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Review Article
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Delayed Coronary Obstruction after Transcatheter Aortic Valve Replacement – An Uncommon But Serious Complication

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As transcatheter aortic valve replacement (TAVR) becomes the mainstream treatment for valvular aortic stenosis, it is vitally important to recognize its associated procedural complications. Among the clinically relevant but uncommonly seen complications, the development of delayed coronary obstruction (DCO) occurring during the early post-procedural phase or even later following the index TAVR procedure, has been reported. These reports have raised concerns as TAVR comes more common in lower-risk patients. In this review article, we explored the implications of DCO for pre-procedural computed tomography evaluation, valve selection and sizing, intra-procedural manipulation, and approaches to post-procedural management.

Key Words: Complication • Delayed coronary obstruction • Transcatheter aortic valve replacement

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has become the mainstream treatment for valvular aortic stenosis (AS).[1,2] Currently, TAVR is undergoing evaluation in prospective, randomized trials compared to surgical aortic valve replacement in younger and/or lower-risk patients.[3-5] It is believed that the use of TAVR may be extended to intermediate- and even low-risk patients in the future; hence, better knowledge concerning its potential complications, risk factors in terms of these complications, and management strategies to deal with them is required.[6]

DELAYED CORONARY OBSTRUCTION AFTER TAVR

Acute coronary obstruction (ACO) during valve implantation is the most clinically relevant although uncommon complication.[7-9] Moreover, delayed coronary obstruction (DCO) has been reported in the early post-procedural phase or even later following the index TAVR procedure.[10-15] It is even rarer but more serious complication, with a high in-hospital death-rate of 50%, especially if DCO occurs ≤ 7 days of the index procedure.[14] As TAVR is increasingly used in lower-risk patients, new concerns arise.

DCO is defined as: 1) obstruction of the left main stem or ostial right coronary artery after a patient has already left the operating room following a successful TAVR in a stable condition; 2) diagnosed by angiogram, surgery, or autopsy at the time of the event; and 3) not solely related to the progression of pre-existing coronary artery disease or in-stent restenosis. According to the largest published international registry of 17,092 TAVRs, the incidence of DCO following TAVR was 0.22% (38 cases).[14] However, it is still vitally important to recognize DCO because of its life-threatening nature.[14-16] DCO can broadly be classified into 2 types: patients in whom obstruction occurs (i) less than (early DCO) and (ii) later than 7 days (late DCO) from the index TAVR procedure.[14]

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DCO may be less uncommon than previously thought, since it can easily go unnoticed as sudden cardiac death outside the hospital can be its first manifestation, if no autopsy is subsequently required or performed. Moreover, patients having undergone a prior coronary artery bypass graft (CABG) may be relatively well protected from the symptoms of coronary obstruction, and the incidence of DCO can be further lowered. As TAVR is increasingly used in lower-risk patients, the incidence of DCO may increase due to a longer life expectancy post-TAVR in those patients.[14-16] It has been estimated that, in a worst case scenario, the frequency of DCO may be as high as 0.5%.[15] In our institution, 2 out of 369 (0.5%) patients who underwent TAVR between March 2013 and December 2018 developed DCO (1 early DCO and 1 late DCO), supporting this hypothesis. These two cases are illustrated in Figure 1 and Figure 2, and serve to highlight the fundamental importance of close cardiac monitoring of patients post-TAVR in order to recognize DCO complications.

STRATIFYING THE PATIENTS AT RISK OF DCO

Two possible distinct pathogenetic mechanisms for DCO were proposed by Jabbour et al.[14] In their series, DCO was most likely to occur within 7 days (n = 24, 63.2%; early DCO); in just over a third of cases, DCO occurred later (n = 14, 36.8%; late DCO). In the early DCO cases, the continuing expansion of a self-expanding valve probably caused an obstruction.[14-16] In addition, DCO occurred more commonly if self-expandable valves were used during the index procedure (0.36% vs. 0.11% balloon expandable; $p < 0.01$). A thrombotic event or heavily calcified valve within the sinus of Valsalva can also cause obstruction; in contrast, certain late DCO probably occurs due to a combination of turbulent flow, which can trigger fibrosis or persistent inflammation, leading to endothelialization and subsequently obstruction. Moreover, DCO occurred more commonly after valve-in-valve procedures (0.89% vs. 0.18%; $p < 0.001$).[14] Furthermore, earlier cases of DCO have been reported to be more likely to appear with cardiac arrest or ST-segment elevation myocardial infarction, and a higher in-hospital mortality rate (up to 62.5%), but later cases have been reported to be more likely to appear with stable or unstable angina and a lower mortality rate.[14,16]

