Cardiac and neuromuscular implications of left bundle branch block in left ventricular hypertrabeculation/noncompaction

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BACKGROUND: Left bundle branch block (LBB) is frequently found in left ventricular hypertrabeculation/noncompaction (LVHT).

OBJECTIVES: To compare LVHT patients with and without LBB regarding LVHT location and extension, left ventricular function, symptoms, electrocardiographic findings, prevalence of neuromuscular disorders (NMDs) and mortality during follow-up.

METHODS: The charts of patients who underwent transthoracic echocardiographic examination at the Krankenhaus Rudolfstiftung (Wien, Austria) between June 1995 and November 2006 were examined.

RESULTS: LVHT was diagnosed in 102 patients (30 women) with a mean ($\pm$ SD) age of 53 ± 16 years (range 14 to 94 years). A specific NMD was diagnosed in 21 patients and an NMD of unknown etiology was diagnosed in 47. The neurological investigation was normal in 14 patients and 20 patients refused the investigation. The 24 patients with LBB were older (61 versus 51 years of age; $P < 0.01$), and suffered from exertional dyspnea (96% versus 59%; $P < 0.01$) and heart failure (79% versus 46%; $P < 0.01$) more often than patients without LBB. LBB patients had less frequent tall QRS complexes (8% versus 47%; $P < 0.01$) and ST-T wave abnormalities (4% versus 50%; $P < 0.01$) than patients without LBB. Patients with LBB had a larger left ventricular end-diastolic diameter (73 mm versus 61 mm; $P < 0.01$), worse left ventricular fractional shortening (15% versus 26%; $P < 0.01$) and more extensive LVHT (1.8 versus 1.5 ventricular segments; $P < 0.05$). The prevalence of NMDs did not differ between patients with and without LBB. Survival did not differ between patients with and without LBB during follow-up.

CONCLUSIONS: LBB is associated with increased age, decreased systolic function and increased extension of LVHT. Whether LBB is a prognostic factor in LVHT remains speculative.

Key Words: Cardiomyopathy; Echocardiography; Electrocardiography; Heart failure; Left bundle branch block; Neuromuscular disorders

Left ventricular hypertrabeculation/noncompaction (LVHT) is an increasingly recognized phenomenon (1). LVHT is frequently associated with cardiac and extracardiac abnormalities. Among these abnormalities, the most prevalent are neuromuscular disorders (NMDs), when systematically searched (2,3). Electrocardiogram (ECG) abnormalities are frequent in patients with LVHT, and left bundle branch block (LBB) is one of the most frequent (4). Little is known about the association between LVHT and LBB. Thus, the present study of a cohort of LVHT patients aimed to compare patients with and without LBB regarding the location and extension of LVHT, left ventricular function, cardiac symptoms, electrocardiographic findings, prevalence of NMDs and mortality rates during follow-up.

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Implications cardiaques et neuromusculaires du bloc de branche gauche dans l'hypertrabéculéon/non-compaction ventriculaire gauche

HISTORIQUE : Le bloc de branche gauche (BBG) s'observe souvent en présence d'hypertrabéculéon/non-compaction ventriculaire gauche (HTVG).

OBJECTIF : Comparer les patients présentant une HTVG avec et sans BBG sur les plans de la localisation et de l'étendue de l'HTVG, de la fonction ventriculaire gauche, des symptômes, des signes électrocardiographiques, de la prévalence des troubles neuromusculaires (TNM) et de la mortalité durant le suivi.

MÉTHODES : Les auteurs ont analysé les dossiers de patients ayant subi un examen échocardiographique transthoracique au Krankenhaus Rudolfstiftung (Vienne, Autriche) entre juin 1995 et novembre 2006.

RÉSULTATS : L'HTVG a été diagnostiquée chez 102 patients (30 femmes) âgés en moyenne ($\pm$ É.-T.) de 53 ± 16 ans (entre 14 et 94 ans). Un TNM spécifique a été diagnostiqué chez 21 patients et un TNM d'étiologie inconnue, chez 47 patients. L'examen neurologique s'est révélé normal chez 14 patients et 20 patients ont refusé de subir l'examen. Les 24 patients présentant un BBG étaient plus âgés (61 ans vs 51 ans, $p < 0,01$) et présentaient une dyspnée à l'effort (96 % vs 59 %, $p < 0,01$) et une insuffisance cardiaque (79 % vs 46 %, $p < 0,01$) plus souvent que les patients indemnes de BBG. Les patients souffrant de BBG présentaient moins de QRS hauts (8 % vs 47 %, $p < 0,01$) et moins d'anomalies du segment ST-T (4 % vs 50 %, $p < 0,01$) que les patients indemnes de BBG. Les patients souffrant de BBG présentaient un diamètre ventriculaire gauche télédiastolique plus gros (73 mm vs 61 mm, $p < 0,01$), un abrègement plus marqué de leur FÉVG (15 % vs 26 %, $p < 0,01$) et une HTVG plus importante (1,8 vs 1,5 segment ventriculaire, $p < 0,05$). Ni la prévalence des TNM ni la survie n'ont été différentes selon que les patients souffraient ou non de BBG au cours du suivi.

