Percutaneous Closure of Paravalvular Regurgitation After Third-Generation Transcatheter Aortic Valve Replacement
Clinical Case Series

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Summary
Significant paravalvular leak regurgitation (PVLR) after transcatheter aortic valve replacement (TAVR) is a well-known complication associated with disabling symptoms related to heart failure and hemolysis or both, with poor prognostic implications. Although challenging and technically demanding, percutaneous closure is an effective treatment option for high-risk patients with symptomatic PVLR. Here, we present two cases of transcatheter PVLR closure after replacement of third-generation (one self-expandable and one balloon-expandable) transcatheter aortic valves, each with peculiar challenges, and the strategies adopted to increase the success rate of percutaneous closure.

Key words: Paravalvular leak regurgitation, Third-generation aortic valves, Transcatheter paravalvular leak closure

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oderate-to-severe PVLR after replacement of first-generation transcatheter aortic valves represented a serious complication with adverse impact on short- and long-term clinical outcomes.1,6 With the development of second-generation transcatheter aortic valves, with the incorporation of an outer skirt at the ventricular side of the stent obtaining better adhesion of the valve at the annular and ventricular levels, the incidence of PVLR has declined and now ranges from 1.5% to 7.7%.3,10 Its incidence has been reported to be higher following the use of self-expandable (SE) valves compared with balloon-expandable (BE) valves,11 probably due to either an inadequate radial strength or an insufficient immediate seal. It has also been reported that the use of SE transcatheter aortic valves is associated with a higher inhospital and 2-year mortality compared with the use of BE transcatheter aortic valves.12 The ongoing refinement and development of third-generation systems promise to drastically resolve or at least mitigate the occurrence of PVLR.

Here, we present two cases of significant PVLR after replacement of contemporary third-generation SE and BE transcatheter aortic valves in patients considered to be at a high risk of reoperation using a specifically designed device for PVL closure.13,14

Case Report

Case 1: The first patient is a 77-year-old man with a history of hypertension, obesity, smoking, chronic obstructive pulmonary disease, abdominal aorta aneurysm, and lower limb arterial disease. In 2007, he underwent triple vessel coronary artery bypass grafting. Due to symptomatic severe aortic stenosis, he was managed with transapical SE supra-annular porcine bioprosthesis self-expandable aortic valve (ACURATE neo™ TA TAVR system, Boston Scientific) in March 2018. The patient’s hospitalization course was eventless. Two-dimensional (2D) transthoracic echocardiography (TTE) upon discharge revealed normal prosthetic valve function, preserved biventricular systolic function, and mild PVLR in the area of non-coronary aortic cusp. In November 2018, the patient was hospitalized due to pleural effusions related to cardiac failure. The brain natriuretic peptide level was > 1,000 pg/mL (the normal range: less than 450 pg/mL). Increased serum lactate dehydrogenase (896 units/L; normal range: 140 to 280 units/L), increased unconjugated bilirubin (1.3 mg/dL, normal range: 0.2-0.8 mg/dL), and decreased haptoglobin (30 mg/dL; normal range: 50-220 mg/dL) confirmed the diagnosis of hemolysis. 2D TEE revealed left ventricular ejection fraction (LVEF) of 62% with an end-diastolic volume of 207 mL, moderate mitral insufficiency, and a 11.7 × 4.5-
A 11.7 × 4.5-mm crescent-shaped, non-coronary aortic cusp PVL (yellow arrows) with moderate regurgitation. LV indicates left ventricle; and Ao, aorta.

Contrast-enhanced computed tomography (CT) was performed, which confirmed the PVL size and location; furthermore, a calcified nodule was shown exactly at the level of the regurgitant jet at the non-coronary aortic cusp (Figure 2A, B). The decision was made by our multidisciplinary heart team to offer percutaneous PVL closure. Written informed consent, after explanation, was obtained from the patient. The procedure was performed in January 2019 under general anesthesia and 2D transesophageal echocardiography (TEE) guidance. Right (for procedure) and left (for control aortography) femoral accesses were obtained using 8- and 6-Fr short introducer sheaths, respectively. A 6-Fr pigtail catheter was advanced from the left femoral artery in the ascending aorta (AA) for baseline angiography (Figure 2C, D), which confirmed severe PVLR in close proximity to the calcified nodule seen previously on CT scan at the non-coronary aortic cusp. With the aim of verifying the possibility of an under-expansion of the previously implanted ACURATE neoTM TA TAVR, a high-pressure semi-compliant 25-mm Cristal balloon (CBV 25 × 40/110, BALT Extrusion SAS) was inflated twice above its nominal level (4 bars) under pacing (Figure 3), but the regurgitant jet remained unchanged. The defect was difficult to cross due to the high sealing skirt and valve frame. The leak was eventually crossed by passing a 6-Fr multipurpose catheter and a hydrophilic-coated 0.035-inch guidewire through the upper cells of the valve frame and then behind the valve at the level of the skirt (Figure 4A). The hydrophilic wire was then replaced with a super stiff 0.035-inch, 260-cm “J” tip guidewire performed with small curve. This allowed the passage of a 7-Fr, 45°-curved, 110-cm-long sheath and then a 7-mm square twist paravalvular leak device (PLD, Occlutech, Helsingborg, Sweden) (Figure 4B-E). A self-expanding, flexible, double-disc device made from nitinol-braided wires (distal LV disc, 17 mm; proximal aortic disc, 16 mm) was deployed with a correct device alignment and a significant decrease of the regurgitant jet without impingement on the bioprosthetic leaflets (Figure 4F). Post-procedural 2D TTE confirmed the resolution of the PVLR (Figure 5). The patient was discharged 3 days after the procedure and was clinically and echocardiographically stable at 6 months follow-up.

