AMERICAN UNIVERSITY OF BEIRUT

# COMPARING PATIENT OUTCOMES OF TRANSCATHETER AORTIC VALVE IMPLANTATION VERSUS SURGICAL AORTIC VALVE REPLACEMENT

by
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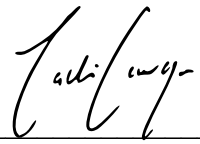

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# ABSTRACT
# OF THE THESIS OF

Dounia Ziad Iskandarani for Master of Science
Major: Nursing

Title: Comparing Patient Outcomes of Transcatheter Aortic Valve Implantation versus Surgical Aortic Valve Replacement

*Background:* Aortic stenosis (AS) is a valvular heart disease that predominantly affects older adults. Valve replacement is the treatment of choice for severe symptomatic AS. However, some older adults cannot undergo open surgical aortic valve replacement (SAVR) due to their higher risk for complications. Over the past decade, transcatheter aortic valve implantation (TAVI) has emerged as the recommended therapy for selected high surgical risk patients and was proven to be non-inferior to SAVR in intermediate and low risk patients.

*Aims:* The aims of the study were to investigate the outcomes of patients who underwent aortic valve replacement (in hospital and 30-day mortality, length of stay and short-term complications including infection and bleeding); and compare these outcomes in SAVR versus TAVI patients within all risk score categories.

*Method:* A retrospective review of 240 consecutive medical charts who underwent SAVR and TAVI at the American University of Beirut Medical Center was conducted to collect relevant data. Univariate descriptive statistics, bivariate correlational analyses, and multiple logistic regression analyses were performed to describe the sample, the study outcomes, and examine predictors of in-hospital and 30 day complications. The approval of the Institutional Review Board at the American University of Beirut was obtained prior to data collection.

*Results:* The mean age of the entire sample (N=240) was 79.49 (standard deviation [SD] = 5.76), with the SAVR population being significantly younger (77.14 ± 4.65) than the TAVI population (81.84 ± 5.83) (P <0.001). The SAVR group had a notably lower Society of Thoracic Surgeons (STS) score of 2.83 (SD = 2.04), whereas the TAVI patients' STS score was nearly double at 4.17 (SD= 2.21), P < 0.001. Patients undergoing TAVI had a relatively shorter average length of stay of 2.16 days (SD=1.88) than SAVR patients, which averaged at 7.11 days (SD=5.01), P < 0.001. There was no significant difference in mortality between the SAVR and TAVI patients (4 deaths in each group). There were no significant differences in complications between both SAVR and TAVI patients, except in type of arrhythmia. New onset atrial fibrillation was found in 42.9% of patients who underwent SAVR versus 0.8% in those who underwent TAVI (P<0.001). On the contrary, a new left bundle branch block was found in 14.4% of TAVI patients versus none in the SAVR patients (P<0.001). Both the type

of procedure and the STS score were significant predictors for in-hospital and follow up complications in the sample.

*Conclusion:* This study identified several important individual characteristics, procedural details, and post-procedure factors that are associated with increased risk of in-hospital and follow up complications. The findings of this study may have implications relevant to nursing education, practice and policy making in the context of assessment of outcomes in patients undergoing aortic valve replacement.

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# CHAPTER 1

# INTRODUCTION

Similar to populations in developed countries, the Lebanese population is aging. In 1995, the Lebanese citizens whose age was above 65 years old, i.e. older adults, constituted 7.1% of the population. By 2025, older adults are expected to constitute 10.2% of the Lebanese population (Chemali et al., 2008).

As the population age increases, the prevalence of age-related diseases will increase as well. Among age-related diseases, aortic stenosis (AS) comes on the top of the list. AS, a disease of older adults, is the most common form of cardiovascular disease in the Western world, exceeded only by hypertension and coronary artery disease (CAD) (Maganti et al., 2010). The prevalence of AS increases dramatically after the age of 65 years, reaching a prevalence of 5% after the age of 80 (Lung, 2018). With no medications proven to treat or attenuate the progression of AS, the only option remains aortic valve replacement (AVR).

Conventional surgical AVR (SAVR) involves an open cardiac procedure in which the native aortic valve is resected and replaced with a mechanical or biologic valve (Thaden et al., 2014). Unfortunately, SAVR is denied in 30-50% of the patients with severe AS due to their high-risk surgical background. The most common reasons for the high-risk status are advanced age, heart failure (HF), neurological concerns or other comorbidities (Thaden et al., 2014). Hence, much effort has been made to overcome this challenge, which led to an innovative and less invasive treatment option that can be adapted to patients with high-risk surgery, known as Transcatheter Aortic Valve Implantation (TAVI). This procedure involves inserting the valve through a

catheter that is inserted through the femoral artery, thus eliminating the need for sternotomy and cardiopulmonary bypass.

Several trials have studied outcomes of patients who underwent SAVR and TAVI in different patient populations including low-risk, intermediate-risk and high-risk patients (Smith et al., 2011; Leon et al., 2016; Mack et al., 2019). Even though both treatment options have been in practice in Lebanon, little is known about the outcomes of patients who undergo SAVR or TAVI.

### 1.1. Aortic Stenosis

The normal aortic valve is comprised of three thin leaflets attached to the aortic annulus and the wall, with a normal aortic valve opening of 3 to 5 $cm^2$ with unimpeded leaflet separation along the commissures during systole. AS wear and tear phenomena begin with leaflet thickening and sclerosis, with progression to hemodynamically significant narrowing, when the aortic valve area (AVA) is less than 1 $cm^2$ (Thaden et al., 2014). Even though aging is considered to be the most important contributor to the development of AS, there are other risk factors for AS similar to those associated with atherosclerotic vascular disease (Bonow & Greenland, 2015).

The pathophysiological processes driving AS can be divided into two phases (Pawade et al., 2015). The initiation phase is characterized by endothelial injury accompanied by infiltration of lipids, lipid oxidation and a pro-inflammatory response. Despite the clear similarities with atherosclerosis, three large randomized trials have failed to show any effect of statins on disease progression or clinical outcomes in AS patients (Pawade et al., 2015). The propagation phase is characterized by the appearance of osteoblast-like cells that coordinate progressive valvular calcium and bone matrix

deposition. This osteogenic phenotype involves many signaling molecules involved in bone formation, and is both self-perpetuating and highly regulated (Pawade et al., 2015). With the aortic valve becoming increasingly restricted, the consequent increase in left ventricular afterload leads to a hypertrophic response of the left ventricle, normalizing wall tension and maintaining cardiac output. However, with time, this hypertrophic response eventually decompensates, resulting in beginning of patient symptoms of dyspnea, angina, syncope and later heart failure and death (Everette et al., 2018).

Treatments such as medical management and balloon aortic valvuloplasty alone do not provide adequate clinical benefits for patients with severe AS (Lichtenstein et al., 2006; Sawaya et al., 2012). Prior to the Food and Drug Administration (FDA) approval of TAVI, SAVR was the conventional and gold standard treatment for patients with severe AS. Nevertheless, at least 30% of patients with symptomatic severe AS were denied SAVR because they were considered too high risk to undergo the surgery (Lung et al., 2005). This led to a less invasive treatment option that could be adapted to patients who had no surgical alternatives. The first percutaneous aortic valve replacement case was introduced in 2002. Today, subsequent clinical trials, including PARTNER and Evolut trials, have validated the clinical use of TAVI in a variety of patient settings and across different risk categories including inoperable, high risk, intermediate risk and recently low risk patients (Harold, 2017; Baron et al., 2019).

## 1.2. Interventions

### *1.2.1. SAVR.*

Until recently, SAVR was the only effective therapy for AS. SAVR requires the use of the heart lung machine to stop the heart and allow access to the aortic valve within the heart. The median sternotomy approach was the traditional approach to expose the heart for bypass and to gain access to the aortic valve. This approach allows excellent access to all cardiac structures but requires complete division of the sternum and sternal spreading. This disrupts the integrity of the chest wall in the early recovery phase, predisposing patients to infection and other complications (Ramlawi, Ramchandani & Reardon, 2011).

### *1.2.2. TAVI.*

Initially, TAVI procedures were performed exclusively via a surgical cut down. Over the past decade, the sheath diameter has been gradually reduced to 14–16 French with the last generation percutaneous heart valves. The trans-femoral (TF) access is currently the default access route, with superior outcomes than trans-apical route and other trans-vascular approaches such as the carotid, aortic, axillary, and caval-aortic. Alternative trans-vascular routes may be considered only in case of unsuitable femoral access (Akodad & Lefevre, 2018). With the refinement of the TAVI procedure, better patient pre-procedural screening, increased operator experience and device improvement, TAVI has become more simple and less time consuming, thus allowing a reduction in staff workload (Akodad & Lefevre, 2018). Recently, the focus has shifted toward an optimized procedural approach with a simplification of the procedure. This strategy involves percutaneous TF vascular access, conscious sedation and local

anesthesia, reduction or elimination of intra-procedural transesophageal echocardiography (TEE) guidance, reduction or elimination of balloon pre-dilatation before valve implantation, pre-specified care plans to encourage rapid ambulation and early hospital discharge, hence decreasing the patient's length of stay (O'Sullivan & Wenaweser, 2017).

