The impact of cardiac rhythm on the mitral valve area and gradient in patients with mitral stenosis

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Abstract

Objective: The aim of this study was to evaluate the effect of cardiac rhythm on the echocardiographic mitral valve area (MVA) and transmitral gradient calculation in relation to net atrioventricular compliance (Cn).

Methods: Patients (n=22) with mild or moderate pure rheumatic mitral stenosis (MS) (MVA <2 cm^2 and MVA >1 cm^2) and atrial fibrillation (AF) were evaluated. All patients underwent transthoracic electrical DC cardioversion under amiodarone treatment. Nineteen of the 22 patients were successfully converted to sinus rhythm (SR). The patients were evaluated with transthoracic echocardiography before and two to three days after DC cardioversion. In order to deal with variable R-R intervals, the measurements were averaged on five to eight consecutive beats in AF. Cn was calculated with a previously validated equation [Cn (mL/mm Hg)=1.270 x MVA/E-wave downslope]. The Cn difference between AF and SR was calculated as follows: [(AF Cn–SR Cn)/AF Cn] x 100. The percentage gradient (mean or maximal) difference between AF and SR was calculated as follows: [AF gradient (mean or maximal) – SR gradient (mean or maximal)]/[AF gradient (mean or maximal)] x 100.

Results: The MVA was lower (MVA planimetric; 1.62±0.29 vs. 1.54±0.27; p=.003, MVA PHT; 1.66±0.30 vs. 1.59±0.26; p=0.01) but transmitral gradient (mean gradient; 6.49±2.51 vs. 8.89±3.52; p=0.001, maximal gradient: 16.94±5.11 vs. 18.57±4.54; p=0.01) and Cn values (5.37±0.77 vs. 6.26±0.64; p<0.001) were higher in the AF than SR. There was a significant correlation between Cn difference and transmitral gradient difference (mean and maximal) (Cn difference–mean gradient difference; r=0.46; p=0.05; Cn difference–maximal gradient difference; r=0.72; p=0.001).

Conclusion: Cardiac rhythm has a significant impact on echocardiographic evaluation of MVA, transmitral gradient, and Cn in patients with MS. *(Anatol J Cardiol 2017; 18: 90-8)*

Keywords: echocardiography, mitral stenosis, atrial fibrillation

Introduction

Rheumatic mitral valve disease frequently complicates with atrial fibrillation (AF) and left atrial thrombus, and at least 30% to 40% patients had AF in long-term follow-up (1, 2). Likewise, AF is independently associated with increased stroke risk in patients with rheumatic mitral valve disease (1, 2). Therefore, AF developing in patients with moderate mitral stenosis (MS) leads to percutaneous mitral commissurotomy indication according to valvular heart disease management guideline (3).

Echocardiography is the standard technique for determining the severity of MS and following up this valve pathology. Several factors can affect the echocardiographic evaluation of mitral valve area (MVA) and gradient. These factors are heart rhythm, heart rate, blood pressure, cardiac output, combined valve diseases, and insufficient echocardiographic image (4–7). If the patient's heart rhythm is AF, echocardiographic assessments may be inaccurate (4, 5). Therefore, echocardiographic measurements should be repeated five to eight times in these patients, and the average value should be taken (4, 5). Another factor is net atrioventricular compliance (Cn), which affects the echocardiographic evaluation in patients with MS and AF. Cn differences play a particularly significant role in MVA derived by pressure half-time (PHT) (8, 9). Atrioventricular pressure gradients, atrioventricular diastolic function, and volume changes affect Cn. Because the Cn differences affect the PHT, they also affect the PHT-derived MVA.

The Cn value can be calculated invasively and noninvasively in MS patients. Schwammenthal et al. (8) compared the invasive and noninvasive Cn determination and found a good correlation between these two methods. Furthermore, the noninvasive Cn calculation value was found to correlate with clinical symptoms (8).

In the literature, there is not enough data about the effect of Cn and cardiac rhythm on echocardiographic measurements in patients with MS. We measured Cn, MVA (derived by PHT and planimetric method), and mitral gradient in patients with MS

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(MVA <2.0 cm^2) and AF before and after cardioversion. In this study, we aimed to investigate the effect of cardiac rhythm on Cn, MVA, and mitral gradient in AF and sinus rhythm (SR).

Method

Study design

Symptomatic patients who were referred to our clinic with the diagnosis of MS and persistent AF were evaluated with a transthoracic echocardiogram (TTE). We assessed the patients, who were eligible for our study entry criteria whether there were thrombi in the LA or LA appendage by transesophageal echocardiography (TEE). Biphasic direct current cardioversion (DCCV) was performed with premedication in intensive care units in patients without thrombus in LA or LA appendage. Two to three days after cardioversion, control echocardiographic examinations were performed on the patients who underwent successful DCCV and in SR. The study protocol was approved by the local Ethics Committee.

Study group

We evaluated 38 patients who had rheumatismal MS and persistent AF. According to TTE assessment, three patients had severe aortic insufficiency, one patient had severe mitral insufficiency, one patient had significant aortic stenosis, two patients had MVA >2 cm^2, and five patients had LA size larger than 5.5 cm. According to TEE assessment, there were thrombi in LA or LA appendage in four patients. These 16 patients were not included the study. We evaluated the 22 patients who were with MS and volunteer and eligible to study inclusion criteria of our observational analytic study. We performed DCCV to these 22 persistent AF patients. SR was not achieved in three of the 22 patients; therefore, we analyzed 19 patients.

Study inclusion criteria were (1) patients who were between 18 and 75 years old, (2) patients with AF who were converted to SR with DCCV, and (3) MVA <2 cm^2. Exclusion criteria were (1) MVA >2 cm^2 or MVA <1 cm^2, (2) patients with significant mitral or aortic insufficiency or aortic stenosis, (3) patients with significant left ventricular (LV) dysfunction (ejection fraction [EF] <40%), (4) patients with coronary artery disease, (5) patients with severe left atrium (LA) enlargement (>5.5 cm), and (6) patients with contraindication for anticoagulation.

