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Subannular perforation of left ventricular outflow tract associated with transcatheter valve implantation: pathophysiological background and clinical implications

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Abstract

OBJECTIVES: Perforation of the subannular left ventricular outflow tract (LVOT) represents an uncommon but almost invariably fatal transcatheter aortic valve implantation (TAVI)-associated complication. The risk factors to predict the occurrence of this devastating complication, particularly in relation to specific LVOT anatomy, have not yet been systematically analysed. We aimed to evaluate the pathophysiological background and possible risk factors for the occurrence of subannular LVOT perforation.

METHODS: A total of 6 (0.7%) consecutive patients (78.8 ± 3.3 years, 83% women) with subannular LVOT perforation complicating TAVI procedure were identified from our institutional TAVI registry, including 900 consecutive patients who underwent TAVI procedure at a single institution between January 2009 and July 2015. Only patients with an intraoperatively confirmed LVOT perforation were included.

RESULTS: The computed tomography (CT)-guided analysis of aortic root/LVOT morphology revealed subannular calcification in close proximity of the anatomically weakest region of muscular LVOT (i.e. in the region of the muscular LVOT between the left fibrous trigone and the left/right commissure) in 5/6 (83%) patients. Moreover, significant annular asymmetry >20% was present in 4/6 (67%) patients and was combined with a severe asymmetric hypertrophy of muscular LVOT.

CONCLUSIONS: Subannular calcification in close proximity of the anatomically unprotected muscular LVOT might represent an important risk factor for the occurrence of subannular LVOT injury. Precise CT-based analysis of patient-specific aortic root anatomy/subannular calcification patterns may be helpful to predict this TAVI-associated complication preoperatively and hence to avoid it in future patients.

Keywords: TAVI • Complication • Annular rupture • Surgery

INTRODUCTION

Over the last decade, transcatheter aortic valve implantation (TAVI) has evolved to a standard of care for severe symptomatic aortic valve stenosis in high surgical risk patients [1, 2]. Decreasing perioperative TAVI-associated mortality and morbidity has been reported with a resulting trend towards expanded indications into intermediate surgical risk patients [3].

Despite significant improvements in preoperative imaging modalities and increasing heart team expertise, the risk of TAVI-associated complications remains real and—to some extent—unpredictable [4]. Recent analyses of large-scale international registries failed to identify any reliable predictors of severe TAVI-associated complications [4, 5]. An important group of severe, life-threatening complications requiring immediate rescue surgery is summarized under the umbrella term of 'annular rupture', which occurs in ∼0.5–1.0% of TAVI procedures [5–8]. Although occurring relatively rarely, it is associated with a high mortality rate with estimates ranging from 50 to 100%, even in recent series [5, 7, 8]. Significant variation in surgical outcomes associated with annular rupture might be explained by the wide spectrum of TAVI-associated lesions included in this definition (i.e. 'device landing zone rupture') as reported by Pasic and colleagues [9]. Injuries to the fibrous aortic annulus may be managed by direct surgical suturing/patching and subsequent surgical aortic valve implantation, a relatively straightforward approach. Quite contrary, injuries to the subjacent left ventricular outflow tract (LVOT) are more complex and difficult to manage. Such injuries almost invariably result in intra-procedural mortality [4, 10].

Based on the functional anatomy of the LVOT and the grim prognosis associated with its injury, we propose a separate term referring to this complication, i.e. 'subannular LVOT perforation'. We also describe a case series of 6 patients with this devastating complication which were diagnosed at our institution over a 7-year period. Moreover, we aim to identify possible risk factors for the occurrence of subannular LVOT perforation based on CT-guided analysis of aortic root/LVOT morphology.

MATERIALS AND METHODS

Study population

A total of 6 (0.7%) consecutive patients with subannular LVOT perforation complicating TAVI procedure were identified from our institutional TAVI registry, including 900 consecutive patients who underwent TAVI procedure at a single institution (Central Hospital Bad Berka, Germany) between January 2009 and July 2015. Only patients with an intraoperatively confirmed LVOT perforation were included.