### 1.3. Management Guidelines for Patients with AS

The European Society of Cardiology (ESC) and the American Heart Association (AHA) guidelines for the management of patients with AS differ in several aspects. The ESC stratifies patients according to their symptom status, while the AHA stratifies the patients according to their risk scores (STS and Euroscore II).

#### *1.3.1. The 2017 European Society of Cardiology (ESC) guidelines.*

In the case of asymptomatic status, the patients are further stratified according to their left ventricular ejection fraction (LVEF). In case LVEF is > 50%, if the patient is physically not active and without risk factors or without risk for surgery, the intervention can be postponed for six months and/or when symptoms occur. If the patient has a positive exercise test or if he/she has risk factors and low individual surgical risk, SAVR is recommended. If the LVEF is < 50%, SAVR is recommended.

In symptomatic patients, medical therapy is recommended in case their general condition or comorbidities make the intervention less likely to benefit them. If the patient has no other access routes that are favorable for TAVI, or if the patient is considered a low risk patient, SAVR is recommended. In case of intermediate or high-risk profile or favorable TAVI access, the heart team should evaluate the case

accordingly and decide on individual basis whether TAVI or SAVR is the best decision for the case (Baumgartner et al., 2017).

### *1.3.2. The 2017 American Heart Association/American College of Cardiology (AHA/ACC) guidelines.*

SAVR is recommended in patients at low surgical risk (STS or Euroscore II < 4%) and no other risk factors that are not included in these scores including porcelain aorta, frailty, sequelae of chest radiation (Evidence class I C). In patients who are at increased surgical risk (STS or Euroscore II > 4%), or with other risk factors that are not included in these scores including porcelain aorta, frailty or sequelae of chest radiation), the decision between SAVR and TAVI should be made by the heart team according to the individual patient characteristics, with TAVI being favored in older adults who are suitable for TF access (Class I B evidence). In patients with high surgical risk, either SAVR or TAVI is recommended (Class I evidence). Finally, TAVI is recommended in patients who are inoperable or with prohibitive surgical risk (Class I B evidence) (Nishimura et al., 2017).

## 1.4. Statement of Problem

By the end of 2019, the center chosen for this study, American University of Beirut Medical Center (AUBMC), had performed over 100 TAVIs since 2017, and over 100 SAVRs since 2015. Due to the lack of official and formal databases for AS and AVR patients in Lebanon, the outcomes of patients undergoing TAVI or SAVR in this population remain unknown. Moreover, predictors of the outcomes of these patients were not investigated, and thus ideal management strategies remain undetermined.

The aim of the study was to investigate the outcomes of AVR patients (in hospital and 30-day mortality, length of stay and short-term complications including infection and bleeding), and compare SAVR versus TAVI patients within all risk score categories. This will allow us to compare the findings of this study to those of other international registries and clinical trials, and to assess the clinical effectiveness and safety of SAVR and TAVI in the treatment of AS in the Lebanese population. This is the first study that will offer an insight about the outcomes of AVR patients in Lebanon and predictors of mortality and complications, both during hospitalization and at 30 days following discharge.

### 1.5. Significance of the Problem

Patient outcomes have important implications for clinical practice and institutions administratively. In general, there is a consensus that reducing length of stay (LOS) is beneficial for patients, especially older adults who are at higher risk for prolonged hospitalization-related complications, de-conditioning, and nosocomial complications (Kleinpell, Fletcher, & Jennings, 2008; Khairudin, 2012). Since the Lebanese population is an increasingly aging population, it is anticipated that more adults will be presenting for degenerative AS who are in need of treatment. Hence, identifying the factors that are associated with increased LOS, complications and mortality, and comparing those by intervention group will aid in better allocation of choice of intervention by the heart team and pre-procedure planning, thus enhancing the quality of patient care.

# CHAPTER 2

# LITERATURE REVIEW

The aim of this study is to compare the outcomes (immediate in-hospital outcomes and short-term outcomes at 30 Days post discharge) of patients who underwent TAVI and those who underwent SAVR. The purpose of conducting this literature review was to appraise the literature findings in relation to the outcomes of patients undergoing TAVI versus SAVR, identify potential variables that influence immediate in-hospital outcomes and short-term outcomes at 30-days post discharge, as well as provide a conceptual framework for this study.

## 2.1. PARTNER Trials

The Placement of Aortic Transcatheter (PARTNER) trials are meticulously designed, prospective randomized controlled trials that examined the safety and effectiveness of the balloon expandable (Edwards Sapien) transcatheter valves and valve delivery systems, in patients with AS at different risk levels (Leon et al., 2016; Mack et al., 2019; Smith et al., 2011).

### *2.1.1 PARTNER 1.*

This was a multicenter study, including 699 patients with severe AS, defined as an aortic valve area (AVA) less than 0.8 $cm^2$, plus either a mean valve gradient (MG) of at least 40 mm Hg or a peak velocity of at least 4.0 m/second. These patients were deemed to be at high risk for operative complications or death according to the risk model developed by the Society for Thoracic Surgeons (STS). High operative risk was

determined to be a score of at least 10% (Smith et al., 2011). This trial revealed that in patients with aortic stenosis who are at high risk for operative complications and death, SAVR and TAVI were associated with similar mortality at 30 days (3.4% in the TAVI group and 6.5% in the SAVR group, P=0.07) and one year (24.2% in the TAVI versus 6.8% in the SAVR group, P= 0.44). More patients undergoing TAVI had an improvement in symptoms at 30 days, but by one year, there was no significant difference between the two groups (Smith et al., 2011). However, at 30 days, major vascular complications, which included aortic dissection, aortic rupture, left ventricle perforation, access site injury such as femoral artery dissection or aneurysm, were significantly more frequent with TAVI than SAVR, while major bleeding and new onset atrial fibrillation were significantly more frequent in the SAVR cohort (Smith et al., 2011). TAVI patients had a significantly shorter length of stay in the intensive care unit (ICU) than SAVR patients (3 days, vs. 5 days) and a shorter index hospitalization (8 vs. 12 days). Ultimately, the findings of this trial suggested that TAVI is a safe alternative for patients who are high risk for surgery with the big first generation devices.

### *2.1.2. PARNTER 2.*

After several small centers reported expanding the use of TAVI to intermediate risk patients, and since most surgical candidates were at low or intermediate risk, the PARTNER 2 trial evaluated the two procedures, SAVR and TAVI, involving intermediate-risk patients, to validate the expansion of use of TAVI to such a population. In this trial, 2,032 intermediate risk patients were enrolled. Intermediate risk was defined as an STS score between 4% and 8%. Again, in intermediate- risk patients with severe symptomatic aortic stenosis, TAVI and SAVR were similar with

respect to the primary end point of death or disabling stroke for up to two years (21.1% in the SAVR group and 19.3% in the TAVI group), and resulted in a similar degree of reduction of cardiac symptoms with P=0.97 (Leon et al., 2016). TAVI resulted in lower rates of acute kidney injury (AKI), severe bleeding, and new-onset atrial fibrillation compared to SAVR, while SAVR resulted in fewer major vascular complications and less paravalvular aortic regurgitation (Leon et al., 2016). TAVI patients had a significantly shorter duration of stay in the ICU than did those in the surgery group (median, 2 vs. 4 days), as well as a shorter index hospitalization (6 days vs. 9 days) (Leon et al., 2016). Again, this trial supported the safety of TAVI as an alternative for patients with severe symptomatic aortic stenosis who are at intermediate risk for surgery.

### *2.1.3. PARNTER 3.*

After establishing that TAVI and SAVR had similar outcomes in patients at high and intermediate risk, the PARTNER 3 study aimed to evaluate the outcomes of patients who underwent TAVI vs SAVR in younger patients with low risk profiles. In this trial, 1,000 patients were recruited from 71 centers. Low risk was defined as an STS score < 4%. Among patients with severe AS who were at low risk of death with surgery, the rate of the composite of death, stroke, or re-hospitalization at one year was significantly lower with TAVI (8.5%) than SAVR (15.1%) (Mack et al., 2019). At 30 days, TAVI resulted in significantly lower rates of new onset atrial fibrillation compared to SAVR. TAVI also resulted in a shorter index hospitalization than SAVR and a lower risk of a poor treatment outcome (death or a low Kansas City Cardiomyopathy Questionnaire score, which represents worse clinical heart failure

symptoms and quality of life) at 30 days. There were also no significant differences between the TAVI and SAVR groups with regards of major vascular complications, new permanent pacemaker implantations, or moderate or severe paravalvular regurgitation. This trial revealed the non-inferiority, if not superiority of TAVI over SAVR in patients with severe symptomatic AS who are at low risk for surgery.

