QUANTIFICATION AND PREVENTION TECHNIQUES 
OF PROSTHESIS-PATIENT MISMATCH

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Abstract: Aortic valve surgery is now the second most commonly performed cardiac operation because nowadays is found an increasingly elderly population. Echocardiography examination (in particular Doppler assessment) is the standard clinical technique for quantifying of hemodynamics after surgical correction of valvar lesion. Analysis can include specifics parameters: mean and peak trans-prosthetic gradients, dimensionless valve index and effective orifice area (EOA) from the continuity equation. Most patients indication for aortic valve surgery will ‘technically’ have some degree of patient – prosthesis mismatch (VP-PM), but this is sometimes severe. Understanding the techniques by which echocardiographic imaging and Doppler technique are used to noninvasively assess aortic prosthesis hemodynamics, and the caveats associated with those methods, are useful for cardiologist to differentiate causes of high trans-prosthetic gradients and prosthesis dysfunction from other causes of obstruction. EOA indexed should be measured in the first 3 weeks postoperatively or at hospital discharge. Assessing the presence and severity of the phenomenon of mismatch is important because that will affect long-term outcomes. Use of the EOA indexed as a continuous variable may help to define the level of severe VP–PM that results in increased mortality, and this may occur at a critical level of obstruction. Prediction of severity of VP–PM is difficult to estimate, that why, the primary goal should be to prevent severe VP–PM by the use of new generation aortic prosthesis with superior hemodynamics and approach with modern surgical techniques. This article summarizes the means by which echocardiography/ Doppler technique is used to assess hemodynamics after aortic valve replacement and the potential caveats associated with its use, and proposes an algorithm for the clinical evaluation of high gradients after aortic surgery.

Keywords: echocardiography technique, aortic valve replacement, mismatch phenomenon, effective orifice area, transprosthetic gradient

I. INTRODUCTION

The aim of the surgical treatment of aortic valve disease is to eliminate the pressure and volume overload of the left ventricle thereby allowing the myocardial remodeling and the regression of left ventricular hypertrophy. The left ventricle’s geometrical shape and the degree of left ventricular hypertrophy influences the patient’s evolution after surgery. [1]

The surgical intervention produces a dramatic change during history of the aortic valve disease, either stenosis or regurgitation. It was reported an improvement in survival [2], in resting hemodynamics [3-4] and the functional NYHA class resulting in enhanced quality of life. These improvements are seen, even though the valve substitutes generate a relative, persistent, but not progressive obstructive stenosis in the ejection of blood. [5]

In the last decades, the postoperative evolution has seen a significant improvement. The important refinements in anesthetics and surgical techniques generate an improvement in myocardial preservation and a better revascularization when coronary artery bypass grafting is associated [6-7]. At the same time, the success of the surgical approach led to increase addressability of patients addressed for valve replacement and to the changing of the basic characteristics of patients proposed for surgery: lately the patients are older and most of them have ischemic heart disease. Measuring the volume, mass and acknowledging the left ventricle’s function can bring valuable data, which are necessary in defining the optimal timing of surgical correction in patients with volume overload in aortic regurgitation or pressure overload generated by the obstruction in left ventricular ejection. In this regard, the prognostic [8-9] utility of the end-diastolic and end-systolic volume, of the ejection fraction, of the left ventricular mass, of the relationship between the systolic stress and the shortening fraction and the end-systolic pressure-volume relationship were investigated in various studies and using different methods of evaluation, both invasive and noninvasive. The end-systolic volume and the ejection fraction seem to be the most useful in predicting the outcome. For certain, the most important

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determinant of the postoperative evolution was the left ventricle’s systolic function.

We thus emphasize the importance of validation of a technique that allows accurate preoperative prediction accuracy of the size of the prosthesis by the surgeon will replace diseased aortic valve (actual size appropriate anatomical conditions and hemodynamic needs of the patient). It follows that the true size of the prosthesis refers to the actual working area rather than the size of the label factory.