All decisions regarding the method of aortic valve replacement (i.e. conventional versus TAVI), choice of the TAVI prosthesis (i.e. balloon-expandable versus self-expandable) and the access route (i.e. transfemoral versus transapical) were made by institutional heart team consisting of cardiologists and cardiac surgeons. Edwards SAPIEN, SAPIEN XT and SAPIEN 3 THVs (Irvine, CA, USA), Medtronic CoreValve THV (Minneapolis, MN, USA), Symetis ACURATE TA and neo THVs (Ecublens, CH) were implanted by transfemoral (n = 623) or transapical (n = 277) approach.

Preoperative imaging

All TAVI candidates underwent preoperative multidetector computed tomography (MDCT) and 2D-echocardiography. The native aortic valve annulus diameter was measured by echocardiography (i.e. parasternal long-axis view and apical five-chamber view in the TTE, mid-oesophageal long-axis view in the TEE) and by means of MDCT analysis. The *syngo.via* software (Siemens Healthcare, Erlangen, Germany) was routinely used for MDCT-based aortic annular measurements (i.e. area-derived and perimeter-derived values) and detailed analysis of calcification patterns (Fig. 1). Aortic valve calcification was graded as mild (small isolated spots), moderate (multiple larger spots) and severe (extensive calcification of all cusps). Aortic annular asymmetry was defined as a relative difference between the largest and the shortest aortic annular diameter [i.e. largest diameter (mm) × 100%/shortest diameter (mm) – 100%]. The LVOT was separately analysed for the presence and exact localization of calcium deposits.

Statistical analysis

Standard definitions were used for patient variables and outcomes. Categorical variables are expressed as percentages, and continuous variables are expressed as mean ± SD with range throughout the manuscript. All statistical analyses were performed with the IBM SPSS 19.0 software (IBM Corp, New York, USA). All P-values of <0.05 were considered statistically significant.

RESULTS

Demographics and preoperative variables of our study cohort are summarized in Table 1. Five of the 6 patients (83%) were women. The mean age was 78.8 ± 3.3 years, and the mean body surface area (BSA) was 1.7 ± 0.2 m^2. Preoperative risk profile was that of a usual TAVI population with a mean logistic Euroscore of 19.5 ± 3.8% and STS score of 10.2 ± 2.9%.

Significant annular asymmetry of >20% was found in 4/6 patients with a mean value of 25 ± 15% (range 4–50%). Cusp calcification was severe in 2 patients and asymmetrically distributed (i.e. localized bulky left coronary cusp calcification) in 2 other patients. Subannular calcification in the region of the muscular

