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ORIGINAL PAPER

Diagnostic superiority of a combined assessment of the systolic and early diastolic mitral annular velocities by tissue Doppler imaging for the differentiation of restrictive cardiomyopathy from constrictive pericarditis

Thomas Butz · C. Piper · C. Langer · M. Wiemer · T. Kottmann · A. Meissner · G. Plehn · H. J. Trappe · D. Horstkotte · L. Faber

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Abstract

Background and aims Echocardiographic tissue Doppler imaging (TDI) has been proposed as diagnostic tool for the differentiation between constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM). The aim of this study was a comprehensive TDI analysis of systolic (S') and early diastolic (E') velocities of the septal and lateral mitral annulus (MA) in patients (pts) with severe diastolic dysfunction caused either by CP or RCM.

Methods and results Sixty consecutive pts (34 men, mean age 61 ± 11 years), 34 pts with proven CP and 26 pts with RCM due to cardiac amyloidosis, were included in the study. Forty-two of the 60 pts were in NYHA class III (70%). In pts with RCM systolic longitudinal velocity (S') was significantly decreased when compared to CP (septal MA 4.1 ± 1.5 vs. 7.3 ± 2.1 cm/s, $p < 0.001$; lateral MA 4.3 ± 1.9 vs. 7.0 ± 1.9 cm/s, $p < 0.001$). In addition, the RCM group showed a significantly decreased early diastolic longitudinal velocity (E'), both on the septal (4.1 ± 1.6 vs. 12.9 ± 4.9 cm/s, $p < 0.001$) and lateral side (4.8 ± 1.9 vs. 11.3 ± 3.7 cm/s; $p < 0.001$) of the mitral annulus. ROC analysis demonstrated an area under the curve of 0.889 (S' septal), 0.823 (S' lateral), 0.974 (E' septal), and 0.915 (E' lateral) for the differentiation of RCM and CP with a cutoff value of <8 cm/s. The combined use of an averaged S' cutoff value <8 cm/s as well as an E' cutoff value <8 at the lateral and septal MA demonstrated 93% sensitivity and 88% specificity for the diagnosis of RCM.

Conclusion TDI provides a diagnostic superiority and an accurate discrimination between RCM and CP by using the combined cutoff value of <8 cm/s for S' and E' at both sides of the MA.

Keywords Constrictive pericarditis · Restrictive cardiomyopathy · Tissue Doppler imaging · Amyloidosis · Echocardiography · Diastolic heart failure

Abbreviations

A	Late component of the transmitral inflow pattern
A'	Late diastolic velocity of the mitral annulus (TDI)
CP	Constrictive pericarditis
DT	Deceleration time of E
E	Early component of the transmitral inflow pattern
E'	Early diastolic velocity of the mitral annulus (TDI)
E/E' ratio	Ratio of the early component of the transmitral inflow pattern and the early diastolic velocity of the mitral annulus
E'/E ratio	Ratio of the early diastolic velocity of the mitral annulus and the early component of the transmitral inflow pattern
MA	Mitral annulus
LVEDP	Left ventricular end-diastolic pressure
PA	Pulmonary artery
PCWP	Pulmonary capillary wedge pressure

T. Butz · C. Piper · C. Langer · M. Wiemer · T. Kottmann · D. Horstkotte · L. Faber
Department of Cardiology, Heart Center Northern-Westphalia, Ruhr-University Bochum, Bad Oeynhausen, Germany

T. Butz (✉) · A. Meissner · G. Plehn · H. J. Trappe
Department of Cardiology and Angiology, Marienhospital Herne, Ruhr-University Bochum, Hölkeskampring 40, 44625 Herne, Germany
e-mail: Thomas.Butz@Marienhospital-Herne.de

RA	Right atrium
RCM	Restrictive cardiomyopathy
RV	Right ventricle
RVEDP	Right ventricular end-diastolic pressure
RVSP	Right ventricular systolic pressure
S'	Systolic velocity of the mitral annulus (TDI)
TDI	Tissue Doppler imaging

