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Short title: Degenerated TAVR

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Key words:
transcatheter aortic valve replacement (TAVR), redo-TAVR, TAV-in-TAV, TAVR explant, coronary artery re-access, coronary artery occlusion, leaflet overhang, neo-skirt

Abstract:

With the expansion of transcatheter aortic valve replacement (TAVR) to younger and lower surgical-risk patients, many younger and less co-morbid patients will be treated with TAVR and are expected to have a life expectancy that will exceed the durability of their transcatheter heart valve. Consequently, the number of patients requiring re-intervention will undoubtedly increase in the near future. Redo-TAVR and TAVR explant followed by surgical aortic valve replacement are the different therapeutic options in the event of bioprosthetic valve failure and the need for re-intervention. Patients often anticipate being able to benefit from a redo-TAVR in the event of bioprosthetic valve failure after TAVR, despite the lack of long-term data and the risk of unfavorable anatomy. Our understanding of the feasibility of redo-TAVR is constantly improving thanks to bench test studies and growing worldwide experience. However, many unknowns remain. In clinical practice, one of the heart team’s objectives is to anticipate the need to re-access the coronary arteries and implant a second or even a third valve when life expectancy may exceed the durability of the transcatheter heart valve. In this review, we address key definitions in the diagnosis of structural valve deterioration and bioprosthetic valve failure, as well as patient selection and procedural planning for redo-TAVR to reduce periprocedural risk, optimize hemodynamic performance, and maintain coronary access. We describe the bench testing and literature in the redo-TAVR and TAVR explant fields.
Over the years transcatheter aortic valve replacement (TAVR) has become the routine therapy for symptomatic severe aortic stenosis in the elderly population across all surgical risk categories and is increasingly used in younger patients. As a result, the number of TAVR procedures in the USA exceeded in 2015 that of isolated surgical aortic valve replacement (SAVR), and in 2019, it even exceeded the total number of SAVR associated with other procedures (coronary artery bypass, surgical procedure on another valve)[1]. The latest American Heart Association/American College of Cardiology (AHA/ACC) guidelines give a class I indication for TAVR and SAVR between the age of 65 and 80 while the 2021 European Guidelines favor TAVR over the age of 75[2, 3]. In 2021, 87.5% of US patients aged 65 to 80 were treated with TAVR for their severe aortic stenosis, compared to less than 50% in 2015 [4].

With the expansion of TAVR to younger and lower surgical risk patients, TAVR penetration could reach 300 cases per million inhabitants in many countries as is already the case in Germany [5]. Knowing that all transcatheter heart valves (THV) are made from biological tissue, they are prone to structural valve deterioration (SVD) over time and, therefore many younger and less co-morbid patients are expected to have a life expectancy that will exceed the durability of their THV. Ultimately the number of patients requiring re-intervention will undoubtedly increase.

Redo-TAVR and TAVR explant followed by SAVR are the different therapeutical options in the event of bioprosthetic valve failure (BVF) and the need for re-intervention. In this review, we address key definitions in the diagnosis of structural valve deterioration (SVD) and BVF, as well as patient selection and procedural planning for redo-TAVR to reduce periprocedural risk, optimize hemodynamic performance, and maintain coronary access. We also describe the bench testing and literature in the redo-TAVR and TAVR explant fields.

**The definition of bioprosthetic valve dysfunction, structural valve deterioration and bio-prosthesis valve failure**

Until recently in studies on SAVR, either survival without aortic valve reintervention or mortality related to the valve have been used as endpoints for long-term success. With this definition, we only captured the most severe cases of SVD and the patients who were well enough to undergo a re-intervention. Indeed, the lack of a well-established definition of bioprosthetic valve dysfunction introduced confusion in the interpretation of the different trials and comparisons between the SAVR and TAVR data [6]. Furthermore, in clinical practice, yearly echocardiographic follow-up is often more routinely performed after TAVR than SAVR, which may underestimate the real SVD in SAVR real-world cohorts.

The first standardized definition of bioprosthetic valve dysfunction was provided in 2017 by the European Association of Percutaneous Cardiovascular Intervention (EAPCI), the European Society of Cardiology (ESC), and the European Association for Cardio-Thoracic Surgery (EACTS)[7]. In 2021, the VARC-3 document provided a modified definition of bioprosthetic valve dysfunction which required not only hemodynamic changes but also permanent morphologic changes of the bio-prosthesis.
before SVD could be confirmed. Hemodynamic changes can be related to other causes than SVD and considering only the hemodynamic criteria may overestimate the incidence of true SVD[6, 8].

Briefly, bioprosthetic valve dysfunction includes four different categories: 1. SVD, meaning intrinsic permanent prosthesis changes (i.e. wear and tear, leaflet disruption, flail leaflet, leaflet fibrosis, and/or calcification, strut fracture or deformation), 2. Non-structural valve deterioration (NSVD) which corresponds to paravalvular regurgitation, prosthesis-patient mismatch, and others (e.g. leaflet entrapment, inappropriate positioning), 3. Thrombosis, 4. Endocarditis. These entities are classified into three stages according to the hemodynamic changes which are described in figure 1. Finally, BVF is also divided into three stages and is an important patient-oriented clinical endpoint.

**Valve durability and incidence of failed THV**

Surgical experience has shown us that the Achilles heel of bio-prostheses is long-term durability. In the TAVR world, little data beyond 5 years exists. There is no data beyond 2 years in patients with bicuspid valves who were excluded from the different randomized controlled trials[8]. TAVR was initially performed in elderly co-morbid patients who often died from non-cardio-vascular causes, preventing long-term follow-up.