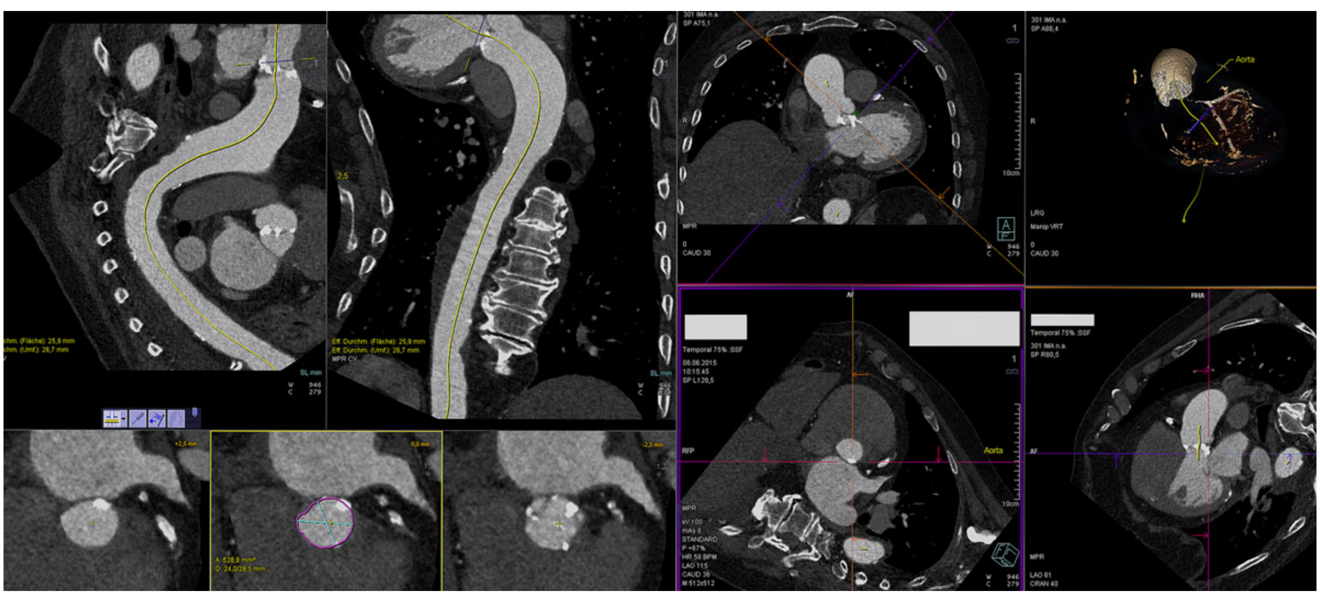

Figure 1: Computed tomography-based analysis of subannular calcifications using *syngo.via* software.

Table 1: Demographics and preoperative characteristics of patients

	Gender	Age (years)	BSA (m^2)	Aortic annular diameter[a] (mm)	LVOT diameter[b] (mm)	Annular asymmetry (%)	Subannular calcification (vulnerable region)	Asymmetric cusp calcification
Patient 1	F	82	1.6	24.5	17	4.2	+	+ (LCC)
Patient 2	F	81	1.6	17.4	13	50.0	+	+ (LCC/NCC)
Patient 3	F	82	1.5	19.7	16	20.0	–	–
Patient 4	F	77	2.1	22.5	20	22.5	+	–
Patient 5	F	74	1.7	22.6	18	32.8	+	–
Patient 6	M	77	1.8	26.4	22	18.8	+	–

BSA: body surface area; F: female; M: male; LVOT: left ventricular outflow tract; LCC: left coronary cusp; NCC: non-coronary cusp.
[a]Area-derived aortic annular diameter, as determined by software-guided MDCT analysis.
[b]CT scan-based measurements at end-systole in the sagittal long-axis view.

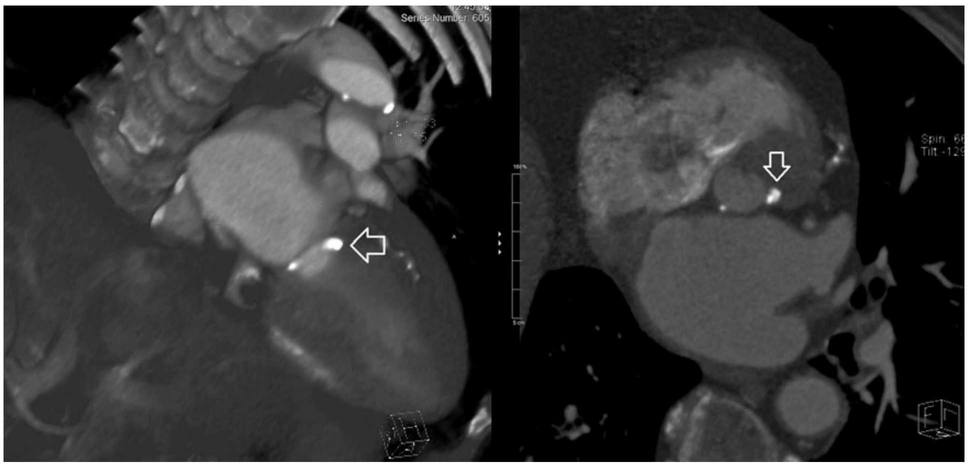

Figure 2: Identification of subannular calcification (arrow) in the region of 'anatomically unprotected' muscular left ventricular outflow tract.

