

The Effect of Heart Rate on Color M-Mode Doppler Flow Propagation Velocity and Continuous-Wave Doppler Parameters in Aortic Insufficiency

Alper O. Onbasili, Tarkan Tekten, Ceyhun Ceyhan, Tunca Piskin

Adnan Menderes University, School of Medicine, Department of Cardiology, Aydin, Turkey

Background and aim of the study: The results of previous studies have suggested that an increase in heart rate (HR) may have a beneficial effect on the hemodynamic condition of patients with aortic regurgitation (AR), and reduce AR severity. An increase in HR was shown to cause a significant increase in regurgitant slope and to significantly shorten the pressure half-time (PHT), both of which are considered to be signs of worsening regurgitation. Color M-mode Doppler flow propagation velocity (FPV) was used to assess AR severity, but no data were available regarding the effects of HR on FPV measurement of AR. The study aim was to evaluate the effect of HR on FPV, and to compare FPV and continuous-wave (CW) Doppler parameter (PHT and slope) variations resulting from an increase in HR.

Methods: Sixty-eight patients (28 males, 40 females; mean age 52 ± 15 years) with AR of various severity were included. Color M-mode Doppler was used in FPV, while CW Doppler was used in PHT and slope

measurements. Atropine sulfate was titrated in all patients to achieve at least a 20% increase in HR. The FPV, PHT, slope and regurgitant fraction (RF) of AR were measured before and after the increase in HR.

Results: An increase in HR (77.8 ± 8.9 versus 103 ± 9.9 bpm; $p < 0.001$) caused a decrease in color M-mode Doppler FPV (51 ± 21 versus 44 ± 19 cm/s), in the PHT of the regurgitant velocity curve (468 ± 154 versus 411 ± 128 ms), and in the RF of the AR (30.2 ± 16.3 versus $26.1 \pm 14\%$). The slope of the regurgitant velocity was increased (291 ± 136 versus 358 ± 122 cm/s²). All of these variations were statistically significant.

Conclusion: An increase in HR caused a decrease in the FPV and RF of the aortic regurgitation, and both changes were signs of improved regurgitation. FPV appears to be a more valuable parameter than CW Doppler parameters in determining improvements in AR resulting from an increase in HR.

The Journal of Heart Valve Disease 2004;13:188-196

At present, several echo-Doppler methods are available for the assessment of aortic regurgitation (AR). Continuous-wave (CW) Doppler measurements provide the parameters of the slope, while the pressure half-time (PHT) is used to evaluate AR severity (1-3). Clinical and laboratory studies have demonstrated that systemic vascular resistance, aortic or ventricular resistance and heart rate (HR) can also influence the AR (4-6). The results of previous studies have suggested that an increase in HR might have a beneficial effect on the hemodynamic condition of patients with AR (7-9). However, an increase in HR has been shown to cause a significant increase in the regurgitant slope

and to shorten significantly the PHT (9), both of which parameters are considered conventionally to be signs of worsening AR. It has been shown previously that the color M-mode Doppler flow propagation velocity (FPV) method can be used to measure the severity of AR (10). To the best of the present authors' knowledge, no data are currently available concerning the effects of these variables on the FPV measurement of AR.

The study aim was first, to evaluate the effect of HR increase on FPV, and second to compare the FPV and CW Doppler parameter (PHT and slope) variations which occur as a result of an increase in HR.

Clinical material and methods

Patients

Sixty-eight patients (28 males, 40 females; mean age 52 ± 15 years) with AR of various degrees of severity were included. All study patients were in sinus rhythm, and the HR ranged from 60 to 90 beats per

Presented in part at the XXIV Congress of the European Society of Cardiology, 31st August-4th September 2002, Berlin, Germany

Address for correspondence:
Ass. Prof. Dr. O. Alper Onbasili, Adnan Menderes University, School of Medicine, Department of Cardiology, 09100, Aydin, Turkey
e-mail: onbasili@isbank.net.tr

minute (bpm). Exclusion criteria were the existence of more than mild regurgitation or stenosis of any valve other than the aortic valve, more than mild stenosis of the aortic valve, intracardiac or extracardiac shunts, previous pacemaker implantation, inadequate Doppler signal visualization of AR due to regurgitant jet eccentricity, or poor echogenicity. The study protocol was approved by the ethical committee of the scientific research programs of Adnan Menderes University Medical School.

The etiology of AR was rheumatic in 36 patients, degenerative in 28, bicuspid valve in two, and aortic aneurysm in two. Forty of these patients had isolated AR, 14 had combined mild aortic stenosis, and 24 had mild mitral regurgitation. Patients were divided into mild ($n = 32$), moderate ($n = 20$) and severe ($n = 16$) AR groups according to aortic regurgitant fraction (RF) measurements. Forty-four patients were assigned to NYHA functional class I, and 24 to class II. All patients were in a stable clinical condition, and none had any clinical history of coronary artery disease.

