Left bundle branch block with and without coronary artery disease: which value for a tissue Doppler-derived post-systolic motion?

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Coronary artery disease; Echo-Doppler; Tissue Doppler imaging.

Background. **An asynchronous contraction occurring during a prolonged relaxation period, defined as post-systolic motion (PSM), has been described as being a consequence of coronary occlusion but also in other conditions including isolated left bundle branch block (LBBB). The aim of this study was to characterize PSM of the interventricular septum at pulsed tissue Doppler in LBBB with or without stenosis of the left anterior descending coronary artery (LAD).**

Methods. **Forty-two patients with chronic, complete LBBB and tissue Doppler-derived septal PSM were divided into two groups on the basis of their coronary angiography: 27 without LAD stenosis and 15 with LAD stenosis (≥ 50%). Standard Doppler echocardiography and tissue Doppler of both the middle posterior septum and lateral mitral annulus were performed in the apical 4-chamber view.**

Results. **Standard Doppler diastolic indexes were comparable between the two groups. Septal tissue Doppler showed lower myocardial systolic (S_m) and atrial peak velocities (both $p < 0.05$), a higher PSM ($p < 0.005$), and a longer relaxation time ($p < 0.02$) and pre-contraction time ($p < 0.05$) in patients with LAD stenosis. A S_m/PSM ratio < 1 was detected in 86% of patients with LAD stenosis and in 22% without LAD stenosis (sensitivity 73%, specificity 77%, positive predictive value 64%, negative predictive value 84%). Tissue Doppler of the mitral annulus showed a significantly longer relaxation time and pre-contraction time and a lower atrial velocity in the presence of LAD stenosis. In the overall population, PSM was positively associated with ejection fraction and negatively with age and septal thickness. In a multiple linear regression analysis, only LAD stenosis ($\beta = 0.42$, $p < 0.005$) and ejection fraction ($\beta = 0.32$, $p = 0.03$) were independent predictors of PSM (cumulative $r^2 = 0.27$, $p < 0.002$).**

Conclusions. **Tissue Doppler may be useful to distinguish septal myocardial asynchrony in LBBB with and without LAD stenosis.**

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Introduction

Left bundle branch block (LBBB) is a common conduction abnormality, often associated with coronary artery disease, systemic arterial hypertension, aortic valve disease, and dilated cardiomyopathy[1]. In a few cases "isolated" LBBB is due to a non-specific fibrosis of the cardiac conduction system[2]. In patients with LBBB an asynchronous contraction of the interventricular septum is often detectable and is due to an altered electrical activation sequence[3].

An asynchronous contraction occurring after normal left ventricular (LV) systolic ejection, during a prolonged relaxation period, has been observed in experimental models[4,5] and in humans at ventriculography[6]. This phenomenon, defined as post-systolic shortening or thickening or post-systolic motion (PSM), has been recently also described at pulsed tissue Doppler (TD)[7], an ultrasound modality which allows the quantification of both the systolic and diastolic segmental myocardial wall velocities[8,9]. PSM has been identified as a consequence of coronary artery occlusion and has also been considered as a hallmark of an ischemic but viable myocardium[5,10-12]. However, TD-derived PSM has been also detected in hypertensive patients with LV hypertrophy[13] and in isolated LBBB[14], i.e. in the absence of angiographically documented coronary artery disease.

In view of the above, the present study was designed to characterize the TD differences in patients with PSM associated with LBBB, with or without angiographic evidence of stenosis of the left anterior descending coronary artery (LAD), in relation to clinical and standard Doppler echocardiographic variables.

Methods

Selection of the study group. This is a prospective multicenter study. The original cohort comprised 53 patients with chronic (> 6 months), complete LBBB and recurrent angina pectoris or atypical chest pain, but without primary cardiomyopathies, hemodynamically significant valvular heart disease, congenital heart disease, previous myocardial infarction, pressure or volume right ventricular overload, permanent pacemaker and abnormal atrioventricular pathways. From this cohort, 42 patients (30 males, 12 females, mean age 59 years) with pulsed TD evidence of interventricular septal PSM were selected, after their informed consent and approval of the Institutional Committee were obtained.

