Türk Kardiyol Dern Arş 2004; 32: 239-245

Effect of Metoprolol Treatment on Pulmonary Venous Flow Pattern Studied by Transesophageal Pulsed Doppler Echocardiography in Mild to Moderate Mitral Stenosis in Sinus Rhythm

Mustafa AYDIN, MD*, Ali ÖZEREN, MD*, Mehmet BİLGE, MD*, Mustafa DEMİRKIRAN, MD, Fatih CAM, MD*, Aydın DURSUN, MD*, Mehmet Ali ELBEY, MD*, Tolga ONUK, MD***

Department of Cardiology, Medical Faculty, Zonguldak Karaelmas University, and Department of Cardiology, SSK Zonguldak Hospital**, Zonguldak, Turkey*

Summary

This study was conducted to evaluate the effect of metoprolol therapy on pulmonary venous flow pattern in patients with mild to modarete mitral stenosis in sinus rhythm. We studied 23 patients with isolated mild to moderate mitral stenosis (mitral valve area 1.6±0.3 cm²). All patients received metoprolol 100 mg once daily orally for 1 month. Pulsed wave Doppler transesophageal echocardiograpic examination of the pulmonary venous flow was performed at the beginning of the study and after 1 month of treatment. Peak systolic pulmonary venous flow (PVs) velocity, PVs velocity time integral (VTI), peak diastolic pulmonary venous flow (PVd) velocity, PVd-VTI, peak pulmonary venous atrial reversal flow (PVa) velocity, PVa-VTI, and PVa duration time were measured.

Peak and mean transmitral gradient, pulmonary artery pressure, systolic and diastolic blood pressure, and heart rate, reduced significantly after metoprolol treatment. The pulmonary venous peak systolic velocity, and pulmonary venous atrial reversal flow velocity duration time increased significantly from 0.55 ± 0.19 m/s to 0.66 ± 0.12 m/s, p<0.05, and from 84 ± 27 to 11 2± 31 msec, p<0.01, respectively). Regarding VTI, PVs-VTI increased from 10.8±3.2 cm to 11.9±4.3 cm (p<0.01), PVd-VTI increased from 5.1± 2.4 cm to 5.4±2.5 cm (p<0.05), and PVa- VTI increased from 2.8±1.1 cm to 3.1±1.3 cm, p<0.05.

Conclusion: Metoprolol treatment increased pulmonary venous flow as an indicator of improved left atrial function in patients with mitral stenosis and sinus rhythm. These results may contribute to disclosing the underlying mechanisms of the favourable effects of beta blockade in mitral stenosis. ***(Türk Kardiyol Dern Arş 2004; 32: 239-245)***

Key words: *Metoprolol, pulmonary venous flow, transesophageal echocardiography*

Özet

Metoprolol Tedavisinin Sinüs Ritimli Hafif-Orta Mitral Darlıklı Hastalarda Transözofajiyal Ekokardiyografi ile Elde Edilen Pulmoner Venöz Akım Paternleri Üzerine Etkisi

Bu çalışma metoprolol tedavisi verilen sinüs ritimli hafif-orta mitral darlıklı hastalarda metoprololün pulmoner venöz dalga ölçümleri üzerine etkisini araştırma amacıyla yapıldı.

Çalışmaya izole hafif-orta şiddette mitral darlığı (mitral kapak alanı 1.6±0.3 cm²) olan 23 hasta alındı. Tüm hastalara 1 ay süreyle günde 100 mg oral metoprolol verildi. Tedavi öncesi ve tedavinin birinci ayında transözofajiyal ekokardiyografi uygulandı. Zirve sistolik pulmoner venöz akım hızı (PVs), PVs hız-zaman integrali (VTI), zirve diyastolik pulmoner venöz akım hızı (PVd), PVd-VTI, zirve pulmoner venöz atriyal geri akım hızı (PVa), PVa-VTI ve PVa süresi ölçüldü.

