

ISCHEMIC HEART DISEASE

Exercise-Induced Left Bundle-Branch Block in Patients with Coronary Artery Disease versus Patients with Normal Coronary Arteries

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Introduction and objectives. Exercise-induced left bundle-branch block does not always denote the presence of underlying coronary artery disease. The aim of this study was to analyze the clinical characteristics and evolution of patients with rate-dependent left bundle-branch block.

Patients and method. 9,318 consecutive exercise stress studies were reviewed. The clinical characteristics and evolution (mean follow-up: 6.9 years) of 20 patients with exercise-induced left bundle-branch block in which coronary angiography had been performed were analyzed.

Results. Eight out of 20 patients had normal coronary arteries (group A) and 12 had coronary artery disease (group B). Peak O_2 consumption, peak myocardial O_2 consumption, and heart rate when block appeared (132 ± 20 vs. 95.4 ± 23 beats/min; $p = 0.002$) were significantly higher in group A. Seven of the 8 patients with normal coronary arteries had chest pain coinciding with the first beat of left bundle-branch block. There were no deaths during follow-up in group A, but permanent left bundle-branch block appeared in 5 patients of this group who experienced disappearance of exercise-related pain. There were 3 deaths in group B and 2 patients had acute myocardial infarction during follow-up. One patient in each group developed atrioventricular block and required pacemaker implantation.

Conclusions. In contrast with patients with left bundle-branch block and coronary artery disease, the prognosis of patients with painful left bundle-branch block and normal coronary arteries is good. However, the development of permanent left bundle-branch block is frequent. Atrioventricular block, although rare, may occur.

Key words: *Conduction. Exercise. Electrocardiography. Scintigraphy. Coronary artery disease.*

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El bloqueo de rama izquierda inducido por el ejercicio en pacientes con y sin enfermedad coronaria

Introducción y objetivos. La aparición de un bloqueo de rama izquierda inducido por el ejercicio no siempre significa presencia de enfermedad coronaria subyacente. El motivo de este estudio fue analizar las características clínicas y evolutivas de los pacientes con bloqueo de rama izquierda dependiente de la frecuencia.

Pacientes y método. Se revisaron 9.318 estudios ergométricos de esfuerzo practicados de forma consecutiva y se estudiaron las características clínicas y evolutivas (seguimiento medio: 6,9 años) de los 20 pacientes que presentaron bloqueo de rama izquierda dependiente de frecuencia y en los que se disponía de coronariografía.

Resultados. Un total de ocho de los 20 pacientes tenían coronarias normales (grupo A) y 12 tenían enfermedad coronaria (grupo B). El consumo máximo de O_2 , el consumo miocárdico de O_2 y la frecuencia cardíaca en el momento de aparición del bloqueo (132 ± 20 frente a $95,4 \pm 23$ lat/min; $p = 0,002$) fueron significativamente superiores en el grupo A. Siete de los 8 pacientes del grupo A presentaron dolor precordial coincidiendo con el primer latido en que apareció el bloqueo. No hubo ningún caso de fallecimiento en el grupo A, y en cinco de los 8 pacientes de este grupo se observó evolución a bloqueo de rama izquierda permanente con desaparición del dolor inducido por el esfuerzo. En el grupo B, 3 pacientes fallecieron y dos presentaron un infarto durante el seguimiento. Un paciente de cada grupo evolucionó a bloqueo auriculoventricular completo.

Conclusiones. A diferencia de los pacientes con bloqueo de rama izquierda dependiente de frecuencia y enfermedad coronaria, el pronóstico de los pacientes con bloqueo de rama izquierda doloroso y coronarias normales es muy bueno en cuanto a mortalidad, aunque pueden evolucionar a bloqueo de rama izquierda permanente y, excepcionalmente, a bloqueo auriculoventricular.

