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Review

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Up to date concepts in valvular heart disease

Actualización de conceptos en cirugía de reemplazo valvular

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ABSTRACT

The prevalence of valvular heart diseases (VHD) has evolved over time. While industrialized countries have reduced the rheumatic fever-related VHD, developing countries still have a substantial number of cases due to this reason. Nevertheless, rheumatic fever is still the main cause of VHD around the world. Regardless of rheumatic or degenerative etiology, it is essential to highlight that left-sided valves still represent the surgery's main indication for valve replacement. The European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) joined forces to write the VHD Guidelines for the first time in 2012 and updated them in 2017. From our perspective, guidelines are useful in guiding the decision-making of health professionals in daily practice. However, patient's options must be individualized and taken carefully by caregiver and physician according to the specific case. Currently, in VHD management, the medical option is still an indication in specific cases, percutaneous procedures and its indications have dramatically increased, and the surgical approach of repair versus replace is dependent upon a variety of factors. We focus this review on the indications of valve replacement and the grafts available when the surgery is indicated.

RESUMEN

La prevalencia de las enfermedades valvulares del corazón (EVC) ha evolucionado con el tiempo. Mientras que los países industrializados han reducido las valvulopatías relacionadas con la fiebre reumática, los países en desarrollo todavía tienen un número sustancial de casos debido a esta razón. Sin embargo, la fiebre reumática sigue siendo la principal causa de EVC en todo el mundo. Independientemente de la etiología reumática o degenerativa, es fundamental destacar que las válvulas izquierdas siguen representando la principales involucradas al momento de indicar una cirugía para el reemplazo valvular. La Sociedad Europea de Cardiología (SEC) y la Asociación Europea de Cirugía Cardio-Torácica (AECCT) unieron sus fuerzas para redactar las guías de EVC por primera vez en 2012 y las actualizaron en 2017. Desde nuestra perspectiva, las guías clínicas representan un sistema que facilita la toma de decisiones de los profesionales de la salud en la práctica diaria, pero cada indicación, decisión clínica y opciones que se ofrecen a los pacientes deben ser individualizadas y tomadas por el cuidador y médico, según el caso específico. Actualmente, en el manejo de la EVC, la opción médica sigue siendo una indicación en casos específicos, los procedimientos percutáneos y sus indicaciones han aumentado dramáticamente, y el abordaje quirúrgico de reparación versus reemplazo depende de una variedad de factores. Centramos esta revisión en las indicaciones de sustitución valvular y los injertos disponibles cuando la cirugía está indicada.

INTRODUCTION

The prevalence of valvular heart diseases (VHD) has evolved over time. Currently, there has been a significant decrease in industrialized countries thanks to better management of rheumatic fever. However, developing countries still have a substantial number of cases due to this reason.[1]

Nevertheless, industrialized countries have increased their life expectancy. In consequence, this implicitly brings an increased rate of degenerative valve disease (DVD). Even though the VHD or DVD are not considered a public health problem, a significant number of patients require an answer to their problem in an ever-changing field of cardiac surgery.[2]

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It is essential to highlight that left-sided valves still represent the surgery's main indication for valve replacement, being the aortic valve the most common, followed by the mitral valve. Currently, at the moment of offering a solution to the patient, either open or percutaneous procedures are available, and specific indication has been established for each one.[3]

In this field, cardiologists and surgeons had joined forces to write the valvular heart disease guidelines for the first time in 2012 when the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) published an unavoidable document to read when we are talking about VHD in Europe.[2]

In 2017, ESC/EACTS updated the guidelines due to new evidence on percutaneous interventional techniques and risk stratification concerning the timing of intervention in VHD. Simultaneously, the American College of Cardiology/American Heart Association (ACC/AHA) also published guidelines for VHD. Many differences between the two major society guidelines have been described and, even a small number of the guideline recommendations seem contradictory. Author of reviews about these differences considers more randomized trials are required to clarify recommendations.[4,5]

From our perspective, guidelines and their recommendations in any specialty are just guides to facilitate decision-making of health professionals in their daily practice. However, every indication, clinical decision and options offered to the patients must be individualized and taken by caregiver and physician according to the specific case.

Particularly in valve heart disease management, the medical option is still an indication in specific cases, percutaneous procedures have dramatically increased in number and indications, and the surgical approach of repair versus replace is dependent upon a variety of factors, including surgical experience, valve morphology, surgical risk, mechanism of the affectation, anticoagulation planning, and patient age.

We focus this review on the indications of surgeries and the grafts available when performing the surgery.

