The Determinants of Systolic Pulmonary Venous Flow Reversal by Transthoracic Pulsed Doppler in Mitral Regurgitation: Its Value in the Quantification of the Severity of Regurgitation

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ÖZET

MİTRAL YETERSİZLİĞİNDE TRANSTORASİK PULSED DOPPLER EKOKARDİYOGRAFİ İLE ELDE EDİLEN SİSTOLİK PULMONER VENÖZ TERS AKIMIN BELİRLEYİCİLERİ VE YETERSİZLİK CİDDİYETİNİ GÖSTERMEDEKİ DEĞERİ

Sistolik pulmoner venöz ters akım (SPVTA) mitral yetersizliğinde (MY) esas olarak transösofageal ekokardiyografik çalışmalarda gösterilmiştir. Ciddi MY için transtorasik ekokardiyografi ile elde edilen SPVTA'ın değerini inceleyen çok az sayıda çalışma vardır. Bu çalışmada, MY'de transtorasik ekokardiyografi ile elde edilen SPVTA'ın belirleyicileri ve ciddiyet tayinindeki değeri araştırıldı.

Metod: Çalışma hastaları, referans olarak kantitatif spektral Doppler uygulanan 50 MY'li hastadan oluşturuldu. Bu hastaların 39 tanesine kardiyak kateterizasyon yapıldı. Bütün hastalarda, SPVTA apikal dört boşluk görüntüsünde hem sağ ve hem de sol pulmoner vende değerlendirildi.

Bulgular: 26 (%52) hastada SPVTA vardı. SPVTA'a sahip olan hastalarda ritm olarak AF'ye ve kateterde III/IV. derece MY'ye sık rastlandı. SPVTA'a sahip hastalarda yetersizlik orifis alanı, yetersizlik hacmi, yetersizlik fraksiyonu, sol atriyum ve ventrikülün çap ve hacimleri SPVTA görülmeyenlere göre daha büyüktü (hepsi için p<0.05). Çok değişkenli analizde, SPVTA'ın tek belirleyicisi yetersizlik fraksiyonu olarak bulundu (p<0.001). Ciddi MY'nin teşhisi için kullanılan SPVTA, yüksek derecede duyarlılığa, özgüllüğe ve doğruluğa sahipti (sırasıyla %89, 95 ve 92).

Sonuç olarak SPVTA, MY ciddiyetinin değerlendirilmesinde faydalı bir metoddur.

Anahtar kelimeler: *Sistolik pulmoner venöz ters akım, mitral yetersizliği, pulsed Doppler ekokardiyografi, kalp kateterizasyonu*

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Though the quantification of valve stenosis has proven easy and reliable for clinical purposes, the quantification of valve regurgitation is still difficult and imprecise. There is currently no single accurate non-invasive method for determining the degree of mitral regurgitation (MR) [1]; therefore, more than one method should be performed during the evaluation [2-8]. The complexity and time consuming nature of some of the techniques forced investigators to seek simpler methods.

The reflux of the contrast media to the pulmonary veins during systole in contrast ventriculography is an angiographic finding of severe MR [9]. This reflux has also been shown during transesophageal echocardiographic (TEE) studies, which corresponded to the systolic flow reversal in pulmonary venous flow tracing [10-12]. This flow reversal was shown to be a sensitive and specific determinant of severe MR [10-12].

It has been previously reported that pulmonary vein flow tracing can also be obtained by transthoracic echocardiography (TTE) [13-19]. There are very limited number of studies which evaluates the relationship between MR severity and the pulmonary flow obtained by TTE [13,20].

In this study, determinants of systolic pulmonary venous flow reversal (SPVFR) and the accuracy of SPVFR obtained with TTE in determining the severity of MR were investigated.

METHODS

Patients: The study group consisted of 73 patients referred to the echocardiography laboratory with the diagnosis of MR. Patients with chronic MR of at least mild degree were evaluated for enrollment. Three patients were excluded for inadequate echogenity, 1 for the presence of intracardiac shunt, 5 for moderate to severe mitral stenosis (mitral valve area < 1.5 cm^2), 2 for moderate to severe aortic stenosis or regurgitation, and 6 patients for the presence of prosthetic valves. Six patients (11%) in whom pulmonary venous flow could not be visualized were also excluded. Thirty-nine of 50 patients (78%) with moderate to severe MR underwent cardiac catheterization. The Declaration of Helsinki' s recommendations for guiding physicians in biomedical research involving human subjects were followed [21].