Palabras clave: *Conducción. Ejercicio. Electrocardiografía. Gammagrafía. Enfermedad coronaria.*

ABBREVIATIONS

AV block: atrioventricular block
 RBBB: right bundle-branch block
 LBBB: left bundle-branch block
 FD-LBBB: frequency-dependent left bundle-branch block
 P-LBBB: permanent left bundle-branch block

INTRODUCTION

The appearance of a bundle-branch block induced by exercise has a variable incidence that, depending on the series, ranges from 0.2% to 1.1%.¹⁻³ On most occasions, the left branch is blocked.^{2,4} Effort-induced right bundle-branch block (RBBB) is related with the presence of coronary artery disease in a high percentage of cases,^{4,5} but the meaning of left bundle-branch block (LBBB) dependent on heart rate is controversial.^{5,6} There are series in which it is estimated that the presence of coronary artery disease in the population with frequency-dependent LBBB (FD-LBBB) can reach 70% and that ischemic heart disease is usually especially severe in these patients.⁶ Nevertheless, in other patients, the induction of LBBB by exercise is not accompanied by coronary artery disease or structural heart disease.⁷

The present study was undertaken to make a retrospective assessment of the clinical, ergometric, scintigraphic, coronariographic, and outcome characteristics of patients with FD-LBBB.

PATIENTS AND METHOD**Patients**

Of 9318 consecutive myocardial perfusion radionuclide scans made during effort (2288 planar and 7030 tomographic) in our hospital between 1985 and 1999, 31 (0.3%) revealed exercise-induced bundle-branch block: 2 RBBB and 29 LBBB. Twenty of these patients had a coronary angiography and were included in the present study. The prescription of effort radionuclide scan and coronary angiography was always issued at the discretion of the cardiologist responsible for the patient.

For the purpose of analyzing the clinical characteristics and studying the evolution of these patients, the medical records of all the patients were reviewed. They were contacted by telephone to analyze the possible evolution to permanent LBBB (P-LBBB), atrioventricular block (AV block), and the complications that appear during follow-up: death, infarction, persistent pain, heart failure, syncope, and pacemaker implantation.

Effort stress test and radionuclide scan

All the patients underwent an effort stress test on an ergometric bicycle with continuous monitoring of the electrocardiogram and blood pressure, beginning with an initial load of 50 watts and applying successive increments of 25 watts every 3 min. The test was stopped when the maximum heart rate was reached or progressive angina, serious fatigue, or arrhythmias appeared. Changes in the ST segment were assessed before and after the appearance of LBBB, as well as the moment of appearance of chest pain, peak O₂ consumption values (MET), and peak myocardial O₂ consumption (heart rate, systolic blood pressure), and heart rate at the moment of appearance of LBBB.

From 30 s to 60 s before concluding the exercise phase, the radionuclide dose was injected (thallium-201, technetium-99m-isonitrile, or technetium-99m-tetrofosmin), and effort and resting images were obtained following a protocol suitable for the radionuclide administered: effort and redistribution at 3 h for thallium,⁸ effort and rest on separate days for technetium-99m-isonitrile,⁹ and effort and rest at an interval of <3 h for technetium-99m-tetrofosmin.¹⁰ The planar radionuclide scans (with thallium-201) were performed with a Picker 4/37 gammacamera and tomographic studies with technetium compounds with an Elscint SP4 gammacamera. Five regions were analyzed: anterior, septal, inferior, lateral, and apical. When a mild, moderate, or severe perfusion defect was observed in at least 2 of 3 views of both effort and resting images, it was considered a «fixed defect», and if it was normalized in the resting images it was considered a «reversible defect».

Coronariography

Coronary angiography was always ordered at the discretion of the attending clinician and in every case it was performed using the Seldinger technique. The catheterization reports were reviewed and the presence or absence of coronary artery disease (stenosis >50% in at least one coronary artery) was corroborated by two expert hemodynamics specialists after reviewing the kinematic images. According to the results of coronary angiography, patients were divided into two groups: group A (patients without coronary artery disease) and group B (patients with coronary artery disease).