Address for Correspondence: Mustafa Aydın, MD, Zonguldak Karaelmas Üniversitesi Uygulama ve Araştırma Hastanesi Kardiyoloji AD, Kozlu, 67600, Zonguldak, Turkey Tel: 90 (372) 261 0169 Fax: 90 (372) 261 0155 e-mail: drmustafaaydin@hotmail.com
Received: 3 March, accepted: 27 April 2004

Zirve ve ortalama transmitral gradiyent, pulmoner arter basıncı, sistolik-diyastolik kan basıncı, ve kalp hızı anlamlı derecede azaldı. Pulmoner venöz zirve sistolik akım hızı, ve pulmoner venöz atriyal geri akım süresi anlamlı düzeyde arttı (sırasıyla 0.55 ± 0.19 m/s'ye karşın 0.66 ± 0.12 m/s, p<0.05, ve 84 ± 27 to 11 2± 31 msn p<0.01). PVs-VTI, 10.8±3.2 cm'den 11.9±4.3 cm'ye yükseldi (p<0.01), PVd-VTI, 5.1± 2.4 cm'den 5.4±2.5 cm'ye yükseldi (p<0.05), ve PVa- VTI 2.8±1.1 cm'den 3.1±1.3 cm'ye yükseldi, (p<0.05).

Sonuç olarak, metoprolol tedavisi sinüs ritmindeki mitral darlığı hastalarında pulmoner venöz akımlarda artışa neden olmaktadır. Bu artış sol atriyal fonksiyonlarda düzelmenin bir göstergesi olabilir. Bu sonuçlar mitral darlıklı hastalarda metoprolol tedavisinin faydalı etki mekanizmasının anlaşılmasına katkı sağlayabilir. ***(Türk Kardiyol Dern Arş 2004; 32: 239-245)***

Anahtar kelimeler: *Metoprolol, pulmoner venöz akım, transözofajiyal ekokardiyografi*

Rheumatic mitral stenosis (MS) continues to be a considerable health problem. Appropriate medical treatment with beta blockers has an important role in patients with MS. In cases with MS an increase in heart rate during exercise elevates the transmitral gradient, thus resulting in increased pulmonary venous pressure and dyspnea [1]. Beta-adrenergic blocking agents reduce the diastolic pressure gradient across the stenotic mitral valve, and thus, pulmonary congestion, by decreasing both heart rate and cardiac output [2]. Beta blockers may have useful effects on the left atrial function in patients with symptomatic isolated MS with sinus rhythm. Pulmonary venous flow which is normally composed of systolic and diastolic forward flows and a small reversal flow during atrial contraction can be examined and assessed by transesophageal echocardiography (TEE). Pulmonary venous flow is pulsatile and is affected by changes in left atrial (LA) pressure, compliance, contractility, cardiac rhythm and left ventricular compliance [3-8]. The properties of the pulmonary venous flow pattern in patients with mitral stenosis and normal sinus rhythm are lower pulmonary venous systolic flow (PVs), pulmonary venous diastolic flow (PVd), and pulmonary venous atrial reversal flow (PVa) velocities [9,10]. Although a variety of altered pattern of pulmonary venous flow have been described in MS, the effect of beta blockade on the pulmonary venous flow in patients with pure MS with sinus rhythm has not been clearly documented [9-14]. The goal of this study was to investigate the effect of beta adrenoreceptor blockade with metoprolol on the pulmonary venous flow in patients with isolated MS in sinus rhythm.