Demographic questions were asked of patients and physical examinations were performed. Peripheral venous blood samples were drawn to analyses the blood count and biochemical markers. Patients were evaluated as hypertensive if their systolic blood pressures were ≥140 mm Hg and/or if their diastolic blood pressures were ≥90 mm Hg on two consecutive measurements or if they used antihypertensive drugs. Patients were evaluated as diabetic if their fasting blood glucose levels were ≥126 mg/dL of blood on two consecutive measurements or if they used oral antidiabetics/insulin. Body mass indices were calculated according to the following formula: weight (kg) / square of the height (m^2). Before and after cardioversion, heart rate was recorded during electrocardiographic monitoring.

The baseline characteristics of the 19 patients are demonstrated in Table 1. The ages of the patients ranged from 32–63 with a mean of 52 years. Sixteen patients (85%) were female, and three (15%) were male. Five (26%) patients had hypertension and four (21%) patients had a history of type-2 diabetes mellitus. The average body mass index of the patients was 27 kg/m^2. Hematological (hemoglobin: 12.97±1.38 gr/dL) and biochemical parameters (glucose: 106.63±10.22 mg/dL; creatinin: 0.83±0.12 mg/dL; Na: 142.95±1.47 mEq/L; K: 4.15±0.37 mEq/L) were within normal limits. Five (26.3%) patients had trivial and 10 (52.6%) patients had mild mitral insufficiency. Six (31.5%) patients had trivial and three (15.8%) patients had mild aortic insufficiency. Six (31.5%) patients had trivial, two (10.5%) patients had mild, and 10 (52.6%) patients had moderate tricuspid insufficiency (Table 1). The mean Wilkin's score of the patients was 9.1±2.0.

Transthoracic echocardiography and calculations

TTE and TEE were performed on all patients (22 patients) before cardioversion using the Vivid 7 Pro Doppler echocardiography system (GE, Hoerten, Norway) (3.5 Mhz probe, multiplan 6 Mhz probe). Echocardiographic examinations were performed and recorded by one operator. The recorded images were evaluated by two operators, and statistical analysis was performed to reveal the average of the two operators' measurements. All echocardiographic images were recorded in the lateral decubitus position. LV, LA diameter, and wall thickness were evaluated in the parasternal long-axis view. Left atrial volume was measured at end-systole using the biplane area–length method. LV EF was calculated by the Teichholz method (10). Mid-diastolic MVA was measured in the planimetric parasternal short-axis view where the mitral orifice was smallest and each commissure could be seen. The velocities of the mitral and tricuspid valves were measured in an apical four chamber view by pulse wave Doppler. Mitral and tricuspid regurgitation were evaluated with color Doppler in the same view. Systolic pulmonary artery pressure (PAP) was calculated from tricuspid regurgitation using continuous wave Doppler and Bernoulli's equation. Deceleration time of mitral E-wave, PHT-derived MVA, Bernoulli's equation derived maximal transmitral gradient were calculated from continuous wave mitral Doppler inflow velocity in apical four chamber view. The area under the curve and mean mitral gradient were measured automatically by the echocardiography device. The ultrasound Doppler beam was oriented to minimize the intercept angle with mitral flow to avoid underestimation of velocities. The Doppler beam was guided by the highest flow velocity zone identified by color Doppler. In order to deal with variable R-R intervals, the measurements were averaged on five to eight consecutive beats in AF. The maximal and mean transmitral gradient was corrected according to the heart rate. This correction was made as follows: maximal and mean transmitral gradient in AF/heart rate in AF, maximal or mean transmitral gradient in SR/heart rate in SR.

Table 1. Baseline characteristics of the study group

Ptients no	Gender (M/F)	BMI (kg/m²)	Age (year)	HT	DM	Hemoglobin (gr/dL)	Glucose (mg/dL)	Creatinine (mg/dL)	Na (mEq/L)	K (mEq/L)	M I	A I	T I
1	F	27.4	61	–	–	10.2	100	0.9	143	3.9	None	Trivial	Moderate
2	F	32.0	55	+	+	14.1	141	1.1	142	5.3	Mild	Mild	Trivial
3	F	24.7	50	–	–	13.8	97	0.9	143	4.3	None	Trivial	Trivial
4	F	24.2	56	–	–	10.7	109	0.8	139	3.9	None	None	Moderate
5	M	26.3	46	–	–	13.7	107	1.0	143	4.5	Trivial	Trivial	Moderate
6	F	32.5	52	–	–	13.4	106	0.9	140	3.9	Mild	None	Trivial
7	F	25.7	45	–	–	13.2	113	0.7	143	3.9	Mild	None	Mild
8	F	23.7	59	+	+	13.2	118	1.0	143	4.0	None	None	Moderate
9	F	21.6	63	–	–	13.6	105	0.8	144	4.2	Mild	Mild	Moderate
10	F	25.7	56	–	+	14.1	110	0.8	145	3.9	Trivial	None	Mild
11	F	25.6	50	–	–	12.7	96	0.9	143	3.9	Mild	None	Moderate
12	F	26.1	48	–	–	13.0	106	0.8	144	4.5	Trivial	Trivial	Trivial
13	F	27.7	47	–	–	9.2	99	0.7	142	4.0	Mild	Trivial	Moderate
14	F	33.5	63	+	–	13.7	98	0.9	144	4.3	Mild	Trivial	Trivial
15	M	26.4	52	–	–	13.1	102	0.8	143	3.9	Mild	Trivial	Moderate
16	F	33.1	58	+	+	14.4	111	0.8	145	4.6	None	None	Moderate
17	M	28.3	51	+	–	13.3	99	0.8	143	4.0	Mild	None	None
18	F	25.2	32	–	–	13.4	101	0.6	143	4.0	None	Mild	Moderate
19	F	32.0	49	–	–	12.6	108	0.7	144	3.9	Mild	None	Trivial

AI - aortic insufficiency; BMI - body mass index; DM - diabetes mellitus; F - female; HT - hypertension; M - male; MI - mitral insufficiency; TI - tricuspid insufficiency

Cn values were calculated using the following formula:

Cn=1.270 (PHT-derivated MVA/E-wave deceleration slope) (8, 9).

The MVA of our study population was between 1 to 2 cm^2 because the Cn formula defined for patients with MVA was between 0.5 to 2.5 cm^2 (9).