### 2.2. NOTION Trial

The Nordic Aortic Valve Intervention (NOTION) trial was the first to randomize all-comers with severe native aortic valve stenosis to either transcatheter aortic valve replacement (TAVR) with the CoreValve (Medtronic) self-expanding bio-prosthesis or SAVR, including a lower-risk patient population (Søndergaard et al., 2016). After two years, the primary outcome measure, a composite of all-cause mortality, stroke, or myocardial infarction at one year, was not statistically different between TAVI and SAVR. The 2-year results of the trial demonstrated the continuous safety and effectiveness of the TAVI procedure in all severe aortic stenosis patients, but with TAVI having higher rates of aortic regurgitation (AR) and pacemaker implantation in comparison to SAVR, while SAVR having higher rates of new onset atrial fibrillation than TAVI cases (Søndergaard et al., 2016).

### 2.3. Variables that Influence Patient Outcomes

In the studies reviewed, particularly the PARTNER trials, clinical variables related to the procedure, including procedural complications, and the patients' individual characteristics were found to play a crucial role in determining the outcomes of patients. The STS risk model was designed to predict operative morbidity and

mortality after adult cardiac surgery, including SAVR. The STS score now plays an important role in predicting morbidity and mortality in TAVI procedures (Balan et al., 2016). For aortic valve replacement (AVR), surgical or transcatheter, the STS score includes different variables consisting of demographic variables, risk factors including comorbidities, previous cardiac interventions, pre-admission cardiac status and hemodynamic stability, pre-AVR workup findings (CT scan and cardiac catheterization findings), and operative status (elective or urgent). Some risk factors are not captured in the STS score, which include porcelain aorta, frailty and hostile chest, even though these factors are considered during patient evaluation (Kappetein et al., 2012).

The Valve Academic Research Consortium (VARC) is a European consensus document that lists standardized definitions of clinical endpoints. The goal of VARC is to arrive at a consensus for selecting appropriate clinical endpoints and standardizing definitions for single and composite clinical endpoints (Zhang & Kolominsky-Rabas, 2017). Recently, an updated version of VARC, the VARC-2, consists of all-cause mortality; cardiovascular and non-cardiovascular mortality (within 30 days), mortality within one year, as well as complications including myocardial infarction, stroke, bleeding, acute kidney injury (AKI), vascular complications (minor and major), and new pacemaker implantation (Zhang & Kolominsky-Rabas, 2017). VARC-2 maintains the original recommendations to use echocardiography as the primary imaging modality for the assessment of prosthetic valve function (Kappetein et al., 2012). The suggested time points for routine follow-up transthoracic echocardiography (TTE) following valve implantation are immediately (before discharge) following the implantation for TF approach, six months following implantation, one year following implantation, and

yearly thereafter. At these endpoints, prosthetic aortic valve stenosis, regurgitation and paravalvular leak (PVL) should be reported (Kappetein et al., 2012).

### 2.4. Study Outcomes

Based on the literature review, the outcomes of the study are as follows:

- The primary outcome is all-cause mortality at 30 days following the procedure (TAVI or SAVR).
- Secondary outcomes include cardiovascular mortality, stroke, cardiac and prosthetic aortic valve complications (myocardial infarction, new onset atrial fibrillation and conduction abnormalities, new pacemaker insertion, PVL, and endocarditis), acute kidney injury (AKI), access-related vascular and bleeding complications, and length of stay.

### 2.5. Conceptual Framework of the Study

Based on the findings in the literature and consultation with clinical experts, a clinical pathway was developed to be used as the underlying conceptual model for this study. In Figure 1, the clinical pathway for aortic valve replacement is divided into four phases based on the clinical process at the study center. The first phase is the “pre-procedural phase”, which extends from the time of referral of the patient by his cardiothoracic surgeon or interventional cardiologist for AVR, until procedure time. Then, the second phase, “intra-procedural phase”, starts at the time of the procedure until its end time. The third phase is the “post procedure phase” and it spans across all the days spent in the coronary care unit (CCU) post procedure. Finally, the fourth phase,

the “outcomes phase”, extends from the point of discharge until 30-days following the SAVR surgery or TAVI procedure.

The following model illustrates the four consecutive phases of the clinical pathway at the American University of Beirut Medical Center, which will be adopted in this study.

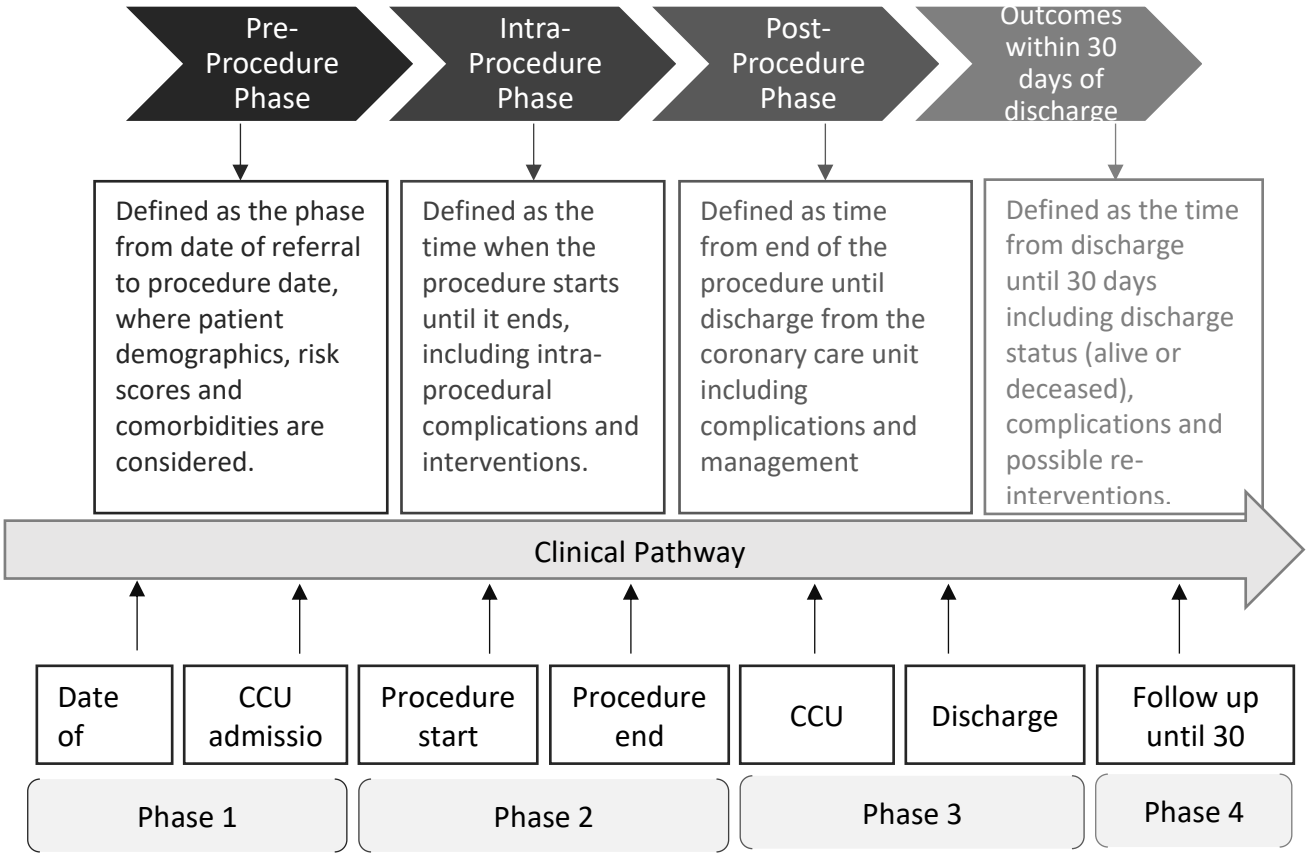


*Figure 1.* Clinical Pathway Model.

Based on figure 1, Figure 2 was built to describe the relevant variables previously discussed in the literature review and categorize them into the appropriate phases.

