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ORIGINAL ARTICLE

Usefulness of dynamic perfusion SPECT with quantitative assessment of myocardial perfusion reserve for the detection of myocardial ischaemia in patients with presumed new left bundle branch block

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Abstract

Aims

The aim of this retrospective study was to evaluate the ability of dynamic SPECT with quantitative analysis of myocardial blood flow (MBF) and myocardial flow reserve (MFR) for the detection of coronary artery disease (CAD) in patients with presumed new left bundle branch block (LBBB).

Methods and results

We evaluated the dynamic SPECT results from 174 consecutive patients with LBBB without a history of CAD from a single center. MBF was assessed at rest and during regadenoson (400 μg). Normal MFR was defined as ≥ 2.1. Left ventricular function and segmental perfusion were assessed from conventional gated SPECT. SPECT abnormalities were found in 17/174 (10%) patients including a reversible SPECT defect in 4 patients (2.3%), a fixed defect in 12 patients (7%), and both in 1 patient. Global left ventricular function was normal despite a significant impairment of septal wall motion. Stress and rest MBF was decreased in the septum and the inferior wall compared with other walls ($P < 0.0001$), resulting in similar MFR. A reduced MFR was associated with a fixed defect ($P = 0.04$). Only 18 patients (10%) presented with a decreased MFR. They were more often referred to subsequent coronary angiography (8/18, 44%) compared with patients with a normal MFR (9/156, 6%, $\chi^2 = 27.382$, $P < 0.0001$). However, significant coronary lesions were finally found in only 4/174 patients (2%).

Conclusion

Although a decreased MFR was associated with a fixed defect on conventional perfusion imaging, the low rate of CAD finally demonstrated in this study questions the relevance of routine screening for CAD in patients with presumed new LBBB.

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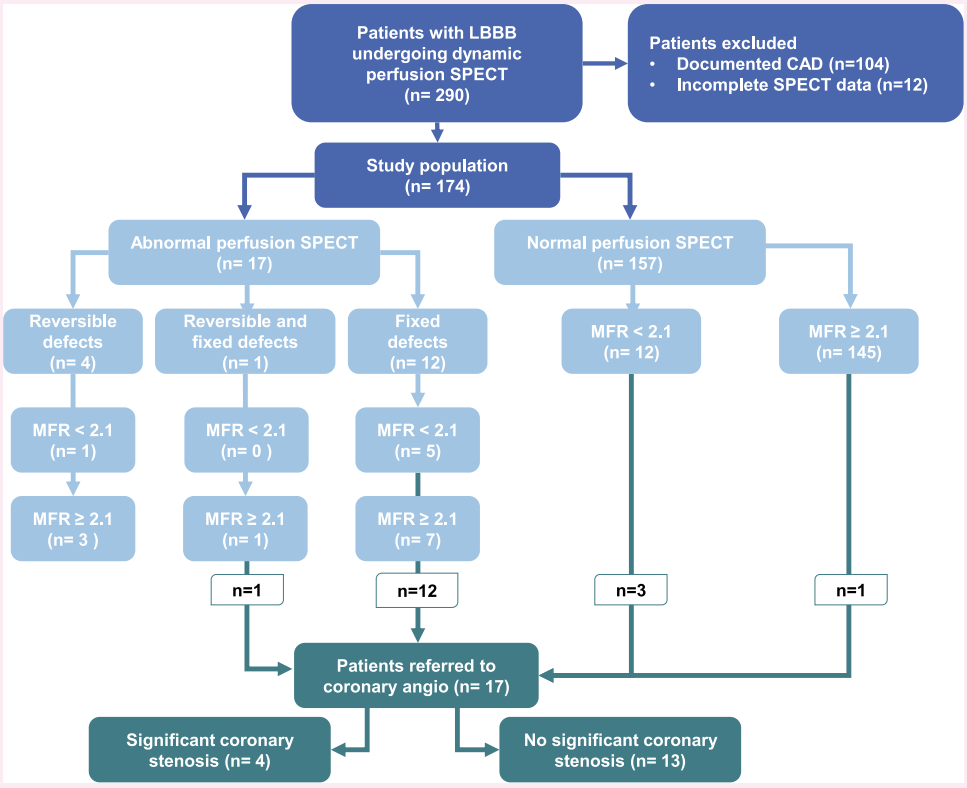
Graphical Abstract