CONCLUSION : Le BBG est associé à l'avancée en âge, à une baisse de la fonction systolique et à un accroissement de l'HTVG. Il reste à déterminer si le BBG est un facteur pronostique dans l'HTVG.

METHODS

All patients who were diagnosed with LVHT at the echocardiography laboratory of the Krankenhaus Rudolfstiftung (Wien, Austria) between June 1995 and November 2006 were included in the study. The echocardiographic equipment used were an Aloka 870 (Aloka Co, Ltd, Japan) (used from June 1995 to April 1998), a VingMed System Five (GE VingMed, Norway) (used from May 1998 until December 2005) and a Vivid 7 (GE VingMed) (used since December 2005) with 2.5 MHz to 3.6 MHz transducers. Two-dimensional and Doppler-echocardiographic criteria for the diagnosis of LVHT were more than three trabeculations protruding from the left ventricular wall (apically to the papillary muscles), visible in one echocardiographic image plane;

intertrabecular spaces perfused from the ventricular cavity, as visualized with colour Doppler imaging; and a ratio of trabeculated to nontrabeculated myocardium measured on end systole of more than 2. Trabeculations were defined as structures with the same echogenicity as the myocardium and moving synchronously with the ventricular contractions (2). To differentiate between trabeculations on the one side and false tendons or aberrant bands on the other side, the transducer had to be angulated, and pictures in atypical views that best delineated LVHT had to be obtained. To obtain the technically best picture quality, the focus was adapted to the region of interest. The location of LVHT was categorized as apical, anterior, lateral or posterior if it involved the corresponding regions of the left ventricular wall. The echocardiographic criteria remained the same throughout the study period. Measurements of left ventricular dimensions and wall thickness were performed in the parasternal short-axis view according to standard recommendations (5). Calculation of the ejection fraction from the two-dimensional picture was not feasible because of the trabeculations. Left ventricular systolic function was assessed by calculating the left ventricular fractional shortening from the M-mode picture. Indications for referring the patient for echocardiography were recorded.

All patients underwent a baseline cardiological examination; they were asked about their family history, medical history, and cardiovascular symptoms and their duration. Patients with heart failure were classified at baseline examination according to the New York Heart Association classification.

A 12-lead ECG was recorded and ECG abnormalities were determined according to previously published criteria (6). LBB was diagnosed if the QRS complex was longer than 0.12 s, and showed a predominantly negative QRS deflection in V1 and a widened R wave in V6. Atypical LBB with left-axis deviation was considered present when the mean frontal QRS axis was between -30 degrees and -90 degrees. Normal LBB was diagnosed if the mean frontal QRS axis was between -29 degrees and $+90$ degrees (7).

All patients were invited for a neurological investigation comprising their medical history and a clinical neurological examination. If there were indications for polyneuropathy, a screening program including blood, cerebrospinal fluid investigation and nerve biopsy was performed. If there were indications for myopathy, muscle enzymes were assessed, and electromyography and, occasionally, muscle biopsy were performed. Family screening was not performed systematically.

Informed consent was obtained from all patients. Patients who were assessed between June 1995 and December 2004 were contacted by telephone between February and April 2005 (8). Patients who were assessed after December 2004 were contacted by telephone in March 2007. Whether the patient was alive was recorded. For cases in which no information could be obtained, the local registration office was contacted. If the patient was deceased, their general practitioner was contacted to assess the cause of death. For patients who died at a hospital, the hospital departments were contacted to obtain information about the terminal diseases and the cause of death.

The *t* test was used for group comparisons of differences in mean values of noncategorical data. Categorical data were analyzed by the χ^2 test and the two-sided Fisher's exact test. Equality of survivor functions was tested using the log-rank test. All statistical analyses were performed using the statistical software package STATA (Stata Statistical Software: Release 8.2; Stata Corporation, USA).

RESULTS

During the study period, 38,377 transthoracic echocardiographic examinations were performed. LVHT was diagnosed in 102 patients (30 women) with a mean ($\pm$ SD) age of 53 ± 16 years (range 14 to 94 years). Ninety-three of these cases, which were diagnosed before December 2005, were published previously (9,10). LVHT did not involve the interventricular septum in any of the patients.