LVOT between the left fibrous trigone and the left/right commissure was detected in 5/6 (83%) patients (Fig. 2). Preoperative echocardiography revealed severe asymmetric subannular LV hypertrophy in 4/6 (67%) (Fig. 3), which was associated with an end-systolic LVOT diameter of 17.7 ± 3.1 mm (range 13–22 mm) in the sagittal CT-scan view in those 4 patients. All 6 patients were diagnosed with very high transvalvular gradients (dp_{max} 112 ± 29 mmHg and dp_{mean} 77 ± 19 mmHg) (Table 2).

Balloon-expandable TAVI prostheses were implanted using a transfemoral approach in all 6 patients. A 23-mm Edwards Sapien XT prosthesis was used in 4/6 (67%) patients. Mild-to-moderate oversizing (i.e. based on the CT-based effective annular diameter) of 10.5 ± 10% was performed during TAVI implantation, and a total of 4 patients had oversizing of a transcatheter valve of less than 10%.

Acute haemodynamic deterioration due to pericardial tamponade was the initial presentation in all 6 patients. Pericardial tamponade occurred immediately after TAVI prosthesis deployment in 4/6 patients and within the first 3 post-TAVI hours in the remaining 2 patients. Rescue cardiopulmonary bypass was established percutaneously through the femoral vessels and pericardial drainage was immediately performed. Due to persisting arterial blood drainage, median sternotomy was performed and uniformly revealed a massive subepicardial haematoma with arterial blood extravasation behind the pulmonary artery trunk and adjacent to the base of left atrial appendage. Intraoperative coronary angiography showed a long-segment 'stenosis' in the proximal

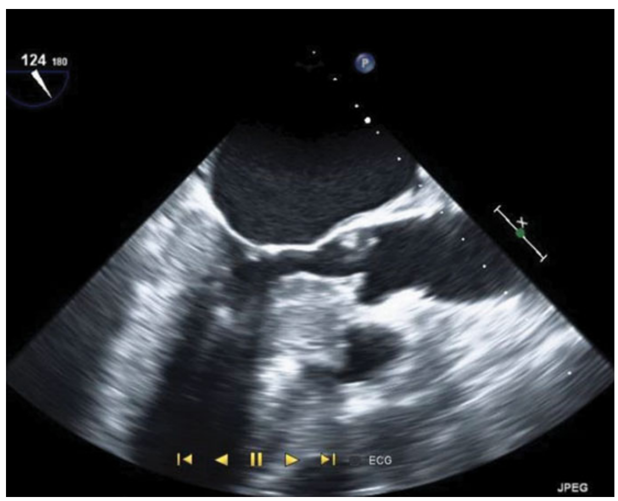

Figure 3: Severe asymmetric hypertrophy of subannular muscular left ventricular outflow tract (as identified echocardiographically in the parasternal long-axis view).

circumflex artery, which was not seen on the preoperative angiography, in 1 patient (Fig. 4). External suturing was attempted in the first 2 cases but was abandoned thereafter because of the lack of success and the risk of coronary artery occlusion. All patients underwent cardioplegic arrest followed by tranverse aortotomy

Table 2: Transcatheter aortic valve implantation procedural variables

	Access route	Balloon size (mm)	TAVI prosthesis	Prosthesis size (mm)	Oversizing (%)	Post-dilatation
Patient 1	TF	23	Sapien XT	26	6	–
Patient 2	TF	20	Sapien XT	23	30	–
Patient 3	TF	20	Sapien XT	23	16	+
Patient 4	TF	20	Sapien XT	23	1	–
Patient 5	TF	20	Sapien XT	23	1	–
Patient 6	TF	26	Sapien 3	29	9	–

TF: transfemoral access route; TAVI: transcatheter aortic valve implantation.