Major ECG criteria required for the diagnosis of complete LBBB were: a duration of the QRS complex > 120 ms (measured in the lead where it was widest), a notched and splintered QRS complex with a predominantly negative QRS (QS or rS) deflection in lead V_1 and a widened slurred R wave in lead V_5, lead V_6 and/or lead I[15].

The presence of TD-derived PSM of the interventricular septum was defined as any clear (≥ 2 cm/s) myocardial velocity occurring upon the baseline between the end of the myocardial systolic velocity and the onset of the myocardial early diastolic velocity.

All the selected patients underwent standard Doppler and TD echocardiography and coronary angiography. Patients were divided into two groups on the basis of their coronary angiography: 27 had no LAD stenosis whereas 15 had significant LAD stenosis (≥ 50%). Of note, among the patients with LAD stenosis, none presented significant stenosis of any coronary branches other than the LAD.

Standard Doppler echocardiography and tissue Doppler. Standard Doppler echocardiograms and pulsed TD were performed with the subjects in partial left decubitus, using the Vingmed System Five (GE, Horten, Norway), Toshiba Powervision 8000 (Toshiba, Tokyo, Japan) and ATL 5000 (ATL Ultrasound, Bothell, WA, USA), all equipped with a variable-frequency phased-array transducer and TD capabilities. Consecutively coded, Doppler echocardiographic and TD tracings were recorded on super VHS videotapes and high-fidelity paper strip (velocity of 150 or 100 mm/s) and examined by two readers using the average of at least 3 cardiac cycles.

Two-guided, M-mode LV analysis and Doppler recording of the LV transmitral diastolic inflow was performed as previously described[16]. The LV mass was calculated using the criteria of the American Society of Echocardiography[17] and normalized for body height[18]. The two-dimensional LV end-diastolic and end-systolic volumes were calculated using the Simpson method[19] and the LV ejection fraction was calculated using the following formula: end-diastolic volume – end-systolic volume/end-diastolic volume × 100.

Pulsed TD was performed at transducer frequencies of 3.5-4.0 MHz, adjusting the spectral pulsed Doppler signal filters to obtain the Nyquist limits of 15 and 20 cm/s, and using the minimal optimal gain. In the apical 4-chamber view, the pulsed Doppler sample volume was subsequently placed in two different regions: middle interventricular septum (the perfusion of which is provided by the LAD) and LV lateral mitral annulus. The apical 4-chamber view was chosen to obtain the quantitative assessment of the regional myocardial wall motion almost simultaneously to the Doppler LV inflow and to minimize the incidence angle between the Doppler beam and the LV longitudinal motion. The following TD measurements were determined as indexes of regional myocardial function: myocardial systolic peak velocity (S_m, m/s), myocardial pre-contraction time (from the onset of the ECG QRS to the beginning of S_m) and contraction time (from the beginning to the end of S_m) (all in ms) as systolic indexes and myocardial early (E_m) and atrial (A_m) peak velocities (m/s) and their ratios, and relaxation time (RT_m) (ms) – corresponding to the time interval elapsing between the end of S_m and the onset of E_m – as diastolic measurements. PSM was identified during RT_m, using the previously mentioned criteria. Our TD methods and reproducibility have been previously described[20].

Coronary angiography. Biplane coronary angiograms using the Judkins technique were performed with a standard cineangiographic system in multiple views. Lumen diameter narrowing was graded as 0, < 25, 25, 50, 75, 90, and 100% in 15 arterial segments. In the present study, the definition of a significant anatomical stenosis implied a ≥ 50% luminal narrowing localized in the first or middle segments of the coronary arterial tree.