RESULTS

Eight of the 20 patients included in the study had angiographically normal coronary arteries (group A, all with a normal ejection fraction) and 12 had coronary artery disease (group B, 5 with previous myocardial infarction). The clinical, ergometric, scintigraphic, coronariographic, and outcome

TABLA 1. Patients with frequency-dependent left bundle-branch block and normal coronary arteries (group A)

N	Sex	Age	Treatment	Baseline			HR	SBP	Pain	Decrease	Gamma ST	Cor	Follow-up	Evolution (years)
				ECG	HR-LBBB	MET								
1	M	55	No	N	115	7.5	118 (71%)	180	Yes	No	N (TI)	N	13.8	P-LBBB, AVB, MCP, without pain
2	M	47	Ni.	Neg T in V1-V3	120	7	128 (78%)	160	Yes	No	+S-R (TI)	N	13.5	P-LBBB, without pain
3	M	37	No	Neg T in V1-V3	151	8	170 (90%)	165	Yes	No	+S-R (TI)	N	12.6	P-LBBB, without pain
4	F	49	No	N	140	6	152 (89%)	150	Yes	No	+S not R (MIBI)	N	10.8	P-LBBB, without pain
5	M	46	No	N	110	6.5	135 (77%)	180	Yes	No	+S not R (MIBI)	N	9.6	FD-LBBB, pain
6	M	43	No	N	170	9	175 (99%)	200	Yes	No	N (tetro)	N	8.4	P-LBBB, without pain
7	F	62	Ni.	Neg T in V1-V3	120	6	152 (96%)	150	No	No	N (tetro)	N	5	FD-LBBB, without pain
8	M	49	No	N	130	8.8	135 (79%)	190	Yes	No	N (tetro)	N	1	FD-LBBB, pain

AVB indicates atrioventricular block; FD-LBBB, frequency-dependent left bundle-branch block; P-LBBB, permanent LBBB; Cor, coronariography; ST depr., ST depression (mm); F, female; HR-LBBB, heart rate at time of appearance of LBBB; HR, maximum heart rate; Gamma, radionuclide scan; M, male; MIBI, technetium-99m methoxy-isobutyl-isonitrile; N, normal; SBP, peak systolic blood pressure (mm Hg); R, reversible; S, septal; F, follow-up; Tetro, technetium-99m tetrofosmin; TI, thallium-201; S, septal.

characteristics of the patients in group A are shown in Table 1 and those of group B, in Table 2. The mean follow-up was 6.9 years (range, 1-13.8 years).

The mean age of the patients in group A was significantly lower than that of the patients in group B (48.5±7.5 years versus 61±8.4 years; *P*=.005).

Although risk factors predominated in the patients in group B (8 smoking, 6 hypertension, 5 dyslipidemia, and 3 diabetes), the differences were not significant with respect to the patients in group A (3 smoking, 3 hypertension, 3 dyslipidemia, and 2 diabetes). MET (7.3±1.12 versus 5.6±1.7; *P*=.02), maximum heart rate

TABLA 2. Patients with frequency-dependent left bundle-branch block and coronary artery disease