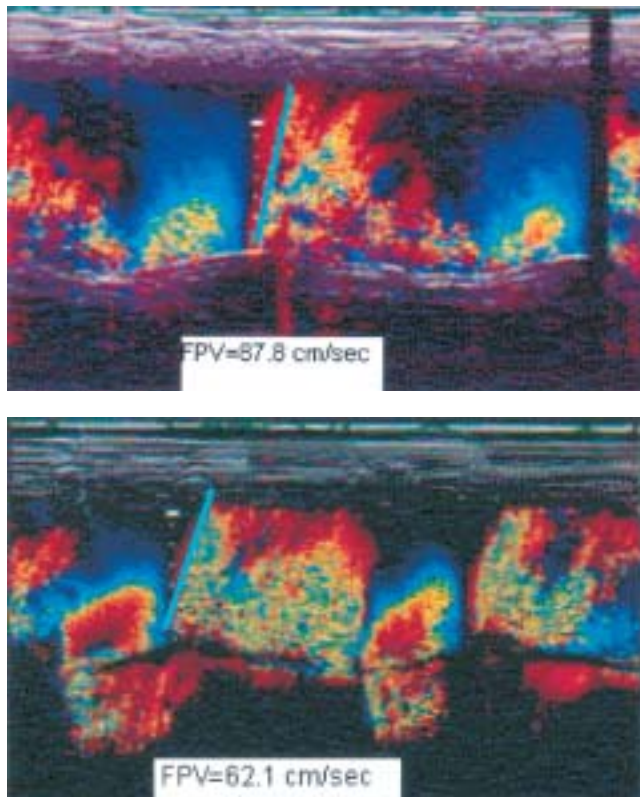


Figure 1: Flow propagation velocity (FPV) measurements of severe aortic regurgitation (AR), recorded at two different heart rates (HR). A) Baseline FPV measurement: HR 76 bpm, FPV 87.8 cm/s, regurgitant fraction (RF) 56%. B) FPV measurements after an increase in heart rate: HR 98 bpm, FPV 62.1 cm/s, RF 51%.

Study protocol

A complete examination, including echocardiography, Doppler and blood pressure measurements using a sphygmomanometer was carried out at baseline and after the HR increase. HR was increased by at least 20% of the baseline value with intravenous administration of atropine sulfate (0.02 mg/kg). In 14 patients, additional atropine sulfate (0.01 mg/kg) was administered intravenously in order to achieve the target HR. The mean total dose of atropine sulfate given intravenously was 1.48 ± 0.3 mg (range: 0.9 to 2.4 mg). All echocardiographic studies were recorded on VHS videotape for subsequent off-line review and analysis.

Echocardiographic evaluation

Echocardiography was performed with patients in the left lateral decubitus position, using a Sonos 5500 instrument (Hewlett Packard, Andover, MA, USA) fitted with a multi-Hz transducer. All echocardiographic measurements were performed according to the rec-

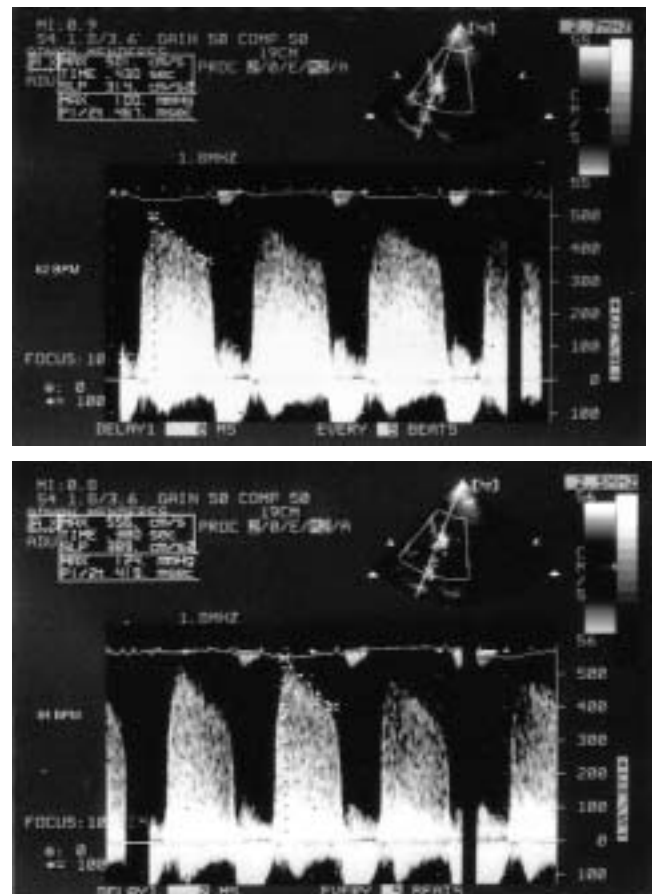


Figure 2: Continuous-wave Doppler measurements of moderate AR, recorded at two different heart rates (HR). A) Baseline pressure half-time (PHT) and slope measurement: HR 62 bpm, PHT 467 ms, slope 314 cm/s^2 . B) PHT and slope measurements after HR increase: HR 84 bpm, PHT 419 ms, slope 389 cm/s^2 .

ommendations of the American Society of Echocardiography (11). Left ventricular volumes were calculated by an ellipsoid monoplane area-length method from an apical four-chamber view. Left ventricular performance was evaluated by measuring fractional shortening (FS) as:

$$EDD - ESD / EDD,$$

where EDD is the end-diastolic diameter and ESD is the end-systolic diameter.

The ejection fraction (EF) was then calculated as:

$$EDV - ESV / EDV,$$

where EDV is the end-diastolic volume, and ESV is the end-systolic volume.