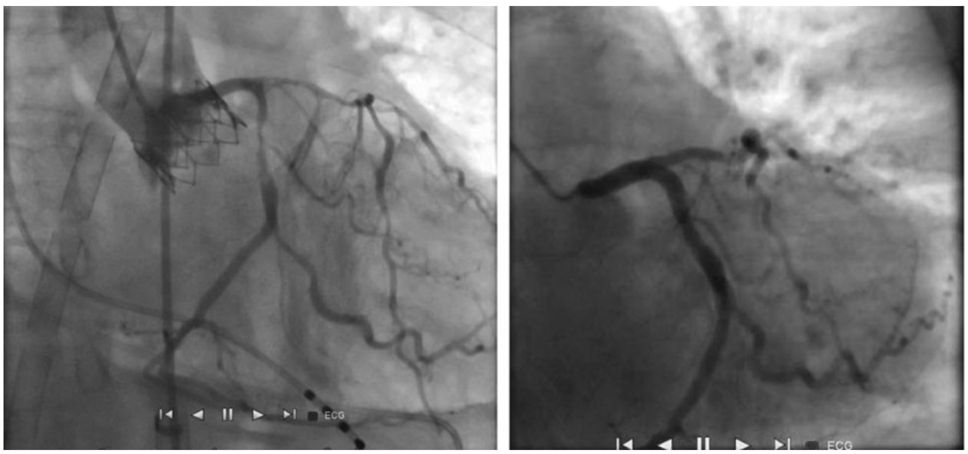

Figure 4: Symmetric stenosis in the proximal circumflex artery (arrow) caused by an expanding subepicardial haematoma.

revealing a normally seated TAVI prosthesis without visible supravalvular injury (Fig. 5A). Following the removal of the balloon-expandable prosthesis, the typical LVOT injury in the most vulnerable subannular region (i.e. between the left fibrous trigone and left/right commissure) was found in all 6 patients (Fig. 5B/C). Due to massive intramyocardial haematoma formation and deep laceration of muscular LVOT extending downwards into the left ventricle towards the anterolateral papillary muscle, all attempts of surgical suturing and pericardial patching were futile and all 6 patients expired intraoperatively.

DISCUSSION

Acute life-threatening complications requiring rescue circulatory support and emergent surgical intervention represent an uncommon but persistent risk of TAVI procedures [4, 6, 7]. A recent meta-analysis was unable to identify any reliable risk factors to predict the occurrence of severe TAVI-associated complications requiring emergent cardiac surgery [4]. Our current report presents a case series and focused overview on the anatomical background of perforation of the subannular muscular LVOT which is a life-threatening TAVI-associated complication.

Functional anatomy of left ventricular outflow tract and pathophysiology of subvalvular injury

Anatomically, the LVOT is composed of two distinct components—the fibrous and muscular portions—which have a significant impact on the pathophysiology of TAVI-associated injuries (Fig. 6). The fibrous component of LVOT is composed of aortomitral continuity between the right/non-coronary commissure and the mid-portion of the left coronary cusp. The fibrous LVOT is formed by the strong and distensible tissue of the aortomitral curtain/anterior mitral leaflet, as well as the membranous septum [11]. Injury in this region is uncommon and may result in acute mitral regurgitation or perimembranous ventricular septal defect. However, catastrophic extracardiac bleeding will not occur. The muscular portion of the LVOT lies underneath the right coronary sinus and the leftward portion of the left coronary sinus. The section under the right coronary sinus is formed by the interventricular septum, which is usually thickened in patients with aortic valve stenosis and is externally supported by the overriding right ventricular outflow tract. This is the 'anatomically protected' part of the muscular LVOT where endocardially induced lesions do not result in catastrophic injury. The small segment of circumference of muscular LVOT located between the left/right commissure and left fibrous trigone represents the only segment of 'anatomically unprotected' LVOT which has no external support and represents the most vulnerable part of the LVOT. Injury here is associated with an imminent risk of catastrophic bleeding (Fig. 7A). We hypothesized that endocardial injuries in close proximity of the anatomically unprotected muscular LVOT may induce haematoma formation in the adjacent soft muscular LVOT which can spread further into the subepicardial fatty tissue and free pericardial space. Externalization of such haematoma formation into the pericardial sac occurs typically in the region of proximal atrioventricular groove, behind the main pulmonary artery trunk and in close proximity to the base of the left atrial appendage and the first segment of