Statistical analysis. Variables are presented as mean ± 1 SD. Analysis of variance was performed to estimate intergroup differences. Linear regression analyses and partial correlation testing using Pearson's method were used to assess univariate relations. The prediction of PSM was made using stepwise, forward, multiple regression analyses that included potential confounding variables not obviously related to each other. The null hypothesis was rejected for $p < 0.05$.

Results

The study population included patients with arterial systemic hypertension (26/42; 62%), aortic valve disease (9/42; 21%) and isolated LBBB (7/42; 17%). With regard to the 15 patients with LAD stenosis, coronary angiography showed a narrowing of 85.5 ± 4.0%. Among these patients, 9 were hypertensive, 5 had mod-

erate aortic regurgitation, and 1 mild aortic valve stenosis. The demographic characteristics of the groups are listed in table I. No differences in gender, age, body mass index, heart rate, blood pressure and ECG-derived QRS duration were found between the two groups. The results of Doppler echocardiographic analysis are reported in table II. Patients with LAD stenosis had a significantly lower septal wall thickness and a greater LV end-diastolic diameter (both $p < 0.01$). No differences of the two-dimensional-derived LV ejection fraction and Doppler indexes of LV diastolic function were found between the two groups.

Table III shows the results of pulsed TD analysis of both the middle posterior septum and LV lateral mitral annulus. At the level of the posterior septum, patients with LAD stenosis had higher amplitude PSM ($p < 0.005$), a longer RT_m ($p < 0.02$) and PCT_m ($p < 0.05$) and a lower A_m and S_m peak velocity (both $p < 0.05$). Of note, we did not find any difference of the PSM amplitude in relation to the different degrees of LAD narrowing in this subgroup. An S_m/PSM ratio < 1 was found in 86% of patients with LAD stenosis but only in 22% of patients without LAD stenosis (sensitivity 73%, specificity 77%, positive predictive value 64%, negative predictive value 84%). Figures 1 and 2 show two examples of LBBB, without and with LAD stenosis respectively: the S_m/PSM ratio is > 1 in the patient without coronary artery disease and < 1 in the patient with LAD stenosis. At the level of the LV mitral annulus patients with LAD stenosis had a longer RT_m ($p < 0.01$) and PCT_m ($p < 0.05$) and a lower A_m peak velocity ($p < 0.05$), without any difference in the E_m/A_m ratio and S_m peak velocity.

Possible univariate relations of the PSM amplitude with demographic and echocardiographic variables were assessed in the overall population. The PSM peak velocity was positively related to LV ejection fraction ($r = 0.32$, $p < 0.05$) and negatively related to both the septal wall thickness and age (both $r = -0.38$, $p < 0.01$). No significant relation of PSM was found with the body mass index ($r = 0.18$), heart rate ($r = -0.10$), systolic and diastolic blood pressure ($r = -0.11$ and $r = -0.10$ respectively) and with the septal S_m ($r = -0.10$) and RT_m ($r = 0.15$). Using a multiple linear regression analysis performed in the overall population and including age, ECG QRS duration, septal wall thickness, LV internal end-diastolic diameter, LV ejection fraction and evidence of significant LAD stenosis (1 = no, 2 = yes) as potential determinants, LAD stenosis (standardized ß coefficient = 0.42, $p < 0.005$) and LV ejection fraction (ß = 0.32, $p = 0.03$) were found to be independent predictors of the PSM amplitude (cumula-

Table I. Characteristics of the study population.

Variable	LBBB with LAD- (n=27)	LBBB with LAD+ (n=15)	p
Gender (M/F)	20/7	10/5	NS
Age (years)	61.7 ± 13.2	57.6 ± 10.5	NS
Body mass index (kg/m^2)	27.5 ± 3.7	26.8 ± 4.1	NS
Systolic BP (mmHg)	137.2 ± 15.6	141.3 ± 23.9	NS
Diastolic BP (mmHg)	79.8 ± 14.5	84.3 ± 11.9	NS
Heart rate (b/min)	78.5 ± 14.5	71.7 ± 11.2	NS
QRS duration (ms)	142 ± 9.1	141 ± 8.6	NS

BP = blood pressure; LAD = left anterior descending coronary artery; LBBB = left bundle branch block. LAD- = patients without significant LAD stenosis; LAD+ = patients with significant LAD stenosis.

