Prevalence and Predisposing Factors for Bundle Branch Block in Patients Starting Dialysis

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Introduction and objectives. Although bundle branch block (BBB) is regarded as a frequent finding, data on its prevalence are scarce in the general population and nonexistent in patients on dialysis. The aims of this study were to determine the prevalence of complete BBB in patients starting dialysis, to identify factors associated with its presence and, secondarily, to explore its association with mortality and the occurrence of cardiovascular events.

Methods. The study involved patients who started dialysis at our institution between November 1, 2003 and December 31, 2006. All underwent cardiological evaluation at the start of treatment. The presence of BBB was determined and its relationship with clinical factors and biochemical and echocardiographic parameters was examined. Patients were followed up until November 30, 2007.

Results. The study included 211 patients (age 65.05[15.7] years; 56.4% male). Of these, 24 (11.4%) presented with BBB: 6 (2.8%) with left BBB and 18 (8.5%) with right BBB. Age (odds ratio [OR]=1.05; 95% confidence interval [CI], 1.008-1.113; *P*=.02) and body mass index (OR=1.12; 95% CI, 1.019-1.234; *P*=.02) were independently associated with BBB. During a mean follow-up period of 23.7(12.9) months, patients who presented with left BBB showed a clear trend towards a poorer outcome than those without a conduction defect.

Conclusions. The prevalence of BBB was high in patients starting dialysis and greater than that observed in the general population. Its presence was independently associated with older age and obesity. During the mean follow-up period of 2 years, patients with left BBB demonstrated a trend towards a poor prognosis.

Key words: *Bundle branch block. Kidney. Risk factors.*

Análisis de la prevalencia y los factores predisponentes de los bloqueos de rama en los pacientes que inician diálisis

Introducción y objetivos. Aunque los bloqueos de rama (BR) se consideran hallazgos frecuentes, la información sobre su prevalencia real en la población general es escasa, y es inexistente en los pacientes en diálisis. El objetivo es establecer la prevalencia del BR completo en la población que inicia diálisis y los factores relacionados con su aparición. Como análisis adicional, se explora su asociación con la mortalidad y con la aparición de un evento cardiovascular.

Métodos. Se incluyó a los pacientes que iniciaron diálisis en nuestro centro entre el 1 de noviembre de 2003 y el 31 de diciembre de 2006. Todos fueron sometidos a valoración cardiológica al inicio de diálisis. Determinamos el BR y su relación con factores clínicos y parámetros ecocardiográficos y bioquímicos. Los pacientes fueron seguidos hasta el 30 de noviembre de 2007.

Resultados. Se incluyó a 211 pacientes (media de edad, 65,05 ± 15,7 años; el 56,4% varones); 24 (11,4%) presentaban BR; 6 (2,8%), BR izquierda y 18 (8,5%), BR derecha. La mayor edad (*odds ratio* [OR] = 1,05; intervalo de confianza [IC] del 95%, 1,008-1,113; p = 0,02) y el índice de masa corporal (OR = 1,12; IC del 95%, 1,019-1,234; p = 0,02) se relacionaron de forma independiente con el BR. Durante un seguimiento medio de 23,7 ± 12,9 meses, hubo una clara tendencia a un peor pronóstico en los pacientes con BR izquierda respecto a los que no tenían defecto de conducción.

Conclusiones. Los pacientes que inician diálisis presentan una alta prevalencia de BR, superior a la de la población general. Mayor edad y obesidad se relacionan de forma independiente con que se produzca. Durante un seguimiento medio de 2 años, los pacientes con BR izquierda mostraron tendencia a un peor pronóstico.

Palabras clave: *Bloqueo de rama. Riñón. Factores de riesgo.*

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Received December 31, 2007.
Accepted for publication March 13, 2008.