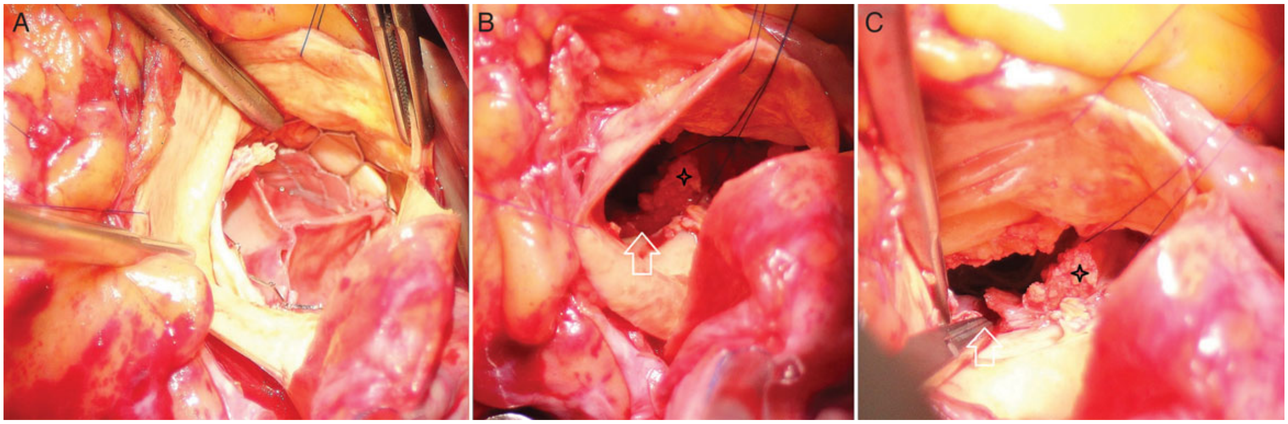

Figure 5: Intraoperative findings in patient with subannular LVOT perforation, showing deep laceration of subannular muscular LVOT (arrow) in the region between left/right commissure and left fibrous trigone (asterisk). LVOT: left ventricular outflow tract.

