Comparison between Patient-Aortic Valve Prosthesis Mismatch Determined by Transthoracic Echo-Doppler at Late Follow-up versus Preoperative Estimation

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SUMMARY

Background
Patient-aortic valve prosthesis mismatch (PPM) is associated with poor postoperative outcomes. Determination of aortic effective orifice area (EOA) indexed for body surface area (BSA) is useful to select suitable type and size of heart valve prosthesis in order to prevent patient-prosthesis mismatch.

Objective
The objective of this study was to compare the PPM estimated by indexed EOA with PPM determined by echo-Doppler at late follow-up.

Material and Methods
Fifty seven patients (43 men) who had undergone an aortic valve replacement in the previous 6 months were retrospectively assessed. After calculating BSA from the surgical report, indexed EOA, postoperative EOA (determined by the continuity equation with transthoracic echo-Doppler), preoperative and postoperative PPM were compared. An indexed EOA < 0.75 cm²/m² was considered aortic PPM.

Results
The prevalence of preoperative and postoperative PPM was 29.8% and 54.4%, respectively (p=0.029); 31% of MMP was severe. The prevalence of overweight in this sample was 80%.

Conclusions
In this group of patients with a high prevalence of overweight and patient-aortic valve prosthesis mismatch, the use of preoperative reference values of EOA indexed for BSA, and the EOA measured by echo-Doppler at late follow-up, showed significant differences between preoperative PPM and postoperative PPM. Further studies should not only include a larger sample, but should also check the method used for calculating valvular area (for example, in the left ventricular outflow tract).

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Key words > Aortic Valve - Echocardiography - Valvular Prosthesis

Abbreviations >

EOA	Effective orifice area	PPM	Patient-aortic valve prosthesis mismatch
GOA	Geometric orifice area	BSA	Body surface area
SD	Standard deviation	LVOT	Left ventricular outflow tract
BMI	Body mass index	LV	Left ventricle

BACKGROUND

The concept patient-aortic valve prosthesis mismatch (PPM) was first coined by Rahimtoola in 1978, (1) who defined it as the ratio between an inadequate prosthetic valvular orifice and patient's body surface area (BSA), meaning that the prosthetic orifice is smaller than the native valve orifice. The PPM produces obstruction of the left ventricular outflow tract (LVOT) generating subsequent high transvalvular

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pressure gradients. (2, 3). PPM is more frequently seen in elder patients (4) with small aortic roots, in women, and is generally associated with severe ischemic heart disease and poor ventricular function. (5)

Several studies have reported less ventricular mass regression, greater incidence of cardiac events and lower survival rates after valve replacement. Nevertheless, the clinical impact informed by other studies during the postoperative follow-up was unremarkable. The estimation of preoperative effective orifice area (EOA) indexed for patient's body surface area (BSA) at the time of surgery using EOA derived from reference values published in the literature for each prosthesis type and size, is a method used in to predict PPM.(6, 9, 10)

Although these reference values are crucial, some differences may exist, that is why some authors use the EOA calculated by cardiac echo-Doppler. (6) Other researchers perform their estimations using the *in vitro* and *in vivo* data supplied by the prosthesis manufacturers. (8, 11) Nevertheless, these values seem to be little reliable to decide the prosthesis size and type to implant in a particular patient according to the individual BSA, type of physical activity and ventricular function status. (6, 12)

The estimation of preoperative EOA based on reference values published for each type of prosthesis and the high prevalence of mismatch calculated by echo-Doppler reported in some series have made us think there might be some differences between both methods which cannot be attributed to mismatch variability. The objective of this study was to compare the PPM estimated by indexed preoperative EOA with PPM determined by transthoracic echo-Doppler at late postoperative follow-up.