Table II. Standard Doppler echocardiographic analysis.

Variable	LBBB with LAD-	LBBB with LAD+	p
Septal wall thickness (mm)	12.0 ± 1.7	10.5 ± 1.9	< 0.01
Posterior wall thickness (mm)	10.2 ± 1.7	9.7 ± 2.0	NS
LV internal diastolic diameter (mm)	53.5 ± 6.4	58.1 ± 7.4	< 0.01
LV internal systolic diameter (mm)	36.7 ± 8.1	39.6 ± 10.2	NS
Two-dimensional ejection fraction (%)	54.6 ± 9.4	54.7 ± 5.5	NS
LV mass index (g/m$^{2.7}$)	43.1 ± 7.1	44.6 ± 7.2	NS
E peak velocity (m/s)	0.56 ± 0.14	0.58 ± 0.10	NS
A peak velocity (m/s)	0.58 ± 0.07	0.61 ± 0.12	NS
E/A peak velocity	0.95 ± 0.21	0.93 ± 0.15	NS
E deceleration time (ms)	198.3 ± 30.0	201.5 ± 34.4	NS
Isovolumic relaxation time (ms)	87.9. ± 14.6	90.1 ± 21.8	NS

LAD = left anterior descending coronary artery; LBBB = left bundle branch block; LV = left ventricular.

Table III. Tissue Doppler analysis of the middle interventricular septum and left ventricular (LV) mitral annulus.

Variable	LBBB with LAD-	LBBB with LAD+	p
Middle interventricular septum			
S_m peak (cm/s)	6.17 ± 1.8	5.19 ± 0.8	< 0.05
PCT_m (ms)	133.1 ± 35.5	143.5 ± 33.5	< 0.05
CT_m (ms)	242 ± 58.1	240.6 ± 55.3	NS
E_m peak (cm/s)	6.7 ± 1.6	7.00 ± 1.9	NS
A_m peak (cm/s)	7.7 ± 3.8	9.91 ± 3.7	< 0.05
E_m/A_m ratio	0.83 ± 0.5	0.76 ± 0.2	NS
RT_m (ms)	133.8 ± 37.2	159.33 ± 27.5	< 0.02
PSM (cm/s)	5.3 ± 1.8	8.0 ± 4.0	< 0.005
S_m/PSM ratio (%)	33 ± 0.3	41 ± 0.3	< 0.001
LV lateral mitral annulus			
S_m peak (cm/s)	7.8 ± 1.24	8.8 ± 2.7	NS
PCT_m (ms)	130.3 ± 42.09	145.6 ± 41.9	< 0.05
CT_m (ms)	232.4 ± 15.2	235.7 ± 13.4	NS
E_m peak (cm/s)	9.2 ± 3.00	9.3 ± 4.8	NS
A_m peak (cm/s)	11.9 ± 2.37	10.2 ± 2.8	< 0.05
E_m/A_m ratio	0.77 ± 0.33	1.10 ± 0.3	NS
RT_m (ms)	89.5 ± 41.0	127.2 ± 50.9	< 0.01

A_m = myocardial atrial peak velocity; CT_m = myocardial contraction time; E_m = myocardial early diastolic peak velocity; PCT_m = myocardial pre-contraction time; PSM = post-systolic motion; RT_m = myocardial relaxation time; S_m = myocardial systolic peak velocity.