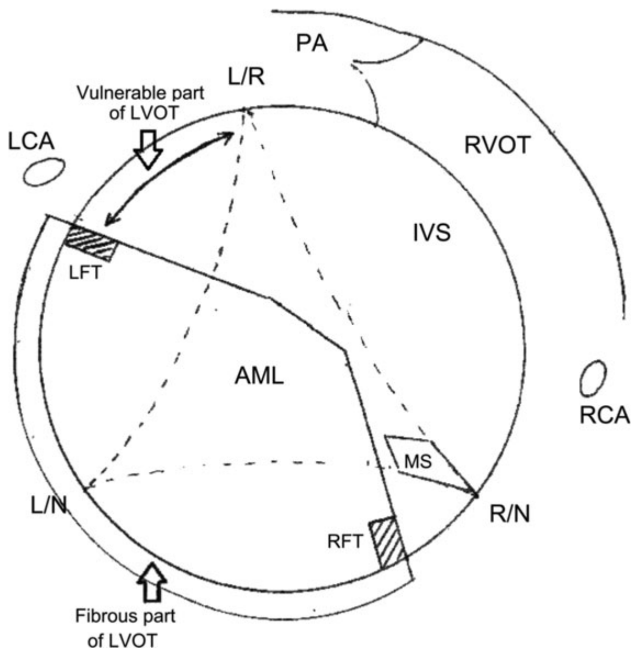

Figure 6: Schematic cross-sectional LVOT view from the surgical perspective. AML: anterior mitral leaflet; IVS: interventricular muscular septum; MS: membranous interventricular septum; LCA: orifice of left coronary artery; LFT: left fibrous trigone; L/N: left/non-coronary commissure; L/R: left/right coronary commissure; PA: pulmonary artery; RCA: orifice of right coronary artery; RFT: right fibrous trigone; R/N: right/non-coronary commissure; RVOT: right ventricular outflow tract; LVOT: left ventricular outflow tract.

the circumflex artery (Fig. 7B). A rapidly expanding subepicardial haematoma may cause external compression of the adjacent left coronary system branches, which may be misidentified as symmetric long-segment stenoses in the proximal circumflex artery (Fig. 4).

From anatomical and pathophysiological point of view, it would be reasonable to describe this process as 'subannular LVOT perforation'. We believe that the term 'annular rupture' should be reserved for those procedural-related injuries that occur in the fibrous portion of the aortic annulus, while 'subannular LVOT perforation' should be used for those injuries that involve the subannular muscular portion of the LVOT. Due to specific architecture of LVOT, we hypothesized that subannular calcification in close proximity of the anatomically unprotected muscular LVOT might represent an important risk factor for the occurrence of this devastating complication.

Risk factors for subannular left ventricular outflow tract perforation

A combination of multiple anatomic and procedural factors rather than a single one is responsible for TAVI-associated 'device landing zone' complications [7, 12]. However, systematic avoidance of patients with any of these characteristics (i.e. narrow aortic root, large amount of calcification in the aortic valve cusps and annulus, the presence of calcification in the LVOT, calcification of supra-annular segment, severe asymmetric subannular LV hypertrophy and global LV hypertrophy in elderly female patients) would result in a very limited proportion of patients being suitable for TAVI procedures. Therefore, identification of more specific factors associated with 'device landing zone' complications is needed.

Although aggressive oversizing (i.e. ≥20%) of a balloon-expandable transcatheter valve has been reported to be a major risk factor [7], it was found in only 1 patient in our series. However, significant annular asymmetry >20% was present in 4/6 patients and was combined with a severe asymmetric hypertrophy of muscular LVOT.

Subannular calcification of LVOT has been previously reported to be a risk factor for aortic root rupture [7, 8, 10], and some efforts were undertaken to quantify the amount of LVOT calcification by the Agatston score [7]. However, the relative impact of specific subannular calcium localization, particularly in relation to adjacent anatomical features, has not yet been systematically analyzed. Based on CT-guided analysis, we detected subannular calcifications in close proximity of the anatomically weakest region of muscular LVOT in 5/6 patients who suffered subannular LVOT perforation in our series.

Based on our findings, we strongly suggest differences in subannular complication risk between calcification in the muscular versus fibrous component of LVOT. While muscular part of LVOT is obviously most vulnerable for such fatal injuries, we are not aware of subannular perforation in case of LVOT calcifications limited to the fibrous aortomitral continuity. All subannular perforations in our series occurred in balloon-expandable device group and, therefore, we intentionally avoid balloon-expandable device whenever the subannular calcification is localized in the muscular LVOT. On the other hand, we are still comfortable to use such devices in subannular calcification limited to the fibrous part of LVOT (e.g. aortomitral continuity) and experienced no complication in this patients' cohort so far. Radial forces of the self-expanding devices, which have been suggested specifically for patients with extensive subannular calcifications, are frequently