MATERIAL AND METHODS

Population and design

We included fifty seven patients (43 men and 14 women) who were assessed by transthoracic echo-Doppler examination from July 2006 to July 2007. Data from the surgical report included weight, height, type, brand and size of the prosthetic device implanted. Anthropometric measurements (BSA, calculated from the Dubois' formula [13] and body mass index [BMI]) were estimated at surgery and before the study. Echo-Doppler, performed by an experienced operator, included measurement of left ventricular outflow tract (LVOT) using the parasternal long axis view closest to the aortic ring, and pulsed Doppler flow velocities with a sample volume positioned 5 mm immediately under the valve prior to flow acceleration or widening of the signal spectrum, in order to assess that both parameters were obtained at the same place. (14) Maximum and mean gradients across the prosthesis were calculated with continuous Doppler from the five-chamber apical view. The continuity equation was used to calculate EOA using the LVOT velocity-time integrals, the flow through the prosthesis and LVOT area. Values were indexed for BSA at the moment of the study. Three and five 2D-echocardiography and Doppler determinations were averaged in patients in sinus rhythm and in atrial fibrillation, respectively.

Preoperative PPM was diagnosed when EOA estimated from charts (Table 1) and indexed for BSA prior to surgery was lower than 0.75 cm^2/m^2 according to the type, brand and size of the implanted prosthesis; this value was associated with long-term survival. (7, 10, 15)

Preoperative PPM was compared to the current prevalence of PPM obtained in the postoperative echo-Doppler.

A BMI > 25 was considered overweight.

Ultrasound was performed with an Esaote My Lab 50 and Hewlet Packard image Point Hx with a 2 to 4 mHz transducer for a second harmonic imaging.

Formulas used

BSA = (weight $kg^{0.425}$) × ($height^{0.725}$) × 0.007184 (7) = m^2

BMI = weight/$height^2$

Continuity equation: EOA = LVOTa × TVI LVOT/ TVI AO = cm^2/m^2

LVOT area: $\pi \times r^2 = cm^2$

Statistical method

Qualitative variables are expressed as percentages, and comparisons were performed using chi-square test or Fisher's exact test. Continuous variables with normal distribution were expressed as mean ± standard deviation and compared with *t* Student's test or Wilcoxon rank test for non parametric distributions. Pearson coefficient of correlation was used to assess the linear association between the gradient

	Brands	Size 19	21	23	25
Biological heart valve prosthesis	St Jude®		1.3 (2)	1.5 (6)	
	Carpentier Edward®		1.5 (2)		2 (1)
	Hancock II®		1.18 (3)		
Bileaflet mechanical heart valve prosthesis	St Jude ®	1.3 (4)	1.73-2.01 (15)	2.13 (6)	2.3 (3)
	Carbomedics®	1.11 (1)			2.1 (1)
	Edward Mira®	1.2 (1)	1.6 (1)	1.6 (1)	
Monoleaflet heart valveprosthesis	Medtronic Hall®	1.19 (2)	1.34 (2)	1.53 (3)	1.9 (3)

Note: EOAs are expressed in cm^2 (number of cases)

Table 1. Effective aortic orifice areas determined by echo-Doppler in prosthesis with different models and sizes obtained from the literature (9, 10)

and the degrees of PPM. A two-tailed p value < 0.05 for was considered significant. Calculations were performed by the statistical packages Statistix 7.1 and Epinfo 3.4.1 for Windows.

RESULTS

Patient characteristics are summarized in Table 2. Most patients were men (75.4%) younger than women (62.8 [9.8] versus 74.3 [6.5] years old [SD], respectively). Men weighted more than women and their body surface area was greater, but the body mass index and the prevalence of overweight was similar between both sexes (weight [SD] 85.5 [14.6)] versus 67.9 [11.5] kg, BSA 1.97 [0.17] versus 1.66 [0.13], p < 0.01; BMI 29.1 [4.6] versus 28.6 [5.1], p = 0.7; overweight 83.7% versus 71.4%, p = 0.31, respectively). Nevertheless, this comparison was not an objective of the study. The prevalence of patients with overweight and obesity was high; yet their mean gradients were not greater than those of non-obese patients (p > 0.20). However, mismatch rate was greater in obese patients (60% versus 27%, p = 0.047). Preoperative and postoperative indexed EOA were similar in both sexes, though slightly lower in men. Most prosthetic valves were mechanical prostheses (77.2%) which had been implanted more then 6 months before the study. St. Jude prosthesis and devices labeled size 21 were more prevalent.

