Transcatheter aortic valve implantation (TAVI) has replaced surgical aortic valve replacement (SAVR) as a therapy for symptomatic severe aortic stenosis in high risk and elderly patients. Before the TAVI-era, patients considered inoperable due to their medical co-morbidities or high age were referred to conservative medical treatment associated with poor short term survival.
Since Cribier et al. performed the first TAVI in 2002, this method has been improved over the last decade and is performed at continuously increasing institutions all over the world.\textsuperscript{4,5} According to a position statement of the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), patients should be evaluated for TAVI or SAVR by a multidisciplinary “heart team” consisting of interventional cardiologists and heart surgeons regarding anatomical feasibility and individual risk profile.\textsuperscript{6} As a tool used for risk stratification in Europe over the last years the “European System for Cardiac Operative Risk Evaluation” logistic EuroSCORE (LES) was established and implementation of TAVI in patients with a LES of 20% or higher is recommended.\textsuperscript{7} Considering a careful patient selection, fewer patients at higher risk should have been treated with SAVR after the introduction of TAVI.

Therefore, the aim of this retrospective single-center study was to compare risk profile, age and outcome of patients with symptomatic severe aortic stenosis undergoing SAVR before and after the inception of TAVI at our institution.

Patients and Methods

The TAVI-program at our center started in 2009. Two years before the introduction of TAVI (2007–2008) and two years after (2010–2011), 357 patients with isolated symptomatic severe aortic stenosis were scheduled for primary isolated SAVR. Meanwhile 135 patients were treated with TAVI in the first two years of our program. Indications for operation were aortic valve area $<1$ cm$^2$ or mean pressure greater than 40 mmHg. Patients with acute endocarditis, under 18 years of age, with surgery on the ascending aorta or any additional cardiac procedure and reoperations were excluded.

Data were divided into two groups considering the years 2007–2008 as group I (n = 191) and the years 2010-2011 as group II (n = 166). We determined patient’s age and gender; LES were calculated retrospectively to estimate expected mortality risk. Follow-up data from our external quality assurance program and internal hospital database were used to calculate observed survival in this study. Data acquisition, definition and statistical analyses were accomplished according to the current guidelines for reporting mortality and morbidity after cardiac valve intervention.\textsuperscript{8}

After patients provided written informed consent, surgery was performed via complete or partial median sternotomy under general anesthesia, normothermic cardiopulmonary bypass and direct aortic clamping using intermittent antegrade warm blood cardioplegia. Mechanical and biological xenograft valve replacements as well as Ross-Procedures were performed.

Statistical Analysis

Data were analyzed using SPSS, version 19.0 (SPSS Inc., Chicago, Illinois, USA). We reported descriptive statistics as means ± standard deviation for continuous data; categorical variables were expressed as frequencies and percentage. Continuous data were tested for normal distribution using the Kolmogorov–Smirnov test. Not normally distributed data were analyzed using Mann-Whitney U test to determine possible associations across variables. Categorical variables were compared using Chi-squared and Fisher’s exact tests. Observed mortality was determined and compared after a time period of thirty days for all patients. In addition, survival rates were calculated in a time-related manner using Kaplan-Meier method including log rank comparison of survival curves. Odds ratios were determined to evaluate variables age and gender as independent risk factors for survival. All tests were two sided. Statistical significance was set at a $p$-value of value of $<0.05$

Results

Risk profiles

Our total sample consisted of 357 patients (44% female; age 70.8 ± 10.0 years; LES 8.6 ± 10.3%). As shown in Table 1 we found that patients undergoing SAVR at our institution after the inception of TAVI were significantly younger than before (p = 0.01). Comparing expected mortality risk represented through LES patients in group II also showed a statistical trend to lower risk profiles (p = 0.07).

