Research Paper Medicine

The correlation of TIMI frame count with pulmonary artery pressure in patients with mitral stenosis

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ABSTRACT

Background: Rheumatic mitral stenosis (MS) is a chronic disease with progressive symptoms and adverse hemodynamicconsequences including pulmonary hypertension.In patients with severe mitral stenosis the increased right ventricle (RV) after load causes RV hypertrophy suggested to impair the coronary blood flow and might lead to cardiac dysfunction.

Methods: patients with severe mitral valve stenosis underwent coronary angiography, cardiac catheterization and echocardiography to evaluate the TIMI frame count, hemodynamic data. Patients with significant valvular involvement other than mitral stenosis, significant ventricular dysfunction and coronary stenosis were excluded.

Results: The mean age of the patients was 49.5±12.7 years and 73.5 % of patients were female.The corrected TIMI frame counts were significantly higher in all vessels compared with normal values ($p<0.001$) and difference between RCA TFC and its normal value was significantly higher than difference between LCX TFC and LAD TFC with their normal values. Moreover, significant positive correlation observed between mean RCA TFC and systolic and diastolic PAP ($p=0.02$ & 0.014 respectively).

Conclusion: the increased TFC in patients with mitral stenosis may be the result of natural progression of disease or atrial fibrillation. Moreover, reduced flow in RCA and its relation with PAP is justified with ventricular hypertrophy and increased vascular resistance or endothelial dysfunction.

KEYWORDS	Mitral stenosis, pulmonary hypertension, TIMI frame count

Introduction

Rheumatic mitral stenosis (MS) is a chronic disease with progressive symptoms and adverse hemodynamicconsequences such as pulmonary hypertension (PH) [1]. Patients present with different symptoms; mostly dyspnea and fatigability but also exertional chest pain in some cases. The angina which is reported to have 15 percent incidence has been attributed to reduced coronary blood flow in severe mitral stenosis [2]. Moreover, in these patients the increased right ventricle (RV) after load causes RV hypertrophy suggested to impair the coronary blood flow and might be the mechanism leading to right ventricular dysfunction [3]. Animal studies of pulmonary hypertension found that RV pressure overload induces a reduction in right coronary artery (RCA) flow [4]. Assessing the coronary blood flow in angiography by means of ThrombolysisinMyocardial Infarction (TIMI) frame countmethod was first described in patients with acute coronary syndrome [5]. Moreover, TIMI frame count (TFC) is used to define coronary slow flow phenomenon [6, 7 and7]. It is simple, quantitative, and reproducible method for assessing coronary blood flow. TFC estimate the epicardialflow and microvascular bed. Coronary slow flow (CSF) phenomenon is related to microvascular disease, endothelial dysfunction and inflammation. It is a marker of attenuated myocardial perfusion. On the other hand study on RCA perfusion with cardiac magnetic resonance imaging (MRI) in patients with PH showed reduced RCA blood flow [9]. Our study aimed at evaluating the coronary blood flow in patients with severe mitral stenosis and its association with pulmonary artery pressure.

Methods

Seventy nine patients with severe mitral stenosiswere initially identified from echocardiogram reports. All the patients were candidate for percutaneous transmitral balloon comissurotomy (PTMC) or mitral valve surgery. Thus cardiac catheterization and coronary angiography performed. Echocardiographic criteria for severe mitral stenosis was mean gradient>10 mmHg or mitral valve area (MVA) <1 cm^2. Exclusion criteria were co-existent valve lesions graded greaterthan mild, right or left ventricular dysfunction greater than mild, poor echocardiographic images, coronary artery stenosis on angiography and atherosclerosis conventional risk factors such as diabetes, hypertension, dyslipidemia and smoking. A total of 50 patients were deemed suitable to enroll into thestudy. The study protocol was approvedby the ethics committee of our center and allpatients gave written informed consent.

Echocardiograms performed by fellowship of echocardiography on available ultrasound device (Vivid 7, General Electric Vingmed Ultrasound). All patients had transthoracic echocardiogram and in case of proper candidate for PTMC transesophageal echocardiogram was also performed. At least three, or in cases of atrial fibrillation(AF), five cardiac cycles were averaged for every measurement. The exam included comprehensive evaluationwith M-mode, 2D, Doppler and tissueDoppler methods. The MVA obtained using median of three methods of direct planimetry, pressure half time,and continuity equations [10]. Mean transmitralpressure gradients were measured by tracing thecontinuous wave Doppler signal across the mitral valve [11]. The left ventricular end-diastolic andend-systolic volumes and ejection fractionwere assessed bymodifiedSimpson's single plane method from the apical four-chamber view. For better estimation of right ventricular (RV) systolicpressure, agitated saline was used to enhancethe tricuspid regurgitation profile [12]. Toestimate peak pulmonaryartery systolic pressure (PAP) simplified Bernoulli equation was used by adding the peak tricuspidregurgitant jet to right atrialpressure obtained from inferior vena cava size and collapse. RV size and function was assessed in four chamber view with peak systolic tricuspid annular velocity.