N	Sex	Age	Previous		Baseline			HR	SBP	Pain	ST depr.		AD	CX	RC	Follow-up (years)	Evolution
			infarction	Treat.	ECG	HR-LBBB	MET				(mm)	Gamma					
9	M	64	Non Q	BB, ACEI	HBA	145	7	150 (96%)	190	No	2	+I not R (TI)	70	0	100	4.1	P-LBBB, surgery
10	M	47	Ant.	Ni, ACEI	QS V1-6	115	5	125 (72%)	170	No	-	+A not R (TI)	90	0	0	11	P-LBBB
11	M	64	-	BB, Ni, Ca	LVH	80	6	100 (64%)	180	No	-	+I R (TI)	< 50	0	90	6.7	P-LBBB, AMI inf, death
12	M	62	-	BB, Ni, IECA	N	80	5.2	90 (57%)	215	No	2	+I R (TI)	0	0	100	10.3	P-LBBB-AVB-MCP
13	M	62	-	BB, Ant Ca, Ni	HBA, T- aVL	80	6.3	100 (63%)	170	No	-	+S-Ap R (MIBI)	70	0	0	8	P-LBBB
14	M	61	-	ACEI	Neg T DI-aVL	120	5	128 (80%)	190	No	-	+A-S-Ap R (MIBI)	90	90	0	7	P-LBBB, AMI ant, EAP, surgery
15	M	47	-	ACEI	HBA	105	4.2	131 (76%)	130	No	1.5	+A-L R (MIBI)	99	100	60	6.3	P-LBBB, ICCV, FV, Impl. def
16	F	68	-	Ni	N	78	4	100 (66%)	190	Yes	1	+A-L R (MIBI)	70	90	50	4.1	FD-LBBB, CX stent
17	F	68	Non Q	Ni, Ca ant, IECA	N	80	4.7	105 (69%)	220	Yes	1	+A-L not R (Tetro)	90	90	0	2	FD-LBBB, PTCA DA and CX, EAP, death
18	M	55	Inf.	BB, Ant Ca, IECA	QS inf. T- V4-6	90	10	110 (67%)	160	No	-	+I-L not R (Tetro)	90	100	0	1.8	FD-LBBB, PTCA DA
19	M	58	-	Ni	T II-III, aVF	95	6	115 (71%)	240	Yes	1	+I-L R (Tetro)	0	0	90	1.5	FD-LBBB, RC stent
20	M	74	Non Q	BB, Ni, IECA	T V2-6	80	4	90 (55%)	165	No	1	+I-L R (Tetro)	99	100	99	1	FD-LBBB, surgery

Ca ant indicates calcium antagonists; A, anterior; Ap, apical; AVB, atrioventricular block; BB, beta-blockers; FD-LBBB, frequency-dependent left bundle-branch block; P-LBBB, permanent LBBB; Cor, coronariography; ST depr., ST depression (mm); Impl. def., implantable defibrillator; ALE, acute lung edema; F, female; HR-LBBB, heart rate at the moment of appearance of LBBB; HR, maximum heart rate; VF, ventricular fibrillation; Gamma, radionuclide scan; M, male; I, inferior; ACEI, angiotensin-converting enzyme inhibitors; L, lateral; MIBI, technetium-99m methoxy-isobutyl-isonitrile; N, normal; SBP, maximum systolic blood pressure (mm Hg); R, reversible; S, septal; F, follow-up; Tetro, technetium-99m tetrofosmin; TI, thallium-201; Treat, treatment.

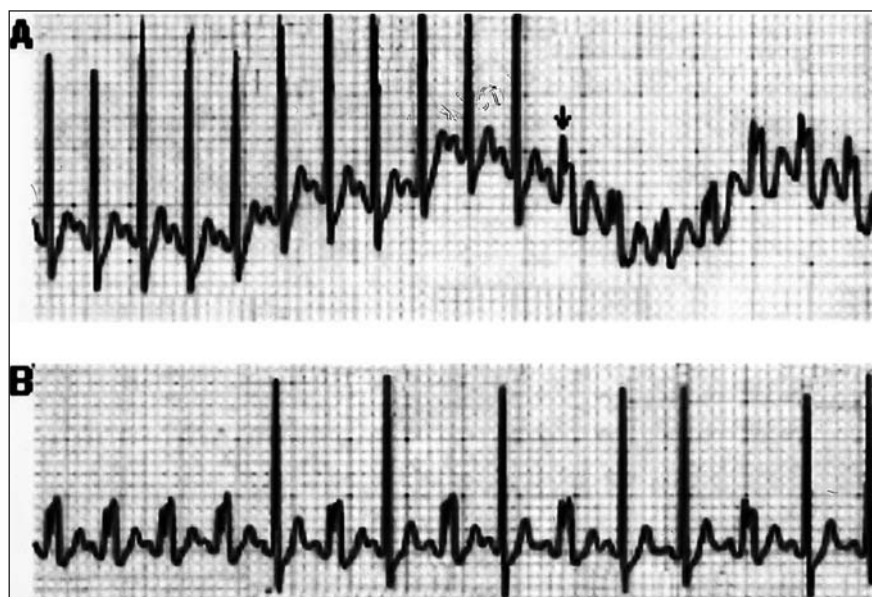


Fig. 1. ECG of a patient with LBBB induced by effort and healthy coronary arteries (case 8). A: the appearance of pain coincides exactly (arrow) with the first beat blocked at a heart rate of 130 beats/min, with no apparent disturbances in the ST segment before the appearance of the LBBB. B: disappearance of LBBB during post-effort without ST segment changes in unblocked beats.