Indeed, data beyond 5 years from randomized controlled trials are still limited since the early population of high-risk patients from PARTNER IA and inoperable patients from PARTNER IB had a 5-year survival rate of 32% (37% when only transfemoral approach was considered) and 28%, respectively [9, 10]. Importantly, the 5-year data of the low-risk PARTNER 3 trial were recently reported [11]. The significantly lower rate of the composite of death, stroke, and rehospitalization in the TAVR group compared to the SAVR group (8.5% versus 15.1%, p<0.001) at one year was attenuated at 5 years (TAVR: 22.8%, SAVR: 27.2%, p=0.07) [11, 12]. Both groups were associated with low clinical event rates (∼1%/year cardiovascular death, ∼1%/year stroke, ∼3% /year cardiovascular rehospitalization).

The hemodynamic performance of the SAPIEN 3 THV was similar to the surgical valves, with a BVF rate of 3.3% in the TAVR group and 3.8% in the SAVR group. In addition, at 5 years, 86.3% and 87.4% of the patients were alive with a durable valve in the TAVR and SAVR groups, respectively.

Furthermore, 71.0% of the TAVR and 71.9% of the SAVR patients were alive with a KCCQ (Kansas City Cardiomyopathy Questionnaire) score > 75.

Concerning post-TAVR survival trends, the all-comer Danish TAVR cohort which consists of 2670 patients since 2007 provides important data on the impact of age and surgical risk on the survival rate [13]. The overall survival rate in this cohort was 58.1% at 5 years and 20.0% at 10 years with more than half of the mortality being of cardiovascular cause. Age and surgical risk significantly affected survival. The survival of low-risk patients remained stable until 80 years old and one-third of the patients less than 75 years old were still alive 10 years post-TAVR. Finally, patients treated in the last period (2017-2021) had a modestly better 5-year survival rate (61.5%) than the patients treated between 2007 and 2011 (52.9%) and between 2012-2016 (56.3%), confirming the impact of better pre-procedural
planning, improved THV design, increased operator experience as well as the selection of lower-risk and younger patients [13].

The longest follow-up in a randomized controlled trial comes from the NOTION (Nordic Aortic Valve Intervention) trial which randomized 120 patients to SAVR and 130 patients to TAVR using the non-recapturable early-generation Medtronic CoreValve device. The 8-year results (52 TAVR and 39 SAVR still alive) were published in 2021[14] and the 10 year-results (34 TAVR and 27 SAVR still alive) were presented at the 2023 ESC meeting [15]. Moderate and severe SVD at 10 years were significantly lower in the TAVR cohort (19.4% and 3.1%) than in the SAVR cohort (36% and 11%). Similar results were found when applying the modified SDV criteria (severe SVD in 0% and 5%, moderate SVD in 15.3% and 19.9% in the TAVR and SAVR cohorts respectively). There was no significant difference in BVF. Of note, 34% of the SAVR valves were externally mounted leaflet bioprosthetic valves, known for early degeneration. One of them, the Trifecta valve (Abbott Vascular) was withdrawn by the manufacturer in 2023.

In summary, treatment of lower-risk and younger patients as well as improvement in technical aspects of the procedure (i.e.; pre-procedural planning, THV design, implantation technique), and operator experience and expertise are likely to result in improved long-term survival and THV durability.

Assessment of bioprosthetic valve dysfunction

Each case with potential hemodynamic THV deterioration should be comprehensively assessed a) to confirm the hemodynamic deterioration (i.e.; stenosis or regurgitation) b) to determine its stage and c) to understand the etiology related to SVD.

Transthoracic echocardiography (TTE) is the cornerstone for the assessment of valve function and hemodynamics. The maximal and mean gradient across the THV can be determined using the simplified Bernoulli formula, knowing that the formula may be controversial in the setting of bioprosthetic and small valves. The effective orifice area of the THV can be calculated using the continuity equation. Additionally, regurgitant orifice and regurgitant volume are both calculated with the help of the proximal isovelocity surface area (PISA) method. Regurgitant volume may also be assessed using the volumetric method.

The assessment of leaflet morphology and the structure of a THV is crucial. Transoesophageal echocardiography (TEE) offers better spatial resolution compared to TTE and superior temporal resolution compared to CT, thus providing a unique assessment of the morphology and motion of the prosthesis leaflets.

Leaflet thickening may be the result of thrombosis, usually in the form of hypo-attenuated leaflet thickening (HALT), infection, inflammation, or calcification. In such cases, a reduced motion of one or
more leaflets is typically observed. Figure 2 demonstrates an example of SVD secondary to infective endocarditis. On the other hand, mechanical degeneration is characterized by excessive leaflet motion, often manifesting as prolapse or tearing. However, degeneration is more often characterized by thickening, restriction, and calcification.

ECG-gated computed tomography (CT) is the gold standard when suspecting valve thrombosis (HALT) because of its higher spatial resolution but it can also help assess paravalvular leaks and inter-chamber fistulas.

**Management of degenerated THV**

TAVR explant followed by SAVR and redo-TAVR (or TAV-in-TAV) are the different therapeutic options in the event of BVF and the need for re-intervention. We describe the clinical worldwide experience with both approaches and bench test studies (focusing on Medtronic and Edwards THV).

**A. TAVR explant followed by SAVR**

TAVR explant beyond 1 year can be technically complex, particularly for self-expanding valves that go up into the ascending aorta with dense endothelization of its upper portion in contact with the aortic wall [16, 17]. It may lead to ascending aorta and aortic root replacement. In an analysis of the Society of Thoracic Surgeons (STS) database, patients with self-expanding devices required more frequent ascending aorta replacement than those with balloon-expandable THV (18.2% versus 8.2%, p=0.009) [18]. However, the rate of aortic root replacement was similar (22.1% versus 18.9%, p=0.52). TAVR explant in the few days or weeks post-implantation will be easier than later when the endothelization process is advanced [16].

