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Wall stress determines systolic and diastolic function — Characteristics of heart failure☆

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ABSTRACT

Introduction: Heart failure can be caused by systolic or diastolic dysfunction. Diagnosing diastolic dysfunction remains challenging, although several criteria have been identified. Ventricular wall stress is crucially involved. It is hypothesized whether increased end-diastolic and end-systolic ventricular wall stress as assessed by the wall stress index is associated with cardiac dysfunction and thus provide novel diagnostic criteria.
Methods: 1050 consecutive patients with suspected non-ischemic heart failure covering a broad spectrum from normal to severely impaired cardiac function were observed. Cardiac magnetic resonance imaging was performed to assess left ventricular (LV) volumes, myocardial mass, peak ejection (PER) and filling rate (PFR).
Results: A reduced PFR was found in 348 patients (33.1%), which resulted from 275 of 422 patients (65.2%) with reduced and from 73 of 628 patients (11.6%) with preserved LVEF ($p < 0.0001$). Increased LV volume and mass was correlated with reduced PER and PFR ($p < 0.0001$). Increased end-diastolic wall stress was the strongest predictor of a reduced PER (OR 4.5 [2.6 to 7.8], $p < 0.0001$) and increased end-systolic wall stress predicted a reduced PFR (OR 1.2 [1.1 to 1.3], $p < 0.0001$). Increased end-systolic wall stress was correlated with increased pulmonary pressure ($p < 0.0001$). Normal end-systolic wall stress < 18 kPa had a favorable predictive value for the absence of an impaired filling and increased pulmonary capillary pressure.
Conclusion: Increased end-diastolic wall stress precedes a reduced ventricular ejection rate and increased end-systolic wall stress determines an impaired diastolic filling. It is thus suggested to add assessment of ventricular wall stress as diagnostic criterion of heart failure.

1. Introduction

Heart failure results from two major components contributing to symptoms in various extent: systolic and diastolic dysfunction. Patients hospitalized for decompensated heart failure suffer from systolic dysfunction in approximately one half of cases. The other half exhibits a normal or near normal systolic function and diastolic dysfunction accounts for symptoms [1]. Diastolic heart failure has been defined as presence of diastolic dysfunction in patients with symptoms of heart failure and normal or near normal, i.e. preserved, LV ejection [2,3]. While an impaired systolic function is characterized by a reduced forward volume, diastolic dysfunction describes an impaired filling, i.e. a disproportion of pressure and filling rate, due to an abnormal diastolic relaxation (active process) and a reduced compliance or distensibility (passive process) regardless of systolic function. Besides the rate of pressure decline during isovolumic relaxation, rate and extent of ventricular filling are crucial. Diastolic dysfunction frequently occurs in left ventricular (LV) hypertrophy of various origin, e.g. following hypertension, in hypertrophic, dilated, restrictive or diabetic cardiomyopathy and in ischemic heart disease [4,5]. Symptoms of heart failure result from an increased LV pressure that is transmitted to the pulmonary veins via an opened mitral valve during diastole accounting for pulmonary congestion and dyspnea. Although echocardiographic criteria, basically including the transmitral flow pattern, have been identified for clinical use [6,7], the diagnosis of diastolic dysfunction remains challenging.

Ventricular wall stress is fundamentally involved in cardiac function. Increased ventricular wall stress is known to exhibit unfavorable consequences in heart failure, e.g. an adverse remodeling [8–10] and imbalance between oxygen consumption and supply [11]. Because of methodological limitations, assessment of ventricular wall stress has not been established as routine diagnostic tool in clinical practice up to now. It is hypothesized whether end-diastolic and end-systolic ventricular wall stress as calculated by the wall stress index based on cavity volume and myocardial mass [12] is associated with ventricular ejection

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and diastolic filling and thus provide novel criteria to diagnose heart failure.