After 48–72 hours of treatment, patients who underwent successful DCCV (19 patients) control of echocardiographic examinations were performed. All successfully cardioverted patients were in SR 48–72 hours after cardioversion. In our study population, left atrial function was impaired because of mechanical etiology (MS). Ongoing mechanical etiology (cause of MS) after DCCV prevents the return of structural changes. However, in the long-term, the AF recurrence ratio increased in this population. So, that, 48–72 hours after cardioversion, the control echocardiographic evaluation could be reliable. TTE measurements were averaged on five to eight consecutive beats in AF and three to five consecutive beats in SR in order to deal with variable R-R intervals.

The absolute difference of heart rate, transmitral gradient, MVA, and PAP were obtained by the AF phase value minus the SR phase value. The percentage difference of MVA was calculated by the following formula: ([MVA measured by PHT –Planimetric MVA] / MVA measured by PHT) x 100. The percentage difference of MVA with cardioversion was calculated by the following formula: for PHT, ([MVA measured by PHT in AF –MVA measured by PHT in SR] / MVA measured by PHT in AF) x 100; for the planimetric method, ([planimetric MVA in AF –planimetric MVA in SR] / planimetric MVA in AF) x 100. The percentage difference of transmitral gradient was calculated by the following formula: ([maximal or mean mitral gradient in AF –maximal or mean mitral gradient in SR] / maximal or mean mitral gradient in AF) x 100.

The percentage difference of Cn was calculated by the following formula: ([Cn value in AF –Cn value in SR] / Cn value in AF) x 100.

Transesophageal echocardiography and cardioversion protocol

Informed consent was obtained from each patient prior to cardioversion and multiplan 6 mhz probe was intubated esophagus after local anesthesia with using oropharyngeal local anesthetic spray. The presence of thrombus in cardiac structures was investigated, particularly the LA appendage. Patients with MS and without thrombus were eligible to DCCV.

Anticoagulation with heparin was given by continuous intravenous infusion (17 U/kg) to all patients before cardioversion and its dose was adjusted to an activated partial thromboplastin time of 1.5–2 times normal. All antiarrhythmic drugs including digoxin were stopped before cardioversion. Amiodarone infusion started (5 mg/kg IV loading dose infused over 10

Table 2. Comparison of echocardiographic characteristics in atrial fibrillation and sinus rhythm

Parameters	AF phase (n=19)	SR phase (n=19)	*P*
LV ejection fraction (%)	60.47±6.84	61.44±6.76	0.83
LV end-systolic diameter, mm	30.15±4.29	30.24±3.40	0.91
LV end-diastolic diameter, mm	46.57±3.50	47.57±3.67	0.85
LA diameter, mm	48.94±3.74	48.94±3.27	0.98
LA volume, mL	92.85±28.97	88.90±27.74	<0.001
E-wave velocity, m/sec	2.14±0.25	2.03±0.30	0.01
sPAP, mm Hg	46.63±13.32	41.57±12.67	0.004
Maximal transmitral gradient, mm Hg	18.57±4.54	16.94±5.11	0.013
Mean transmitral gradient, mm Hg	8.89±3.52	6.49±2.51	0.001
Corrected maximal transmitral gradient, mm Hg.minute/beat	0.16±0.031	0.22±0.062	<0.001
Corrected mean transmitral gradient, mm Hg.minute/beat	0.076±0.025	0.086±0.030	0.198
PHT-derivated MVA, cm^2	1.59±0.26	1.66±0.30	0.011
Planimetric MVA, cm^2	1.54±0.27	1.62±0.29	0.003
Cn value, mL/mm Hg	6.26±0.64	5.37±0.77	<0.001
Heart rate, beat/minute	114±18	75±10	<0.001

AF - atrial fibrillation; Cn - net atrioventricular compliance; LA - left atrium; LV - left ventricle; MVA - mitral valve area; PHT - pressure half-time; sPAP - systolic pulmonary artery pressure; SR - sinus rhythm

minutes followed by 10–15 mg/kg/hour infusion over 24 hours) (11) to patients who did not have intracardiac thrombus on TTE and TEE studies and patients were sedated with intravenous midazolam during the procedure. After that, transthoracic electrical cardioversion was performed with delivery of synchronized biphasic DC shocks of 200, and 270 J in the intensive care unit. After cardioversion, if SR continued for ≥1 minute, it was considered successful. We performed DCCV to our patients under amiodarone treatment, and the AF recurrence risk is high and success rate is low in patients with AF recurrence in one minute after cardioversion. The AF recurrence rate is not increased in patients with SR one minute after cardioversion (12). Patients who achieved SR were anticoagulated with warfarin with a therapeutic International Normalized Ratio of 2.0–3.0. Amiodarone was maintained with oral therapy after discharge (200 mg, 2 x 1) (11).

Statistical analysis

The data were analyzed using the SPSS 10.0 statistics package (SPSS Inc, Chicago, IL, USA). Averages were calculated using descriptive statistics test. Continuous variables were reported as means±standard deviation, and categorical variables are reported as percentages. To compare pre- and post-DCCV variables, the Wilcoxon signed rank test was used. The relationship between MVA-transmitral gradient and Cn was assessed using Pearson's correlation test. The interobserver correlation was assessed by Pearson's correlation test. There was a good interobserver correlation between the two operators measurements ($r=0.91$, $p<0.001$). In all statistical analyses, a p value of <0.05 was considered significant.

Results

Heart rate and echocardiographic measurements of the 19 patients before and after DCCV were evaluated. LV EF, LA diameter, LV systolic and diastolic diameter measurements were similar before and after cardioversion (Table 2). Heart rate ($p<0.001$), Cn ($p<0.001$), pulmonary artery pressure ($p=0.004$), LA volume ($p<0.001$), E-wave velocity ($p=0.01$), and maximal ($p=0.013$) and mean ($p=0.001$) transmitral gradients were significantly higher in AF compared with SR (Table 2). However, MVA measured by planimetry and PHT methods were significantly lower in AF compared with SR (Table 2). The average of percentage difference of the echocardiographic measurements before and after cardioversion were calculated and are given in Table 3.