(145.6 ± 20 versus 112 ± 18 beats/min; $P=.003$), the percentage of tachycardization ($84.9 \pm 10\%$ versus $69.5 \pm 11\%$; $P=.008$) and the heart rate at the moment of appearance of LBBB (132 ± 20 versus 95.4 ± 23 beats/min; $P=.002$) were significantly superior in group A compared with group B.

Two of the 8 patients in group A and 10 of the 12 patients in group B were receiving antianginal treatment (beta-blockers, nitrites, or calcium antagonists) at the moment that the effort stress test was performed. During exercise testing, only 3 patients in group B presented precordial pain that required the interruption of effort, whereas 7 of the 8 patients in group A presented precordial pain coinciding with the first beat in which LBBB appeared. The cessation of pain was also abrupt and coincided with the disappearance of LBBB. In no patient in group A was ST-segment depression observed before the appearance of LBBB or immediately after its cessation (Figure 1), whereas in 7 of the 12 patients in group B, there was a horizontal change or depression of the ST segment ≥ 1 mm before the appearance of LBBB (Figure 2).

The perfusion radionuclide scan was normal in 4 patients in group A (Figure 3). In the other 4 patients, mild septal uptake defects were observed, which were reversible in 2 cases and fixed in the other 2. In group B, all the radionuclide scans revealed perfusion defects, with good agreement between the region with a reversible defect and the most stenotic artery (in patients without previous infarction) and between the nonreversible defect and the location of necrosis (in patients with previous infarction) (Figure 4).

In group A there were no cases of death or acute myocardial infarction during follow-up. Progression to

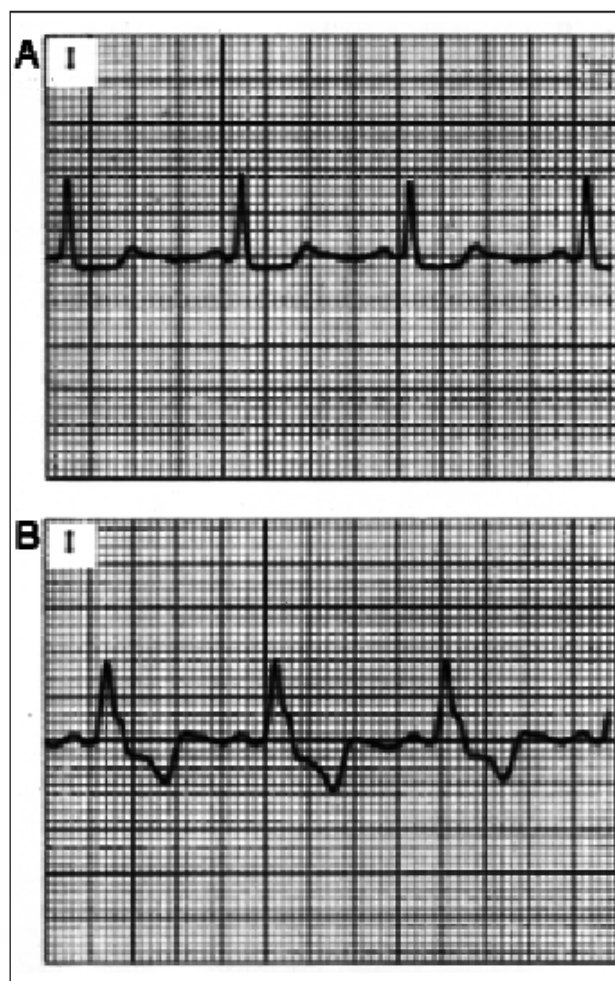


Fig. 2. ECG of a patient with LBBB induced by effort and coronary artery disease (case 16). A depression of 0.1 mV in the ST segment is visible in I (A), just before the appearance of LBBB at a heart rate of 78 beats/min (B) (case 16).