Indications for valvular replacement were as follows: 63.2% were pure aortic stenosis, 26.3% aortic regurgitation and 10.5% mixed aortic valve disease. Most procedures (73.7%) were non-combined surgeries. The majority of patients (66.7%) were in functional class I-II and 29.8% were free of symptoms. The incidence of severe mismatch (EOA < 0.65 cm^2/m^2) was high (31.55%) and 22.85% of patients had mild to moderate PPM (EOA 0.65-0.85 cm^2/m^2); nevertheless only 15.7% of patients had a maximum gradient greater than 45 mm Hg and the linear correlation between the degree of PPM and the gradient across the prosthetic valve was low (r: 0.35; p < 0.007). Table 4 shows the statistically significant difference between the prevalence of preoperative and postoperative PPM in the whole group (p = 0.029). No differences were reported when sub-groups were analyzed according to sex.

Table 2. Population characteristics

	Mean (IC 95%)
N	57
Age (years)	65.6 (57-75)
Body mass index	28.9 (27.7-30.2)
LV Diastolic diameter (cm)	5.08 (4.82-5.35)
LV Outflow tract (cm)	1.95 (1.89-2.02)
Overweight/obesity (%)	80.7%
Maximal gradient across the prosthesis (mm Hg)	30.45 (13-45)
Mean gradient across the prosthesis (mm Hg	16.7 (11.65-38.3)
Biological / mechanical heart valve prosthesis (%)	22.8% / 77.2%
Time after surgey (months)	43 (33-52)

NOTA: Media (intervalo de confianza del 95%).

DISCUSSION

The clinical relevance of PPM reported by different studies implies that mismatch should be prevented at the moment surgery using indexed EOA derived from reference values based on published papers which included a great number of patients. There are no data reached by consensus in national or foreign guidelines, therefore we based our discussion on values reported by two representative papers from the literature currently available. (3, 18) EOA determined by the continuity equation is less flow-dependent (16) and it is related not only to the prosthesis characteristics but also to the left ventricle and the outflow ventricular tract properties. Nevertheless, several papers have reported some discrepancies with the use of this determination. (6) The same prosthesis may have different EOAs attributed to real biological variations, such as subvalvular geometry which might influence the size of the vena contracta, or errors in the measurement and overestimation or underestimation which might occur when the prerequisites of the principle of continuity are not met. It is well-known that the measurement of the left ventricular outflow tract and the estimation of the Doppler velocities are subjected to errors (Table 3), and that the concept of the EOA is functional, as opposed to the GOA, an static measurement derived from the internal diameter of the prosthesis. (17). For this reason, it has been demonstrated that the GOA is not a precise diagnostic weapon which does not reflect the complexity of valvular hemodynamics, as it does not take into account *in vivo* factors, such as the surrounding tissue, suturing techniques or the position of the prosthesis.

The diagnosis of preoperative and postoperative PPM using indexed EOA derived from reference values showed differences in our observational study, performed on a retrospective sample of patients who had undergone an aortic valve replacement due to diverse conditions. The power of the study is limited by the sample size; however, the positive predictive value of the EOA previously published in medical literature for the diagnosis of PPM is 64% (6) which highlights the difficulties to predict PPM and to choose an adequate prosthesis prior to surgery. Rubio et al (18) reported that overweight is a confounder factor for the diagnosis of PPM. The presence of severe PPM in patients with overweight may be related to an over-

Cause of variation	Results
Measurement errors	
Incorrect LVOT area	Overestimation or underestimation of the EOA
LVOT velocity angle error	Underestimation of the EOA
Peak aortic velocity angle error	Overestimation of the EOA
The prerequisites of the continuity equation are not met	
Non-uniform subvalvular velocity profile	Overestimation or underestimation of the EOA
Non-uniform prosthetic velocity profile	Underestimation of the EOA

Table 3. Principal causes of variation of the EOA measured by continuity equation for prosthesis of the same size (16)

	Presurgical	Current	p
Weight (kg)	79.2 (13)	81.2 (15)	0.09
Body surface area (m^2)	1.88 (0.19)	1.9 (0.21)	0.56
Mismatch (%)	29.8	54.4	0.029
Indexed EOA (cm^2/m^2)	0.91 (0.21)	0.87 (0,42)	0.01

NOTE: Mean ± standard deviation.

