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Review

Timing of Surgery in Valvular Heart Disease: Prophylactic Surgery vs Watchful Waiting in the Asymptomatic Patient

Linda D. Gillam, MD, MPH,[a] Leo Marcoff, MD,[a] and Sofia Shames, MD[b]

[a] *Morristown Medical Center, Morristown, New Jersey, USA*

[b] *Columbia University Medical Center, New York, New York, USA*

ABSTRACT

In the absence of randomized controlled trial data, the management of patients with severe valvular heart disease without symptoms, ventricular dysfunction, or other identified triggers for surgery is controversial. In this review, we frame the debate between prophylactic surgery vs close follow-up until triggers occur (watchful waiting) for severe aortic stenosis and degenerative mitral regurgitation (MR), the 2 conditions for which the pros and cons of these approaches are best articulated. Classic high-gradient severe aortic stenosis is generally accurately diagnosed. In asymptomatic patients, stress testing can be used to confirm asymptomatic status and identify high-risk features including reduced exercise tolerance, exercise-induced symptoms, and absolute or relative hypotension. Resting echocardiographic predictors of disease progression and/or adverse events include very high gradients, rapid progression, and extensive calcification. Surgical risk calculators can help estimate perioperative morbidity/mortality with the ultimate choice of a medical vs a prophylactic surgical approach to be made after discussion with the patient. With degenerative MR, severity can be inaccurately estimated. Stress testing might clarify whether the patient is truly asymptomatic and identify features asso-

RÉSUMÉ

En l'absence de données d'essais cliniques aléatoires, la prise en charge des patients asymptomatiques souffrant de cardiopathie valvulaire grave sans symptômes, ni dysfonction ventriculaire, ni autres facteurs déclenchants de la chirurgie est controversée. Dans cette revue, nous structurons le débat entre la chirurgie prophylactique *vs* le suivi étroit jusqu'à ce que les facteurs déclenchants de la sténose aortique grave et de la régurgitation mitrale (RM) dégénérative apparaissent (attente vigilante), 2 affections pour lesquelles les avantages et les inconvénients de ces approches sont mieux définis. La forme habituelle de la sténose aortique grave à gradient élevé est généralement diagnostiquée avec précision. Chez les patients asymptomatiques, l'épreuve d'effort peut être utilisée pour confirmer l'état asymptomatique et déterminer les caractéristiques à risque élevé, soit la diminution de la tolérance à l'effort, les symptômes induits par l'exercice, et l'hypotension absolue ou relative. Les prédicteurs échocardiographiques au repos de la progression de la maladie ou des événements indésirables comprennent les gradients très élevés, la progression rapide et la calcification étendue. Les calculateurs de risques chirurgicaux peuvent aider à estimer la morbidité

The definitive therapy for patients with valvular heart disease is mechanical intervention, with surgery currently serving as the gold standard, notwithstanding advances in catheter-based approaches. Although the onset of symptoms is an accepted indication for surgery, the timing of surgery in the asymptomatic patient remains a clinical dilemma. Additional surgical triggers based on the response of the heart and/or pulmonary vascular bed to the pathologic load imposed by valve dysfunction have been identified. However, there is considerable controversy concerning the timing of surgery in the patient who is asymptomatic and without such triggers. In this article, we review the arguments for early prophylactic surgical intervention and an approach based on close medical surveillance until either symptoms or other triggers emerge, the so-called watchful waiting strategy. The discussion is limited to the consideration of valve surgery as the primary procedure in patients with severe valvular aortic stenosis (AS) or degenerative mitral regurgitation (MR), the 2 conditions in which this debate has been clearly articulated.[1-5] That controversy as to the optimal clinical approach to such patients continues is a reflection of the fact that there has been no prospective randomized clinical trial to inform decision-making.

The following considerations will form the framework for this discussion: (1) the reliability with which the diagnosis of severe disease can be made, the assumption being that surgery is not indicated for patients with moderate or mild disease unless as an add-on to surgery for another indication; (2) the degree to which symptoms or other triggers for surgery are inevitable and predictable; and (3) the relative risks of surgery (perioperative and long-term) vs waiting. The importance of

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Corresponding author: Dr Linda D. Gillam, Department of Cardiovascular Medicine, Morristown Medical Center, 100 Madison Ave, Morristown, New Jersey 07962, USA. Tel.: +1-973-971-4947; fax: +1-973-290-7145.