ABBREVIATIONS

BBB: bundle branch block
LAHB: left anterior hemiblock
LBBB: left bundle branch block
RBBB: right bundle branch block

INTRODUCTION

The bundle branch block (BBB) concept was introduced more than a century ago by Eppinger et al.[1] Since then it has generated considerable interest in the medical literature, and is now a familiar finding for all physicians involved in clinical practice. Nonetheless, despite the extensive available literature, which agrees on the association of BBB with advanced age, there are considerable discrepancies regarding the prevalence of BBB and its association with other heart diseases and cardiovascular risk factors. The relationship between BBB and hypertension, coronary disease, and heart failure has been the subject of numerous research efforts and the source of conflicting results in major epidemiologic studies.[2-7]

Although there is agreement on the importance of BBB as an indicator of a poor prognosis in patients with myocardial infarction, whether treated with thrombolysis or not,[8-10] and in chronic coronary disease, regardless of the degree of systolic dysfunction or extent of the coronary lesions,[11] the role of BBB itself as a predictor of cardiovascular mortality or morbidity is not well established.

More than 30 years ago an association was observed between cardiovascular disease and chronic kidney disease,[12] and now this is a fully recognized fact.[13] Nevertheless, some specific aspects of cardiovascular disease occurring in dialysis patients have not been fully investigated. Conditions such as atrial fibrillation and peripheral arterial disease, which are quite important in the general population, have received little attention in this group of patients.[14-17] To our knowledge, there are no published studies analyzing the relationship between chronic kidney disease under dialysis treatment and intraventricular conduction defects.

The aim of this study is to establish the prevalence of complete BBB in patients starting dialysis and to analyze the factors associated with BBB or that predispose to its appearance. In addition, the associations between BBB and mortality and the development of cardiovascular events are investigated.

METHODS

All patients starting hemodialysis or peritoneal dialysis for the first time at our hospital or affiliated outlying centers between November 1, 2003 and December 31, 2006 were included in the study.

During the first month under treatment, a cardiologist assessed all patients by performing a clinical history, physical examination, electrocardiography, and color Doppler echocardiography. Complete BBB was established when the following criteria were present on electrocardiography:

– Left bundle branch block (LBBB): *a)* QRS duration ≥120 ms; *b)* QS or rS complex in lead V_1; *c)* slurred R wave in leads I, aVL, V_5, or V_6, or rS pattern in V_5, or V_6; and *d)* absence of Q wave in leads V_5, V_6, or I
– Right bundle branch block (RBBB): *a)* QRS duration ≥120 ms; *b)* R or rSR' pattern in leads V_1 or V_2; and *c)* slurred S wave in leads I, V_5, or V_6. In RBBB, the QRS axis in the frontal plane was taken into account, such that an axis of less than –30° was considered attributable to a left anterior hemiblock (LAHB) and indicative of bifascicular block

An analysis was performed to determine the relationship between the conduction defect and the following factors: age, sex, diabetes, hypertension, pulse pressure, smoking, body mass index, history of coronary disease, stroke, and atrial fibrillation, analytical values for troponin I, hemoglobin, urea, creatinine, albumin, cholesterol, triglycerides, calcium, phosphorus, and parathyroid hormone, as well as the size of the left atrium and ascending aorta, left ventricular hypertrophy, ejection fraction, E/A ratio for mitral flow, and annular or valvular calcifications. Hematological and biochemical parameters were determined at the start of treatment.

Patients were considered to have hypertension when their blood pressure value at the time of enrollment was >140/90 mm Hg or they were under drug therapy to control blood pressure. Patients were considered to have diabetes when they were taking antidiabetic drug treatment, and were classified as smokers if they were actively smoking at the time of enrollment or had stopped smoking within the 3 months prior to enrollment. A history of coronary disease was established when the patient had experienced a myocardial infarction or showed significant obstructive lesions on coronary angiography. Color Doppler echocardiography studies were performed by the same operator. Left atrial and ascending aorta dimensions were determined using a long-axis parasternal view. Left ventricular ejection fraction was calculated in M mode applying the Teichholz formula, and left ventricular mass was estimated following the Penn convention method.