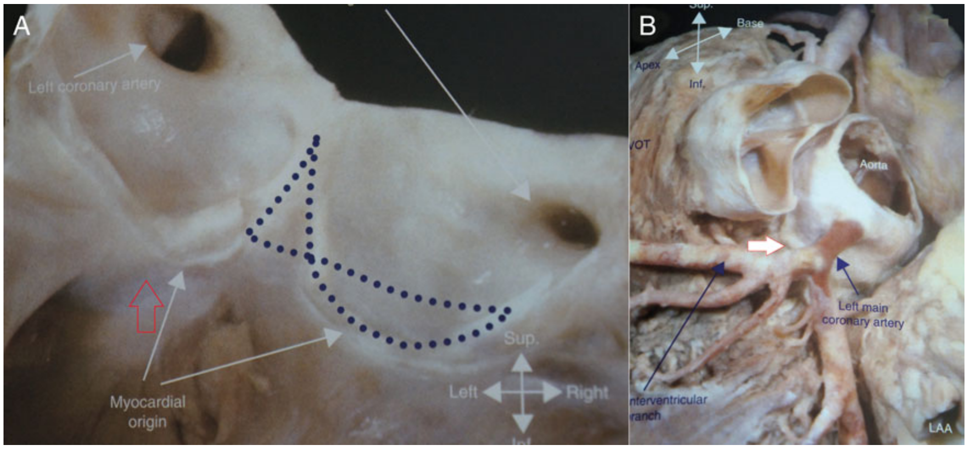

Figure 7: The region of 'anatomically unprotected' muscular left ventricular outflow tract from intracardiac view (**A**)—arrow showing the typical area of endocardial injury; and from extracardiac view (**B**)—arrow showing the typical area of extravasation, behind the main pulmonary artery trunk and in close proximity to the base of the left atrial appendage. Reproduced with permission from Wilcox BR, Cook AC, Anderson RH. Surgical Anatomy of the Heart—3rd edition. Cambridge: Cambridge University Press, 2005.

not sufficient enough to fully expand and seal subannular calcification spots, especially if no balloon pre/post-dilatation was performed. Obviously, there is no universal solution to address this morphological challenge, and we strongly believe that CT-based analysis of LVOT calcification patterns (i.e. muscular versus fibrous part of the LVOT) is of utmost importance when choosing the most appropriate prosthesis (i.e. balloon expanding versus self-expanding versus conventional AVR) for an individual patient.

The impact of subannular calcifications underneath the left coronary cusp might be aggravated in the presence of a narrow LVOT due to asymmetric septal hypertrophy, which was found in 4 of our 6 patients. Hypothetically, a pronounced oval-shaped LVOT that is associated with a reduced anteroposterior diameter may further magnify the stress on the posterior annular circumference during TAVI implant and thus increase the risk of subannular LVOT injury.

From clinical point of view, older female patients with small BSA $\leq$1.8 m^2 and severe asymmetric septal hypertrophy (Table 1) might be particularly prone to this devastating complication, especially in the presence of above-mentioned subannular calcification.

Precise analysis of patient-specific aortic root anatomy/calcification patterns using preprocedural imaging data may be helpful in avoiding such complications (Fig. 1). Based on our observations, we believe that this nearly uniformly fatal type of TAVI procedure-related complication can be predicted preoperatively and hence avoided in future patients.

CONCLUSIONS

Subannular calcification in close proximity of the anatomically unprotected muscular LVOT might represent an important risk factor for the occurrence of subannular LVOT injury. Precise CT-based analysis of patient-specific aortic root anatomy/subannular calcification patterns may be helpful to preoperatively predict this nearly uniformly fatal type of TAVI procedure-related complication and hence to avoid it in future patients.

Conflict of interest: Evaldas Girdauskas and Lenard Conradi are proctors for Symetis. All other authors none declared.

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