BACKGROUND

CHAPTER I.

Introduction

Aging of the population is an established fact. Caregivers are regularly confronted by the clinical challenges of treating older patients with advanced cardiovascular diseases and co-morbidities. With escalating healthcare costs in both private and social medicine, it has become imperative to examine the outcomes of patients undergoing surgical and catheter laboratory-based interventions in old age.

As the population ages, more and more elderly patients will need surgery. Decision making in patient care cannot anymore ignore this aspect. Surgeons are especially confronted with this reality when considering risk and benefits of surgical procedure in older patients.

Degenerative aortic stenosis (AS) is the most prevalent valvular heart disease in the elderly population and is becoming even more prevalent as the population ages.[1] This condition can be fatal if not treated especially when symptoms develop. The prognosis is dismal with survival rates of only 15 to 50% at 5 years.[1] According to the Society of Thoracic Surgeons (STS) adult cardiac surgery database, 270,376 patients underwent an aortic valve replacement for AS in the last 10 years and the median age was 70 years old.[2]

Traditionally, the standard of care for the management of aortic stenosis has been a surgical aortic valve replacement (SAVR) via a minimally invasive or full median sternotomy surgical approach. However now, with the advancement of new technologies and with the goal of doing less invasive procedures, an alternative procedure known as transcatheter aortic valve replacement (TAVR) was used to replace the aortic valve first in a human. This was performed, in France, by Alain Cribier in April 2002.[3] Since then, TAVR has been proven to be a disruptive technology, as cardiac surgeons and cardiologists join forces and combine resources to determine

its ultimate utility. The prevalence of degenerative aortic stenosis in the growing elderly population has contributed to the demand for innovative and less invasive new technology for aortic valve replacement. Though surgical results are traditionally excellent, many patients are not offered surgical aortic valve replacement (SAVR) due to high surgical risk or inoperability despite the fact that, as noted above, untreated aortic stenosis carries a mortality of up to 15 to 50 percent at five years.[1] This transformative procedure, TAVR, can be done through a multitude of access points: transfemorally via a surgical cutdown or percutaneously via the femoral artery or less commonly the femoral vein, surgically via the subclavian or carotid arteries, an upper median sternotomy via the ascending aorta (transaortic), or left mini-thoracotomy via the apex of the heart (transapically).

The development of this new technology started with important clinical trials in the US in 2006 with the Edwards-Sapien balloon expandable valve (Edwards Lifesciences, Irvine, CA). The PARTNER (Placement of AoRtic TraNscathetER Valves) study evaluated patients with severe symptomatic AS who were considered inoperable (Cohort B)[4] or high risk (Cohort A)[5] for traditional surgical therapy. In the inoperative patients, 358 patients were randomized to either medical treatment or TAVR.[6,7] The 1-year conclusion of this study was that TAVR significantly reduced the rates of death from any cause, the composite endpoint of death from any cause or repeat hospitalization and cardiac symptoms despite the higher incidence of major strokes and major vascular events.[6,7] Those results were sustained at 5 years.[4,5] The second study randomized 699 high-risk patients to either TAVR or SAVR. The one-year results of this landmark trial showed equivalence between treatments in terms of mortality, reduction in symptoms, and improved valve hemodynamics.[6,7] However, patients who had a TAVR had higher rates of post-implant paravalvular leak (PVL), incidence of stroke, and major vascular complications.[8] At five

years, overall survival in these high-risk patients was shown to be similar and leading to the majority of patients considered to be high-risk surgical patients to undergo the TAVR procedure.[5]

Based on the results of this study, the first generation Sapien valve was the first TAVR valve to be approved in the US by the FDA in 2011 for inoperable patients and in 2012 for high-risk patients. To address the early complications of the TAVR valves, the companies performed device iterations that have led to smaller valve sheaths and paravalvular leak prevention modifications by sewing a cuff around the annulus of the valve. This technology has led to multiple trials in intermediate risk patients including the randomized PARTNER-2A trial and PARTNER-2 S3i registry.[9] The PARTNER-2A study was the first randomized trial comparing outcomes between TAVR and SAVR in an intermediate-risk cohort of patients with severe aortic stenosis. This trial demonstrated that at two years, the rate of death and disabling stroke was similar between TAVR using the 2nd generation SAPIEN XT valve and SAVR (p=0.001 for non-inferiority).[9] TAVR resulted in greater improvement of aortic valve areas and aortic gradients than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation. Surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.[9]

The second most important trial is the Corevalve Pivotal trial (Medtronic Corporation, Minneapolis, MN) that include 795 high- and extreme risk patients. High-risk patients were randomized to conventional surgery versus the TAVR. The results showed that TAVR patients had a lower rate of death from any cause at 1 year compared to the surgical group (14.2% versus 19.1%).[10] This self-expandable TAVR received FDA approval in 2014. The Corevalve has also had device iterations to the Corevalve Evolut-R, allowing repositionability and changes to decrease the pacemaker rate that has been ~25% in this technology. The intermediate trial of this

device randomized patients to either the Corevalve Evolut-R (the second generation valve) to SAVR and was published in 2017. This trial demonstrated the non-inferiority of TAVR compared to SAVR in terms of clinical and hemodynamic results.[11] Moreover, in the United States, trials for a multitude of other valves have emerged over the past 2 years, including the Lotus Valve (Boston Scientific, Germany, Europe), the Portico valve (St. Jude Medical, Minneapolis, MN), and the Directflow valve (Directflow, Santa Rosa, CA).

Following those important trials, the U.S. Food and Drug Administration (FDA) approved in 2014 the use of the Sapien XT valve for high-risk and inoperable patients and in 08/2016 for intermediate-risk patients (Sapien 3). Following this, there was an obvious paradigm shift in the treatment of aortic stenosis. To monitor the use of this new technology in the US, the Society of Thoracic Surgeons and American College of Cardiology among others, have developed the Transcatheter Valve Therapies (TVT) registry. The mean age for the TAVR procedure is commonly in the 80's, but it is not uncommon for those in the 90's to undergo the TAVR procedure.[12]

Through September 2015, there are 396 sites performing TAVR in the US and ~37,768 procedures have been entered in the national US TVT registry. Although there has been a well-adopted clinical use of TAVR in those patients with aortic stenosis (AS) considered high- or extreme-risk for surgical therapies, the economic burden for using TAVR has not been completely elucidated. The use of TAVR in Europe has grown rapidly and is estimated to be now around 23% of the total AVR done in which a biological valve is used in high-risk patients. In the US, the cost of the commercially available TAVR devices is approximately ~$30,000 to $32,500 compared to a conventional surgical bioprosthetic valve that costs between ~$4,000 to $6,000. However, it is plausible that the TAVR procedure will require less resource utilization since the

median length of stay in the hospital for high-risk patients who underwent TAVR in the TVT registry was 3 days compared to 5 days for SAVR.[13]