Echocardiographic study: Transthoracic echocardiography was performed using a Hewlett-Packard Sonos 1500 equipment and a 2.7 MHz phased array transducer. All the patients were examined by one cardiologist who was unaware of the clinical status and the catheterization results of the patients. The recordings were taken in patients positioned in left lateral decubitis position. Simultaneous ECG recordings were also taken. The mean of three consecutive measurements from a good quality tracing were taken in patients in sinus rhythm for every parameter. Five measurements were taken in patients with atrial fibrillation for every parameter. M-mode echocardiographic measurements (left ventricle and atrium diameters) were taken according to established standards [22]. The left ventricular end-diastolic and end-systolic volumes were measured using modified Simpson's rule [23]. The left atrial volume was measured using the biplane area-length method at the end-systole.

Evaluation of the pulmonary venous flow: The heart was viewed in the apical four-chamber view and the sample volume of the Pulsed Doppler was placed 0.5 to 1 cm distal to the junction of the left atrium and right and left pulmonary vein [19]. A Doppler signal below the baseline during systole was considered as the systolic flow reversal. Systole was considered as the interval between the beginning of QRS and the end of T wave in ECG (Fig.1). In eccentric jets, the presence of SPVFR in the pulmonary vein which the jet was directed to, was defined as "concordance" and that in the opposite pulmonary vein was defined as "discordance".

Quantitative Doppler measurements: Mitral stroke volume was obtained with the method proposed by Ascah et al [24]. This method assumes that mitral annulus is an ellipse. The area of the ellipse was calculated by mitral annular diameters obtained from apical two and four-chamber views. The mitral stroke volume was calculated as the product of this area and the time-velocity integral (TVI) of mitral annular Doppler tracing. Similarly, the aortic stroke volume was calculated as the product of the area of the left ventricular outflow tract and the TVI of aortic annular Doppler tracing [15]. The following parameters were calculated by using the related formulae:

Regurgitant volume (RV) of mitral regurgitation (MR);

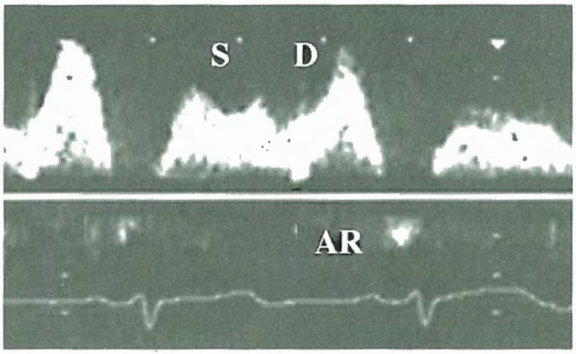
"RV(cm^3) = (mitral stroke volume) - (aortic stroke volume)"

Regurgitant fraction (RF);

"RF= RV/ (mitral stroke volume)"

Regurgitant orifice area (ROA);

"ROA (cm^2)= RV/(TVI of MR Doppler tracing)"



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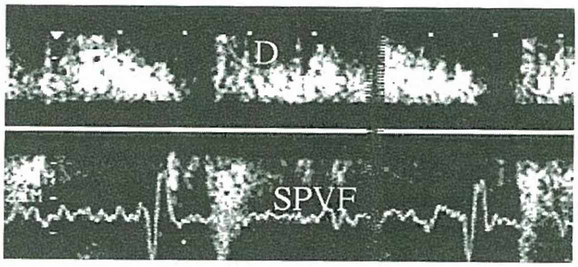

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Figure 1: The pulmonary venous flow Doppler tracing of two patients with mitral regurgitation are given. **(A)** A patient without systolic pulmonary venous flow reversal, **(B)** with systolic pulmonary venous flow reversal. AR; atrial reverse flow, D; diastolic flow, S; systolic flow, SPVFR; systolic pulmonary venous flow reversal.

The TVI of the MR jet was obtained by using CW Doppler tracings derived from the apical four chamber view. ROA was standardized according to body surface area.

Cardiac catheterization: Thirty-nine (78%) of the patients underwent cardiac catheterization in the following 1 month. Left ventriculography was performed with a 7F pigtail catheter in the 30° right oblique position. Injection of the contrast media was performed by a pump at a speed of 14 cc/sec. and a volume of 35-40 cc. MR was graded according to the Sellers classification, which grades MR into 4 grades; mild (I), moderate (II), moderate-severe (III), and severe (IV) [25]. We have separated the patients into 2 groups in which the first group consisted of patients with grade I-II MR whereas the second group consisted of patients with grade III-IV MR.