Table 1 further provides a comparison of gender specific age and risk profiles between both study groups. The fact that men scheduled for SAVR (compared to women) are younger (group I: p <0.001; group II: p = 0.007) and had lower LES counts (group I: p <0.001; group II: p <0.001) remained similar before and after the introduction of TAVI. Women’s age and LES, however, decreased significantly after the introduction of TAVI (age: p = 0.004; LES: p = 0.04). Female gender in the SAVR patient population was reduced by 7% after the inception of TAVI, which was not statistically significant (p = 0.2).
Table 1 Preoperative demographics

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall, n (%)</td>
<td>191 (54)</td>
<td>166 (46)</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>90 (47)</td>
<td>67 (40)</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>101 (53)</td>
<td>99 (60)</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>71.9 ± 10.6 (34–92)</td>
<td>69.5 ± 9.2 (39–87)</td>
<td>0.01</td>
</tr>
<tr>
<td>Female</td>
<td>75.6 ± 8.5 (55–88)</td>
<td>71.6 ± 9.0 (44–87)</td>
<td>0.004</td>
</tr>
<tr>
<td>Male</td>
<td>68.6 ± 11.2 (34–92)</td>
<td>68.1 ± 9.0 (39–86)</td>
<td>0.6</td>
</tr>
<tr>
<td>Logistic EuroSCORE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>9.8 ± 12.3 (1.5–92.5)</td>
<td>7.2 ± 7.2 (1.5–67.1)</td>
<td>0.07</td>
</tr>
<tr>
<td>Female</td>
<td>13.9 ± 15.9 (2.1–92.5)</td>
<td>9.6 ± 9.9 (2.1–67.1)</td>
<td>0.04</td>
</tr>
<tr>
<td>Male</td>
<td>6.1 ± 5.8 (1.5–39.8)</td>
<td>5.6 ± 4.1 (1.5–19.0)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation (range) unless otherwise specified. Group I indicates patients of years 2007–2008; Group II indicates patients of years 2010–2011.

Table 2 Operative data

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Group I</th>
<th>Group II</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologic SAVR, n (%)</td>
<td>186 (97)</td>
<td>159 (96)</td>
<td>345 (97)</td>
</tr>
<tr>
<td>Sorin Freedom Solo®, n (%)</td>
<td>71 (37)</td>
<td>63 (38)</td>
<td>134 (38)</td>
</tr>
<tr>
<td>ATS 3fr, n (%)</td>
<td>43 (23)</td>
<td>66 (40)</td>
<td>109 (31)</td>
</tr>
<tr>
<td>Vascutek Elan®, n (%)</td>
<td>13 (7)</td>
<td>10 (6)</td>
<td>23 (6)</td>
</tr>
<tr>
<td>SJM Toronto®, n (%)</td>
<td>6 (3)</td>
<td>0</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Laborc TLPB®, n (%)</td>
<td>0</td>
<td>5 (3)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Shelhigh Super Stentless®, n (%)</td>
<td>4 (2)</td>
<td>0</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Ross-Procedure, n (%)</td>
<td>49 (26)</td>
<td>15 (9)</td>
<td>64 (18)</td>
</tr>
<tr>
<td>Mechanical SAVR, n (%)</td>
<td>5 (3)</td>
<td>7 (4)</td>
<td>12 (3)</td>
</tr>
<tr>
<td>Valve size of biologic AVR</td>
<td>24.9 ± 2.1 (19–29)</td>
<td>24.8 ± 2.1 (21–29)</td>
<td>24.8 ± 2.1 (21–29)</td>
</tr>
<tr>
<td>Valve size of mechanical AVR</td>
<td>24.2 ± 3.0 (21–29)</td>
<td>25.6 ± 3.4 (21–29)</td>
<td>25.0 ± 3.2 (21–29)</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation (range) unless otherwise specified. Group I indicates patients of years 2007–2008; Group II indicates patients of years 2010–2011. SAVR: surgical aortic valve replacement.

Operative data

Table 2 summarizes procedures, prosthetic material and valve sizes of the study population. Implanted valves were mostly biologic (97%), including 64 Ross-Procedures. We compared xenograft valve-sizes of both study groups (Ross-Procedures were not regarded since pulmonary autograft was not sized). Mean size of prostheses remained the same (25 mm) in the TAVI era. Review of institutional guidelines in 2009 led to less Ross-Operations in group II.