The severity of AR was assessed according to the RF measurements (12). RF was calculated as: Aortic regurgitant volume / Aortic forward stroke volume.

Aortic regurgitant volume was calculated as the difference between the forward stroke volume across the aortic valve (which represents both forward and regurgitant flow), and forward stroke volume across the

pulmonary valve (cardiac output), which represents only forward flow.

Hence:

$$RF = \text{Regurgitant volume} / \text{Aortic forward stroke volume}$$

$$= (\text{Aortic forward stroke volume} - \text{Pulmonary forward stroke volume}) / \text{Aortic forward stroke volume}$$

The aortic forward stroke volume was calculated as: Cross-sectional area (CSA) × velocity time integral (VTI) of the left ventricular outflow tract.

Pulmonary forward stroke volume (cardiac output) was calculated as:

$$CSA \times \text{VTI of the right ventricular outflow tract.}$$

The severity of AR was graded as either mild (RF <20%), moderate (RF 20-40%), or severe (RF >40%).

Color M-mode Doppler evaluation

Color M-mode Doppler measurements were obtained from an apical five-chamber view or from an

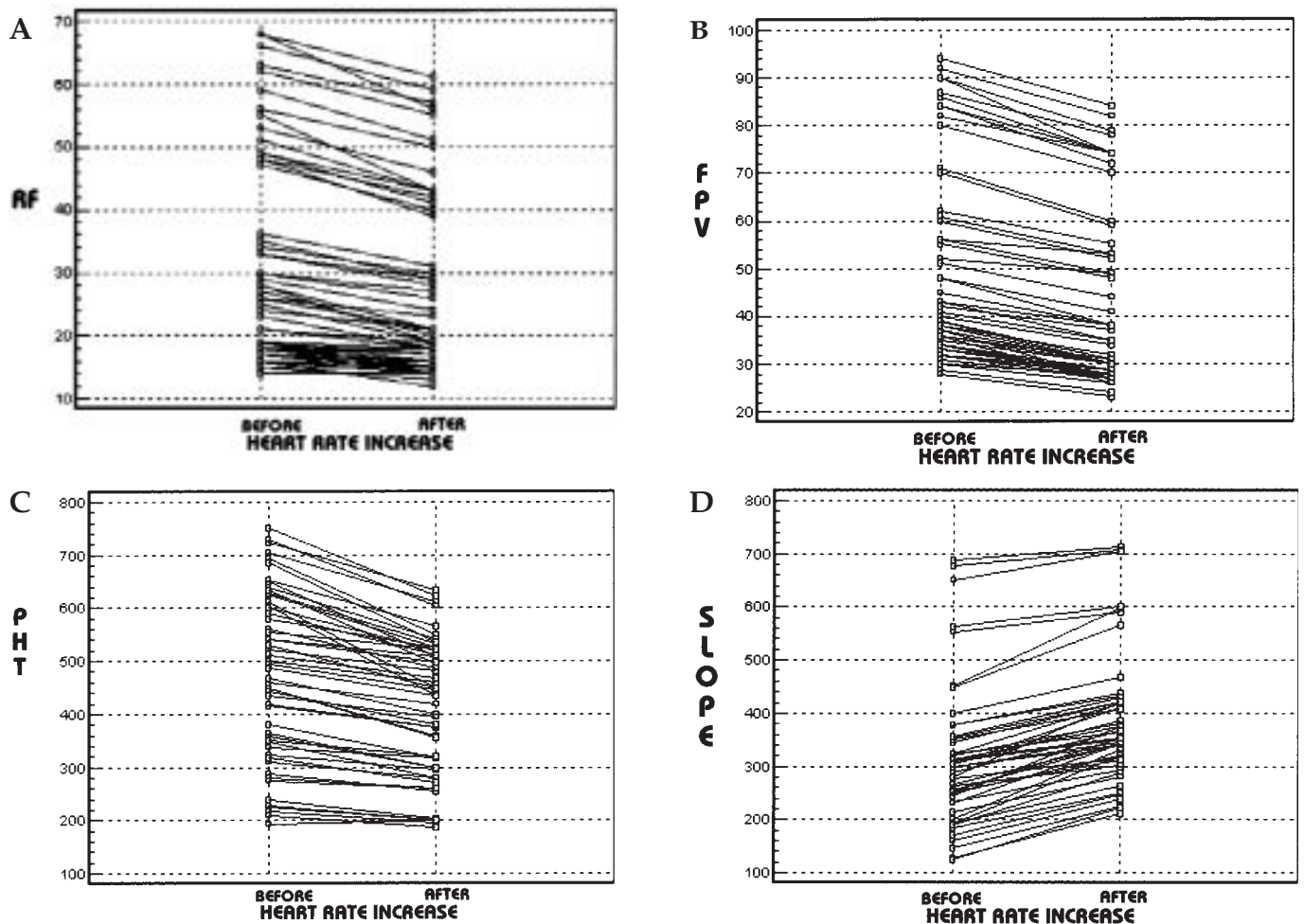


Figure 3: Changes in: A) Regurgitant fraction (RF, %); B) Flow propagation velocity (FPV, cm/s); C) Pressure half-time (PHT, ms); D) Slope (cm/s²) during an increase in heart rate (HR).