The correlation between MVA, transmitral gradients, pulmonary artery systolic pressure, and Cn values were evaluated. In AF, a significant correlation was not observed between Cn values and MVA, which was measured by planimetry and PHT methods before cardioversion (Table 3). There was no correlation between heart rate and Cn values before and after cardioversion (Table 3). However, there was a significant negative correlation between Cn values and pulmonary artery systolic pressure and maximal and mean transmitral gradients (and corrected maximal and mean gradients) (Fig. 1a–d) (Table 3). Similar results were seen in patients with SR (Table 3) (Fig. 2a–d). A significant negative correlation was observed between maximal and mean transmitral gradients' difference in AF-SR and Cn difference in AF-SR (and corrected maximal and mean gradients' difference in AF-SR) (Fig. 3a–d). Significant positive correlation was observed between percent change of Cn and percent change of heart rate difference in AF-SR (Table 3).

Table 3. Percent and absolute changes of the echocardiographic parameters with cardioversion and the correlation between Cn and echocardiographic parameters

Parameters	Mean		Minimum/Maximum	
	Percent	Absolute	Percent	Absolute
Change of C_n	13.99	0.88	-1.48/31.50	-0.10/2.10
Change of maximal transmitral gradient	9.05	1.63	-20.0/35.71	-3.0/5.0
Change of mean transmitral gradient	24.95	2.40	-14.29/51.43	-1.0/8.0
Change of PHT-derivated MVA	-4.76	-0.07	-19.74/8.67	-0.30/0.13
Change of planimetric MVA	-5.38	-0.08	-18.67/10.34	-0.28/0.15
Change of sPAP	10.41	5.05	-9.09/24.00	-5.0/15.0
Change of heart rate	33.54	39.78	18.69/50.00	19.0/74.0
Parameters	**r**		***P***	
In AF				
Cn and PHT-derivated MVA	0.22		0.35	
Cn and Planimetric MVA	0.18		0.44	
Cn and sPAP	-0.47		0.04	
In SR				
Cn and PHT-derivated MVA	0.06		0.78	
Cn and Planimetric MVA	0.03		0.89	
Cn and sPAP	-0.43		0.06	
Percent change with cardioversion (AF and SR)				
Percent change of Cn and percent change of PHT-derivated MVA	-0.01		0.93	
Percent change of Cn and percent change of planimetric MVA	-0.24		0.31	
Percent change of Cn and percent change of heart rate	0.76		<0.001	
Percent change of Cn and percent change of sPAP	-0.43		0.07	

C_n - net atrioventricular compliance; AF - atrial fibrillation; MVA - mitral valve area; PHT - pressure half-time; sPAP - systolic pulmonary artery pressure; SR - sinus rhythm

Discussion

In this study, we evaluated the effect of cardiac rhythm on Cn, MVA, and transmitral pressure gradient in patients with MS. We showed that (1) MVA (calculated by PHT and planimetry) was significantly higher in patients with SR than in patients with AF, (2) transmitral pressure gradient (maximal and mean) was significantly higher in patients with AF than in patients with SR however the heart rate adjusted transmitral pressure gradient was higher in patients with SR than in patients with AF, (3) net Cn was higher in patients with AF than in patients with SR, (4) there was a significant negative correlation between the transmitral pressure gradients and Cn (in AF and SR) (5) there was a significant negative correlation between the differences of Cn and the differences of transmitral pressure gradient with cardioversion.

Assessment of the MVA by PHT method remains controversial in patients with MS because it can be affected by a variety of clinical conditions including AF, tachycardia, impaired atrial and LV compliance, and nonlinear Doppler velocity curves (6, 13–18).

In our analysis, patients with AF were found to have higher Cn values than those with SR. The underestimating PHT-derived MVA and rise in Cn before cardioversion led to a lengthening of PHT. However, in our study, although EF was similar before and after cardioversion, MVA was lower in AF phase. In general, the low EF in AF patients depends on the causal heart rate. Calculated EF is usually found to be similar if it is done with five to eight different cycle environments or the longest cycle length. A large number of recent studies have found that MVA in AF is lower than in SR (7, 14, 19, 20).

Two-dimensional planimetry-derived MVA is generally accepted as reference standard for other measurements, but also, this method can be affected by mitral valve calcification, LA pressure, cardiac output, and LV function (5). Our study population's mean Wilkin's score was 9.1. Four patients had moderate leaflet calcification; however, we performed the MVA measurements at the same patients before and after cardioversion.

In our study, we demonstrated a significant increase of MVA by planimetry after cardioversion. This increase can be associated with improvement of diastolic filling with synchronization of cardiac cycles. Previous studies well demonstrated the increase of MVA derived by planimetry with rising of LA pressure and improvement of diastolic functions (8, 14, 21). Although we demonstrated that transmitral pressure gradient (maximal and mean) was significantly higher in patients with MS and AF when