METHODS

Patients: The study included 23 patients (21 women and 2 men, mean age 38 ± 13 years) who met the following criteria: patients with pure or predominant MS in sinus rhythm at the time of TEE; no evidence of moderate or severe mitral regurgitation by TEE [15] (a maximal regurgitation jet area between 1.5 and 4 cm^2 predicted mild mitral regurgitation); no echocardiographic evidence of aortic stenosis, aortic regurgitation and tricuspid stenosis; adequate resting heart rate on no current therapy with beta adrenergic blocker, calcium channel blockers or digitalis (heart rate>60 beats/min); normal left ventricular systolic function determined by two-dimensional echocardiography; no evidence of obstructive pulmonary or coronary heart disease and hypertension; systolic blood pressure>100 mm Hg; good quality Doppler and standard echocardiographic tracings and those patients who could tolerate repeat TEE and agreed to undergo this procedure during follow-up.

Their diagnosis of rheumatic MS was based on echocardiographic examinations. All patients were in sinus rhythm at the time of the studies. Although it is not possible to completely rule out episodes of asymptomatic atrial fibrillation, patients had no electrocardiographic documented episodes of atrial fibrillation in the past. No patients had a history of embolic event. At the time of echocardiographic studies, 17 patients were receiving aspirin, and one was receiving oral anticoagulant treatment with warfarin. The remaining 5 patients were not receiving anticoagulation or antiplatelet therapy. Demographic features are described in Table 1. The study protocol was

Table 1. Basal clinical and echocardiographic characteristics of study patients

N	23
Age (yrs)	38 ± 13
Men/women	2/21
Left atrial diameter (cm)	4.2 ± 0.5
Mitral valv area (cm^2)	1.6 ± 0.3
Left ventricular end-diastolic diameter (cm)	4.7 ± 0.4
Left ventricular end-systolic diameter (cm)	2.8 ± 0.6
Left ventricular ejection fraction (%)	63 ± 4
Mitral regurgitation (mild/absent)	17/6
History of embolism	0
Aspirin therapy	17 (74%)
Warfarin therapy	1 (4%)
Prophylaxis with benzathine penicillin G	18 (78%)

approved by the Science and Ethics Committee of our institution. Informed consent was obtained from each patient.

Echocardiographic studies: Before the transesophageal evaluation, all patients underwent a complete transthoracic examination using a commercially available Doppler echocardiography unit (GE Medical Systems,Vivid FiVe, Horten, Norway) with a 2.5 MHz probe. Left ventricular end-diastolic diameter, left ventricular end-systolic diameter and left atrial diameter were measured from parasternal M-mode recordings accordings to standard criteria [16]. Left ventricular ejection fraction was determined from apical views using a modified Simpson's rule [17]. The mitral valve area was measured by continuous-wave Doppler, according to the pressure half-time method [18]. The mean transmitral pressure gradient was estimated from the maximal transvalvular flow velocity using a modified Bernoulli equation [19]. Pulmonary artery systolic pressure (PASP) was estimated with the modified Bernoulli equation, PASP = $4V^2$ + RAP, where V = peak systolic velocity of the tricuspid regurgitation jet recorded by continuous wave Doppler and right atrial pressure (RAP) was assumed to be 10 mm Hg [20].

TEE was performed using a 5 MHz multiplane probe (GE Medical Systems,Vivid FiVe). All patients were studied in the fasting state using 10% lidocaine spray for posterior pharyngeal anesthesia. No sedation or atropine was administered. The TEE probe was inserted with the subject lying in the left lateral position. The procedure was performed with continuous monitoring of heart rate, blood pressure and a one lead electrocardiogram. All images were recorded on Super VHS videotapes for subsequent analysis. TEE was well tolerated by all patients, and there were no complications.

The pulmonary venous flow was measured by positioning the pulsed wave Doppler sample volume in the left upper pulmonary vein approximately 1 cm proximal to its entrance to LA. The Doppler beam was oriented as parallel as possible to the flow and no angle correction was used. From the pulmonary venous flow velocity tracing PVs velocity, PVs velocity time integral (VTI), PVd velocity, PVd-VTI, PVa velocity, PVa-VTI, and PVa duration time were measured. Three cardiac cycles were averaged for quantitation.