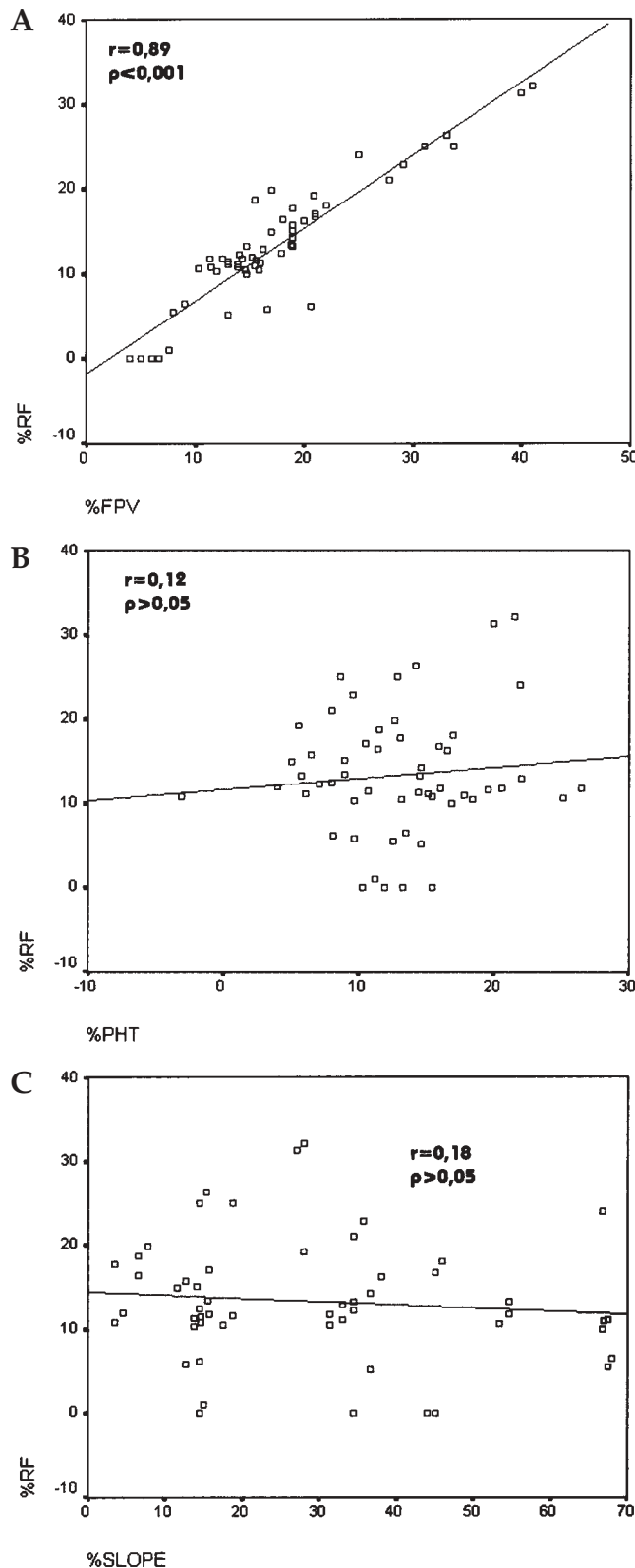


Figure 4: Correlations of percentage variations in regurgitant fraction (RF) with: A) Percentage variation in flow propagation velocity (FPV); B) percentage variation in pressure half-time (PHT); and C) percentage variation in slope.

apical long-axis view. Attempts were made to place the M-mode cursor as parallel as possible to the AR flow obtained by color Doppler. Before color M-mode Doppler measurements were made, the color scale of the equipment was adjusted for aliasing. The narrowest sector angle that allowed best visualization of the regurgitant jet was used, and color M-mode Doppler recording was performed. Adjustments were made to obtain the longest column of flow from the aortic valve to the left ventricle. Color M-mode Doppler echocardiograms were recorded on videotape using a sweep speed of 100 mm/s. The FPV was measured as the slope of the first aliasing velocity from the aortic valve to the left ventricular cavity (cm/s) (Fig. 1). The slope of the color M-mode flow was described as the slope of a line (drawn by hand) along the color/no-color border as described by Brun et al. (13). Three measurements of cardiac cycles were made in all patients, and the average value was calculated.

Continuous-wave Doppler evaluation

Continuous-wave Doppler recordings were obtained from the cardiac apex using either apical five-chamber or apical long-axis views. Color Doppler was used to align the Doppler beam parallel to the flow. The slope of diastolic deceleration was determined as the slope of a straight line drawn along the peak velocities throughout diastole (Fig. 2A and B). The PHT was defined as the time required for the initial early diastolic transvalvular pressure gradient to be halved (Fig. 2A and B). Three measurements of cardiac cycles were made in all patients, and the average value was calculated.

Inter- and intra-observer variabilities

In order to determine inter-observer variability, color M-mode and CW Doppler measurements were made by a second observer from the video sequences. To determine intra-observer variability, all patients were re-analyzed by the first observer two weeks later. Observer variability was defined as: (Absolute difference between two observations)/Mean value, with the result expressed as a percentage.

Statistical analysis

All values were expressed as mean \pm SD. Variations in the parameters at different heart rates were evaluated using a paired-sample *t*-test. Correlations between FPV, CW Doppler parameters and RF values were obtained using the Pearson correlation and linear regression analysis. A p-value <0.05 was considered to be statistically significant.

