Prognostic Value of a Restrictive Mitral Filling Pattern in Patients With Systolic Heart Failure and an Implantable Cardioverter-Defibrillator

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In patients with chronic heart failure and reduced systolic function, an implantable cardioverter-defibrillator (ICD) improves the prognosis, but morbidity and mortality remain high. We attempted to identify the prognostic impact of Doppler echocardiography and QRS duration in such patients. We prospectively enrolled 84 patients with chronic heart failure, an ICD, and impaired systolic function (mean ejection fraction $29 \pm 10\%$). Echocardiographic measurements included left ventricular dimensions/volumes, ejection fraction, mitral E/A ratio, deceleration time, and tissue Doppler analysis of mitral annular velocities (S′, E′, A′). A cardiac event (death from pump failure or appropriate ICD therapy, i.e., antitachycardia pacing/shock due to sustained ventricular tachycardia or ventricular fibrillation) was defined as the study end point. During a follow-up of 373 ± 254 days, 22 patients (26%) had an event (death from pump failure, n = 7; patients who received an appropriate ICD therapy, n = 16). In patients with an event, the QRS duration was longer (169 ± 41 vs 146 ± 37 ms, p = 0.023), the mitral E/E′ ratio was higher (16.0 ± 6.5 vs 12.8 ± 5.9, p = 0.044), and a restrictive filling pattern was more frequent (44% vs 9%, p = 0.017). Stepwise multivariate Cox regression analysis identified a restrictive filling pattern as the only independent predictor of an event (hazard ratio 3.65, 95% confidence interval 1.54 to 8.64, p = 0.003). For patients with a restrictive filling pattern, the outcome was markedly poorer than that for patients with a nonrestrictive pattern (event-free survival rate 38% vs 72%, p = 0.005). In conclusion, in patients with chronic heart failure, an ICD, and systolic dysfunction, a restrictive filling pattern is an independent predictor of adverse cardiac events.   © 2006 Elsevier Inc. All rights reserved. (Am J Cardiol 2006;97:676–680)

This prospective study was designed to assess the prognostic value of Doppler echocardiography and tissue Doppler imaging in patients with heart failure (HF) and an implantable cardioverter-defibrillator (ICD) and to compare it against traditional markers, such as New York Heart Association (NYHA) functional class, ejection fraction, and QRS duration.

Methods

Study patients: The study population consisted of a consecutive series of 98 patients who were followed after receiving ICDs between 2000 and 2003 at our institution (Hospital of the University of Münster). Patients were prospectively included if they fulfilled the following criteria: a history of chronic HF according to the Framingham criteria,[1] left ventricular ejection fraction <45% as detected by echo-

cardiography, and clinical stability after ≥2 months on standard medical therapy. Patients with severe valvular disease (n = 5) or atrial fibrillation (n = 9) were excluded, so that 84 subjects formed the final study cohort. Of these patients, 62 (74%) received ICDs for secondary prevention and 22 (26%) for primary prevention of sudden cardiac death. All implanted devices were capable of storing intracardiac electrograms and had antitachycardia pacing capabilities in combination with cardioversion/defibrillation treatment features. All treated episodes were classified as inappropriate or appropriate by 1 experienced cardiologist (RG), who had no knowledge of the remaining clinical data.

Electrocardiographic analysis: The QRS duration was measured on a 12-lead electrocardiogram using leads V_3 to V_6. A mean of ≥3 QRS complexes was used for further analysis. Left bundle branch block was diagnosed on the basis of a QRS duration >120 ms, absent Q waves, and wide slurred R waves in V_5 and V_6, and monophasic QS or rS waves in leads V_1 and V_2.

