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On site cardiac surgery for structural heart interventions: a fence to mend?

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Current evidence supports device-based transcatheter interventions for the management of patients with structural heart disease, proving well their safety and efficacy; transcatheter aortic valve implantation (TAVI), transcatheter edge-to-edge repair (TEER) of mitral or tricuspid valves, and left atrial appendage occlusion (LAAO) are expanding their role in contemporary practice. Currently, guidelines recommend performing TAVI in 'Heart Valve Center' with interventional cardiology and institutional on-site cardiac surgery (iOSCS), while no site limitation has been defined for TEER and LAAO. The growing number of candidates for transcatheter interventions generates long waiting times with negative consequences on mortality, morbidity, hospitalization, and functional deterioration. Therefore, a debate on the feasibility of TAVI in centres without iOSCS has been set up. Data from randomized controlled trials and registries failed to document any difference in outcomes and in conversion rate to emergent surgical bailout in centres with or without iOSCS; on the other hand, a direct relationship with TAVI complications has been clearly documented for learning curve and centre volume. Therefore, the role of iOSCS for TAVI, as well as for other transcatheter interventions, should be carefully explored.

Introduction

Transcatheter aortic valve implantation (TAVI), transcatheter edge-to-edge repair (TEER) of mitral or tricuspid valve, left atrial appendage occlusion (LAAO) are device-based transcatheter interventions for a wide range of structural heart diseases which are expanding their role in contemporary clinical practice due to a well-proven safety and efficacy. Previously restricted to patients with surgical contraindications or at very high risk, now these techniques are comparable or even superior to surgery in terms of short- and long-term outcomes even in intermediate risk patients. With the imminent expansion of TAVI indications, the number of candidates is growing and the rate of TAVI has increased exponentially.

Current European[1] and American[2] guidelines on valvular heart disease (VHD) recommend performing TAVI in 'Heart Valve Centers' with interventional cardiology and institutional on-site cardiac surgery (iOSCS) with 24 h/7-day services. In addition, a hybrid catheterization laboratory is desirable and multimodality imaging, education programmes, operator, diagnostic, and interventional imager training must be achieved.

European guidelines[1] endorse a structured collaborative multidisciplinary Heart Team (HT) composed by clinical and interventional cardiologists, cardiac surgeons, imaging specialists with expertise in interventional imaging, cardiovascular anaesthesiologists, meeting on a frequent basis and working with standard operating

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procedures. American guidelines[2] further define 'primary' centres, performing basic transcatheter and surgical procedures (transfemoral TAVI, percutaneous aortic valve balloon dilation, surgical aortic valve, and mitral valve replacement) and 'comprehensive' centres, fulfilling more complex strategies [TAVI by alternative accesses, paravalvular leak closures, TEER, valve-sparing, and aortic root enlargement, extensive use of mitral valve repair for both primary and secondary mitral regurgitation (MR)].

Therefore, TAVI in centres without iOSCS is not endorsed at present.

Though, the continuous growth of candidates to transcatheter interventions prompts an increase in waiting times with negative consequences on mortality, morbidity, repeated hospitalizations, and functional deterioration. Some reports have estimated that about 1–10% of candidates die while awaiting TAVI. Therefore, there is now a debate to expand TAVI and other transcatheter procedures to centres without iOSCS.

The topic of performing TAVI at sites without iOSCS can be compared with the previous debate on percutaneous coronary intervention (PCI), now fully legitimized in centres without iOSCS,[3] although it must be acknowledged that the diffusion of PCI has been related to the time-dependence treatment of acute coronary syndromes.

Transcatheter aortic valve implantation

Aortic stenosis (AS) is the most common valve disease in industrialized countries. Severe symptomatic AS is associated with poor short and mid-term prognosis if not treated. Until recently, surgical aortic valve replacement (SAVR) was the gold standard and TAVI was an option only for patients with prohibitive surgical risk and elderly people. In the last decade, randomized controlled trials demonstrated the non-inferiority and even superiority of TAVI compared with SAVR in high and intermediate surgical risk, with some evidences also in young low-risk patients, marking a new era in the treatment of AS.[4]

Need for emergent cardiac surgery

Despite advancement in technical equipment and operator's skills, TAVI still carries the risk for major postprocedural and intraoperative complications that may require emergent surgical bailout treatments, such as device malpositioning, or embolization, coronary artery occlusion, aortic dissection, annular rupture, pericardial tamponade, and vascular injury.