Table I: Changes in clinical and echocardiographic parameters during increase in heart rate (HR)*.

Parameter	Baseline (I)	After atropine sulfate (II)	Absolute difference between baseline and after HR increase	Percentage difference between baseline and after HR increase	p-value (I versus II)
HR (bpm)	77.8 ± 8.9	103 ± 9.9	26 ± 8	35 ± 13	<0.001
SBP (mmHg)	147 ± 31	142 ± 32	5.1 ± 7.4	3.4 ± 3.6	NS
DBP (mmHg)	76 ± 21	80 ± 19	3.5 ± 12	3.2 ± 13.2	NS
LVEDD (mm)	51.4 ± 4.9	50.9 ± 5.4	1.5 ± 1.2	3.1 ± 2.5	NS
LVESD (mm)	32.1 ± 3.5	31.8 ± 3.8	0.8 ± 0.6	1.7 ± 1.5	NS
EF (%)	66.8 ± 4.5	67.2 ± 4.3	1.3 ± 1.4	2.8 ± 3.1	NS
FS (%)	37.2 ± 3.5	38.1 ± 3.7	0.6 ± 1.0	1.3 ± 2.2	NS
RF (%)	31.2 ± 16	26.7 ± 13.9	4.5 ± 2.7	14.2 ± 6.3	<0.001
FPV (cm/s)	51 ± 21	44 ± 19	7.1 ± 2.8	14.6 ± 4.5	<0.001
PHT (ms)	468 ± 154	411 ± 128	63 ± 48	12.8 ± 5.2	<0.001
Slope (cm/s ²)	291 ± 136	358 ± 122	67 ± 31	22.5 ± 13.7	<0.001

*Values are mean ± SD.

DBP: Diastolic blood pressure; EF: Ejection fraction; FPV: Flow propagation velocity; FS: Fractional shortening; LVEDD: Left ventricular end-diastolic diameter; LVESD: Left ventricular end-systolic diameter; NS: Not significant; PHT: Pressure half-time; RF: Regurgitant fraction; RV: Regurgitant volume; SBP: Systolic blood pressure.

Results

Variations in HR, systolic and diastolic blood pressures, left ventricular end-diastolic and end-systolic dimensions, EF, FS, FPV, PHT and slope of AR during the HR increase are listed in Table I. In addition, absolute and percentage differences in the measured parameters between baseline and after HR increases are listed in Table I.

Changes in RF, FPV, PHT and slope during HR increases are illustrated in Figure 3A-D. There was a highly significant correlation between the percentage variation in RF and in FPV ($r = 0.89$, $p < 0.001$), though the variation in RF did not correlate with the variation in PHT and slope (Fig. 4).

The percentage variation in HR did not correlate with the percentage variation in PHT, slope, FPV and

RF in all patients (Fig. 5). In the subgroup analysis of patients with mild, moderate and severe AR, the percentage variation in HR did not correlate with the percentage variation in RF, FPV, PHT and slope in all of the AR subgroups.

The increased ratio of HR was $35 \pm 13\%$. However, the decreased ratios of RF, FPV and PHT values were $14.2 \pm 6.3\%$, $14.6 \pm 4.5\%$ and $12.8 \pm 5.2\%$, respectively, while the increased ratio of the slope value was $22.5 \pm 13.7\%$ (Tables I and II). The percentage variations in RF and FPV values with an HR increase were more prominent in the mild AR subgroup than in the moderate and severe AR subgroups (Table II).

Inter- and intra-observer variability

Inter- and intra-observer variability was assessed by linear regression between measurements, and also as a

Table II: Baseline and post-heart rate increase (HRI) values and change from baseline to post-HR increase (Δ BL-HRI; %) of regurgitant fraction (RF), flow propagation velocity (FPV), pressure half-time (PHT) and slope in mild, moderate, severe aortic regurgitation (AR) subgroups.

Severity of AR	RF			FPV			PHT			Slope		
	Baseline	Post-HRI	Δ BL-HRI	Baseline	Post-HRI	Δ BL-HRI	Baseline	Post-HRI	Δ BL-HRI	Baseline	Post-HRI	Δ BL-HRI
Mild	18.3±0.9	15.1±1.3	17.3±5.3	34.0±3.1	28.2±2.1	16.2±5.3	560±87	486±67	12.4±3.7	220±57	276±45	24.6±12.9
Moderate	29.1±5.7	24.9±5.3	13.9±2.6	48.1±8.4	41.4±8.2	14.0±3.7	505±118	428±98	15.6±6.1	269±49	320±36	18.8±13.3
Severe	55.9±8.2	49.4±7.4	11.8±7.6	85.1±7.1	74.1±7.2	12.6±2.7	259±44	232±39	9.4±3.8	432±166	536±148	23.6±14.1
Total	31.2±16	26.7±13.9	14.2±6.3	51±21	44±19	14.6±4.5	468±154	411±128	12.8±5.2	291±136	358±122	22.5±13.7

percentage of variability for the color M-mode, CW Doppler and RF measurements of AR. The intra-observer variability was $6 \pm 4\%$ for the FPV, $9 \pm 4\%$ for the PHT, $8 \pm 4\%$ for the slope, and $8 \pm 5\%$ for the RF. The inter-observer variability values for these parameters were $7 \pm 4\%$, $8 \pm 5\%$, $9 \pm 4\%$ and $9 \pm 6\%$, respectively.