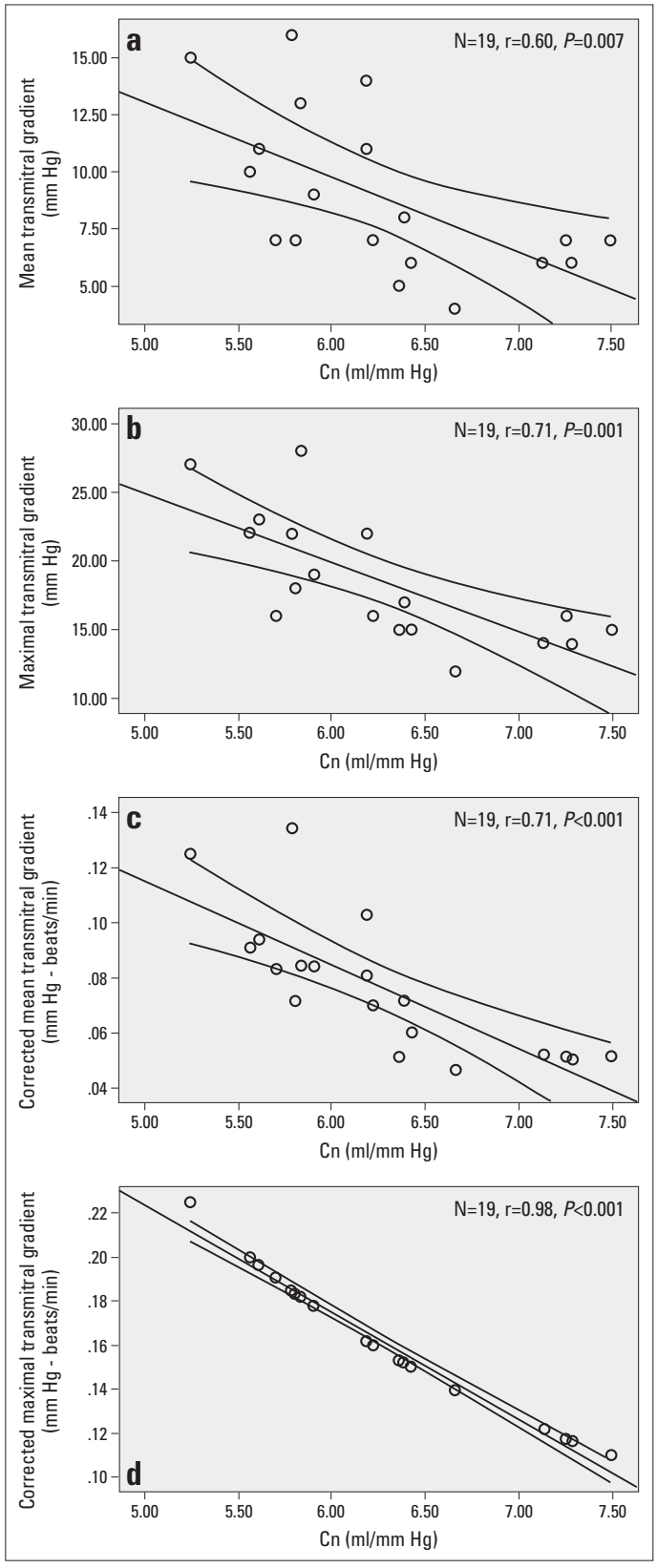

Figure 1. Correlation between Cn and transmitral gradient in AF. (a) Correlation between Cn and mean transmitral gradient in AF, (b) Correlation between Cn and maximal transmitral gradient in SR, (c) Correlation between Cn and corrected mean transmitral gradient in SR, (d) Correlation between Cn and corrected maximal transmitral gradient in SR

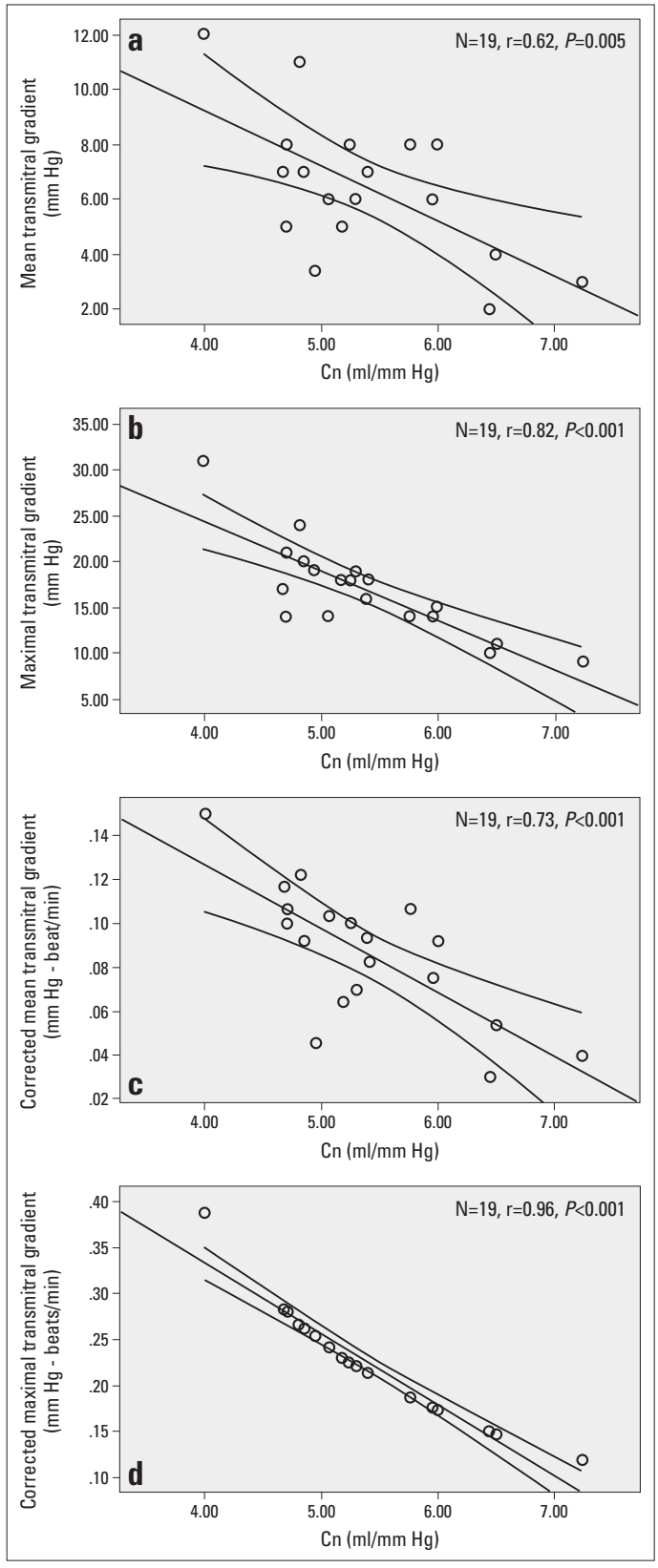

Figure 2. Correlation between Cn and transmitral gradient in SR. (a) Correlation between Cn and mean transmitral gradient in SR, (b) Correlation between Cn and maximal transmitral gradient in SR, (c) Correlation between Cn and corrected mean transmitral gradient in SR, (d) Correlation between Cn and corrected maximal transmitral gradient in SR