SUMMARIZING SURGICAL INDICATIONS

Aortic stenosis (AS) is the most common valvular disorder in Europe, and the 2017 ESC/EACTS guidelines consider balloon aortic valvotomy, transcatheter aortic valve implantation (TAVI), or surgical aortic valve replacement (SAVR) as suitable options in patients requiring intervention.[2,6]

For establishing indications, symptomatic versus asymptomatic patients must be differentiated. Indications could be summarized as follow:

- Intervention is indicated in symptomatic patients with severe, high-gradient aortic stenosis (mean gradient ≥ 40 mmHg or peak velocity ≥ 4.0 m/s). It is also indicated if severe low-flow, low-gradient (< 40 mmHg) aortic stenosis with reduced ejection fraction and evidence of flow (contractile) reserve excluding pseudo-severe aortic stenosis.
- Patients with low-flow, low-gradient (< 40 mmHg) and aortic stenosis should undergo surgery if they have normal ejection fraction after careful confirmation or if they have a reduced ejection fraction without flow (contractile) reserve, particularly when CT calcium scoring confirms severe aortic stenosis.
- Symptomatic severe AS demands intervention in nearly all clinical circumstances. However, quality of living, benefits for the patient, comorbidities or surgical risk must be analyzed before indicating the surgery.
- Asymptomatic patients have indications only if severe aortic stenosis and systolic LV dysfunction (LVEF) not due to another cause, an abnormal exercise test showing symptoms on exercise related to aortic stenosis or an abnormal exercise test showing a decrease in blood pressure below baseline.
- In Asymptomatic patients should indicate a surgery if they have low surgical risk and very severe aortic stenosis defined by a Vmax > 5.5 m/s, or severe valve calcification and a rate of Vmax progression ≥ 0.3 m/s/year or markedly elevated BNP levels

confirmed by repeated measurements without other explanations or in cases of severe pulmonary hypertension without other explanation.[2]

Specific details about open surgery or percutaneous, or concomitant aortic valve surgery at the time of other cardiac/ascending aorta surgery procedure is beyond this review, and we strongly recommend reviewing the 2017 ESC/EACTS guidelines.[2]

Regarding aortic regurgitation, every symptomatic patient or anyone with acute aortic regurgitation requires surgical intervention, and the latter often demands emergent surgical intervention. Asymptomatic patients have an indication of surgery if resting left ventricular ejection fraction (LVEF) < 50%. Also, should be considered the surgery for asymptomatic patients with resting ejection fraction > 50% with severe LV dilatation: LVEDD > 70 mm or LVESD > 50 mm (or LVESD >25 mm/m^2 BSA in patients with small body size). Surgery is indicated in patients undergoing CABG or surgery of the ascending aorta or another valve.[2,6]

Mitral regurgitation (MR) remains the second most common indication for valve surgery in Europe. Patients with acute severe mitral regurgitation must be provided for urgent surgical intervention, according to the 2017 ECS/EACTS guidelines. In contrast, for deciding about surgery in chronic MR, symptomatic and asymptomatic patients must be differentiated.[2,6]

The surgery is indicated for symptomatic patients with MR if LVEF > 30%. For asymptomatic patients, surgery is indicated in asymptomatic patients with LV dysfunction (LVESD ≥ 45 mm and/or LVEF 60%) and atrial fibrillation secondary to mitral regurgitation, as well as, patients with pulmonary hypertension. Indication of surgery should be considered in asymptomatic patients with preserved LVEF (> 60%) and LVESD 40-44 mm when a durable repair is likely, surgical risk is low, the repair is performed in a heart valve center, and presence of flail leaflet or significant Left Atrium (LA) dilatation in sinus rhythm.[2,6]

The guidelines exposed recommendation IIa and IIb for specific techniques, valve repair, valve replacement or percutaneous procedures. However, these details go beyond our scope, and we strongly recommend to review the ECS/EACTS guidelines for this information.

The scenario is different for patients with Mitral stenosis because surgery has been displaced by percutaneous mitral commissurotomy (PMC). Currently, only symptomatic patients who are not suitable for PMC or asymptomatic patients with unfavorable anatomic and clinical characteristics undergo surgery. For all the other patients with moderate or severe mitral stenosis requiring intervention, PMC is the mainstay.[2,6]

Regarding right-sided valves, the 2017 ES/EACTS guidelines recommend surgery for symptomatic patients with severe tricuspid stenosis. Surgery is also indicated for patients with severe tricuspid stenosis who are undergoing left-sided valve surgery. In cases of tricuspid regurgitation (TR), indications of surgery have been established for symptomatic patients but also should be considered in asymptomatic patients when progressive right ventricle (RV) dilatation or decline of RV function is observed as well as, patients with severe primary tricuspid regurgitation undergoing left-sided valve surgery. Mildly symptomatic (or asymptomatic) patients with progressive RV dysfunction and severe primary tricuspid regurgitation.[2,6]

GRAFTS FOR VALVE REPLACEMENT

Once the indication of valve replacement has been established according to the guidelines or because individualization of the case lead to think this is the best option, surgeons will have a wide range of options to choose. However, this selection seems to be related to geographical areas, personal experiences, research conducted in specific locations, regional/national guidelines and/or an attempt to adjust the grafts to the patient.