Patients were followed-up until November 30, 2007 except when there was a change of residence that implied continuing dialysis treatment at another center, death, or transplantation. We analyzed the relationship between BBB and overall mortality and the development of cardiovascular events, defined as coronary disease (acute

TABLE 1. **Clinical Characteristics of the Study Population**

Men, n (%)	119 (56.4)
Age at start of dialysis, y	65.05 (15.7)
BMI	27.42 (5.3)
Diabetes, n (%)	57 (27)
Hypertension, n (%)	184 (87.2)
Smoking, n (%)	55 (26.1)
Documented coronary disease, n (%)	16 (7.6)
Prior stroke, n (%)	18 (8.5)
AF detected at any time, %	33 (15.6)
Pulse pressure, mm Hg	55.6 (20.8)
Troponin, ng/mL	0.09 (0.6)
Hemoglobin, g/dL	0.4 (1.5)
Urea, mg/dL	144.2 (50.9)
Creatinine, mg/dL	6.6 (2.4)
Albumin, g/dL	3.5 (0.5)
Cholesterol, mg/dL	159 (40)
Triglycerides, mg/dL	137.6 (72.5)
Calcium, mg/dL	8.9 (0.9)
Phosphorus, mg/dL	5.2 (1.7)
Parathyroid hormone, pg/dL	249.1 (249.2)

AF indicates atrial fibrillation; BMI, body mass index.
Values are expressed as the mean (SD), except where otherwise indicated.

TABLE 2. **Echocardiographic Parameters of the Study Population**

Left ventricular size, mm	41.08 (7.4)
Aortic root size, mm	32.7 (3.9)
Left ventricular mass, g/m^2	199.5 (75.7)
Patients with EF <50%, n (%)	12 (5.6)
EF, %	64.9 (10.1)
E/A velocity ratio for mitral filling	0.89 (0.4)
Patients in SR with mitral E/A ratio >1, n (%)	42 (21.8)
Patients with calcifications, n (%)	99 (46.9%)

EF indicates ejection fraction; SR, sinus rhythm.
Values are expressed as the mean (SD) except where otherwise indicated

myocardial infarction or coronary angiography showing >70% lesions in epicardial coronary arteries), stroke, or pacemaker requirement. All patients were in a dialysis program and in permanent contact with the hospital; hence, collection of data related to their evolution did not pose any problems.

Statistical Analysis

Univariate analysis (Student *t* test for quantitative variables and Fisher's exact test for qualitative variables) was used to examine whether there were differences between patients with and without BBB for candidate variables that would be predisposing factors to this condition. Logistic regression models were developed to measure the association between the predisposing factors and BBB. The models estimated the odds ratio (OR) and 95% confidence interval (CI). A *P* value of <.05 was considered statistically significant in the hypothesis testing.

RESULTS

The study included 211 patients. The clinical characteristics and echocardiographic parameters of the study population are presented in Tables 1 and 2. Twelve (5.6%) patients had ejection fraction values of <50%. Left ventricular mass was >120 g/m^2 in 93.3% (111/119) of men and >100 g/m^2 in 94.6% (87/92) of women.

Among the 211 patients, 24 (11.4%) presented complete BBB, including 6 (2.8%) LBBB and 18 (9%) RBBB. Among the latter, 7 patients (38% of all RBBB and 3.3% of the total number of patients) presented RBBB plus LAHB (bifascicular block).

None of the patients with BBB had EF <50%. Left ventricular mass was >120 g/m^2 in men with BBB and >100 g/m^2 in women with BBB.

The differences in the presentation of BBB between men and women are shown in Figure 1. BBB was more common in men than in women (15/119 [12.6%] and 9/92 [9.8%], respectively), although the difference did not attain significance. Among men, RBBB were predominant, accounting for 86.6% of the BBB detected (13/15). The percentage was more balanced among women, with LBBB detected in 4 of the 9 patients with BBB (44.4%).