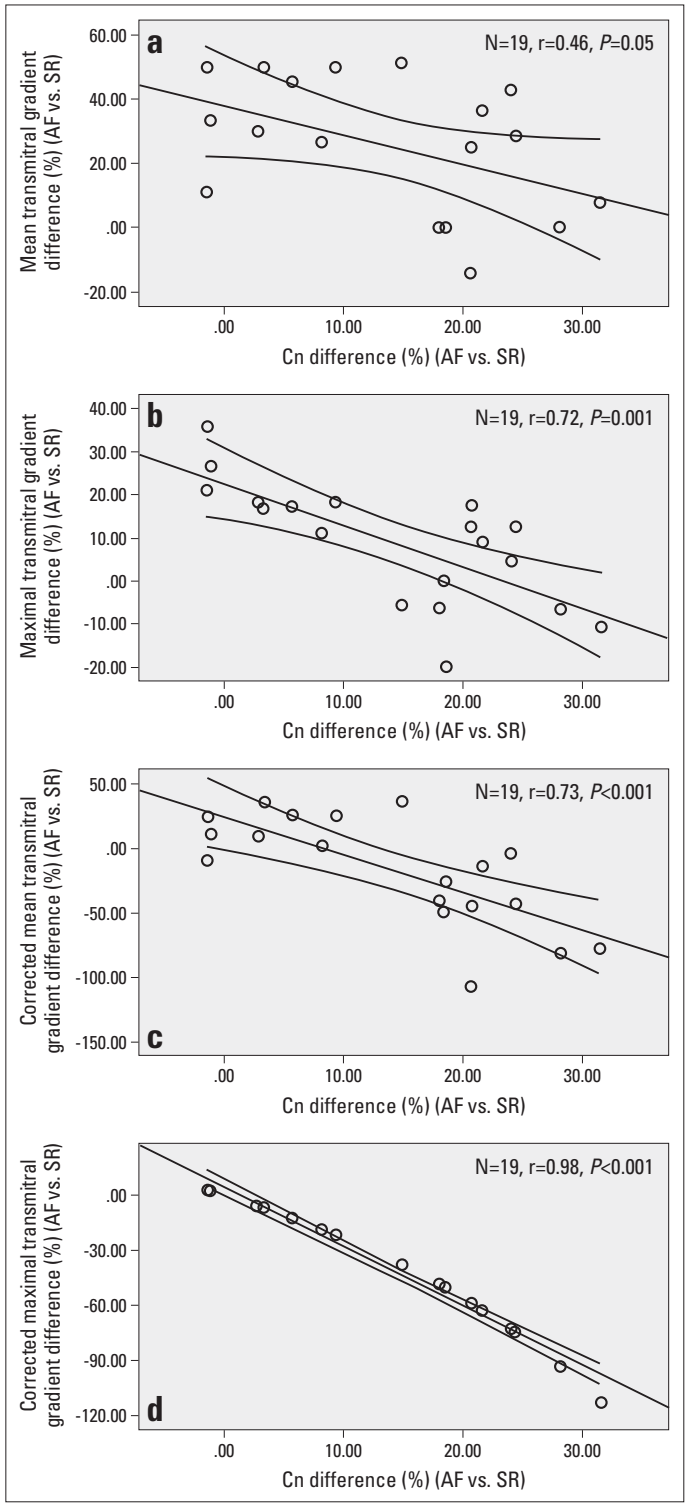

Figure 3. Correlation between the differences of Cn and differences of transmitral pressure gradient in cardioverting from AF to SR. (a) Correlation between the differences of Cn and differences of mean transmitral pressure gradient in cardioverting from AF to SR, (b) Correlation between the differences of Cn and differences of maximal transmitral pressure gradient in cardioverting from AF to SR, (c) Correlation between the differences of Cn and differences of corrected mean transmitral pressure gradient in cardioverting from AF to SR, (d) Correlation between the differences of Cn and differences of corrected maximal transmitral pressure gradient in cardioverting from AF to SR

compared with those in SR after the correctly adjusted for the heart rate, the maximal transmitral pressure gradient was found higher in the SR group in comparison to AF. Adjusted transmitral pressure gradients for the heart rate are more valuable to determine MVA and mitral valve functions because exercise and tachycardia significantly increase the transmitral pressure gradients (8, 15, 22–24). In addition, mitral orifice stretching can not be maximal in patients with AF because of higher value of Cn due to this, MVA can be under-estimate. The current reports showed that MVA could be under-estimated in patients with MS and higher value of Cn (6, 7, 14, 20).

In our study, we found no correlation between Cn values and MVA (planimetric and PHT-derivated); in addition, there was no correlation between differences of Cn and MVA (planimetric and PHT-derivated) after cardioversion. Cn value is affected by left atrial and ventricular parameters, atrioventricular gradient, and heart rate. MVA alone may not explain the Cn value and its changes. Evaluation of the sum of these parameters may provide more descriptive information about the Cn value and its changes (14, 20, 25).

Although higher Cn values with AF are observed, transmitral pressure gradient is increased in this group of patients because of tachycardia before cardioversion. Most studies show that tachycardia, exercise, and other hyperdynamic conditions may increase the transmitral pressure gradient (8, 14, 21, 26, 27). In our study, after adjusting transmitral pressure gradients according to the heart rate, the maximal transmitral pressure gradient was higher in the SR group, but the mean pressure gradient was similar in both groups.

AF is usually associated with increased LA volume and lower LA pressure because of LA enlargement and loss of contraction function. And this lower LA pressure caused increased Cn level in patients with AF. In our population, LA volume and Cn were found higher in AF group when compared to SR group. Many studies support this data (6, 7, 14, 25). We showed that pulmonary artery systolic pressure is inversely correlated with Cn values in the AF group. Increased pulmonary artery systolic pressure is related with elevated LA pressure, and elevated LA pressure leads to decreased Cn values.

LV functions also have an impact on the differences of Cn values. Diastolic heart failure is characterized by increased resistance to diastolic filling, and also, LV compliance or distensibility is reduced, the dynamics of filling are altered, and the end-diastolic pressure is increased (28, 29). As a result, Cn values are reduced because of increased compensatory LV filling pressure and LA pressure (29, 30). In our trial we showed that the percent change of Cn and the percent change of heart rate are positively correlated. This data supports the relation of diastolic function and Cn value. Similar results were published by Schwammenthal et al. (8). Furthermore, systolic function is related with Cn value, because the systolic function of left ventricle determines the left ventricle end-diastolic pressure. The strain assessment of the left ventricle could determine the subclinical dysfunction of the

left ventricle (29). In this study, we did not evaluate the strain parameters of the left ventricle. This evaluation and the relation between the Cn and LV strain parameters could provide more reliable data about the rheumatismal MS (29).