Factors to consider when choosing a prosthesis heart valve are: age of the patient, comorbid conditions: cardiac and non-cardiac, expected life span of patient, probability of adherence and compliance with anticoagulant therapy, patient’s wishes and expectations. More need to consider to choose a prosthesis that does not require root replacement for isolated aortic valve disease, with long-term follow-up outcomes that are at least as good as the best of the available prosthesis, with which individual physicians and medical centers have the necessary skill and experience.

II. VALVE PROSTHESIS-PATIENT MISMATCH

A. Definition

The term ‘mismatch’ was proposed in 1978 by Rahimtoola. The mismatch appears when the effective aortic orifice area of the prosthesis is smaller than the patient’s body surface area thus generating an abnormally high transprosthetic gradient (VS/AscAo) after surgery.

The main criterion generally used to identify the mismatch is the indexed effective orifice area (EOA) of the prosthesis to the patient’s body surface area (m²BSA). The mismatch in the case of the prosthetic valves in aortic position is defined as EOA < 0.85 cm²/m² BSA and is quantified as:
- moderate when EOA = 0.65-0.85 cm²/m²
- severe when EOA ≤0.65 cm²/m².

In specialty literature, the prevalence of the severe mismatch is between 2-11%. [10]

The mismatch phenomenon is associated with:
- the lower improvement of symptoms and of functional NYHA class
- a lower improvement of left ventricular hypertrophy
- an increase in cardiac events.

This phenomenon has a significant impact on short and long-term outcome, especially when it is associated with left ventricular dysfunction. [11]

B. Mismatch mechanisms

The mismatch phenomenon is produced through the following mechanisms:
- the discrepancy between the prosthesis and the cardiac structures (the lack of correlation between the dimensions of the prosthesis and the body surface area)
- patients who had replacement valve surgery at a young age (the growth of the cardiac structures with age)
- women (because of the smaller size and the necessity of using small dimensions prosthesis resulting in sub-optimal hemodynamics), Fig. 1.

- normal dimensions of the prosthesis but the patient develops exercise dysfunction (lack of adjustment to increased hemodynamics needs)
- the mismatch appears more frequently in aortic prosthesis

Attention: the high gradients observed at the valvular orifices can also appear in case of increased cardiac output or severe valve regurgitation.

The valve-prosthesis patient mismatch must be differentiated from the acquired obstructions:
- the correct acknowledgement of the prosthetic function and of the mobility of the movable element
- information regarding the size of the prosthesis correlated with body surface area index
- the quantitative evaluation of the stroke volume
- excluding other causes of prosthesis dysfunction

How important is the mismatch? [12]

- In subjects with left ventricular dysfunction recent research have shown a strong relationship between the mismatch phenomenon and the decreased left ventricular function the additional hemodynamic load is less tolerated in an insufficient left ventricle than in a left ventricle with a normal function. Therefore, it is taken into account any technique to prevent the phenomenon of mismatch in these patients with systolic dysfunction of the left ventricle.
- In young patients - probably because they have the need for a higher cardiac output
- In athletes there must be obtained an EOA ≥1cm²/m²BSA
- In obese patients there was questioned whether using the body surface area for indexing doesn’t overestimate the mismatch. But indexing the aortic EOA to height or weight doesn’t represent a solution because it is known that obesity generates an increase of the cardiac output with 10-30%.

The best parameter which predicts the apparition of the valve prosthesis-patient mismatch during surgery is the aortic EOA indexed to the reference values reported in the studies. Contrasting, the aortic EOA designed by the industrie in vitro has a very low sensitivity. The data obtained through in vivo echocardiography must be used.
C. Techniques for quantifying the phenomenon patient - prosthesis mismatch

Most prostheses used for correction of aortic valve lesions were suboptimal hemodynamic to native valve. This had especially to mechanical prostheses. Therefore, all prostheses were implanted in the aortic position by themselves a degree of stenosis. This phenomenon is known and accepted, especially since the degree of obstruction is hemodynamically insignificant and not alter the postoperative course of the patient's prosthesis. In contrast correction prosthetic valve lesion reduce pressure or volume overload of the left ventricle with the beneficial hemodynamic effects in the short and long term.