Most clinicians are used to looking at a new therapy and asking if it will make their patient live longer and /or better. Cost-effectiveness analysis adds the financial dimension to this decision. The most commonly used metric is "quality-adjusted life years" (QALY). QALYs provide a common currency to assess the extent of the benefits gained from a variety of interventions in terms of health- related quality of life and survival for the patient.[14] When combined with the costs of providing the interventions, cost–utility ratios result; these indicate the additional costs required to generate a year of perfect health (one QALY). QALY is a composite of the extra years of life gained with a treatment and the quality of that life as measured by a utility. The utility is a scale of 0 to 1, where 0 is no different from death and 1 is perfect health.[15] This utility number is then multiplied by the additional survival to obtain QALY. The utility score is generally an empiric measurement extracted from patient interviews or quality of life questions.[15] Although QALY is the most commonly used metric to compare cost-effectiveness, clinicians recognize that utility scores are subjective and may not always match the wishes of subjective patients. However, despite these limitations, QALY is the most commonly used tool in the literature for cost-effectiveness studies.[14] In 2012, Reynolds and colleagues published a cost-effectiveness analysis of the 1st generation TAVR device compared to SAVR in the PARTNER high-risk trial using quality-adjusted life-years (QALYs).[16] They showed that the 12-month costs and QALYs were similar for TAVR and SAVR in the overall population; however, they noted some differences when stratifying his analysis according to the access site used. For patients who had a transfemoral approach (the most commonly used approach for TAVR), the total 12-month costs were slightly lower with TAVR and QALYs were slightly

higher meaning that TF-TAVR was economically dominant/attractive compared to SAVR. When they stratified for the alternative access approaches, TAVR was economically dominated by SAVR and not economically attractive. The results obtained in the alternative access approaches could be due to early experience, steep learning curve, and lower number of patients performed in this analysis.[16] The balance between newer less-invasive technology and the higher cost associated with these innovations remains a robust discussion among the multiple stakeholders within our society; it is especially worth noting that the use of those devices is expanding to lower risk groups of patients. As the new technology continues to mature with new iterations of the devices, as in the case of the transcatheter valves, early procedural complications diminish, and benefit to patients continues to be more pronounced.[15]

As transcatheter valve technology evolved with improved delivery systems, valve design and patient selection, the likelihood of indications is now being expanded to include low-risk patients with the PARTNER-3 trial that is currently on-going. The question on everyone's mind is how far will this go and what will be the role of standard surgical aortic valve replacement? Since the major trials such as the PARTNER trial and the CoreValve Pivotal US trials, TAVR programs have become increasingly prevalent across North America and Europe. The indications for TAVR have expanded, availability has increased, and outcomes have improved.[4,5,6,7] As this technology is relatively new, we still have to wait for long-term data to unfold. However, there is no doubt that the field of cardiothoracic surgery will look very different than it did 20 years ago with respect to the treatment of valvular diseases. In recent years, there was an overall growing interest in assessing and improving health care quality. On-going changes to the United States healthcare system involve a greater emphasis on public reporting of quality as well as a direct link between quality and coverage (or reimbursement).[15] The economics of TAVR are complex

and must be considered against the backdrop of medically managed symptomatic aortic stenosis, which, on average, incurs an annual cost of $29,278 to cover 1.9 hospital admissions totalling 11.5 days per patient-year.[15] The Medicare coverage determination and reimbursement algorithm significantly impacts the economics of TAVR in the United States because the vast majority of TAVR patients are aged ≥ 65 years (the qualifying age for Medicare coverage) .[15] Furthermore, both the accompanying hospital charges associated with TAVR and the reimbursement through Medicare vary significantly according to institution, location, and academic status. [15] Reimbursement for the same TAVR procedure on equivalent patients at two different hospitals can vary from $32,000 to more than $60,000 based on adjustments for location alone.[17] Hospitals with training programs also receive more reimbursement per diagnostic-related group (DRG) from Medicare, making a TAVR program at a private hospital less financially attractive.[17]

This thesis uses data performed in a single institution academic centre. For patients on Medicare, they reimburse TAVR hospital charges using the same diagnosis related group (DRG)'s as surgical aortic valve replacement. The appropriate DRG is assigned based on the severity of clinical comorbidities and complications.

Because TAVR is much less invasive, we tend to believe that the complications related to TAVR have less of an impact on mortality than SAVR especially in those high-risk patients. No study yet has examined the association between the complications related to TAVR and the complications related to SAVR on mortality and on hospital cost.

The increased cost of TAVR compared to SAVR can make the TAVR procedure unattainable for some countries especially those with socialized medicine. The effect of complications following SAVR versus the complications following TAVR on 30-day mortality and hospital cost in a

cohort of patients who underwent either of those procedures had never been evaluated in the United States.

Purpose of the study

To assess if complications related to TAVR have less impact on 30-day mortality and are less costly than complications related to SAVR at Emory University Hospitals, Atlanta, Georgia, United States of America, in a cohort of patients who had either of those procedures between 01/2011 and 07/2017

Public health purpose: If the cost and burden of complications related to TAVR are less than for SAVR, the healthcare centres could justify the extra cost related to the transcatheter heart valve (THV) and expand its use to any risk categories of patients.

Goals of the study: The goals are: 1) identify complications which predict 30-day mortality; 2) find which complications are predictors of increase in the overall cost and 3) estimate the differential cost of complications between TAVR and SAVR.

CHAPTER II.

III. Manuscript chapter (article to be published in Annals of Thoracic Surgery)

Assessment of Outcomes and Cost of Complications following Surgical and Transcatheter Aortic Valve Replacement

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Abstract

BACKGROUND: TAVR and SAVR are two well-adopted therapies for the treatment of severe aortic stenosis. However, analyses related to the clinical and economic cost of complications during these procedures are less defined. The purpose of this study is to assess outcomes and costs associated with complications following TAVR and SAVR.

METHODS: 3,337 patients undergoing SAVR (N=1,765) or TAVR (N=1,572) from 1/2011 and 1/2017 were included in this retrospective analysis from an academic US institution. The complications included the neurological, respiratory, cardiovascular, renal and gastrointestinal systems. Unadjusted and adjusted analyses were done using logistic regression for 2 possible associations: 1) cost and complications and 2) 30-day mortality and complications. Differential cost between SAVR and TAVR were calculated excluding and including the cost of the implant and categorizing it by the number of complications. A p-value of <0.05 was considered statistically significant.

