

Review Article

Valvular leak after transcatheter aortic valve implantation: a clinician update on epidemiology, pathophysiology and clinical implications

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Abstract: During transcatheter aortic valve implantation (TAVI) the native valve is not removed but crushed. Thus, a slight prosthesis insufficiency is not uncommon and has been reported in about 70% of patients for both available types of percutaneous valves. However, the definition of clinically “significant” valve regurgitation is not fully established yet. In most cases, aortic insufficiency is mild and clinically acceptable, however, severe insufficiency can occur. Paravalvular insufficiency is usually prevalent, and it may be the consequence of prosthesis/patient mismatch due to an undersizing of the implanted device or to an incomplete expansion of the prosthesis stent frame, or also to incorrect site of prosthesis implantation. Thus, an accurate assessment of the aortic valve annulus before TAVI is mandatory in order to select the optimal size of the valve. The presence of large calcium burden or bicuspid valve as well as the correct implantation of the device are other key determinants of final valve insufficiency. When severe regurgitation is present, an integration of hemodynamic, angiographic, transthoracic and TEE data is necessary to tailor the best clinical decision on a per-patient basis.

Keywords: Valvular leak, transcatheter aortic valve implantation

Introduction

A 77-year man with high-risk severe aortic stenosis (EuroSCORE 25.61%) was referred for Transcatheter Aortic Valve Implantation (TAVI). Aortic annulus was 24 mm at transesophageal echocardiogram; 24.4 mm (sagittal) and 25.7 mm (coronal) at angioTC assessment. Peripheral vessels were suitable for transfemoral approach. Thus a 26 mm transfemoral Edwards Sapien XT valve implantation was planned (**Figure 1A**). After valve deployment, a relevant aortic regurgitation was detected (**Figure 1B**). What further evaluation and treatment is indicated?

Epidemiology of Valvular Leak after TAVI

Percutaneous TAVI has extended our ability to treat patients with severe symptomatic aortic stenoses being no or poor candidates for open

heart surgery [1]. At the present time two different devices are available, one self-expandable, porcine pericardial leaflets, and nitinol frame, and the other one balloon-expandable, bovine pericardial leaflets, and Cobalt-Chromium frame. Both devices have shown good performance once implanted, with transvalvular gradient and effective orifice area that are respectively lower and higher than that observed in surgical valves [2-8]. However, TAVI may result in severe complications, starting with vascular injuries, cerebral or peripheral embolisation, pericardial effusion, ventricular rupture, conduction abnormalities, aortic dissections and aortic regurgitation.

Regurgitation originating between the prosthetic sewing ring and the native valve annulus is a well-known phenomenon reported as paravalvular, perivalvular and peri/ or paraprosthesis leaks. In surgical series, the occurrence of para-

