[Review article]

The clinical challenge of concomitant aortic and mitral valve stenosis

Philippe UNGER[1], MD; PhD; Patrizzio LANCELLOTTI[2], MD; PhD; Didier de CANNIÈRE[3], MD, PhD

[1]Department of Cardiology, CHU Saint-Pierre, Université Libre de Bruxelles, Brussels, Belgium; [2]Department of Cardiology, GIGA Cardiovascular Sciences, Heart Valve Clinic, University Hospital Sart Tilman, University of Liège Hospital, Liège, Belgium; [3]Department of Cardiac Surgery, CHU Saint-Pierre, Université Libre de Bruxelles, Brussels, Belgium.

Abstract The coexistence of mitral and aortic stenosis is not exceptional. Whereas rheumatic fever is currently plummeting in the Western countries, the incidence of degenerative disease is inversely increasing. The haemodynamic interactions which may interfere both with the usual echocardiographic parameters and with the invasive assessment may render the diagnosis difficult. The therapeutic challenges raised by this entity should not be underestimated. The increased morbidity and mortality of multivalvular surgery has to be balanced with the risk of a second operation down the line if one valvular involvement, deemed of a lesser importance, is neglected. This complex situation requires the multidisciplinary approach of a heart team involving surgeons, cardiologists, geriatrists if need be and imaging specialists.

Keywords *Aortic stenosis – mitral stenosis – valvular heart disease – multiple valve disease – cardiac imaging.*

INTRODUCTION

Multivalvular heart disease is a frequent situation, but there is only scarce medical literature about its management[1]. Diagnosis can be difficult because of haemodynamic interactions that may interfere with the usual echocardiographic parameters, most of which have been validated only in patients presenting with an isolated mono-valvular dysfunction. Similarly, the invasive haemodynamic assessment that is usually recommended in the event of inconclusive or confusing non-invasive tests can be also difficult to interpret or even misleading due to diagnostic pitfalls. Finally, the therapeutic decision can be challenging to the heart team, and require to balance the increased risk of multiple valve surgery against that of a second operation should an initially and less significant valve dysfunction be left untreated, raising the question of a prophylactic intervention on a moderately dysfunctional valve.

The combination of aortic (AS) and mitral stenosis (MS) is a particularly illustrative example. This situation is far from being exceptional. It was reported in 17% of 170 consecutive patients undergoing combined mitro-aortic surgery at the Zurich University Hospital[2].

Demographics vary between different regions of the world. In the so-called industrialized countries, coexisting severe or critical AS and MS are less frequently observed since this combination is usually very poorly haemodynamically tolerated, and access to care is usually sought before the occurrence of full-blown deterioration. Similarly, improved access to healthcare for young and ageing population altogether have led to a paradigm shift in the aetiology of multiple heart valve disease, from rheumatic fever to degenerative calcified heart valve disease. Typically, rheumatic MS is associated with diastolic "doming" of the mitral valve and symmetric fusion of the commissures, whereas degenerative MS usually results from progressive annular calcifications involving the base of the leaflets and progressively reducing the functional valvular orifice, without commissural fusion. The resulting obstruction is generally less severe than in rheumatic valve disease, thus decreasing the prevalence of double critical stenosis. Other

Address for correspondence:

Philippe Unger, M.D.,
Cardiology Department, CHU Saint-Pierre,
322 rue Haute, B-1000 Brussels, Belgium.
E-mail: punger@ulb.ac.be

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causes of combined MS and AS such as congenital (Shone's complex, mucopolysaccharidosis), drug-induced or post-radiation therapy are exceptional.

DIAGNOSTIC PITFALLS

As is common in the case of serial valve involvement, the clinical signs of the upstream lesion usually prevail. Accordingly, when the severity of AS and MS are balanced, the clinical presentation will be dominated by haemoptysis and pulmonary congestion. Systemic embolisms can occur at the onset of atrial fibrillation that will usually be poorly tolerated in patients with left ventricular hypertrophy and stiffness resulting from AS.

The physical examination can be misleading. Even in the absence of atrial fibrillation, the presence of MS can suppress the AS-related 4th heart sound, and both the systolic aortic and the diastolic mitral murmurs can be blunted by the decreased transvalvular flow.