Keywords dynamic perfusion SPECT • myocardial blood flow • myocardial flow reserve • left bundle branch block

Introduction

Left bundle branch block (LBBB) is a conduction disorder resulting from an interruption of the normal ventricular activation sequence through the left branch of the His–Purkinje system. Although incidence increases with patient age, the prevalence is low and is even lower without underlying heart disease.[1] The Framingham study[2] reported that LBBB was associated with an increase in cardiac mortality. Particularly, LBBB was identified as a strong predictor of mortality in patients with coronary artery disease (CAD)[3] as well as a risk factor for progression in heart failure.[4] Even in asymptomatic patients, the presence of LBBB is a marker of increased prevalence of cardiovascular disease[5] and is related to higher mortality risk, mostly because of coronary death in the longer term.[6] Consequently, the search for underlying cardiac disease, especially CAD, is a primary goal in the investigation of patients with a presumed new- or recent-onset LBBB. However, non-invasive diagnosis of CAD in these patients remains challenging because of the suboptimal accuracy of functional imaging within this population, and although pharmacological stress testing reduces septal perfusion artefacts, myocardial perfusion SPECT has only moderate specificity for the detection of CAD in patients with LBBB.[7]

In recent years, technological improvements realized with the introduction of dedicated cardiac cadmium–zinc–telluride (CZT) detector SPECT cameras have considerably improved myocardial perfusion imaging because of better spatial and energy resolution and the increased sensitivity enabled by a cardiac-centric acquisition geometry.[8] In addition, the design of such dedicated CZT-based cameras allows dynamic perfusion acquisitions which provide quantitative measurement of both myocardial blood flow (MBF) and myocardial flow reserve (MFR), with high accuracy when compared with PET imaging and to fractional flow reserve.[9] Nevertheless, the diagnostic value of dynamic myocardial perfusion CZT-SPECT imaging has not yet been reported in patients with LBBB. The aim of this retrospective study was to evaluate whether the addition of MBF and MFR data to the perfusion SPECT improves the detection of CAD in patients with presumed new LBBB and no overt heart disease.

Methods

Study population

We retrospectively evaluated SPECT results in patients with presumed new LBBB and without documented CAD who underwent dynamic myocardial perfusion imaging at a single Nuclear Medicine centre between April 2018 and February 2022. In patients who underwent more than one SPECT examination, only the first one was considered for this study. In our department, routine reports are structured according to the EANM/EACVI joint position paper[10] and included age, gender, history of cardiac or vascular disease, coronary risk factors, symptoms, results of previous non-invasive tests or coronary angiogram, ongoing treatment, stress test data, SPECT perfusion results indicating the number of reversible (i.e. ischaemic) or fixed defects using a 17-segment model of the LV, stress and rest LV function, and finally MBF and MFR. Data from patients with previously documented CAD

or with missing stress or rest data were not included. The pre-test probability (PTP) of CAD was calculated using the 2019 ESC guidelines,[11] adapted from the Diamond and Forrester classes, according to age, sex, and the nature of the symptoms and categorized as low (<5%), intermediate (5–15%), or high (>15%) risk of CAD. The use of the data for this retrospective study was approved by the institutional review board (ID-3907).