Introduction

The differentiation between constrictive pericarditis (CP) and restrictive cardiomyopathy (RCM) remains challenging for echocardiographers. During the last decade, tissue Doppler imaging (TDI) has been introduced into clinical practice for a less load dependent, quantitative assessment of systolic and diastolic myocardial function [1–5]. The assessment of E' has been proposed as a new method for the differentiation between restrictive and constrictive physiology, because intrinsic mechanical elastic properties of the myocardium are usually preserved in CP, but not in RCM [6, 7]. The differentiation of both entities is very important, because there are different promising treatment options for these diseases (e.g. pericardiectomy in CP, chemotherapy and bone marrow transplantation in some forms of amyloidosis; [8–10]).

Previous studies were limited by the small number of patients examined, and they predominantly focused on the analysis of the early diastolic velocity E' of the lateral mitral annulus [6, 7, 11]. Furthermore, it has been recently shown that TDI analysis of the motion of the lateral mitral annulus might be affected by severe pericardial calcification [12–17]. Moreover, quantitative assessment of systolic myocardial velocities (S'), which have been reported to be reduced in myocardial diseases, e.g. RCM and hypertrophic cardiomyopathy, has been rarely used for the differentiation between CP and RCM [18, 19].

Thus, we hypothesized that the comprehensive analysis of the systolic and early diastolic velocities of the lateral and septal mitral annulus in a large patient population with either proven constrictive or restrictive heart disease by TDI may be useful in differentiating those conditions by echocardiography, and that this diagnostic approach may provide a superior diagnostic accuracy.

Methods

Study design

In a single center study we studied 60 consecutive patients who were referred to the echocardiographic laboratory from January 2000 to September 2007 for evaluation of predominant right sided heart failure with normal or near normal ejection fraction, and suspected severe diastolic dysfunction caused either by CP or RCM due to cardiac amyloidosis. The patients were categorized on the basis of clinical assessment and the results of a multi-dimensional diagnostic approach, including transthoracic and transesophageal echocardiography, magnetic resonance imaging (MRI), multi-slice computed tomography (MSCT), cardiac catheterization, endomyocardial biopsy, and surgical findings [7, 14–17]. All patients had a complete echocardiographic and hemodynamic assessment within 1–5 days during the same hospital stay.

The diagnosis "constrictive physiology" was confirmed in all 34 patients by the surgical findings during pericardiectomy. The presumed etiology of pericardial disease was previous cardiac surgery in 13, chest irradiation in 3, and unknown or idiopathic in the remaining 18 patients.

In all 26 patients with "restrictive physiology" due to cardiac amyloidosis, the diagnosis was confirmed by histology and immunohistochemical findings of the myocardial biopsy taken during catheterization (20 patients had AL-lambda, 2 AL-Kappa, 4 ATTR-amyloidosis).

Echocardiographic examination

Echocardiographic assessment was performed according to the Guidelines of the American Society of Echocardiography [20–23], and included the analysis of the transmitral inflow pattern, the respiratory variation of the transtricuspidal and transmitral inflow, and the analysis of the systolic (S') and early diastolic component (E') of mitral annulus motion by TDI. All patients were examined at rest in the left lateral decubitus position with a commercially available ultrasound system (Vingmed System Five and Vivid Seven, General Electrics, Horten, Norway) equipped with TDI capabilities [1, 6, 7, 11]. A multifrequency 1.5- to 4.0-MHz transducer was used for all two-dimensional, M-mode and Doppler echocardiographic examinations. Two-dimensional studies were recorded from the parasternal long- and short-axis, and the apical four- and two-chamber views in the harmonic imaging mode. End-diastolic and end-systolic volumes were obtained from the apical four-chamber view. Ejection fraction was calculated off-line using the modified Simpson's method [7]. From the apical window, the pulsed-wave Doppler sample volume was placed at the mitral valve tips, and 5–10 cardiac cycles were recorded [6]. A respiratory variation of >25% in mitral and of >40% in transtricuspidal inflow peak E velocity was considered suggestive for CP [1, 6, 7, 11].