Cardiac Catheterization and Coronary Angiography performed in all patients, coronary angiography was performedby femoral artery approach using the Judkins technique.Coronary arteries were visualized in right and left obliqueplanes with cranial and caudal angulations. Cineframes recorded ata film rate of 30 frame/seconds. Two independent cardiologists, who were blinded to the study, assessed the coronaryflow in coronary arteries using the TIMI frame count method [13]. In this method, thenumber of cine frames required forthe contrast to first reach standard distal coronary landmarksin left anterior descending (LAD), left circumflex (LCX) and rightcoronary arteries (RCA) were counted. LAD distal landmarkconsidered-its distal bifurcation referred as the 'pitchfork' or 'whale's tail'. For LCX distal bifurcationof the segment with the longest total distance from the origin and for RCA the first branch of the posterolateral artery were also defined. The TIMI frame count for LADwas then divided by 1.7 to obtain the corrected TIMI frame count because the LAD is usually longer than the RCA and LCX.For statistical Analysismean TIMI frame count of each artery compared with corrected cut-off values of normal coronary arteries used from literature (22.3±2.6 frames for LAD, 22.2±4.1 frames for LCX and 20.4±3 framesfor RCA) [14]. Continuous data were presented as means ± standard deviation.Differences in continuous variables between the groupswere determined by Student's t-test or Mann Whitney U-testfor variables with or without normal distribution, respectively. Pearson correlation analysis was performed to assess the correlation between TIMI frame count and hemodynamic data.Linear regression analysis was used to evaluate the relation between TIMI FC and PAP. Value less than 0.05 considered significant.

Results

Echocardiographic, cardiac catheterization and angiographic data of patients are summarized in Table 1. The mean age of the patients was 49.5±12.7 years and 73.5 % of patients were female. Seventy eight percent of patients were in AF rhythm and 11 patients had sinus rhythm. The corrected TIMI frame counts were significantly higher in all vessels compared with normal values ($p<0.001$). Moreover, difference between RCA TFC in this group and its normal value (D RCA) was significantly higher than difference between LCX TFC and LAD TFC with their normal values (DLCX and DLAD respectively) (Table2). Therefore, RCA showed more increment in TIMI FC than two other vessels (Figure 1). Interestingly, significant positive correlation observed between mean RCA TFC and PAP and pulmonary capillary wedge pressure (PCWP) (Table 3). This correlation was not seen with LCX or LAD. The relation between RCA TFC and PAP was modeled as linear regression and PAP was predicted by present calculation (Systolic PAP in catheterization = 24.35 + 1.72 * RCATFC) (Figure 2).

Discussion

The main finding of the study is the coronary slow flow (CSF) phenomenon in patients with significant mitral stenosis and positive correlation between pulmonary artery pressure and right coronary artery TFC. To our knowledge this is the first report showing the increase of TFC in MS without coronary artery stenosis and effect of PAP on RCA TFC.

Coronary slow flow is described in patient with acute coronary syndrome and X syndrome, chronic valvular involvements such as aortic regurgitation, chronic obstructive pulmonary disease, insulin resistance and inflammation and atrial fibrillation in the absence of coronary artery stenosis [6, 7 and 15, 16]. The pathopysiological mechanism underlying the CSF is not fully understood. It may be explained by endothelial and microvascular dysfunction, initial phase of atherosclerosis or inflammation. In mitral stenosis coronary hypo perfusion as result of low cardiac output and high right atrium pressure is proposed. Moreover, progressive inflammatory basis of disease and concomitant atrial fibrillation seems to contribute in CSF. In our patients prevalence of atrial fibrillation was high. The rapid ventricular heart rate is suggested to cause changes in cardiomyocytesand vascular endothelial cells leads to microvascular and endothelial dysfunction [16].