Proposed risk factors for ACO following TAVR (Table 1) may be of limited value in terms of predicting DCO, especially in cases of late DCO. According to the report by Jabbour et al., although two thirds of the patients had at least one classic risk factor for ACO, left and right coronary heights exceeded 12 mm in more than one half and about two thirds of the patients, respectively. Another 44% of the patients had a mean sinus of Valsalva diameter greater than 30 mm, and only about half of

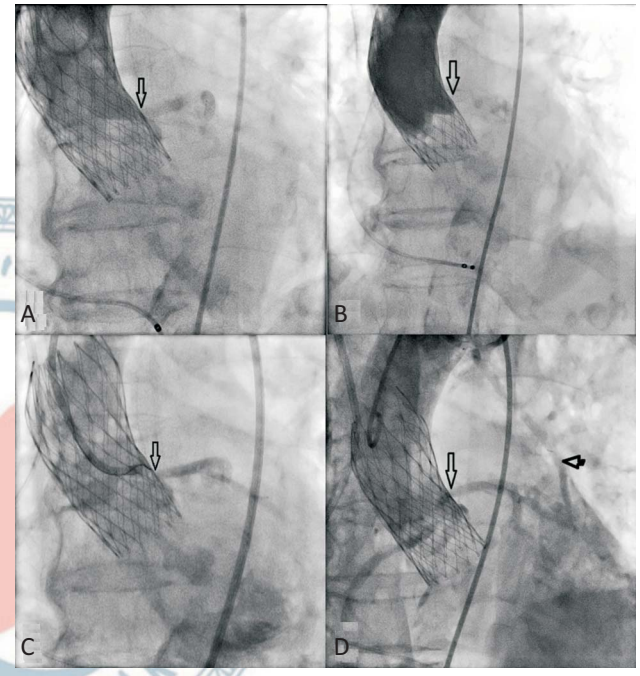

Figure 1. *An 84-year-old woman was admitted with symptomatic, severe aortic stenosis for transcatheter aortic valve replacement. Her aortic valve annulus measured 19.4 mm on three-dimensional computed tomography imaging. The left and right coronary ostial height was 9 mm and 10 mm, respectively. A 26 mm CoreValve (Medtronic) was deployed in a good anatomical position. Aortic root angiography suggested the presence of bioprosthetic valve struts and tissue close to, but not obstructing, the left coronary ostium (A, arrow). As the patient remained hemodynamically stable, sheaths were removed and the arteriotomy at the femoral artery was closed. However, about 1 hour later, she became abruptly hypotensive, and severe ST-segment elevation appeared on electrocardiograph monitor was noted. Hemodynamic status deteriorated rapidly and cardiopulmonary resuscitation was initiated. Emergency percutaneous coronary intervention was planned, but total occlusion of the left main stem (LMS) by the CoreValve with obliteration of the space between the bioprosthesis and the coronary orifice (B, arrow), which precluded the engagement of guiding catheter and wiring of the coronary arteries, was demonstrated (C, arrow). Therefore, emergency coronary artery bypass grafting was performed. Post-operative aortogram showed improved left ventricular function, patent LMS (D, arrow) and left internal mammary artery graft to left anterior descending artery (D, small arrow).*