To obtain mitral annular velocities by TDI, we placed a 5–10 mm sampling gate within the bright lateral and septal side of the mitral annulus. The peak velocities of systolic excursion (S'), and the peak early (E') and late (A') diastolic velocities were measured from the apical four-chamber view by TDI. Spectral pulsed-wave (PW) Doppler signal filters were adjusted to obtain a Nyquist limit of 20 cm/s, with the lowest wall filter settings, and the minimal optimal gain, to eliminate the signals produced by transmitral flow. TDI assessment was obtained with frame rates between 50 and 100 fps. Three beats were recorded at a sweep speed of 50–100 mm/s, and averaged for each of these measurements. In patients with atrial fibrillation the TDI values of 5–10 cycles were averaged [1, 11, 24].

Moreover, the index of mitral inflow peak E velocity and peak early diastolic (septal and lateral) annular velocity (E/E') was calculated as previously described [25–27].

Statistical analysis

Descriptive statistics were used to summarize the data; for categorical variables, this included frequencies and percentages, and for continuous variables, this included mean ± standard deviation (SD). Commercially available software has been used for analysis (SPSS 15.0, SPSS Inc., Chicago, Illinois, USA). Comparisons between patients with CP and RCM were performed with the unpaired t test for each of the different methods, and Pearson's chi-square test. Differences were considered statistically significant when the probability value (p) was <0.05. Receiver operating characteristic (ROC) curves methods were used to determine the summary measure of relative accuracy for the various approaches as a function of specificity and sensitivity (area under the curve, AUC).

Results

Subject characteristics

From the 60 patients investigated (34 men, 26 women; mean age 61 ± 11 years, range 24–87 years), 34 had CP, and 26 RCM. Due to the specific point in time of manifestation of the underlying diseases, the RCM patients were significantly older (65 ± 9 years) than the CP patients (58 ± 12 years; $p < 0.05$). 37/60 patients (62%) had sinus rhythm, and 23/60 patients (38%) were in atrial fibrillation (CP: 16/34, 47%; RCM: 7/26, 26%), which is a common finding in these conditions. Forty-two of the 60 patients were in NYHA class III (70%), 13 (21%) in NYHA class II, and five patients were in NYHA class I.

M-mode and two-dimensional echocardiography

Systolic left ventricular function was normal in all patients with CP [ejection fraction (EF), 67 ± 10%]. Twenty-one RCM patients had a normal (EF, 61 ± 9%), two a borderline normal (2D-EF, 50–55%), and three patients a slightly impaired systolic left ventricular function (2D-EF, 40–50%).

The end-diastolic thickness of the interventricular septum and the posterior wall was significantly increased in RCM when compared to CP (see Table 1). A pericardial effusion was detected in 15 of the 26 RCM patients (58%), but in no case of the CP group. On the other hand, pericardial thickening and/or pericardial calcifications were detected by 2D-echocardiography in the majority of CP patients (30/34 pts, 88%).

Table 1 Patients and echocardiographic characteristics of all patients ($n = 60$)

	RCM	CP	p Value
Age (years)	64.6 ± 8.8	57.9 ± 12.3	<0.05
Male/female (number)	16/10	18/16	0.80
2D-echo			
LV end-diastolic diameter (mm)	44.7 ± 7.5	46.3 ± 7.2	0.43
Left atrial diameter (mm)	49 ± 6	49 ± 11	0.88
LV thickness septum (mm)	16.4 ± 4.6	8.5 ± 1.6	<0.001
LV thickness posterior (mm)	13.5 ± 2.0	8.8 ± 1.5	<0.001
Pericardial effusion	15/26	0/34	<0.01
Pericardial thickening/calcification	0/26	30/34	<0.01
Transmitral flow			
E (cm/s)	84.3 ± 17.6	108.3 ± 40.9	<0.05
A (cm/s)	43.76 ± 25.24	51.6 ± 22.4	0.31
E/A ratio	2.3 ± 1.1	2.0 ± 0.9	0.37
Deceleration time (ms)	149.1 ± 61.7	131.8 ± 36.3	0.22

Mitral inflow pattern and respiratory variation of transtricuspidal and transmitral flow

The data of the transmitral flow pattern analysis is summarized in Table 1.

