Screening, complications and outcome of aortic valve implantation
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Chapter 10

Discussion
Patients with symptomatic aortic valve stenosis have an increased mortality and morbidity risk. Current guidelines include TAVI as the preferred treatment for inoperable patients and as a good, less invasive, alternative for surgical aortic valve replacement in patients with high to intermediate surgical risk (1). However, the majority of the TAVI population is still typically old and frail. For this population, all examinations prior to the procedure are cumbersome. Ideally, the entire TAVI work-up would take place within one day. The results of the study in Chapter 2 help us in this respect as we demonstrated that for patients with an impaired renal function, hydration before and after the computed tomography angiography (CTA) could be decreased from 24-hours to only 1-hour hydration prior to the scan. By incorporating the short hydration protocol in the clinical workflow, flexible planning of CTA in an outpatient setting will reduce hospital admission days without compromising patient’s safety. With current technological advances of CTA, there is a trend of decreasing necessary volumes of contrast agents (2). It is conceivable that with lower doses of contrast volume, risks for kidney injury after CTA will further diminish. Moreover, very recently the Radiological Society of the Netherlands, agreed on a new guideline, only advising hydration for CTA in patient with an estimated glomular filtration rate (eGFR) <30 ml/min/1.73m2) (3). Because the majority of TAVI patients have an eGFR ≥ 30 ml/min/1.73m2, implementation of the new guideline will further reduce the burden of TAVI work-up. Future randomized studies with low-volume intravenous contrast CTA are needed to verify if intravenous hydration is still necessary at all.

CTA could be the corner stone to further reduce the burden of TAVI work-up. It has the potential to evaluate presence of coronary artery disease. Use of CTA for this purpose could reduce the number of coronary angiographies, decreasing the contrast dose administered in TAVI work-up. Moreover, CTA could play a larger role in patient selection. Current imaging techniques allow evaluation of cardiac function and left ventricular hypertrophy. As we demonstrated in Chapter 3, the discussion on incidental findings on CTA has just started. The potentially malignant incidental findings are very common in the TAVI population and frequently pose a TAVI team for dilemmas. We demonstrated that patients with an incidental finding have a worse prognosis than patients without such a finding. Future studies are mandatory to analyze if there are specific findings that influence short- and long-term outcome. It should be evaluated if the incidental findings themselves cause the increased mortality rate, or if an incidental finding should be considered as a sign of a patient’s poor general health. This last hypothesis is reasonable, as we have shown a variety of causes of death besides malignancy in the patients with incidental findings. Moreover, future studies should also focus on the burden of incidental findings because repeated testing and possible overtreatment of the findings remain a concern.
For a patient, good counseling is crucial to make a well-informed choice about the wish to undergo TAVI. In this counseling, information on the expected outcome is essential. Major complications including thromboembolic- and vascular complications should be discussed. As demonstrated in our case series in Chapter 4, the impact of a thromboembolic event varies greatly. Regarding the cause of stroke, we illustrated that manipulation of the aortic valve and vessel wall may cause embolization. In addition, the prosthesis implantation itself may induce platelet aggregation, activating of coagulation pathways, ultimately leading to thromboembolic events during or shortly after TAVI. Moreover, it is suggested that valve thrombosis plays a role in development of thromboembolic events. But although valve thrombosis is frequently seen at post-procedural CTA, recent studies do not report a significantly increased risk for stroke in those patients with valve thrombosis (4). Nevertheless, the risk of transient ischemic attacks (TIA) may be increased but it is unknown whether this association is causal or whether it is a reflection of the patient’s status (4). Histopathological analysis of thrombectomy material can be the key in detecting the causes of stroke after TAVI and should be performed more frequently to identify potential risk factors. Data on what constitutes the best perioperative preventive management are scarce. Both pharmacotherapeutic and mechanical preventive strategies have been suggested to reduce stroke incidence. Trials suggest that single antiplatelet therapy is just as effective as dual antiplatelet therapy. However, introduction of this single therapy as a clinical standard will not decrease stroke incidence more than dual therapy does. Also mechanical protection with embolic protection devices has still not proven to reduce the stroke risk or mortality (5). Consequently we are still waiting for the Holy Grail for perioperative stroke prevention. While awaiting this development, there is an increasing availability of mechanical thrombectomy, with proven clinical benefits if performed within 6 hours after symptom onset (6). Considering the high risk of stroke related to TAVI, in-hospital cerebral thrombectomy service should be available to perform this procedure. In Chapter 5, we show that vascular complications have not yet been diminished with the latest generation balloon-expandable SAPIEN 3 (Edwards Lifesciences, Irvine, California, USA). We did find a relative low incidence for major vascular complications as compared to older generation prostheses. Nevertheless, major vascular complications were associated with an increased 30-day mortality risk, indicating that it is important to reduce the incidence of major vascular complications. Hopefully in the near future, refinements of prosthesis, using smaller devices, will do so. As part of the clinical routine, early surveillance of the access site and quick anticipation on possible complications are pivotal for the outcome, for example by using an endovascular stent. A recent study has demonstrated using such a stent may lead to a good clinical
outcome (7). Of course, the possible use of a stent should be included when informing a patient about the TAVI procedure. Moreover studies should evaluate if there are no long-term effects of the stent on peripheral arterial patency, especially if the stent is used in patients with lower surgical risk and thus an expected longer survival.