Pineda *et al.*[5] analysed data from the Society of Thoracic Surgeons/American College of Cardiology TVT Registry on 47 546 patients undergoing TAVI from 2011 to 2015, and documented a 1.2% rate of cardiac surgery bailout. The most frequent indications were valve dislodgment (22%), ventricular rupture (20%), aortic valve annular rupture (14%), aortic dissection (8%), and coronary occlusion (6%). A complication needing surgical bailout has a tremendous clinical relevance, as all-cause in-hospital mortality in patients undergoing emergent surgery were extremely high (49.6%), significantly different from those who did not need surgical conversion (3.5%; $P < 0.0001$).

Learning curve and centre volume

Transcatheter aortic valve implantation learning curve is associated with better outcomes and a significant reduction in the need for surgical bailout.

Wassef *et al.*,[6] collecting data of more than 3400 patients from 16 centres, chronologically ordered all cases per centre into initial (1–75), early (76–150), intermediate (151–225), high (226–300), and very high (>300) experience institutions for TAVI learning curve characterization. In addition, participating institutions, were stratified by annual TAVI case volume into low-volume (<50), moderate-volume (50–100), and high-volume (>100) groups. A progressive improvement in clinical outcomes with lower major adverse events was associated with increasing TAVI experience. In fact, on multivariate analysis, 30-day-mortality was significantly higher for initial [9.6%, odds ratio (OR): 3.83; 95% confidence interval (CI): 1.93–7.60], early (7.9%, OR: 2.41; 95% CI: 1.51–5.03), and intermediate (5.8%, OR: 2.53; 95% CI: 1.19–5.40) experience groups when compared with the very high experience centres (3.3%). In addition, the early safety endpoint, defined as the composite of death, stroke, major bleeding, vascular complications, surgical conversion, and renal failure, was significantly worse for all the groups when compared with the very high experienced group (from 27.5% for the initial experience to 14.9% for the very high-experienced group; $P < 0.001$). Of note, these data were driven mostly by reduction of major bleeding and major vascular complications.

In the analysis by annual volume, low-volume TAVI institutions had significantly higher 30-day all-cause mortality compared with the moderate- and high-volume groups (8.8% in low-volume group vs. 3.9% in high-volume group; $P = 0.003$). The same results have been showed also in early safety endpoint and major bleeding. A number of 225 overall TAVI procedures per operator was identified as a threshold beyond which 30-day mortality significantly reduces. Notably, early safety endpoint continues to improve even beyond this threshold.

Moreover, data from TRITAVI Registry[7] supported the direct correlation between the red blood cell transfusion after TAVI and increased mortality and early acute kidney injury; in agreement with the significant reduction of TAVI complications with operator's experience and centre volume, also blood derivates were less frequently used in in higher-volume centres and more experienced operators.

'Without on-site surgery' experiences

In the last 10 years, a few reports on TAVI performed in centres without iOSCS have appeared in the literature.

In the absence of iOSCS, the two adopted options are represented by a visiting surgical team for back-up during intervention or an external facility with cardiac surgery onsite (*Figure 1*).

The AQUA Registry[8] analysed the 2013–14 datasets of TAVI and SAVR procedures performed in Germany and