Left atrial spontaneous echo contrast (SEC) was diagnosed by the presence of dynamic "smoke-like" echoes in the left atrial cavity with a characteristic swirling motion distinct from a white noise artifact after properly adjusting the gain setting. The presence or absence of thrombus and the degree of spontaneous echo contrast was determined by 2 independent observers unaware of clinical history. The presence of spontaneous echo contrast was diagnosed when dynamic, swirling intracavitary smoke-like echoes were detected, which were differentiated from white noise artifact by their characteristic swirling pattern and by careful attention to the gain settings. The degree of SEC was categorized as previously described [21]. Mild SEC was defined as being present if dynamic intracavitary microechoes were seen only with high gain, whereas severe SEC was present if SEC was noted with low gain. Echocardiographic characteristics of the patient population are described in Table 1.

Metoprolol treatment: Baseline parameters included heart rate, blood pressure, mean transmitral pressure gradient, PASP, and left atrial spontaneous echo contrast intensity. Each patient was given a intravenous bolus dose of 5 mg metoprolol. Ten minutes later, a second set of assessments were performed. After the first TEE studies were performed, each patient was given metoprolol succinate controlled release 100 mg once daily for 1 month. A second TEE study was performed after 1 month of continuous oral metoprolol treatment at maintenance dose and the measurements were repeated.

Table 2. Clinical and echocardiographic parameters before treatment, 10 minutes after metoprolol 5 mg intravenously, and 1 month after oral metoprolol treatment

	Before	10 min after metoprolol	1 month after metoprolol
Heart rate (beats/min)	85 ± 11	73±10§	68 ± 19†
Systolic blood pressure (mm Hg)	128 ± 12	126±12	118 ± 5†
Diastolic blood pressure (mm Hg)	78 ± 6	76±6	71 ± 3†
Mean mitral valve gradient (mm Hg)	8.8 ± 3.8	7.8±3.2§	6.9 ± 2.5‡
Maximal mitral valve gradient (mm Hg)	16.2 ± 5.1	15.8±4.8	12.5 ± 3.8‡
Pulmonary artery pressure (mm Hg)	44±9	42±8	41±10α
Spontaneous echo contrast (n)	6	6	6

Values are expressed as the mean±S.D; NS, non-significant
† p value <0.001 vs before treatment
‡ p value <0.01 vs before treatment
α p value <0.02 vs before treatment
§ p value <0.05 vs before treatment

p<0.001, respectively). The beta blocker therapy significantly attenuated transmitral pressure gradient (at baseline 8.8 ± 3.8mm Hg) at 10 minutes 7.8±3.2 mm Hg (p<0.05) and at 1 month 6.9±2.5 mm Hg (p<0.01). At 10 minutes, there was no significant change in pulmonary arterial systolic pressure with metoprolol (at baseline 44±9 mm Hg and at 10 minutes 42 + 8 mm Hg) but 1 month later significantly decreased (41±10, p<0.02).

Statistics

Data are presented as mean ± SD. The differences of parameters between before and after beta blocker therapy were assessed by the paired t test. Significance was accepted at the p<0.05 level. The data were processed using the software packages SPSS versions 8.0 statistics programme (SPSS Inc, Chicago, IL, USA).

RESULTS

The mean mitral valve area for patients in this study was 1.6±0.3 cm^2. All patients were in New York Heart Association functional class I or II. During the study period, all patients tolerated the treatment well, and there were no complications or adverse effect.