RESULTS: Median age was 82 (76-86) years for TAVR and 70 (62-77) years for SAVR. Majority of patients were male and median STS score was 9.6% (4.6-14.3) for TAVR and 2.8% (1.6-4.8) for SAVR. The 30-day mortality was 3.9% for TAVR and 3.1% for SAVR. Complications associated with 30-day mortality are shown in Table 1. The mean number of complications for TAVR was 1.3 and SAVR 2.2. When excluding the cost of the implant, the SAVR cost was more than TAVR by $650 for patients who had 1 complication; $104 for 2; $1,862 for 3; $158 for 4; and $6,147 for ≥5. Including the cost of the implants, the TAVR cost was more than SAVR by $ 26,523 for patients who had 1 complication; $28,066 for 2; $27,095 for 3; $30,458 for 4; and $31,060 for ≥5. The differential cost between the SAVR and TAVR devices was $25,985.

CONCLUSIONS: When the cost of the implant is considered, the costs related to TAVR complications are higher than the costs related to SAVR complications. However, if the cost of the implants is removed, the costs of TAVR complications, even in a high-risk cohort, are much less than the costs of SAVR complications in a low-risk cohort. When the cost of the TAVR implant decreases in the future, the economic advantage of TAVR over SAVR becomes more pronounced.

Introduction

Aortic stenosis (AS) is highly prevalent in elderlies. For decades the standard for treating aortic stenosis was an open cardiac surgery via a sternotomy approach. However in 2002, the future of treating these patients was changed when Dr Alain Cribier performed the first transcatheter aortic valve replacement (TAVR).[3] Transcatheter aortic valve replacement (TAVR) is proving to be disruptive technology, as cardiac surgeons and cardiologists join forces and combine resources to determine its ultimate utility. The prevalence of degenerative aortic stenosis in the growing elderly population has contributed to the demand for innovative and less invasive new technology for aortic valve replacement.[1] Though surgical results are traditionally excellent, many patients are not offered surgical aortic valve replacement (SAVR) due to high surgical risk or inoperability despite the fact that untreated aortic stenosis carries a mortality of up to 50 percent at five years.[1] The transcatheter approach has been proven to be an effective aortic valve replacement option for patients with aortic stenosis who are either very high risk or not candidates for conventional surgical therapy.[4,5,7] As transcatheter valve technology evolved with improved delivery systems, valve design and patient selection, the indications has been expanded and FDA approved to include intermediate risk patients and now, current trials are on-going for low-risk patients. The question on everyone's mind is how far will this go and what will be the role of conventional surgical aortic valve replacement? Since the PARTNER trial, TAVR programs have become increasingly prevalent across North America and Europe. The indications for TAVR have expanded, availability has increased, and outcomes have improved. As this technology is relatively new we still have to wait for the long term data to unfold, however there is no doubt that the field of cardiothoracic surgery will look very different than it did 20 years ago with respect to the treatment of valvular diseases.

However, the drawback of this transcatheter valve is its cost. Actually, it is sold at a price of approximately 30,000 US$ compared to 5,000 US$ for a conventional surgical valve prosthesis. Not every cardiac surgery centre can afford paying for a lot of those valves and access to this technology can be limited especially in country with a socialized free healthcare system such as Canada for example. Spending money on this technology becomes a societal choice especially if those valves are implanted in inoperable/high-risk and elderly patients where the procedure can be considered futile. The cardiac surgical and cardiology communities have joined with industry and regulatory agencies to both implement and study the use of TAVR in the United States and worldwide. This collaboration serves to expedite the acquisition of information that will eventually determine the best option for each patient in need of aortic valve replacement.

Because TAVR is less invasive, we tend to believe that the complications related to TAVR have less of an impact on mortality than SAVR especially in those high-risk patients. No study yet has examined the association between the complications related to TAVR and the complications related to SAVR on 30-day mortality and on hospital cost. This study can have a public health impact if the cost and burden of complications related to TAVR are less than for SAVR, which can justify for the healthcare centres the extra cost related to the transcatheter heart valve (THV). The goal of this study is to assess if complications related to TAVR have less effect on 30-day mortality and are less costly than complications related to SAVR at Emory University Hospitals, Atlanta, Georgia, USA in a cohort of patients who had either of those procedures between 01/2011 and 01/2017.

Material and Methods

Data source:

Patients were identified by querying Emory University Hospitals Society of Thoracic Surgeons (STS) Adult Cardiac Database for consecutive qualified patients between 1/2011 and 07/2016. A total of 3,337 patients undergoing aortic valve replacement with or without concomitant CABG/PCI were included. Exclusion criteria included any other concomitant procedures. Of them, 1,765 patients underwent surgical aortic valve replacement and 1,572 underwent transcatheter aortic valve replacement.

The study was approved by the Emory University Institutional Review Board in compliance with Health Insurance Portability and Accountability Act regulations and the Declaration of Helsinki and waived individual patient consent for these patients.

Study population:

Patients included in this study were low, intermediate high- and extreme-risk. High-risk patients were defined as patients with an STS score of more than 8% with no other comorbidities or anatomic factors that made them inoperable. For extreme-risk patients, we adopted the definition used in the PARTNER-B trial for "inoperable" patients. It includes patients with an STS risk score of 10% or higher or those who had coexisting conditions that would be associated with a predicted risk of death of 15% or higher by 30 days after surgery, or those those who were not considered to be suitable candidates for surgery because they had coexisting conditions that would be associated with a predicted probability of 50% or more of either death by 30 days after surgery or a serious irreversible condition. The intermediate risk patients were defined by a STS score of between 3-8% and the low risk patients were the ones with an STS less than 3%.[4]

Surgical technique

The access site for the procedure were transfemoral (TF), transapical (TA), direct aortic (TAo), and other (including, transcaval or transcarotid). Patients underwent TAVR with either balloon-expandable valve (SAPIEN, SAPIEN XT, or SAPIEN 3, Edwards LifeSciences) or self-expanding valve (CoreValve, Medtronic) or other (LOTUS, Boston, Scientific, PORTICO, St-Jude Medical). In some patients, TAVR was performed via the standard technique under general anaesthesia and utilizing transesophageal echocardiography, while others underwent minimalist TAVR with conscious sedation and transthoracic echocardiography.[18] The heart team determined whether a patient received standard or minimalist TAVR.

For the patients who underwent surgery, standard cardiopulmonary bypass (CPB) and cannulation techniques were used for all cases. Surgical approach, valve prosthesis or repair techniques, and conduct of CPB and myocardial protection were left to the discretion of the attending cardiac surgeon. SAVR was performed via full-length redo median sternotomy or through a mini-sternotomy. Patients received either a mechanical or a bioprosthetic valve.
According to institutional protocol, epiaortic ultrasonography was performed before central aortic cannulation and cross clamp placement. When extensive aortic calcification was encountered, axillary or femoral artery cannulation was performed for arterial inflow. Typically, conventional CPB was performed utilizing roller head pumps, membrane oxygenators, cardiotomy suction, arterial filters, cold antegrade and retrograde blood cardioplegia, and moderate systemic hypothermia (32-34°C). For patients with class 4 or 5 renal failure, the mean arterial blood pressure was maintained at or above 70 mmHg throughout the duration of CPB. The operative field was routinely flooded with carbon dioxide and de-airing maneuvers were performed in all

cases before releasing the cross clamp. A modified version of zero-balance ultrafiltration was initiated near the termination of CPB. All patients received 30-day follow-up.