Analysis of a large multi-center American database including all patients who underwent TAVR between 2012 and 2017 showed that the overall incidence of TAVR explant was low at 0.2% (n=227, 71% between the 30th day and 12 months)[19]. The average age of the cohort was 73.7 years, while 30-day and 1-year mortality were as high as 13.2% and 22.9% respectively.

More data are available in the international EXPLANT-TAVR (EXPLANTation After Transcatheter Aortic Valve Replacement Failure) registry, which included 269 patients in 42 centers between 2009 and 2020 (retrospective analysis, exclusion of reinterventions during index TAVR hospitalization)[20]. The mean age of patients was 72.7±10.4 years and the median STS score at the time of TAVR explant was 5.6% (IQR: 3.2%-9.6%) with a median time between TAVR and TAVR explant of 11.5 months (IQR 4.0-32.4 months). THV explanted were Edwards THV in 50.9% and self-expanding or mechanically expandable THV in 49.1%. The causes of TAVR explant were endocarditis (43.1%), SVD (20.1%), paravalvular leak (18.2%), and prosthesis-patient mismatch (10.8%). A redo-TAVR was considered not feasible in as many as 26.8% of cases due to unfavorable anatomy. Aortic root replacement was performed in 13.4% and, 54.6% of cases had an associated cardiac procedure. Per-
procedure mortality was only 0.7%, but the mortality and stroke rates were respectively 13.1% and 8.6% at 30 days and 28.5% and 18.7% at 12 months. Therefore, the risks associated with TAVR explant were not negligible and similar to the large multi-center American database [19]. After adjustment, in multivariate analysis, the independent factors of 30-day mortality were a history of stroke (OR: 3.4; 95%CI: 1.4-8.6), pulmonary hypertension (OR: 2.8; 95%CI: 1.1-7.0), and an associated procedure on the mitral and/or tricuspid valve during TAVR explant (OR: 3.8; 95%CI: 1.5-9.4).

Jawitz et al analyzed 123 patients from the STS database who underwent TAVR explant between 2011 to 2015 with a median age of 77 years (IQR: 67-84) and median time from TAVR to explant of 2.5 months (IQR: 0.7-13) [21]. Indications for reoperation were paravalvular leak (15%), SVD (11%), sizing or position issues (11%), and endocarditis (10%). The STS score was <4% in 17% of cases, between 4 and 8% in 24% and >8% in 59%, respectively. The 30-day mortality (17.1%) was higher than the expected mortality rate following conventional reoperation after SAVR. It reached 14% for patients at low surgical risk, 10% for those at intermediate risk, and 21% for those at high risk. The average operating time (321 min) was almost double the time reported for surgical reoperation of a degenerated surgical aortic bioprosthesis valve (around 200 min). The median cardiopulmonary bypass time (146 min) was longer than the 111 min reported in a study of SAVR in patients who already had coronary artery bypass grafting [22]. Only 7% of patients required aortic root replacement.

Recently, Hawkins et al reported all SAVR with prior aortic valve intervention (29306 prior SAVR, 1126 prior TAVR, 674 prior SAVR +TAVR) from the STS Adult Cardiac Surgery Database between 2011 and 2021 [23]. The most common exclusion criteria were prior non-bioprothetic valve, emergent TAVR explant, and prior root replacement. The unadjusted operative mortality was the highest (17%) in the TAVR-SAVR group, whereas the operative mortality rate was 12% for the SAVR-TAVR-SAVR patients and 9% in the SAVR-SAVR patients. In a propensity-matched group with 433 SAVR-SAVR patients and 433 TAVR-SAVR patients, the operative mortality was significantly higher for the TAVR-SAVR (11.3%) than for the SAVR-SAVR (6.7%, p=0.02), but the rate of major morbidity was not different between both groups (28% versus 24%, p=0.223). However, the TAVR-SAVR patients had more renal failure and longer intensive care unit stays with fewer patients discharged directly home.

In 2023, Fukuhara et al reported the results of the State of Michigan after redo-TAVR (n=54) and TAVR-explant (n=34) between 2012 and 2019 from a cohort of 9694 TAVR [24]. The number of re-interventions increased over time and, the contraindications for redo-TAVR were unfavorable anatomy (75%), need for other cardiac surgery (29%), other structural issues caused by the THV (18%, i.e.; mitral valve impingement, partial coronary obstruction and ventricular septal defect) and endocarditis (12%). Importantly, in this series, the rate of concomitant procedure at the time of TAVR explant was high at 68% and corresponded to aortic repair (32%), mitral repair or replacement (29%), coronary artery bypass graft (21%), tricuspid repair (18%) and ventricular septal defect repair (3%). In an earlier study from the STS database assessing 784 patients with TAVR explant, Fukuhara et al found that the 30-day
mortality was significantly lower after isolated TAVR explant versus TAVR explant and concomitant procedure (14.8% versus 23.8%, p=0.002) [18]. Ultimately, TAVR explant years after implantation is technically more demanding than standard SAVR given the longer operating times and higher rates of complications and 30-day mortality. The latest generation of THV, with their external sealing skirts, can increase tissue development and potentially add challenges to TAVR explant. In addition, compared to SAVR, during TAVR explant, the risk of aortic root replacement following THV stent dissection/de-insertion and the risk of anterior mitral leaflet injury are higher. Overall, the 30-day mortality after TAVR explant varies between 11% and 23.8% in the series described above, with the highest mortality rate found in the group of TAVR explant associated with concomitant procedures [18-21, 23]. The concept of the volume-outcome relationship applies to this potentially challenging surgery [25]. In the 2023 Michigan State report, 12% of the cardiac surgeons have been exposed to TAVR-explant with a median of only 1 procedure per surgeon (IQR:1-2; range 1-10 per surgeon) at 10 hospitals representing 30% of the cardiac centers in the State[18]. The 30-day mortality rate after TAVR explant has the potential to decrease when treating lower-risk and younger patients by more experienced and exposed surgeons to this surgery. However, TAVR explant is the gold standard therapy for THV endocarditis or thrombosis, significant paravalvular leak, patient-prosthesis mismatch, or in the context of unsuitable anatomy for redo-TAVR.