Patient survival

Follow up at 30 days was 100% complete. Observed survival of all 357 patients at this time point was 97.2%. Comparing subgroups, total mortality rate decreased from 4.2% (8 patients) in group I to 1.2% (2 patients) in group II. However, due to the low count of patients who died, this difference is only a statistical trend ($\chi^2$: p = 0.09) which appears similar in Kaplan-Meier survival analysis as presented in Figure 1.

We further divided the study population into both genders (Table 3) and found that survival of all female patients, which was 94.3%, was significantly worse than 99.5% survival of all male (p <0.01). A similar pattern was found for SAVR-patients before the inception of TAVI: female survival in group I was 92.2% which was significantly worse compared to 99% male survival (p = 0.03). Even though male survival in group II was 100%, compared to 97% female survival this difference in gender specific survival did not reach statistical significance (p = 0.2).

Predictors of lethal events

We evaluated risk profiles of all death cases (n = 10). Preoperative age of all patients who died was 79.5 ± 6.8 years. Calculated expected mortality risk (LES) was 38.3 ± 29.5%. To compare both group’s fatalities is a statistical challenge because there were only two in group II. Dead patients in the pre-TAVI era (group I)
were 80.9 ± 6.7 years old. The two patients in the TAVI era (group II) were 71 and 77 years old (p = 0.3). Risk profiles specified by LES stayed similar (group I: 37.8 ± 30.1%, group II: 13.0 and 67.1%; p = 0.7).

Table 4 shows evaluation of risk factors age and gender as predictors for patient survival. Results reveal that women undergoing SAVR before the introduction of TAVI were at significantly higher risk for mortality than men. In the TAVI era this phenomenon does not reach statistical significance any longer.

### Discussion

Therapy of symptomatic severe aortic stenosis is becoming more challenging due to the higher life expectancies of patients and the rapidly increasing prevalence of aortic stenosis in aged people. In the group of 75-year-olds it is 2.5% whereas ten years later it amounts to 8.5%. Mortality rates from onset of symptoms are >25% in the first year and ~50% after two years with a high risk of sudden death.

SAVR is the indicated therapy and showed good results in the last decades with 3-year-survival of 87%. Comorbidities, such as low left ventricular function, chronic obstructive pulmonary disease (COPD) with the need for permanent bronchodilatory drug intake, peripheral vascular disease (PVD) or renal insufficiency as well as higher age are associated with a significantly higher mortality risk with conventional surgery and can impede causal therapy. Patients with high risk profiles are therefore nowadays referred to the TAVI-method with satisfactory outcome so far.

The aim of this study was to find out if these elderly, high risk patients are really missing in the current conventional SAVR patient population because they are provided with TAVI today. We further compared mortality rates of patients undergoing SAVR before and after the introduction of TAVI to evaluate changes in survival due to the assumed lower count of high risk patients.

Patients receiving SAVR after the inception of TAVI at our center were significantly younger. This owns to the fact that elderly patients were more often scheduled for TAVI due to the rising mortality risk of SAVR in higher aged patients. We also noticed a trend to lower patient risk profiles for SAVR — assessed by LES — in the TAVI era.

Assigning results of variables age and LES to specific genders showed that operated women had significantly lower LES (p = 0.04) and were significantly younger (p <0.01) after the introduction of TAVI. On the other hand, age and LES of male patients stayed similar. Since female gender is a counting factor in the LES algorithm, women have higher LES counts than men with comparable comorbidity-profiles. Therefore we conclude that women are scheduled for TAVI more frequently. Recent TAVI-studies support this assumed aspect of gender mal-distribution (female > male) in the total TAVI patient population (Grube et al.: 65% female TAVI-patients, Tamburino.
et al.: 56% female TAVI-patients).12,13 The loss of female SAVR-patients after the introduction of TAVI in the present study (−7%) also underpins this finding. According to our results, these female patients missing in the SAVR patient population are high aged, afflicted with a high mortality risk (LES) and referred to the TAVI method with good outcome so far. Observed 30-day survival of female TAVI patients in our center is 3.4%.14