Pre and perioperative Variables:

Before analysis, preoperative risk factors were identified and extracted from the Emory STS database (which include 30-day outcome data). Standard STS definitions for risk factors and outcomes were used. Race was dichotomized as Caucasian or non-Caucasian. New York Heart Association (NYHA) heart failure class was dichotomized as class III/IV or I/II. STS discharge location was used to determine where the patients were discharged following their procedure. VARC-2 criteria were used to define major and minor stroke[19]. Renal failure was defined, according to STS criteria, as an increase in serum creatinine level more than 4.0 mg/dl or 3 times greater than the baseline creatinine; acute rise must be at least 0.5 md/dl or a new requirement for dialysis postoperatively. Other clinical outcomes used were defined according to STS criteria.[2] Patients' charts were reviewed for the subsequent re-hospitalizations in any Emory University Hospitals. The date, the causes of readmission and the discharge location following the hospitalization for readmission were recorded in our database. Follow-up visit or emergency visit notes during the one-year period following their procedure were also reviewed. We also reviewed the notes from our valve nurse navigator and/or valve coordinator who receive phone calls from all patients or family when they were readmitted at any hospitals. Patients were instructed following their index procedure to call them if they experienced any re-hospitalizations. The coordinator recorded readmission status as well as the causes of readmission.

Statistical analysis:

We examined crude association between outcomes variable and mortality using Chi-square test. We computed crude prevalence odds ratios (cORs) and 95% confidence intervals (95% CIs). Outcomes that were significantly associated with mortality were selected in a full model.

Unconditional logistic regression was used to estimate the association between the risk of 30-day mortality those complications: 30-day all-cause mortality, neurological events, acute kidney injury, renal failure requiring dialysis, new pacemaker, conversion to open surgey, deep stenal wound infection, atrial fibrillation, blood product transfusions, pneumonia, gastrointestinal bleeding, prolonged ventilation, myocardial infarction, intensive care unit (ICU) and hospital length of stay, readmission to ICU and 30-day readmission. Estimation of the adjusted odds ratios (cORs and aORs, respectively) and corresponding 95 % confidence intervals (CIs) were performed for the TAVR group and for the SAVR group on their risk of 30-day mortality. For adjusted analysis, all the aforementioned complications were included in the regression models based as well as age, race and sex. A backward regression was performed to evaluate the possible confounders and to find our adjusted final models (TAVR and SAVR). For the cost-analyses, complications had been divided into 5 categories (1 complication, 2 complications, 3 complications, 4 complications and 5 and more complications). The mean cost of the total patient's encounter according to the procedure received was calculated for each of the category of complications including and excluding the cost of the implant/device. The differential in cost for all levels of complications was calculated and this was unadjusted for preoperative mortality risk. Adjusted analyses using logistic regression were also performed to assess which complications were associated with increase in overall cost. A two-sided P value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were conducted using SAS_

version 9.4 (SAS Institute Inc., Cary, NC.

Results

Demographics

The median age of the patients in the TAVR group was 82 (76-86) years old and 70 (62-77) years old in the SAVR group. The majority of patients were males in both groups (TAVR: 54.6%; SAVR: 64.9%). The median STS-PROM at 30-day was 9.6 (4.6-14.3)% in the TAVR group and 2.8 (1.6-4.8) % in the SAVR group. (Table 1)

Operative data

Majority of the patients had an elective procedure (TAVR: 58.1%; SAVR: 57.9%). The main indication was for aortic stenosis in both groups (TAVR: 77.2%; SAVR: 7.0%)

In the SAVR group, majority of the valves implanted were of sizes 23 mm (31.1%) and 25 mm (23.5%) and 67.2% of those patients had an isolated AVR.

In the TAVR group, majority of the valves implanted were the Sapien XT or Sapien 3 (85%) and the most commonly valve sizes used were 23 mm (38.5%) and 26 mm (40.5%). The most commonly approach used was transfemoral (60%). (Table 2)

Post-operative outcomes

Thirty-day all-cause mortality was 3.9% for TAVR and 3.1% for SAVR. The median length of stay in the intensive care unit for the TAVR patients was 29 (22.5-53.1) hours and for SAVR it was 49.1 (26.6-94.6) hours. Median post-operative length of stay was 3 (2-6) days for TAVR and 6 (5-9) days for SAVR patients. Rate of readmission was 4.8% for TAVR and 7.8% for SAVR. Complications rates are shown in Table 3. (Table 3)

Unadjusted and Adjusted logistic regression analyses: odds ratio for death and individual procedure complications SAVR and TAVR

The unadjusted logistic regression is shown in table 4. After performing the adjusted analysis, the predictors that were found to be associated with 30-day mortality in the TAVR group were re-exploration for bleeding, prolonged mechanical ventilation, post-operative renal dysfunction and readmission to ICU. (Table 5) The ones associated with SAVR were post-operative pneumonia, prolonged ventilation, post-operative renal dysfunction and packed red blood cells transfusions requirements. (Table 6)

Distribution of complications TAVR and SAVR

The distribution of complications is shown in table 7. The main complications related to SAVR were blood product requirements, atrial fibrillation, 30-day readmission, pacemaker, prolonged ventilation, new renal failure and readmission to ICU. The main complications related to TAVR were blood product requirements, pacemaker, atrial fibrillation, 30-day readmission and prolonged ventilation.

The mean cost of the TAVR implant was $32,217 and the mean cost of SAVR implant was $6,232.

The differentials in costs per complications between TAVR and SAVR (including and excluding the cost of the implant) are illustrated in table 8. The mean number of complications for TAVR was 1.3 and SAVR 2.2. When excluding the cost of the implant, the SAVR cost was more than TAVR by $650 for patients who had 1 complication; $104 for 2; $1,862 for 3; $158 for 4; and $6,147 for ≥5. Including the cost of the implants, the TAVR cost was more than SAVR by $ 26,523 for patients who had 1 complication; $28,066 for 2; $27,095 for 3; $30,458 for 4; and

$31,060 for ≥5. The differential cost between the SAVR and TAVR devices was $25,985. (Table 8)

Adjusted regression analyses have been done to assess the association between complications and increase in the overall cost and are shown in Tables 9 and 10 for TAVR and SAVR respectively. For both TAVR and SAVR, the complications that were mainly associated with the most increase in the overall cost were post-op renal dysfunction requiring dialysis, prolonged mechanical ventilation and post-operative pneumonia. Post-op renal dysfunction was associated with the higher increase in overall cost for SAVR, but not for TAVR. (Table 9 and Table 10)

Discussion

This study demonstrated the main complications that were associated with 30-day mortality following TAVR and SAVR. It also shows higher complications rate in the SAVR group compared to the TAVR group. In term of the differential in cost between the two procedures, it was demonstrated that when excluding the cost of the implant, for the same number of complications, the complication-related cost for TAVR was less than for SAVR despite the fact that TAVR patients were at higher risk. However, while considering the cost of the implant, the cost of TAVR remains higher despite its lower complications-related cost.