A significantly increased respiratory variation of both, the transtricuspidal and transmitral flow, was detected in 14 of 18 patients (78%) with CP and sinus rhythm, whereas only three of the 19 RCM patients with sinus rhythm showed an increased respiratory variation. The analysis of the respiratory variation in patients with atrial fibrillation gave inconsistent results due to the irregular cycle length.

Tissue Doppler Imaging (TDI)

Systolic longitudinal velocity (S') as assessed by TDI was significantly decreased in patients with RCM when compared to patients with CP (Table 2; Fig. 1). S' at the septal and lateral mitral annulus (MA) showed a significant inverse correlation with the thickness of the interventricular septum (IVSD; −0.598, resp. −0.550, $p < 0.01$) and the thickness of the posterior wall (PW; −0.479, resp. −0.464, $p < 0.01$).

There was no correlation between age and the S' velocities neither in the CP nor in the RCM group, indicating that there was no bias caused by the above mentioned difference in age between the two groups.

The previously proposed cutoff value for S' <8 cm/s showed 100% sensitivity and 53% specificity at the septal MA and 92.3% sensitivity and 50% specificity at the lateral MA for the diagnosis of RCM (Fig. 2). ROC analysis demonstrated in an area under the curve (AUC) of 0.889 (S' septal) and 0.823 (S' lateral; Fig. 3).

Early diastolic longitudinal velocities (E') on the septal and lateral side of the mitral annulus were lower in patients with RCM than in CP patients, reaching high statistical significance (Fig. 1). E' at the septal and lateral MA showed a significant inverse correlation with the thickness of the interventricular septum (IVSD; −0.666, resp. −0.655, $p < 0.01$) and the thickness of the posterior wall (PW; −0.622, resp. −0.625, $p < 0.01$). There was a significant inverse correlation between age and the septal E' velocity in the CP group ($r = -0.352$, $p < 0.05$), but no correlation between age and the E' velocities in the RCM group.

Moreover, patients with RCM had a significant higher E/E' ratio at the septal MA and at the lateral MA (Table 1). All RCM patients demonstrated an E/E' ratio >8, and 20/26 patients (77%) had an E/E' ratio >15, which usually indicates elevated filling pressures [17, 18]. In contrast, only 6/34 CP patients (18%; septal and lateral mitral annulus) showed an E/E' ratio >15, predominantly due to a post-radiation syndrome.

Septal E' was <8 cm/s in all RCM patients, and lateral E' was <8 cm/s in 24/26 (92%) of the RCM patients. In

Table 2 Comparison of the mitral annular velocities as assessed by TDI and of the hemodynamic findings between patients with RCM and CP

	RCM	CP	p Value
TDI			
S' septal (cm/s)	4.1 ± 1.5	7.3 ± 2.1	<0.001
S' lateral (cm/s)	4.3 ± 1.9	7.0 ± 1.9	<0.001
Averaged S' (lateral S' + septal S'/2)	4.2 ± 1.6	7.1 ± 1.8	<0.001
E' septal (cm/s)	4.1 ± 1.6	12.9 ± 4.9	<0.001
E' lateral (cm/s)	4.8 ± 1.9	11.3 ± 3.7	<0.001
Averaged E' (lateral E' + septal E'/2)	4.4 ± 1.6	12.1 ± 4.0	<0.001
E/E' (septal)	23.4 ± 10.2	10.4 ± 7.3	<0.001
E/E' (lateral)	20.2 ± 8.6	11.5 ± 7.8	<0.001
Averaged E/E' [E/(lateral E' + septal E'/2)]	21.3 ± 8.5	10.7 ± 7.3	<0.001
Ejection fraction, EF (%)	61 ± 9	67 ± 10	0.09
Hemodynamic data			
Coronary artery disease (CAD)	31% (8/26)	29% (10/34)	0.91
LVEDP (mmHg)	22 ± 6	23 ± 4	0.83
Mean RA pressure (mmHg)	12 ± 4	16 ± 5	<0.01
Systolic RV pressure (mmHg)	48 ± 13	40 ± 7	<0.01
Systolic RV pressure ≥ 50 mmHg	38% (10/26)	12% (4/34)	<0.05
Mean PA pressure (mmHg)	32 ± 8	26 ± 4	<0.01
Mean PCWP (mmHg)	23 ± 7	21 ± 4	0.33
RVEDP/RVSP < 1/3	81% (21/26)	26% (9/34)	<0.01
LVEDP-RVEDP ≥ 5 mmHg	73% (19/26)	32% (11/34)	<0.05
Dip-plateau sign	23% (6/26)	73% (25/34)	<0.01