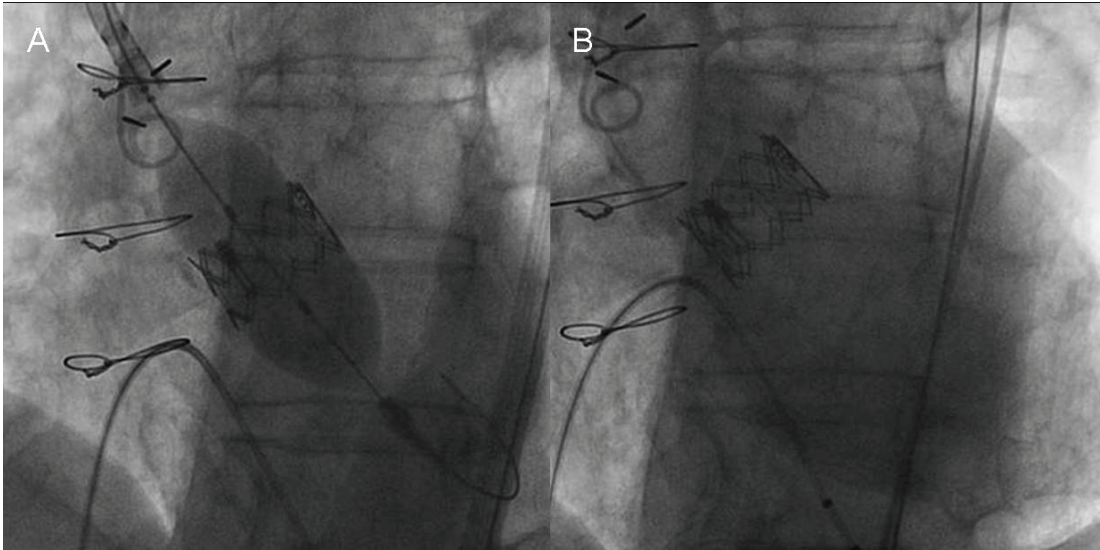


Figure 1. PVL after TAVI. Figure shows a 26-mm transfemoral Edwards Sapien XT valve implantation (Panel A) and a severe valve regurgitation after prosthesis implantation (Panel B).

valvular leak (PVL) has been reported in very few cases, being 2% and 8% after a bioprosthesis or mechanical prosthesis implantation, respectively [9]. Thus, it does not represent a main issue in the context of surgical aortic valve replacement and is not addressed in the current guidelines for valvular heart disease [9-10].

In contrast to surgical aortic valve replacement, during TAVI procedure the native valve is not removed but crushed. Thus, a slight aortic insufficiency is not uncommon and has been reported in about 70% of patients for both available types of percutaneous valves [11-14]. On the other hand, a moderate regurgitation has been observed in up to 40% of the cases [11-12]. In most cases, aortic insufficiency is clinically acceptable, however, severe insufficiency can occur and although current reports mention treatment of such severe insufficiencies only very briefly [3, 7], the problem is not trivial because the underlying pathophysiology can be very different (see below). It should be also acknowledged that discrepancies in the prevalence of valve regurgitation after TAVI [2-7,15-16] are mainly due to the absence of standardized definition and protocols to detect (i.e. angiography versus echocardiography) and score (qualitative or semiquantitative methods) the leak. Moreover the definition of clinically "significant" PVL is not fully established because of the lack of evidence exploring the

pathophysiology of the valvular leak and its impact on outcome. More recently the Valve Academic Research Consortium provided a consensus aimed to standardize definitions on technical and clinical end-points in TAVI procedure [17]. Nevertheless, trying to estimate and quantify the valve regurgitation they adopted arbitrarily a standard classification that is commonly used to describe regurgitation in native valve.

Mechanisms of valvular leaks

The aortic insufficiency after TAVI might be classified taking into account the type of regurgitation, its mechanism, and the etiology (**Table 1**). The vast majority of valve regurgitation is due to PVL, intraprosthetic or combined leaks being 6% and 17%, respectively [18]. The underlying pathophysiology of the leaks can be very different as shown in Figure 2. Paravalvular insufficiency may derive from a prosthesis/patient mismatch due to an undersizing of the implanted device or to an incomplete expansion of the prosthesis stent frame, or also to incorrect site of prosthesis implantation (i.e. too low or too high; **Figure 2**). On the other hand, intravalvular insufficiency might be due to the opening failure of the prosthesis' leaflets, to leaflets damage occurring during the crimping manoeuvre or during the implantation phase (i.e. postdilatation) or again to a prosthesis/patient mismatch because of an incorrect sizing of the valve.

Valvular leak after TAVI : clinician update

Table 1. Aortic Regurgitation after TAVI

Classification	Mechanism	Ethiology
Paravalvular (PVL)	<ol style="list-style-type: none"> 1. Prosthesis/patient mismatch 2. Incomplete valve adherence to aortic annulus 3. Low/high implantation of the valve 	Incorrect size Calcium Bicuspid LVOT/Aorta angle Technique of implantation
Valvular	<ol style="list-style-type: none"> 1. Prosthesis/patient mismatch 2. Valvular damage 	Incorrect size I o II valve dysfunction