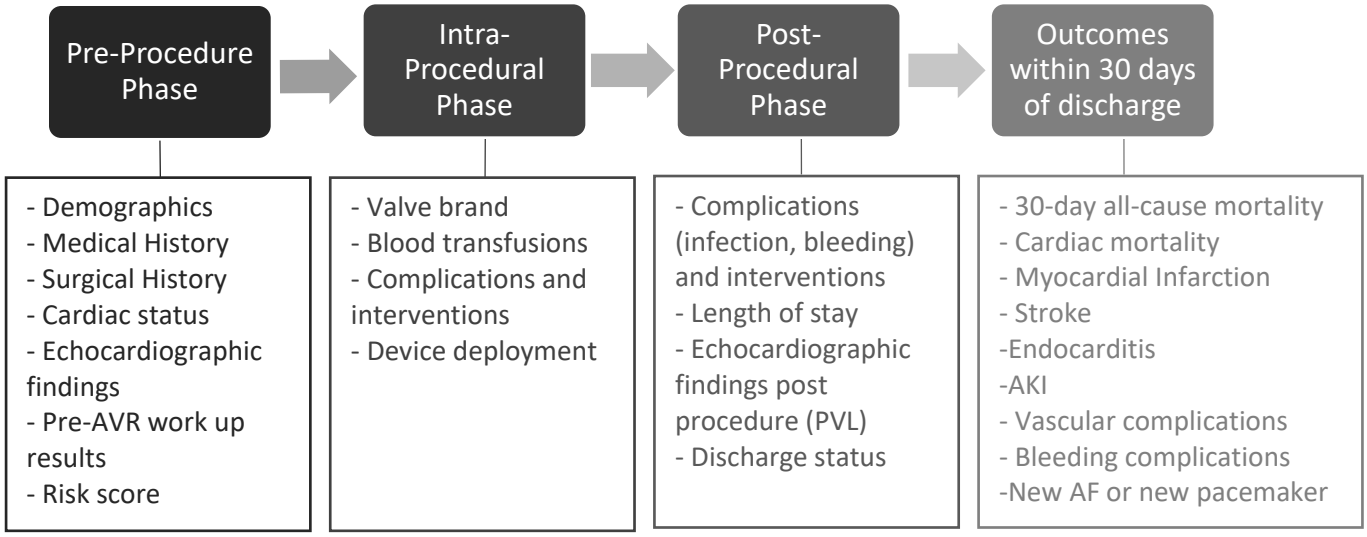


*Figure 2.* Predictors and Outcomes of TAVI vs SAVR.

### *2.5.1. Pre-procedural phase.*

The first phase is the "pre-procedural phase", typically from the date of referral of the patient by his cardiothoracic surgeon or interventional cardiologist for the AVR procedure. During this phase, the individual characteristics of the patient will be taken into consideration, including demographics such as age and gender, and the STS risk score.

The medical history includes history of cardiac diseases (including heart failure and coronary artery disease), pulmonary diseases including chronic obstructive pulmonary disease (COPD), cerebrovascular accidents (CVA) including transient ischemic attacks (TIA), peripheral artery disease (PAD) such as carotid stenosis, estimated glomerular filtration rate (eGFR) to assess kidney function, and finally conduction abnormalities including atrial fibrillation (AF), bundle branch block (right or left BBB). History of cardiac surgery includes previous coronary artery bypass graft

(CABG), percutaneous coronary interventions (PCI) and device implantation such as a pacemaker, an implantable cardioverter defibrillator (ICD) or cardiac re-synchronization therapy with defibrillator (CRTD). Cardiac status and hemodynamic stability include the status of the patient if he had a myocardial infarction (MI) within 72 hours, heart failure exacerbation within 72 hours, or if he were in cardiogenic shock.

Pre-TAVI work up includes a CT Angiogram of the Chest, Abdomen, and Pelvis, in which the aortic valve morphology is revealed to be bicuspid or tricuspid. This also includes a cardiac catheterization, to rule out vessel diseases or abnormal coronary arteries. Echocardiographic findings include the LVEF, AVA, and MG.

### *2.5.2. Intra-procedural phase.*

The second phase, "intra-procedural phase", which starts at the time of the procedure until its end time, includes all procedural details; such as valve brand (balloon expandable or self-expanding). Intra-procedural complications will be included according to the VARC-2 criteria, and if necessary these include all emergent interventions that needed to take place. The complications include all-cause mortality, cardiac complications (such myocardial infarction, cardiac tamponade or dissection), device complications such as device embolization or thrombosis, stroke, bleeding, vascular complications, and conduction abnormalities.

### *2.5.3. Post-procedural phase.*

The third phase is the "post procedure phase" and it spans across all the days spent in the coronary care unit (CCU) post procedure. It includes post-procedural complications, namely infection and bleeding and possible interventions, as well as

echocardiogram findings that assess the valve function and paravalvular leak (PVL). The third phase is also defined as the length of the stay (LOS).

### *2.5.4. Outcomes within 30-days post discharge.*

The fourth phase, the "outcomes phase", extends from the point of discharge until 30 days post-op. Similarly, this includes the 30-day all-cause mortality and complications including cardiac, renal and vascular complications and bleeding, and/or re-interventions.

## 2.6. Simplified Conceptual Model

Based on figure 1 and figure 2, a simplified conceptual model is shown to guide the study procedures: data collection and statistical analysis.

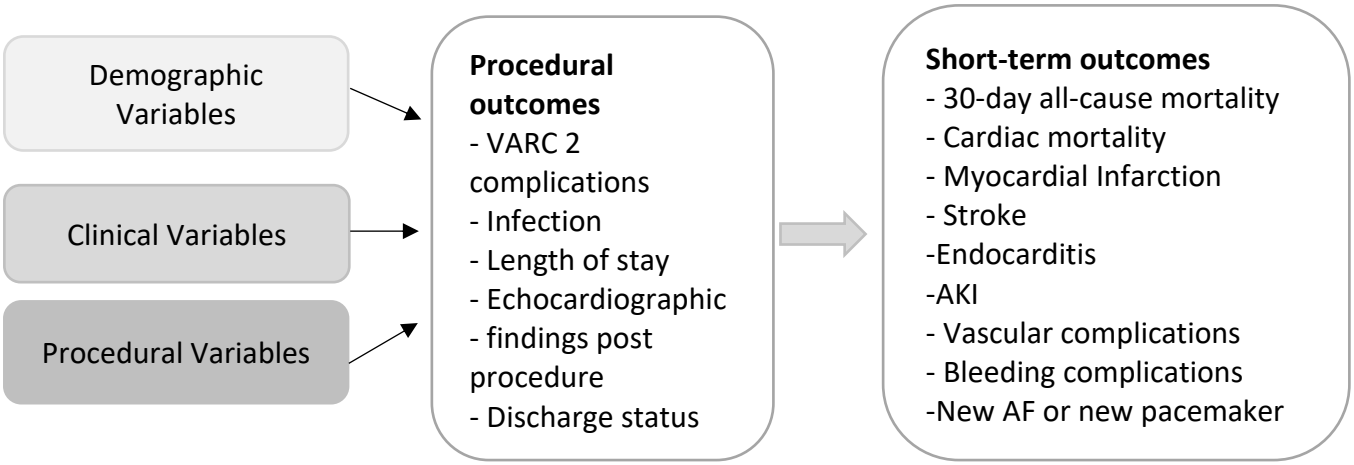


*Figure 3.* Simplified TAVI vs SAVR Conceptual Model.

In line with the above, the specific aims of the study are:

1. To examine short-term outcomes (in hospital and 30-day mortality) and procedural outcomes, namely length of stay and complications, in patients with AVR treated at AUBMC.
2. To compare the outcomes of patients undergoing SAVR to those undergoing TAVI.

2.a. Hypothesis: Patients undergoing TAVI will have significantly lower in-hospital and 30-day mortality rates, and lower complication rates compared with those who undergo SAVR.

3. To identify the predictors of mortality and complications in the sample.

# CHAPTER 3

# METHODOLOGY

## 3.1. General Description of the Research Design

A retrospective observational/descriptive study design was used to answer the research questions**.** Data were retrieved from the medical records at the American University of Beirut Medical Center. To ensure the consistency in data extraction and enhance the quality of data extracted, the Data Collection Form was developed and attached, with its code manual (see Appendix).

The medical records of all consecutive patients who underwent TAVI and SAVR at AUBMC from January 2011 to June 2020 were accessed. This period for data collection was chosen for two reasons. First, due to the consistency in the techniques used in SAVR with one surgeon performing surgeries, patients from January 2011 to June 2020 were included. In the case of TAVI, the program at AUBMC started in 2013. The first few years of the TAVI program witnessed a very small number in procedures (around one per year), and these were performed with older generation devices and using inconsistent techniques. Therefore, TAVI patients that were included are those who underwent the procedure between January 2017 and June 2020.

## 3.2. Study Sample and Eligibility Criteria

### *3.2.1. Eligibility criteria.*

Eligible patients included those aged 70 years or older, with severe degenerative AS with or without symptoms (see Table 1). As patients who undergo TAVI are older in age, all patients were chosen to be 70 years or older in an attempt to

compare groups that are as homogenous as possible by controlling for age. Patients must be suitable for both SAVR and TAVI, hence patients with porcelain aorta who can only undergo TAVI and patients with bicuspid valve who are only undergoing SAVR were excluded. Patients with previous aortic valve interventions (including aortic balloon valvuloplasty) were excluded to eliminate confounding factors. Table 1 displays the sample inclusion and exclusion criteria.