Stress procedure and dynamic CZT-SPECT examination

All examinations were routinely performed as previously described[9] using a D-SPECT camera (Spectrum Dynamics, Caesarea, Israel) and ^{99m}Tc-labelled radiopharmaceutical (sestamibi: $n = 120$ and tetrofosmin: $n = 54$) with the patient in supine position. The patients were refrained from all caffeine-containing food and beverages for 12 h prior to SPECT examination and underwent pharmacological stress testing (regadenoson 400 μg). An initial dose of ~37 MBq of ^{99m}Tc-labelled tracer was used to position the patient's heart within the field of view before rest imaging. A dose of 3.7 MBq/kg and a dose of 10 MBq/kg were injected for rest and stress imaging, respectively, while rest and stress dynamic acquisitions were completed within 75 min, without attenuation correction. Perfusion SPECT was analysed on reconstructed images using a 17-segment model of the left ventricle. Segments demonstrating moderate to severe uptake reduction on stress imaging were considered abnormal. An increased uptake in the same segments on rest imaging was interpreted as ischaemia. A perfusion defect was considered to be artefact if there was decreased uptake on rest imaging only, a defect with a wider extent at rest compared with stress imaging, or a defect present at both stress and rest imaging with either a normal segmental wall motion or a paradoxical septal wall motion in the case of a septal defect.[12] Left ventricular function was evaluated using QGS software (Cedars Sinai, Los Angeles, CA, USA) and reported normal limits.[13] Segmental wall motion was analysed as 1 = normal, 2 = hypokinesia, 3 = akinesia, and 4 = dyskinesia.

Dynamic imaging data were analysed using Corridor 4DM software (v2018, INVIA, Ann Arbor, MI, USA) as previously described,[9] providing global and regional quantitative perfusion analysis from perfusion polar plots. Regional perfusion was assessed according to a five-territory segmentation (i.e. septal, anterior, lateral, inferior, and apical). The cut-off value for abnormal global MFR was defined as < 2.1.[9] All images were reviewed by nuclear medicine physician with an experience > 20 years in nuclear cardiology (A.M. and D.A.).

Coronary angiography

Coronary angiography was performed according to standard techniques at Caen University Hospital or at Hôpital Privé Saint Martin (Caen, France), and the results were retrieved from hospital records. A significant obstructive coronary stenosis was routinely defined as > 50% diameter reduction. If several stenoses were observed in the same artery, it was classified according to the status of the most stenotic segment. A left main coronary artery stenosis was classified as two-vessel disease.[14]

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical variables as percentages. The association of the following categorical variables to an abnormal MFR (<2.1) was tested using a χ^2 test: significant ischaemia (ischaemia > 10% of the LV), septal perfusion defect, positive coronary angiogram, multivessel CAD, and coronary angioplasty. A P-value ≤ 0.05 was considered significant. All statistical analyses were performed using JMP 11 software (SAS Institute, Cary, NC, USA).

Results

Patients characteristics

During the period April 2018–February 2022, a total of 290 patients with LBBB underwent dynamic perfusion SPECT as part of routine clinical management. Of them, 104 patients were excluded because of having previously documented CAD and 12 because of incomplete SPECT data required for further analysis, leaving 174 patients (45% women; mean age 71 ± 8 years) with a presumed new LBBB for study analysis. Most patients were asymptomatic (66% without dyspnoea and 83% without chest pain), and 59% of patients had a pre-test CAD probability range over 15%, measured according to ESC guidelines. Patient characteristics are summarized in *Table 1*.

Perfusion SPECT results

Among these 174 patients, myocardial ischaemia was noted in five cases (3%), including two patients (1%) with significant ischaemia (>10% of the LV) and one patient (0.4%) with both ischaemia and fixed defects. In 12

Table 1 Patient characteristics

	Whole population ($n = 174$)
Female gender, *n* (%)	79 (45)
Age (years)	71 ± 8
Weight	
BMI (kg/m^2)	27.7 ± 5.7
Not overweight, *n* (%)	55 (32)
Overweight, *n* (%)	61 (35)
Obesity, *n* (%)	58 (33)
Cardiovascular risk factors and comorbidities	
Hypertension, *n* (%)	122 (70)
Diabetes, *n* (%)	48 (28)
Tobacco, *n* (%)	56 (32)
Dyslipidaemia, *n* (%)	78 (45)
DCM, *n* (%)	15 (9)
PAD, *n* (%)	18 (10)
AF, *n* (%)	27 (15.5)
No symptoms, *n* (%)	98 (56)
Dyspnoea	
NYHA I–II, *n* (%)	46 (26)
NYHA III–IV, *n* (%)	14 (8)
Chest pain	
Angina, *n* (%)	14 (8)
Atypical, *n* (%)	15 (9)
Current medication	
Beta-blocker, *n* (%)	64 (37)
Ivabradine, *n* (%)	0 (0)
Statine, *n* (%)	57 (33)
Other cholesterol-lowering drugs, *n* (%)	14 (8)
ACEI, *n* (%)	95 (55)
Diuretics, *n* (%)	52 (30)
Calcium channel blockers, *n* (%)	42 (24)
Insulin, *n* (%)	6 (3)
OAD, *n* (%)	23 (13)
PTP range	
Mean	0.19 ± 0.09
<0.05, *n* (%)	0 (0)
0.05–015, *n* (%)	72 (41)
>0.15, *n* (%)	102 (59)