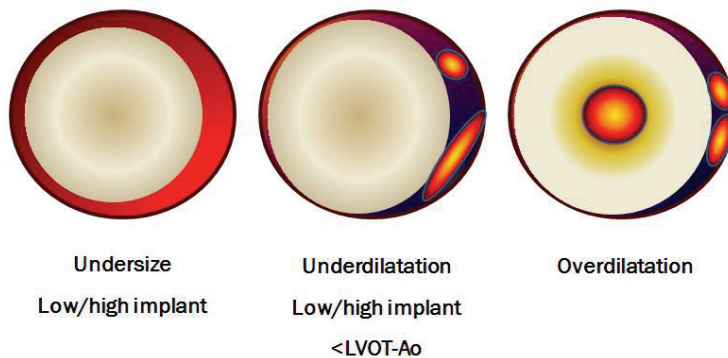


Figure 2. Valvular leak mechanisms. Incomplete valve adherence is due to prosthesis-patient mismatch or to incorrect site of implantation, resulting in large paravalvular leak (left panel); asymmetrical coverage of native aortic root may be due to incomplete prosthesis expansion because of remaining material of the native valve (mid panel). In right panel is shown an intravalvular leak secondary to inappropriate overexpansion of the valve.

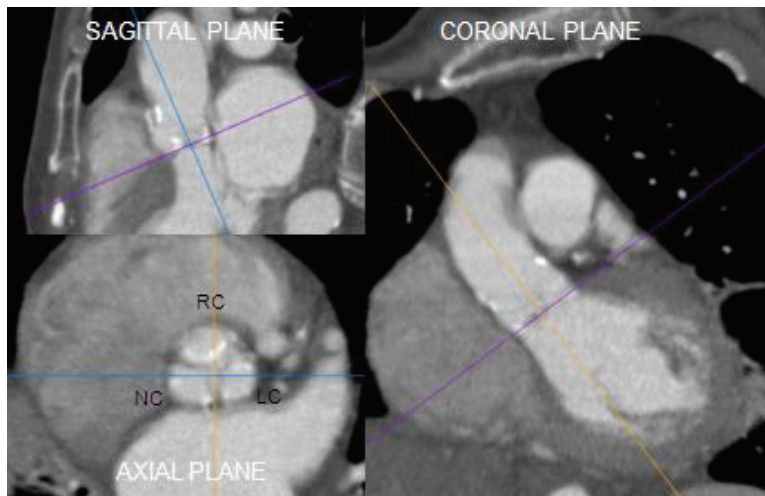


Figure 3. Pre-TAVI assessment. Annulus evaluation by using different imaging showing that significant inter-test disagreement might exist because different anatomical planes are explored by MDCT, TTE and TEE respectively. The combined assessment may reduce the chance for error and provide a more comprehensive definition of the annular size and shape in patients considered for TAVI.

Differently from surgical series, the direct sizing of native aortic annulus is not possible during TAVI, thus an accurate assessment of the latter is mandatory during the screening phase of the patient. It is noteworthy that the selection of the prosthesis that matches properly with the native aortic annulus is paramount to final procedural success, as the goal is to displace the native valve leaflets and deploy the device within the

valve annulus. The native annulus should be identified with the virtual basal ring below the nadir of the aortic cusps, which provides the right plane of the annulus, that is not the anatomic ventriculo-aortic junction [19]. Different methods are used to assess aortic annulus measurement: echocardiogram (transthoracic or transesophageal), angiography, and computed tomography (**Figure 3**). There is not a gold