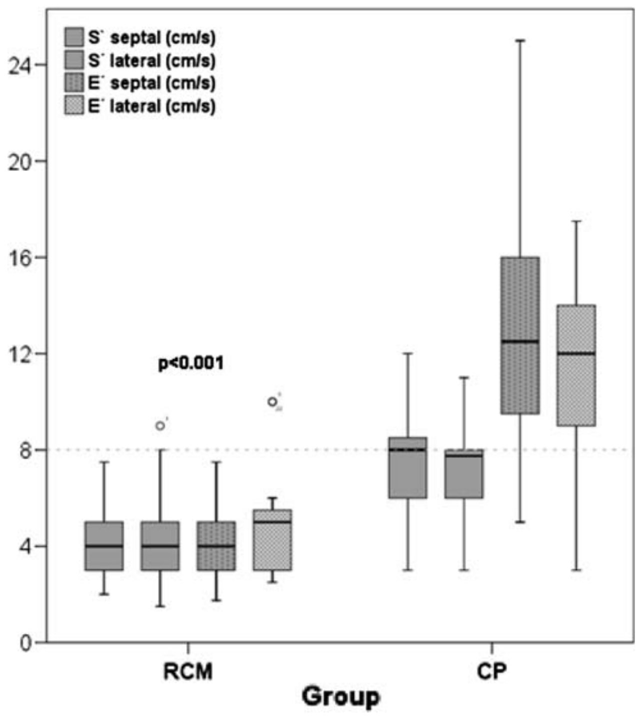

Fig. 1 Peak systolic velocity S' and early diastolic velocity E' at the septal and lateral mitral annulus in restrictive cardiomyopathy (*RCM left side*) and constructive pericarditis (*CP right side*)

contrast, septal and lateral E' was $\geq$8 cm/s in 29/34 CP patients (85%). The four CP patients with E' <8 cm/s at the septal and lateral MA either showed severe pericardial calcification or had a post-radiation syndrome (two patients). One patient with calcification of the lateral mitral annulus, showed an E' <8 cm/s at the lateral MA, but an E' $\geq$8 cm/s at the septal MA.

A cutoff value <8 cm/s for E' at the septal and lateral MA resulted in a sensitivity of 93% and a specificity of 85% for the diagnosis of RCM (Fig. 2). The combined use of an S' cutoff value <8 cm/s and an E' cutoff value <8 at both sides of the MA (lateral and septal MA) demonstrated 93% sensitivity and 88% specificity for the diagnosis of RCM.

ROC analysis demonstrated in an area under the curve (AUC) of 0.974 (E' septal) and 0.915 (E' lateral; Fig. 3).

Hemodynamic assessment

The findings of left and right heart catheterization are summarized in Table 2.

Left ventricular angiography revealed normal left ventricular systolic function with a mean ejection fraction (EF) of 67 ± 10% in all patients with CP. In the RCM group the mean EF was 61 ± 9% due to three patients with borderline (EF, 50–55%) or slightly decreased EF (EF, 40–50%). Mean pulmonary arterial pressure (32 ± 8 vs. 26 ± 4 mmHg; $p < 0.01$) and systolic right ventricular pressure (48 ± 13 vs. 40 ± 7 mmHg; $p < 0.01$) were significantly increased in RCM when compared to CP. In contrast, there was no significant difference of the mean pulmonary capillary wedge pressure (PCWP) and the left ventricular end-diastolic pressure (LVEDP) between both groups. Typical hemodynamic findings of CP, like end-diastolic pressure-equilibration and dip-plateau phenomena, were present in the majority of CP patients (see Table 2).