**B. Redo-TAVR**

Redo-TAVR has emerged as an alternative therapy for BVF in the lifetime management of aortic stenosis, particularly for patients at high surgical risk. Although TAV-in-SAV (transcatheter aortic valve in surgical aortic valve) has already proved to be safe and effective in the treatment of degenerated surgical valves[26], data on the use of THV in degenerated THV prostheses (redo-TAVR) are still scarce and do not exceed 12 months. Redo-TAVR requires a tailored approach for each patient taking into account the risk and pitfalls of implanting a second THV in a THV. Similar to TAV-in-SAV procedures, in addition to the difficulty of re-accessing the coronary arteries or the risk of coronary obstruction, there is a risk of leaflet thrombosis and patient/prosthesis mismatch, especially for valves smaller than 23mm, which leads to an increased mean gradient. To reduce patient/prosthesis mismatch, routine pre- and post-dilatation are typically performed. SAPIEN THV can be dilated to a diameter that is approximately 3 mm larger than nominal[27]. However, for valves smaller than 23 mm or when expecting a patient/prosthesis mismatch, TAVR explant remains the best approach when surgery can be reasonably undergone.

The preprocedural planning is of utmost importance and requires a very good knowledge of the THV-specific characteristics as well as the patient individual anatomy and position of the index THV in
relation to the anatomy. Importantly, the balloon-expandable SAPIEN THV is the only device that is approved in the USA and Europe for redo-TAVR. Current implantation recommendations favor high implantation during the initial TAVR, intending to reduce the risk of conduction disorders. However, this approach may be unfavorable for future redo-TAVR because a high THV is more likely to cause coronary occlusion during redo-TAVR by occluding the entire sinus of Valsalva, particularly when the sinuses of Valsalva are at the lower size limit required for the initial TAVR. Indeed, data have shown that many redo-TAVR combinations could be at risk of coronary obstruction or sinus sequestration. Bench test studies provide information on the best combinations of valves to perform a redo-TAVR and how to position the second THV. They also provide critical insight into the implications of creating a double stent layer and neo-skirt that can complicate coronary re-access and reduce the flow in the sinuses of Valsalva in diastole. The concepts of leaflet overhang and neo-skirt need explanation before discussing CT analysis, bench test studies, and worldwide experience.

**Leaflet overhang**

Leaflet overhang corresponds to the extent of index THV leaflets that are entrapped by the second THV. Indeed, it contributes to the orifice blockage considering the inward flexing of the unpinned portion of the initial THV leaflets. The lower the second THV is implanted, the higher the percentage of leaflet overhang there will be. It may affect valve performance, durability, and coronary access.

**Neoskirt**

It corresponds to the height of the covered tube which is formed by the leaflets of the initial failed THV with its leaflets blocked in an opened position by the second THV. The height of the neoskirt varies according to the index THV, the design of the second THV, and the height of the initial implantation. It can be measured between 15.4 mm in the case of a balloon-expandable valve in a balloon-expandable valve and 31.6 mm in the case of a balloon-expandable valve positioned high in a self-expanding valve [28, 29]. The functional neoskirt corresponds to the height of the neoskirt that is situated above the annular plane and thus is influenced by the initial THV implantation depth. The height of the neoskirt has important implications for the periprocedural risk for coronary obstruction and future coronary access.

**Importance of CT scan analysis**

CT scan analysis of the valve and aortic root is paramount for planning TAVR procedures, and even more so for redo-TAVR. Indeed, when considering redo-TAVR, the CT scan of the initial TAVR as well as the one with the BVF should be carefully assessed. Figure 3 and 4 show an example of redo-TAVR with an Edwards SAPIEN S3 in a degenerated Evolut THV.
**Pre-Index TAVR CT Analysis**

If the pre-index CT is available, it permits the evaluation and sizing of the native aortic annulus and root and particularly the identification of unfavorable characteristics such as severe annulus or left ventricular outflow tract calcifications, bicuspid anatomy, anatomy with narrow sinuses of Valsalva or low coronary ostia.

Indeed, small anatomy presents significant challenges for redo-TAVR due to the potential higher risk of coronary obstruction or flow impairment as well as patient-prosthesis mismatch.

**Pre-Redo TAVR CT analysis**

Its analysis is crucial to evaluate the commissural alignment and position of the index THV in relation to the surrounding structures and hence the feasibility of redo-TAVR[30]. A systematic step-by-step approach (table 1) can help to plan redo-TAVR[30]. It is essential to understand the characteristics (self-expanding versus balloon-expandable, supra- or intra-annular), design (frame/struts, skirt and leaflets), and size of the initial THV. Assessment of the index THV expansion is also important. Measurements should be performed at every stent frame node level to evaluate the neosinus, specifically the valve-to-coronary (VTC), valve-to-sino-tubular junction (STJ) for both the left and right coronary sinuses, and valve-to-aorta (VTA) at the neoskirt plane in cases of Evolut-in-Evolut (figure 5). It is important to be aware that the neoskirt-to-aorta distances can be shorter than the VTA distance depending on the second THV size and index THV expansion. Indeed, it has been shown that implantation of a balloon-expandable valve inside a failed Evolut THV can result in up to a 5-mm increase in the Evolut THV diameter, particularly if the balloon-expandable valve is implanted high in the self-expandable valve [31].

**Access to the coronary arteries and risk of coronary obstruction**

When the THV covers the coronary ostia, as is frequently the case following supra-annular valve implantation, access to the coronary arteries after the initial TAVR may already be challenging, and it becomes even more difficult when a THV commissure is in front of the coronary ostium.