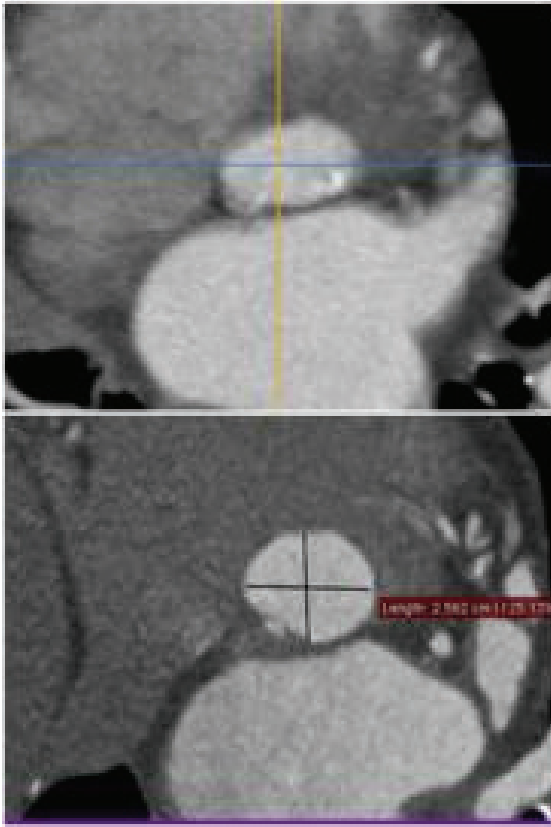


Figure 4. Aortic Valve and annulus morphology. Aortic annulus is a complex 3D structure. The annulus is often oval shaped, as has been observed by MDCT.

standard for annulus measurement, and a multimodal assessment is strongly recommended [20], since the aortic annulus is not circular but might be ovoid in shape (**Figure 4**).

Tops et al. [21] reported that the annulus had an oval configuration in approximately 50% of patients evaluated for TAVI, with a mean difference between coronal and sagittal measurements of 3.0 ± 1.9 mm. An oval configuration of the annulus was also noted by Delgado et al. [22], who reported a significant difference between mean coronal (25.1 ± 2.4 mm) and sagittal (22.9 ± 2.0 mm) measurements in 53 patients with severe aortic stenosis. This oval geometry of the annulus has been previously underappreciated on imaging but has been well described in the surgical literature. There have been a number of published methods for measurement of the aortic annulus on MDCT, but it is important to consider that different techniques

might explore different plane and thus provide different dimensions of the annulus. For instance, the sagittal diameter of annulus as assessed by CT relate to the annulus diameter assessed by transesophageal echo in long-axis view, on the other hand, the coronal CT diameter matches with the measurements of the annulus assessed by angiography. The assumption of a circular geometry of the aortic annulus and the left ventricular outflow tract might lead to significant underestimation of their “true” cross-sectional area by use of two-dimensional assessment. Therefore multiple measurements in different planes are recommended. To this regard, the clinical use of 3D echocardiogram may improve pre-TAVI evaluation, when compared to 2D echo, by the assessment of the aortic annulus in 3 planes. Moreover, a balloon-based annular measurement is an adjunctive tool to select the proper valve size. In fact, intraoperative evaluation of aortic regurgitation during balloon inflation for valvuloplasty increases the accuracy of the optimal device size selection [23].

Although, the selection of the correct sizing of the device is of utmost importance to avoid valve insufficiency, it is not the only issue. The presences of large calcium burden or unidentified bicuspid valve as well as incorrect implantation of the device are other key determinants of final valve insufficiency. Moreover the presence of a bicuspid valve should be taken into consideration, because of its association to asymmetrical stent frame expansion [24]. To note, this condition is frequently observed also in the elderly, accounting for up to 38% of patients as reported in surgical series [25].

The incorrect expansion of the frame is the second more frequent mechanism of paravalvular insufficiency [24,26]. For that reason, the pre-TAVI assessment should consider the analysis of the calcium burden and distribution (**Figure 5**). Although the calcium provides an anchorage to the stent frame, it may also interfere with the complete and symmetrical frame expansion. Para-valvular insufficiency due to incomplete valve adherence to the aortic annulus because of remaining material of the native valve or a prosthesis-patient mismatch may be overcome by post-dilatation [13], which is normally discouraged or by implantation of a plug device [27-28] or in less severe cases by “faithful watching”. It has been reported in case also the possibility of a further expansion of the self-expanding Core-