Table 1

*Inclusion and Exclusion Criteria*

| Inclusion criteria |
| --- |
| • Severe degenerative AS with AVA <1.0 $cm^2$, MG > 40mmHg, or confirmed low-flow low-gradient AS<br>• Age 70 years old or older<br>• Candidate for both SAVR and TAVI (based on clinical and anatomical characteristics) |
| Exclusion criteria |
| • Mixed aortic valve disease (AS and AR with predominant AR grade 3+)<br>• Previous SAVR<br>• Echocardiographic evidence of intra-cardiac mass or tumor<br>• Stroke or TIA within 30 days<br>• Hemodynamic instability requiring inotropic therapy or hemodynamic support<br>• Severe ventricular cardiomyopathy with LVEF <20%<br>• Porcelain aorta<br>• Bicuspid aortic valve |

*Legend.* AS, aortic stenosis; AVA, aortic valve area; MG, mean gradient; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; AR, aortic regurgitation; PCI, percutaneous coronary intervention; TIA transient ischemic attack; LVEF, left ventricular ejection fraction.

### *3.2.2. Sample size.*

The study was designed to test the hypothesis that TAVI is associated with lower mortality and complications compared to SAVR. A power analysis revealed that, when using logistic regression, 25 patients are needed for every predictor. Based on the study of Søndergaard et al. (2016), and estimated occurrence of the primary outcome measure (mortality) of 15% in the SAVR group and 5% in the TAVI group during the first year following the procedure, corresponding to an absolute risk reduction of 10% and a chosen power of $1 - \beta = 80\%$ and two-sided $\alpha = 5\%$, then a sample of 240 patients (120 per group) is needed.

## 3.3. List of Variables

As discussed in the literature review chapter and based on the conceptual model, a collection of variables was selected and classified against the procedural phases as shown in table 2.

Table 2

*List of Variables*

| **Pre-Procedural Phase Variables** | | |
|---|---|---|
| ***Demographic Variables*** | ***Medical History*** | ***Surgical History*** |
| Age (years) | HTN, DM, DL | Previous PCI |
| Gender (Male/Female) | CAD, PAD | ICD/ CRTD/ PPM |
| Smoking Status (Smoker or none) | Previous MI | Previous CABG |
| BMI ($kg/m^2$) | Previous Stroke | ***Pre-op Status*** |
| BSA ($m^2$) | BBB (Right/Left) | STS score (%) |
| ***Echocardiographic Findings*** | Atrial Fibrillation | STS Category |
| AVA ($cm^2$) | Chronic Lung Disease | eGFR |
| MG (mmHg) | Heart Failure | |
| LVEF (%) | | |

| | |
|---|---|
| **Intra-Procedural Phase Variables** | |
| ***AVR Procedural Data*** | ***Complications*** |
| Valve brand | MI, tamponade |
| Anesthesia type | Cardiac arrest |
| Total procedure time (minutes) | Conduction abnormality |
| Cross Clamping Time (minutes) | TIA, stroke |
| Aborted procedure | Vascular complications (minor, major) |
| Access site | Bleeding (minor, major, fatal) |
| Intra-procedural death | Valve embolization, migration or thrombosis |
| Blood transfusion (units) | |
| **Post-Procedural Phase Variables** | |
| ***LOS*** *(days)* | ***Complications*** |
| ***Discharge status*** *(alive/ deceased)* | MI, tamponade |
| | Endocarditis |
| ***Echocardiographic findings*** | Conduction abnormality (new PPM) |
| MG (mmHg) | TIA/ Stroke |
| PVL | AKI (with or without dialysis) |
| | Vascular complications (minor, major) |
| | Bleeding (minor, major, fatal) |
| | Pleural/pericardial effusion |
| | Pneumonia |
| **Outcomes within 30 days** | |
| ***Status*** *(alive/ deceased)* | ***Complication/ requiring re-admission*** |
| *All-cause mortality* | MI, tamponade |
| | Endocarditis |
| | Conduction abnormality (new PPM or AF) |
| | TIA/ Stroke |
| | AKI (with or without dialysis) |
| | Vascular complications (minor, major) |
| | Bleeding (minor, major, fatal) |
| | Pleural/pericardial effusion |
| | Pneumonia |

*Legend.* AKI, acute kidney injury; AVA, aortic valve area; BBB, bundle branch block; BMI, body mass index; BSA; body surface area; CABG: coronary artery bypass graft; CAD, coronary artery disease; CRTD, cardiac re-synchronization therapy with defibrillator; DL, dyslipidemia; DM, diabetes mellitus; eGFR, estimated glomerular filtrate rate; HTN, hypertension; ICD, implantable cardioverter defibrillator; LOS, length of stay; LV, left ventricle; LVEF, left ventricular ejection fraction; MG, mean gradient; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; PPM, permanent pacemaker; PVL, paravalvular leak; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation; TIA, transient ischemic attack.

### 3.4. Level of Measurement of the Variables

Since most of the variables in this study are self-explanatory, such as demographics and echocardiographic findings, only variables such as risk scores and complications are described next. Most variables including the mortality outcome were expressed as categorical variables, except for STS, which is a continuous variable.

#### *3.4.1. STS score.*

According to the Society of Thoracic Surgeons (STS), the STS score was designed to predict operative morbidity and mortality after adult cardiac surgery. The STS score is a sensitive predictor of 30-day mortality for both SAVR and TAVI (Balan et al., 2016). As noted above, the STS score is based on demographic variables, risk factors including comorbidities, previous cardiac interventions, pre-admission cardiac status and hemodynamic stability, pre-AVR workup findings (CT scan and cardiac catheterization findings), and operative status (elective or urgent). Patients are considered low risk for surgery if the STS score is less than 4%, intermediate risk if the score falls between 4% and 8%, and high risk if the score is greater than 8%.

#### *3.4.2. All-cause mortality.*

3.4.2.1. Cardiovascular mortality.

Based on the VARC-2 classification, cardiovascular mortality is defined as death due to proximate cardiac cause that is immediate death directly related to a cardiac cause, such as a myocardial infarction, cardiac tamponade or heart failure exacerbation. It can also be caused by non-coronary vascular conditions such as a stroke, pulmonary embolism, ruptured aortic aneurysm, or dissecting aneurysm. In

addition, all procedure-related deaths including complications of the procedure or treatment for a complication of the procedure is considered as cardiovascular death (Kappetein et al., 2012).

3.4.2.2. Non-cardiovascular mortality.

Non-cardiovascular mortality is defined as death in which the primary cause is due to another condition such as cancer.

### *3.4.3. Myocardial infarction.*

According to the VARC-2 criteria, within 72 hours from the TAVI or SAVR procedure, an MI is based on clinical criteria and cardiac biomarkers. Any new ischemic signs such as new ST-segment changes, new pathological Q waves, or hemodynamic instability, AND elevated cardiac biomarkers (peak value exceeding 15x the upper reference limit for troponin or 5x for CK-MB) will be considered a peri-procedural MI.

After 72 hours from the procedure, new ECG changes indicative of new ischemia such as new ST-T changes or new left bundle branch block (LBBB), or pathological Q-waves, or sudden unexpected death are indicative of a spontaneous MI (Kappetein et al., 2012).

### *3.4.4. Stroke and TIA.*

Any acute episode of focal or global neurological deficit with at least one of the following: change in the level of consciousness, hemiplegia, hemiparesis, numbness or sensory loss affecting one side of the body, dysphagia or aphasia, or other neurological symptoms consistent with stroke should be assessed by a neurologist (Kappetein et al.,

2012). If these symptoms resolve within less than 24 hours, with no neuroimaging demonstrating a hemorrhagic stroke or infarct, then it is a transient ischemic attack (TIA). In case these symptoms continue for more than 24 hours, or neuroimaging confirms a hemorrhage or infarct, then this is a stroke. A stroke will be classified as ischemic (caused by infarction of the central nervous system due to a thrombus in one of the cerebral arteries) or hemorrhagic (caused by intra-parenchymal, intraventricular, or subarachnoid hemorrhage) (Kappetein et al., 2012).

### *3.4.5. Bleeding.*

#### 3.4.5.1. Fatal bleeding.

According to the Bleeding Academic Research Consortium (BARC), a fatal bleeding is any bleeding that is present in a critical organ such as intracranial, intra-spinal, intraocular, or pericardial bleeding that necessitates pericardiocentesis, or intramuscular with compartment syndrome (Kappetein et al., 2012). Fatal bleeding is also considered to be any bleeding that causes hypovolemic shock or severe hypotension necessitating vasopressors or a surgical intervention. Clinically, fatal bleeding can be defined as a drop of hemoglobin more than 5 g/dL or blood transfusion, requiring four or more units of whole blood or packed red blood cells (pRBC).

#### 3.4.5.2. Major bleeding.

Major bleeding is defined as a drop in the hemoglobin level of at least 3 g/dL, or necessitating blood transfusion of two or three units of whole or pRBCs, or any bleeding that causes hospitalization or permanent injury, or requires surgical intervention but does not meet the criteria for fatal bleeding.

3.4.5.3. Minor bleeding.

Any bleeding that is minimal such as an intravenous access site hematoma.

### *3.4.6. Acute kidney injury.*

Acute kidney injury can be defined as an increase in serum creatinine or by urine output within 48 hours. AKI will be defined as an increase in creatinine at least 0.3 mg/dL more than baseline, or urine output that is less than 0.5mL/kg/h for at least 6 hours, with or without a new requirement for hemodialysis (Kappetein et al., 2012).