The impact of TAVR-related complications

A sub-study of the PARTNER (Placement of AoRTIc TraNscathetER) 1A and 1B trials included 419 patients who underwent TF-TAVR. The goal of this study was to evaluate the predictors of vascular complications as well as its impact on mortality. They found that major vascular complication was associated with increased 30-day (HR: 4.87 [95% CI: 2.02-11.75], p <0.0001)

and 1-year all-cause mortality (HR: 2.04 [95% CI: 1.30 to 3.19], p =0.001) as well as 30-day (HR: 4.75 [95% CI: 1.87-12.04], p <0.0003) and 1-year (HR: 3.75 [95% CI: 2.06-6.83], p <0.0001) cardiovascular mortality. However, they reported that the incidence and impact of major vascular complications seems to decrease in a lower-risk population (STS <4%).[20] In a study by Ducroq et al., major vascular complication was associated with more transfusions and also with more episodes of acute renal failure requiring dialysis.[21] The patients who experienced major vascular complication in our study were the ones who experienced severe hemodynamic collapse that lead to more transfusions, the need for conversion to open surgery or the need for hemodynamic support devices reflecting the severity of the initial vascular insult and all this could have lead to the development of acute kidney injury (AKI). All these predictors were related to increase in 30-day mortality in our study. A review was done evaluating the impact of AKI on mortality following TAVR. They found that 30-day mortality rate in patients with AKI ranged from 13.3% to 44.4% and was 2-6 fold higher than in patients without AKI.[22] Interestingly and this was demonstrated in many studies except one, the amount of contrast agent during the procedure was not associated with the occurrence of AKI.[22-24] A group from Florida assess the impact of AKI on mortality after TAVR. They found also that AKI was associated with increase in mortality up to 2 years following the TAVR procedure. They also recommended that blood transfusion should be administered restrictively in order to prevent AKI. In our study, even if blood transfusions were not directly associated with 30-day mortality in the TAVR group of patient, it could potentially lead to AKI and this predictor was strongly predictive of 30-day mortality.

<u>The impact of SAVR-related complications</u>

Magruder et al. in a propensity-matched analysis assessed the impact of severe bleeding

following any cardiac surgery compared to patients who had minimal bleeding. In their analysis, they found that as compared to matched dry patients, bleeding patients were more likely to experience the primary outcome of any morbidity/mortality (36.8% vs. 13.2 %, p = 0.002), as well as ventilation >24 hrs (33.8% vs. 7.4 %, p <0.001) and 30-day mortality (11.8% vs. 1.5 %, p = 0.02).[25] In our current analysis, we did not find that re-exploration for bleeding was associated with increase in 30-day mortality in this cohort of surgical low-risk patients. However, the amount of blood transfusions received was associated with an increase in mortality which may reflect sicker patients. Probably, if recognized early, the bleeding source can be controlled without too much damage and without requiring too many blood transfusions. A retrospective cohort study comparing 4,028 patients undergoing cardiac surgery compared the postoperative complications between patients with blood transfusion versus non-blood transfusion. The authors did not find any difference in survival between groups, however patients who received blood transfusions had more infectious episodes as mediastinitis, respiratory infection, acute renal failure, stroke and sepsis.[26] Mortality associated with the development of ARF is as high as 60% in some studies but likely averages 15 to 30%, depending on the definition of ARF and the postoperative period studied (hospital discharge or 30-day mortality).[27-29] In patients who require dialysis, the mortality is uniformly high in all studies and averages 60 to 70%.[30,31] Chertow et al. found that AKI was an independent determinant of the risk for death with an odds ratio of 7.9.[32]

The group by the National Institutes of Health and Canadian Institutes of Health Research Cardiothoracic Surgical Trials Network enrolled prospectively 5,158 patients who underwent cardiac surgery and examine the timing, pathogens, and risk factors, including modifiable management practices, for postoperative pneumonia and estimate its impact on clinical outcomes. Pneumonia was associated with a marked increase in mortality (HR, 8.89; 95% CI, 5.02-15.75)

and longer length of stay of 13.55 ±1.95 days (95% CI, 10.31-16.58).[33] We found the same in our study.

Cost-effectiveness studies TAVR, SAVR or medical treatment

TAVR versus medical treatment

A study from the results of the PARTNER-1B cohort was done on cost-effectiveness of TAVR compared with standard care among inoperable patients with severe aortic stenosis.[4] TAVR has been shown to improve survival and quality of life compared to patients who received the medical treatment ; however, the cost and cost-effectiveness of this strategy was not well known. Follow-up costs through 12 months were lower with TAVR ($29 289 versus $53 621) because of reduced hospitalization rates, but cumulative 1-year costs remained higher for TAVR ($106, 076 versus $53, 621).[34]

TAVR versus SAVR

Then, the same group published the cost-effectiveness result of the PARTNER-1A trial comparing the cost related to TAVR to SAVR. They found that although 12-month costs and QALYs were similar for TAVR and SAVR in the overall population, there were important differences when results were stratified by the access site used for the patients who underwent TAVR. In patients who received a transfemoral approach, the total 12-month costs were slightly lower with TAVR and QALYs were slightly higher such that TF-TAVR was economically dominant compared with AVR in the base case and economically attractive (incremental cost-effectiveness ratio < $50,000/QALY) in 70.9% of bootstrap replicates. In patients who received a transapical approach, the 12-month costs remained substantially higher with TAVR, whereas QALYs tended to be lower such that TA-TAVR was economically dominated by AVR in the base case and economically attractive in only 7.1% of replicates. This excess initial cost with TF-

TAVR was offset by shorter length of stay (LOS; ~6 days, including ~2 ICU days) such that index hospitalization costs similar ($73,219 vs. $74,067). With TA-TAVR, however, the higher procedural cost ($40,368 vs. $15,076) was not offset because LOS was only 1 to 2 days shorter than SAVR. [16] In this current study, we did not have the cost data to separate the patients who received a transfemoral approach versus an alternative approach, we could however speculate that the complications cost would be lower in patients who receive a transfemoral approach and this differential in cost between SAVR and TAVR would be greater and in favor of TAVR, but this needs to be demonstrated.

