Regurgitant Flow Rate Estimation Using Doppler Color Flow Imaging in Children with Mitral Regurgitation

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ÇOCUKLARDA MİTRAL YETERSİZLİK JETİ AKIM HIZININ RENKLİ DOPPLER EKOKARDİOGRAFİ İLE DEĞERLENDİRİLMESİ

Mitral yetersizliğinin (MY) Doppler ekokardiografi ile derecelendirilmesinde çeşitli kantitatif metodlar önerilmiştir. In vitro şartlarda yeni bir metod olan proksimal eş hızlı hemisferlerin yüzey alanı (PISA) kullanılarak akım hızının doğrulukla ölçülebildiği gösterilmiştir. Aynı prensibin renkli Doppler ekokardiografi ile klinikte de kullanılarak, belirli bir kan haciminin akım hızının (cm3/sn) = PISA (cm^2) x aliasing hızı (cm/cn) formülü ile hesaplanabileceği düşünülmüştür. MY olan çocuklarda bu metodun klinik kullanımını belirleyen ilk çalışma olması nedeni ile bu araştırma yapılmıştır. Yaşları sekiz ay ile 12 yıl arasında (ortalama : 3.1 yıl) olan 37 hasta çalışmaya dahil edilmiştir. PISA-Doppler ölçümleri ile kateterizasyon sonuçları arasında anlamlı bir ilişki saptanmıştır ($r=0.93$, $p<0.0001$). MY jet alanının sol atrium alanına orantısı anjiografik derecelendirme ile karşılaştırıldığında yine anlamlı bir ilişki bulunmuştur ($r=0.92$, $p<0.0001$). Ancak, anjiografi ile karşılaştırıldığında PISA metodu ile elde edilen sonuçların jet alanı orantısına kıyasla daha iyi bir korrelasyon gösterdiği saptanmıştır. Sonuç olarak, mitral kapak yetersizliğinin noninvaziv kantitatif derecelendirilmesinde PISA metodu ile elde edilen sonuçların hastaların takibinde kullanımının güvenilir olduğu kanaatine varılmıştır.

Anahtar kelimeler: *Mitral yetersizlik, jet akım hızı, eş hızlı hemisferlerin yüzey alanı.*

Over the recent years Doppler echocardiography has emerged as the noninvasive method of choise for confirming the diagnosis and severity of mitral regurgitation. Color flow mapping and calculation of regurgitant fraction have been the most widely studied methods (1-5). A new method, which quantitates the proximal isovelocity surface area (PISA), more recently addressed as the flow convergence region (FCR), on the left ventricular side has been investigated in only a few clinical studies (6-11). According to the hydrodynamic theory, flow approaches an orifice in a series of concentric hemispheric shells of increasing velocity known as the FCR. Doppler color flow mapping of FCR may be accomplished once the blue-red aliasing radius is identified on the left ventricular side. Volume flow rate (ml/sec) can be calculated as PISA (cm^2) x aliasing velocity (cm/sec). Flow calculations with this technique has been examined in vitro studies and seem to be less influenced by technical factors and orifice shape which alter jet appearance (12-18). Recently the technique was shown to allow in understanding the pathophysiology of the regurgitation (11). The purpose of this study is to correlate the results of the PISA and jet area methods to angiographic grading in a clinical setting.

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MATERIALS and METHODS

Thirty-seven patients, aged from eight months to 12 years (mean: 3.1 years) with varying degrees of mitral regurgitation were included in the study. All of the patients were in sinus rythm. The etiologly of the mitral regurgitation included residual mitral regurgitation present in late post-operative period following mitral annuloplasty in 18 patients, dilated congestive cardiomyopathy in nine patients, mitral valve prolapse in four patients, rheumatic carditis in six patients. Patients with arrhythmias, aortic valve disease, mitral stenosis, intra-cardiac shunts and eccentric regurgitant jets were excluded.

Angiographic grading was available in all of the patients. Cardiac catheterization was carried out after obtaining a written consent and within 1-2 hours of the echocardiographic examination. Left ventriculography was imaged in 60 degrees left anterior oblique and 20 degrees cranial and 45 degrees right anterior oblique projection using Iopromid at a maximum total dose of 5 ml/kg. Qualitative angiographic grading was done into four grades by an observer blinded to the echocardiographic results. 1+ was regurgitant jet with minimum opacification of the left atrium which cleared rapidly. 2+ was regurgitant jet with moderate opacification of the left atrium which cleared rapidly. 3+ when the left atrium was as intense as that of the left ventricle and aorta on late films. 4+ when left atrium was more intense than that of the left ventricle and aorta, and intense opacification persisted throughout the entire series of films [19].