### *3.4.7. Vascular complications.*

Based on the VARC-2 criteria, vascular complications can be divided into two categories, major and minor complications.

3.4.7.1. Major vascular complications.

Major vascular complications include any aortic dissection, aortic rupture, annulus rupture or left ventricle perforation. All access site or access-site related vascular injury such as dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudo-aneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure leading to death are considered major complications. Major complications also include distal embolization from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage. Any unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment, or access site related nerve injury that might necessitate surgery, will be considered a major vascular complication.

3.4.7.2. Minor vascular complications.

Minor vascular complications are similar to the major complications but do not result in death, life threatening major bleeding, amputation or irreversible end-organ damage.

### *3.4.8. Conduction disturbances and arrhythmias.*

During the 72-hour monitoring phase post procedure, any new or worsened cardiac conduction disturbance that might or might not require a new pacemaker was recorded. This included any new or worsened first degree atrioventricular (AV) block, second degree AV block, third degree AV block, incomplete or complete right bundle branch block (RBBB), incomplete or complete left bundle branch block (LBBB), left anterior fascicular block or left posterior fascicular block, atrial fibrillation or any new arrhythmia that resulted in hemodynamic instability or requires therapy.

### *3.4.9. Other complications.*

Other complications that were noted included conversion of TAVI to open sternotomy secondary to any procedure related complication, or conversion from SAVR to TAVI due to severely calcified aortic valve.

Another complication that might occur during TAVI and were noted is coronary obstruction by the valve prosthesis itself, the native leaflets, calcification or dissection during the TAVI procedure. Any ventricular septal perforation, cardiac tamponade associated with hemodynamic instability and endocarditis were also recorded. Any valve related complication such as valve thrombosis or mal-positioning (migration, embolization or ectopic deployment) were also documented.

### 3.5. Ethical Considerations

The approval of the Institutional Review Board at the American University of Beirut was obtained prior to data collection. Medical record review was initiated after securing approval of the administration of the affiliated Medical Center. As this is a retrospective medical record review, no consent was secured from the patients. The medical records officers provided access to the patients' files to the student, who transcribed data on the data collection form (see Appendix).

Confidentiality of the records was maintained to the maximum extent possible. Personal information was key-coded. Subjects' personal information were handled at all times in accordance with appropriate confidentiality standards and all applicable data protection and privacy regulations. To ensure confidentiality, the assigned student retrieved data from the patient's medical records discretely and entered them into the excel sheet in a coded manner. The participants' names were kept on the Principal Investigator's password protected database and were linked only with a study identification number for this research. All computer entry and networking programs were done using study identification codes. The information from the data collection sheets were entered on the SPSS sheet and the papers shall be stored for a period of three years after study completion, according to AUB policy. Stored data were secured in lockers and only accessible to the PI. After this duration of time, the destruction of the data collection sheets will be done by shredding the papers and electronic files will be deleted.

### 3.6. Statistical Analysis

To appropriately address the study aims, a step wise approach was executed.

Step 1: A data collection form (Appendix 1) was developed based on the literature review, clinical experience, and consultation with experts at the study center. A corresponding code manual (Appendix 2) was developed and based on the VARC-2 criteria and STS ACC TAVI registry. Once data collection was done on an excel file, it was imported into the Statistical Package for Social Sciences (SPSS) software for statistical analysis.

Step 2: In SPSS, univariate descriptive statistical analyses were performed to describe the measures of central tendency and distributions of the variables. Frequencies and percentage were used to describe the categorical variables whereas means and standard deviations were used for continuous variables.

Bivariate descriptive analysis was performed to compare the differences between SAVR and TAVI on all the variables. Differences in continuous variables between the TAVI and SAVR groups were examined using the independent sample Student t-test. Differences in categorical variables between the two groups were examined using the Chi-squared test or Fisher's exact test as appropriate. The effect of using TAVI versus SAVR on mortality and complications parameters were presented as odds ratios (ORs) and 95% confidence intervals (CIs).

Step 3: An analysis of all complications (intra-operatively and at discharge) was performed to determine the relationship between complications and type of procedure and STS category of patients.

Step 4: An analysis of all complications at one month post procedure was performed to determine the relationship between complications and the type of procedure and STS category of patients.

Step 5: Multiple logistic regression analysis was performed to predict the outcomes that differed significantly between the two groups. For this analysis, the presence of any complication was coded as zero if none and 1 if any complication occurred, for both in-hospital complications and 30-day complications at follow up.

# CHAPTER 4

# RESULTS

In this chapter, a sample description is first provided. The results of bivariate descriptive statistical analysis of demographic and pre-operative echocardiography variables is discussed, followed by univariate descriptive analysis of operative variables. Then, bivariate analysis of intra-operative, post-operative and follow up complications are presented. Finally, results of logistic regression analysis with select variables (STS and type of procedure) are presented.

## 4.1. Demographic Characteristics

### *4.1.1. Sample description.*

Table 4.1 shows the sample characteristics for the whole sample and by group (TAVI and SAVR). As shown in Table 4.1, the mean age of the entire sample (N=240) was 79.49 (standard deviation [SD] = 5.76), with the SAVR population being significantly younger (77.14 ± 4.65) than the TAVI population (81.84 ± 5.83) (P <0.001). There was no significant difference in gender between the two groups, where in both SAVR and TAVI patients the male gender accounted for almost half of the group (55.8% and 48.3% respectively, P=0.245).

### *4.1.2. Risk scores.*

There was a noteworthy dissimilarity in the STS score between the SAVR and the TAVI patients in which the SAVR group had a notably lower STS score of 2.83 (SD

= 2.04) whereas the TAVI patients' STS score was nearly double at 4.17 (SD= 2.21), P < 0.001. This is significantly reflected in the STS category of the patients undergoing AVR, with 85% of the patients who underwent SAVR in the low risk category versus 55% of those who underwent TAVI. Moreover, intermediate and high risk patients were more frequent in the TAVI population (35.8% and 9.2% respectively) than in the SAVR population (10.8% and 4.2% respectively).

#### *4.1.3. Body measurements.*

Body measurement variables varied significantly between the two groups, with the BSA of patients who underwent SAVR markedly higher (1.82 ± 0.20) than that of those who underwent TAVI (1.77 ± 0.21) (P <0.05). The other body measurement variable, the BMI, was significantly different among the two groups. Patients who underwent SAVR tended to be more overweight (44.9%) and obese (47.5%) than those who underwent TAVI with overweight patients at 39% and those obese 38.1%; overall p value = 0.006.

#### *4.1.4. Medical history.*

Comorbidities were well balanced between the two groups except for hypertension, eGFR and arrhythmias. Patients who underwent TAVI had a slightly impaired (30-59) glomerular filtration rate (50.8%) more than those who underwent SAVR (25%), P <0.001. More patients in the TAVI group had hypertension than in the SAVR group (99.2% vs. 91.7%, p = 0.01). Patients who underwent TAVI had more frequent ECG disturbances including more frequent atrial fibrillation (28.3% vs. 10.8%) and left bundle branch block (12.5% vs.4.2%), P < 0.001 and P=0.02, respectively.

The majority of patients (61%) had heart failure with preserved ejection fraction, with only 8% who had heart failure with a reduced ejection fraction, with no difference between the two groups. There was a significant variance between the two groups in terms of previous coronary interventions. TAVI patients were more prone to have either prior PCI (24% vs.10.0%) or CABG (17.5% vs. 2.5% ) than SAVR patients; P=0.004 and P <0.001, respectively.

### 4.1.5. Length of stay.

Patients undergoing TAVI had a relatively shorter period length of stay of an average of 2.16 days (SD=1.88) than SAVR patients which averaged at 7.11 days (SD=5.01), P < 0.001.