Heart rate, blood pressure, transmitral pressure gradient and pulmonary arterial systolic pressure: Before the treatment, baseline heart rate was 85±11 beats/min. Metoprolol significantly decreased heart rate at 10 minutes (73±10 beats/min, p<0.005) and at 1 month (68±19 beats/min, p<0.001). The treatment by metoprolol caused a significant reduction in systolic and diastolic blood pressures (128±12 / 78±6 mm Hg at baseline, 124±8 / 75±3 mm Hg at 10 minutes and at 1 month 118±5 / 71±3 mm Hg, p<0.05,

Pulmonary venous flow velocity and velocity time integral: Pulmonary venous flow velocity profiles before and after treatment were evaluated (Figures 1,2). There was no change significantly in pulmonary venous flow velocities at 10 minutes after intravenous 5 mg metoprolol administration (Table 3). Metoprolol treatment resulted in a significant increase in PVs from 0.55±0.19 m/s to 0.66±0.12 m/s, (p<0.05). Peak atrial reversal flow duration time increased from 84 ± 27 msec to 112±31 msec, (p<0.01). Pulmonary venous diastolic flow and atrial reversal flow velocity measurements did not differ significantly before and after metoprolol treatment (p>0.05). In velocity time integral, PVs-VTI increased from 10.8±3.2 cm to 11.9±4.3 cm, (p<0.01), PVd-VTI increased from 5.1± 2.4 cm to 5.4±2.5 cm (p<0.05), and PVa- VTI increased from 2.8±1.1cm to 3.1±1.3 cm, (p<0.05).

Spontaneous echo contrast: Before initiation of beta blocker therapy, 6 patients (26%) had a left atrial SEC graded as mild in 4 patients (17%) and as severe in 2 (9%). After intravenous and oral metoprolol therapy, SEC intensity did not change in any patients. Diagnostic disagreement between the observers in the classification of SEC were not found in any patient.

Table 3. Pulmonary venous flow data before and after metoprolol treatment in mitral stenosis in sinus rhythm

Pulmonary venous flow	Before	10 min after metoprolol	1 month after metoprolol
PVs (m/sec)	0.55±0.19	0.57±0.16	0.66±0.12‡
PVs- VTI (cm)	10.8±3.2	11±3.5	11.9±4.3†
PVd (m/sn)	0.38±0.9	0.39±0.9	0.40±0.8
PVd- VTI (cm)	5.1± 2.4	5.1±2.4	5.4±2.5‡
PVa (m/sn)	0.22±0.6	0.24±0.6	0.28±0.7
PVa- VTI (cm)	2.8±1.1	2.9±1.1	3.1±1.3‡
PVa-DT (msec)	84± 27	88±22	112±31†

Values are expressed as the mean±S.D; PVs, peak systolic pulmonary venous flow velocity; PVd, peak diastolic pulmonary venous flow velocity; PVa, peak pulmonary venous atrial reversal flow velocity; VTI, velocity time integral; PVa-DT, pulmonary venous atrial reversal flow duration time.
† p value <0.01 vs before treatment
‡ p value <0.05 vs before treatment

ved to be the prominent determinants of pulmonary venous systolic flow. In mitral stenosis, the left atrial pressure overload persists throughout the cardiac cycle. This obstructs left atrial filling of blood that drains from the pulmonary veins, because of the reduced or blunted systolic flow [12]. During systole, blood flows from the pulmonary veins to the left atrium at a relatively higher velocity because of the suction effect caused by atrial relaxation [25]. With atrial contraction, reversed atrial flow in late diastole becomes pronounced because of retrograde transmission of the high left atrial pressure to the pulmonary veins.

DISCUSSION

Blunted pulmonary venous flow and reduced left atrial function has been described in patients with mitral stenosis but the effect of beta blockade on pulmonary venous flow is not well known in patients with mitral stenosis in sinus rhythm [8,10,12,22,23]. A decrease in distensibility can result from an increase in left atrial pressure, volume, or both. Therefore, left atrial distensibility may be the most important mechanism [24]. Thus left atrial size and function are believed to be the prominent determinants of pulmonary venous systolic flow. In mitral stenosis, the left atrial pressure overload persists throughout the cardiac cycle. This obstructs left atrial filling of blood that drains from the pulmonary veins, because of the reduced or blunted systolic flow [12]. During systole, blood flows from the pulmonary veins to the left atrium at a relatively higher velocity because of the suction effect caused by atrial relaxation [25]. With atrial contraction, reversed atrial flow in late diastole becomes pronounced because of retrograde transmission of the high left atrial pressure to the pulmonary veins.