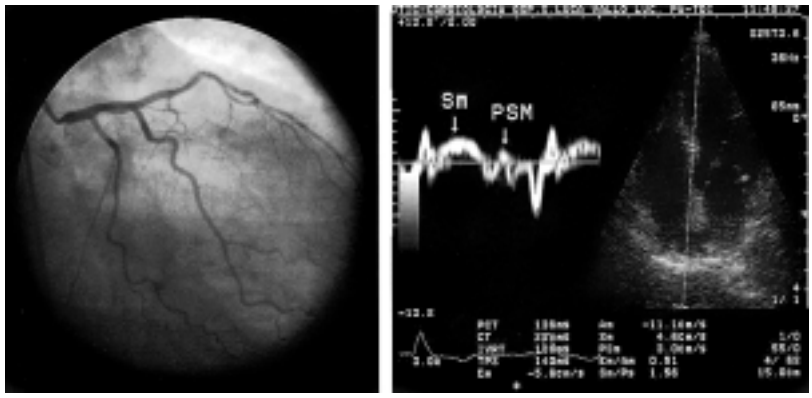

Figure 1. *Coronary angiography* (left panel) *and pulsed tissue Doppler pattern of the posterior septal wall* (right panel) *in a patient with left bundle branch block but without left anterior descending coronary artery stenosis. The post-systolic motion (PSM) is lower than the myocardial systolic peak velocity (S_m) (S_m/PSM = 1.56).*

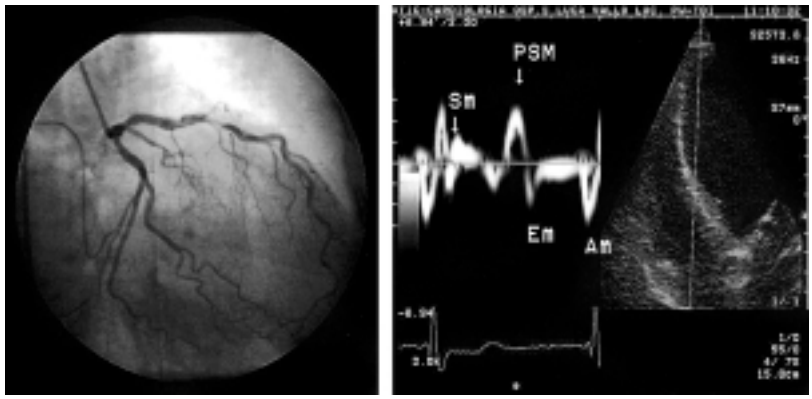

Figure 2. *Coronary angiography* (left panel) *and pulsed tissue Doppler pattern of the posterior septal wall* (right panel) *in a patient with left bundle branch block and significant left anterior descending coronary artery stenosis. Note the higher amplitude of the post-systolic motion (PSM) and the myocardial systolic peak velocity (S_m)/PSM ratio < 1. A_m = myocardial atrial peak velocity; E_m = myocardial early peak velocity.*

tive $r^2 = 0.27$, standard error 2.11 cm/s, $p < 0.002$). After removing the effect of LAD stenosis and of LV ejection fraction from the model, the partial relation coefficients of the other variables versus PSM were found to be not significant.

Discussion

LBBB is characterized by a delay in the onset and completion of the systolic ejection phase and by a shortening of the LV diastolic period. This abnormally prolonged activation is often associated with late asynchronous contraction of the interventricular septum[3] that often alters the assessment of the LV global and segmental functions at usually employed noninvasive imaging[21]. LBBB may develop both in patients with and without coronary artery disease. The non-invasive diagnosis of LAD stenosis in this subset is particularly difficult because of the well known ECG limitations[1], possible myocardial scintigraphic antero-septal perfusion defect artifacts[22] and echocardiographic abnormal septal wall motion[21,23] occurring also in patients free of LAD stenosis. Stress echocardiography has already been proved to be superior to myocardial scintigraphy for the detection of significant LAD stenosis in patients with LBBB[24] and its prognostic value in this clinical setting is recognized[25].