Table 3

*Baseline Characteristics of AVR patients (N = 240)*

| | **Total N=240** | **SAVR (N=120)** | **TAVI (N=120)** | **P-value** |
|---|---|---|---|---|
| **Age** (Mean ± standard deviation [SD]) | 79.49 ± 5.76 | 77.14 ± 4.65 | 81.84 ± 5.83 | **<0.001** |
| **Gender** (Males) | 125 (52.0) | 67 (55.8) | 58 (48.3) | 0.245 |
| **Society of Thoracic Surgeons Category** | | | | **<0.001** |
| *Low Risk* | 168 (70.0) | 102 (85.0) | 66 (55.0) | |
| *Intermediate Risk* | 56 (23.0) | 13 (10.8) | 43 (35.8) | |
| *High risk* | 16 (7.0) | 5 (4.2) | 11 (9.2) | |
| **STS Score** (Mean ± SD) | 3.49 ± 2.22 | 2.83 ± 2.04 | 4.17 ± 2.21 | **<0.001** |
| **Smoking Status** | 33 (14.0) | 17 (14.2) | 16 (13.3) | 0.851 |
| **Body Mass Index** ($kg/m^2$) | | | | **0.006** |
| *Underweight< 18.5* | 1 (0.4) | 0(0.0) | 1(0.8) | |
| *Normal: 18.5-24.9* | 35 (14.8) | 9 (7.6) | 26 (22.0) | |
| *Overweight: 25-29.9* | 99 (42.0) | 53 (44.9) | 46 (39.0) | |
| *Obese: > 30* | 101 (42.8) | 56 (47.5) | 45 (38.1) | |
| **Body Surface Area** | 1.79 ± 0.20 | 1.82 ± 0.20 | 1.77 ± 0.21 | **0.037** |
| **Hypertension** | 229 (95) | 110 (91.7) | 119 (99.2) | **0.010** |
| **Diabetes Mellitus** | | | | 0.605 |
| *On oral medication* | 72 (30) | 36 (30.0) | 36 (30.0) | |
| *On Insulin* | 9 (3.8) | 3 (2.5) | 6 (5.0) | |
| *Insulin +Medication* | 1 (0.4) | 0 (0.0) | 1 (0.8) | |

| | | | | |
|---|---|---|---|---|
| **Chronic Obstructive Pulmonary Disease** | 39 (16.0) | 17 (14.2) | 22 (18.3) | 0.382 |
| **Dyslipidemia** | 142 (59.0) | 68 (56.7) | 74 (61.7) | 0.431 |
| **Estimated Glomerular Filtration Rate** | | | | **<0.001** |
| *Dialysis* | 6 (2.5) | 2 (1.7) | 4 (3.3) | |
| *<29* | 8 (3.3) | 6 (5.0) | 2 (1.7) | |
| *30-59* | 91 (38) | 30 (25.0) | 61(50.8) | |
| *>60* | 135 (56.2) | 82 (68.3) | 53 (44.2) | |
| **Peripheral Artery Disease** | 5 (2.0) | 0 (0.0) | 5 (4.2) | 0.060 |
| **Cerebrovascular Accident** | 9 (3.7) | 2 (1.7) | 7 (5.8) | 0.171 |
| **Transient Ischemic Attack** | 4 (2) | 1(0.8) | 3 (2.5) | 0.622 |
| **Carotid Stenosis** | 2 (0.8) | 1 (0.8) | 1 (0.8) | 1.00 |
| **Heart Failure** | | | | 0.185 |
| *HFrEF* | 19 (8.0) | 8 (6.7) | 11(9.2) | |
| *HFpEF* | 146 (61.0) | 69 (57.5) | 77 (64.2) | |
| *HFrEF & HFpEF* | 17 (7.0) | 7 (5.8) | 10 (8.3) | |
| **Percutaneous Coronary Intervention** | 31 (13.0) | 12 (10.0) | 29 (24.0) | **0.004** |
| **Previous Coronary Artery Bypass Graft** | 24 (10.0) | 3 (2.5) | 21(17.5) | **<0.001** |
| **Implantable Cardioverter Defibrillatror** | 3 (1.2) | 0 (0.0) | 3 (2.5) | 0.247 |
| **Permanent Pacemaker** | 4 (2.0) | 1 (0.8) | 3 (2.5) | 0.622 |
| **Left Bundle Branch Block** | 20 (8.0) | 5 (4.2) | 15 (12.5) | **0.020** |
| **Right Bundle Branch Block** | 10 (4.0) | 3 (2.5) | 7 (5.8) | 0.333 |
| **Atrial Fibrillation** | 47 (20.0) | 13 (10.8) | 34 (28.3) | **0.001** |
| **Length of stay** (days) (Mean ± SD) | 4.63 ± 4.51 | 7.11 ± 5.01 | 2.16 ± 1.88 | **<0.001** |

*Legend.* HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons; TAVI, transcatheter aortic valve implantation. Values are count and % unless indicated otherwise

### 4.2. Pre-Operative Echocardiographic Findings

Pre-operative echocardiographic results including pre-operative LVEF, AVA, MG and AR for the SAVR and TAVI groups are presented in Table 4.2. As shown in the table, the two groups were homogenous, with no substantial disparity noted, particularly in systolic function.

Table 4

*Pre-Operative Echocardiographic Findings*

| | SAVR (N=120) | TAVI (N=120) | P-value |
|---|---|---|---|
| **Pre-LVEF** (%) | | | 0.637 |
| *<50%* | 17 (14.0) | 22 (18.0) | |
| **AVA** ($cm^2$)* | 0.76 ± 0.15 | 0.74 ± 0.16 | 0.380 |
| **MG** (mmHg)* | 50.58 ± 16.23 | 46.40 ± 14.11 | 0.107 |
| **Aortic Regurgitation** | | | 0.567 |
| *No* | 42 (35.0) | 44 (36.7) | |
| *Trace/Trivial* | 3 (2.5) | 6 (5.0) | |
| *Mild* | 75 (62.5) | 70 (58.3) | |

*Legend.* AVA, aortic valve area; LVEF, left ventricular ejection fraction; MG, mean gradient; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.
*These variables were skewed so Mann Whitney test was used.

### 4.3. Procedural Variables

Table 4.3 shows the results of the intra-procedural variables for both the SAVR and TAVI groups.

#### *4.3.1. TAVI.*

The average time of a TAVI procedure was 109 minutes (SD=40.16) and mainly local anesthesia (95%) was used, with only five patients requiring inotropic support. The main access was femoral (96.7%). Balloon expandable valves accounted for 40.3% of the cases versus self-expandable valves that accounted for the majority of the cases (59.7%).

#### *4.3.2. SAVR.*

All patients underwent the procedure under general anesthesia with an average time of 205 minutes (SD=103) with the aortic cross clamp duration averaging at 70.47 minutes (SD=41.5). Only three patients had a mechanical valve implanted (2.5%) while

97.5% of the patients had a bio-prosthetic valve implanted. Only ten patients required inotropic support during the procedure**.**

Table 5

*Procedural Details (N = 240)*

| | **TAVI (N=120)** | | **SAVR (N=120)** |
|---|---|---|---|
| **Time** (minutes) (Mean ± SD) | 109.12 ± 40.16 | **Time** (minutes) | 205.20 ± 102.95 |
| | | *Cross Clamp Time* | 70.47 ± 41.51 |
| **Anesthesia** | | | |
| *General* | 6 (5.0) | 120 (100.0) | |
| *Local* | 114 (95.0) | | |
| **Access** | | | |
| *Femoral* | 116 (96.7) | *Full Sternotomy* | 120 (100.0) |
| *Axillary* | 2 (1.7) | | |
| *Subclavian* | 1 (0.8) | | |
| *Transcaval* | 1 (0.8) | | |
| **Valve** | | | |
| *Edwards* | 48 (40.3) | *Edwards* | 4 (3.3) |
| *Medtronic* | 46 (38.7) | *Medtronic* | 24 (20.0) |
| *Boston* | 13 (10.9) | *St Jude Biocor* | 39 (32.5) |
| *Abbott* | 12 (10.1) | *LabCor* | 49 (41) |
| | | *CardiaMed* | 3 (2.5) |
| | | *Mech* | |
| **Implantation** | 118 (98.3) | 119 (99.2) | |
| **Inotropes** | 5 (4.2) | 10 (8.4) | |

*Legend.* SAVR, surgical aortic valve replacement; SD, standard deviation; TAVI, transcatheter aortic valve implantation.
*Note:* Results are presented as frequency and percent unless otherwise indicated

### 4.4. Intra-Operative Complications

Intra-operative complications and mortality rates are presented in Table 4.4. Out of the 120 patients who underwent TAVI, two patients were deceased intra-operatively; one due to a stroke and the other due to a tamponade and its complications. Out of the 120 patients who underwent SAVR, only one patient had an intra-operative hemodynamic instability and was deceased. There were no significant group differences in intra-operative complications nor mortality. Unplanned interventions that took place

included an intra-operative thrombectomy for a SAVR patient and an embolectomy for a TAVI patient who had an ischemic stroke intra-op.

Table 6

*Intra-Operative Complications (N = 240)*

| | SAVR (N=120) | TAVI (N=120) | P-value |
|---|---|---|---|
| **Intra operative status** | | | 1.000 |
| *Alive* | 119 (99.2) | 118 (98.3) | |
| *Deceased* | 1 (0.8) | 2 (1.7) | |
| **Tamponade** | 0 (0) | 1 (0.8) | 1.000 |
| **Unplanned intervention** | 1 (0.8) | 1 (0.8) | 1.000 |
| **Complete AV Block** | 1 (0.8) | 2 (1.7) | 1.000 |
| **New Device Embolization** | NA | 2 (1.7) | 0.498 |
| **New Onset Stroke** | 0 (0.0) | 2 (1.7) | 0.498 |
| **Vascular Complications** | | | 0.247 |
| *Minor* | (0.0) | 3 (2.5) | |

*Legend.* SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

### 4.5. Post-Operative Complications

Table 4.5 shows the mortality and complications during the CCU stay. There was no significant difference in mortality between the SAVR and TAVI patients. Three SAVR patients had post-operative complications that resulted in the patients being pronounced deceased in CCU. These complications included 1) tonic-clonic seizure, 2) cardiogenic shock and 3) high rate atrial fibrillation. Only one TAVI patient passed away in CCU, which was mainly due to multiple complications including pericardial tamponade. There were no significant differences in complications between both SAVR and TAVI patients, except in type of arrhythmia. New onset atrial fibrillation was found in 42.9% of patients who underwent SAVR versus 0.8% in those who underwent TAVI ($P<0.001$). On the contrary, a new left bundle branch block was found in 14.4% of TAVI patients versus none in the SAVR patients ($P<0.001$). The unplanned

interventions that took place in the two TAVI patients included PVL closure for a patient after noting severe PVL on TTE and another patient who required surgical drainage of a tamponade. There was also a somewhat higher risk for pneumonia in the SAVR group compared to the TAVI group, although the difference did not reach statistical significance.

