Relation Between Echocardiographically Estimated and Invasively Measured Filling Pressures in Constrictive Pericarditis

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The ratio of early transmitral flow velocity (E) to mitral annular velocity (E′) is considered a predictor of pulmonary capillary wedge pressure (PCWP). In a previous small study, the paradoxical relation between PCWP and E/E′ ratio has been described in patients with constrictive pericarditis (CP). We sought to test this paradoxical relation in a larger cohort. We retrospectively identified 49 patients with surgically confirmed CP (40 men; mean age 61 ± 10 years) who underwent right-sided cardiac catheterization with PCWP measurement, preceded by an echocardiographic study. Of these, 48 patients underwent either computed tomography or magnetic resonance imaging to measure pericardial thickness on the lateral side of the left ventricular wall. Mean interval time between echocardiogram and right-sided cardiac catheterization was 1.5 ± 3.8 days. There were no significant correlations between mean, medial, or lateral E/E′ and PCWP (r = −0.17, 95% confidence interval [CI] −0.43 to −0.12; r = −0.17, 95% CI −0.43 to −0.12; and r = −0.12, 95% CI −0.39 to −0.17, respectively). Similarly, there was no correlation between mean E/E′ and brain natriuretic peptide (Spearman r = −0.17, p = NS). Patients with increased pericardial thickness (defined as >4 mm) had both lower lateral peak systolic annular velocity (S′) and lower lateral S′ integral (7.8 ± 2.4 vs 9.6 ± 2.4, p = 0.02 and 13.2 ± 4.2 vs 15.9 ± 4.7, p = 0.04, respectively). In patients with CP, there were no correlations between septal, lateral, or mean E/E′ and PCWP. In conclusion, E/E′ is not predictive of filling pressures in patients with CP, and perhaps the "annulus paradoxus" phenomenon should be revisited. The relation between the mitral annular velocity and thickness of the parietal pericardium may affect this phenomenon. **(Am J Cardiol 2014;113:1911−1916)**

Constrictive pericarditis (CP) is characterized by impedance to diastolic filling caused by the external constraints of fibrotic or inflamed pericardium.[1,2] Pericardiectomy is generally the definitive treatment in patients refractory to medical treatment.[3] Although patients still commonly undergo cardiac catheterization before surgical intervention to ascertain the severity of CP,[4] the combination of multimodal noninvasive imaging methods of echocardiography,[5] computed tomography (CT), and cardiac magnetic resonance imaging (MRI) can be used to give more insight into this complex diagnosis.[6] Diagnosis of CP is challenging as it necessitates the integration of seemingly disparate changes in myocardial function and blood flow velocities into the unifying diagnosis of CP. In addition, noninvasive imaging methods lack the accuracy of intracavitary pressure estimation. The most commonly used method of echocardiographic estimation of left ventricular (LV) filling pressure (LVFP) is the ratio of transmitral flow velocity (E) to tissue Doppler velocity of the mitral annulus (E′; i.e., E/E′). Although increased E/E′ ratio appears to correlate with increased LVFP in many disease states because of a decreased E′,[7] it seems to be less accurate in patients with advanced decompensated heart failure or LV hypertrophy.[8,9] Furthermore, patients with CP often show preserved annular motion and therefore preserved E′ despite severe impairment of LV filling,[10−12] thus making the E/E′ ratio less accurate. Ha et al[7] showed in a small cohort of patients with CP (n = 10) that there is a paradoxical relation between LVFP and E/E′ ratio (r = −0.74, p = 0.014) because of a preserved E′. However, given the small number of patients in this study, and the heterogeneous nature of CP, we sought to investigate whether these findings could be reproduced in a larger cohort of patients with surgically confirmed CP.

Methods

This was a retrospective study of consecutive patients who underwent pericardial stripping for CP without any additional procedures at Cleveland Clinic in a period from the year 2000 to 2010. The inclusion criteria were (1) comprehensive echocardiography and right and left catheterization studies done at the Cleveland Clinic, with echocardiography preceding right-sided cardiac catheterization but by not more than 2 weeks, (2) normal sinus rhythm, (3)

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Table 1
Clinical and hemodynamic patient characteristics