Some studies have suggested that beta blockers may be useful in patients with MS [26,27]. Beta blockers are expected to alleviate the symptoms of pulmonary congestion and decrease the transmitral pressure gradient. On one hand, beta blockers decrease heart rate, prolong the diastolic filling period and attenuate the transmitral pressure gradient. On the other hand, negative atrial inotropism is potentially harmful [28].

Based on this information, we investigated whether beta blocker therapy may affect LA

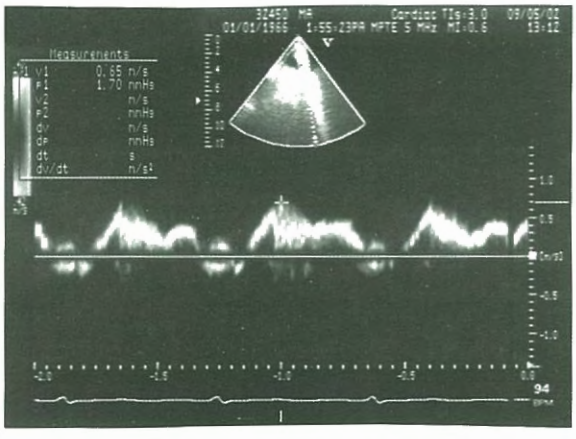

Figure 1. Transesophageal Doppler echocardiographic recordings showing remarkably blunted pulmonary venous peak systolic velocity in a patient with mitral stenosis before metoprolol treatment

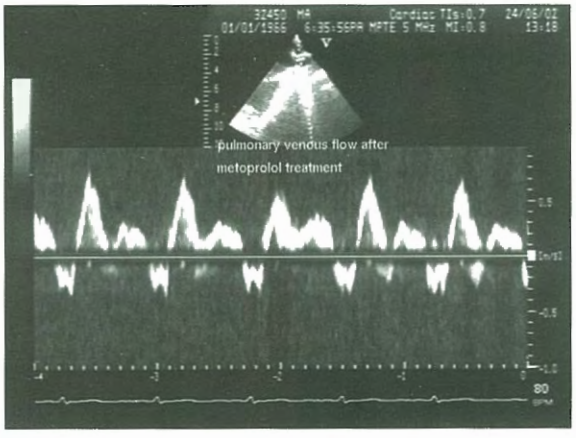

Figure 2. Relatively increased pulmonary venous peak systolic velocity after 1 month of oral metoprolol treatment. (Pulmonary venous peak systolic velocity increased from 64 to 75 cm/s).

function in patients with MS, and, we observed that metoprolol could be favourable on pulmonary venous flow velocities in patients having mild and moderate MS with sinus rhythm. To the best of our knowledge, this is the first clinical report assessing the effects of a beta blocker on pulmonary venous flow velocities in patients with MS.

A positive effect of metoprolol was the reduction in mean transmitral pressure gradient and heart rate at 10 minutes and at 1 month. These changes were associated with a significant improvement in pulmonary venous flow velocities. The mechanism underlying the improvement in PVs velocity after the administration of metoprolol is not clear. A possible explanation for this result is that the decrease in transmitral pressure gradient and left atrial pressure induced by metoprolol could have contributed to an improvement in PVs velocity. Tabata et al. found that PVs and PVd flows were decreased significantly in MS patients compared to controls [9]. These results could demonstrate that evaluation of the pulmonary venous flow velocities may be helpful in understanding the hemodynamic events between the left atrium and left ventricle in patients with mitral stenosis.