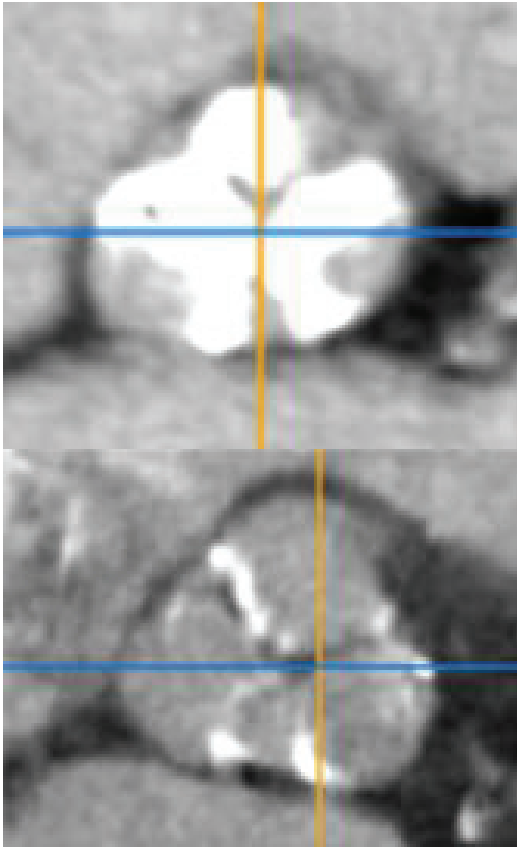


Figure 5. Two clinical examples of different calcium burden and distribution.

Valve during the days following the implantation resulting in a decrease of the regurgitation [29], but data are anecdotal.

The third mechanism of paravalvular insufficiency is the misemployment of the valve in the aortic annulus, such as too-high or too-low implantation. To this regard, some differences between the two transcatheter valves should be highlighted. The implantation of the balloon-expandable Edwards SAPIEN valve (Edwards Lifesciences, Irvine, CA, USA) provides a “one-shot” procedure, thus deserve careful evaluation of the device position before definite deployment. A proper rapid pacing during the deployment phase is necessary to ensure a steady and accurate device delivery, that may further be enhanced using a “two steps” inflation of the balloon for an improved control of the valve position. The “first step” consists in an incomplete inflation of the balloon expandable valve followed by an angiographic assessment of the

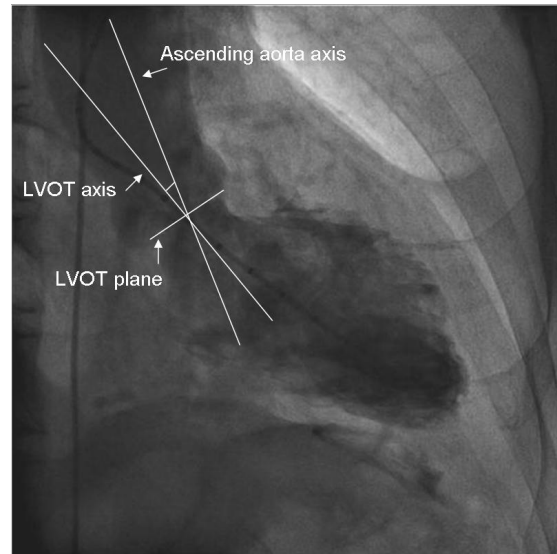


Figure 6. Clinical example of evaluation of the angle between the ascending aorta axis and left ventricular outflow tract axis.

proper position of the valve, and only then “second step” by a complete deployment of the device. On the other hand dedicated imaging assistance workstation, such as real-time angiography-based C-THV (Paieon Inc, NY, USA), may help to optimize the device implantation, especially during the learning curve period.

On the opposite, the self-expandable Medtronic CoreValve device (Medtronic, Minneapolis, Minnesota, USA) can be released step-by-step, thus allowing, at least in theory, a more controlled release of the valve during its deployment. Indeed, also with this valve, the appropriate positioning might be challenging in particular anatomic subset such as the case of angulated ascending aorta (**Figure 6**). To this regard, the angle between the aortic root axis and left ventricular outflow tract, has been shown to be a major predictor of paravalvular leak after CoreValve implantation, together with the depth of implantation [9]. Moreover, although minimal late repositioning or adjustment are possible in case of too low implantation of the valve by snaring and pulling the device upward [30,31], we should notice that this trick is technically difficult, and may also threaten the patient because of the risk of valve dislocation and stroke. To this regard, a para-valvular insufficiency due to too low implantation of both the types of valve might be succeeded by implantation of