Variable	CP (n = 49)	Controls (n = 49)
Age (yrs)	61 ± 11	59 ± 8
Men/Women	40/9	29/20
New York Heart Association functional classification (I/II/III/IV)	0/6/18/25	49/0/0/0
BNP (pg/ml)*	138 (79−183)	
Echocardiographic data		
End-diastolic volume index (ml/m^2)	33 ± 16	48 ± 14†
End-systolic volume index (ml/m^2)	13 ± 4	18 ± 6†
Ejection fraction (%)	59 ± 5	63 ± 7†
Interventricular septal thickness (cm)	1.0 ± 0.1	1.0 ± 0.1
Posterior wall thickness (mm)	1.0 ± 0.1	0.9 ± 0.1
Left atrial volume index (ml/m^2)	29 ± 9	18 ± 5†
Septal mitral annulus velocity (cm/s)	13 ± 4	9 ± 2†
Lateral mitral annulus velocity (cm/s)	14 ± 4	11 ± 3†
Ratio between early diastolic mitral inflow and mitral annulus velocity	7 ± 3	7 ± 2
Ratio between early diastolic mitral inflow and late diastolic mitral inflow	2.2 ± 1.2	1.1 ± 0.3†
Deceleration time (ms)	147 ± 40	221 ± 26†
Respiratory variation of mitral inflow (%)	28 ± 22	—
Echo to right-sided cardiac catheterization interval (days)	1.5 ± 3.8	—
Invasive data		
Left ventricular systolic pressure (mm Hg)	118 ± 17	—
Left ventricular end-diastolic pressure (mm Hg)	20 ± 6	—
Right ventricular systolic pressure (mm Hg)	42 ± 13	—
Right ventricular end-diastolic pressure (mm Hg)	19 ± 5	—
Right atrial pressure (mm Hg)	17 ± 5	—
PCWP (mm Hg)	21 ± 5	—
Cardiac output (L/min)	4.9 ± 1.3	—
Cardiac index (L/min/m^2)	2.4 ± 0.7	—

* BNP was measured in 39 patients; median (twenty-fifth to seventy-fifth).
† $p \leq 0.01$ for comparison between groups.

no mitral valve disease (defined as ≥2+ regurgitation or any degree of stenosis), (4) no previous mitral valve surgery, and (5) surgically and pathologically confirmed CP. Consecutive patients were selected if they were in sinus rhythm and had a comprehensive echocardiography study performed to evaluate for CP 1.5 ± 3.8 days before right-sided cardiac catheterization. For comparative purposes, we used echocardiography data of 49 healthy controls aged ≥38 years selected from our database of healthy control subjects. Study design was approved by the Cleveland Clinic Institutional Review Board. All healthy controls gave written informed consent. In the diagnosis of CP, a constellation of clinical, hemodynamic, and echocardiographic findings were considered; however, the final diagnosis of CP was confirmed by surgical inspection and pathology specimen assessment in all study patients. We measured the maximal pericardial thickness of the lateral wall of the left ventricle obtained from reconstructed horizontal sections of the heart of contrast-enhanced CT or cardiac MRI data at any short axis.[13] Right- and left-sided cardiac catheterizations were performed under a light sedation in a supine position using a Swan-Ganz catheter for the assessment of pulmonary capillary wedge pressure (PCWP) and pigtail catheter for the assessment of LV pressures. All measurements were done in end-expiration. Cardiac output was measured by a Fick method using estimated total-body oxygen consumption. Serum brain natriuretic peptide (BNP) levels were obtained in 39 patients on the day of echocardiography using the Biosite assay (San Diego, California).[14]

CP was assessed in our institution in a standardized method and in accordance with the published guidelines using a combination of echocardiographic variables. LV volume, LV ejection fraction, and left atrial volume were calculated using the biplane method of disks from apical 4-chamber and 2-chamber views and traced by an experienced single observer. Tissue Doppler−derived indexes were measured using the apical 4-chamber view. Peak systolic (S′), early diastolic (E′), and late diastolic (A′) mitral annular velocities were calculated by averaging septal and lateral mitral annular velocities. The values for 2-dimensional echocardiographic parameters were obtained after averaging 3 consecutive cycles. To assess the role of E/E′ in predicting LVFP, we focused on analyzing the predictors of E′ as predictors of E-wave velocity are already well described. We used a framework described in Popovic et al,[15] which relies on the facts that the profiles of the velocities of the mitral inflow and of the diastolic mitral annulus velocities are intrinsically similar and that upward displacement of the mitral annulus (S′ integral) is identical to its downward displacement (i.e., E′ + A′ integral), to calculate an estimate of lateral, septal, and mean E′. Perfect correlation between thus estimated and measured E′ indicates that E′ velocities depend solely on long-axis systolic function and mitral flow pattern. Absence of correlation would indicate that E′ velocity is governed by other factors such as relaxation. The time constant of isovolumic pressure decay with a zero-asymptote assumption (τ) was estimated by the equation that is previously described.[16]