2. Methods

A total of 1050 patients consecutively undergoing cardiac magnetic resonance (CMR) imaging due to suspected cardiomyopathy were examined. Patients had been admitted because of symptoms of heart failure, e.g. overt chronic heart failure, exertional dyspnea or chest pain. Patients with at least 16 years of age were included. Patients with chronic heart failure were on guideline-adjusted heart failure therapy [13]. Patients with coronary artery or valvular heart disease, patients with implanted cardiac devices such as pacemakers or cardioverter/defibrillators, patients with cardiac storage diseases or hypertrophic cardiomyopathy, patients with malignancies, severe kidney or liver disease were not included. The enrolled cohort covered a broad spectrum of cardiac function ranging from normal to severe dilated cardiomyopathy and poor function.

In a subgroup of 269 patients, left and right heart catheter procedures (Swan Ganz) had been performed for clinical reasons before entry into the study. Aortic, pulmonary artery and capillary wedge pressure was assessed by using Statham manometers. Patients' characteristics are summarized in Table 1. The study is in accordance with the institutional guidelines and approved by the ethics committee. This trial is registered as DRKS00007756.

2.1. LV volume, function and wall stress by cardiac magnetic resonance

CMR examinations (1.5 T, Siemens, Germany) were performed in all study participants. For measurement of LV volumes, function and mass, a stack of short-axis views covering the complete LV from base to apex was acquired using ECG-gated steady-state free precession sequences (TrueFISP) [14]. End-diastolic (LVEDV) and end-systolic volume (LVESV), ejection fraction (LVEF), and LV mass (assuming a solid density of 1.05 kg/l) was assessed.

The time varying course of LV volume characterized by systolic ejection and diastolic filling was obtained during retrospective gating at 25 equally distributed reading points, marked by ECG R–R intervals, covering the cardiac cycle. If required, the built-in semiautomatic procedure for contour detection of the endocardium on LV short-axis views was corrected manually. Beside this volume versus time curve (V/Δt), also its first derivate characterizing the rate of LV volume changes versus time (ΔV/Δt) was assessed (Fig. 1) [15,16]. Thereby, peak ejection rate (PER, normalized to LVEDV), peak ejection time (PET), peak filling rate (PFR, normalized to LVEDV) and peak filling time after end systole (PFT) was assessed by using approved analyzing software (Argus, Siemens, Germany) [17,18]. PER and PFR of less than 2.5 EDV/s was considered to be abnormal [19–23].

For calculation of ventricular wall stress [σ], the wall stress index [σ_i], based on a thick-walled sphere model of the LV, was used [12,24]. LV cavity volumes (V_{lum}) and myocardial volume (V_{myo}) were inserted as measured by CMR [14]. Details are described elsewhere [25,26].

$$\sigma_i = \left[\left(\frac{V_{lum} + V_{myo}}{V_{lum}}\right)^{2/3} - 1\right]^{-1}$$

An intraventricular pressure [P] of 16 mm Hg at end diastole and 130 mm Hg at end systole was assumed to approximate wall stress as described in detail previously [12].

$$\sigma = P \times \sigma_i$$

Since pressure was standardized, the obtained wall stress [σ] is a resultant of the proportion of LV dilatation and myocardial hypertrophy.

2.2. Statistics

Chi square test was used for comparisons of categorical variables. For between-group comparisons, the Mann–Whitney rank sum test was performed. Comparisons between

Table 1
Characteristics of patients.