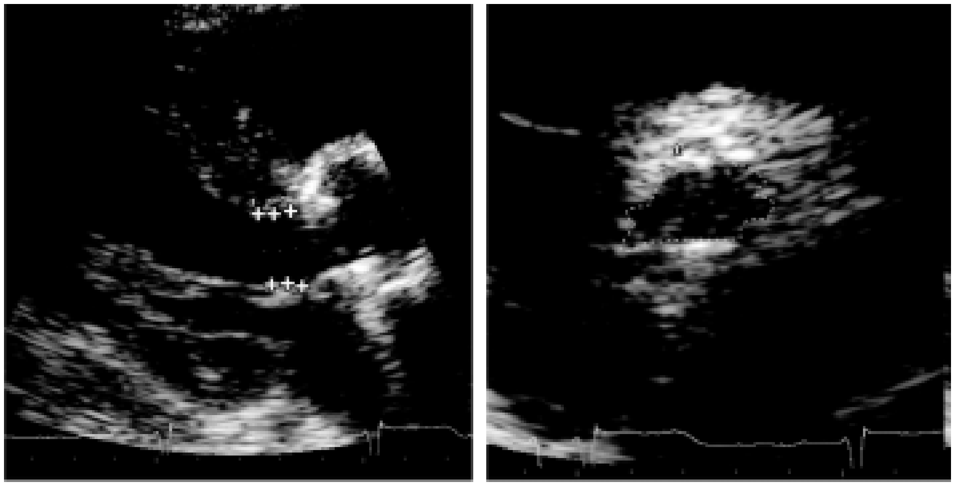
Table 4. Anthropometric measurements and mismatch prevalence

estimation, and it is not associated with high gradients across the prosthesis or with a deterioration of the functional class. A curvilinear relationship between the mean transvalvular gradient and the EOAs has already been established (r = 0.79), and when EOA is lower than 0.85 cm^2 the gradient increases significantly. (3) Surprisingly, the correlation between the degree of PPM and gradients in our study was weak. Overweight might also explain the differences between our study and the literature, as the prevalence of mild to moderate PPM (indexed EOA 0.65-0.85 cm^2/m^2) ranges from 20% to 70%, while severe PPM (indexed EOA < 0.65 cm^2/m^2) varies from 2% to 11% of valvular replacements. (3) No significant differences in patients' preoperative and postoperative weight and body surface area were reported in this study (Table 2).

A possible explanation related to preoperative and postoperative PPM might be that EOA reference values have been established in populations anthropometrically different from our sample. Surgical techniques used in the different centers which established the reference values might have been different. The postoperative gradient is mainly determined by the internal diameter of the prosthesis, but additional variables may also play some roles; for example, the shape and the type of mechanical valves, as well as the opening and closing angles and the orientation of the valve which may produce different flow patterns. (19-21). The EOA of heart valve bioprosthesis may depend on cardiac output, ventricular function, stent flexibility, the degree of aortic root decalcification and the distensibility of the surrounding tissues. These reasons explain the EOA variation among prosthesis of the same size. For example, EOA of a 23-mm Carbomedics mechanical heart valve prosthesis ranges from 1.63 and 1.8 cm. (2, 9, 10) In turn, EOAs tend to be a 10% to 15% smaller than GOAs (16). (9) Although GOA is a fixed parameter for each prosthesis size, it has a low predictive value for postoperative morbidity and mortality as it does not take into account the hemodynamic function of the prosthesis as was previously mentioned.