TD is an easy-to-use ultrasound tool, which permits the measurement of the systolic and diastolic velocities of the regional myocardial walls[8,9] and the identification of myocardial asynchrony[26]. The findings of the present study indicate that septal PSM can be documented by means of this technique in LBBB and utilized to distinguish LBBB patients with or without coronary artery disease.

Post-systolic motion in patients with and without coronary artery disease. The first documentation of PSM was made in the 1970s in experimental studies after myocardial infarction[10]. The regional myocardial function was assessed in open chest animal models using sono-micrometry and a decrease in systolic shortening with an increase in PSM was described as an effect of progressive myocardial ischemia[27]. More recently, other studies performed in animal models demonstrated that post-systolic contraction occurs both in case of moderate ischemia (when the myocardium is hypokinetic or akinetic and it should be due to active contraction) as well as in case of severe ischemia (when the myocardium is dyskinetic and it should be due to an entirely passive mechanism)[5]. PSM has also been observed in humans at ventriculography after acute anterior myocardial infarction[6] and at pulsed TD during percutaneous transluminal coronary angioplasty[7] and has been interpreted as a marker of myocardial ischemia and viability[11]. However, PSM also occurs in subsets of patients free of coronary artery stenosis, including those with LV hypertrophy[13] and LBBB[14]. In accordance with these previous observations, we found PSM even when LBBB was not associated with LAD stenosis. Of note, we chose the middle posterior septum for TD analysis since the interventricular septum is more often involved than the other LV walls in the paradoxical motion induced by LBBB and the perfusion of the middle portion of this wall is provided by the LAD.

Differences of post-systolic motion in left bundle branch block with or without left anterior descending coronary artery stenosis. Although the presence of septal PSM was the main selection criterion in the present study, a TD septal pattern with PSM was often evidenced in our overall original population of LBBB (42/53 patients; 79%). Among the 42 selected patients, the group with LAD stenosis was characterized by a higher PSM peak velocity and a lower S_m peak velocity. PSM occurs during the myocardial relaxation period which, according to previous observations[28], is lengthened in the presence of coronary stenosis. In non-ischemic conditions, PSM could be simply secondary to a wall motion heterogeneity due to prolonged intraventricular conduction. In LBBB associated with LAD stenosis, a lower S_m is an obvious consequence of a reduced myocardial contraction while the higher PSM amplitude could be explained by the additive effect of the delayed myocardial tension which is more prolonged during the relaxation phase[4]. Of interest, a S_m/PSM ratio < 1 was evident in 86% of patients with LAD stenosis but only in 22% of those without coronary artery disease. This ratio might be useful to exclude significant LAD stenosis in LBBB patients since it showed good sensitivity and specificity and a negative predictive value of 84%.

With regard to temporal analysis, a prolonged precontraction time and RT_m were found at the level of both the septal wall and LV mitral annulus in patients with LAD stenosis. Asynchronous contraction associated with LBBB is likely to lead *per se* to a delayed myocardial relaxation[3]. Additionally, the longer relaxation time in the presence of coronary artery disease could be due to a further effect of myocardial ischemia. Of note, except for minor changes of the A_m, the systolic and diastolic peak velocities of the LV mitral annulus were not significantly modified in patients with LAD stenosis. This finding is consistent with the observation of a globally preserved LV longitudinal function identified in this set of patients also at standard echocardiography.

Associations of post-systolic motion in the overall left bundle branch block population. In the overall population, PSM was negatively related to age and septal wall thickness, in agreement with the changes in myocardial elastic properties developing with aging and LV wall hypertrophy[13]. In addition, the PSM amplitude was positively associated with LV ejection

fraction, i.e. to LV systolic function. This finding suggests a possible effect of a good LV global systolic function in sustaining a prolonged delayed motion of the asynchronous myocardium by the neighboring normally contracting LV walls. A recent assessment by means of strain Doppler echocardiography supports the hypothesis that the abnormal contraction developing during isovolumic relaxation in a dyskinetic area may reflect the work performed on that area by other myocardial segments[5]. The multiple linear regression model provided additional information by adjusting the above associations for clinical and echocardiographic confounders. By this analysis, the presence of LAD stenosis and, to a lesser extent, LV ejection fraction were the only independent predictors of the PSM amplitude. The independent association between evidence of significant coronary stenosis and a higher PSM peak velocity is consistent with previous studies[4-6,27] and suggests a potential clinical role of TD in the identification of coronary artery disease in patients with LBBB.