Case 2: The second patient is an 82-year-old female with type 2 diabetes, previous coronary angioplasty and stenting of the left descending artery and obtuse marginal branch, hypertension, obesity, dyslipidemia, and symptomatic severe aortic stenosis managed with transfemoral TAVR using 20-mm Myval THV (Meril Life Sciences Pvt. Ltd.), a BE aortic anti-CA-treated bovine pericardium trileaflet valve in November 2020. Following TAVR, TTE demonstrated a LVEF of 40% with a moderately dilated
Figure 2. A, B: Multidetector computed tomography angiography (MDCTA) scans with acquired frames in the axial (A) and coronal (B) views showing the location of the leakage (green arrows) and the calcified nodule located at the level of the regurgitant jet at the non-coronary aortic cusp. C: Baseline ascending aorta angiogram (left anterior oblique projection) confirming a severe paravalvular regurgitation after self-expandable supra-annular bioprosthesis aortic valve (ACURATE neo™) implantation in close proximity to the calcified nodule (black arrow) at the non-coronary cusp; note the severely diseased and ulcerated ascending aorta (white arrows). D: Fluoroscopic image (right anterior caudal projection) showing the self-expandable aortic bioprosthesis valve in place and the calcified nodule (yellow star) and its indentation (black arrow) on the non-coronary cusp adjacent commissure. NCC indicates non-coronary cusp; and AA, ascending aorta.

Figure 3. A, B: 2D TEE X-plane imaging of the first (upper line) and the second (bottom line) balloon valvuloplasty with high-pressure semi-compliant 25-mm Cristal balloon (CBV 25 × 40/110, BALT Extrusion SAS) valvuloplasty catheter. C: Fluoroscopic image showing the balloon inflated across the ACURATE neo™ TAVR; note the calcified nodule (yellow star) and its indentation (white arrow) on the adjacent commissure.
left ventricle and an antero-laterally located moderate PVLR. Unfortunately, there was only slight improvement in the heart failure symptoms, and the patient’s health deteriorated over the next 2 months. In January 2021, she was readmitted due to cardiac failure. 2D TEE color Doppler revealed a 12.9-mm-diameter PVL with moderate-to-severe regurgitation (Figure 6). After heart team discussion and due to prohibitive surgical risk, it was decided to address her recurrent PVLR post-TAVR using a catheter-based technique. The patient was consented after the local ethics committee has approved the use of the device. The procedure was performed in mid-February 2021 in a hybrid operating room under general anesthesia and continuous real-time 2D TEE color flow Doppler and fluoroscopic guidance. Baseline angiography in the AA (Figure 7A) revealed moderate-to-severe PVLR. The irregularly shaped defect was initially crossed using a slippery wire and JR4 (Cordis) catheter, but neither the 6-Fr sheath nor the long 6-Fr sheath could pass. This was overcome firstly by dilating the leak using a 0.035-inch-guidewire-compatible balloon PTA catheter (diameter: 6 mm; length: 40 mm) (Figure 7B) and secondly by looping the slippery wire in the left ventricle and passing it back through the center of the prosthetic aortic valve up to the AA (Figure 7C). The slippery wire was then replaced with a super stiff 0.035-inch, 260-cm “J” tip guidewire and, finally, with this extra support, through a 7-Fr, 45°-curved, 110-cm-long sheath a 10 × 4-mm rectangular waist PLD (distal LV disc, 19 mm; proximal aortic disc, 17 mm) (Figure 7D, E) was successfully deployed with significant decrease of the regurgitant jet (Figure 7F). Post-procedural 2D TEE confirmed the almost-complete abolition of the PVLR (Figure 8) with the presence of a tiny peri-device residual leak. The patient was discharged 2 days after the procedure in better clinical conditions. At 2 months follow-up, she had a significant clinical improvement, and TTE confirmed the stable position of the device with trivial residual leak.