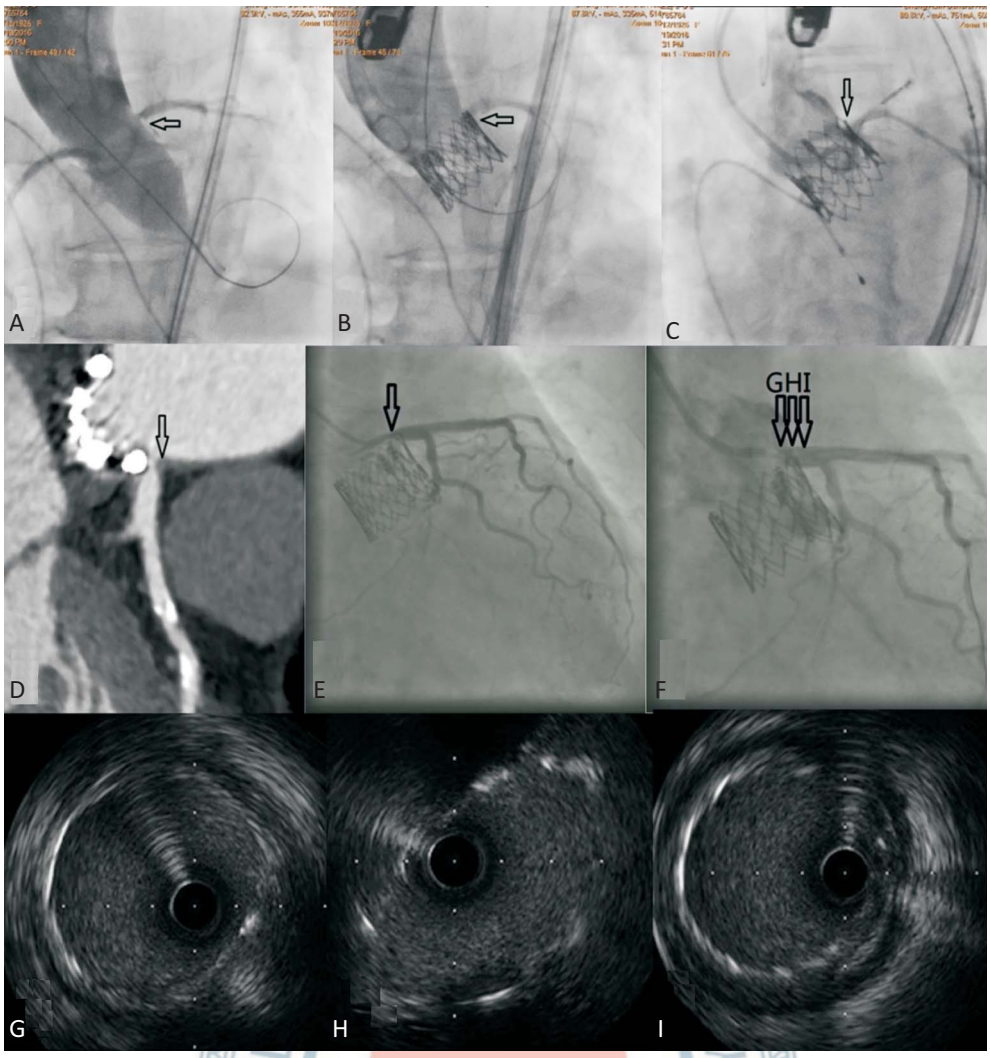

Figure 2. *A 90-year-old woman was admitted with symptomatic, severe aortic stenosis for transcatheter aortic valve replacement (TAVR). Pre-implantation computed tomography indicated left and right coronary ostial heights of 13.4 mm and 17.6 mm, respectively. During balloon valvuloplasty for pre-dilatation with a 25 mm × 40 mm balloon, the left aortic leaflet was displaced toward the left coronary ostium (A, arrow); therefore, we decided to perform coronary protection. A 29 mm SAPIEN XT valve (Edwards Lifesciences) was then implanted. Aortography suggested the presence of stent frames of TAVR device close to, but not obstructing, the left coronary ostium (B, arrow). A post-TAVR selective angiography also showed a patent left main stem (LMS) with TIMI 3 flow (C, arrow). The patient was discharged uneventfully but a computed tomography follow-up six month after TAVR showed new tissue growth near the ostium of LMS (D, arrow). The patient declined percutaneous coronary intervention at that time because she continued to do well. Another 5 months passed, the patient was admitted for unstable angina and the LMS was stented with a 4.0 mm × 12 mm integrity resolute stent (Medtronic) (E, arrow). Post-dilatation with a 4.5 mm non-compliant balloon led to improvement in the angiographic appearance of the stent (F, arrows). Intravascular ultrasound examination demonstrated improvement in minimum lumen area and diameter, but residual ovoid-shaped stented segment discovered at the site of the impingement of stent frames of the TAVR device (G-I).*