Discussion

It has been shown previously that FPV attains higher values as the severity of AR is increased, and is also highly correlated with the angiographically assessed AR degree (10). To the best of the present authors' knowledge, this is the first study to analyze the effect of HR on FPV, and to show that FPV was decreased as a result of an increase in HR.

The results of previous studies have suggested that an increase in HR might have a beneficial effect on the hemodynamic condition of patients with AR (8,14,15).

Such an increase causes a shortening of the diastolic time in which regurgitation occurs, and may also lead to a decrease in the regurgitant volume (9). In the present study, an increase in HR caused a significant reduction in the RF, which was indicative of an improvement in the regurgitation.

In the present study, a shortening of the PHT and an increase in the slope of AR - both of which are regarded as signs of worsening regurgitation - were found as a result of an increase in HR. The PHT and slope of aortic regurgitant velocity curve obtained by CW Doppler echocardiography reflect the rate at which the aortic and left ventricular pressures equilibrate across the regurgitant orifice during diastole (4,6). Several studies have shown a good correlation between the slope and PHT of the regurgitant flow curve with AR severity (2,9,16). The rate of decrease in aortic diastolic pressure is greater in patients with more severe regurgitation; therefore, a rapid equilibration of the aortic

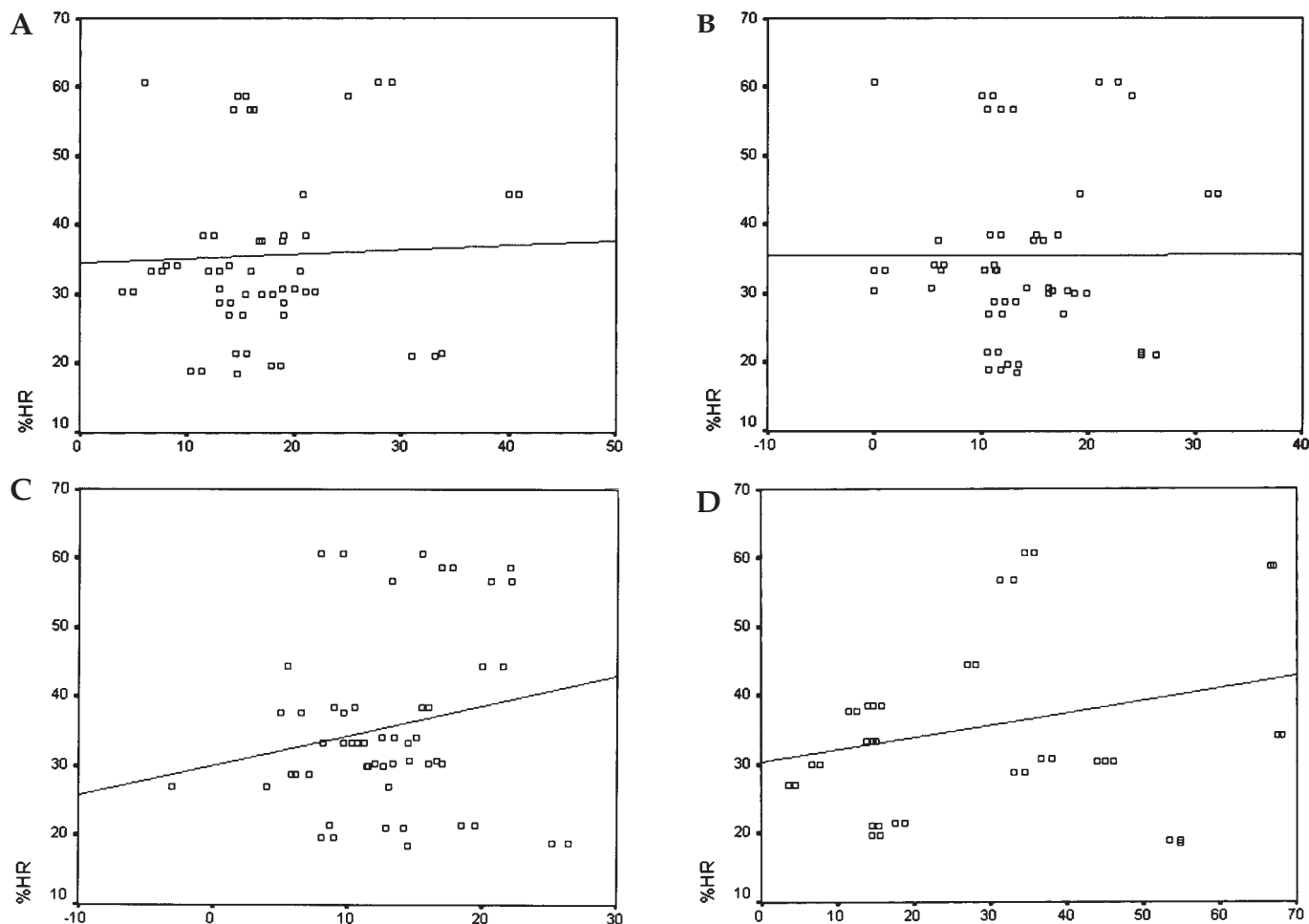


Figure 5: Correlations of percentage variations in heart rate (HR) with: A) Percentage variation in FPV; B) percentage variation in regurgitant fraction (RF); C) percentage variation in pressure half-time (PHT); and D) percentage variation in slope.

and left ventricular pressures reflects severe regurgitation. A short PHT or a steep slope are considered to be conventional signs of severe regurgitation (1-6). An increased HR decreases the left ventricular end-diastolic pressure and influences the rate of fall in aortic diastolic pressure (14-17). These variations cause a more rapid equilibration of aortic and left ventricular pressure, resulting in a steeper slope and shorter PHT (9). This variation in the slope and PHT of aortic regurgitation occurs in the presence of a prevalent hemodynamic improvement.