Echocardiography: Echocardiographic images were taken according to the guidelines of the American Society of Echocardiography.[2] Peak velocities of early (E) and late

Table 1
Clinical characteristics of study patients

Variable	Total (n = 84)	Event		p Value
		Yes (n = 22)	No (n = 64)	
Age (yrs)	60 ± 12	61 ± 12	60 ± 12	0.78
Men/women (%)	80/20	73/27	82/18	0.34
Body surface area (m^2)	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	0.39
Ischemic/nonischemic cardiomyopathy	74%/26%	59%/41%	68%/32%	0.46
NYHA functional class	2.7 ± 0.5	2.8 ± 0.5	2.7 ± 0.5	0.31
QRS duration (ms)	153 ± 39	169 ± 41	146 ± 31	0.023
Left bundle branch block	31 (37%)	9 (41%)	22 (35%)	0.78
Medication				
Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker	94%	91%	95%	0.48
Diuretics	91%	95%	90%	0.44
Digoxin	70%	71%	69%	0.83
β Blockers	90%	86%	92%	0.46
Class III antiarrhytmic agents	31%	30%	31%	0.93

Table 2
Echocardiographic characteristics of study patients

Variable	Total (n = 84)	Event		p Value
		Yes (n = 22)	No (n = 64)	
Left atrial diameter (cm)	5.0 ± 0.8	5.1 ± 0.7	5.0 ± 0.9	0.87
LV diastolic diameter index (cm/m^2)	3.6 ± 0.5	3.7 ± 0.5	3.5 ± 0.5	0.20
LV systolic diameter index (cm/m^2)	3.0 ± 0.5	3.1 ± 0.5	3.0 ± 0.5	0.32
LV diastolic volume index (ml/m^2)	129 ± 46	143 ± 46	125 ± 47	0.079
LV systolic volume index (ml/m^2)	93 ± 40	102 ± 40	90 ± 40	0.19
LV ejection fraction (%)	29 ± 10	29 ± 10	29 ± 10	0.87
Fractional shortening (%)	18 ± 7	19 ± 6	18 ± 7	0.51
Puked Wave Doppler				
Mitral E/A ratio	1.93 ± 1.16	2.25 ± 1.18	1.82 ± 1.14	0.105
Deceleration time	188 ± 80	173 ± 68	193 ± 84	0.26
Restrictive filling pattern	16 (22%)	12 (44%)	4 (9%)	0.017
Tissue Doppler				
S′ (cm/s)	4.64 ± 1.12	4.25 ± 0.93	4.77 ± 1.16	0.069
E′ (cm/s)	5.85 ± 1.75	5.43 ± 1.41	6.00 ± 1.84	0.30
A′ (cm/s)	6.30 ± 2.35	6.41 ± 2.99	6.27 ± 2.13	0.607
E/E′ ratio	13.6 ± 6.2	15.9 ± 6.5	12.8 ± 5.9	0.045

LV = left ventricular.

(A) diastolic filling and deceleration time were derived from transmitral Doppler recordings. A restrictive filling pattern was defined by an E/A ratio >2, a deceleration time of <150 ms, and a mitral annular E′ velocity of <8 cm/s.[3] Tissue Doppler-derived peak systolic (S′) and early (E′), and late (A′) diastolic velocities were derived from the septal and lateral mitral annulus, and averaged for each patient.[4] The inter- and intraobserver correlation for conventional echocardiographic measurements and tissue Doppler variables reached 0.92 and 0.98, respectively.

Outcome measurements and statistical analysis: To study the prognostic impact of Doppler echocardiography and tissue Doppler imaging in our study population, the follow-up period started at the time of the index echocardiogram. Patients were seen regularly on an outpatient basis at 3- to 6-month intervals, and the device was interrogated for treated episodes at each visit. Detailed follow-up infor-

mation was also obtained by telephone interview with the patients or their physicians. A cardiac event (death from pump failure or appropriate ICD therapy, i.e., antitachycardia pacing or shock due to sustained ventricular tachycardia or ventricular fibrillation) was defined as the combined study end point.

The numerical values are expressed as means ± SDs. Continuous variables were compared between groups using an unpaired *t* test (for normally distributed variables) or the Mann-Whitney *U* statistic test (for non-normally distributed variables). Chi-square analysis was used to compare categorical variables. Clinical, electrocardiographic, and echocardiographic variables were evaluated for the combined study end point in a Cox proportional hazard model. Receiver-operating characteristic curves were generated to define the cut-off values for the variables with a significant association (p <0.05) with the end point. Multivariate re-