The handle http://hdl.handle.net/1887/28521 holds various files of this Leiden University dissertation

**Author:** Katsanos, Spyridon
**Title:** Outcomes of transcatheter aortic valve implantation
**Issue Date:** 2014-09-04
Chapter 1

General introduction and outline of the thesis
Degenerative severe aortic valve stenosis is a frequent valvular disease affecting 3% of patients aged >75 years and its prevalence is expected to increase. (1) Elderly patients with symptomatic severe aortic stenosis have poor outcome if medically treated, whereas surgical aortic valve replacement reduces the 1-year mortality rates significantly. (2,3) However, at least 30% of symptomatic severe aortic stenosis patients are considered of excessive surgical risk and are not referred to or are denied for surgical treatment. (4) Balloon aortic valvulotomy is associated with limited clinical improvement, does not show any prognostic improvement and is associated with high rate of recurrence of aortic stenosis (80% at 1 year follow up). (5,6) Transcatheter aortic valve implantation (TAVI) has been an important therapeutic breakthrough for patients with symptomatic severe aortic stenosis and contraindications for surgical aortic valve replacement.

The first-in-human TAVI was successfully performed in 2002, in a critically ill patient with severe aortic stenosis in whom previous balloon valvulotomy had failed. (7) The prosthesis device and implantation technique were further developed and the results of the cohort B Placement of Aortic TranScatheterER Valves (PARTNER) trial demonstrated that TAVI is a safe and effective treatment for patients with symptomatic severe aortic stenosis and contraindications for surgery, improving the outcome of these patients compared with patients who were conventionally treated (medically or with balloon aortic valvulotomy): 1 year mortality 30.7% vs. 50.7%, respectively. (8) Subsequently, the Food and Drug Administration approved TAVI as an alternative to surgical aortic valve replacement for non-operable patients. The results of the cohort A PARTNER trial, randomizing patients with severe aortic stenosis and high operative risk to TAVI or surgical aortic valve replacement demonstrated that TAVI was also safe in this subgroup of patients and led to comparable outcomes at follow-up (1-year mortality: 24.2% with TAVI vs. 26.8% with surgical treatment). (9) The results of these randomized trials and the numerous national registries have established TAVI as a safe and feasible alternative for patients with symptomatic severe aortic stenosis who are non-surgical candidates or have high surgical risk. Furthermore, TAVI is currently included in the 2012 European Society of Cardiology guidelines for the management of patients with symptomatic severe aortic stenosis and contraindications or high-risk for surgery, with class IB and IIa B indications, respectively. (10)

However, TAVI is also associated with complications. The rate of stroke was higher in the group of patients treated with TAVI compared with surgically treated group. (8,11) Moreover paravalvular aortic regurgitation (AR) was more frequently observed in TAVI compared to surgically treated patients, having important prognostic implications since moderate and severe paravalvular AR were related to increased mortality at follow-up. (11) Patients treated with TAVI also showed a higher rate of new conduction abnormalities.
A number of additional complications of this relatively new procedure that may affect the clinical course of patients were also acknowledged: perioperative myocardial infarction, acute kidney injury, pericardial effusion, vascular and bleeding complications.

The patient characteristics are one of the main determinants of the risk of procedural complications. The rate of the observed complications may also differ between trans-

<table>
<thead>
<tr>
<th>Device-Company</th>
<th>Expansion mechanism</th>
<th>Valve material</th>
<th>Stent material</th>
<th>Repositionable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapien Edwards</td>
<td>Balloon-expandable</td>
<td>Bovine pericardium</td>
<td>Cobalt Chromium</td>
<td>No</td>
</tr>
<tr>
<td>CoreValve ReValving system Medtronic</td>
<td>Self-expandable</td>
<td>Porcine Pericardium</td>
<td>Nitinol</td>
<td>No</td>
</tr>
<tr>
<td>Portico</td>
<td>Self-expandable</td>
<td>Bovine pericardium</td>
<td>Nitinol</td>
<td>No</td>
</tr>
<tr>
<td>CoreValve Evolut R</td>
<td>Self-expandable</td>
<td>Bovine Pericardium</td>
<td>Nitinol</td>
<td>No</td>
</tr>
<tr>
<td>Sapien III</td>
<td>Balloon-expandable</td>
<td>Pericardium</td>
<td>Cobalt Chromium</td>
<td>Yes</td>
</tr>
<tr>
<td>Direct Flow Direct Flow Medical</td>
<td>Polymer-injected</td>
<td>Equine pericardium</td>
<td>Polymer</td>
<td>Yes</td>
</tr>
<tr>
<td>JenaValve JenaValve Technology</td>
<td>Self-expandable</td>
<td>Pericardium</td>
<td>Nitinol</td>
<td>Yes</td>
</tr>
<tr>
<td>Lotus Sadra Medical</td>
<td>Self-expandable</td>
<td>Bovine pericardium</td>
<td>Nitinol</td>
<td>Yes</td>
</tr>
</tbody>
</table>
catheter aortic valve manufacturers. Currently, the balloon-expandable Edwards SAPIEN (Edwards SAPIEN or SAPIEN XT, Edwards Lifescience, Irvine, CA) and the self-expandable CoreValve (CoreValve system, Medtronic, Minneapolis, MN) are widely commercially available although a plethora of new designs have been clinically studied (Table 1). (14)

The Edwards SAPIEN valve can be implanted both through transfemoral and transapical access whereas the CoreValve system is implanted mainly through transarterial access (transfemoral, transsubclavian, transaxillary or direct transaortic). The design of the frames has undergone several modifications in order to optimize its deployment in the aortic root and avoid related complications. The optimal recommended deployment of the frame is not easy to achieve and a shallow or deep implantation of the valve in the left ventricular outflow tract may be observed, which may increase the risk of acute coronary ostia occlusion, paravalvular regurgitation or prosthesis migration. (15) In addition, it is acknowledged that some complications may be expected more frequently in specific transcatheter valve designs. For example, in patients treated with the CoreValve device, pacemaker implantation is more frequent compared with patients treated with the Edwards SAPIEN valve. (14)

It is becoming apparent that in order to optimize the management of TAVI candidates there should be an emphasis on careful selection of patients that will benefit most from this procedure, in combination with an effort to minimize procedural complications that influence their post-operative clinical course. Consequently, understanding the pathophysiology of TAVI complications and defining the outcome of specific high risk groups may be of clinical importance.