In previous studies, it was determined that β-blocker therapy significantly improves exercise capacity in patients with symptomatic isolated MS with sinus rhythm. This improved effort tolerance was due to reduction of the exercise-associated sinus tachycardia by beta adrenergic blockade, allowing a longer diastolic filling period and better left atrial decompression [26,27]. Metoprolol is thought to cause a significant increase in pulmonary venous flow secondary to decreased left atrial pressure. Lee et al. investigated the relation between left atrial pressure and pulmonary vein systolic pressure in the patients with MS. They performed percutaneous balloon valvuloplasty and found that as the left atrial pressure increases, pulmonary venous systolic flow decreases [13]. Similarly, we demonstrated that beta blockade could cause an increase in pulmonary venous systolic flow by decreasing left atrial pressure.

In the present study, we observed a significant improvement of PVs, PVs-VTI, PVd-VTI, PVa-VTI, and PVa duration time after 1 month use of metoprolol. These findings may show that metoprolol has beneficial effects on pulmonary venous flow pattern in MS patients. These changes were consistent with marked reductions in left atrial wall tension and in transmitral gradient as indicator of LA pressure. It is likely that LA inflow dynamics could change after metoprolol treatment.

Study limitation

Only the left upper pulmonary vein was interrogated in all the studies because this was the most readily visible vessel. Since the study was limited to one month, long term results of the beta blocker therapy can not be predicted. Besides, effects of beta blockade on SEC and thrombus formation on long term are not known. We chose to examine patients with sinus rhythm as the study group because patients with mild to moderate degrees of MS are generally in sinus rhythm. Therefore our results may not be extrapolated to patients with MS in atrial fibrillation. Further studies are necessary to evaluate whether these favourable results of beta blockade on pulmonary venous flow can be extrapolated to patients with MS and atrial fibrillation. This study had a rather small patient population, however the measurements of pulmonary venous flow velocities were assessed on a prospective basis.

Conclusion

This study suggests that metoprolol therapy may have a beneficial effect on pulmonary venous flow velocities in patients with MS in sinus rhythm.

REFERENCES

1. Gorlin R, Lewis BM, Haynes FW: Factors regulating pulmonary capillary pressure in mitral stenosis. Am Heart J 1951;41: 834-54

2. Meister SG, Engel TR, Feitosa GS, Helfant RH, Frankl WS: Propanolol in mitral stenosis during sinus rhythm. Am Heart J. 1977;94:685-88

3. Rajagopalan B, Friend JA, Stallard T, Lee GD: Blood flow in pulmonary veins: I. Studies in dog and man. Cardiovasc Res 1979;13:667-76

4. Klein AL, Tajik AJ: Doppler assessment of pulmonary venous flow in healthy subjects and in patients with heart disease. J Am Soc Echocardiogr 1991:4:379-92

5. Keren G, Sherez J, Megidish R, Levitt B, Laniado S: Pulmonary venous flow pattern--its relationship to cardiac dynamics. A pulsed Doppler echocardiographic study. Circulation 1985;71:1105-12

6. Keren G, Meisner JS, Sherez J, Yellin EL, Laniado S: Interrelationship of mid-diastolic mitral valve motion, pulmonary venous flow, and transmitral flow. Circulation 1986;74:36-44

7. Keren G, Sonnenblick EH, LeJemtel TH: Mitral anulus motion. Relation to pulmonary venous and transmitral flows in normal subjects and in patients with dilated cardiomyopathy. Circulation 1988;78: 621-29

8. Klein AL, Hatle LK, Burstow DJ, et al: Doppler characterization of left ventricular diastolic function in cardiac amyloidosis. J Am Coll Cardiol 1989:13: 1017-26

9. Tabata T, Oki T, Fukuda N, et al: Transesophageal pulsed Doppler echocardiographic study of pulmonary venous flow in mitral stenosis. Cardiology 1996;87:112-18

10. Stojnic BB, Radjen GS, Perisic NJ, Pavlovic PB, Stosic JJ, Prcovic M: Pulmonary venous flow pattern studied by transesophageal pulsed Doppler echocardiography in mitral stenosis in sinus rhythm: effect of atrial systole. Eur Heart J 1993;14:1597-601