Echocardiophic studies were done with Acuson XP-128 and 3 or 5 MHz transducers. The Nyquist limit ranged from 43 to 64 cm/sec. The gain level was kept just below that which produced a noise in the color signal. The results were obtained in the apical four chamber and parasternal long axis views. The radius of the proximal flow convergence region was measured at a point in midsystole from the first aliasing limit to the ventricular edge of the mitral leaflets nearest to the regurgitant orifice and staying as parallel as possible to the direction of the transducer in the apical four chamber view. The measurements were analyzed using the Freeland computer system. The following equation was used to calculate the instantaneous regurgitant flow where r= radius of the aliasing surface, NL= Nyquist limit, Q= instantaneous flow in L/min [7].

$$Q = \frac{2nR^2 \times NL \times 60}{1000}$$

The resultant value was subsequently indexed for body surface area.

Principle: Since color Doppler is capable of showing spatial relations of laminar flow reliably, the area of convergence region can be quantified. The aliasing boundary with a known velocity and a measurable radial distance from the center of the orifice to the color change can be used to determine an isovelocity hemisphere. The zone of proximal flow acceleration is made up of concentric hemispheric shells of equal and accelerating velocities, the smallest hemisphere being near the orifice having the highest velocity. Fluid dynamics theory states that the flow through any of these isovelocity surfaces is identical and equal to the velocity multiplied by the surface area. The velocity at which aliasing occurs multiplied by the calculated first isovelocity surface area yields the instantaneous regurgitant flow rate.

Mitral regurgitation was also quantified by measuring the jet area at its maximum turbulent area both in the apical four chamber and parasternal long axis views. The results were expressed as an average of the ratio of jet area to the area of the left atrium in two orthogonal planes.

Fifteen randomly selected patients were analyzed by two observers blinded to the results. Interobserver variability was measured for regurgitant flow rates. The radius of the proximal isovelocity surface was measured by the same observer on two consecutive days to calculate the intraobserver variability.

Statistics

Data are expressed as mean±1 SD. Differences between angiographic grades were expressed with the use of student's t test for unpaired data. Spearman's rank correlation method was used to assess the association between the color Doppler results and the left ventricular angiographic degree of mitral regurgitation. A comparison between instantaneous regurgitant flow rate and jet area percentage was done by means of linear regression analysis. Comparisons of measurements of heart rates and blood pressures were made with student's t test for paired values. The level of statistical significance was defined at $p<0.05$.

RESULTS

By angiography, nine patients had 1+, 11 had 2+, 14 had 3+ and four had 4+ mitral regurgitation. There was no statistically significant differences in heart rate or blood pressure obtained during the noninvasive measurements and at the time of the catheterization ($p>0.05$). Regurgitant jet area percentage, flow rate index, mean aliasing radius and mean Nyquist limit values obtained in the four angiographically-determined severity degrees of MR are presented in Table 1.

The relationship between the calculated regurgitant flow rate using the PISA method correlated highly

Table 1. Regurgitant jet area percentage, flow rate indices, mean aliasing radius and mean Nyquist limits according to angiographically determined degrees of severity of mitral insufficiency.

	Angiographic grading						
	1+ (n=9)	p	2+ (n=11)	p	3+ (n=14)	p	4+ (n=4)
Area % :	6.2±2.3	< 0.001	9.04±2	< 0.001	13.4±2.1	< 0.001	32±8.8
Regurgitant flow rate index : (L/min/m2)	3±1.3	< 0.05	6.7±3.6	< 0.0001	14.9±1.6	< 0.0001	34±13.7
Mean aliasing radius (mm)	1.38±3.4	< 0.05	3.5±1	< 0.05	7.5±2.4	< 0.05	11.8±4.6
Mean Nyquist limit (cm/sec)	57±7	> 0.05	53±7	> 0.05	52±0.8	> 0.05	50±4.9

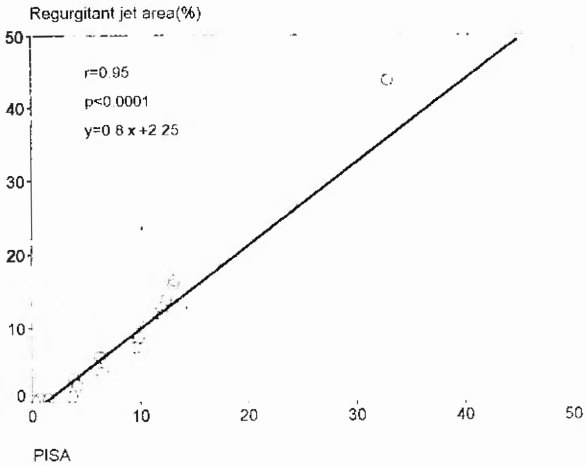

Fig 1. Correlation between regurgitant flow rate using the proximal isovelocity surface area (PISA) method on the x axis and ratio of color Doppler regurgitant jet area on the y axis. (r: 09.95, p<0.0001)

significantly with the ratio of regurgitant jet area to left atrial area (Fig. 1).