Recently, net Cn, derived echocardiography by Doppler, has been shown to be an important physiologic parameter in patients with MS (6, 8, 14, 24, 26). It was found that Cn was a strong independent predictor of exercise capacity, prognosis and timing of treatment in patients with MS (8, 14). Cn value must be calculated especially when there is an inconsistency between transmitral pressure gradient and symptom of patient. Recent studies showed that Doppler-derived net Cn can be used for predicting the timing of mitral valve replacement or percutaneous mitral commissurotomy and determinant of prognosis (14, 25, 27). Especially the patients with lower Cn values have a poor prognosis.

Previous studies demonstrated that there was an inverse ratio between transmitral pressure gradient and Cn values (transmitral pressure gradient = [PHT x MVA by planimetry] / [11.6 x Cn]) (14). In this present study, we found that there was a significantly negative correlation between Cn values and mean and maximal transmitral pressure gradient. In addition, this correlation was demonstrated in both the SR and AF groups. The correlation in AF and SR was similar but correlation coefficients are higher in SR than AF. In SR phase the heart rate is lower and regular, the Cn, LV and LA systolic and diastolic function were more stable. Because of that, the correlation coefficients are higher in SR phase. Similar results were presented by Kim et al. (14).

In the present study, we found a significant negative correlation between differences of Cn and transmitral pressure gradient after cardioversion. Cn values reduced with restoration of SR by cardioversion in patients with AF. This reduction ratio was associated with Cn value and transmitral pressure gradient. High reduction ratio is concluded with lower Cn values and less decrease of transmitral pressure gradient and also, transmitral pressure gradients are increased by reduction of compliance.

Scarsoglio et al. (31) evaluated the effect of AF on left valvular heart disease by computational fluid dynamics modeling and showed that the hemodynamic effects of AF on LA and LV were more evident in regurgitant valve disease than stenotic valve disease. In the severe MS and AF patients LA volume and LA pressure were higher, LV performance index (Cardiac Output, EF, Stroke Volume) were lower than lone AF patients (31). The same study also evaluated the LA probability density function, and showed that LA probability density dispersion was lower in AF and severe MS patients than in lone AF patients (31). In AF and severe MS patients, the LA probability density dispersion was lower than lone AF patients because LA pressure and volume were continuously elevated in AF and severe MS patients. Lower heart rate, decreased LA volume and increased LV volume decreased Cn value; on the contrary, tachycardia increased Cn value. Similarly, in our study, we showed that there was a positive correlation between Cn changes and heart rate changes.

Cardiac catheterization is the best procedure to measure Cn value (6, 8, 32). But this procedure is invasive, not suitable for following up the Cn changes at different period, and not suitable for every patient. Therefore, a simple equation was developed for quantitative assessment of Cn from transmitral velocity profiles (8). Cn can be calculated noninvasively by TTE data, and the calculation is well correlates with invasively determined values.

Cn is an important predictor of adverse outcome, adding prognostic information; therefore, Cn assessment should be done for clinical risk stratification and monitoring in all MS patients.

Study limitations

Several limitations need to be acknowledged. First, this study was retrospective in design, but it is the first study of assessment of Cn values of both SR and AF rhythm with the same patients. Second, this study was limited by the relatively small number of patients enrolled; therefore, it could not reflect generalizable values of the entire population. Moreover, we excluded patients with MVA >2 cm^2 or MVA <1 cm^2 from our study. Third, the R-R intervals could affect the TTE measurements in the AF period in order to deal with variable R-R intervals the measurements were averaged on five to eight consecutive beats in AF. However, the average of five to eight consecutive beats may not be sufficient to guarantee the statistical stability of the results. Another limitation was that the follow-up duration was too short.

Conclusion

Cardiac rhythm can have an impact on transmitral pressure gradient, MVA, and Cn value in patients with MS. Although there is a negative correlation between Cn value and transmitral pressure gradient, there is not a correlation between MVA and Cn value. There is a negative correlation between Cn value and pulmonary systolic pressure in AF period. There is a significant positive correlation between the percentage difference of the heart rate and Cn. It should be kept in mind that cardiac rhythm could affect the TTE evaluation in patients with MS. We expect this study will be helpful for future works.

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References

1. Darby AE, DiMarco JP. Management of atrial fibrillation in patients with structural heart disease. Circulation 2012; 125: 945-57. [CrossRef]