Study limitations. In the present study, among the LV myocardial walls pulsed TD sampling was limited to the interventricular septum and to the LV lateral mitral annulus, which corresponds to the overall LV longitudinal motion. Although it is well known that the contraction asynchrony of LBBB is particularly overt at the septal level[3], it could have been more comprehensive to evaluate even other LV myocardial segments, possibly influenced by the abnormal electrical conduction present in LBBB. Another limitation is due to the assessment exclusively of the LV longitudinal motion (since our TD recording was performed only in the apical 4-chamber view), without considering the circumferential shortening (in the parasternal short-axis view). Our choice, however, was mainly due to the assumption that, because of a reduced translation movement, the pulsed TD septal pattern is more easily obtainable in the apical views. A further limitation arises from the population selection criteria and our findings cannot be extrapolated to the general population with LBBB because they are limited to those presenting with PSM. However, it has to be taken into account that TD detected PSM in the majority of the assessed patients. Further studies including larger cohorts of patients with LBBB are needed to confirm our data.

In conclusion, despite its main prognostic implications[25], the evidence of coronary artery disease in patients with LBBB is difficult to unmask using the traditional non-invasive tools[21]. The present study demonstrates that TD provides two different patterns of septal asynchrony due to LBBB, where PSM presents different characteristics in patients with and without significant LAD stenosis. Pulsed TD could be a relevant tool for the detection of the coexistence of LBBB and coronary artery disease in the clinical setting.

References

1. Schneider JF, Thomas HE Jr, Sorlie P, et al. Comparative features of newly acquired left and right bundle branch block in the general population: the Framingham study. Am J Cardiol 1981; 47: 931-40.
2. Fahy GJ, Pinski SL, Miller DP, et al. Natural history of isolated bundle branch block. Am J Cardiol 1996; 77: 1185-90.
3. Grines CL, Bashore TM, Boudolas H, et al. Functional abnormalities in isolated left bundle branch block. The effect of interventricular asynchrony. Circulation 1989; 79: 845-53.
4. Takayama M, Norris RM, Brown MA, et al. Post-systolic shortening of acutely ischemic canine myocardium predicts early and late recovery of function after coronary artery reperfusion. Circulation 1988; 78: 994-1007.
5. Skulstad H, Edvardsen T, Urheim S, et al. Postsystolic shortening in ischemic myocardium: active contraction or passive recoil? Circulation 2002; 106: 718-24.
6. Hosokawa H, Sheean FH, Suzuky T. Measurement of postsystolic shortening to assess viability and predict recovery of left ventricular function after acute myocardial infarction. J Am Coll Cardiol 2000; 35: 1842-9.
7. Jamal F, Kukulski T, D'hooge J, De Scheerder I, Sutherland G. Abnormal postsystolic thickening in acutely ischemic myocardium during coronary angioplasty: a velocity, strain, and strain rate Doppler myocardial imaging study. J Am Soc Echocardiogr 1999; 12: 994-6.
8. Isaaz K, Thompson A, Ethevenot G, et al. Doppler echocardiographic measurement of low velocity motion of the left ventricular posterior wall. Am J Cardiol 1989; 64: 66-75.
9. Sutherland GR, Stewart MJ, Groundstroem KW, et al. Color Doppler myocardial imaging: a new technique for the assessment of myocardial function. J Am Soc Echocardiogr 1994; 7: 441-58.
10. Kerber RE, Abboud FM. Echocardiographic detection of regional myocardial infarction: an experimental study. Circulation 1973; 47: 997-1005.
11. Barletta G, Del Bene R, Lo Sapio P, et al. Post-ejection thickening as a marker of viable myocardium. An echocardiographic study in patients with chronic coronary artery disease. Basic Res Cardiol 1998; 93: 313-24.
12. Brown MA, Norris RM, Takayama M, White HD. Post-systolic shortening: a marker of potential for early recovery of acutely ischemic myocardium in the dog. Cardiovasc Res 1987; 21: 703-16.
13. Pai GR, Gill K. Amplitudes, durations and timings of apically directed left ventricular myocardial velocities: II. Systolic and diastolic asynchrony in patients with left ventricular hypertrophy. J Am Soc Echocardiogr 1998; 11: 112-8.
14. Galderisi M, Cicala S, Sangiorgi G, et al. Tissue Doppler-derived post-systolic motion in a patient with left bundle branch block: a sign of myocardial asynchrony. Echocardiography 2002; 19: 79-81.
15. Rowlands DJ. Intraventricular conduction disturbances. In: Rowlands DJ, ed. Clinical electrocardiography. London: Gowers, 1991: 110-43.
16. Galderisi M, Paolisso G, Tagliamonte MR, et al. Is insulin action a determinant of left ventricular relaxation in uncomplicated essential hypertension? J Hypertens 1997; 15: 745-50.
17. Sahn DJ, DeMaria A, Kisslo J, Weyman A, for the Committee of M-Mode Standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072-83.
18. Galderisi M, Lauer MS, Levy D. Echocardiographic determinants of clinical outcome in subjects with coronary heart