Statistics: Numeric values were given as mean ± standard deviation. In the comparison of groups; Student's t test was performed for numeric values and chi-square test was performed for non-numeric values. Spearman linear regression analysis was performed to analyze the correlation of the variables with SPVFR. Logistic regression analysis with backward likelihood ratio was performed with the variables which were found to have significant correlation in the univariate analysis. The analysis was carried out in two parts, first with parameters used for quantification of MR (RF, RV, ROA, grade III/IV MR by angiography) and other parameters found to be significant. The parameters found significant in these two analyses were pooled and analyzed again and significant parameters were considered as independent markers of SPVFR.

The specificity, sensitivity, positive and negative predictivity of SPVFR for severe MR were calculated in all patients. Receiver operating characteristic (ROC) curve for SPVFR was drawn according to the values of RF. The criteria for severe MR was taken as a RF of greater than 50% (26).

RESULTS

The mean age of the patients were 36 ± 18 years, and 31 (62%) of the patients were female. The etiology of MR was rheumatic in 23 (46%) patients, prolapsus in 20 (40%) patients, flail leaflets in 3 (6%) patients and cardiomyopathy in 4 (8%) patients. The jets were eccentric in 32 (64%) patients and central in 18 (36%) patients. Eighteen (36%) of the patients had atrial fibrillation (AF). Left ventricular systolic dysfunction was present in the 7 (14%) of the patients. SPVFR was present in 26 (52%) patients. The presence of AF was more frequent in patients who had SPVFR (58% vs. 13%, p=0.001). The ROA, RV, RF, and left atrium/ventricle diameters/volumes were higher in SPVFR patients. On univariate analysis, SPVFR was significantly correlated to the presence of AF, left ventricular dimension and volume, left atrial diameter and volume, RV, ROA, and RF. When ROA was standardized according to body surface area the calculated correlation was slightly increased (r=0.73 increased to 0.77). The single and powerful determinant of SPVFR was found to be RF on multivariate analysis (Table-I).

Sixteen of 39 (41%) patients had grade II MR in left ventriculography whereas 10 of them (26%) had grade III and 13 of them (33%) had grade IV MR. SPVFR was present in 2 (13%) patients with grade II MR, 6 (60%) patients with grade III MR and all (100%) patients with grade IV MR. SPVFR was

Table 1. Distribution of clinical, echocardiographic and hemodynamic findings according to the presence of SPVFR and correlations of these variables with SPVFR

	SPVFR (+) n=26	SPVFR (-) n=24	p Value*	r coefficient †	p Value †
Age (yr)	37±17	35±19	0.61	0.13	0.38
Men (no)	10	9	1	0.01	0.95
Heart rate (beats/min)	92±18	86±13	0.13	0.19	0.18
AF (no)	15	3	0.001	0.47	0.001
Eccentric jet (no)	16	16	0.80	-0.05	0.71
LV dysfunction (no)	4	3	1	0.04	0.78
LVDd (cm)	6.4±0.7	5.6±0.7	<0.001	0.57	<0.001
LVSd (cm)	4.3±0.7	3.6±0.6	0.001	0.47	0.001
EDV (cm^3)	211±48	170±50	0.01	0.41	0.006
ESV (cm^3)	86±36	68±43	0.16	0.32	0.035
EF (%)	59±13	61±13	0.67	-0.8	0.59
LAd (cm)	6.3±0.7	4.6±1.1	<0.001	0.59	<0.001
ROA (cm^2)	0.59±0.19	0.26±0.12	<0.001	0.73	<0.001
RV (cm^3)	77±22	39±17	<0.001	0.69	<0.001
RF (%)‡	60±8	35±8	<0.001	0.81	<0.001
III/IV MR (no)	19	4	<0.001	0.69	<0.001
Jet velocity (cm/sec)	492±72	501±57	0.64	-0.13	0.37
LAV (cm^3)	223±110	105±48	0.001	0.59	0.001

**: With SPVFR vs without SPVFR (p>0.05 for NS), †: Correlations between parameters and SPVFR, ‡: The most powerful determinant of SPVFR, +: presence, -: absence*

