Transcatheter heart valve failure: the sword of Damocles over our heads?

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This editorial refers to ‘Transcatheter heart valve failure: a systematic review’, by D. Mylotte et al. on page 1306.

Transcatheter aortic valve implantation (TAVI) has emerged as the treatment of choice in inoperable patients with severe aortic stenosis and as an alternative treatment strategy in high-risk patients, which is non-inferior to surgical aortic valve replacement (SAVR). The recently published results of the US CoreValve High Risk cohort even showed that TAVI was associated with a significantly higher rate of survival at 1 year than SAVR in patients at increased surgical risk. It is estimated that >100,000 TAVIs have been performed between 2002 and 2013. Over the years, a rapid development in prosthetic valves has been witnessed, with the introduction of so-called next-generation devices, which are addressing transcatheter heart valve- (THV) specific shortcomings such as paravalvular aortic regurgitation (AR), conduction disturbances with the need for pacemaker implantation, and vascular complications by modifications of the valve design (paravalvular sealing mechanisms), repositionability, and smaller delivery sheath size.

As approximately 200,000 patients worldwide undergo SAVR annually, with significantly higher usage of bioprosthetic surgical heart valves, and TAVI is currently evaluated for treatment of so-called ‘intermediate risk’ patients, an exponential increase in the use of TAVI can be expected over the next years. Since the existing rationally clinical trials have been designed to show non-inferiority of TAVI compared with SAVR in elderly patients with (at least in part) life-limiting co-mobilities, the question of durability and long-term outcome of THVs will play a pivotal role in future studies with the consideration of younger and healthier patients for TAVI.

Durability is determined by numerous factors including the characteristics of the valve tissue, tissue treatments, and valve design, as well as multiple clinical factors such as proper deployment of the prosthesis with symmetric leaflet coaptation and the final transvalvular gradients. THVs are often delivered in an oval-shaped fashion due to the predominantly non-circular form of the left ventricular outflow tract (LVOT), which represents the landing/anchoring zone of the THV stent frame, and the calcified leaflets of the native aortic valve. In particular, deployment of THVs in patients with a bicuspid valve anatomy leads to an elliptical distortion of the THV geometry with unknown impact on longevity. In addition, patient age itself plays a crucial role for durability. Mechanical stress and collagen fibre disruption of the prosthetic leaflets may favour early calcification of the leaflets and valve degeneration. Anticalcification treatment of the leaflets may prevent these degenerative changes. Finally, the pre-crimping process inherent to transcatheter aortic valves as well as the deployment of a THV by balloon expansion or balloon post-dilation for the reduction of paravalvular AR may cause structural changes of the collagen and elastic fibres of the leaflets. The impact of these changes on long-term durability of THVs is still completely unknown. Although the data of the first 5-year follow-up studies are encouraging, the existing studies were too small to address valve failure as a safety endpoint. To assess the durability and longevity of THVs, objective performance criteria analogous to that of surgical bioprosthetic heart valves will have to be used.

Mylotte and colleagues should be congratulated on this important manuscript, as their review is the first systematic description of THV failure. The authors summarize failure modes typical of surgical bioprosthetic valves and define others that are unique to the THV-specific design such as prosthesis compression or late embolization. Five failure modes are described, which could be supplemented by another THV-specific, procedure-related failure mechanism: paravalvular AR (Figure 1).

Transcatheter heart valve endocarditis according to the VARC-2 criteria is defined as fulfilment of the Duke endocarditis criteria or evidence of abscess, paravalvular leak, pus, or vegetation confirmed as secondary to infection by histological or bacteriological studies during a re-operation. In a large, multicentre registry from Italy and Germany, the overall incidence of infective endocarditis after TAVI was 1.1% (29 of 2572 patients). The majority of patients presented with fever and heart failure symptoms. Comparable with what is stated in the review by Mylotte and colleagues, staphylococci, enterococci, and streptococci were the predominant causative organisms.

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microorganisms. Echocardiography was positive in 86% of the patients with prosthetic vegetations as the most common finding.