Echocardiography usually provides the diagnosis clues. The typical high pressure gradients of isolated severe MS and AS can occasionally be recorded. However, several pitfalls should be kept in mind. As described in the early sixties, the reduction of cardiac output is usually more dramatic than it is in isolated valvular stenosis[3]. The occurrence of a low flow situation can account for smaller pressure gradients in the case of severe stenosis. Indeed, a low mean aortic pressure gradient (< 30 mmHg) is not infrequent in presence of severe AS (aortic valve area below 0.8 cm^2), and a relatively low pressure gradient (< 10 mmHg) is also not exceptional even when mitral valve area stands below 1 cm^2 [4]. Therefore, multiple valve involvement particularly warrants the assessment of the valvular areas because a low pressure gradient does not allow in itself ruling out severe valvular stenosis. Underestimating the severity of AS can lead to dramatic consequences: the left ventricle is usually small, stiff and hypertrophied, and "protected" from overload by the concomitant MS. Rapid relief of the mitral obstacle following balloon dilatation or surgery will abruptly increase preload which may eventually lead to acute left ventricular failure and "flash" pulmonary oedema.

Left ventricular abnormal relaxation resulting from AS can increase mitral E wave half-pressure time whereas the latter will be reduced in situations where left ventricular compliance is impaired, leading to an overestimation of mitral valve area[5]. The pressure half-time method that is commonly used in rheumatic MS should therefore not be used when there is concomitant AS. Because of an excellent correlation with the anatomical surface of explanted valves, echocardiographic two-and three-dimensional planimetry are usually considered as the gold-standard measurements to evaluate mitral valve area, even in the presence of AS. However, the heavy calcifications found in degenerative MS most of the time impair the accuracy of planimetry. Moreover, whereas mitral orifice is funnel-shaped in rheumatic valve disease, with the limiting orifice at the free edge of the leaflets, degenerative MS is characterized by a limiting orifice mostly located at the level of the restricted native annulus. The proximal isovelocity surface area method remains useful to quantify mitral valve area in patients with bivalvular rheumatic disease, but it has yet not been validated in degenerative calcified mitral valve disease. The continuity equation remains accurate to assess both aortic and mitral valve area, but it cannot be used to assess the mitral valve area in the presence of concomitant mitral and/or aortic regurgitation.

If uncertainty about one or the other measure persists after a thorough echocardiographic evaluation, the importance of a correct diagnosis is such that a left and right heart catheterization may be warranted[6]. However, when the cardiac output is particularly reduced, as may sometimes happen in these patients, the Gorlin formula may overestimate the aortic valve area[7]. Conversely, the Gorlin formula underestimates aortic and mitral valve area in the presence of aortic and mitral regurgitation, respectively. Occasionally, the combination of a moderate AS and a moderate MS will lead to severe functional intolerance. In this case, assessing the NT-pro BNP level can be a useful adjunct as a global marker of the functional repercussions of the double stenosis[8].

THERAPEUTIC ISSUES

According to the Society of Thoracic Surgeons database, the operative mortality is three times higher for double valve surgery when compared to isolated aortic valve replacement[9]. Long-term post-operative survival after multiple valve surgery is also lower, with a high New York Heart Association class, a lower left ventricular ejection fraction and/or a dilated left ventricle, a need for myocardial revascularization and/or the presence of pulmonary hypertension as risk factors[2,10]. In double valve replacement, although the risk of a thromboembolism is higher after double mechanical valve replacement than it is after single valve replacement[11], the use of the same type of prosthesis in both places (bioprosthesis or mechanical) is recommended in order to avoid superimposing the risk of anticoagulation to the one of bioprosthesis deterioration. In a retrospective study from the Cleveland Clinic, mitral valve repair seemed to provide a survival benefit when compared to replacement in double-valve (aortic and mitral) surgery[12].

Importantly, the rheumatic or degenerative aetiology needs to be accounted for in the decisional algorithm.

The American Heart Association/American College of Cardiology Guidelines on Valvular Heart Disease mainly address rheumatic valve disease and therapeutic strategies may be different in the presence of degenerative mitral valve, disease (table 1)[13,14]. For example, transcatheter aortic valve implantation is usually targeted at patients with AS of degenerative aetiology whereas mitral valve repair is usually not an option in patients with degenerative mitral valve disease.

Rheumatic aetiology

Double-valve surgery is preferable in patients with severe MS combined with severe AS (table 1)[13,14]. In case of a severe "surgical" AS, the coexistence of a moderate MS represents a IIb (level of evidence C) recommendation for a "passing" mitral replacement according to the American guidelines (table 1) [14]. According to the same guidelines a "passing" aortic valve replacement can be contemplated in the presence of a severe MS requiring surgery coexisting with a moderate AS (IIa recommendation, level of evidence C). The latter can also indirectly rely upon the superior outcomes of a "passing" aortic valve replacement for moderate AS when it coexists with coronary artery disease due for surgical revascularization[15]. However, when feasible, balloon valvuloplasty may be the preferred option in this case, enabling to defer surgery[13]. In patients with double valve rheumatic stenosis due for surgery, open mitral commissurotomy delivers satisfactory long-term outcomes. In a series of 276 patients undergoing open surgical commissurotomy, 55 (19.9%) had an associated aortic valve procedure. Despite an operative mortality of 7.3%, freedom from mitral valvular failure at 10 years was 87% among the whole cohort of operative survivors[16].