Abbreviations: AF; *atrial fibrillation,* ***EDV;*** *left ventricle end diastolic volume,* ***EF;*** *ejection fraction,* ***ESV;*** *left ventricle end systolic volume,* ***LAd;*** *left atrial diameter,* ***LAV;*** *left atrial volume,* ***LV;*** *left ventricle,* ***LVDd;*** *left ventricle diastolic diameter,* ***LVSd;*** *left ventricle systolic diameter,* ***MR;*** *mitral regurgitation,* ***RF;*** *regurgitant fraction,* ***ROA;*** *regurgitant orifice area,* ***RV;*** *regurgitant volume,* ***SPVFR;*** *systolic pulmonary venous flow reversal.*

more frequent in patients with grade III/IV MR than the patients with grade I/II MR (73% vs. 27%, p<0.001) (Fig. 2).

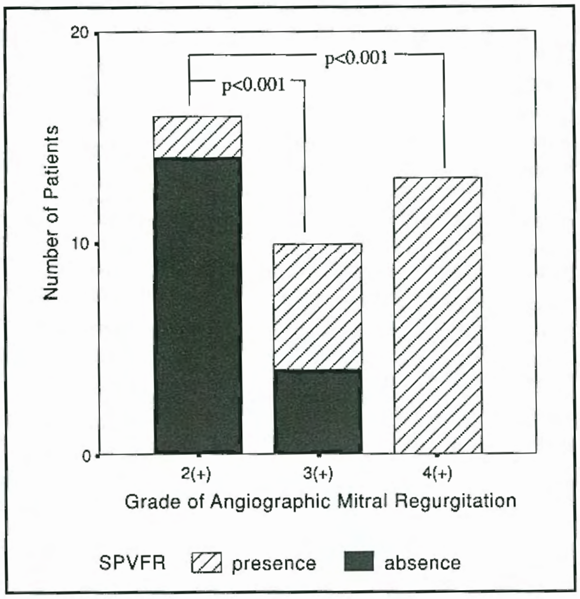

Figure 2. Diagram shows the distribution of patients with or without systolic pulmonary venous flow reversal according to angiographic mitral regurgitation grading.

SPVFR had a high degree sensitivity, specificity and accuracy for the diagnosis of severe MR (89%, 95% and 92%, respectively). The ROC curve is given in Fig. 3. All SPVFR patients excluding 1 were in the severe MR (RF ≥ 50%) group (Fig. 4).

Thirty-two (64%) patients had eccentric MR jet. Eleven (69%) of 16 patients with SPVFR and eccentric jets had a jet directed to the left pulmonary vein and the jets of 7 (44%) patients were discordant. Among the patients with the jet oriented to the left, SPVFR was observed in right pulmonary vein in 2 (18%), left pulmonary vein in 6 (55%) and both pulmonary veins in 3 (27%) patients. Among 5 (31%) patients with the jet oriented to the right, SPVFR was present in right pulmonary vein in 3 (60%) and both pulmonary veins in 2 (40%) patients. When central and eccentric jet subgroups were analyzed strong correlation of SPVFR with RF was found (r=0.74 and 0.84; p<0.001, respectively).

The intra and inter-observer variability were evaluated in randomly selected 10 patients with linear regression analysis by using the videotape records and angiographic films. There was an excellent inter-

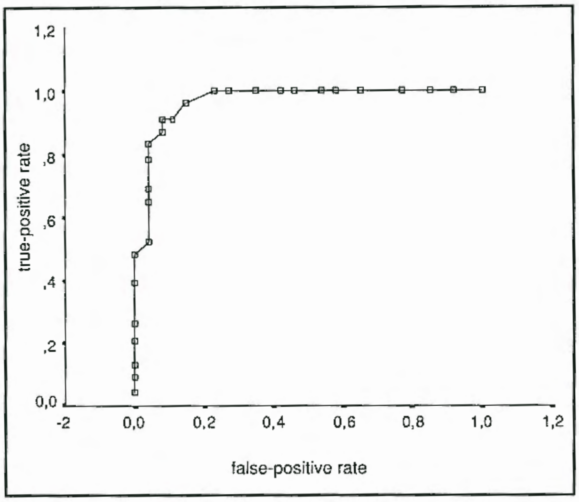

Figure 3. ROC curve of SPVFR drawn according to the values of regurgitant fraction