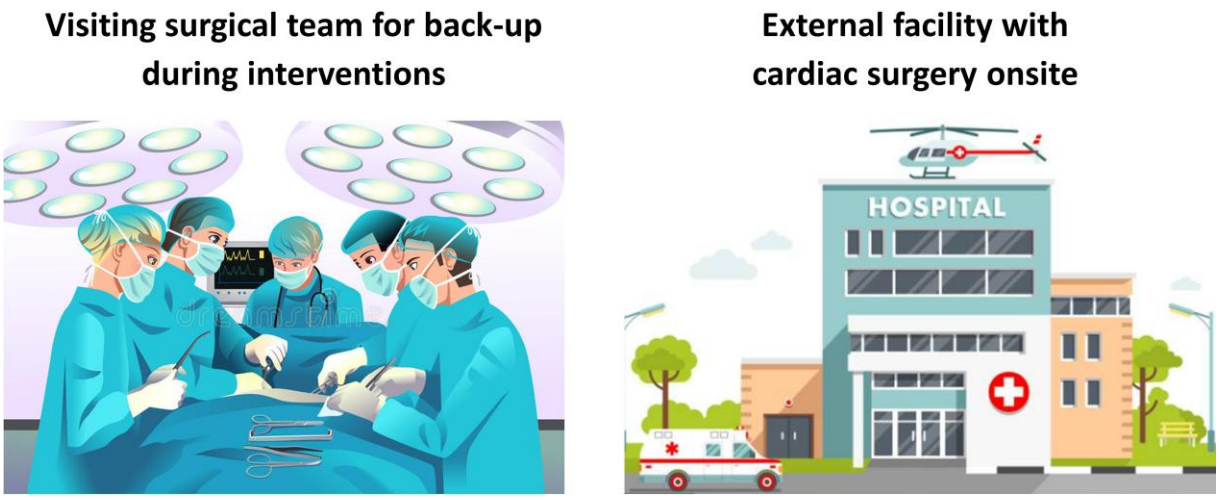

Figure 1 In the absence of institutional on-site cardiac surgery, the two currently adopted options are either a visiting surgical team for back-up during intervention or an external facility with cardiac surgery onsite.

showed that intraprocedural complications requiring emergency cardiac surgery occurred in 3.4% of patients undergoing TAVI at no-iOSCS hospitals and in 3.9% in iOSCS hospitals (P = NS); conversion to surgery at no-iOSCS was similar to the iOSCS group (13.0 vs. 16.5%; P = NS) and in-hospital mortality of patients who underwent a surgical conversion was 50% in no-iOSCS and 62% in iOSCS hospitals (P = NS).

In Spain an observational TAVI registry analysed safety and feasibility of TAVI at 10 no-iOSCS centres with a reference cardiac and vascular surgery institution <90 km away.[9] In the 384 cases included, technical success was high (96%), and conversion to open-heart surgery was required in only one case (0.3%), due to left ventricle perforation. Other major periprocedural complications, such as coronary obstruction (0.8%), cardiac tamponade (1.6%), valve malposition (1.6%), were solved without the need of surgical bailout. In-hospital and 1-year mortality were 2.1 and 12.2%, respectively.

In an analysis of the Austrian TAVI registry,[10] 1822 patients from nine centres performing TAVI were evaluated from 2011 to 2016. Of these, 15.9% of cases underwent TAVI at three no-iOSCS centres, whereas the others were treated in six iOSCS centres. The no-iOSCS group had a higher perioperative risk (EuroSCORE 20.9 vs. 14.2%; $P < 0.001$) compared with the iOSCS group; procedural survival was 96.9% in no-iOSCS centres and 98.6% in iOSCS centres ($P = 0.034$), 30-day survival was 93.1 vs. 96.0% ($P = 0.039$) and 1-year survival was 80.9 vs. 86.1% ($P = 0.017$), respectively. After propensity score matching, these differences disappeared, thus suggesting that the worse outcomes in no-iOSCS centres were mostly driven by the higher baseline risk profile of the treated patients. However, the relative small sample size and the low rate of severe complications might have obscured differences in outcome that would have been significant in a larger patient population.

Despite such promising clues from 'without iOSCS' experiences, it must be acknowledged that complications proportionally decrease with growing operator's experience, thus promoting an expansion of TAVI to 'peripheral' centres unable to guarantee high annual procedural volumes of procedures may be a double-edged sword.

Transcatheter edge-to-edge repair

MitraClip is the leading transcatheter mitral valve repair technique with over 110.000 devices implanted worldwide, since its introduction in 2003.[11]

The latest European VHD guidelines[1] recommend mitral TEER as the first-line option when compared with surgical replacement for the treatment of symptomatic patients with secondary MR under optimal guideline-directed treatment of heart failure, provided an acceptable left ventricular function. For primary MR, TEER may be considered in symptomatic patients who fulfil the echocardiographic criteria of eligibility, deemed inoperable, or at high surgical risk by the HT, provided the procedure is not considered futile.