Discussion

The principal finding of this study is the diagnostic superiority of a combined and comprehensive tissue Doppler imaging (TDI) analysis of systolic and early diastolic

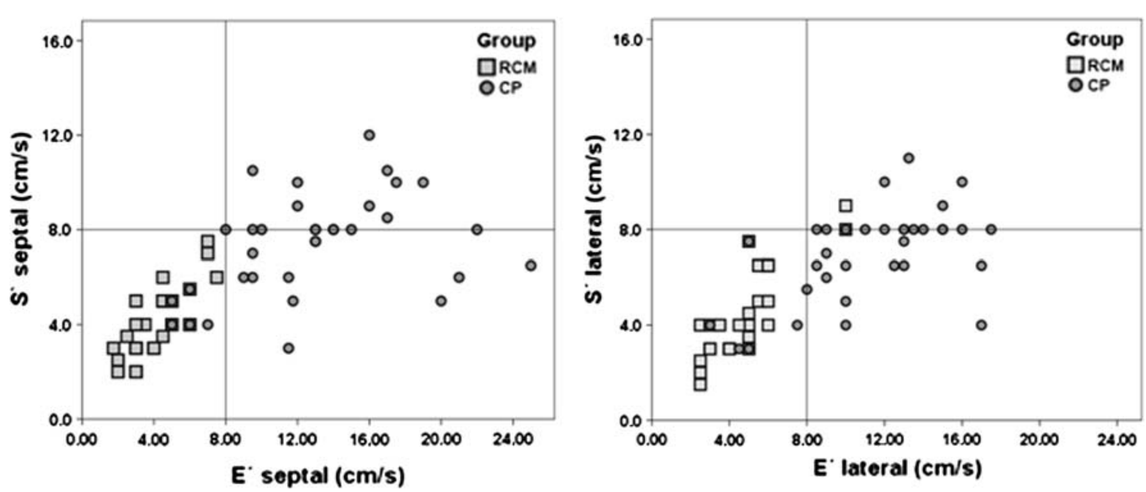

Fig. 2 Combined use of an S' cutoff value <8 cm/s and an E' cutoff value <8 at the septal (*left side*) and lateral (*right side*) of the mitral annulus for patients with RCM and CP

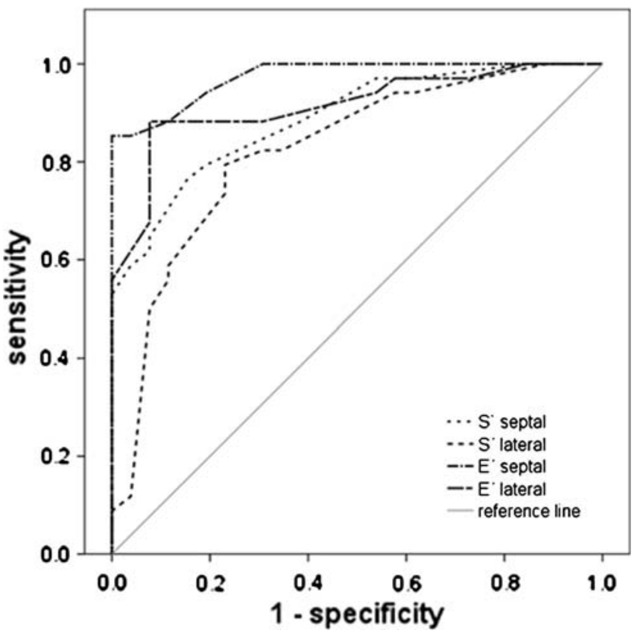

Fig. 3 ROC curves for peak systolic velocity S' and early diagnostic velocity E' at the septal and lateral mitral annulus in restrictive cardiomyopathy (*RCM*) and constructive pericarditis (*CP*)

velocities of the lateral and septal mitral annulus in a large cohort of patients for the differentiation of severe diastolic filling abnormalities caused either by a restrictive or a constrictive physiology.