The basic noninvasive technique for the assessment of aortic valve prosthesis hemodynamics is quantification of transprosthetic gradients. By definition, pressure increases proximal to a restrictive orifice; the difference between the pressure proximal and distal to the orifice is a reflection of the degree of obstruction.

Doppler echocardiography technique takes advantage of the acceleration of flow across a restrictive orifice, and the relationship defined by the Bernoulli equation between velocity and pressure, to assess gradients. Using the Bernoulli equation, the difference in pressure across a restrictive orifice is defined as:

\[ \Delta P = P_1 - P_2 = 4 \left( V_2^2 - V_1^2 \right) \]

where \( P_1 \) and \( V_1 \) are the pressure and velocity, respectively, proximal to the restrictive orifice; and \( P_2 \) and \( V_2 \) are the pressure and velocity, respectively, distal to the orifice - in our case restricted orifice is the orifice valve prosthesis.[19]

Characteristics of the spectral Doppler envelope beyond simple velocity quantification also can provide information pertinent to the function of prostheses. The Doppler envelope associated with normal prosthetic AV function is triangular in shape, and peaks in early systole.

The mismatch was frequently observed, mainly for two reasons. In the first place, patients with aortic valve disease frequently present aortic annulus calcification and fibrosis, as well as left ventricular hypertrophy, these pathological processes can reduce the size of the aortic annulus.

Secondly, because the prosthesis is inserted inside the aorta and has its own structural support, the surface of the prosthesis is smaller than the surface of a normal native valve on the same aorta. The supporting apparatus of the biological prosthesis with stents or of the mechanical valves generates a relative flow obstruction, and it has been demonstrated that the EOA Ao available for the bloodflow represents 40-70% of the total surface occupied by the valve. The stentless bioprosthesis have been created in order to diminish this particular problem and they generally ensure a larger EOA indexed to the

\[ \text{EOA} = \frac{4}{\pi} \times \left( \frac{D^2}{4} - \text{EOA} \right) \]

where \( D \) is the diameter of the orifice.

Effective orifice area is determined using echocardiography Doppler and the continuity equation, and is a reflection of the minimal cross-sectional area of the outflow jet.

The dimensionless valve index (DVI) is a unitless ratio of the velocity proximal to and through the prosthetic valve. Typically expressed as the ratio of velocity-time integrals, DVI also can be expressed as the ratio of peak velocities. Similar to EOA, DVI should reflect hemodynamics independent of flow, and can be especially useful for serial assessment.

High transprosthetic gradients after aortic valve replacement can be due to 1 or more of several potential etiologies. Some, but not all, are associated with obstruction to left ventricular outflow tract.

High gradients after AVR can occur without LV outflow obstruction in the setting of measurement error, high-flow states, and pressure recovery. In a high-flow state, valve layout, EOA, DVI, and the contour of the spectral Doppler envelope all should remain normal.

High gradients after AVR can be caused by obstruction at the level of the valve due to prosthesis dysfunction, pannus, or prosthesis–patient mismatch (PPM); or due to obstruction above or below the level of the aortic valve.