E-mail: linda.gillam@atlantichealth.org

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ciated with worse prognosis and symptom onset. Selecting patients with high probability of repair can be challenging. Perioperative risk and postoperative risks including those of unanticipated valve replacement and recurrent MR after repair are also considerations. In aggregate, management of patients with valvular disease who are asymptomatic and who have no clear trigger for surgery is complex, requires individualization, and should be carried out by or in collaboration with a heart valve centre of excellence.

et la mortalité périopératoires afin de prendre la meilleure décision entre l'approche médicale et l'approche chirurgicale prophylactique après en avoir discuté avec le patient. Quant à la RM dégénérative, la gravité peut être estimée de manière inexacte. L'épreuve d'effort clarifierait si le patient est vraiment asymptomatique et déterminerait les caractéristiques associées au plus sombre pronostic et à l'apparition de symptômes. La sélection des patients ayant une forte probabilité de réparation peut s'avérer complexe. Le risque périopératoire et les risques postopératoires, soit ceux liés au remplacement valvulaire non anticipé et à la récurrence de la RM après la réparation sont également à prendre en considération. En somme, la prise en charge des patients souffrant de valvulopathie qui sont asymptomatiques et qui ne présentent pas de facteurs déclenchants clairs de la chirurgie est complexe, exige l'individualisation et devrait être réalisée par ou en collaboration avec un centre d'excellence en matière de valves cardiaques.

stress testing to confirm the patient's asymptomatic status will also be noted as patients might subconsciously scale back activities to avoid symptoms.

Severe AS

> *"The problem whether or not to recommend operation for patients with few symptoms but with severe stenosis is unsettled."*
> —*Ross and Braunwald*[6]

That the onset of symptoms—angina, syncope, or heart failure—portends a poor prognosis for the patient with AS has been recognized for decades with the result that surgery for symptomatic patients with classic high-gradient severe AS carries a class I indication in the most recent American College of Cardiology (ACC)/American Heart Association (AHA)[7] and European Society of Cardiology (ESC)[8] guidelines. Indeed, mortality in symptomatic patients approximates 2% per month. Surgery for asymptomatic patients with reduced left ventricular (LV) ejection fraction (EF) (< 50%) also carries a class I indication for surgery.[7,8] Thus, for purposes of this discussion, the asymptomatic patient who is a candidate for watchful waiting is one with severe AS and normal LVEF.

Reliability of diagnosis

Although cardiac catheterization and novel noninvasive imaging techniques such as planimetry using 3-D echocardiography, computed tomography, or magnetic resonance imaging (MRI) and velocity-encoded phase contrast MRI application of the continuity equation might play a role in the identification of the patient with severe AS, echocardiography is the major diagnostic tool for AS quantitation.

The accurate diagnosis of classic severe AS (peak velocity $\geq$ 4 m/s, mean gradient $\geq$ 40 mm Hg and valve area < 1.0 cm^2 or 0.6 cm^2/m^2 regardless of LVEF) should be within the skill set of most clinical echocardiography laboratories. Indeed, the Intersocietal Accreditation Commission demands proficiency in the assessment of AS for echocardiography laboratory accreditation. Where deficiencies exist, they will typically result in underestimation of transvalvular gradient and the severity of obstruction, making it unlikely that a prophylactic surgical strategy would send someone with mild or moderate disease for intervention if the decision were based predominantly on valve gradient. However, the diagnosis of severe AS based on reduced calculated aortic valve area (AVA) despite low gradients asks more of the echocardiography laboratory.

Patients with small AVAs can have low gradients in the presence of reduced stroke volume (SV) on the basis of reduced LVEF. In this setting, dobutamine stress echocardiography (DSE) can help separate those with true severe AS from those whose cusp opening is limited, in part, by reduced opening forces (pseudosevere AS). The guidelines recommend surgery (class IIA) for symptomatic patients with low-gradient low-flow reduced-EF AS who, with DSE, are shown to have severe rather than pseudosevere stenosis with flow reserve.

Additionally, the existence of low-gradient, low-SV (< 35 mL/m^2), preserved LVEF ($\geq$ 50%) severe AS is generally accepted.[9,10] However, this diagnosis mandates the accurate assessment of SV because it might be impossible to increase gradients to typical severe AS levels with DSE or other interventions so that the diagnosis of severe AS is based on AVA alone. SV is typically calculated echocardiographically as the product of the LV outflow tract (LVOT) cross-sectional area (CSA) and the LVOT pulsed Doppler velocity time integral. The LVOT is assumed to be circular with CSA calculated as $\pi(d/2)^2$ where d is the LVOT diameter. With the recognition that the LVOT is often not circular, that image quality might limit measurement accuracy, and that small errors in LVOT diameter measurement are amplified in the calculation of CSA, SV might be underestimated and a patient with moderate or mild stenosis might be incorrectly categorized as having severe AS based on AVA calculation alone. Additionally, there is some controversy as to the validity of defining reduced SV as < 35 mL/m^2, particularly in obese subjects. This adds to concerns that one can overestimate the severity of stenosis in the obese if severe AS is defined exclusively as a body surface area-corrected AVA $\leq$ 0.6 cm^2/m^2. Finally, recognizing the interplay between systemic blood pressure and AS as determinants of LV afterload, a concept captured in the calculation of valvulo-arterial impedance,[11] it should be noted that hemodynamics should be assessed when the patient is normotensive. The guidelines recommend surgery (class IIA) for symptomatic patients with low-gradient low-flow preserved-LVEF AS whose symptoms are believed to be on