Degenerative aetiology

The absence of commissural fusion and the calcifications mostly located at the annulus and at the very base of the leaflets preclude both balloon dilatation and surgical commissurotomy. The surgical mitral valve replacement can be made very difficult by the "bar" calcifications at the fragile level of the posterior atrioventricular groove, with an increased risk of the lethal complication of atrioventricular dehiscence, especially in small annuli and previously irradiated patients, where extensive decalcification may be required.

In addition, patients exhibiting such degenerative valvular diseases are usually frail and elderly, and present with numerous co-morbidities. In this setting, medical treatment including diuretics and heart-rate reducing agents may occasionally be beneficial until invalidating symptoms occur. However, one must bear in mind from the Euro Heart Survey study pertaining to isolated AS that patients who are usually dismissed because they are regarded as being too frail or too old might be those who could benefit the most from a valve replacement

Table 1 European Society of Cardiology/European Association for Cardio-Thoracic Surgery and American College of Cardiology/American Heart Association Guidelines[13,14]

Clinical setting	2012 European Society of Cardiology/European Association for Cardio-Thoracic Surgery Guidelines[13]	2014 American College of Cardiology/American Heart Association Guidelines[14]
Severe mitral stenosis and severe aortic stenosis	• Severe concomitant aortic valve disease is a contraindication to percutaneous mitral commissurotomy. • In patients with severe MS combined with severe aortic valve disease, surgery is preferable • Aortic valve replacement is indicated in patients with severe aortic stenosis undergoing surgery of another valve. (Class I, level of evidence C)	• Concomitant mitral valve surgery is indicated for patients with severe MS (mitral valve area ≤ 1.5 cm^2) undergoing other cardiac surgery (Class I, level of evidence C) • AVR is indicated for patients with severe AS when undergoing other cardiac surgery (Class I, level of evidence B)
Severe mitral stenosis and non-severe aortic stenosis	• In cases with severe MS with moderate aortic valve disease, PMC can be performed as a means of postponing the surgical treatment of both valves • Aortic valve replacement should be considered in patients with moderate aortic stenosis undergoing surgery of another valve (Class IIa, level of evidence C)	• Aortic valve replacement is reasonable for patients with moderate aortic stenosis (aortic velocity 3.0-3.9 m/s) who are undergoing other cardiac surgery (Class IIa, level of evidence C)
Severe aortic stenosis and non-severe mitral stenosis		• Concomitant mitral valve surgery may be considered for patients with moderate mitral stenosis (mitral valve area 1.6-2.0 cm^2) undergoing other cardiac surgery (Class IIB, level of evidence C)
Non-severe aortic stenosis and non-severe mitral stenosis	• Intervention can be considered for non-severe multiple lesions associated with symptoms or leading to left ventricular impairment	

procedure, and it is not unlikely that rejecting patients "per principle" for the same reason may be a redundant error[17]. The advent of transcatheter aortic valve replacement has significantly impacted this paradigm, allowing treating high-risk patients with severe AS despite concomitant moderate MS. Transcatheter mitral valve implantation in a calcified mitral annulus is currently under development[18,19], but this challenging procedure has only rarely been carried out and its precise role in the therapeutical armamentarium remains elusive.

In the case of a suitable mitral and aortic anatomy and a prohibitive surgical risk, a percutaneous treatment combining mitral balloon valvuloplasty and transcatheter aortic valve implantation can be considered[20], but this scenario is expected to be extremely uncommon, since, as mentioned above, mitral balloon valvuloplasty and transcatheter aortic valve implantation usually do not cover the same patient population.

CONCLUSIONS

The coexistence of MS and AS is not exceptional. If rheumatic fever is currently plummeting in the Western countries, the incidence of degenerative disease is inversely increasing. It is important not to underestimate the diagnostic and therapeutic challenges raised by this entity. The increased morbidity and mortality of multivalvular surgery has to be balanced with the risk of a second operation down the line if one valvular involvement, deemed of a lesser importance, is neglected. These complex situations require the multidisciplinary approach of a heart team involving surgeons, cardiologists, geriatrists if need be and imaging specialists.

CONFLICT OF INTEREST: none.

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