In contrast to the review of Mylotte et al. with a survival of 75%, only 38% survived until hospital discharge in the multicentre registry published by Latib et al. This emphasizes the importance of the question of how to treat these patients suffering from THV endocarditis, in whom TAVIs had been preferred over SAVRs due to several reasons such as patient age and co-morbidities. Although antibiotic therapy might be sufficient in some cases, a heart team is needed to decide whether and especially when a patient suffering from THV endocarditis should undergo surgical intervention.

Many TAVI centres administer peri- and post-procedural antibiotic prophylaxis, but it will be hard to prove if this treatment strategy helps to prevent endocarditis. Prophylaxis against THV endocarditis is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa, but seems not to be necessary before non-dental procedures (e.g. transoesophageal echocardiography, oesophagogastroduodenoscopy, colonoscopy, or cystoscopy) in the absence of active infection. Furthermore, the debate as to whether a cardiac catheterization laboratory is sterile enough for a heart valve implantation compared with a hybrid suite or surgical theatre will be ongoing and needs to be addressed in future studies.

Transcatheter heart valve thrombosis predominantly occurred after implantation of the Edwards-SAPIEN prosthesis (14 of 15 patients), as outlined in the review of Mylotte et al. These patients presented with progressive dyspnoea and increasing transvalvular gradients. According to the VARC-2 criteria, valve thrombosis is defined as any thrombus attached to or near an implanted valve that occludes part of the blood flow path, interferes with valve function, or is sufficiently large to warrant treatment. Although leaflet thickening and immobility in combination with increasing transvalvular gradients might give a diagnostic clue, the diagnosis of THV thrombosis is not easy to confirm and needs to be differentiated from endocarditis.

Figure 1 Transcatheter heart valve failure modes. Failure modes that are similar to those of surgical bioprosthetic valves are endocarditis (A), thrombosis (B), and structural failure of the transcatheter heart valve (THV) (C). Failure modes that seem to be unique to the specific design of THVs comprise paravalvular aortic regurgitation (D), late THV embolization (E), and THV compression (F).
before initiating a specific therapy. Considering the review of Mylotte et al., the treatment of choice in these patients might be the administration of oral anticoagulation, since the transvalvular gradients diminished towards the post-procedural gradient and leaflet mobility normalized in patients treated with this regimen. Taken together, however, this again raises the question of how long dual antiplatelet therapy (DAPT) with aspirin and clopidogrel is necessary in TAVI patients and whether we need specific regimens depending on the valve type. Future studies will have to elucidate not only the optimal duration of DAPT but also whether oral anticoagulation may be reasonable for the first 3 months after TAVI as recommended by the American guidelines after SAVR with a surgical bioprosthesis.12

Structural THV failure has been reported in a few cases after TAVI due to chronic degenerative processes leading to severe leaflet calcification, cusp rupture, or tissue ingrowth (pannus).9 The aetiology of THV degeneration seems to be very similar to that of surgical bioprostheses. However, THV-specific characteristics such as incomplete frame expansion or elliptically deployed prostheses as well as the pre-crimping process might predispose for degeneration and negatively impact THV durability. Although we and others have shown that structural THV failure independent from the failure mechanism (leaflet calcification with severe restenosis13 or cusp rupture with severe transvalvular regurgitation14) can be treated successfully by THV-in-THV implantation, the major focus should be on this failure mode, as it will be the most frequent reason for THV failure over time and will play the pivotal role for long-term durability—especially for the use of TAVI in younger patients.