Research using post-TAVR or post-redo-TAVR CT scans is an important element in assessing the risk of sinus sequestration and coronary access failure [32-34]. In the Evolut Low-Risk trial, 204 patients underwent high-quality post-TAVR CT scans, which were analyzed using 3Mensio software (Pie Medical Imaging) after virtual SAPIEN S3 (in different positions) and Evolut THV implantation to assess the feasibility of redo-TAVR [32]. When a SAPIEN S3 valve was implanted in an Evolut THV, the analysis predicted that 80% of the patients would have a low risk of coronary flow compromise. The most favorable coronary access was achieved when the SAPIEN S3 valve was implanted at node 4. However, when Evolut in Evolut redo-TAVR was performed, only 29% of the patients were considered at low risk for coronary flow compromise and all cases were predicted to be challenging or at high risk of coronary access failure. Figure 6 displays the risk stratification for coronary flow compromise as reported by Grubb K et al [32].
Using post-TAVR CT scans, T Ochiai et al. assessed the risk of coronary obstruction associated with the sinus of Valsalva sequestration during redo-TAVR in a cohort of 66 Evolut THV and 345 SAPIEN 3 THV cases [33]. They used specific CT scan criteria to predict this risk, including THV commissures rising above the sino-tubular junction or a distance between the THV and the sino-tubular junction less than 2mm. They showed that CT scans allowed the identification of a risk of sinus sequestration at one or both coronary ostia in 45.5% of Evolut cases (39.4% for the left ostium and 24.2% for the right) and 2% of SAPIEN 3 cases (2% for the left ostium and 0.6% for the right ostium). This risk was even higher when the height of the sinuses of Valsalva was low.

Another study assessed coronary access using post-redo-TAVR CT scans from 45 patients. It revealed that the coronary ostia were located below the upper part of the neo-skirt in 90% of supra-annular Medtronic THV cases and 67% of intra-annular Edwards valve cases [34]. Using various criteria, such as the relationship between the coronary ostia and the neo-skirt, a distance < 3 mm between the THV and the aortic wall, and misalignment of the bioprosthetic commissures, the risk of coronary access failure was identified in 27% of cases post initial Medtronic THV implantation and 10% of cases post initial Edwards THV implantation [34].

Leaflet modification techniques

In the context of degenerated surgical aortic prosthetic valves, several publications have demonstrated the feasibility of the BASILICA (bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction) procedure to reduce the risk of coronary obstruction [35]. However, its technical complexity limits its use. A new device namely the ShortCut system appears promising as it may facilitate the technique of leaflet modification [36]. Nevertheless, in the context of redo-TAVR, there is limited clinical experience. Bench test studies using the Evolut R, SAPIEN XT, SAPIEN 3, and Lotus THV showed a lower success rate of the BASILICA procedure compared to surgical aortic bioprosthetic valves [37]. An effective leaflet splay was demonstrated for the SAPIEN XT and Lotus valves, but BASILICA procedures on the SAPIEN 3 and the Evolut THV were associated with a less effective leaflet splay. For the Evolut THV, leaflet splay was achieved only high above the annulus. In addition, the commissure of the second THV might obstruct the splayed leaflet post BASILICA. J Khan et al do not recommend “BASILICA TAVR-in-TAVR roulette” since, despite an adequate leaflet splay, it might not help to re-access the coronary arteries, especially when the predicted mechanism of obstruction is narrow sinuses of Valsalva [37]. In addition, poor commissural alignment makes the leaflet modification technique ineffective. Finally, when performing BASILICA procedure in a nitinol frame, there is a theoretical risk of electrical conduction from the nitinol alloy to the aortic annulus (potentially more important with the Evolut R considering the single and inner layer of tissue), which may result in damage at the annulus level. This question should be answered using bench testing.

Data from the bench test studies
In EuroIntervention, Sathananthan J et al. reported in 2021 the safety and feasibility of different combinations of valve type, size, and positioning [38]. Indeed, in a SAPIEN XT and an Evolut R, the implantation of different THV (SAPIEN 3, Evolut Pro, ACURATE neo, ALLEGRA, and Portico) was tested ex vivo using different sizes. The results showed that in a 29 mm SAPIEN XT the 27 mm Allegra THV had an insufficient anchoring while the 29 mm Portico embolized in all the different depth of implantation tested. When a 20-mm SAPIEN 3 was implanted in a 23 mm Evolut R or when a 23 mm SAPIEN 3 was implanted in a 26/29 mm Evolut R at nominal volume, dislodgement of the SAPIEN 3 was noted in cases of high implantation. On the other hand, when the SAPIEN 3 was implanted high in an Evolut R but overexpanded by increasing the volume in the balloon to simulate a larger valve (limited sizes of the different valves available to perform the study), there was no dislodgement or embolization. Post-procedure gradients were favorable. In conclusion, the majority of combinations were stable in the first THV, and the different valves implanted in a SAPIEN XT or an Evolut R were associated with favorable hydrodynamic performances.

In 2022, Akodad et al. published an important in vitro study to evaluate the optimal position of a SAPIEN 3 in an Evolut R taking into account the expansion of the THV, changes in the height of the neo-skirt, overhang of the leaflets, and hydrodynamic performance [31, 39]. In vitro testing was performed under physiological testing conditions in collaboration with the Cardiovascular Translational Laboratory (Vancouver, Canada) and Medtronic Inc. (Santa Ana, California). They implanted the SAPIEN 3 THV at different depths, at nodes -4, -5, and -6 of the Evolut R. Since the SAPIEN 3 shortens on the “inflow” side (ventricular side), they concluded that it was more predictable to align the SAPIEN 3 using the outflow (aortic side).