BMI, body mass index; NYHA, New York Heart Association functional class; PAD, peripheral artery disease; ACEI, angiotensin-converting enzyme inhibitors; OAD, oral antidiabetic drugs.

patients (7%), perfusion SPECT showed a non-reversible perfusion defect compatible with myocardial infarction without residual ischaemia. A septal perfusion defect considered to be a LBBB-related artefact was noted in 20 patients (11%). The mean global left ventricular function was normal, but segmental wall motion was impaired in the septum compared with all other territories (see *Tables 2* and *3*) because of paradoxical septal wall motion. The mean stress and rest left ventricular ejection fraction (65 ± 14 and 62 ± 14%, respectively) as well as stress and rest EDV (106 ± 39 and 103 ± 39 mL, respectively) and stress and rest ESV (42 ± 32 and 43 ± 32 mL, respectively) were normal for these patients. Regarding segmental wall motion in each vascular territory, the wall motion score was 1.1 ± 0.3 (anterior wall), 1.1 ± 0.3 (apical wall), 1.1 ± 0.3 (lateral wall), 1.2 ± 0.4 (inferior wall), and 1.7 ± 1.1 (septum). Perfusion SPECT results are summarized in *Tables 2* and *3*.

Table 2 Perfusion SPECT results

	Whole population ($n = 174$)
Perfusion	
Normal perfusion, *n* (%)	157 (90.2%)
Reversible defects, *n* (%)	4 (2.3%)
Abnormal fixed defects	12 (6.9%)
Reversible and abnormal fixed defects, *n* (%)	1 (0.6%)
Septal perfusion defect, *n* (%)	20 (11%)
Left ventricular function	
LVEF stress (%)	65 ± 14
LVEF rest (%)	62 ± 14
EDV stress (mL)	106 ± 39
EDV rest (mL)	103 ± 39
ESV stress (mL)	42 ± 32
ESV rest (mL)	43 ± 32
MBF and MFR	
Stress MBF	3.0 ± 1.0
Rest MBF	1.2 ± 0.5
MFR	2.7 ± 0.7

LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume.

Dynamic SPECT data demonstrated a decrease in both stress and rest MBF in the septum compared with the anterior, lateral, and apical walls ($P < 0.0001$) as well as in the inferior wall (*Table 3*). However, the resulting MFR was similar in all myocardial walls. In the 20/174 patients presenting a septal perfusion defect, global MFR was not different compared with the rest of the population ($P = 0.9571$, ns) (*Table 4*).

Eighteen patients (10%) had a decreased MFR (<2.1), including 5 patients with fixed defects and 12 with normal SPECT results, and fixed defects were associated with impaired MFR ($\chi^2 = 13.243$, $P = 0.04$). The patients with MFR <2.1 were more often referred to coronary angiogram (8/18, 44%) compared with patients with a normal MFR (9/156, 6%, $\chi^2 = 27.382$, $P < 0.0001$) (*Table 4*). Finally, the SPECT results were not different between clinically symptomatic or asymptomatic patients (see *Table 5*). An illustrative case is depicted in *Figure 1*.