Unlike TAVI, European guidelines[1] do not mention the necessity to perform TEER with iOSCS, while a detailed multidisciplinary HT evaluation is strongly recommended; in contrast, American guidelines[2] suggest performing TEER in 'comprehensive' centres such as other more complex procedures.

Multiple randomized, controlled trials and retrospective registries confirmed the low complication rate with high procedural performance for MitraClip therapy; moreover, the major adverse periprocedural event rate decreased over time from 15% in 2005 to <3.5% in 2020, and in-hospital mortality had the same trend.[12]

MitraClip complications can be considered as procedural- or device-related. Among the first, pericardial effusion, and cardiac tamponade are rare complications (0-0.5%) with a downwards trend over the years; the rate of persistent atrial septal defect is 57, 50, and 25% after 1, 6, and 12 months post-procedure with data suggesting a frequent spontaneous closure. Device-related

complications such as clip embolization (0.7%) after complete detachment of both leaflets, and leaflet injury/chordal rupture during grasping (0–2%) are rare.

Accordingly, TEER can be considered a safe procedure, but major complications, although rare, increase dramatically the morbidity and the mortality.

Isogai *et al.*[13] retrospectively identified patients who underwent TEER from 2014 to 2017, reporting a surgical bailout rate of about 1.4%, which was in turn associated with a high in-hospital mortality; such incidence progressively decreased during the 4 years of observation (from 5.26% in 2014 to 0.43% in 2017) and was higher in lower-volume hospitals.

Therefore, it seems plausible to expand TEER procedures also to non-primary centres, even if such experiences in the literature have not been systematically reported. However, in order to reduce complications and avoid the surgical bailout, physicians must be aware of these adverse events and their risk factors and be familiar with their preventive strategies and treatment options. Randomized clinical trials comparing outcomes of TEER in iOSCS and no-iOSCS centres should be welcomed, although barely feasible.

Left atrial appendage occlusion

Poor data available on LAAO experiences demonstrated the rarity of major procedural complications but at the same time a clear association was documented with major morbidity and mortality. Death, stroke, device embolization, and cardiac tamponade are the possible LAAO complications and surely pericardial effusion is the most important one.[14]

In PROTECT AF-trial, the first landmark LAA closure study using the Watchman device, pericardial effusion requiring intervention was reported in 4.3% and steadily declined to 1.9%.[15] In the most recently published Amulet Post-marketing Registry, the incidence of cardiac tamponade was 1.2%. Most pericardial effusions occur early, 89% within 24 h of the procedure and are related to procedural mishaps. Although we believe that LAAO should be performed in centres with on-site cardiac or, in its absence, at least a thoracic surgical backup, emergency pericardiocentesis is generally resolutive. Early recognition of pericardial effusion, prompt haemodynamic resuscitation and percutaneous drainage can be sufficient.

Device embolization remains one of the most feared complications of the LAAO procedure, with incidence ranging from 0.2 to 0.8% in leading trials and main registries. Recent data from Watchman clinical trials and registries reported an average incidence of 0.25%. A systematic review showed that most of device embolizations were acute (69%), and localized in the left ventricular (43%), aorta (43%) and in the left atrium (14%). Instead, about 31% of device embolizations were detected later (1–7 months), but probably here several early embolizations were missed. The embolized devices are often clinically silent and, similarly to pericardial effusion, do not require ECS.

Moreover, likewise TAVI and TEER, a decline in the incidence of LAAO-related complications over time was associated with improved operators' skills.

Therefore with stringent guidelines on operator training, competency requirements and procedural-technical refinements, LAAO seems to be performed safely with low complication rates also in no-iOSCS centres.

Conclusions

Several TAVI registries have shown similar outcomes including surgical bailout requirement and in-hospital mortality, in iOSCS and no-iOSCS centres. However, complications proportionally decrease with growing operators' experience and in high annual-volume centres, therefore legitimizing TAVI in no-iOSCS centres can turn over a double-edged sword.

Although TAVI can be potentially performed in no-iOSCS centres, likewise mitral TEER and LAAO, questions remain at what price and to what end; the appropriate balance to allow access of this growing population to these treatments remains a matter of debate.

Conflict of interest: None declared.

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