In all the configurations tested, the leaflet function of the SAPIEN 3 was preserved and the degree of leaflet overhang did not have a significant impact on the hydrodynamic performances of the SAPIEN 3. In addition, low implantation of a SAPIEN 3 in an Evolut R may facilitate future coronary access after redo-TAVR.

D Meier et al. reported the effect of pre- and post-dilatation on final THV expansion when ex-vivo redo-TAVR was performed using a SAPIEN 3 in a SAPIEN XT or a SAPIEN 3 [27]. Without pre- or post-dilatation, the SAPIEN S3 was under-expanded particularly in its mid-portion for all combinations. To obtain nominal expansion with a SAPIEN S3 in a SAPIEN S3, the authors concluded that pre- and post-dilatation should be performed. When implanting a SAPIEN S3 in a SAPIEN XT, the SAPIEN S3 remained under-expanded despite pre- and post-dilatation. All combinations had acceptable hydrodynamic performance, but the under-expanded samples had worse leaflet pinwheeling. Under-expansion of the SAPIEN S3 is known to be associated with an increased risk of hypo-attenuated leaflet thickening (HALT). When a SAPIEN S3 was implanted in a SAPIEN XT, since the SAPIEN S3 is 20% taller than the SAPIEN XT, it was positioned 20% above the outflow of the SAPIEN XT to reduce the mean gradient and the transvalvular leak.
Importantly, bench-test studies may not fully reflect how a THV would perform in a degenerated THV implanted in a patient's native annulus.

**Worldwide clinical experience**

Redo-TAVR data are limited. The international Redo-TAVR registry analyzed 212 redo-TAVR procedures from 37 centers out of a total of 63876 TAVR, corresponding to an incidence of 0.33%[40]. The procedures were performed during the first year after the initial TAVR in 35% while 65% took place beyond 1 year. The cases treated during the first year are potentially more linked to a procedural failure rather than true SVD. The average time between TAVR and redo-TAVR was 5 years (3-6 years) when considering the 138 patients with more than 12 months between the initial procedure and redo-TAVR. The majority of cases with BVF during the first year (73%) presented with aortic regurgitation, whereas beyond the first year, the presentation was aortic stenosis (37%), a combination of stenosis and regurgitation (33%) and finally isolated aortic regurgitation (30%). Redo-TAVR was successful in 85% of cases with a high residual gradient as the primary cause of failure. The mean gradient found at 30 days (12.6±7.5mmHg) remained stable at 12 months (12.9±9.0mmHg). There was no mortality related to the procedure and patients significantly improved their quality of life. The 30-day and 1-year survival rates were respectively 94.6% and 83.6% for cases treated within one year post TAVR and 98.5% and 88.3% for those treated more than one year post TAVR. The rate of 30-day complications after redo-TAVR was low (mortality: 2.9%, stroke: 1.4%, coronary occlusion: 0.9%). However, the population was selected and we do not know how many patients were initially evaluated but ultimately refused for a redo-TAVR due to unfavorable anatomy (i.e.; risk of coronary obstruction).

Interestingly, similar THV types were used in 59% of cases of redo-TAVR. In the case of a degenerated Medtronic self-expanding THV, redo-TAVR was performed using a similar supra-annular Medtronic THV (off-label) in 55 cases (58% of the redo-TAVR in Medtronic THV) [40].

Propensity score matching was applied using the Redo-TAVR registry data, and 165 redo-TAVR were matched with 165 TAV-in-SAV[41]. Procedural success was higher in the redo-TAVR group, due to a lower residual mean aortic gradient, but there was no difference in early safety and mortality up to one year. However, the frequency and degree of aortic regurgitation were higher after redo-TAVR than after TAV-in-SAV.

The international TRANSIT (Transcatheter Aortic Valve Replacement for Degenerated Transcatheter Aortic Valves) registry, involving 28 centers and 40000 TAVR, also reported a very low redo-TAVR rate of 0.4%, corresponding to 172 patients [42]. In 33% of cases (n=57), the cause of BVF was stenosis, in 56% of cases (n=97) regurgitation, and in 11% of cases (n=18) a combination of both. All patients had a first TAVR which met the success criteria (gradient <20 mmHg or paravalvular leak ≤ grade 1). Only 3.5% of the patients underwent redo-TAVR during the first year post-TAVR. The EuroScore II and the STS score were 8.8±3.4% and 6.1±5.7%, respectively. The success rate of redo-TAVR was 79%
and procedural failure was secondary to a significant residual mean gradient in 14% of cases and an aortic regurgitation in 7%. The second valve was in 61% a self-expanding valve. Similar to the redo-TAVR registry, more than half of the degenerated CoreValve THV (63%, n=53) had an Evolut THV implanted, whereas 29% (n=25) had an Edwards THV. For degenerated Edwards THV, a second Edwards THV was implanted in 55% of cases (n=33), whereas an Evolut THV was implanted in 35% (n=21). The all-cause mortality and in-hospital stroke rates were 4.1% and 3.5%, respectively. At 30 days, all-cause mortality was 7.0% with no new cases of cardiovascular mortality since hospital discharge. The 30-day rehospitalization rate was 3.6%. Valves treated for stenosis had a higher mean post-redo-TAVR gradient and valves treated for regurgitation had a higher rate of post-intervention aortic regurgitation. At 12 months, all-cause mortality reached 10%, cardiovascular mortality 5.8%, whereas in the international redo-TAVR registry all-cause mortality was 11.7%. No cases of valve thrombosis were reported and <1% of coronary occlusion. The very low rate of coronary occlusion was certainly linked to a rigorous selection of cases on CT scan.

The results of these two multicentric registries are promising, however, follow-up beyond 12 months is lacking and these cases are selected and performed in centers recognized for their expertise. Furthermore, we do not know how many patients with BVF were turned down and what happened to them.

