference in the poststress/rest EDV and ESV between group 1 and group 2, but no difference in LVEF. The abnormal septal contraction typical of LBBB patients may cause an increase in both EDV and ESV. In fact, it is well established that LBBB is often accompanied by LV dilatation, even in the absence of CAD. In a recent study by Vernooy *et al.* [24], the LV dilatation was attributed to the asynchronous ventricular activation during LBBB, which leads to redistribution of circumferential shortening and myocardial blood flow and, in the long run, to LV remodeling. Nichols *et al.* [25] reported that in the QGS program analyses, EDV equal to $84 \pm 26$ ml and ESV equal to $33 \pm 17$ ml were considered normal. In accordance with this report, in our study population, group 1 showed LV volumes in the normal range, whereas group 2 had EDV and ESV values higher than normal ($98.2 \pm 51.1$ and $49.0 \pm 44.4$ ml, respectively, for EDV rest and ESV rest). Furthermore, the variation of EDV between rest and poststress was different in patients with LBBB when compared with controls (1.32 vs. −2.21 ml). In fact, poststress EDV increased in group 1 patients and decreased in the LBBB population. We hypothesize that this difference may be related to the enhanced paradoxical movement of the septum in LBBB patients, which might determine an altered pattern of ventricular filling. However, in our study population, this diastolic dysfunction was not followed by a decrease in systolic performance, as demonstrated by the LVEF values, which are just slightly below the normal range. The lack of systolic dysfunction could be explained by the low coronary risk of our population.

### Prognosis

After $32 \pm 19$ months of follow-up, cardiac events occurred in 22 patients (six of group 1 and 16 of group 2). Four were major and 18 were minor cardiac events. The latter finding is consistent with the low risk of our patients. Ten Cate *et al.* [26] concluded that the cardiac prognosis of patients with LBBB and septal perfusion defects alone on SPECT imaging is the same as that in patients with normal myocardial perfusion. In our study population, many cardiac events occurred in patients with the LBBB disorder, and 16 out of 18 (89%) were hospitalizations for cardiac causes. Moreover, nine events occurred in the group of 14 patients with nonseptal perfusion defects and just one event occurred among the 11 patients with LBBB-related perfusion defects (64 vs. 7%, $P < 0.005$). Furthermore, patients who experienced cardiac events had higher EDV and ESV values ($113.7 \pm 80.7$ and $62.4 \pm 71.9$ poststress, $111.1 \pm 70.0$ and $59.2 \pm 63.3$ at rest, respectively), and the extension of perfusion defects (SSS values) helped in further stratifying the prognosis of LBBB patients.

### Clinical implications

It is not known whether LV dilatation in patients with LBBB is the cause of the abnormal conduction or whether the activation disturbance is a marker of a more progressive disease state [27]. In LBBB patients, the early identification of LV dilatation, which anticipates systolic dysfunction, could improve outcome by suggesting a more aggressive therapy. The literature reported that LVEF reduction is one of the strongest predictors of cardiac events [28]. According to our findings, we hypothesize that in patients with LBBB, the absence of an increase in EDV between poststress and rest could be considered as a marker of ventricular dilatation, which might anticipate diastolic dysfunction and LVEF reduction. Gated SPECT, allowing an earlier detection of LV dilatation, could be considered a useful tool to identify patients who need a closer follow-up.

### Study limitations

First, this is an observational retrospective study; thus, selective bias is possible (i.e. population-based analysis). Second, 26% of the LBBB patients underwent a treadmill exercise test on the basis of the cardiologist's decision, possibly increasing the percentage of false-positive anteroseptal defects. Third, it was not possible to perform attenuation correction of SPECT images. Fourth, the physiological effects of physical exercise and coronary vasodilators (e.g. dypiridamole) on LV indices are not exactly the same. Nevertheless, even on stratifying our patients according to the stress method, the trends in poststress LV indices were similar to those reported in the present report. Finally, gated SPECT was performed in 84% of patients because, in the remaining population, heart rate was irregular.

## Conclusion

Functional and perfusion parameters obtained by gated SPECT were different among patients with and without LBBB. In particular, the presence of higher EDV and ESV in patients with abnormal ventricular activation has to be considered an important finding. To our knowledge, this is the first study to recognize the decrease in EDV between rest and poststress in LBBB patients as a possible marker of diastolic dysfunction, which might anticipate LVEF reduction. Functional and perfusion data obtained by gated SPECT could aid the assessment of LBBB patients' prognosis when higher EDV, ESV, and SSS values are found. These results indicate that a prospectively conducted study evaluating the predicting value of functional parameters obtained by gated SPECT in LBBB low coronary-risk patients is warranted.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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