The chronicity of high gradients after AVR can offer an important clue to the underlying etiology. The ability to compare later postoperative transprosthetic gradients to those early after AVR is an important reason to perform routine baseline echocardiography/Doppler technique relatively early after surgery, at a time when hemodynamics and echocardiography windows have returned to normal, and when normal prosthesis function is still relatively certain. Among the potential causes of high gradients that are associated with LV outflow obstruction, PPM and subvalvular obstruction should be present early after surgery and on all subsequent echocardiograms. [20]

D. The clinical and hemodynamic impact of the mismatch phenomenon

Various echocardiographic research have shown that most of the prosthetic valves have a slight degree of stenosis and, that immediately after surgery increased gradients can be obtained, in spite of the normal function of the prosthesis. The variable which is best correlated with the gradient of the prosthesis, both at rest or during exercise, is the indexed effective prosthesis area. The mismatch develops when the indexed effective orifice area of the prosthesis is reduced, namely when the orifice of the prosthesis is too small in relation to the body surface area. In order to avoid an increased gradient at rest or during exercise the indexed EOA should not be smaller than 0.85-0.90 cm²/m².

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The valve prosthesis-patient mismatch has been identified by the American Society of Thoracic Surgery as a nonstructural dysfunction of the prosthesis. The mismatch phenomenon is not rare and it can be found in 52% of the patients with stent bioprosthesis (Fig. 3).[12]

The mismatch appears more probably in larger or older patients, in case of a valvular prosthesis with a smaller EOA and when the dominant lesion is aortic stenosis. Patients with valvular prosthesis with dimensions under 21 mm have increased gradients, but the mismatch can also appear when the artificial valve’s dimensions are over 21 mm. Patients with aortic stenosis have a smaller annulus than those with aortic regurgitation. [14]

The main consequence of the mismatch consists of generating increased transvalvular pressure gradients given a normal functioning valve. An increased pressure gradient will generate an increased mechanical work of the left ventricle and an increased wall tension and thus preventing (according to the Laplace law) the regression of the left ventricular hypertrophy.

The trans-prosthetic gradient increases exponentially with the decreasing of the indexed EOA, and even a small reduction of the EOA causes a relatively important increase of the pressure gradient. The medium pressure gradient of the patients with an EOA ≤ 0.85 cm²/m² was 22±8 mmHg, by comparison, the medium pressure gradient of the patients without mismatch was 15±6 mmHg.

The patients with a valvular prosthesis with an EOA ≤ 0.65 cm²/m² have a trans-prosthetic pressure gradient of 32±2 mmHg. Furthermore, the long term follow up has shown a reduction of the hemodynamic parameters only in the patients with mismatch. Thus, the cardiac index, which was similar in the patients with or without mismatch right after surgery, after three years has dropped significantly only in the patients with mismatch. [15]

Although the reduction of the EOA was similar in both groups, the medium trans-prosthetic gradient has increased significantly during follow up only in the patients with mismatch. The most important impairment of the cardiac index and of the pressure gradient was reported in patients with severe mismatch (EOA ≤ 0.65 cm²/m²).

Studies have shown that an increase of the medium trans-prosthetic gradient during maximum exercise is directly linked to the indexed EOA at rest. In the patients with aortic bioprosthesis there is a strong inverted relationship between the medium pressure gradient during maximum exercise and the indexed EOA at rest. So, in patients with mismatch, the medium increase of the medium gradient was 30±10 mmHg, which is similar to that of the patients with mild-moderate aortic stenosis, meanwhile, in the patients without mismatch the medium increase was 10±5 mmHg. [16]

Studies using exercise echocardiography have shown that the surface of the bioprosthesis has the potential to increase during exercise. By contrast, the area of the mechanical valves doesn’t increase during exercise, resulting in a greater increment of the gradient.

The impact of the mismatch can be overestimated in patients with a smaller aortic root because of the pressure recovery phenomenon.