2. Farman MT, Sial JA, Khan N, Rahu QA, Tasneem H, Ishaq M. Severe mitral stenosis with atrial fibrillation a harbinger of thromboembolism. J Pak Med Assoc 2010; 60: 439-43.
3. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J 2012; 33: 2451-96. [CrossRef]
4. Baumgartner H, Hung J, Bermejo J, Chambers JB, Evangelista A, Griffin BP, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. Eur J Echocardiogr 2009; 10: 1-25. [CrossRef]
5. Braunwald Heart Disease : A Textbook of cardiovasculer medicine, 6th edition Saunders, 2001.p.1643-53.
6. Flachskampf FA, Weyman AE, Gillam L, Liu CM, Abascal VM, Thomas JD. Aortic regurgitation shortens Doppler pressure half-time in mitral stenosis: clinical evidence, in vitro simulation and theoretic analysis. J Am Coll Cardiol 1990; 16: 396-404. [CrossRef]
7. Mohan JC, Mukherjee S, Kumar A, Arora R, Patel AR, Pandian NG. Does chronic mitral regurgitation influence Doppler pressure half-time-derived calculation of the mitral valve area in patients with mitral stenosis? Am Heart J 2004; 148: 703-9. [CrossRef]
8. Schwammenthal E, Vered Z, Agranat O, Kaplinsky E, Rabinowitz B, Feinberg MS. Impact of atrioventricular compliance on pulmonary artery pressure in mitral stenosis: an exercise echocardiographic study. Circulation 2000; 102: 2378-84. [CrossRef]
9. Flachskampf FA, Weyman AE, Guerrero JL, Thomas JD. Calculation of atrioventricular compliance from the mitral flow profile: analytical and in vitro study. J Am Coll Cardiol 1992; 19: 998-1004. [CrossRef]
10. Teichholz L, Kreulen T, Herman M, Gorlin R. Problems in echocardiographic volume: Echocardiographicangiographic correlations in the presence or absence of asynergy. Am J Cardiol 1976; 37: 7-11.
11. Fuster V, Ryden LE, Cannom DS, Curtis AB, Ellenbogen KA, Halperin JL, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation—Executive Summary. J Am Coll Cardiol 2006; 48: 854-906. [CrossRef]
12. Yu WC, Lin YK, Tai CT, Tsai CF, Hsieh MH, Chen CC, et al. Early recurrence of atrial fibrillation after external cardioversion. Pacing Clin Electrophysiol 1999; 22: 1614-9. [CrossRef]
13. Nakatani S, Masuyama T, Kodama K, Kitabatake A, Fujii K, Kamada T. Value and limitations of Doppler echocardiography in the quantification of stenotic mitral valve area: comparison of the pressure half-time and the continuity equation methods. Circulation 1988; 77: 78-85. [CrossRef]
14. Kim HK, Kim YJ, Chang SA, Kim DH, Sohn DW, Oh BH, et al. Impact of cardiac rhythm on mitral valve area calculated by the pressure half time method in patients with moderate or severe mitral stenosis. J Am Soc Echocardiogr 2009; 22: 42-7. [CrossRef]
15. Ikawa H, Enya E, Hirano Y, Uehara H, Ozasa Y, Yamada S, et al. Can the proximal isovelocity surface area method calculate stenotic mitral valve area in patients with associated moderate to severe aortic regurgitation? Analysis using low aliasing velocity of 10% of the transmitral velocity. Echocardiography 2001; 18: 89-95. [CrossRef]
16. Voelker W, Regele B, Dittmann H, Mauser M, Ickrath O, Schmid KM, et al. Effect of heart rate on transmitral flow velocity profile and Doppler measurements of mitral valve area in patients with mitral stenosis. Eur Heart J 1992; 13: 152-9. [CrossRef]
17. Gonzalez MA, Child JS, Krivokapich J. Comparison of two-dimensional and Doppler echocardiography and intracardiac hemodynamics for quantification of mitral stenosis. Am J Cardiol 1987; 60: 327-32. [CrossRef]
18. Sunil Roy TN, Krishnan MN, Koshy C, Sajeev CG, Francis J, Velayudhan CC, et al. Comparison of proximal isovelocity surface area method and pressure half-time method for evaluation of mitral valve area in patients undergoing balloon mitral valvotomy. Echocardiography 2005; 22: 707-12. [CrossRef]
19. Thomas JD, Wilkins GT, Choong CY, Abascal VM, Palacios IF, Block PC, et al. Inaccuracy of mitral pressure half-time immediately after percutaneous mitral valvotomy. Dependence on transmitral gradient and left atrial and ventricular compliance. Circulation 1988; 78: 980-93. [CrossRef]
20. Kim HK, Kim YJ, Shin JI, Hwang SJ, Jo SH, Park JS, et al. Echocadiographic and hemodynamic findings in patients with mitral stenosis having percutaneous mitral commissurotomy comparing those with chronic atrial fibrillation versus those with normal sinus rhythm. Am J Cardiol 2007; 100: 1153-6. [CrossRef]
21. Thomas JD, Weyman AE. Fluid dynamics model of mitral valve flow: description with in vitro validation. J Am Coll Cardiol 1989; 13: 221-33. [CrossRef]
22. Hurst's. The Heart 10th edition Mc Graw-Hill. Rahiimtoola SH: Valvuler Heart disease 2001.p.1697-728.
23. Dahan M, Paillole C, Martin D, Gourgon R. Determinants of stroke volume response to exercise in patients with mitral stenosis: a Doppler echocardiographic study. J Am Coll Cardiol 1993; 21: 384-9
24. Schwammenthal E, Vered Z, Rabinowitz B, Kaplinsky E, Feinberg MS. Stress echocardiography beyond coronary artery disease. Eur Heart J 1997; 18: 130-7. [CrossRef]
25. Salem Omar AM, Tanaka H, AbdelDayem TK, Sadek AS, Raslaan H, Al-Sherbiny A, et al. Comparison of mitral valve area by pressure half-time and proximal isovelocity surface area method in patients with mitral stenosis: effect of net atrioventricular compliance. Eur J Echocardiogr 2011; 12: 283-90. [CrossRef]
26. Leavjtt JI, Coats MH, Falk RH. Effects of exercise on transmitral gradient and pulmonary artery pressure in patients with mitral stenosis or a prosthetic mitral valve: a Doppler echocardiographic study. J Am Coll Cardiol 1991; 17: 1520-6. [CrossRef]
27. İnci S, Erol MK, Bakırcı EM, Hamur H, Değirmenci H, Duman H, et al. Effect of percutaneous mitral balloon valvuloplasty on right ventricular functions in mitral stenosis: Short- and mid-term results. Anatol J Cardiol 2015; 15: 289-96. [CrossRef]
28. Litwin SE, Grossman W. Diastolic dysfunction as a cause of heart failure. J Am Coll Cardiol 1993; 22:49-55. [CrossRef]
29. Gerede DM, Ongun A, Kaya CT, Acıbuca A, Özyüncü N, Erol Ç. Use of strain and strain rate echocardiographic imaging to predict the progression of mitral stenosis: a 5-year follow-up study. Anatol J Cardiol 2016; 16: 772-7. [CrossRef]
30. Lnihan DJ, Gerson MC, Hoit BD, Walsh RA. Mechanisms, diagnosis and treatment of diastolic heart failure. Am Heart J 1995;130:153-66. [CrossRef]
31. Scarsoglio S, Saglietto A, Gaita F, Ridolfi L, Anselmino M. Computational fluid dynamics modelling of left valvular heart diseases during atrial fibrillation. Peer J 2016;26:4: e2240
32. Kim HK, Kim YJ, Hwang SJ, Park JS, Chang HJ, Sohn DW, et al. Hemodynamic and prognostic implications of net atrioventricular compliance in patients with mitral stenosis. J Am Soc Echocardiogr 2008;21:482-6. [CrossRef]