Coronary angiogram

Only 17/174 patients (10%) underwent coronary angiography within 3 months after the SPECT examination, including 14 patients with perfusion abnormalities (fixed defects: 12; ischaemia: 1; and both fixed defects and ischaemia: 1) and 3 patients with normal perfusion SPECT but abnormal MFR. Significant coronary lesions were found in 4/17 patients: two with a single-vessel disease and two with multivessel disease, leading to coronary angioplasty in three patients. These four patients had non-reversible perfusion defects (three segments in three cases

Table 3 Regional SPECT results (MBF, MFR, and wall motion) according to the left ventricular territories

	Anterior	Apex	Lateral	Inferior	Septum	Global *P*-value
Stress MBF (mL/min/g)	3.3 ± 1.1	3.3 ± 1.4	3.4 ± 1.1	2.7 ± 1.2*	2.6 ± 0.9*	<0.0001
Rest MBF (mL/min/g)	1.4 ± 0.5	1.3 ± 0.6	1.4 ± 0.5	1.1 ± 0.5*	1.0 ± 0.4*	<0.0001
MFR	2.5 ± 0.8	2.7 ± 1.2	2.6 ± 0.8	2.6 ± 1.0	2.7 ± 0.9	NS
Wall motion grade	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.2 ± 0.4	1.7 ± 1.1**	<0.0001

*$P < 00\,001$ vs. apex, lateral and anterior walls; **$P < 00\,001$ vs. apex, lateral, anterior, and inferior walls.

Table 4 Comparison of categorical variables according to the presence of an abnormal MFR in the whole population (results are expressed as a percentage of their categories)

	MFR < 2.1 ($n = 18$)	MFR ≥ 2.1 ($n = 156$)	χ^2	*P*-value
Myocardial perfusion SPECT				
Ischaemia ≥ 10%, *n* (%)	0 (0)	2 (1)	1.955	NS
Septal perfusion defect, *n* (%)	2 (11)	18 (12)	0.003	NS
Coronary angiogram				
Patient referred to coronary angio, *n* (%)	8 (44)	9 (6)	27.382	<0.0001
Significant obstructive CAD, *n* (%)	1 (6)	3 (2)	0.948	NS
Multivessel CAD, *n* (%)	0 (0)	2 (1)	0.233	NS
Angioplasty, *n* (%)	1 (6)	2 (1)	1.739	NS

Table 5 Patient characteristics and coronary angiography results according to the presence of symptoms (chest pain or dyspnoea)

	Asymptomatic (*n* = 99)	Symptomatic (*n* = 75)	*P*-value
Gender (*n*, %)	40 (40)	39 (52)	NS
Age [mean (SD)]	71 (7)	71 (9.44)	NS
PTP [mean (SD)]	0.17 (0.07)	0.22 (0.11)	<0.001
Cardiovascular risk factors and comorbidities			
Hypertension (*n*, %)	69 (70)	53 (71)	NS
Diabetes (*n*, %)	34 (34)	14 (19)	0.034
Tobacco (*n*, %)	33 (33)	23 (31)	NS
Dyslipidaemia (*n*, %)	49 (49)	29 (39)	NS
PAD (*n*, %)	13 (13)	5 (7)	NS
Weight			
BMI [mean (SD)]	27.2 (5.6)	28.4 (5.7)	NS
Obesity (*n*, %)	31 (31)	27 (36)	NS
Overweight (*n*, %)	31 (31)	30 (40)	
Normal weight (*n*, %)	37 (37)	18 (24)	
Insulin (*n*, %)	3 (3)	3 (4)	NS
OAD (*n*, %)	15 (15)	8 (11)	NS
AF (*n*, %)	11 (11)	16 (21)	NS
Left ventricular function			
LVEF stress (%) [mean (SD)]	65 (13)	65 (16)	NS
LVEF rest (%) [mean (SD)]	62 (13)	60 (15)	NS
EDV stress (mL) [mean (SD)]	105 (38)	107 (40)	NS
EDV rest (mL) [mean (SD)]	103 (38)	102 (40)	NS
ESV stress (mL) [mean (SD)]	41 (31)	43 (33)	NS
ESV rest (mL) [mean (SD)]	43 (31)	44 (33)	NS
MBF and MFR			
MBF stress (mL/min/g) [mean (SD)]	3.04 (0.9)	2.86 (1.0)	NS
MBF rest (mL/min/g) [mean (SD)]	1.19 (0.4)	1.08 (0.4)	NS
MFR [mean (SD)]	2.7 (0.7)	2.8 (0.7)	NS
MFR < 2.1 (*n*, %)	10 (10)	8 (11)	NS
Perfusion SPECT			
Normal SPECT	88 (89)	69 (92)	NS
Reversible defects	3 (3)	1 (1)	
Fixed defects	7 (7)	5 (7)	
Reversible and fixed defects	1 (1)	0 (0)	
Coronary angiography			
Referred to coronary angio (*n*, %)	10 (10)	7 (9)	NS
Significant CAD (*n*, %)	2 (2)	2 (3)	—
Coronary lesions			
LM (*n*, %)	0 (0)	0 (0)	—
LAD (*n*, %)	1 (10)	1 (14)	—
LCX (*n*, %)	0 (0)	1 (14)	—
RCA (*n*, %)	2 (20)	1 (14)	—
MVD (*n*, %)	1 (50)	1 (50)	—
PCI (*n*, %)	1 (10)	2 (27)	—