Eighty-two patients (80%) underwent at least one neurological investigation; the remaining 20 patients refused investigation. A specific NMD was diagnosed in 21 patients (including metabolic myopathy

[*n*=14]; Leber's hereditary optic neuropathy [*n*=3]; myotonic dystrophy [*n*=2]; Becker's muscular dystrophy [*n*=1]; and Duchenne muscular dystrophy [*n*=1]. An NMD of unknown etiology was diagnosed in 47 patients, and the neurological investigation was normal in 14 patients.

LBB was diagnosed in 24 patients and was the fourth most frequent ECG abnormality. An atypical LBB with left-axis deviation was identified in 11 of these patients. Patients with atypical LBB had two or more ECG abnormalities more often than patients with normal LBB (55% versus 0%; *P*<0.05). No other differences were detected between patients with typical and atypical LBB.

Patients with LBB were older than patients without LBB (61 versus 51 years of age; *P*<0.01), and the indication for echocardiography was heart failure more often in patients with LBB (79% versus 64%, *P*<0.01). LBB patients suffered from exertional dyspnea (96% versus 59%; *P*<0.01) and heart failure (79% versus 46%; *P*<0.01) more often than patients without LBB. The ECG and echocardiographic findings of the 102 patients according to the presence or absence of LBB are listed in Table 1. Regarding ECG abnormalities, LBB patients had less frequent tall QRS complexes and ST-T wave abnormalities than patients without LBB. Echocardiographically, patients with LBB had a larger left ventricular end-diastolic diameter, worse systolic function and a thinner posterior wall than patients without LBB. The location of LVHT did not differ between patients with and without LBB, but LBB patients had more extensive LVHT. No differences were detected regarding the prevalence of NMDs in patients with and without LBB.

During follow-up, it was determined that 22 patients had died due to cardiac failure (*n*=7; one patient with LBB), pneumonia (*n*=4; two patients with LBB), sudden cardiac death (*n*=3; one patient with LBB), malignancy (*n*=3; one patient with LBB), pulmonary embolism (*n*=2; one patient with LBB), abdominal sepsis (*n*=1), stroke (*n*=1) and hepatic failure in cirrhosis (*n*=1). Survival did not differ between patients with and without LBB (*P*=0.5940, log-rank test) (Figure 1). Eight of the LBB patients had received a cardiac resynchronization device in the meantime.

DISCUSSION

Among 102 LVHT patients, LBB was the fourth most frequent electrocardiographic abnormality, affecting 24% of the patients. Patients with LBB were older, suffered more often from exertional dyspnea and heart failure, had less frequent tall QRS complexes and ST-T wave abnormalities, had a larger left ventricular end-diastolic diameter, worse systolic function and a thinner posterior wall than patients without LBB. The location of LVHT did not differ between patients with and without LBB, but LBB patients had more extensive LVHT. Survival did not differ between patients with and without LBB.

LBB is characterized by impaired myocardial conduction. The relationship of LBB with dilated left ventricle and systolic dysfunction may be explained by impaired myocardial conduction. The occurrence of LBB was associated with increasing left ventricular dimensions and decreasing left ventricular fractional shortening in epidemiological studies (11,12).

The etiology of LVHT is unknown. LVHT may be a congenital abnormality, possibly as a result of a disturbed morphogenesis of the myocardium. LVHT may also develop as a compensatory mechanism of an impaired myocardium (1,13). LBB is a rare finding in children with LVHT, but occurs more frequently in adults (14-19).

Presently, it is unknown why cardiac conduction is impaired in LVHT. It is unknown if there is a specific alteration of the conduction system or if the LBB results from primary myocardial damage. The first possibility is substantiated by two LVHT patients with LBB whose left ventricular function improved after receiving a cardiac resynchronization device (20,21).

Left-axis deviation in LBB was found to be a marker for organic heart disease (7). That patients with LBB and left-axis deviation did not differ from LBB patients with a normal QRS axis in the present study may be due to the small study population.

TABLE 1
Clinical, electrocardiographic and echocardiographic findings in 102 patients with left ventricular hypertrabeculation/noncompaction (LVHT) according to the presence of left bundle branch block (LBB)