The variables showing the most significant differences between patients presenting conduction defects and those that did not are presented in Table 3. Older age, elevated body mass index, diabetes, increased pulse pressure, and calcifications were significantly related to the presence of BBB. A history of hypertension was documented in 92% of patients with BBB and 89% of those without.

The associations between BBB and all the variables in Table 3 are shown in Table 4. As can be observed, older age and higher body mass index are independently associated with a higher probability of developing BBB.

There was a higher percentage of diabetic subjects among the patients with bifascicular block than among those with RBBB or LBBB alone. Patients with LBBB had a lower ejection fraction and higher frequency of documented coronary disease and atrial fibrillation than those who had RBBB or bifascicular block. Differences according to the location of the conduction defect are shown in Table 5.

Patients were followed up for a mean (SD) of 23.7 (12.9) months. Over the follow-up period, 67 (31.7%) patients died, 15 (7.1%) underwent transplantation, and 5 (2.4%) moved to a residence outside the catchment area of our institution. In addition, 25 (11.8%) had a

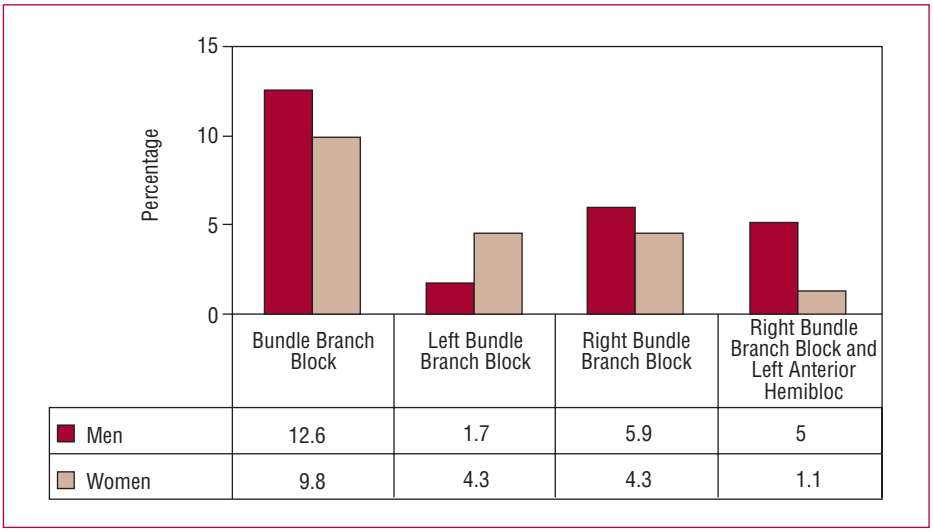

Figure 1. Distribution of bundle branch blocks by site and sex. Values are expressed as percentages of the total population of men and women.

TABLE 3. **Factors Related With the Presence of Bundle Branch Blocks**

	With BBB (n=24)	Without BBB (n=187)	*P*
Men, n (%)	15 (62)	104 (55.6)	NS
Age, y	72.8 (8.9)	64 (1.9)	.001
BMI	29.4 (4.5)	27.1 (5.3)	.02
Diabetes, n (%)	10 (41.7)	47 (25.1)	.009
Pulse pressure, mm Hg	63.6 (15.7	54.5 (21.29)	.01
Troponin, ng/dL	0.05 (0.04)	0.1 (0.6)	.05
Annular or valvular calcifications, n (%)	16 (66.6)	83 (44.3)	.03
E/A velocity ratio for mitral filling	0.76 (0.3)	0.9 (0.4)	.07
AF detected at any time, n (%)	7 (29.2)	26 (13.9)	.05
Documented coronary disease, n (%)	4 (16.7)	12 (6.4)	.09