Table 1. Proposed risk factors for acute coronary occlusion following transcatheter aortic valve replacement

A short distance between the aortic annulus and the coronary ostia (< 10 mm).
A narrow aortic root (< 28 mm at the sinuses of Valsalva).
Bulky calcification of the native leaflets.
Signs of coronary compromise during balloon aortic valvuloplasty, such as ST-segment elevation in the electrocardiogram, and extrinsic compression of or reduced flow in the coronary artery on angiogram or transesophageal echocardiogram.
A leaflet length to coronary sinus height ratio greater than 1.
High implantation depth.

the occlusions involved implantation depths that were considered to be high. Therefore, the individual predictive value of any one or combination of these measurements or risk factors has not been proven, and DCO remains largely unpredictable.[14-16] Nevertheless, we suggest that detailed anatomical information is mandatory and may be useful in mitigating this devastating complication.

For early DCO cases, the presence of risk factor(s) for ACO can still play an important role in causing this catastrophic complication. For example, continuing expansion of a relatively highly-implanted self-expandable device in a small aortic root may be prone to the development of early DCO; hence, pre-procedural computed tomography (CT) evaluation is of paramount importance during the TAVR evaluation process, and may offer valuable information regarding detailed information on the risk factors for coronary obstruction, including, sinus of Valsalva width, coronary height, bulky calcium nodules and their distribution or excessively long leaflets, which may obstruct the coronary ostia.[14-16]

THE SELECTION OF VALVE TYPE AND SIZE TO LOWER THE RISK

Prosthesis type and sizing is part of the patient selection process, and allows the operator to prevent coronary obstruction. For example, although feasible, it can be technically challenging to re-cannulate the coronary arteries, especially in the case of self-expanding valves [CoreValve (Medtronic Inc.) or Venus-A valve (VENUS MEDTECH)] with a longer frame that extends above the coronary ostia.[17,18] In this regard, valves with larger stent cell sizes [Portico™ valve (Abbott Vascular)] may facilitate future access to the coronary orifices.[19] While there is no reliable way to control the TAVR valve commissural orientation in relation to the coronary ostia, nor is there an easy way to orient the valve to optimize future coronary access, the use of newer generation devices [Lotus Edge™ (Boston Scientific), Portico, Evolut™ R (Medtronic Inc.)], which are retrievable and more advantageous in high-risk coronary obstruction cases are highly recommended.[19-21] Theoretically, before final release of a partially deployed self-expanding valve, an aortogram can determine the commissural position and the coronary patency. However, in practice, it is not always possible to recapture the valve and move it to the descending aorta to reorient it before attempting deployment again. Hence, certain newer generation TAVR devices [ACURATE Neo™ (Boston Scientific), JenaValve™ (JenaValve), J-Valve (JC Medical)] are fixed in place by using a direct anchoring mechanism to either the calcified native leaflets or surgical valve leaflets, which would mitigate the risk of future valve tissue prolapse and coronary obstruction. Although experience with the use of these valves is relatively limited, the results have been encouraging.[22-25]

Another important factor to be taken into consideration is valve sizing. Since most of the currently approved TAVR valves use a radial force-dependent mechanism to fix the prosthesis in place, oversizing of some sort is recommended, even though radial force will not prevent the native aortic valve leaflets from prolapsing. The stent frames of the implanted TAVR valve and displaced valve tissues and calcium may partially obliterate the space between the expanded device and the coronary orifice, which may cause turbulent flow in the space and trigger fibrosis and/or persistent inflammation, leading to endothelialization and then obstruction of the coronary orifices over time.[14-16] In other words, too aggressive oversizing exceeding the upper limits of those recommended in the sizing charts of individual devices should be avoided in the selection of valve size.