When measures of instantaneous regurgitant flow rate were correlated with angiographic grade of mitral regurgitation, a correlation coefficient of r=0.93 (p<0.0001) was obtained with a mild overlap between the groups (Fig. 2). The correlation between the ratio of jet area to left atrial area and the angiographic grade of mitral regurgitation was significant with a correlation coefficient of r=0.92, (p<0.0001). There was mild overlap between the groups (Fig. 3).

The interobserver variability was 1.4 % ± 3.9 % for calculated regurgitant flow rates. The intraobserver variability for the radius measurements was 0.6 ± 2.9 % (mean difference ± SD).

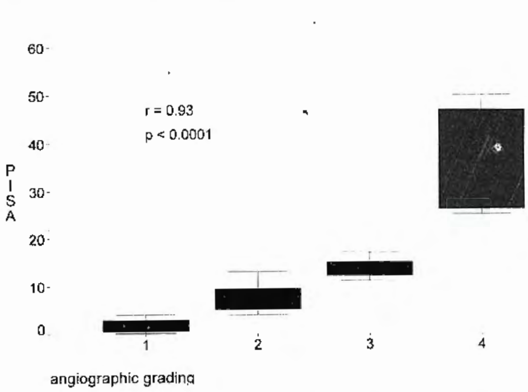

Fig 2. Boxplot showing comparison of color-flow Doppler imaged instantaneous regurgitant flow rate calculation for each angiographic grade of mitral regurgitation in 37 patients. Standard deviation values for each angiographic group are shown. Black areas represent values between 25th and 75th percentile

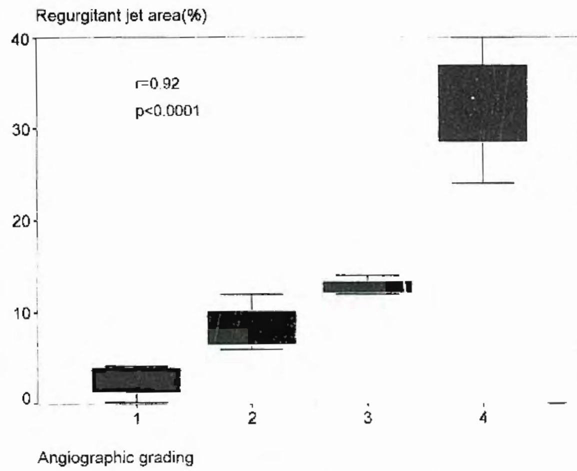

Fig 3. Correlation showing comparison of the ratio of color flow Doppler regurgitant jet area to left atrial area calculation with angiographic grade of mitral regurgitation in 37 patients. Standard deviation values for each angiographic group are shown. Black areas represent values between 25th and 75th percentile.

DISCUSSION

With the introduction of two-dimensional color Doppler flow imaging, measurements of jet length, width and area were used for the quantification of valvular regurgitation [1,2]. Some authors have estimated 1+ mitral regurgitation by echocardiography when the jet was located immediately posterior to the mitral valve and 4+ when the flow was present diffusely all over the atrium [3]. This sort of grading faces problems when the regurgitant jet is narrow and reaches the roof of left atrium. To minimize such problems, some authors have chosen to grade regurgitation as a fraction of regurgitant area to left atrial area [1,2].

Unfortunately, mechanical factors such as gain, transmitted frequency, wall filter and pulse repetition frequency interfere with accuracy of mitral regurgitation quantification [20-40]. Hemodynamic factors including blood viscosity, afterload, preload, orifice area, regurgitant flow velocity and flow duration have been shown to effect Doppler color jet area [1,2,25,26]. Analysis of the converging flow proximal to a restrictive orifice has been proposed as an alternative method in the quantification of flow rate in regurgitant lesions [13,14].

Yamamura et al. have previously reported that minimum color encoded velocity area proximal to the reguritant orifice correlates well with angiographic severity of mitral regurgitation [27]. Later, minimum color encoded velocity area was shown to be affected by ultrasound machine factors, unlike the proximal isovelocity aliasing surface (22). In vitro studies, the color aliasing radius was shown to correlate extremely well with the actual flow rate (r=0.99) (14,17,18). In addition, this approach has the advantage over other color Doppler methods in that the PISA is apparently not affected by changes in machine factors (7,14-16).