The differences in PPM diagnosis make us think the possibility of reexamining the EOA reference values for our population and/or the method of determination. We think it would be important to assess the possible impact of the measuring procedure of the left ventricular outflow tract area. (22, 23) The echocardiographic assessment of heart valve prosthesis presents several difficulties related to reverberations of the non-biological material and to the presence of remaining calcium in the aortic root. According to the literature, the shape of the LVOT in systole is circular. (14) Nevertheless, if this condition was not met, the resulting error in calculation would cause a further deviation from the real value.

As an example, in some cases we examined the hypothesis considered, which would be subject for a future research study. Figure 1 shows an elliptical outflow tract; as the anteroposterior axis passes by the minor diameter, the effective aortic area calculated with the continuity equation would be underestimated, as this equation uses the surface of the circle to estimate the area of the left ventricular outflow tract. This hypothesis is also supported by the low gradients measured despite the great rate of severe mismatch found in patients without a significant deterioration of ventricular function.



LVOT area 2.83 cm^2 LVOT area 3.25 cm^2

Fig. 1. LVOT area calculated by short axis planimetry (B) versus the circular area estimated from the long axis diameter (A)

Limitations

This is a retrospective study, with a small sample size, a low rate of women and a high prevalence of patients with overweight. It was not possible to establish a relationship between the prostheses and the PPM due to the small number of prosthesis of each type, brand and size.

Reported sensitivity and specificity for the diagnosis of PPM varies from 54% and 71%, and 67% and 83%, respectively, with a positive predictive value from 64% to 67%. This diagnostic accuracy is another factor to be considered in the result of this study.

CONCLUSION

In this group of patients with a high prevalence of overweight and patient-aortic valve prosthesis mismatch, the use of preoperative reference values of EOA indexed for BSA, and the EOA measured by transthoracic echo-Doppler at late follow-up, showed significant differences between preoperative PPM and postoperative PPM. Further studies should not only include a larger sample, but should also check the method used for calculating valvular area (for example, in the left ventricular outflow tract).

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Competing interests
None declared.

RESUMEN

Introducción
El *mismatch* paciente-prótesis (MPP) aórtica se asocia con peor evolución posoperatoria. La utilización del área del orificio aórtico efectivo (AOE) para cada tipo de prótesis, indexado por la superficie corporal (SC) en el momento quirúrgico, puede permitir la elección de un tamaño de prótesis adecuado para cada paciente y así evitar el MPP.

Objetivo
Comparar la estimación de MPP por las AOE tabuladas con la diagnosticada en el posoperatorio alejado por eco-Doppler.

Material y métodos
Se analizaron retrospectivamente 57 pacientes, 43 hombres, con prótesis aórtica, operados más de 6 meses antes del estudio. Se calculó la SC del parte quirúrgico y el AOE indexada tabulada, el AOE posquirúrgica con eco-Doppler transtorácico por la ecuación de continuidad y se comparó el MPP prequirúrgico y posquirúrgico. Se consideró MPP aórtico un AOE indexada < 0,75 cm^2/m^2.

Resultados
Se observó una prevalencia de MPP preoperatorio del 29,8% y posoperatorio del 54,4% ($p = 0{,}029$), con el 31% de MMP grave. La prevalencia de sobrepeso en la muestra estudiada fue del 80%.

Conclusiones
En este grupo de pacientes con alta prevalencia de sobrepeso, la estimación del AOE preoperatoria indexada por SC de cada tipo de prótesis para predecir el MPP posoperatorio mostró diferencias significativas entre el diagnóstico del MPP estimado en el preoperatorio y el calculado por eco-Doppler en el posoperatorio. En futuros estudios es necesaria la inclusión de un grupo poblacional mayor, así como la revisión del método de cálculo del área valvular (p. ej., del tracto de salida del ventrículo izquierdo).

Palabras clave > Válvula aórtica - Ecocardiografía - Prótesis valvular

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