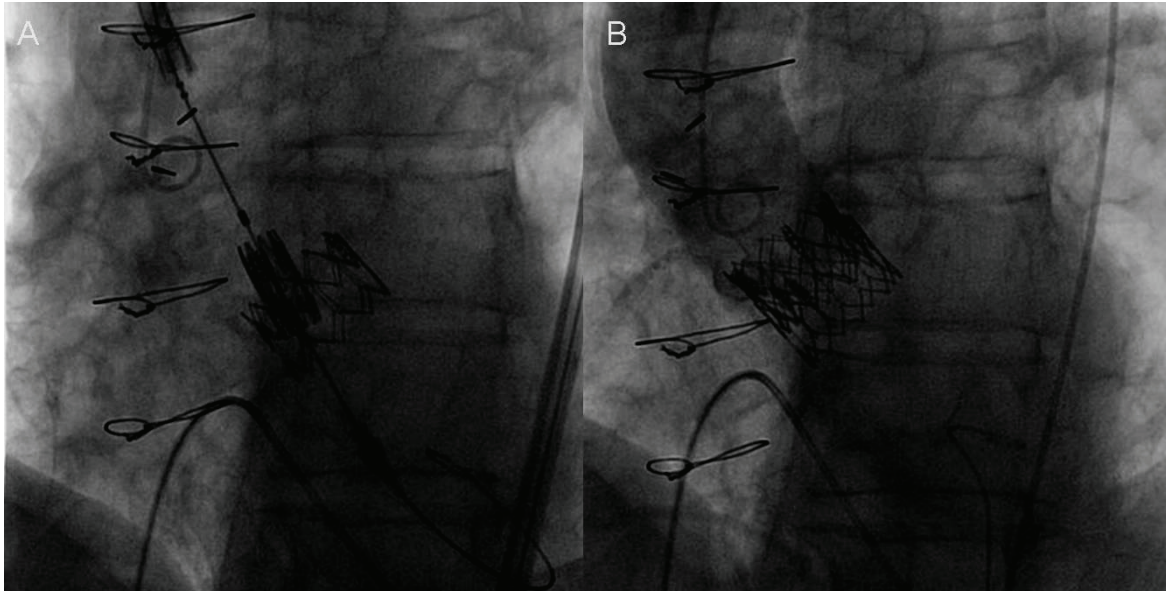


Figure 7. Valve-in-Valve procedure to overcome a severe regurgitation after a “too low” valve implantation (Panel A). The Aortic angiography after second valve implantation confirmed the resolution of valve regurgitation (Panel B).

the second, the so-called “valve-in-valve”, that will be lower or higher according to the position of the first implanted valve. This procedure results frequently in a significant reduction of the valve insufficiency as reported by others [2,32].

Clinical implications

Clinical implications of valvular leak are not fully established. Although, in most cases, aortic insufficiency is stable during follow-up [7,11, 33] and clinically acceptable, severe insufficiency can occur. More recently, some authors have shown that even less than severe valvular leak might be related to higher 1-year mortality after TAVI [7]. When severe regurgitation is present, a multimodality imaging for an accurate assessment of the underlying pathophysiology of the valve regurgitation is of utmost importance to select the adequate therapy.

The exact diagnosis may be troublesome because angiography gives only the severity of the insufficiency but not always the underlying pathophysiology, whereas echocardiography may be difficult due to interference of the metal of the prosthesis with the ultrasound as well as underestimation of the severity of aortic insufficiency in the case of paravalvular leaks. Therefore, an integration of all available data, that is, hemodynamic data, post-implantation angiogra-

phy, auscultation, transthoracic, and TEE, as well as the clinical course is necessary to make a good judgement [10]. Finally, there will be a learning curve for exact judgement of post-implantation aortic insufficiency in TAVI.

Case discussion and conclusion

The cause of the severe regurgitation was a too low implantation leading to paravalvular leakage through the uncovered cell of the prosthesis, as assessed by transesophageal echo. The left ventricular end diastolic pressure was 22 mmHg and the pulse pressure 130/40 mmHg. In this case the regurgitation cannot be overcome by post-dilatation that we commonly discourage in case of balloon expandable prosthesis. Thus, a second valve was implanted into the first valve with a complete resolution of the leak (**Figure 7A and B**). This case shows the importance to determine, by multimodality approach, the degree and the pathophysiology of the aortic regurgitation after TAVI procedures to select the most adequate therapy and to avoid “oculo-regurgitation” reflex.

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