11. Castello R, Pearson AC, Lenzen P, Labovitz AJ: Effect of mitral regurgitation on pulmonary venous velocities derived from transesophageal echocardiography color-guided pulsed Doppler imaging. J Am Coll Cardiol 1991;17:1499-1506

12. Klein AL, Bailey AS, Cohen GI, et al: Effects of mitral stenosis on pulmonary venous flow as measured by Doppler transesophageal echocardiography. Am J Cardiol 1993;72:66-72

13. Lee MM, Park SW, Kim CH, et al: Relation of pulmonary venous flow to mean left atrial pressure in mitral stenosis with sinus rhythm. Am Heart J 1993;126:1401-07

14. Ara N, Nishimura RA, Tajik AJ, Redfield MM: Pulmonary venous velocity patterns in mitral stenosis. J Am Soc Echocardiogr 1995;8:643-46

15. Yoshida K, Yoshikawa J, Yamaura Y, Hozumi T, Akasaka T, Fukaya T: Assessment of mitral regurgitation by biplane transesophageal color Doppler flow mapping. Circulation 1990;82: 1121-27

16. Sahn DJ, De Maria A, Kisslo J, Weyman A: The committee on M-mode standardization of the American Society of Echocardiography. Recommendations regarding quantification in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58: 1072-81

17. Schiller NB, Shah PM, Crawford M, et al: Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography. Committee on standards, subcommittee on quantitation of two-dimensional echocardiograms. J Am Soc Echocardiogr 1989;2: 358-67

18. Hatle L, Brubakk A, Tromsdal A, Angelsen B: Noninvasive assessment of pressure drop in mitral stenosis by Doppler ultrasound. Br Heart J 1978;40:131-40

19. Hatle L, Angelsen B: Doppler ultrasound in cardiology: physical principles and clinical applications. 2nd ed. Lea & Febiger Press, Philadelphia. 1985. pp. 167

20. Yock PG, Popp RL: Noninvasive estimation of right ventricular systolic pressure by Doppler ultrasound in-patients with tricuspid regurgitation. Circulation 1984;70:657-62

21. Daniel WG, Nellessen U, Schroder E, et al: Left atrial spontaneous contrast in mitral valve disease: an indicator for an increased thromboembolic risk. J Am Coll Cardiol 1988;11: 1204-11

22. Jolly N, Arora R, Mohan JC, Khalilullah M: Pulmonary venous flow dynamics before and after balloon mitral valvuloplasty as determined by transesophageal Doppler echocardiography. Am J Cardiol 1992;70:780-84

23. Oki T, Iuchi A, Tabata T, et al: Left atrial contribution to left ventricular filling in patients with mitral stenosis: combined analysis of transmitral and pulmonary venous flow velocities. Echocardiography 1998;15:43-50

24. Keren G, Sherez J, Megidish R, Levitt B, Laniado S: Pulmonary venous flow pattern--its relationship to cardiac dynamics. A pulsed Doppler echocardiographic study. Circulation 1985;71:1105-12

25. Chen YT, Kan MN, Lee AY, Chen JS, Chiang BN: Pulmonary venous flow: its relationship to left atrial and mitral valve motion. J Am Soc Echocardiogr 1993;6:387-94

26. Stoll BC, Ashcom TL, Johns JP, Johnson JE, Rubal BJ: Effects of atenolol on rest and exercise hemodynamics in patients with mitral stenosis. Am J Cardiol 1995;75:482-84

27. Giuffrida G, Bonzani G, Betocchi S, et al: Hemodynamic response to exercise after propranolol in patients with mitral stenosis. Am J Cardiol 1979;44:1076-82

28. Pollak A, Falk RH: Aggravation of postcardioversion atrial dysfunction by sotalol. J Am Coll Cardiol 1995;25: 665-71