PAD, peripheral artery disease; BMI, body mass index; OAD, oral antidiabetic drugs; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume; LM, left main trunk; LAD, left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery; MVD, multivessel disease; PCI, percutaneous intervention.

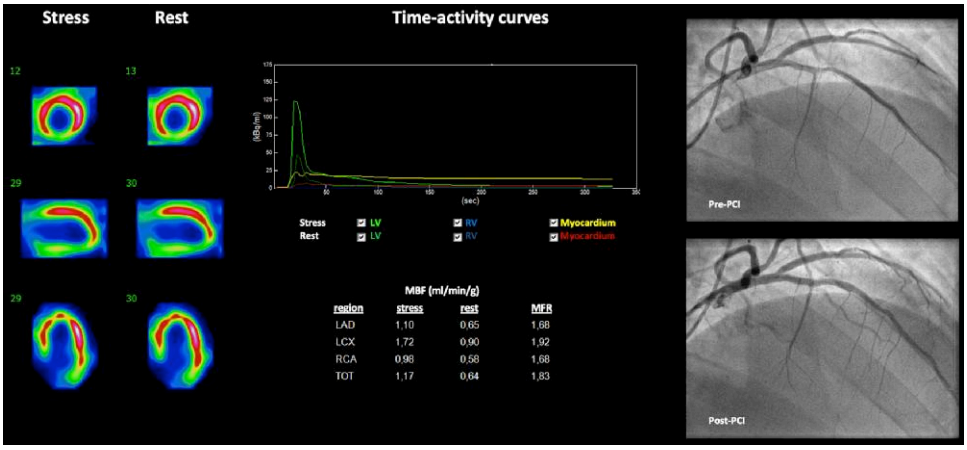


Figure 1 Illustrative case, with perfusion SPECT (left panel) showing a non-reversible perfusion defect involving the inferior myocardial wall, MBF, and MFR(middle) demonstrating a decreased global (TOT) MFR, and coronary angiogram depicting a coronary lesion in the left anterior descending artery (right) before and after percutaneous coronary intervention.

and four segments in one case) with wall motion abnormalities within the same segments, without reversible defect but with abnormal MFR in one case. In 13 patients with false-positive perfusion SPECT, seven patients had a final diagnosis of dilated cardiomyopathy (DCM). These data are summarized in *Table 5*. The rate of positive angiographic results was too low to allow a statistical comparison, but there was a trend towards increased coronary lesions in symptomatic (28.6%) compared with asymptomatic patients (20%), in agreement with a higher PTP of CAD. When comparing the data in patients with MFR <2.1, it was observed that the patients who were not referred to coronary angio ($n = 9$) tended to have a preserved stress MBF [median value 2.55 (range 1.66–4.20)] compared with patients ($n = 3$) who finally underwent coronary angiography [median value 1.70 (range: 1.62, 2.12)]. In addition, five out of these nine patients had an almost normal MFR between 2 and 2.09.