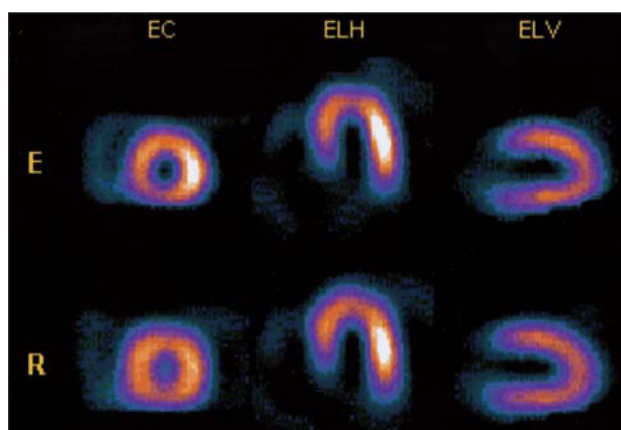


Fig. 3. Myocardial perfusion SPECT corresponding to the patient in Figure 1 in which no perfusion defects are observed during effort (E) or at rest (R). EC indicates short axis; ELH: horizontal long axis; ELV: vertical long axis.

P-LBBB was observed in 5 of the 8 patients, with the effort-induced pain disappearing in all of them. Only one patient evolved to complete AV block and required the implantation of a pacemaker.

In group B, 2 patients died of left heart failure refractory to treatment and two of the 7 patients without previous infarction presented it during follow-up. A total of 7 patients were revascularized (3 by surgery, 2 by angioplasty, and 2 by stent implantation). Four patients progressed to P-LBBB, one to complete AV block requiring the pacemaker implantation, and another patient required the implantation of a defibrillator after an episode of ventricular fibrillation.

DISCUSSION

The appearance of a FD-LBBB does not necessarily imply the existence of underlying coronary artery disease. Wieweg et al¹¹ in 1976 described for the first time patients who presented chest pain that coincided with the appearance of LBBB in the course of a effort stress test. These patients showed healthy coronary arteries in catheterization studies, which is why this clinical condition was later designated «painful LBBB».¹² The characteristics of the pain that these patients present are similar to those of angina pectoris, since it is triggered by exercise, but the pain is usually not so intense, is not radiated, is not accompanied by vegetative symptoms, and precludes continuing exercise. In every case its onset was abrupt and always coincided with the first blocked beat. The duration of discomfort varied and usually concluded abruptly.^{1,3,7} Likewise, in no case was the appearance of LBBB during exercise testing preceded or followed by changes in the ST segment that suggested an ischemic origin of the blockade.⁷ Two theories are

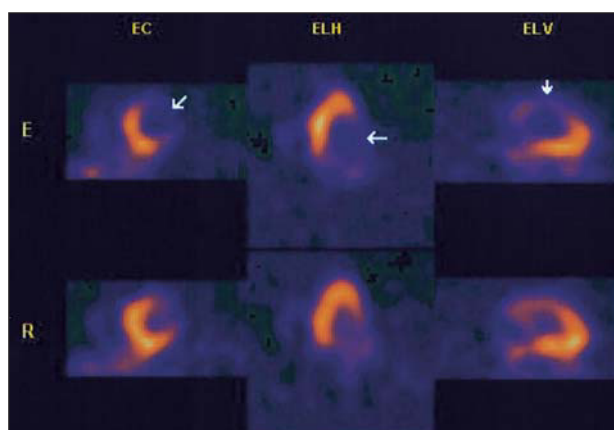


Fig. 4. Myocardial perfusion SPECT corresponding to the patient in Figure 2. A severe perfusion defect (arrows) is visible in the lateral and anterior regions during effort (E) that is partially reversible at rest (R). EC indicates short axis; ELH: horizontal long axis; ELV: vertical long axis.