The function of the prosthesis plays an important role in the clinical outcome. In Chapter 6 the hemodynamic performance of stented and stentless surgical implanted prostheses were evaluated one year after surgery by using 4D flow magnetic resonance imaging (MRI). Obstructed blood flow over the prosthesis may lead to worse long-term outcome and potentially the need for re-intervention. We assume ideally that a prosthesis should provide unobstructed central laminar blood flow comparable to the native aortic valve, without substantial energy loss and shear stress on the aortic wall. Although this performance was best resembled by stentless prostheses, we found in our study that both prostheses remained associated with some degree of obstruction. To achieve a hemodynamic performance that is comparable to that of the native aortic valve, there is still a long way to go in the further development and improvement of aortic valve bioprostheses. The new 4D flow MRI technique could also be used to evaluate TAVI prostheses and to compare them with surgical prostheses. The use of this technique can be helpful, but it is noteworthy that currently, longitudinal follow-up data of 4D flow MRI parameters are missing. Future studies are necessary to acquire comprehensive advanced baseline MRI data with long-term follow-up of enrolled patients. Ideally, 4D flow MRI will be combined with sequences for tissue characterization and clinical outcome of different aortic valve prostheses to determine prognostic parameters for individual outcome and patient specific risk stratification. Refinements of existing prostheses have been made to improve its function.

Adjustments of the balloon-expandable SAPIEN prosthesis resulted in the SAPIEN XT and then in the SAPIEN 3 (Edwards Lifescience, Irvine, CA, USA). In Chapter 7 we demonstrated favorable procedural and mid-term outcomes of the SAPIEN 3 as compared to the SAPIEN XT in patients who underwent transfemoral TAVI with low to intermediate surgical risk. This included a higher device success, less paravalvular leakage and less major bleeding complications, but we did not show a significant difference in 3-year survival between the prostheses. However, it is conceivable that less severe paravalvular leakage as a consequence of using the SAPIEN 3 will positively influence long-term clinical outcome. In Chapter 8, we described the evolution of TAVI care in our hospital, and it’s positive effect on clinical outcome. From 2009 onwards, we described a clear shift towards a lower-risk TAVI population and improved clinical outcome, including more symptom
relief and lower complication rates. Along with the shift in the eligible population, there has been a remarkable evolution in the procedure itself, including the use of CTA imaging for optimal sizing of the prosthesis, a reduction in delivery sheath size and the move to a minimalist approach under local anesthesia. Mortality after TAVI declined impressively, mainly as a consequence of improved 30-day clinical outcome. The decline in mortality rates was not only a consequence of treatment of a lower risk population but was, most likely, also influenced by the increased operator and center experience combined with procedure- and device-related changes. To further improve clinical outcome, it is important to analyze the pathophysiology of periprocedural complications. In Chapter 9, we used autopsy for this purpose and found that per time interval after TAVI there were differences in the causes of death. Moreover we found that there were large discrepancies between the clinical diagnosis and cause of death at autopsy, which underscores the significance of autopsy. Autopsy should be considered a helpful instrument to assess the results after TAVI and to evaluate necessary technical refinements in order to improve short and long term outcome after TAVI.

The focus of this thesis is mainly on clinical outcome, but for patients it is important that survival after TAVI also yields in a good quality of life. Ideally a risk score for potential TAVI candidates will provide a more accurate prediction of expected morbidity and mortality, which could help in patient selection. Furthermore, although there is increasing evidence for the short-term safety of TAVI, more information on long-term outcomes and valve durability is required. To reach long-term valve durability, valve sizing and positioning must be optimal. Against this background, there are an increasing number of TAVI devices coming on the market besides the standard self-expandable and balloon-expandable prostheses (8). Nevertheless, there are only small trials evaluating prostheses quality (9). Large randomized trials should answer to the question which prosthesis is preferable for which patients and to evaluate which patients benefit from the procedure at all. Although 5-year outcomes look promising, long term, 10-years and 20-years results of TAVI are eagerly awaited (10,11). Presumably, future improvements will result in a further expansion of clinical indications for TAVI and eventually it may even replace surgical valve replacement for most indications.
REFERENCES