TDI has advanced to an additional method for quantitative assessment of systolic and diastolic myocardial function, and for the evaluation of diastolic heart failure, especially in CP and restrictive cardiomyopathy, within the last decade [1, 6, 7, 11, 14]. It has been previously demonstrated that a peak myocardial longitudinal expansion E' velocity of <8.0 cm/s at the lateral mitral annulus as assessed by TDI can be used to differentiate patients with RCM and CP with high diagnostic accuracy [28–34]. Reduction of the S' and E' velocity of the mitral annulus in RCM is due to an impairment of myocardial function, and E' is supposed to be an important measure of left ventricular relaxation [11].

Hence, the definition of "RCM" in the reported study groups was quite heterogeneous and imprecise [1, 6, 7, 11], we consequently assessed a clearly defined and homogeneous study group with restrictive physiology (RCM) due to cardiac amyloidosis in order to obtain optimal TDI data.

In contrast, E' is usually well preserved or even accentuated in CP despite increased filling pressures, and consecutive diastolic heart failure. This finding might be due to elevated filling pressures in patients with CP causing increased longitudinal motion of the mitral annulus, precisely because the lateral expansion of the entire heart is limited by the constricting pericardium [35, 36]. The more severe the constriction, the higher are the filling pressures, and the more accentuated is the longitudinal motion of the mitral annulus. This explanation is supported by the finding that E' decreases after pericardiectomy [35, 36]. The previous finding of an annulus reversus [37], which is characterized by significant lower E' velocities at the lateral MA than the E' velocities at the septal MA, could not been confirmed by our data, because there was no significant difference of the septal and lateral E' velocities in CP.

However, in the majority of the previously published studies only the E' velocity of either the lateral [7, 11] or the septal [6] mitral annulus, but not of both sides of the mitral annulus, have been analyzed (Table 3). Moreover, S' has been rarely analyzed in previous reports, and most of the reported studies were performed in a limited number of patients [1, 6, 7, 11, 14]. Most of the previous published studies have shown no differences between constriction and restriction with regard to peak S' and peak A' values, although some overlap of these data had been evident between the two groups [1, 11].

In contrast to these findings, our study demonstrated significantly decreased peak S' values in the RCM group as compared to the CP group, confirming the results of two recently published studies [37, 38].

The present study is the first one that combined the comprehensive TDI analysis of the S' and the E' velocities of the lateral as well as septal mitral annulus in a large cohort of patients with these rare entities.

The overall sensitivity and specificity of TDI for differentiating between RCM and CP (cutoff value for E' <8 cm/s) has been reported as 74 and 91%, respectively [6, 11]. Our study demonstrated a superior diagnostic accuracy with a sensitivity of 92% (averaged E'; 92% for E' lateral, 100% for E' septal) and a specificity of 85.3% (E' septal, E' lateral, and averaged E') for the cutoff value for E' <8 cm/s.

The four CP patients with an E' and a S' <8 cm/s had either severe pericardial calcification, especially at the

Table 3 Comparison to the previously published studies with TDI analysis in CP and RCM

Author	CP	RCM	S' septal	S' lateral	E' septal	E' lateral
Sengupta [1]	45	11			X	X
Ha [6]	23	52			X	
Garcia [7]	8	7		X		X
Rajagopalan [11]	19	11		X		X
Reuss [37]	14	10	X	X	X	X
Choi [38]	17	12	X		X	
Butz	34	26	X	X	X	X
Total number	160	129				

lateral MA, or post-radiation syndrome, which has been previously shown as a limitation of TDI analysis in these particular conditions [1, 13, 14, 39].

The cutoff value for S' <8 cm/s demonstrated a sensitivity of 100% (averaged S'; 92% for S' septal, 100% for S' lateral) and a specificity of 53% (averaged S'; 50% for S' lateral, 53% for S' septal). In addition, an even better diagnostic approach could have been achieved by the combined use of an averaged (lateral and septal MA) cutoff value <8 cm/s for S' as well as for E', which demonstrated a 93% sensitivity and an 85% specificity for the diagnosis of RCM in our study.