Arnold et al. sought to estimate the effect of periprocedural complications on in-hospital costs and length of stay of TAVR. They developed multivariable models to estimate the incremental cost and length of stay associated with specific periprocedural complications. Mean cost for the initial hospitalization was $79 619± 40 570 ($50 891 excluding the valve); 49% of patients had ≥ 1 complication. They found seven complications associated with an incremental hospital cost: major and minor stroke, major vascular complications, major bleeding, renal insufficiency and failure and arrhythmia. Death, repeat TAVR and surgical AVR were also significantly associated with an incremental hospital cost. A repeat TAVR procedure was associated with ≈$120 000 in additional hospitalization costs. Renal failure and death were also expensive, with adjusted incremental costs of ≈$68 000 and $42 000, respectively. Also, a total of 6 complications were independently associated with increased LOS and these included death, renal failure, major bleeding, vascular complications, major arrhythmia, and pacemaker implantation.[17] Those were mainly the complications that we found to be more associated with 30-day mortality in our cohort of patients.

TAVR complications on cost

A retrospective observational study was done from the German DRG statistic on patients' characteristics and in-hospital outcomes of all isolated TAVR procedures for a total of 9147 patients. The authors evaluated the impact of post-procedural complications on length of stay and reimbursement. Of all the complications, they found that bleeding events were associated with the highest additional reimbursement (€ 12,839,$p< 0.001$), extra length of stay (14.58 days, $p< 0.001$), and increased likelihood of mechanical ventilation for more than 48 hrs (OR 17.91, $p< 0.001$). Also, a more moderate complication-related impact on resource use and reimbursement was found for acute kidney injury (additional reimbursement: € 5963, $p<0.001$; extra length of stay: 7.92 days, $p< 0.001$ and ventilation more than 48 hrs: OR 6.93, $p<0.001$).[35] In our current study, the OR related to reoperation for bleeding was significant and had a major impact on 30-day mortality as well as prolonged mechanical ventilation.

Limitations

Selection bias cannot be ruled out in this study, as the TAVR had a greater percentage of risk patients than SAVR. However, despite this difference in preoperative risk, the cost of complications is still lower in the TAVR group. Estimating the actual cost differential is difficult due to the selection bias, but the significance of the direction of the difference is noteworthy. Also, it was impossible for us to determine the different types of hospital costs in this analysis and to differentiate between payment, charges and economic costs as well as who were Medicaid and Medicare patients and for the others which insurance companies were doing the reimbursement and at which percentage. However, here we used charges that can also be a proxy for cost. Using this gives us an idea of the direction of the difference more than the magnitude.

Conclusions

When the cost of the implant is considered, the costs related to TAVR complications are higher than the costs related to SAVR complications. However, if the cost of the implants is removed, the costs of TAVR complications, even in a high-risk cohort, are much less than the costs of SAVR complications in a low-risk cohort. When the cost of the TAVR implant decreases in the future, the economic advantage of TAVR over SAVR becomes more pronounced.

CHAPTER III.

Discussion

This study demonstrated the main complications that were associated with 30-day mortality following TAVR and SAVR. It also shows higher complication rates in the SAVR group compared to the TAVR group. In term of the differential in cost between the two procedures, it was demonstrated that when excluding the cost of the implant, for the same number of complications, the complication-related cost for TAVR was less than for SAVR despite the fact that TAVR patients were at higher risk. However, while considering the cost of the implant, the cost of TAVR remains higher despite its lower complications-related cost.

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CHAPTER IV. Summary, Public Health Implications and Future Directions

Future directions and public health implications

While looking at the costs for SAVR according to the preoperative risk categories based on the STS-PROM, it was demonstrated that there was an increase in mean total costs from the low- (n=2,002) to intermediate- (n=415) to high-risk (n =113) category ($35,021 ± $22,642 vs $46,101 ± $42,460 vs $51,145 ± $31,655; $p < 0.001$). Higher STS-PROM was significantly associated with higher postoperative mortality, complications, length-of-stay, and costs. The SAVR cost data provide a basis for the analysis of TAVR cost-effectiveness and its impact on payment systems.[36] Because a higher STS-PROM score was also associated with higher postoperative mortality, complications, length-of-stay and costs, cost-effectiveness studies comparing TAVR and SAVR in this category of patients remains relevant despite the higher cost of a transcatheter

heart valve (THV). The major component of increased procedural costs for TAVR over SAVR is the cost of the transcatheter heart valve itself, and this is expected to change driven by eventual market forces and the greater availability of competitor products and the cost effectiveness of TAVR depends considerably upon the health economy in which it is used.[37] Across multiple analyses, TAVR has been found to be more cost-effective than medical therapy in inoperable patients with incremental cost-effectiveness ratios ranging from ~ $33,000 to ~ $55,000 per life-year gained.[38] The cost-effectiveness of TAVR versus SAVR in high-risk, operable patients is less favorable and varies by analysis. Same thing applies for cost-effectiveness study done in an intermediate cohort of patients who underwent TAVR.[39] In general, a lower operative risk is associated with higher and less favorable cost-effectiveness ratio for TAVR.

Options to reduce the cost related to TAVR could potentially include the use of the "minimalist approach" (MA) versus the use of the hybrid operating room. The minimalist approach does not require the presence of the anesthesiologist because the procedure is performed under local anesthesia with minimal conscious sedation and is performed in the catheterization laboratory. It also uses a fully percutaneous access site entry and closure and transthoracic echocardiography. No invasive monitoring is necessary.[40] The structural heart group of physicians from Emory who are pioneers of this technique, showed that it can be performed with minimal morbidities and mortality and equivalent effectiveness compared with the hybrid operating room TF TAVR. They have also demonstrated that the shorter length of stay and lower resource use with MA-TF TAVR significantly lowers hospital costs.[40] Until the cost of the transcatheter heart valve prosthesis decrease, other strategies need to be used to help decrease the cost related to this costly technology. Cost-analyses studies should be performed in different hospital settings using different strategies for TAVR in order to assess the economic benefits of using this technology on

short-, mid-, and longer-terms.

LIMITATIONS

This study includes selection bias as the sicker patients were attributed the TAVR procedure and the lower risk the SAVR procedure. However, the results go in the sense that despite the higher risk patients the cost of complications is still lower in the TAVR group. Also, it was impossible for us to determine the different types of hospital costs in this analysis and to differentiate between payment, charges and economic costs as well as who were Medicaid and Medicare patients and for the others which insurance companies were doing the reimbursement and at which percentage. However, here we used charges that can also be a proxy for cost. Using this gives us an idea of the direction of the difference more than the magnitude.

CONCLUSIONS

When the cost of the implant is considered, the costs related to TAVR complications are higher than the costs related to SAVR complications. However, if the cost of the implants is removed, the costs of TAVR complications, even in a high-risk cohort, are much less than the costs of SAVR complications in a low-risk cohort. When the cost of the TAVR implant decreases in the future, the economic advantage of TAVR over SAVR becomes more pronounced.