Recently, the international registry EXPLANTORREDO-TAVR included, over 13 years, 396 patients from 29 centers performing both surgical (46.4%, n=181) and transcatheter reintervention (54.3%, n=215) for BVF in a separate admission from the index TAVR [43]. Among the 66760 TAVR patients treated in the participating centers between May 2009 and February 2022, 0.59% (with a rising trend during the study period) required a re-intervention for BVF, which is 3 times more than in TAVR-EXPLANT [20], twice more than in the international redo-TAVR registry [40], and 1/3 more than in TRANSIT [42]. In this registry, TAVR explant compared with redo-TAVR had a shorter median time from the initial procedure to reintervention (17.6 vs 45.7 months, p<0.001), less SVD (51.9% vs 63.7%, p=0.023), but more prosthesis-patient mismatch (17.1% vs 0.5%, p<0.001) and emergency procedures (38.6% vs 20.8%, p<0.001). In the cohort of TAVR explant, aortic root replacement was performed in 10.7% and concomitant procedure in 55.8% (i.e.; mitral valve surgery: 20.4%, tricuspid valve surgery: 2.8%, coronary artery bypass grafting: 17.7%, ascending aorta replacement: 6.1%). The decision to perform one or the other approach was made by the local heart teams. There were no differences in the re-intervention approach for balloon-expandable valves (54.7% of redo-TAVR vs 45.3% of TAVR explant, p=0.92) or self-expandable or mechanical valves (54.0% of redo-TAVR vs 46.0% of TAVR explant, p=0.92). Independent risk factors for mortality after TAVR explant were dialysis, pulmonary hypertension, and concomitant mitral valve surgery. The 30-day and one-year mortalities were higher after TAVR-explant (13.6% vs 3.4%, p<0.001 and 32.4% vs 15.4%, p=0.001, respectively), but when surviving the first 30 days post-TAVR explant, the survival was similar to redo-TAVR, with a mortality rate around 30% at 4 years.
Finally, redo-TAVR is less invasive, but TAVR explant is preferred in operable patients when the anatomy is not favorable for redo-TAVR or a suboptimal hemodynamic result is expected.

**Perspective**

Redo-TAVR is a desirable approach that is not always feasible, and some patients may benefit from a TAVR explant with the implantation of a surgical bioprosthetic valve. Lifetime management of aortic stenosis requires anticipation of a second procedure, especially when discussing patients whose life expectancy exceeds valve durability. Indeed, these patients remain a subject of debate. Should we perform SAVR followed by TAV-in-SAV or TAVR followed by THV explant with implantation of a surgical bioprosthetic valve or redo-TAVR?

Considering the lack of data after 12 months for redo-TAVR and the high mortality risk when performing TAVR explant, a SAVR-first approach remains the safer option for patients who are expected to survive their first bioprosthetic valve.

Chatfield et al. proposed an algorithm for the lifetime management of aortic stenosis in which the choice between surgery and TAVR is made based on the patient's initial anatomy evaluated on a CT scan. They consider the width of the sinuses of Valsalva and the height of the coronary ostia as criteria to select the best initial approach [44]. In the case of first-line surgery, they recommend the implantation of a valve favorable to TAV-in-SAV. Of note, in the Cleveland Clinic series, hospital mortality associated with isolated reoperation after SAVR has declined from 3.4% in 1985 to 1.3% in 2011, which is similar to the mortality after primary isolated SAVR [45]. Therefore, the decision regarding reoperation after SAVR should be made on an individual basis taking into account valve durability and the need for future reinterventions rather than solely focusing on avoiding reoperation.

In the case of initial TAVR, the lowest risk of coronary access failure is in the configuration of a SAPIEN THV in a SAPIEN THV, the intermediate risk occurs when combining a SAPIEN THV with an Evolut THV regardless of which one is implanted first. Finally, the highest risk is when two valves such as the Evolut whose frame goes up to the ascending aorta have been implanted.

TAVR explant will remain the treatment of choice in patients with endocarditis, patient-prosthesis mismatch, and those with unfavorable anatomy for a redo-TAVR. Given the growing experience of the surgical community with this potentially challenging procedure, the mortality rate after TAVR explant has the potential to decrease when treating lower-risk and younger patients by experienced surgeons. Nevertheless, research and development teams should design devices dedicated to redo-TAVR to secure and facilitate future access to the coronary arteries. Bench test and CT scan studies have shown that implanting a second supra-annular Medtronic THV in a first similar valve is not the optimal strategy to reduce the risk of coronary obstruction and coronary access failure.

Given the potential higher risk of valve thrombosis with two THV, the strategy of anticoagulation or anti-platelet therapy should be evaluated. In addition, patients with a residual mean gradient post-redo-
TAVR should be closely monitored to detect early degeneration of the new valve. Conceptually, in a small intra-annular 20mm SAPIEN THV, a TAVR explant or a supra-annular self-expanding valve should be favored to reduce the gradients, especially with an initial post-TAVR mismatch.

Conclusions

Patients often anticipate being able to benefit from a redo-TAVR in the event of bioprosthetic valve failure after TAVR, despite the lack of long-term data and the risk of unfavorable anatomy. Our understanding of the feasibility of redo-TAVR is constantly improving thanks to bench-test studies and growing worldwide experience. However, many unknowns remain. One of the heart team’s objectives is to anticipate the need to re-access the coronary arteries and implant a second or even a third valve when life expectancy may exceed the durability of the bioprosthetic valve. CT scan assessment is crucial in assessing the risk of coronary access failure. At this stage, patients should be informed transparently, and members of the Heart Team should anticipate possible new procedures when making their initial choice of treatment.
Table
Table 1: Systematic step-by-step approach to assess the feasibility and plan redo-TAVR -

- Assess the pre-index TAVR CT scan
  - valve morphology: native bicuspid or tricuspid valve
  - native aortic annulus/LVOT and aortic root dimensions
  - coronary artery height
  - calcium distribution