postulated to explain pain in patients with angiographically normal coronary arteries. The first interpretation defends an ischemic cause on the basis of an increase in lactate in the coronary sinus, the appearance of minor ECG disturbances such as elevation of the R wave and reduction of the Q wave in V₅ before the appearance of LBBB, and alleviation with nitroglycerin.¹³ The second, more widely accepted interpretation postulates the existence of dysnergic contraction that stimulates mechanoreceptors and causes chest discomfort.^{3,12,14}

In our series, patients with FD-LBBB and coronary artery disease were characterized as being older and reaching a smaller peak O₂ consumption and a smaller myocardial O₂ consumption than patients with FD-LBBB and normal coronary arteries. The fact that the group of patients with coronary artery disease was receiving antianginal treatment explains why the heart rate systolic blood pressure product was low. Different authors report the same results.^{1,6,15} Vasey et al¹ noted that the criteria that characterized patients with FD-LBBB and associated coronary artery disease were the presence of typical angina and the appearance of blockade with heart rates of less than 125 beats/min. Although it is certain that this last criterion was met by all the patients with coronary artery disease in our series except one, half of the patients with normal coronary arteries presented LBBB with heart rates of less than 125 beats/min.

A smaller proportion of the patients with FD-LBBB and coronary artery disease in our series presented chest pain during the effort stress test than the patients with normal coronary arteries (3/12 versus 7/8). This, without doubt, must be attributed to the fact that the majority were being treated with antianginal drugs at the time that the exercise stress test was carried out. In the 3 patients with coronary artery disease who

presented angina during the test, angina did not coincide with the first blocked beat, it appeared later and required effort to control it. The perception of discomfort with the first blocked beat is, in our opinion, the most characteristic finding of patients with painful LBBB and healthy coronary arteries.

Although the myocardial perfusion radionuclide scan showed, in general, more severe and extensive defects in patients with coronary artery disease, mild septal perfusion defects were also observed with effort, which were more or less reversible with rest, in patients with LBBB and normal coronary arteries.¹⁵⁻¹⁸ These scintigraphic patterns are similar to those described in patients with underlying LBBB. Four of the 8 patients with normal coronary arteries presented an abnormal scintigraphic pattern and 3 of them progressed to permanent LBBB. Therefore, there are cases in which doubts still appear with respect to the presence of coronary artery disease after observing the radionuclide scans. Some authors have communicated that effort echography,¹⁹ the use of dipyridamole or adenosine,²⁰ and the use of technetium compounds instead of thallium²¹ make it possible to increase the specificity of the noninvasive techniques for the diagnosis of coronary artery disease in patients with LBBB, but coronary angiography is always required in order to establish a firm diagnosis.

Various authors have reported a good medium and long-term prognosis in patients with FD-LBBB and normal coronary arteries with regard to infarction and mortality,^{15-17,22,23} which was corroborated in our series. In these patients, progression to P-LBBB with the disappearance of symptoms is not infrequent during follow-up. This occurred in 5 of the 8 patients in our series without coronary artery disease and in 5 of the 12 patients with coronary artery disease. Progression to advanced AV block, with the consequent need for pacemaker implantation, was observed in one patient in each group. This progression to complete cardiac block could explain some cases of sudden death that have been reported in patients with healthy coronary arteries.^{4,15}

The prognosis of patients with FD-LBBB and coronary artery disease is much worse. In our series, 3 of the 12 patients died during follow-up, one required implantation of a defibrillator after cardiac arrest due to ventricular fibrillation, 3 suffered acute myocardial infarction, and 7 had to be revascularized.

CONCLUSIONS

The appearance of LBBB induced by exercise does not always reflect the presence of coronary artery disease. A group of relatively younger patients exists presents abrupt chest pain during effort, coinciding with the first beat of LBBB and unaccompanied by

vegetative symptoms, that does not force exercise to be stopped. Coronary artery disease is not found in these patients. The prognosis of these patients is very favorable compared with that of patients with FD-LBBB and coronary artery disease. In the latter cases the coronary artery disease is usually very severe and has a high mortality. Although underlying coronary artery disease does not exist, it is advisable to carry out periodic follow-up examinations in these patients due to the possibility of progression to P-LBBB and, exceptionally, to more advanced forms of AV block.

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