Furthermore, increase in RCA TFC was significantly greater than LAD and LCX and positive correlation was present with systolic and diastolic PAP. Previous studies showed that patients with other etiologies of pulmonary hypertension (PH) have reduced RCA systolic blood flow. Accordingly, change of RCA flow from simple monophasic to biphasic pattern like

LAD was observed. The total mean flow in whole cardiac cycle was not reduced. However, there was strong negative correlation between right ventricle mass and RCA flow in ml pergram myocardial mass of the right ventricle [3, 9]. Myocardial systolic compression is thought to reduce RCA flow in patients with pulmonary hypertension. Compression of myocardial fibers in this situation decreases the diameter of microvascular bed and increase the vascular resistance. The role of inflammation and endothelial dysfunction in PH is under investigation [17].

It is demonstrated that the subendocardial flow is reduced in RV hypertrophy[4]. Whether this decreased RCA flow leads to ventricular dysfunction needs further study.

In conclusion the increased TFC and coronary hypo perfusion in patients with mitral stenosis may be the cause of angina in these patients. It may results from natural progression of disease or atrial fibrillation. Moreover, reduced flow in RCA and its relation with PAP is justified with ventricular hypertrophy and increased vascular resistance and endothelial dysfunction.

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Fig 1
The mean±SD TIMI frame counts of coronary arteries are shown and RCA has significantly higher TIMI frame count compare to LAD and LCX.

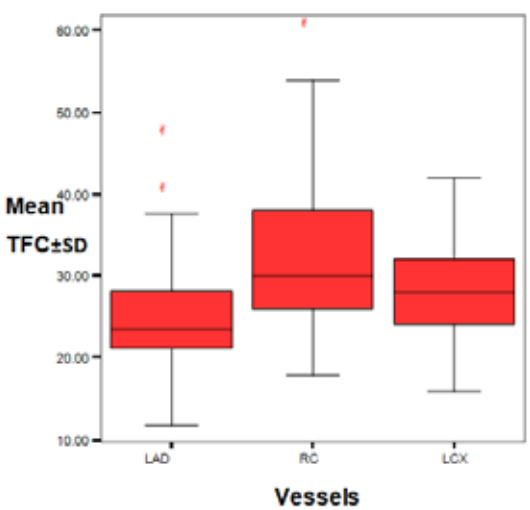
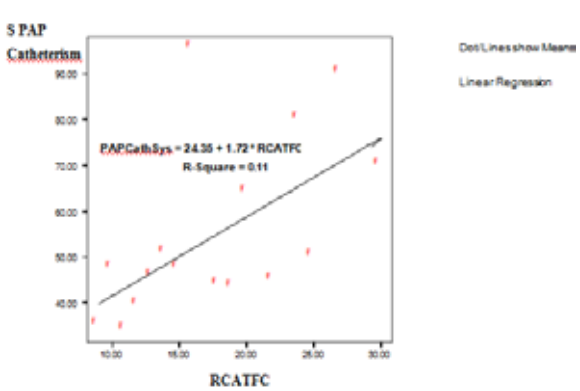


Fig 2
Linear regression of systolic pulmonary artery pressure acquired during catheterization (SPAP cath) on right coronary artery TIMI frame count (RCA TFC) with r square=0.11.



Tables

Table 1 data are shown in mean±SD

Echocardiographic data		Catheterization data		Angiographic data	
PAP	50.1±18.3	PAP systolic	52.1±23.4		
LA area	28.4±7.3				
MV area	0.9±0.2	PAP diastolic	24.3±11.1	LAD TFC	43.3±6.94
MV gradient	9.6±5.3				
EF	51.4±5.9	RVEDP	11.2±3.8		
LV size	4.6±0.6			LCX TFC	27.6±6.7
RV size	3.2±0.6	LVEDP	13.8±4.1		
TAPSE	19.4±4.3				
S' RV	10.8±2.1	PCWP	22.5±7.8	RCA TFC	32.2±9

Table 2 data are shown as mean±SD

	Patient TFC	Normal TFC	P value				P value
RCA	32.2±9	20.4±3	<0.001	DRCA	12.1±8.9	DRCA vs DLAD	0.004
LCX	27.6±6.7	22.2±4.1	<0.001	DLCX	5.6±3.7	DRCA vs DLCX	<0.001
LAD	25.5±6.9	22.3±2.6	0.001	DLAD	7.6±6.8	DLAD vs DLCX	0.14

Table 3 Correlation between RCA TF and hemodynamic factors

	Correlation coefficient	P value
RCA TF & SPAP (Echo)	0.34	0.017
RCA TF & SPAP (Cath)	0.33	0.02
RCA TF & DPAP (Cath)	0.35	0.014
RCA TF & PCWP	0.56	<0.001

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