**Discussion**

PVLR remains an important complication associated with replacement of first- and second-generation transcatheter aortic valves that can be prevented by accurate annulus measurements using three-dimensional (3D) techniques and adequate valve sizing. Furthermore, accurate positioning of the valves may reduce the risk of post-TAVR PVLR. Among others, the goal of the ongoing re-

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**Figure 4.** Fluoro-angiography procedural steps. A: Ascending aorta angiogram (left anterior oblique projection) showing severe PVL regurgitation post-ACURATE neo™ TAVR and the super stiff 0.035-inch, 260-cm “J” tip guidewire across the PVL in the left ventricle; B: over the stiff guidewire, a 7-Fr, 45°-curved, 110-cm-long delivery sheath was then advanced into the left ventricle; C: opening of the distal LV disc (white arrow); D–E: the 7-mm square twist PLD (black arrow) still connected to the Flex II pusher and finally deployed in the correct position; F: immediate post-procedure angiographic control with the device *in situ* (black arrow) showing just a mild-to-moderate regurgitant jet. AA indicates ascending aorta; and ST PLD, square twist paravalvular leak device.
finement and development of third-generation transcatheter aortic valves is to drastically reduce the incidence of leakage regurgitation.

The risk factors for PVLR after contemporary TAVR include tissue frailty, mismatch between the annulus and prosthesis diameters, prosthetic valve underinflation, suboptimal prosthetic valve implantation, bicuspid valve, and most importantly, a high degree of valve calcification, which is measured by the aortic valve calcium scoring (AVCS). Indeed, the AVCS identifies patients at risk for a significant PVLR and may even have more impact on the postoperative result in terms of the persistence of PVL and residual stenosis.

Accurate quantification of PVLR after SE- and BE-TAVR is challenging. AA angiography is an established technique for assessing PVL in the cath lab during interventional procedure. 2D/3D TTE/TEE color Doppler are the primary imaging tools for identifying and monitoring PVLR after TAVR but often fail to obtain good pictures due to interference from the valve frame itself. Cardiac CT allows further definition of the size and orientation of PVL in cases in which acoustic shadowing affects the interpretation of echocardiographic images. Magnetic resonance imaging may be superior to the current 2D TTE/TEE modalities when attempting to quantify the degree of PVL, particularly in the case of multiple paravalvular defects.

More recently, Sinning, et al. reported that the aortic regurgitation (AR) index can be useful for defining the severity of AR, with a value of < 25, suggesting severe AR with an increased mortality risk. The Valve Academic Research Consortium suggests a semiquantitative evaluation using the proportion of the circumference of the prosthesis that involves the PVL, measured in the short-axis view. They define mild, moderate, and severe paravalvular AR as < 10%, between 10% and 29%, and >30% of the extent of the prosthesis frame circumference, respectively.

Moderate-to-severe PVLR immediately after TAVR should be managed with valve repositioning and postdilation without delay. Nevertheless, when incomplete adherence to the annulus is observed due to calcified nodule, as demonstrated in our first case, or post-implant balloon dilation cannot be performed or has been suboptimal, as demonstrated in our second case, percutaneous PVL closure is the only available option to avoid progressive heart failure and surgery.

Percutaneous treatment using occluder devices adapted from other indications has been previously reported. Nowadays, PVL post-TAVR percutaneous closure
occluders have been developed, such as Amplatzer™ Vascular Plug (AVP) (St. Jude Medical, St. Paul, MN) devices and among them the most commonly used AVP IV, a low-profile device that is 4- or 5-Fr-compatible. More recently, Occlutech PLD devices with a unique rectangular/square design especially designed for PVLs have been used and may be useful tools in the device armamentarium of interventional cardiologists.

Similar to the PVL of surgical valves, the vast majority of the leaks of the SE transcatheter aortic valves are irregular, mostly crescent-shaped, and challenging to be crossed due to the prosthetic heart valve apparatus itself. As widely reported in the literature and also in our two cases, the presence of high sealing skirts is a serious challenge when attempting to cross the leak with wires and catheters.

The rapidly evolving TAVR technology is expanding to new indications, such as younger, intermediate, or lower-risk individuals and patients with asymptomatic severe aortic stenosis. Therefore, advances in technology are mandatory to improve not only paravalvular sealing with specific skirts and new cuffs to better seal the annular region but also to reduce the risk of stroke, to avoid heart block and the need for pacemaker implantation, to increase valve durability, and to facilitate accurate transcatheter aortic valve implantation. At the same time, lower-profile and more flexible delivery sheaths will also facilitate leakage crossing and closure device delivery, thus reducing vascular complications and the procedure time. Longer-term follow-up and greater numbers of patients are needed to confirm if those technological advancements will really improve clinical outcomes.

**Conclusion**

Catheter-based closure of moderate-to-severe PVLR after third-generation SE- and BE-TAVR is a complex procedure with serious potential complications, requiring optimal patient selection, thorough intraprocedural imaging guidance, expert operators, and trained centers to optimize the success rate of the procedure. Further development of dedicated closure devices and more versatile delivery sheaths are essential steps to improve clinical outcomes and patient prognosis.

**Disclosure**

Conflicts of interest: Eustaquio Maria Onorato is a consultant for Occlutech, manufacturer of the device. The remaining Authors declare no commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions: All authors listed have made a
Figure 8. Post-procedure 2D TEE color Doppler imaging at 120° (A–C) and 73° (D) views showing the almost-complete abolition of the regurgitant jet with the presence of a tiny peri-device residual leak.

substantial, direct and intellectual contribution to the work, and approved it for publication.

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