PERIPROCEDURAL STRATEGY TO LOWER THE RISK

Many techniques that are usually applied to prevent ACO during TAVR should be carefully carried out. However, despite following state-of-the-art practices with caution, there is no easy way to prevent DCO. In the presence of risk factors for coronary obstruction, a pre-implant balloon valvuloplasty with simultaneous associated aortography may be useful to ensure the patency of the coronary ostia during balloon inflation. If the coronary ostium is occluded by the calcified cusps crushed against the wall of the sinuses of Valsalva when the balloon is fully inflated, several strategies should be considered: 1) terminating the procedure and considering other options; 2) implanting the prosthesis slightly

lower into the left ventricle outflow tract to reduce movement of the cusps towards the coronary ostia and the sinus walls; and 3) performing coronary protection.[14-17]

DCO can still occur, however, even if an ostial coronary stent is deployed during the index procedure. Of note, Jabbour et al. reported that DCO occurred in 27% of their patients in whom an ostial coronary stent was deployed to protect the left main ostium.[14] Another possible way to mitigate the risk of DCO is to use excessively protruding 'chimney' stents or stents with greater radial strength to prevent stent deformation from the native valve leaflets or transcatheter heart valve.[14-16] Performing a novel technique called the bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction for valve-in-valve procedures prior to TAVR insertion with the use of catheters to direct an electrified guidewire to traverse and lacerate through the centre of the aortic valve leaflet should also be considered.[14-16,26,27] The future development of a fully retrievable device even after deployment may be even more beneficial, since DCO is defined as occurring after a patient has left the operating room in a stable condition following a successful TAVR.

In terms of preventing coronary obstruction, the importance of implantation depth cannot be over-emphasized, since a significant proportion of DCO patients (n = 18; 47.4%) have been reported to have high implantation depths.[14] Consequently, to optimize future coronary re-access, implantation depth is a critical issue, especially if the ostial height is < 10 mm. For example, because the skirt height of the Evolut-PRO (Medtronic Inc.) is 13 mm, it is recommended to implant it at least 4 mm below the annular plane to ensure that the skirt is not overlaying the coronary artery.[17] The future development of devices designed to minimize the profile of the skirt is anticipated as this could potentially prevent DCO, since DCO has occurred with self-expanding valves due to prosthesis skirt obstruction.[28] Moreover, it would also be advantageous if the commissural tabs of self-expanding valves could be easily identified on fluoroscopy, and if a simple mechanism could be developed to align the prosthetic valve commissures with those of the native valve so as to optimize its placement in relation to the coronary arteries, although this is not available with current devices.[17]

Close cardiac monitoring of post-TAVR patients, especially during the early post-procedural phase, may enable effective complication management. The index of suspicion for late DCO cases is never high because their post-implant aortography or selective coronary arteriograms confirms a lack of obstruction, unless DCO is incidentally recognized during CT follow-up or when the patients become symptomatic. Accordingly, there needs to be a lower threshold for imaging the coronary system post-TAVR. For example, whenever the patients present with newly developed symptoms, especially in TAVR cases with most of the sinus obliterated, even though they may leave the operating theater after a successful procedure. Once it occurs, timely revascularization is the only effective bailout.[14-16]

STRATEGIES TO INCREASE THE ODDS OF RESCUING CORONARY OBSTRUCTION

In the series of Jabbour et al., percutaneous coronary intervention (PCI) was the most common management option, and the overall success rate was 74.3% for left main PCI and 60% for right coronary artery PCI, respectively.[14] If the patency of the coronary artery cannot be restored and the hemodynamics are poor, urgent or emergent CABG or mechanical hemodynamic support are required. If possible, the valve should immediately be snared (CoreValve), or removed from its anatomical position by using an oversized balloon (i.e. SAPIEN prosthesis) and pulled up, out, and into the ascending aorta to allow coronary perfusion to be re-established.[17] This highlights the need to be aware of this rare, life-threatening complication of TAVR, which requires a dedicated heart team involved not only in decision-making, but also in the procedure itself.

Thrombus embolization from a prosthetic valve or the obliteration of the space between the expanded device and the coronary orifice can be a cause of DCO. Under these circumstances, the use of oral anti-coagulant drugs after a successful TAVR may be required. As in people on anticoagulants for valve-thrombosis prevention, those anticoagulants may protect the sinus against filling with clots.[14-16] However, future large clinical trials are needed to verify this hypothesis.[29]

CONCLUSIONS

Before the indications of TAVR are extended to lower-risk and/or younger patients, the net risk-benefit ratio should be evaluated, especially as complications and mortality after TAVR continue to decrease. DCO is a relatively newly identified complication but is it is becoming increasingly important. Therefore, understanding this rare, but potentially lethal complication can help medical professionals to make the right decisions for their patients.

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CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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