	All patients n = 1050	LVEF >50% n = 628	LVEF ≤50% n = 422	p Value *	Subgroup pressure measurement n = 269
Baseline characteristics					
Age [years]	47.83 ± 16.29	46.31 ± 15.94	50.09 ± 15.36	<0.001	50.94 ± 15.21
Male/female gender	627 (59.71%)	340 (54.14%)	287 (68.01%)	<0.001	183 (68.03%)
Body mass index [kg/m^2]	26.27 ± 4.63	26.06 ± 4.63	26.57 ± 4.81	0.147	26.4 ± 4.59
Body surface area [m^2]	1.94 ± 0.22	1.93 ± 0.22	1.97 ± 0.23	0.006	1.97 ± 0.21
Medication					
Betablockers	62.14%	50.45%	76.92%	<0.001	67.46%
ACE inhibitors/AT antagonists	56.35%	42.34%	70.07%	<0.001	64.29%
Aldosterone antagonists	27.42%	7.21%	52.99%	<0.001	35.32%
Diuretics	29.18%	14.19%	48.15%	<0.001	41.67%
Left ventricular volume, mass and function by CMR					
LVEDV [ml]	155.96 ± 74.29	127.29 ± 37.29	198.50 ± 92.10	<0.001	166.51 ± 79.16
LVEDV [ml/m^2]	79.73 ± 35.47	65.85 ± 16.41	100.38 ± 44.35	<0.001	84.14 ± 38.45
LVESV [ml]	85.3 ± 70.49	49.84 ± 15.10	137.89 ± 84.76	<0.001	99.47 ± 76.07
LVESV [ml/m^2]	43.42 ± 34.69	25.77 ± 7.00	69.68 ± 41.51	<0.001	50.22 ± 37.75
LVSV [ml]	69.52 ± 25.98	76.09 ± 26.32	59.75 ± 23.62	<0.001	66.79 ± 24.80
LVSV [ml/m^2]	36.31 ± 11.61	40.08 ± 10.85	30.70 ± 10.63	<0.001	33.92 ± 11.52
LV mass [g]	156.14 ± 69.03	132.23 ± 53.31	191.60 ± 72.89	<0.001	174.43 ±73.03
LV mass [g/m^2]	79.41 ± 31.42	67.81 ± 23.65	96.69 ± 33.65	<0.001	87.85 ± 33.93
LVEF [%]	50.23 ± 16.23	61.17 ± 5.41	33.95 ± 11.86	<0.001	45.81 ± 17.68
Left ventricular wall stress					
End-diastolic [kPa]	3.93 ± 1.05	3.88 ± 1.01	3.99 ± 1.13	0.205	3.75 ± 1.09
End-systolic [kPa]	17.32 ± 7.39	13.77 ± 3.53	22.61 ± 8.08	<0.001	18.04 ± 8.48
Left ventricular ejection and filling					
Heart rate [1/min]	69.47 ± 14.30	68.56 ± 13.06	70.80 ± 15.85	0.0618	68.96 ± 14.11
PER [EDV/s]	3.52 ± 1.53	4.15 ± 1.44	2.58 ± 1.26	<0.001	3.32 ± 1.61
PET [ms]	136.36 ± 77.01	125.91 ± 69.64	152.28 ± 92.38	<0.001	126.83 ± 84.66
PFR [EDV/s]	3.23 ± 1.55	3.88 ± 1.37	2.26 ± 1.32	<0.001	2.82 ± 1.50
PFT [ms]	182.26 ± 150.47	180.93 ± 167.38	184.29 ± 147.21	0.517	191.14 ± 155.50
Number of PFR <2.5 EDV/s	348 (33.1%)	73 (11.6%)	275 (65.2%)	<0.0001	117 (43%)
Aortic pressure					
Systolic [mm Hg]					129.57 ± 23.64
Diastolic [mm Hg]					69.94 ± 13.63
Mean [mm Hg]					92.39 ± 15.51
Pulmonary artery pressure					
Systolic [mm Hg]					30.79 ± 12.76
Diastolic [mm Hg]					12.56 ± 7.62
Mean [mm Hg]					19.31 ± 9.32
Mean capillary wedge [mm Hg]					12.01 ± 8.09

Abbreviation: LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVSV, left ventricular stroke volume; LVEF, left ventricular ejection fraction; PER, peak ejection rate; PET, peak ejection time; PFR, peak filling rate, PFT, peak filling time after end systole.

* Indicate differences among groups with LVEF ≤50% and >50%.