Therefore, we propose this approach of a combined assessment of systolic and early diastolic velocities of the septal and lateral mitral annulus, and an additional calculation of the E/E'-ratio as diagnostic algorithm for an accurate and substantial differentiation between CP and RCM.

A comprehensive echocardiographic approach in severe diastolic heart failure should combine the traditional non-TDI Doppler approaches, like respiratory variation of mitral and tricuspid E-waves, and Doppler evaluation of hepatic and pulmonary vein flow, as well as assessment of thickness of the interventricular septum, septal bounce, and pericardial morphology (thickening, calcification, or effusion) with the above mentioned combined TDI analysis of S' and E' at the septal and lateral mitral annulus to differentiate between RCM and CP [20–34, 40].

Limitations for the TDI analysis in CP and RCM in a clinical setting

There are several limitations for the TDI analysis in heart failure patients due to CP or RCM which should be taken into account during the diagnostic workup.

First, it has been shown in a study by Sengupta et al. [1], two recent case reports [12, 13] and in our study, that the early diastolic mitral annular velocity can be artificially decreased and misleading in patients with extensive annular calcification at the lateral mitral annulus, which may affect mitral annulus motion [12–17]. Thus, nonuniform pericardial thickening and calcification may confound the use of mitral annular velocities to identify constriction. It has been proposed that coexistent myocardial dysfunction in CP (due to the extension of an inflammatory process into deeper layers of the myocardium, or simultaneous involvement of myocardium and pericardium by a common etiology, e.g. radiation exposure) may cause decreased E' velocities in some patients with CP [1]. Thus, TDI analysis in patients with myocardial dysfunction due to radiation, inflammation or previous myocardial infarction can be misleading. Heart failure in patients with cardiac post-radiation syndrome can be caused by a combination of myocardial dysfunction and pericardial constriction. In our study, an E' <8 cm/s was demonstrated only in CP patients with either severe pericardial calcification or post-radiation syndrome [1, 13, 14, 39].

Some of the previously published studies used inconsistent definitions for "restrictive cardiomyopathy" [1, 6, 7, 11], and it must be taken into account that the definition and classification of certain forms of cardiomyopathy with restrictive physiology is still a matter of debate. Normal TDI velocities ($E' \geq 8$ cm/s) have been demonstrated in some forms of RCM, e.g. endomyocardial fibrosis [1, 41]. Therefore, it must be pointed out that the reported results of TDI analysis may not be transferred to each form of RCM. We purposefully focused on patients with restrictive physiology due to biopsy-proven amyloidosis in order to analyze a homogeneous and clearly defined cause of RCM, but this approach might cause a selection bias due to the very well defined patient groups on the other hand. Further studies with all different causes and forms of a restrictive physiology, e.g. endomyocardial fibrosis, in large patient cohorts are needed.

Atrial fibrillation, which is quite common in severe diastolic heart failure, because left atrial pressure increases to maintain cardiac output, was present in 38% of the patients in the study. Patients with atrial fibrillation had been enclosed in most of the previously published studies [1, 7, 11, 14]. However, there are only few data available about the diagnostic accuracy of TDI in patients with atrial fibrillation. The analysis of the transmitral inflow pattern and the respiratory variation of transmitral flow have been shown to be less accurate or even impossible in atrial fibrillation. Thus, we propose to use the averaged velocities of S' and of E' in patients with normofrequent atrial fibrillation as a very helpful tool in patients with severe diastolic heart failure and atrial fibrillation.

Conclusion

TDI analysis in patients with diastolic heart failure demonstrated decreased systolic and diastolic velocities of the mitral annulus in patients with RCM and allows for an accurate differentiation between patients with RCM and CP independent of cardiac rhythm. The combined assessment of the peak systolic and early diastolic velocities at the lateral and septal side of the mitral annulus by TDI with a cutoff value of 8 cm/s for S' and E' in combination with the traditional echocardiographic parameters should be used for the echocardiographic workup in these entities. However, the diagnostic value of TDI analysis in CP can be limited in patients with severe pericardial calcifications, systolic dysfunction, and post-radiation syndrome.

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