AF indicates atrial fibrillation; BMI, body mass index.
Hypertension, smoking, prior stroke, hemoglobin, urea, creatinine, albumin, cholesterol, triglycerides, calcium, phosphorous, parathyroid hormone, left ventricular size, aortic size, ejection fraction, and left ventricular mass were statistically non-significant. *P* values were calculated using the Student *t* or Fisher exact test.
Values are expressed as the mean (SD), except where otherwise indicated.

cardiovascular event during follow-up, which consisted of pacemaker implantation in only 2 cases. Mortality was higher in the group of patients with BBB (54.2% vs 28.9%). Five of the 6 patients with LBBB (83.3%), and 8 of the 18 patients with RBBB (44%) died during follow-up. In addition, cardiovascular events occurred in a higher proportion of patients with BBB than in those with no conduction defect (16.6% vs 11.2%). As was seen for mortality, LBBB was more closely related to development of a cardiovascular event, which occurred in 16.7% of patients with LBBB and 11.1% of those with RBBB. Because of the limited number of patients included, however, the differences were not statistically significant. One of the 2 patients who required pacemaker implantation had a bifascicular block.

TABLE 4. **Associations Between Bundle Branch Block and the Most Significant Variables**

	OR	95% CI	*P*
Men	1.57	0.56-4.92	.43
Older age	1.05	1.008-1.113	.02
Higher BMI	1.12	1.019-1.234	.02
Diabetes	0.51	0.17-1.49	.22
Higher pulse pressure	1.01	0.98-1.04	.35
Higher troponin value	0.68	0.05-9.12	.77
Presence of calcifications	0.78	0.24-2.42	.64
Higher mitral E/A ratio	0.44	0.08-2.27	.32
AF	0.44	0.11-1.77	.25
Heart disease	0.65	0.12-3.55	.62

AF indicates atrial fibrillation; BMI, body mass index; CI, confidence interval; OR, odds ratio.

TABLE 5. **Differences in Some of the Clinical Parameters According to the Site of the Conduction Defect**

	LBBB (n=6)	RBBB Alone (n=11)	RBBB+LAHB (n=7)
LVEF, mean %	57	72	65
History of hypertension, %	100	91	86
Documented coronary disease, %	33	6	14
AF detected at any time, %	50	27	14
Diabetes, %	33	36	57
Annular or valvular calcifications, %	83	72	43

AF indicates atrial fibrillation; LAHB, left anterior hemiblock; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; RBBB, right bundle branch block.

DISCUSSION

As this study shows, complete BBB is highly prevalent among patients starting dialysis. Our results cannot be compared with similar studies because there are no published reports analyzing this aspect of cardiovascular disease in the population of dialysis patients. Nonetheless, were able to carry out some estimates regarding the differences with respect to the general population. Our findings concur with epidemiological studies showing that BBB is associated with older age. In the Framingham study,[2] the finding of a QRS complex >0.12 s was exceptional in individuals under 50 years, but reached a prevalence of almost 11% in men in the 8th or 9th decade of life. In a study of men in Sweden,[3] the prevalence of BBB was 1.2% at age 50, 12.2% at 75, and 17% at 80. In the present study, age was independently related with BBB; only 1 (2.4%) of the 41 patients under 51 had the conduction defect, whereas BBB was documented in 19.4% of patients over 75. The relationship between BBB and age in our study group was similar to the trend seen in the general population. However, same cannot be said for the prevalence. In our analysis, the prevalence of BBB among men ≥70 years old was 19.2% and among women, 14.3%. These figures are much higher than those of the general population. In the Framingham study,[2] the prevalence of BBB in a population of similar age was 11% in men and 5% in women. In the Swedish study, which only included men, the prevalence was 12.2% at age 75 and 17% at age 80.[3] The Reikiavik[4,5] study reported that 4.1% of men and 1.6% of women aged 75 to 79 years presented BBB. The higher prevalence of conduction defects among men in our study is also similar to the general population,[2,4,5] although the differences between sexes occurring in our population were smaller.