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Table 1: Demographics

Demographics	**TAVR (n=1572)**	**SAVR (n=1765)**
Age	82 (76-86)	70 (62-77)
Sex male	859 (54.64)	1145 (64.87)
Race white	1381 (88.02)	1484 (84.13)
BMI	26.6 (23.3-31.0)	28.6 (25.1-32.9)
STS risk score (%)	9.6 (4.6-14.3)	2.8 (1.6-4.8)
Pre-op LVEF (%)	55 (45-60)	58 (50-60)
NYHA functional • III • IV	 518 (33.00) 855 (54.40)	 504 (28.6) 247 (14.0)
Cardiogenic shock	5 (0.32)	6 (0.34)
Atrial fibrillation	254 (16.2)	171 (9.7)
Previous MI	485 (30.87)	339 (19.23)
Previous PCI	562 (35.8)	322 (18)
Previous Cardiac intervention	1096 (69.70)	618 (35.00)
Peripheral arterial disease	492 (31.30)	227 (12.86)
Previous TIA/Stroke	234 (14.89)	134 (7.59)
Diabetes	677 (43.07)	634 (35.92)
Hypertension	1528 (97.20)	1550 (87.82)
Chronic Obstructive Pulmonary Disease • Moderate • Severe • O_2 dependent	 187 (12.10) 200 (12.94) 106 (6.70)	 105 (6.03) 90 (5.17) 29 (1.6)
End-stage renal disease on dialysis	59 (3.76)	47 (2.66)
Previous chest radiation	82 (5.41)	31 (2.01)
Immunocompromised	195 (12.40)	109 (6.18)
Liver disease	60 (3.95)	74 (4.79)

BMI: Body mass index; STS: Society of Thoracic Surgeons; LVEF: Left ventricular ejection fraction; NYHA: New York Heart Association; MI: Myocardial Infarction; PCI: Percutaneous coronary intervention; TIA: Transient Ischemic Attack; O_2: Oxygen; TAVR: Transcatheter aortic valve replacement; SAVR: Surgical aortic valve replacement.

Table 2: Operative data

Operative data	**TAVR (n=1572)**	**SAVR (n=1765)**
Elective status	914 (58.14)	1021 (57.85)
Etiology of aortic valve disease • aortic stenosis • aortic insufficiency • mixed	 1213 (77.16) 0 359 (22.84)	 1253 (71.00) 200 (11.33) 312 (17.68)
Aortic valve orifice area (cm2)	0.62 (0.52-0.70)	0.8 (0.6-0.93)
Mean aortic gradient (mmHg)	49 (41-54)	40 (30-49)
Surgical procedure		
Full sternotomy Mini sternotomy Right anterior thoracotomy	N/A	1712 (97) 52 (3) 1 (0)
Aortic valve prosthesis • 19mm • 21mm • 23mm • 25mm • 27mm • 29 mm	N/A	 72 (4.1) 321 (18.2) 549 (31.1) 414 (23.5) 204 (11.6) 205 (11.6)
Prosthesis type • Mechanical • Edwards (Magna ease or Perimount,) • St-Jude Medical bio • Carbomedics • Medtronic freestyle • Medtronic Mosaic • Sorin Mitroflow • Sutureless • Homograft • Unspecified	N/A	 170 (10) 714 (40.5) 195 (11) 8 (0.1) 312 (18) 276 (15.6) 60 (3.4) 26 (1.5) 1 (0.1) 3 (0.2)
Surgery Type • Isolated AVR • AVR + CABG • AVR+PCI	 1374 (87.40) N/A 198 (12.60)	 1186 (67.20) 579 (32.80) N/A
Isolated AVR • Cardiopulmonary bypass time • Cross-clamp time AVR + concomitant procedure • CPB time • Cross-clamp time	N/A	 104 (91-125) 82 (69-95) 144 (123-166) 116 (97-135)
TAVR procedure		
TAVR valve type • Sapien, Sapien XT or Sapien 3	1336 (85)	N/A

• Other	236 (15)	
TAVR valve sizes (mm) • 20 • 23 • 25 • 26 • 27 • 29 • 31	 32 (2) 605 (38.5) 10 (0.01) 636 (40.5) 10 (0.6) 275 (17.5) 4 (0.0)	N/A
Minimalist TAVR	815 (52)	N/A
Access • Transfemoral • Transapical • Direct Aortic • Other	 943 (60) 314 (20) 220 (14) 94 (6)	N/A
Need for a second valve implanted	94 (6)	N/A
Need of postoperative balloon dilatation	424 (27)	N/A
Post-op IABP	44 (3)	102 (5.8)

AVR: Aortic valve replacement; CABG: Coronary artery bypass graft; PCI: Percutaneous coronary intervention; TAVR: Transcatheter aortic valve replacement; IABP: Intra-aortic balloon pump; SAVR: Surgical aortic valve replacement.

Table 3: Post-operative outcomes

Outcomes	**TAVR (n=1572)**	**SAVR (n=1765)**
30-day all-cause Mortality	62 (3.94)	54 (3.06)
Neurological events TIA Stroke	 4 (0) 24 (2.0)	 4 (0) 48 (3.0)
Acute kidney injury	22 (1.4)	35 (2.0)
Renal failure requiring dialysis	13 (0)	22 (1.2)
Re-exploration for bleeding (major vascular complications, mediastinal re-exploration)	16 (1.0)	65 (3.7)
New Post-operative pacemaker	102 (6.49)	87 (4.93)
Conversion to open surgery	15 (1)	--
Deep sternal wound infection/mediastinitis	2 (0)	7 (0)
Post-op new atrial fibrillation	112 (7.1)	664 (37.6)
Post-operative Transfusion requirement • PRBC • Platelets • Cryoprecipitate • Fresh frozen plasma	 2 (1-3) 0 0 0	 2 (1-4) 0 (0-1) 0 (0-2) 0 (0-2)
Pneumonia	26 (1.7)	69 (3.9)
Gastrointestinal bleeding	26 (1.7)	58 (3.3)
Post-op prolonged ventilation	80 (5.1)	265 (15.0)
Myocardial infarction	2 (0)	0 (0)
ICU length of stay (hrs)	29 (22.5-53.1)	49.1 (26.6-94.6)
Readmission to ICU	53 (3.4)	103 (5.8)
Postoperative Hospital length of stay	3 (2-6)	6 (5-9)
30-day readmission	75 (4.8)	137 (7.8)

TIA: Transient Ischemic Attack; PRBC: Packed red blood cells; ICU: Intensive care unit; TAVR: Transcatheter aortic valve replacement; SAVR: Surgical aortic valve replacement.