In this study, PISA method was applied clinically for estimating regurgitant volume flow in children with mitral regurgitation. The correlation of instantaneous flow rate using the PISA method to the jet area-to-left atrial area ratio was significant with a correlation coefficient of r=0.95 (9) (p<0.0001, Fig. 1). In our study population, a good correlation was observed between the jet area and angiographic degree of mitral regurgitation (r=0.92, p<0.001, Fig. 3). Helmcke et al (1) have reported a modest correlation (r=0.78) in a nonsimultaneous comparison between angiographic grading and jet/left atrial area ratio. Later Spain et al (2) reported similar results with a modest correlation (r=0.76) between maximal jet area and aniographic grading, but in contrast to Helmcke et al (1) found no improvement in correlation when a ratio of jet size to left atrial area was used (r=0.71). The limitation regarding these studies was nonsimultaneity of color Doppler and angiography. The results observerd in our study is better (r=0.92), probably owing to the study design in which the patients were examined using different techniques with close proximity in timing.

Factors contributing to the disparity between color Doppler jet area and angiography are technical factors such as gain setting, depth and pulse repetition frequency (28). The distribution of jet area within the left atrium is not uniquely dependent on the amount of regurgitation, but also on the pressure gradient between the chambers (26). Another limitation in the analysis of jet area is eccentricity of the jet which leads to the underestimation of the degree of the mitral regurgitation (29). Because the FCR is located in the high pressure chamber, PISA technique appears to be independent of the direction of the jet allowing for an accurate prediction of the severity of the regurgitation (8).

The proximal FCR method has been studied several times in computer simulations and in in-vitro flow models (12,14,17,18). Until now clinical experience with the PISA method has been limited (8-11). The principle of flow convergence was also used in the assessment of shunt flow across a ventricular septal defect (6). In this study, similar to previous clinical studies there was a significant correlation between PISA-Doppler and catheterization results (r=0.93, p<0.001, Fig. 2). Bargiggia et al (8) have found a close correlation between the Doppler derived regurgitant flow rate and angiographic degree of mitral regurgitation in 52 adults (r=0.91, p<0.001). They also found a significant correlation between angiographic regurgitant volume and flow calculated by Doppler (r=0.93, SEE:123 ml/sec) (8). Among several comparisons made in their study, Utsunomiya et al (7) found significant correlation between the mitral regurgitant stroke volume using the PISA method and regurgitant jet area ratio (r=0.84, p<0.001). The formula they used was derived from previous in-vitro studies, such that regurgitant stroke volume = 8.05 x r2, where r is the maximum aliasing radius and 8.05 is the constant. The authors have concluded that the constant 8.05 may not be applicable to all cases of mitral regurgitation (7). We have used a separate formula and found a better correlation between the instantaneous regurgitant flow rate and jet area ratio (r=0.95, p<0.0001). However, our number of patients were smaller.

Rivera et al (9) compared proximal FCR method to the regurgitant stroke volume and regurgitant fraction calculated by pulsed Doppler and found very good correlations for both comparisons, r=0.93 and r=0.89, respectively.

Lower aliasing velocities using zero-baseline shift technique allows to detect the aliasing radius in patients with mild mitral regurgitation. Hence, care must be taken to avoid inappropriate use of low alias velocities which result in elongation of the aliasing contuor. Zero shifting below 50 % of the Nyquist limit must be avoided (11). The aliasing velocities in this study ranged from 43 cm/sec to 64 cm/sec which allowed for adequate visualization of the proximal FCR in all of the patients. Measuring the FCR radius in the direction of the transducer would execute major problems in the calculation of flow rates with conical shaped aliasing zones. The size of the regurgitant jet area was shown to vary during the regurgitant period [11]. This fact may account for discrepancies between the Doppler and angiographic data. In our opinion, the good agreement between the instantaneous regurgitant flow rate and angiographic grading demonstrate that the limitations do not pose a major problem.

Despite its various limitations, left ventricular angiography is still the most often used method of assessing the severity of mitral regurgitation. The sensitivity and specifity for the diagnosis of mitral valve repair or replacement of mitral regurgitation, using angiography as the gold standart were 100% and 93% by Doppler echocardioraphy as compared to 95% and 85% by clinical evaluation [3,30].

In conclusion, calculating mitral regurgitant flow rate from PISA provides excellent agreement with angiography and has the advantage of being a non-invasive clinical method.

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Düzeltme

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1) 111. sayfa 1. sütun 6. satırdaki $p<0.05$ yerine $p>0.05$ olacaktır.

2) Tablo 1'deki 15 ve 20. sıradaki olgulardaki değerler 1'er sütun kaymıştır. Dolayısı ile işlem öncesi gradientler eşlik eden hastalık hanesine gelmiştir. İki olguda 1'er sütun sağa kaydırma yapılırsa veriler düzelecektir.