In the present study, however, an increase in HR was found to cause a decrease in FPV, which is a sign of improving regurgitation. A reduction in flow velocity, according to the Bernoulli equation, occurs as a result of a reduction in the pressure gradient. Therefore, the flow velocity between two chambers will vary directly with pressure gradient. With AR, the aortic valve is a restrictive orifice that controls the rate of diastolic flow from the high-pressure aorta to the low-pressure left ventricle. Gozzelino et al. (9) showed that an increase in HR, obtained either by cardiac pacing or with atropine sulfate administration, caused a significant decrease in the difference in the aortoventricular gradient between proto- and end-diastole constantly, and also a decreasing trend in the mean diastolic gradient per minute, which was expressing the total force per minute causing regurgitant flow (9). This reduction in diastolic aortoventricular pressure gradient might explain the decrease in FPV which occurs as a result of an increase in HR.

In the present study, the percentage variation in RF correlated well with the percentage variation in FPV. However, the variation in RF did not correlate with the variation in PHT and slope, both of which are related to pressure equilibration between the aorta and left ventricle. Although these parameters are dependent upon the size of the regurgitant orifice, they may be influenced by other factors, such as systemic vascular resistance and aortic or ventricular compliance (4-6,18). Heart rate changes may also affect these factors, and may be responsible for the finding that there is no association between the RF and PHT or slope. This result might show that FPV is affected by mainly the regurgitant fraction, and is either minimally affected or not affected by other factors such as systemic vascular resistance and aortic or ventricular compliance.

In the present study, there was no correlation between the percentage variation in PHT, slope, FPV and RF with the percentage variation in HR. This may be explained by the effect of HR on the diastolic time during which aortic regurgitation occurs. Especially in severe AR, a shortening of diastolic time with increasing HR appears to influence to a lesser extent the regurgitant volume because the majority of this vol-

ume occurs in early diastole (4,19-23). It was also found that the percentage variations in RF with HR increases were less prominent in the severe AR subgroup than in the moderate and mild AR subgroups. Therefore, HR changes do not correlate with regurgitant fraction and other Doppler parameter changes.

In the subgroup analysis of patients with AR, the percentage variation in HR did not correlate with the percentage variations in RF, FPV, PHT and slope in all subgroups, most likely because of the interactive effect of multiple determinants of the color M-mode and CW Doppler aortic regurgitant velocity curves (4,6).

Study limitations

A major limitation of the present study was that the 'gold standard' echocardiographic RF method used to assess AR may be prone to measurement errors, with accurate measurements being both time-consuming and tedious. Poor lateral resolution may affect the measurement of pulmonary artery diameter, and minor changes in calculating aortic or pulmonary stroke volumes would lead to significant errors in the RF. The inter-observer variability was therefore relatively high. However, quantitation of RF is the most direct method to assess AR severity, and corresponds most closely to the quantitative angiographic 'gold standard' (24). When aortic RF was determined as the difference between Doppler-derived aortic and pulmonary flow in patients with AR, an excellent correlation of 0.94 with the invasively determined RF was recorded (25). The presence of mitral regurgitation may affect calculation of the total left ventricular stroke volume, though in the present study the presence of more than mild mitral regurgitation was an exclusion criterion. Despite these limitations, this approach provides quantitative, ordered data which, when measured accurately in appropriate patients, should provide a reasonable estimation of AR. Alignment between the flow and the ultrasound beam is crucial, as a beam that is incorrectly oriented due to regurgitant jet eccentricity may lose flow close to the aortic valve orifice and induce a false low propagation speed. Hence, regurgitant jet eccentricity was accepted as an exclusion criterion. Visual linear fitting of the AR flow velocity curve may be another important source of error. The PHT measurement is most accurate in steep aortic regurgitation flow velocity curves, but in flat curves it is very sensitive to small changes in visual fitting. This may explain the higher PHT variability with a small RF than with severe AR. The design of the present study did not include invasive measurements, which would have provided a 'gold standard' assessment of the aortic regurgitant fraction. However, use of the angiographic RF rather than echocardiographic grading of AR as a standard reference will not provide

practical standardization. Even a very slight change in calculating either stroke volume or cardiac output will lead to a significant error in the calculated RF. The pressure drop across the aortic valve is dependent on left ventricular compliance, systemic vascular resistance and loading conditions. Previous studies have demonstrated the effect of these variables on the deceleration slope and PHT measurements (4,5). These factors, which affect the pressure drop across the aortic valve, may have adverse effects on FPV measurements. In the present study, the effects of these parameters on FPV measurements were not examined, and this might be considered another limitation.

In conclusion, FPV and CW Doppler parameters of the AR were seen to be rate-dependent. An increase in HR caused a decrease in RF and FPV of the aortic regurgitation, and both of these changes are indicative of improving regurgitation. Hence, FPV is considered to be a more valuable parameter than PHT and slope in determining improvements in AR as a result of an increase in HR.