Table 4: Logistic regression Odds ratio for death and individual procedure complications SAVR and TAVR-Unadjusted analysis

	TAVR (n=1572)		SAVR (n=1765)	
Outcomes	**Odds ratio 95%CI**	**p-value**	**Odds ratio 95%CI**	**p-value**
Acute kidney injury	19.56 (8.01-47.76)	<0.0001	37.50 (17.91-78.49)	<0.0001
Stroke	1.06 (0.14-7.98)	0.95	2.18 (0.66-7.24)	0.20
Renal failure requiring dialysis	23.01 (7.49-70.69)	<0.0001	26.14 (10.63-64.29)	<0.0001
Re-exploration for bleeding (major vascular complications, mediastinal re-exploration)	38.34 (6.29-233.78)	<0.0001	12.37 (3.81-40.19)	<0.0001
Myocardial infarction	----	---	----	-----
New permanent pacemaker	0.23 (0.03-1.67)	0.15	0.74 (0.18-3.07)	0.67
Deep sternal wound infection/mediastinitis	-----	----	----	---
Post-op new atrial fibrillation	0.65 (0.20-2.12)	0.48	0.90 (0.51-1.58)	0.71
Transfusion requirement				
PRBC	1.17 (1.04-1.31)	0.0075	1.18 (1.11-1.25)	<0.0001
Platelets	1.68 (1.29-2.20)	0.0002	1.33 (1.16-1.53)	<0.0001
Cryoprecipitate	1.34 (1.06-1.71)	0.02	1.20 (1.09-1.32)	0.0002
Fresh frozen plasma	1.58 (1.22-2.04)	0.0005	1.22 (1.12-1.32)	<0.0001
Pneumonia	7.98 (3.09-20.65)	<0.0001	13.17 (6.91-25.10)	<0.0001
Gastrointestinal bleeding	3.29 (0.96-11.26)	0.0581	5.78 (2.59-12.88)	<0.0001
Post-op prolonged ventilation	13.77 (7.69-24.66)	<0.001	9.22 (5.27-16.16)	<0.0001
Readmission to ICU	1.49 (0.45-4.90)	0.52	0.69 (0.21-2.25)	0.54
30-day readmission	1.02 (0.31-3.32)	0.98	1.45 (0.45-4.69)	0.54

PRBC: Packed red blood cells; ICU: Intensive care unit; TAVR: Transcatheter aortic valve replacement; SAVR: Surgical aortic valve replacement.

Table 5: Logistic regression analysis adjusted odds ratio for death and individual procedure complications transcatheter aortic valve replacement (TAVR)

Predictive Outcomes	OR (95%CI)	P-value
Re-exploration for bleeding (major vascular complications, mediastinal reexploration)	64.66 (7.59-550.88)	0.0001
Prolonged mechanical ventilation (<48hrs)	11.46 (5.91-22.19)	<0.0001
Post renal dysfunction	9.42 (2.96-29.98)	0.0001
Readmission to ICU	0.21 (0.05-0.93)	0.04

ICU: Intensive care unit; TAVR: Transcatheter aortic valve replacement.

Table 6: Logistic regression analysis adjusted odds ratio for death and individual procedure complications surgical aortic valve replacement (SAVR)

Predictive Outcomes	OR (95%CI)	P-value
Pneumonia	2.92 (1.22-6.99)	0.02
Prolonged ventilation	2.52 (1.14-5.56)	0.02
Post renal dysfunction	7.64 (2.98-19.62)	<0.0001
PRBC transfusion	1.08 (1.01-1.15)	0.03

PRBC: Packed red blood cells; SAVR: Surgical aortic valve replacement.

Table 7: Distribution of complications TAVR and SAVR

	TAVR (N=1572)	SAVR (N=1765)
Complication =0 N=1423	1031 (65.6)	392 (22.2)
Complication=1 N=962	323 (20.5)	639 (36.2)
Complication=2 N=525	125 (8.0)	400 (22.7)
Complication=3 N=219	46 (2.9)	173 (9.8)
Complication=4 N=115	27 (1.7)	88 (5.0)
Complication>5 N=93	20 (1.3)	73 (4.1)

TAVR: Transcatheter aortic valve replacement; SAVR: Surgical aortic valve replacement.

Table 8: Differential in cost TAVR-SAVR including and excluding cost of the implant

	TAVR without implant	**SAVR without implant**	**Differential cost TAVR-SAVR without implant**	**TAVR cost with implant**	**SAVR cost with implant**	**Differential cost TAVR-SAVR with implant**
No complication TAVR N=1031 SAVR N=392	$10,736	$15,200	$ - 4,464	$42,211	$21,124	$21,087
1 any complication TAVR N=323 SAVR N=639	$17,463	$18,113	$ - 650	$50,638	$24,115	$26,523
2 any complications TAVR N=125 SAVR N=400	$21,485	$21,589	$ -104	$55,879	$27,812	$28,066
3 any complications TAVR N=46 SAVR N=173	$30,375	$32,237	$ - 1,862	$66,083	$38,987	$27,096
4 any complications TAVR N=27 SAVR N=88	$40,571	$40,729	$ - 158	$78,448	$47,990	$30,458
5 or more any complications TAVR N=20 SAVR N=73	$55,529	$61,677	$ -6,147	$100,033	$68,972	$31,061

Transcatheter aortic valve replacement; SAVR: Surgical aortic valve replacement.

Table 9: Logistic regression analysis adjusted odds ratio for overall cost and individual procedure complications transcatheter aortic valve replacement (TAVR)

Predictive Outcomes	OR (95%CI)	P-value
Re-exploration for bleeding (major vascular complications, mediastinal reexploration)	4.32 (4.05-4.40)	<0.0001
Post-op renal dysfunction requiring dialysis	4.36 (4.24-4.46)	<0.0001
Prolonged mechanical ventilation (<48hrs)	4.36 (4.32-4.40)	<0.0001
Post-op pneumonia	4.36 (4.27-4.43)	<0.0001
Post-op permanent stroke	4.27 (4.20-4.33)	<0.0001
PRBC transfusion	3.68 (3.57-3.77)	<0.0001
Readmission to ICU	3.99 (3.89-4.08)	<0.0001

ICU: Intensive care unit; TAVR: Transcatheter aortic valve replacement.

Table 10: Logistic regression analysis adjusted odds ratio for overall cost and individual procedure complications surgical aortic valve replacement (SAVR)

Predictive Outcomes	OR (95%CI)	P-value
30-day mortality	3.83 (3.60-3.99)	0.03
Re-exploration for bleeding (major vascular complications, mediastinal reexploration)	4.02 (3.91-4.11)	<0.0001
Post-op pneumonia	4.11 (4.04-4.18)	<0.0001
Prolonged ventilation	4.09 (4.03-4.13)	<0.0001
Post-op renal dysfunction requiring dialysis	4.11 (3.87-4.27)	0.02
Post renal dysfunction	4.47 (4.41-4.54)	<0.0001
Post-op atrial fibrillation	3.28 (3.05-3.43)	0.01
Post-op permanent stroke	3.86 (3.68-3.98)	0.003
Post-op insertion IABP	3.88 (3.77-3.96)	<0.0001
Readmission to ICU	3.51 (3.20-3.69)	<0.0001
PRBC transfusion	3.71 (3.64-3.77)	0.03

PRBC: Packed red blood cells; SAVR: Surgical aortic valve replacement; IABP: intra-aortic balloon pump.