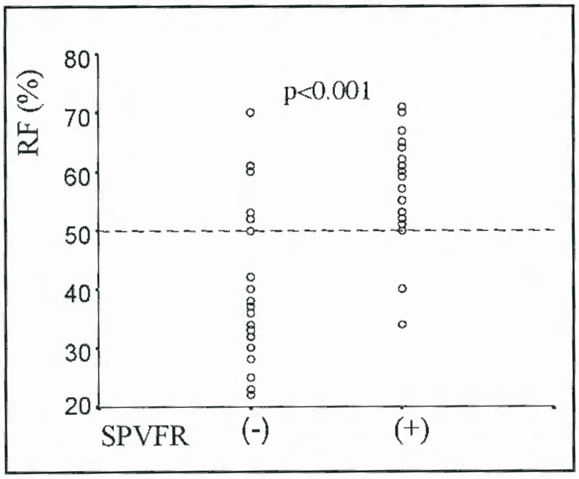

Figure 4. Diagram shows that patients with systolic pulmonary venous flow reversal take place in the severe mitral regurgitation (RF>50 %) group. RF; regurgitant fraction

and intra-observer agreement for the measurement of the left ventricle systolic and diastolic diameters and volumes, the left atrium diameter and volume, mitral and aortic stroke volumes, presence of SPVFR and angiographic grading of MR (r= 0.93, 0.94, 0.88, 0.87, 0.96, 0.89, 0.85, 0.91, 1, 1; p<0.05, respectively).

DISCUSSION

The reflux of contrast media to pulmonary veins in systole is an angiographic finding of severe MR in left ventriculography [9]. It has been reported that this reflux corresponds to SPVFR in TEE studies and that it is a sensitive and specific determinant of severe MR (10-14). In this study, PVSFR as obtained by TTE was found to be strongly correlated to mitral regurgitant fraction and showed high degree of sensitivity, specificity and accuracy in the diagnosis of severe MR.

Enriquez-Sarano et al. (13) had reported ROA as the most powerful determinant of SPVFR. In another study (20), a better correlation with RF and pulmonary venous flow was found compared to ROA. RV is a factor used in calculating both RF and ROA. ROA is affected by body mass in addition to degree of MR. When we standardized ROA by body surface area, it showed a slightly better correlation with SPVFR but not as much as RF did.

Results of our study show that SPVFR has a good sensitivity, specificity and accuracy for diagnosing severe MR. Enriquez-Sarano had reported that SPVFR had a low sensitivity and correlation for severe MR (13). In that study they had evaluated only the right upper pulmonary vein for SPVFR. In another study, low sensitivity was reported for single sided SPVFR with TEE (27). Klein et al (28) emphasized that both right and left upper pulmonary veins should be evaluated for pulmonary venous flow. Both Klein (11) and Pieper (27) have reported a discordance between the flows of two upper pulmonary veins in a group of patients. This may be due to the eccentricity of the jet, the angle between the Doppler beam and the veins or the size of the left atrium. We have evaluated both of the pulmonary veins by TTE and we have considered the presence of SPVFR in any of these veins as significant.

Since many of our patients had flail or prolapsed valves, we observed eccentric jets more frequently (64%). The eccentric jets were directed towards right or left pulmonary veins. Since we evaluated both of the pulmonary veins, we found an excellent accuracy for SPVFR in severe MR even in patients with eccentric jets (91%). Though they used a single pulmonary vein, Pieper et al have had reported similar results for eccentric jets (29). On the other hand, Enriquez-Sarano had reported that eccentric and long jets alter pulmonary venous systolic flow regardless of degree of MR (13). Although the effects of eccentric jets on pulmonary venous flow is not clear enough, the jet may have a local effect on the pulmonary vein orifices. But it is not possible to explain the formation of SPVFR only by the local effect of eccentric jets because; half of the jets in our study was discordant with SPVFR, and it is a fact that the distance between the pulmonary vein orifices and the regurgitant orifice increases in the dilated left atrium.

In this study we managed to visualize the pulmonary vein flow in the 89% of the patients by TTE. This was comparable to ratios obtained in other studies by TTE (13,19). The measurements obtained from TTE were also found to be strongly correlated to measurements obtained by TEE (11,20,27,29). Therefore transthoracic pulmonary vein tracings could be used in a high fraction of the MR patients increasing its utility.

It was concluded that PVF is obtainable in majority of the patients with TTE. This was simple, less time consuming and more comfortable to the patient compared to TEE. Severe MR was found to be related with the formation of SPVFR as measured by quantitative Doppler and angiographic methods.

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