Discussion

The present study evaluated the usefulness of dynamic perfusion SPECT using a CZT D-SPECT camera for the detection of CAD in patients with LBBB and no overt heart disease. The main finding of our study was the low rate of positive SPECT results in this population (8%), with 8% additional patients presenting with altered MFR and normal perfusion SPECT, suggesting balanced ischaemia. Despite these results, the final diagnosis of CAD was confirmed in only 2% of the referred population (see *Graphical Abstract*).

In our study, the rate of abnormal SPECT perfusion was 14/174 (8%, fixed defects: 12; ischaemia: 1; and both fixed defects and ischaemia: 1), in contrast to previous studies reporting a rate ranging from 50 to 60%.[15,16] This difference may be explained by several potential factors. First, we excluded septal LBBB-related artefacts (20/174, 11%) from the definition of myocardial ischaemia or fixed defects, a common finding in patients with LBBB, especially when exercise stress testing is performed.[7] In addition, the mean pre-test likelihood of CAD was 0.19, and the study population consisted with patients without personal history of CAD, with a high number of asymptomatic patients (56%). The clinical utility of referring an asymptomatic patient for non-invasive testing for detection of CAD is questionable. In a recent ACC/AHA report on the appropriate use criteria for detection of chronic coronary disease, Winchester *et al.*[17] considered that referring an asymptomatic patient for a diagnostic procedure may be appropriate where there is a high risk of atherosclerotic cardiovascular disease (>20% based on the ACC risk estimator). The recently updated 2024 ESC guidelines for the management of chronic coronary syndromes[18] do not recommend non-invasive functional imaging in patients with pre-test likelihood <15%, pre-test likelihood being calculated as a risk factor-weighted clinical likelihood (RF-CL) further adjusted based on clinical findings and eventually using coronary calcium score.[18] Given that a presumed new LBBB may suggest chronic coronary syndrome, referring cardiologists often consider LBBB as increasing the likelihood of CAD. In our study, 59% of patients had a PTP > 15% of CAD but SPECT images were abnormal in only 10%. This discrepancy may be explained by the lack of accuracy of a Diamond and Forrester class-based approach in predicting obstructive CAD compared with the RF-CL[18] as well as considering a presumed new LBBB as increasing the PTP of CAD.

In our study, a final diagnosis of CAD was scarce (4/174, 2%), in contrast to previous results reporting CAD in 10–40% of patients with LBBB,[16,19] mostly in the presence of typical angina. Engbers *et al.*[19] evaluated 218 symptomatic patients with LBBB and without history of CAD. In their study, SPECT was abnormal in 57% of patients, although when coronary CT angiography was performed, it excluded CAD in 72% of them, leading to a final CAD rate of 10%. In a series of 47 consecutive high-risk patients with permanent LBBB referred for perioperative SPECT examination for non-cardiac surgery, Karavidas *et al.*[16] reported a significant CAD in 11 patients (23%). In a study comparing cardiac MRI to stress echocardiography in 82 consecutive patients with LBBB with typical features of ischaemia and without history of CAD, coronary angiography documented a significant CAD in 34 patients (41%).[20]

Clerc *et al.*[21] evaluated 101 patients with LBBB with low-to-moderate PTP and 303 controls without LBBB using coronary CT angiography. The prevalence of CAD was similar in patients with LBBB and matched controls (15 vs. 16%, respectively). In this study, the PTP of CAD was 33 ± 18%, and 40% of patients with LBBB were asymptomatic. Interestingly, on multivariate analysis, age, gender, typical angina, and coronary risk factors, but not LBBB, were predictors of significant CAD.