References

1. Teague SM, Heisimer JA, Anderson JJL, et al. Quantification of aortic regurgitation utilizing continuous Doppler ultrasound. *J Am Coll Cardiol* 1986;8:592-599
2. Labovitz AJ, Ferrara RP, Kern MJ, et al. Quantitative evaluation of aortic insufficiency by continuous-wave Doppler echocardiography. *J Am Coll Cardiol* 1986;8:1341-1347
3. Masuyama T, Kodama K, Kitabatake A, et al. Noninvasive evaluation of aortic regurgitation by continuous-wave Doppler echocardiography. *Circulation* 1986;73:460-466
4. Griffin BP, Flachskampf FA, Siu S, et al. The effects of regurgitant orifice size, chamber compliance, and systemic vascular resistance on aortic regurgitant velocity slope and pressure half-time. *Am Heart J* 1991;122:1049-1056
5. Griffin BP, Flachskampf FA, Reimold SC, et al. Relationship of aortic regurgitant velocity slope and pressure half-time to severity of aortic regurgitation under changing hemodynamic conditions. *Eur Heart J* 1994;15:681-685
6. Samstad S, Hegrenars L, Skjaerpe T, et al. Half-time of diastolic aortoventricular pressure difference by continuous-wave Doppler ultrasound: A measure of the severity of aortic regurgitation. *Br Heart J* 1989;61:336-343
7. Firth BG, Dehmer GJ, Nicod P, et al. Effect of increased heart rate in patients with aortic regurgitation. *Am J Cardiol* 1982;49:1860-1867
8. Laniado S, Yellin EL, Yoran C, et al. Physiologic mechanisms in aortic insufficiency. I. The effect of changing heart rate on flow dynamics. II. Determinants of Austin Flint Murmur. *Circulation* 1982;66:226-235
9. Gozzelino G, Aletto C, Curti MT, et al. The effect of heart rate on the slope and pressure half-time of the Doppler regurgitant velocity curve in aortic insufficiency. *J Am Soc Echocardiogr* 1996;9:516-526
10. Onbasili OA, Tekten T, Ceyhan C, et al. A new echocardiographic method for the assessment of the severity of aortic regurgitation: Color m-mode flow propagation velocity. *J Am Soc Echocardiogr* 2002;15:1453-1460
11. Henry WL, De Maria A, Framiak R, et al. Report of the American Society of Echocardiography Committee on nomenclature and standards in two dimensional echocardiography. *Circulation* 1980;62:212-217
12. Otto CM, Pearlman AS. *Textbook of Clinical Echocardiography*. WB Saunders Co., Philadelphia, 1995:255-263
13. Brun P, Tribouilloy C, Duval AM, et al. Left ventricular flow propagation during early filling is related to wall relaxation: A color M-mode Doppler analysis. *J Am Coll Cardiol* 1992;20:420-432
14. Judge TP, Kennedy JW, Lowell B, et al. Quantitative hemodynamic effect of heart rate in aortic regurgitation. *Circulation* 1971;44:355-367
15. Nakamura T, Nezu S, Sawayama T, et al. The effect of heart rate on cardiac hemodynamics in patients with aortic regurgitation. *Kokju-To-Junkan* 1992;40:169-174
16. Wilkenshoff UM, Kruck I, Gast D, et al. Validity of continuous wave Doppler and color Doppler in the assessment of aortic regurgitation. *Eur Heart J* 1994;15:1227-1234
17. Meyer TE, Sarelli P, Marcus RH, et al. Beneficial effect of atrial pacing in severe aortic regurgitation and role of M-mode echocardiography in determining the optimal pacing interval. *Am J Cardiol* 1981;67:398-403
18. Vanoverschelde JJ, Taymans-Roberts AR, Raphael DA, et al. Influence of transmitral filling dynamics on continuous wave Doppler assessment of aortic regurgitation by half-time methods. *Am J Cardiol* 1989;64:614-619
19. Judge TP, Kennedy JW. Estimation of aortic regurgitation by diastolic pulse analysis. *Circulation* 1970;41:659-665
20. Rackley CE, Edwards JE, Karp RB, et al. Aortic valve disease. In: Hurst W (ed.), *The Heart*. McGraw-Hill, New York, 1990:244-301
21. Libanoff AJ. A hemodynamic measure of aortic regurgitation. Half-time of fall in aortic pressure during diastole. *Cardiology* 1973;58:162-173

22. Croft CH, Lipscomb K, Mathis K. Limitation of qualitative angiographic grading in aortic or mitral regurgitation. *Am J Cardiol* 1984;53:1593-1598
23. Gozzelino G, Molendi V, Pizzetti F, et al. Influence of heart rate on Doppler aortic regurgitant velocity curve. *Echocardiography* 1999;16:1-9
24. Weyman AE, Griffin BP. Left ventricular outflow tract. In: Weyman AE (ed.), *Principles and Practice of Echocardiography*. Lea & Febiger, Philadelphia, 1994:538-541
25. Kitabake A, Ito H, Inou M, et al. A new approach to noninvasive evaluation of aortic regurgitant fraction by two-dimensional Doppler echocardiography. *Circulation* 1985;72:523-529