The impact on left ventricular hypertrophy (Fig. 4) – a major consequence of high residual gradients consists of the delay of the postoperative regression of the left ventricular hypertrophy. Other study has demonstrated that regression of the left ventricular hypertrophy is better in patients with the dimensions of the prosthetic valve > 21 mm than in patients with the dimensions < 21 mm. Other studies have shown that using a stentless bioprosthesis is associated with a greater reduction of the trans-valvular gradient and of the left ventricular wall tension, as well as a more complete regression of the left ventricular hypertrophy than when using stent valves. [17]

The clinical impact – the postoperative improvement of the functional capacity (exercise tolerance) is an important objective of the surgical correction. The reduced physical capacity is also associated with a high rate of late mortality. There are studies which show that the size of the prosthesis is an independent prediction factor of exercise tolerance after valve replacement.
E. The impact on morbidity and mortality

Most studies have shown that there is a link between the indexed EOA and the incidence of complications like pulmonary embolism, hemorrhage, structural deterioration and the need to intervene surgically. However, other studies on patients with stent bioprosthesis suggest that the mismatch phenomenon can cause a predisposition towards developing, in the long-term, chronic heart failure. [18]

The mismatch is associated with a higher mortality and a greater incidence of heart failure in patients with EF < 50%, but it does not influence the prognosis in patients with normal systolic function. The mismatch phenomenon has been associated with an increased mortality and a high trans-prosthetic gradient, which appears to be caused by an acquired von Willebrand syndrome (e.g. valve thrombosis, calcification, tissue deposits-pannus) and especially if there was a progressive deterioration in hemodynamics and an increased mortality in the long-term, they must be frequently evaluated.

Regarding the impact on the postoperative mortality, various studies have demonstrated that the mortality was higher in patients with smaller size valve prosthesis (≤ 21mm). Other studies have shown that 5 year survival was significantly lower in patients with smaller size valve prosthesis (63%) than in general population (87%). Some authors have reported that the 10 year postoperative mortality was higher when they used a 19mm or 21mm St. Jude prosthesis in patients with BSA > 1.9 m². In addition, a smaller size prosthesis can be an indicator of other additional risk factors, like: a small aortic root with calcification, a large BSA and an increased left ventricular hypertrophy. Finally, the implantation of a prosthesis in a calcified aortic root can be technically challenging and it necessitates a longer clamping time, which is a major risk factor. The mismatch is associated with a short and long term reserved prognosis, causing an increased mortality, and its effect is accentuated in patients with the ejection fraction < 40% (EF). The importance of ejection fraction was noted in other studies. The mismatch is associated with a higher mortality and a greater incidence of heart failure in patients with EF < 50%, but it does not influence the prognosis in patients with normal systolic function.

In a study which included 1400 patients the following results were found:

- Mismatch, defined as EOA ≤ 0.75 cm²/m², was present in 51% of the bioprosthesis and in 11% of the mechanical valves.
- The 10 year survival of the patients with bioprosthesis was significantly lower in case of mismatch associated with patients under 60 years old, but not in older patients. [19]

The mismatch phenomenon has been associated with decreased survival and increased bleeding (observed also in the patients with severe aortic stenosis) which appears to be caused by an acquired von Willebrand syndrome (the destruction of factor VIII during the passage through the narrow valve). An alternative for the patients with a small aortic annulus is to enlarge the aortic root or to use a stentless valvular conduct. [20]

F. The management of valve prosthesis-patient mismatch

The discovery of an increased trans-prosthetic gradient is often associated with diagnostic difficulties. The high postoperative gradients can appear because of a high cardiac output or because of the presence of mismatch. The most logical approach in determining the intrinsic performance of the prosthesis is by comparing the EOA measured in the echocardiography exam with the reference values for that type of prosthesis.

A substantially lesser value suggests an intrinsic stenosis (e.g. valve thrombosis, calcification, tissue deposits-pannus) and especially if there was a progressive reduction of the EOA over time.

In these cases, reintervention should be considered because intrinsic stenosis is usually progressive.

If the high gradient is caused by mismatch, as indicated by the EOA compared to the reference values, but the indexed EOA ≤ 0.85 cm²/m², there is a lack of this situation in the guidelines. Because these patients have a better prognosis in the medium term, but they present a deterioration in hemodynamics and an increased mortality in the long term, they must be frequently evaluated.

