Review article

DURABILITY OF BIOLOGICAL PROSTHESES USED FOR MANAGEMENT OF DEGENERATIVE AORTIC STENOSIS – TAVR vs. SAVR

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ABSTRACT:
The only known treatment for high grade degenerative aortic stenosis until the beginning of this century was surgical replacement with a biological or mechanical valve. For the high risk or inoperable patients this treatment was unacceptable, with a high mortality rate in both operated and non-operated cases. The new concept of transcatheter valve implantation was developed especially for this group of patients, which number continues to increase. It is a really attractive idea, being able to offer a non-invasive and low risk procedure for a patient who is not considered a good candidate for conventional operation. The increase in the operators experience reduces the rate of mortality in TAVI even more. Both TAVI and surgical valves are biological. The technology used for production of the balloon expandable and self-expandable valves is much more advanced. The biological tissue used in both types of valve is prone to degeneration due to different factors and can lead to valvular dysfunction. The surgical valves are made from porcine or bovine tissue and have a lifespan between 10 and 15 years. In some cases, the dysfunction occurs much sooner. If that happens the patient needs a re-replacement valve surgery. Since such a procedure is risky the patient is usually referred for valve-in-valve TAVI.

Keywords: Transcatheter aortic-valve implantation (TAVI), aortic stenosis, bioprosthetic valvular dysfunction

INTRODUCTION:
The surgical treatment of degenerative aortic valve disease is in general cutting out the old diseased valve and replacing it with an artificial one – mechanical or biological [1]. The drawback of the mechanical ones is the requirement for life-long anticoagulation. The biological valves tend to degenerate over time and that leads to increase in gradient. The patients with high surgical risk are not good candidates for an operation, because of the high mortality rates. For many years an alternative for surgery was wanted. First emerged the transcatheter balloon valvuloplasty – first attempted and described by Cribier et al in the distant 1985 [2]. Because of the high early restenosis rate (more than 80%

of the patients in the first year), this procedure was abandoned, even though it temporary improved the quality of life [3, 4]. Òhe first transluminal valve was implanted by A. Cribier in 2002 [5]. This event marked the beginning of a new era in medical history, characterised by fast progression of new technologies. This new and remarkable method is not without its issues.

The market for TAVI valves is dominated by the Edwards "Sapien" (first generation balloon expandable valve) (Irvine, California) and Medtronic CoreValve (self-expanding valve) (Minneapolis, Minnesota). Two different valve technologies and one common thing: the leaflets are made by biological structures, just like a surgical bioprosthesis.

The term "bioprothesis" includes homografts, pericardial bioprostheses, pulmonary autografts, stented and stentless porcine autografts.

A TAVI valve that doesn't need any sutures, allows for rapid deployment, anchors itself within the aortic annulus, facilitates a minimally invasive approach and reduces the duration of anesthesia. Both the balloon-expandable and the self-expanding transcatheter valves are made from bovine or porcine pericardium.

Both surgical bioprostheses and transcatheter ones are vulnerable to structural degeneration. This is a dysfunction of the valve mediated by multifactorial processes, leading to accumulation of connective tissue and calcium. This results in secondary stenosis in ~40% of the valves, regurgitation in ~30% of the valves, or combined stenosis and regurgitation in ~30%. These complications in TAVI valves are often unrecognized or underestimated due to lack of knowledge about the normal and pathological appearance of one such valve.

Valvular dysfunction means appearance of at least a moderate aortic regurgitation with or without presence of mean gradient of more than a 20mmHg, which is not related to endocarditis and is not present in the first 30 days of follow up. There is no unified consensus regarding the definition yet though.

Bovine pericardial valves tend to develop stenosis in relation to calcification more often. Porcine valves are vulnerable to leaflet tear and regurgitation. Stenosis appears

usually in stented valves. Leaflet tear and regurgitation is typical for the stentless valves.

Some studies suggest that, in addition to the passive processes, active mechanisms that trigger inflammation can contribute to calcification and consequently- dysfunction. The fixation of the leaflets in glutaraldehyde decreases tissue antigenicity, but does not eliminate entirely the risk for an immune response leading to accelerated tissue mineralization. Early post-implantation valvular thrombosis does happen up to some degree in 15% of the patients. Even in successfully treated cases it triggers inflammation and a subsequent fibro-calcific remodeling of the leaflets.

AIM OF THE STUDY:

Our purpose is to review the durability of all biological valves – surgical and transluminal. We want to analyze retrospectively databases, containing patients with post-implantation aortic valve dysfunction. Information regarding dysfunction of TAVI valves is scarce mainly due to the newness of the procedure. We will try to find out what is the proper treatment in case of prosthetic valvular dysfunction.

In the literature there are many studies regarding the structural valve dysfunction in surgical valves. Most studies reveal less than 20% incidence of degeneration during the first decade after SAVR with a bioprosthesis.