Paravalvular AR is a procedure-related failure mode, which is caused by incomplete apposition of the prosthesis with the aortic annulus, since THVs are implanted in a sutureless fashion using oversized to anchor the prosthesis stent frame at the level of the native aortic annulus.15 As next-generation devices are addressing paravalvular AR by paravalvular sealing mechanisms and repositionability of the prosthesis itself during the deployment process, this issue will hopefully overcome in the future.4

Late THV embolization represents a new, TAVI-specific failure mode, which predominantly has been associated with the balloon-expandable Edwards-SAPIEN prosthesis and occurred as retrograde embolization into the LVOT in most of the patients.16 This phenomenon might be associated with the anchoring mechanism of the prosthesis, deep implantation, and undersizing of the THV. As most patients develop abrupt left ventricular failure, an urgent intervention is needed: in most of the cases, emergent cardiac surgery was needed to retrieve the prosthesis from the LVOT. Late THV embolization can be addressed by several considerations: precise valve sizing by three-dimensional measurement of the aortic annulus, the use of a self-expanding prosthesis, especially in borderline cases, and repositioning of THVs, which have been deployed in a ‘too ventricular’ fashion. Taken together with the introduction of next-generation THVs, late prosthetic embolization might also be a thing of the past in TAVI patients.

Another failure mechanism, which seems to be unique to the balloon-expandable Edwards-SAPIEN prosthesis, is THV compression after cardio-pulmonary resuscitation.9 Whether self-expanding THVs may be less susceptible to deformation seems to be obvious but remains speculative, until in vitro or in vivo experiences for this scenario are reported. Nonetheless, this characteristic seems to be an achilles’ heel of non-self-expanding THVs, which has to be taken into account when a younger patient undergoes TAVI.

The review of Mylotte and colleagues very nicely summarizes the failure mechanism of THVs, which occur very rarely, have not been collected systematically, and, therefore, might have been under-reported so far. The durability of the currently available THVs appears adequate for elderly patients with limited life expectancy. However, further questions remain. Will the durability of the THVs match that of surgical bioprostheses? Should our limited experience with valve durability and THV failure be a contraindication to treat younger, so-called ‘intermediate risk’ patients with TAVI in the future? Moreover, the durability of the next-generation valves and the outcome of valve-in-valve procedures needs to be determined.

The only way to answer these burning questions and to assess whether certain THV types are more prone to certain failure modes than others is the careful continuation of large, nationwide surveillance registries with long-term follow-up such as the German Aortic Valve Registry (GARY) or the US Transcatheter Valve Therapy (TVT) registry. Only then we can get rid of the sword of Damocles hanging over our heads, and prove whether the durability of THVs is equivalent to that of surgical bioprosthetic heart valves.

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References


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**CARDIOVASCULAR FLASHLIGHT**

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How to re-shape a transcatheter heart valve

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A 82-year-old female patient suffering from severe aortic stenosis presented with progressive dyspnoea NYHA class III after syncope. Due to severe calcifications of the ilio-femoral arteries, she underwent uneventful transapical transcatheter aortic valve implantation with a balloon-expandable Edwards SAPIEN 3 (23 mm) prosthesis. Three hours postoperatively, the patient had a sudden cardiac arrest due to ventricular fibrillation (VF). After 4 min of cardiopulmonary resuscitation (CPR) normal sinus rhythm was restored. Since neither signs of cardiac ischaemia (no ST-segment alterations in the electrocardiogram) nor troponin elevation were seen myocardial ischaemia could be ruled out as reason for VF. TEE after CPR confirmed a correct intra-annular position of the transcatheter heart valve (THV) but revealed a severe prosthesis deformation with consecutive paravalvular leakage (Panels A and B). To overcome this THV-specific failure mode, which has been described recently for balloon-expandable THVs, we decided to re-dilate the SAPIEN 3 prosthesis via transfemoral access (Supplementary material online, Video S1), using a 9-French 20 mm Tyshak II Balloon Dilatation Catheter (NuMED Inc., Hopkinton, NY, USA).

After the first inflation of the balloon (Supplementary material online, Video S2), the prosthesis appeared reshaped in fluoroscopy without any signs of migration or any remaining transvalvular gradient. Furthermore, the significant paravalvular leakage had completely disappeared after re-dilation of the prosthesis stent frame, which now appeared round-shaped again (Panels C and D). The further clinical course of the patient was uneventful.

Long-term follow-up has to show whether re-dilation might impact stability of the stent frame or durability of the valve itself but this case demonstrates how to address successfully THV compression.

Supplementary material is available at *European Heart Journal* online.

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