Characteristic	Total (n=102)	With LBB (n=24)	Without LBB (n=78)
Age, years, mean $\pm$ SD	53.2 $\pm$ 15.7	60.6 $\pm$ 15.3	50.9 $\pm$ 15.2**
Female sex, n (%)	30 (29.4)	9 (37.5)	21 (26.9)
Below median age, n (%)	51 (50.0)	10 (41.7)	41 (52.6)
ECG findings			
No ECG abnormality, n (%)	9 (8.8)	0 (0)	9 (11.5)
2 or more ECG abnormalities, n (%)	49 (48.0)	9 (37.5)	40 (51.3)
Tall QRS complex, n (%)	39 (38.2)	2 (8.3)	37 (47.4)**
ST-T wave abnormality, n (%)	40 (39.2)	1 (4.2)	39 (50.0)**
Ventricular ectopic beats, n (%)	13 (12.7)	3 (12.5)	10 (12.8)
Pathological Q waves, n (%)	8 (7.8)	0 (0)	8 (10.3)
Atrial fibrillation, n (%)	15 (14.7)	5 (20.8)	10 (12.8)
Left anterior hemiblock, n (%)	7 (6.9)	0 (0)	7 (9.0)
Right bundle branch block, n (%)	5 (4.9)	0 (0)	5 (6.4)
Low voltage, n (%)	4 (3.9)	0 (0)	4 (5.1)
Sinus tachycardia, n (%)	3 (2.9)	0 (0)	3 (3.8)
WPW syndrome, n (%)	3 (2.9)	0 (0)	3 (3.8)
ECG abnormalities/patient, n, mean $\pm$ SD	1.5 $\pm$ 0.8	1.5 $\pm$ 0.7	1.5 $\pm$ 0.9
Echocardiographic findings			
Left ventricular end-diastolic diameter, mm, mean $\pm$ SD	63.9 $\pm$ 12.8	72.8 $\pm$ 11.6	61.2 $\pm$ 11.9**
Left ventricular fractional shortening, %, mean $\pm$ SD	23.1 $\pm$ 11.3	15.2 $\pm$ 6.9	25.6 $\pm$ 11.3**
Interventricular septal thickness, mm, mean $\pm$ SD	12.4 $\pm$ 3.1	11.5 $\pm$ 2.5	12.7 $\pm$ 3.2
Left ventricular posterior wall thickness, mm, mean $\pm$ SD	12.4 $\pm$ 2.9	11.4 $\pm$ 2.0	12.7 $\pm$ 3.0*
Valvular abnormalities, n (%)	55 (53.9)	17 (70.8)	38 (48.7)
LVHT location			
Apex, n (%)	95 (93.1)	23 (95.8)	72 (92.3)
Anterior wall, n (%)	3 (2.9)	2 (8.3)	1 (1.3)
Posterior wall, n (%)	17 (16.7)	5 (20.8)	12 (15.4)
Lateral wall, n (%)	45 (44.1)	13 (54.2)	32 (41.0)
LVHT extension, ventricular segments, mean $\pm$ SD	1.6 $\pm$ 0.7	1.8 $\pm$ 0.9	1.5 $\pm$ 0.7*

* $P < 0.05$; ** $P < 0.01$. ECG Electrocardiogram; WPW Wolff-Parkinson-White

It is surprising that patients with LBB had a more extensive LVHT than patients without LBB, and this remains unexplained. It can be speculated, however, that abnormal motion of the interventricular septum due to LBB results in compensatory growth of the left ventricular myocardium. An argument against this speculation is that the interventricular septum is only very rarely affected by LVHT. It can be further speculated that conduction prolongation is a consequence of changed myocardial morphology, which is heavily trabeculated in extensive LVHT. A third theory explains the growth of extensive LVHT in LBB as a compensation for asynchronous contraction, leading to and promoting systolic dysfunction.

It is not surprising that the prevalence of NMDs did not differ between patients with and without LBB because LBB is only a rare manifestation of cardiac involvement in myopathies.

It is surprising that LBB was not a prognostic indicator in the follow-up study, since it was associated with more severe degrees of heart failure at baseline. It is also in contrast to epidemiological studies that found a worse prognosis when LBB was associated with dilated cardiomyopathy and myocarditis (22). This may be explained by the

Figure 1) Kaplan-Meier survival curves of patients with left ventricular noncompaction regarding the presence or absence of left bundle branch block (LBB)

fact that LVHT patients with LBB responded well to cardiac therapy and, at least in some cases, to the cardiac resynchronization device (23). Furthermore, LBB was not associated with NMDs, which have been identified as indicators of a higher mortality rate. Thus, no final assessment about the role of LBB as a prognostic factor of LVHT can be made.

Limitations of the study are the low number of patients, that not all patients were investigated neurologically and that follow-up was only by telephone and restricted to the assessment of vital status. Medication was recorded neither at baseline nor during follow-up. The New York Heart Association class was only assessed at baseline and not during follow-up. Left ventricular systolic function was only assessed by the calculation of left ventricular fractional shortening. Left ventricular ejection fraction was not calculated because the trabeculations impeded planimetry of the two-dimensional images.

CONCLUSIONS

The present study shows that LBB is a frequent finding in adults with LVHT. LBB is associated with increased age, decreased systolic function and increased extension of LVHT. Whether LBB is a prognostic factor in LVHT remains speculative.

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