If the patient develops symptoms compatible with aortic stenosis (angina, dyspnea or syncope) and has an indexed EOA similar to severe aortic stenosis (≤ 0.6 cm²/m²) then the patient must undergo surgery. It is very important that the new prosthesis insures a bigger EOA either using a bigger size or changing the type of the prosthesis.

In order to avoid mismatch, the BSA should be calculated using the Dubois formula, then a minimum EOA should be determined in order to ensure an indexed area > 0.85 cm²/m². After that, there is selection of the type and size of the prosthesis (according to reference values) in order to ensure the calculated area (Fig. 5).

For the same size of the prosthesis, the EOA can significantly vary, depending on the type of the prosthesis. Thus, obviously, mechanical valves tend to have a bigger EOA than bioprosthesis, except stentless bioprosthesis. [21]

Inserting a bigger prosthetic valve may necessitate the enlargement of the aortic root, if this is the case the increased operative risk must be balanced against the estimated benefits. Other alternatives to prevent mismatch include an implantation over the annulus or choosing a different type of prosthesis (especially stentless bioprosthesis). Other alternative surgical techniques involve grown aortic clamping time and significantly more bleeding. That is why the increased operative risk should be balanced against the estimated benefits. A mild mismatch can be acceptable when there is an increased surgical risk, while severe mismatch is not taken into account. The level of the patient’s physical activity (age, profession, lifestyle) must be also considered.
G. Can mismatch be prevented?

Bleiziffer et al. [9] have compared the mismatch prevalence before and after the introduction of the thorough calculus of the estimated EOA during surgery. The moderate mismatch prevalence was reduced from 44% to 30%, and the prevalence of the severe mismatch was reduced from 9% to 1%. Considering the risk of mismatch during intervention, the correct prosthesis can be chosen. That is why it is highly recommended to systematically calculate the indexed suitable EOA of the prosthesis, and, if mismatch is anticipated alternative procedures should be used, like: enlargement of the aorta, over annulus bioprostesis, stentless valves, homografts or the Ross procedure. [9]

Indexed projected EOA must be incorporated to other parameters, like: age, the level of physical activity, left ventricular function and accompanying procedures, in order to choose the proper technique. The prevalence of mismatch becomes mandatory in case of left ventricular dysfunction.

III. CONCLUSIONS

In patients with proof of the phenomenon aortic prosthesis–patient mismatch hemodynamic and clinical improvement were suboptimal after aortic valve surgery. This becomes more evident in terms of effort.

More long-term postoperative course, especially haemodynamic status, progressively deteriorates during follow-up, and mismatch has negative impacts on the regression of LV hypertrophy, as well as on long-term survival.

This phenomenon occurs post prosthetic and overshadows the postoperative course of patients, of different categories of age and especially active people, who make effort in everyday life, can be anticipated and prevented by some calculations estimate. Calculating, before the operation, the indexed EOA from reference values for the EOA of the prosthesis being implanted and the patient’s BSA, considering that for optimal valve performance at rest and exercise. Avoiding the mismatch, can be done through a particular surgical approach, techniques specific - enlargement plasty of the left ventricular outflow tract – performed by surgeon in order to implant a prosthesis size as close to the patient’s hemodynamic needs. These operational techniques increase the complexity of the intervention and at the same time patient risk.

Following trials industry has developed new types of prostheses with optimal hemodynamics as similar to the native valve, there are now newer generation mechanical and bioprosthetic valves who manage the most potentially severe cases of mismatch.

Transprosthetic gradients determined using Doppler echocardiography technique in general correlate well with invasive measures among patients after aortic valve replacement. The accuracy, noninvasive method, availability and versatility have consecrated this technique as the standard for the clinical assessment of hemodynamics after surgical repair.

However, caveats exist for the noninvasive assessment of aortic hemodynamics in general, and the presence of a prosthetic valve can introduce additional confounders.

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