disease. The Framingham Heart Study. Am J Cardiol 1992; 70: 971-6.
19. Schiller NB, Shah PM, Crawford M, et al, for the American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989; 2: 358-67.
20. Galderisi M, Caso P, Severino S, et al. Myocardial diastolic impairment caused by left ventricular hypertrophy involves basal septum more than other walls: analysis by pulsed Doppler tissue imaging. J Hypertens 1999; 17: 685-93.
21. Vaduganathan P, Zuo-Xiang HE, Raghavan C, et al. Detection of left anterior descending coronary artery stenosis in patients with left bundle branch block: exercise, adenosine, or dobutamine imaging? J Am Coll Cardiol 1996; 28: 543-50.
22. Jazmati B, Sadaniantz A, Emaus SP, Heller GV. Exercise thallium-201 imaging in complete left bundle branch block and the prevalence of septal perfusion defects. Am J Cardiol 1991; 67: 46-9.
23. Gleijnse ML, Vigna C, Kasprazak JD, et al. Usefulness and limitations of dobutamine-atropine stress echocardiography for the diagnosis of coronary artery disease in patients with left bundle branch block. A multicentre study. Eur Heart J 2000; 21: 1666-73.
24. Mairesse GH, Marwick FH, Arnese M, et al. Improved identification of coronary artery disease in patients with left bundle branch block by use of dobutamine stress echocardiography and comparison with myocardial perfusion tomography. Am J Cardiol 1995; 76: 321-5.
25. Cortigiani L, Picano E, Vigna C, et al. Prognostic value of pharmacologic stress echocardiography in patients with left bundle branch block. Am J Med 2001; 110: 361-9.
26. Bruch C, Bartel T, Schmermund A, Schaar J, Erbel R. Asynchrony of ventricular contraction and relaxation - pathophysiologically recognized phenomenon, now can be clinically assessed. Herz 1998; 23: 506-15.
27. Leone BJ, Norris RM, Safwat A, Foex P, Ryder WA. Effects of progressive myocardial ischemia on systolic function, diastolic dysfunction, and load dependent relaxation. Cardiovasc Res 1992; 26: 422-9.
28. Garcia-Fernandez MA, Azevedo J, Moreno M, et al. Regional diastolic function in ischemic heart disease using pulsed wave Doppler tissue imaging. Eur Heart J 1999; 20: 496-505.