Although myocardial perfusion PET has been reported to yield higher sensitivity and specificity compared with conventional SPECT

imaging for the detection of CAD in patients with LBBB,[22] the impact of using quantitative perfusion results as an adjunct to increase sensitivity has not been reported yet. In patients with non-ischaemic cardiomyopathy and LBBB, a decreased rest MBF was reported in the septum (septal-to-lateral MBF ratio: 0.68 ± 0.18) using dynamic PET perfusion imaging, and a similar pattern was observed for myocardial 18F-FDG uptake and oxygen consumption.[23,24] Using ^{82}Rb-PET, Falcão *et al.*[25] found that MFR was decreased in the septum compared with patients without LBBB but remained within normal limits, whereas it was impaired in patients with LBBB and CAD.[25]

The recently published EURECA registry[26] confirmed that the prevalence of significant CAD or ischaemia in patients with stable chest pain is relatively low (24 and 19%, respectively). In our study, the rate of positive SPECT perfusion studies was much lower. This discrepancy could be explained by the occurrence of balanced ischaemia characterized by a normal perfusion and a decreased MFR found in a high number of patients (12/174, 7%). This rate is relatively high compared with the 4.5% reported by Maaniitty et al.[27] in their study using water PET in patients with suspected CAD on CT angiography. In addition, a significant number of these patients with either preserved stress MBF or a MFR within a grey zone between 2 and 2.09 were finally not referred to coronary angio. Although the WATERDAY study demonstrated that a cut-off value of 2.1 for dynamic SPECT MFR was highly predictive of ischaemia by radiolabeled water PET in patients with stable CAD,[9] it is likely that this threshold may be overestimated for the diagnosis of significant coronary lesions. Determining the normal limits of MBF and MFR yielded by dynamic perfusion SPECT will likely improve the reliability of this technique in a diagnostic setting, especially as these thresholds may vary depending on the camera and post-processing methods used.[28]

In the present study, dynamic SPECT demonstrated a significant decrease in both stress and rest MBF within the septum compared with other left ventricular walls, which resulted in a preserved MFR. Despite this, there was a high rate of false-positive results in patients with LBBB who were finally referred to invasive coronary angiography. In 13 patients with false-positive SPECT examination, seven had a final diagnosis of DCM, a situation associated with a poor diagnostic value of perfusion SPECT.[29] It is likely that not referring patients with documented DCM, which is commonly associated with LBBB, to SPECT examination would lead to a significant decrease in false-positive results.[30] More importantly, as the four patients with angiographically proven CAD in the present study had a positive SPECT on conventional imaging, our results do not support the addition of MFR to perfusion SPECT for CAD detection in patients with LBBB.

These data also demonstrated that perfusion SPECT in patients with LBBB led to the identification of only a small number of patients with CAD, even when adding MFR quantification. The results call into question whether such screening is relevant in patients with LBBB, with no history of CAD, and only mild clinical symptoms. Applying to patients with LBBB, the updated algorithm proposed in the recent 2024 ESC Guidelines for the management of chronic coronary syndromes, based on a risk factor-weighted likelihood, clinical findings and coronary calcium score, will likely help to improve patients selection for functional imaging.

Limitations of the study

This is an observational and retrospective single-centre study. Consequently, a selection bias remains possible as the epidemiology of cardiovascular disease may vary within and across regions and countries,[31] and compliance to current guidelines may differ across countries using cardiac imaging for the diagnosis of chronic coronary syndromes.[26] In addition, the study would have benefited from a control group comparison; however, this is not yet available. Moreover, attenuation correction is not available with the D-SPECT camera, which could give rise to false-positive scans and to potential errors in MBF assessment. In the WATERDAY study, stress and rest MBF acquired on D-SPECT without attenuation correction was overestimated compared with PET. However, the resulting MFR was similar between the two techniques,[9] thus supporting its usage in the majority of centres with no access to myocardial perfusion PET.

Conclusion

Although a decreased MFR was associated with fixed perfusion defects on conventional MPI, this study does not support the addition of global MFR to CZT-SPECT perfusion data for the detection of CAD in patients with presumed new LBBB. The low rate of perfusion abnormalities in this study underlines the need to improve the selection of patients with LBBB referred to perfusion SPECT imaging.

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Conflict of interest: D.A. received consulting fees and support for attending meetings from Spectrum Dynamics and participated to an advisory board for GE Healthcare.

Consent

The use of previously acquired data for this retrospective study was approved by the institutional review board (Comité Local d'Ethique de la Recherche en Santé, CLERS #ID-3907). According to French regulation, the patients were previously informed.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Lead author biography

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