**EMERGING ROLE OF MULTI-DETECTOR ROW COMPUTED TOMOGRAPHY TO PREDICT OUTCOMES IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE IMPLANTATION**

Multi-detector row computed tomography (MDCT) is an important imaging technique to evaluate patients with symptomatic severe aortic stenosis who are candidates for TAVI. The superb spatial resolution of this imaging technique permits accurate sizing of the aortic annulus, key to select the most appropriate transcatheter valve size. Studies have shown that the choice of valve size based on MDCT measurements, as opposed to echocardiography or angiography measurements, has led to less postoperative paravalvular AR and therefore MDCT is emerging as the “gold standard” method for valve sizing in patients undergoing TAVI (Figure 1). (16)

MDCT is also used to assess dimensions of various components of the aortic root such as the height of the coronary ostia relative to the aortic annulus, and moreover it can be used to clarify the size and morphology of the peripheral arteries (ilio-femoral arterial
system), assisting the decision for the appropriate the procedural access (transfemoral, transarterial or transapical) (Figure 1).(17)

The use of post-operative MDCT has also shed light into many procedural related complications in TAVI patients. Optimal expansion of the frames has been evaluated with MDCT and interestingly under-expanded frames may be found in 8% of patients which has been related with significant paravalvular AR and prosthesis migration.(18) The pathophysiology of paravalvular AR has also been investigated with post-operative MDCT.(17) Moreover, post-operative MDCT studies have shown that deep implantation of the frame in the left ventricular outflow tract may be responsible for new conduction disorders after TAVI.(19) In a few patients with perioperative coronary ostia occlusion successfully treated with immediate percutaneous coronary artery intervention MDCT has also revealed the possibility of direct impingement of the coronary ostia by the frame.(20)
In real-world clinical practice, patients with symptomatic severe aortic stenosis that do not strictly fulfil the inclusion criteria of PARTNER trial (cohort A and B) may receive a so-called “off-label” treatment with TAVI. These patients are deemed at excessive surgical risk and TAVI may be a last resource treatment.

Indeed, TAVI may be a successful alternative treatment, with acceptable rate of in-hospital and long-term mortality rates, in patients with pure native aortic valve regurgitation deemed inoperable.(21) Moreover, patients with concomitant severe aortic stenosis and severe mitral regurgitation may receive TAVI treatment, although generally these cases were excluded from large randomized trials.(22) TAVI may reduce concomitant mitral regurgitation in this group. However, it remains unclear how to identify the patients that will show an improvement in mitral regurgitation after TAVI.(22)

Registries have also shown low complication rates and acceptable survival for high-risk patients with failing bioprostheses treated with transcatheter valve-in-valve.(23) However, so far there has not been a direct comparison with a similar group of high-risk patients undergoing surgical treatment (Figure 2).

**Figure 2.** Transcatheter aortic valve implantation may have an “off-label” use for failing bioprosthetic valves. Successful implantation of a 23 mm Edwards SAPIEN valve in a failing 23 mm Carpentier Edwards PERIMOUNT aortic bioprosthesis.

**OBJECTIVES AND OUTLINE OF THE THESIS**

The objective of this thesis was to investigate the role of MDCT to predict outcomes in patients undergoing TAVI and also to focus on the outcome of specific populations undergoing this procedure.

In part I, the role of MDCT to predict the occurrence of procedural complications will be evaluated, focusing on the combination of pre- and post-procedural MDCT for the definition of the underlying mechanisms of complications such as paravalvular regurgitation (Chapter 2) or new onset rhythm conduction disturbances (Chapter 3). Addition-
ally, the deployment of the frame in relation to the coronary ostia will be systematically studied with post-operative MDCT and its implications for percutaneous coronary interventions at follow-up will be carefully addressed (Chapter 4). The combination of pre- and post-procedural MDCT images in addition to echocardiography measurements may also help us better identify the prevalence of late pericardial effusion in patients treated with TAVI (Chapter 5). Patients undergoing transfemoral TAVI do not experience pleuro-pericardial surgical trauma and they are expected to develop less frequently late pericardial effusion as compared with patients treated with transapical TAVI.

In part II the outcomes of specific populations undergoing TAVI will be studied. The predictive value of valvuloarterial impedance (ZVa) will be tested in patients undergoing TAVI (chapter 6). Ideally high baseline ZVa values would help us to identify a subgroup of patients with poor outcome, and this measurement could be included in future TAVI risk scores. Patients with more than mild mitral regurgitation represent also a special subgroup of interest (Chapter 7). There are few studies investigating predictors of mitral regurgitation improvement post-TAVI and they are based only in semiquantitative methods for grading mitral regurgitation severity. Patients with significant baseline mitral regurgitation will be followed up to 12 months after the procedure. Quantitative measurements of baseline mitral regurgitation severity will be evaluated for their ability to predict post-operative mitral regurgitation improvement. Finally, the subgroup of patients with failing bioprostheses treated with TAVI will be investigated (Chapter 8). The long-term survival of these patients will be compared with the survival of patients with similar surgical risk undergoing valvular redo surgery.
REFERENCES