The higher prevalence of BBB we found can be attributed to the fact that almost all the patients included had a current or prior history of hypertension. Nonetheless, the relationship between hypertension and intraventricular conduction defects has been, and continues to be, a subject of controversy. In contrast to the Framingham[2] study, the one performed in Iceland found no association between hypertension and LBBB,[5] but did establish a link between hypertension and RBBB in men and women under 60 with this condition.[4] Data from studies by Eriksson et al[3] and Ostander[6] have also shown a lack of significant relationships between conduction defects and hypertension, whereas other authors have reported an association only in bifascicular block.[7] Therefore, we believe that attributing the higher prevalence of BBB found in our study only to hypertension is not supported by a high enough level of evidence. In addition, this higher prevalence is similar to that found in other clinical manifestations of cardiovascular disease in patients with chronic end-stage renal disease.[16-18] The higher proportion of RBBB than LBBB is an almost constant finding in the general population,[2-5] although there is no overall agreement on this point either.[19]

We do not have an explanation for the relationship between BBB and high body mass index seen in our patients, which has not been described previously. Nor have we found descriptions of the association between BBB and pulse pressure documented in our patients. There has been some mention,[4,5] although it is not constant,[3] of the association we found between conduction defects and diabetes.

The relationship between valvular calcifications and conduction disorders was reported many years ago[20,21] and the association between valvular calcifications and chronic kidney disease is well established.[22-24] Thus, the association we found between conduction defects and annular or valvular calcifications is not surprising, and, in fact, has been indicated in a previous study.[25]

As was the case of hypertension, left ventricular hypertrophy was present in a quite significant percentage of our cohort, a fact that makes it difficult to establish differences for this parameter in patients with and without conduction disorders.

When the factors associated with BBB were analyzed in relation to the location of the conduction defect, we found that LBBB was associated with a higher incidence of coronary disease, atrial fibrillation, and valvular calcifications, although the limited patient sample makes it difficult to establish statistical significance.

As is true for the BBB-related factors, the influence of conduction defects on the clinical evolution of the patient remains poorly delimited. The recent Swedish

study[26] showed that the presence of RBBB in 50-year-old men without myocardial infarction or stroke increased the risk of developing a high-grade atrioventricular block, but did not change the estimated life expectancy or development of cardiovascular events. However, LBBB was associated with both atrioventricular block and a higher risk of death due to ischemic causes. The Framingham[27] study concluded that LBBB is more closely associated than RBBB with the development of cardiovascular disease in men, whereas in women, both conduction defect sites showed a similar clinical correlation. In the analysis to determine the significance of isolated BBB, that is, in the absence of heart disease or cardiovascular risk factors, LBBB had a poorer prognosis than RBBB.[28,29]

The duration of follow-up in our study was shorter than that of the studies performed in the general population mentioned above. This short follow-up and the small number of patients included are the main limitations of the study. It should be kept in mind, however, that the population under study (patients initiating dialysis) is a relatively small group with a much higher mortality rate than that of the age-matched general population. The present study includes all patients starting dialysis in the catchment area of our center (650 000 inhabitants) over a period of 3 years, who had a yearly mortality rate of approximately 15%. Taking into account these limitations, our study showed a poorer prognosis in patients presenting BBB at the start of dialysis, which was more pronounced in those with LBBB.

CONCLUSIONS

In summary, patients starting dialysis present a high prevalence of BBB as compared to similar age groups in the general population. This high prevalence can probably be attributed to several factors, as has been reported for other clinical manifestations of cardiovascular disease.[29,30] Among these related factors, we should highlight those that have shown a relationship with interventricular conduction defects in the general population and that are present in a high percentage of these patients, such as hypertension, left ventricular hypertrophy, and calcifications. The presence of BBB in a patient starting dialysis should be considered a factor indicative of a poor prognosis, particularly when the conduction defect is an LBBB.

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