In a study by the Division of Cardiovascular Surgery of Toronto General Hospital and the University of Toronto (Toronto, Ontario, Canada), Göran Dellgren et al. describe the late hemodynamic and clinical outcomes of aortic valve replacement with the Carpentier-Edwards Perimount bioprosthesis [6]. In the study are included 254 patients in which the bioprosthetic valve is implanted in the period from January 1984 to December 1995. The results are 11 early deaths (4%) and 58 late deaths. The percentage of patients that remain alive at 5, 10, and 12 years are around 80%, 50%, and 36%. At 12 years the freedom from cardiac death is ~73%, from valve-related death 84%, from valve reoperation ~ 83%, from thromboembolism 67%, and the freedom from endocarditis is 98%.

In another study with the same valve, Frater et al. describe 267 patients, that got operated on between September 1981 and December 1983 [7]. Valvular dysfunction leading to explantation was seen in around 0.9%, with an associated mortality of 0.1%. At 14 years post implantation, the freedom from overall and valve-related death is 39.3% and 78.8%, the freedom from valve dysfunction is between 70.4% and 81.7%. The freedom from valve explantation as a result of dysfunction is 85.1% in all patients.

In a study using Hancock Porcine Bioprosthesis, Aldo Milano et al. review 196 patients [8], operated from 1970 to 1983. The reported actuarial freedom from valve-related deaths, valve failure, and overall valve related complications at 14 years are 66.3%, 34.3%, and 30%, respectively.

The high actuarial and actual freedom from structural valve dysfunction support the long-term durability of surgical bioprosthesis.

Most of the patients enrolled in TAVI studies are elderly, with severe comorbidity and the mortality that is not related to the valve is respectively high.

A big study in Italy, including 8 centers and 353 patients, who received TAVI implants implanted between June 2007 and August 2009, Marco Barbanti et al. shows the clinical outcomes during a 5 years of follow-up. A low rate of significant prosthetic valvular degeneration was reported - 1.4%. A late prosthesis failure occurred in 5 patients, redo TAVI was performed in 2 patients due to symptomatic prosthetic restenosis. The 3 other cases of prosthesis failure did not require an intervention.

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry contains promising data [9]. No matter that the mortality rate is high it is not connected to valvular dysfunction. In this study the strong predictors of death are other comorbidities like renal dysfunction, the presence of coronary artery disease, non-transfemoral approach, left ventricular dysfunction with ejection fraction <30%, the presence of post-procedural severe aortic regurgitation and chronic obstructive pulmonary disease.

The first study for TAVI durability by Dannny Dvir from St. Paul's Hospital, Vancouver, Canada [10], describes the implantation of TAVI valves in an increasingly younger patients at low surgical risk. The goal of this study is to assess long-term valve deterioration risk. In the study are involved 378 patients. In 35 patients valvular degeneration criteria are met – 23 have regurgitation and 12 stenosis. Significant valve degeneration is revealed between years 5 and 7 and is often associated with kidney failure.

DISCUSSION:

The treatment for bioprosthetic surgical valve dysfunction is either re-do surgery or transcatheter valve-in-valve procedure. Valve-in-valve within a degenerated surgical valve is recommended by the AHA/ACC guidelines for high-risk patients [11], since this is the less-invasive option.

Despite the adequate durability of the surgical valve, there are many publications describing degeneration. The best course of action in case of biological valve dysfunction is yet unknown.

In case of TAVI failure it is feasible to implant another valve. A few centers reveal their experience with implanting a valve at the place of a degenerated bioprosthesis [12] [13]. The publications confirm the feasibility of this new, promising transcatheter valve implantation like an alternative treatment for a degenerated aortic bioprosthesis.

A study in two German centers reviews the clinical outcomes after implantation of transcatheter valve in a degenerated surgical valve [14]. 19 patients are involved between October 2011 and November 2015. The most common indication for a redo procedure is paravalvular regurgitation. The procedural success is high with low post-procedural gradients and no severe mismatch. Good valvular functional status is observed after 12 months, but mortality rates are still high, due to comorbidities.

In case of a TAVR prosthesis dysfunction, a new TAVI procedure is advisable and associated with excellent hemodynamic results. It is possible to shrink the aortic annulus after a few prosthetic implantations. This is called Curzen Syndrome. One has to be aware of it when multiple re-do procedures are done.

CONCLUSION:

The new generations of transcatheter valves show a low rate (1.4%) of significant prosthetic valve degeneration. Since it is a new method of treatment it has its specific complications (for example paravalvular leak). Surgical valves have good long-term durability, with low rates of dysfunction, but in case of a failure the patient is referred for interventional treatment. This kind of patients are considered to be high risk for re-operation, according to Valve Academic Research Consortium (VARC) [15]. The long-term results after TAVR implantation are still being investigated, but at the moment the results sound promising.

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