- Confirm the index THV type and size and look at
  - design of stent/struts, skirt and leaflets, supra- or intra-annular
  - frame dimensions (height, waist diameter, inflow and outflow diameter)
  - skirt and commissure (neo-skirt) heights

- Determine the mechanism of THV failure:
  - stenosis versus regurgitation
  - patient prosthesis mismatch
  - paravalvular leak
  - endocarditis
  - thrombosis

- Assess the post-index TAVR CT scan
  - implantation depth of the TAVR
  - appropriate expansion and sizing
  - frame dimensions (height, waist diameter, inflow and outflow diameter)
  - commissural post alignment
  - coronary ostia height and different distances (VTC, VTSTJ, VTA)

adapted from [30] LVOT: left ventricular outflow tract, VTA: valve to aorta distance at the neoskirt plane, VTC: valve to coronary distance at the midpoint plane, VTSTJ: valve to sino-tubular junction distance at the sino-tubular junction plane

Figure legends

Figure 1: bioprosthetic valve dysfunction classification and definition. DVI: doppler velocity index, EOA: effective valve area, SVD: structural valve deterioration, NSVD: non-structural valve deterioration

Figure 2: demonstrates an example of SVD secondary to infective endocarditis. Panel A: TEE, mid-esophageal biplane view focused on the aortic prosthesis in a patient who underwent TAVR 2 years ago. Note the prosthesis leaflet calcification which results in reduced prosthesis opening. Panel B: same view with color Doppler in systole showing color Doppler aliasing and non-circular transprosthetic flow.
Figure 3: A-C: Pre-index TAVR CT, measurements of the annulus and aortic root, and simulation with a 26-mm Medtronic Evolut THV.

D-H: Pre-Redo-TAVR CT scan analysis with the failed 26-mm Evolut R with simulation using a 23-mm Edwards Sapien S3. If the Sapien S3 THV is implanted at Node 4, the risk plane (top of the neoskirt) is just below the coronary ostia, which very important in this case with short VTC distance and VTSJ distances. LCA=left coronary artery, RCA = right coronary artery, STJ = sino-tubular junction, VTC = valve to coronary distance, VTSJ = valve to STJ

Figure 4: A-C: Fluoroscopic images of the redo-TAVR planned in figure 3: A 23-mm Edwards SAPIEN S3 is deployed in the 26-mm degenerated Evolut R THV

Figure 5: The different measurements to perform on CT scan when assessing redo-TAVR with a SAPIEN S3 in an Evolut THV

LM: left main, RCA: right coronary artery, VTC: valve to coronary distance at the midpoint plane, VTSJ: valve to sino-tubular junction distance at the sino-tubular junction plane.

Figure 5: Stratification of the risk of coronary flow compromise with redo-TAVR. VTA: valve to aorta distance at the neoskirt plane, VTC: valve to coronary distance at the midpoint plane, VTSJ: valve to sino-tubular junction distance at the sino-tubular junction plane. Adapted from [32]
References:


Bioprosthetic valve dysfunction (BVD)

Aetiology
- Structural valve deterioration (SVD)
- Non-structural valve deterioration (NSVD)
- Thrombosis
- Endocarditis

Stage according to haemodynamic changes

Stage 1: morphological valve deterioration
- Evidence of SVD, NSVD, thrombosis or endocarditis without significant hemodynamic changes

Stage 2: moderate hemodynamic valve deterioration
- Increase in mean transvalvular gradient ≥10 mmHg resulting in mean gradient ≥ 20 mmHg, with concomitant decrease in EOA ≥ 0.3 cm² or ≥ 25% and/or decrease in DVI ≥ 0.1 or ≥ 20% compared with an echocardiography 1–3 months post-procedure
  OR
- new occurrence increase of ≥ 1 grade of intraprosthetic AR resulting in ≥ moderate AR

Clinical consequences
- Subclinical BVD
  - any BVD associated with absent or mild hemodynamic changes AND absent symptoms and sequelae

Bioprosthetic valve failure (BVF)

Stage 1:
- Any BVD associated with clinically expressive criteria (new-onset or worsening symptoms, LV dilation/hypertrophy/dysfunction, or pulmonary hypertension)
  OR
- irreversible stage 3 haemodynamic valve deterioration

Stage 2:
- Aortic valve reoperation or re-intervention

Stage 3:
- Valve-related death

Stage 3: severe hemodynamic valve deterioration
- Increase in mean transvalvular gradient ≥20 mmHg resulting in mean gradient ≥ 30 mmHg, with concomitant decrease in EOA ≥ 0.6 cm² or ≥ 50% and/or decrease in DVI ≥ 0.2 or ≥ 40% compared with an echocardiography 1–3 months post-procedure
  OR
- new occurrence increase of ≥ 2 grades of intraprosthetic AR resulting in severe AR
Post-TAVI CT assessment for each coronary artery

Is neoskirt below coronary ostium midpoint?
  No
  Is neoskirt below the STJ?
    No
    Is VTSTJ ≥ 2 mm?
      No
      High risk of coronary flow compromise and coronary access failure
    Yes
    (Evolut-in-Evolut only)
    Is VTA ≥ 2 mm?
      No
      High risk of coronary flow compromise and coronary access failure
    Yes
    Is VTC ≥ 4 mm?
      No
      Low risk of coronary flow compromise and coronary access failure
    Yes
    Yes
    Low risk of coronary flow compromise but challenging coronary access

Low risk of coronary flow compromise:
  S3 in Evolut

check the neoskirt height
  below the midpoint of the coronary ostium (optimal)
  below the STJ but $VTC \geq 4\, mm$
  above the STJ but $VTSTJ \geq 2\, mm$ and $VTC \geq 4\, mm$

Evolut-in-Evolut
  same criterion
  $VTA \geq 2\, mm$ at the neoskirt plane