Guidelines limit the choice between a mechanical and a biological valve. This selection is made based on the risk of anticoagulation-related bleeding and thromboembolism with a mechanical valve versus the risk of structural valve deterioration with a bioprosthesis. Although the patient's life expectancy and

lifestyle are considered for this selection, the guideline does not go beyond to thought the emerging alternatives.

Allografts are one of these alternatives to grafts. At the moment, cryopreserved human heart valve allografts still represent almost perfect substitutes for heart valves. In fact, valve allografts have wide acceptance, and they have been in several indications. However, the most common procedure where the valve allografts are used is the Ross procedure. This technique dates back to 1967, when Donald Ross transferred the patient's pulmonary valve into the aortic root. An allograft replaces the pulmonary valve. Since the 60s, excellent long-term results and the possibility of combination with other techniques have encouraged to continue this technique.[7]

However, the Ross procedure is a complex operation; careful patient selection and experienced surgeons are mandatory requirements to achieve satisfactory results.[7]

In Europe, several groups have worked with allografts, and new variants have been proposed with the aims of creating a graft with improved durability compared to routinely used valve substitutes. The most significant and more exciting proposal involving allografts and tissue-engineered aortic valve (TEV) came in 2013 from the Department of Cardiothoracic, Transplant and Vascular Surgery at the Hannover Medical School. This project has evolved and currently is called ARISE. Now, it is a European Commission-funded project, led by the Hannover Medical School, nine hospitals, six tissue banks and an innovative biotechnology company providing the decellularization service that came together for the world-wide first prospective study on cell-free allografts for aortic valve replacement.[8,9]

After extensive preclinical work and their first publication in 2013 performed in sheep, the group leader, Haverich et al., have used decellularized allogenic heart valve matrices for aortic valve replacements (AVR) based on compassionate use in 34 patients with tentative assessment showing favorable initial clinical results. However, transferring this regenerative approach to routine clinical application necessitates controlled prospective clinical trials lacking to date.[8]

Simultaneously, tissue-engineering heart valve (TEHV) has emerged as an interesting alternative to find a solution for the increasing demand for cardiac valves. TEHV has centered on its research lines in creating an ideal scaffold to be seeded by cells, which are expected to proliferate to resemble a natural human heart valve. Scaffolds materials can be classified into natural and synthetic. Natural scaffolds are decellularized xenografts purified from animal valves, and the synthetics as they are called come mainly from polycarbonate urethane and polyether urethane. To avoid an immune reaction, cells to seed in the scaffold must come from an autologous source.[10]

A combination of the natural and synthetic scaffold has also been developed. Decellularized bovine pericardium extracellular matrix modified with synthetic polymers by coating the structure with a layer of polycaprolactone-chitosan (PCL-CH) nanofibers have been previously described as an attractive hybrid scaffold with superior mechanical properties and promising results.[11]

Tissue-engineered heart valves are an increasing alternative with the hope of eventually to develop an ideal and clinically suitable cardiac valve replacement to cover the growing demand. Currently, TEHV is considered the only technology is working on the potential creation of tissues analogous to a native human heart valve, with longer sustainability and fewer side effects.[10]

Other exciting alternatives to valve replacement are the xenografts. In this regard, an endovascular alternative worth to be highlighted. The melody transcatheter valve (Medtronic, Minneapolis, MN, USA) is a heart valve from a cow's vein attached to a wireframe that has demonstrated to be safe and effective in pediatric patients with excellent short- and mid-term follow-up hemodynamic results. However, their approved indications are limited to treat bioprosthetic valves dysfunction, mainly in pulmonary position.[12]

The melody transcatheter valve (Medtronic, Minneapolis, MN) has emerged in the era of percutaneous cardiac valves. Another percutaneous alternative is SAPIEN S3 from Edward Lifesciences (Edwards, Irvine, CA, USA). However, transcatheter valve replacement is

not the scope of this review, and we will not go deep into this alternative.

Among the xenografts, also highlight The Edwards Inspiris Resilia® valve (Edwards Lifesciences, Irvine, CA, USA), which is bovine pericardial tissue transformed by a preservation technique which was primarily designed as the aortic valve, but because of availability of small size have been tested in children. Currently, The Edwards Inspiris Resilia® valve (Edwards Lifesciences, Irvine, CA, USA) has been accepted to be potentially used in mitral position in children. However, there are not robust clinical trials, and more studies are required.[13]

Regarding synthetic valve replacement, the classical concept is that by implanting a mechanical valve, the patient will require permanent anticoagulation. However, Lapeyre et al. have performed a preclinical assessment of a trileaflet mechanical valve. They have tried to develop a mechanical valve that will not require permanent anticoagulation.[14,15]

Finally, it is essential to highlight that the decellularization technique and valves fully built with polyurethane are being developed. However, until having enough trials and studies, these options are also too young to extract conclusions.

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