Many recent studies revealed that several available risk algorithms including LES and north-American pendant STS-score seem to over-predict the actual risk of mortality for aortic valve surgery patients especially in the group of high risk elderly patients.15,16 Therefore in our multidisciplinary heart team we did not only consider the isolated results of calculated LES, but evaluated and discussed every patient’s morbidity profile individually. That is why sometimes even patients with higher LES would yet receive a SAVR instead of TAVI if the heart team responsibly decided so; this could explain why we only found a statistical trend for the decrease of preoperative LES count after the introduction of TAVI regarding all patients. This aspect is congruent to results of other recent studies that report risk profiles of patients undergoing conventional surgical and transcatheter aortic valve replacement.17 However, estimating the risk of SAVR in the group of high risk elderly patients is challenging. This has led to intense interest in risk stratification systems currently. LES and STS score have been updated lately and are readily available in the internet.18 Their clinical performance is presently being evaluated.19,20 A promising new algorithm called German Aortic Valve Score has been developed by the German Aortic Valve Registry (GARY) and needs to prove efficiency in clinical everyday life.21,22 Survival rates were assessed as hospital-mortality at 30 days postoperatively for every patient in the study. Overall detected mortality (n = 357) was 2.8%. Other studies with larger patient cohorts evaluating the hospital-mortality after primary isolated SAVR report frequencies ranging from 3.1% for single aortic stenosis to 5.6% for all aortic valve diseases.23–25 Long-term follow up studies provide results of time periods beginning at 1 year reporting a survival of 89% to 15 years 46%.10,24

Our results revealed that hospital mortality rate decreased after the introduction of TAVI (group I: 4.2%, group II: 1.2%); however, due to the low number of patients who died, this is only a statistical trend. Nevertheless, improved outcome of SAVR patients is obviously attributed to the introduction of the TAVI-method. According to European consensus papers TAVI is reserved for very sick, high-risk-patients.60 Consequently these patients do not undergo high-risk, or “ultima ratio” surgery any longer and do logically now ensure better survival statistics of conventional SAVR. Results of our TAVI-program are also encouraging: 30-day mortality rate of our 135 TAVI patients (first two years of the program) is 4.4%. Adding survival-rates of group II reveals a 30-day-mortality of 2.7% for the total cohort of surgically and interventionally treated patients. In conclusion we assess, that the introduction of TAVI also contributed the improvement of clinical results of all symptomatic severe aortic stenosis patients.

We further evaluated the gender specific survival. Being female is a known risk factor in aortic valve surgery as in general cardiac surgery and is thus listed in the LES and other recent risk stratification systems such as the mentioned new German aortic valve score.21 This gender aspect matches our results for mortality of SAVR before the inception of TAVI (group I) as survival of women was significantly worse than survival of men. Interestingly, we found that this mismatch would compensate after the introduction of TAVI.

When looking at mortality, we found that high risk (LES: 37.8 ± 30.1%) elderly (age: 80.9 ± 6.7 years) patients dying after SAVR in group I as expected. Since there were only two patients who died in group II, sensible statistical analysis with causal conclusions is challenging. Anyway, a univariate statistical risk model (Table 4) revealed results fitting to our conclusion that female patients benefit from the invention of TAVI: today female gender is no longer a significant risk factor for mortality after SAVR.

**Limitations**

The present study represents results from a single centre and may not be generalized to all centres. Low number of deaths makes survival analyses challenging. Dividing the study population into genders further lowers this count. Especially, the statistical “underpower” of only two patients who died in group II has to be considered when analysis of risk factors for mortality is performed.

**Conclusions**

This single centre study evaluating SAVR for isolated symptomatic severe aortic stenosis pre and post TAVI introduction indicates that especially women benefit from the inception of TAVI. We found that age and risk profiles (LES count) of female patients significantly lowered after the introduction of TAVI. We conclude that today especially
female high risk patients are provided with TAVI; therefore being female is no longer a significant risk factor for survival of SAVR. Consequently, overall detected survival rates at 30 days improved from 95.8% in the pre-TAVI era to 98.8% after the inception of TAVI.

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Disclosure Statement

Conflict of interest: none declared.

References