Table 7

*Post Procedural Complications (N = 237)*

| | SAVR (N=119) | TAVI (N=118) | P-value |
|---|---|---|---|
| **Post-operative status** | | | 1.000 |
| *Alive* | 116 (97.5) | 117 (99.2) | |
| *Deceased* | 3 (2.5) | 1 (0.8) | |
| **New Onset AF** | 51 (42.9) | 1 (0.8) | **<0.001** |
| **Pacemaker Intervention** | 3 (2.5) | 6 (5.1) | 0.333 |
| **Pericardial Effusion** | 3 (2.5) | 0 (0.0) | 0.247 |
| **Pleural Effusion** | 5 (4.2) | 1 (0.8) | 0.213 |
| **Tamponade** | 0 (0.0) | 1 (0.8) | 0.498 |
| **Bundle Branch Block** | | | **<0.001** |
| *LBBB* | 0 (0.0) | 17 (14.4) | |
| *RBBB* | 1 (0.8) | 0 (0.0) | |
| **Unplanned Intervention** | 0 (0) | 2 (1.7) | 0.247 |
| **AKI** | 4 (3.4) | 6 (5.1) | 0.622 |
| *Yes on hemodialysis* | 3 (2.5) | 1 (0.8) | |
| **Neurological Complication** | 1 (0.8) | 0 (0.0) | 1.000 |
| **Vascular Complications** | | | 0.622 |
| *Minor* | 1 (0.8) | 2 (1.7) | |
| **Bleeding Complication** | | | 0.247 |
| *Major* | 3 (2.5) | 0 (0.0) | |
| **Wound Infection** | 1 (0.8) | 0 (0.0) | 1.000 |
| **Pneumonia** | 7 (5.9) | 1 (0.8) | 0.066 |

*Legend.* AF, atrial fibrillation; AKI, acute kidney injury; LBBB, left bundle branch block; RBBB, right bundle branch block; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation.

### 4.6. Post-Operative Echocardiography Findings

The TTE findings prior to discharge are presented in Table 4.6. There was no striking difference in LVEF between the SAVR and TAVI groups. Yet, the SAVR group had significantly higher aortic MG with an average of 15.73 mmHg (SD=7.49)

while those who underwent TAVI had post-operative aortic MG of 9.49 mmHg (SD=3.97), P<0.001. The post-operative TTE also showed that TAVI patients had notably higher grades of PVL (P<0.001). PVL in patients who underwent SAVR ranged between none to mild PVL (84% and 16% respectively), whereas patients who underwent TAVI had PVL ranging from none to even one patient with severe PVL that required intervention of vascular plugs to reduce the PVL.

Table 8

*Post Echocardiographic Findings (N = 224)*

| | SAVR(N=106) | TAVI (N=118) | P-value |
|---|---|---|---|
| **Post-LVEF** (%)* | | | 0.345 |
| *<50%* | 17 (16.0) | 16 (14.0) | |
| **MG** (mmHg) Mean ± SD | 15.73 ± 7.49 | 9.49 ± 3.97 | **<0.001** |
| **PVL** | | | **<0.001** |
| *None/Trace* | 89 (84.0) | 75 (63.6) | |
| *Mild* | 17 (16.0) | 26 (22.0) | |
| *Mild/Moderate* | 0 (0.0) | 12 (10.2) | |
| *Moderate* | 0 (0.0) | 4 (3.4) | |
| *Severe* | 0 (0.0) | 1 (0.8) | |

*Legend.* LVEF, left ventricular ejection fraction; MG, mean gradient; PVL, Paravalvular leak; SAVR, surgical aortic valve replacement; SD, standard deviation; TAVI, transcatheter aortic valve implantation.
*LVEF data was missing for 16 patients, 14 from the SAVR group and two from the TAVI group
*Note:* Results are presented as frequency and percent except when indicated otherwise

### 4.7. Follow Up Complications

Post discharge mortality, re-admission and complication rates are presented in Table 4.7. There was no significant difference between the SAVR and TAVI group in mortality within 30 days. Only one TAVI patient passed away after suffering a stroke within two weeks post discharge and spending another two weeks in the ICU prior to a sudden cardiac arrest. Also, there was no difference between the two groups of patients regarding the VARC-2 criteria. Yet, cumulative complications led to a significantly

higher re-admission rate in the SAVR patients. Patients who underwent SAVR were more likely to be re-admitted (19%) versus 4.3% of those who underwent TAVI (P<0.001). The unplanned intervention that took place in the SAVR group included an embolectomy after presenting to the hospital for acute limb ischemia. The SAVR group also tended to have pleural effusion more than the TAVI group, though the difference did not reach statistical significance.

Table 9

*30-Day Complications (N = 233)*

| | SAVR (N=116) | TAVI (N=117) | P-value |
|---|---|---|---|
| **Follow up status** | | | 1.000 |
| *Alive* | 116 (100) | 116 (99.1) | |
| *Deceased* | 0 (0.0) | 1 (0.9) | |
| **Readmission** | 22 (19.0) | 5 (4.3) | **<0.001** |
| **Follow up AF** | 1 (0.9) | 0 (0.0) | 0.498 |
| **Endocarditis** | 1 (0.9) | 0 (0.0) | 0.498 |
| **Pacemaker Insertion** | 2 (1.8) | 2 (1.8) | 1.000 |
| **Pericardial Effusion** | 3 (2.6) | 0 (0.0) | 0.122 |
| **Pleural Effusion** | 4 (3.4) | 0 (0.0) | 0.060 |
| **Tamponade** | 1 (0.9) | 0 (0.0) | 0.498 |
| **Unplanned Intervention** | 1 (0.9) | 0 (0.0) | 0.498 |
| **Neurological Complication** | 0 (0.0) | 1 (0.9) | 1.000 |
| **Vascular Complications** | | | 0.498 |
| *Minor* | 1 (0.9) | 0 (0.0) | |
| **Wound Infection** | 1 (0.9) | 0 (0.0) | 0.498 |
| **Pneumonia** | 3 (2.6) | 1 (0.9) | 0.370 |

*Legend.* AF, atrial fibrillation; SAVR, surgical aortic valve implantation; TAVI, transcatheter aortic valve implantation.

### 4.8. Regression to Predict In-Hospital Complications

Due to the non-significant difference between the SAVR and TAVI group on the primary outcomes, i.e. in-hospital and 30-day mortality and the very small number of deceased patients overall, no multivariate analyses were conducted for these two primary outcome variables. A logistic regression analysis was conducted to investigate the predictors of in-hospital complications and the results are presented in Table 4.8.

The predictor variables used were STS category and type of AVR procedure. These predictors were selected because most of the other baseline variables are already included in the STS score. Since the high-risk STS category had a small number of patients (N=16), the high-risk category was merged with the intermediate risk category. Thus, STS was recoded into two categories: low risk, and intermediate or high risk. The model was significant ($\chi^2 = 35.68$, $p < 0.001$) and correctly classified 65% of participants in terms of whether or not they had in- complications (63.2% of those who did not have complications and 67.3% of those who did have complications).

The Nagelkerke $R^2$ suggested an 18.5% of the variance in complications explained by the predictors. The Hosmer and Lemeshow test showed a significance of 0.545, which is not statistically significant, meaning that the data fit the model. The predictor variable type of procedure, having TAVI as a reference, was found to significantly contribute as predictor ($B = 1.739$, $P < 0.001$). The odds ratio showed a six times more likelihood (Exp(B)=5.692) for having an in-hospital complication in those who underwent SAVR than TAVI. The other predictor, the STS category with the low risk category as reference, was also found to significantly contribute to the model ($B=1.227$, $P < 0.001$). The odds ratio showed a three times higher likelihood (Exp(B)=3.412) for having an in-hospital complication if a patient is a high or intermediate surgical risk patient in comparison to a low risk patient. Thus, patients who underwent SAVR and were at intermediate or high surgical risk were more likely to have in-hospital complications than those who underwent TAVI or had low surgical risk.

Table 10

*Logistic regression to predict occurrence of In-hospital Complications (N = 240)*

| | B | S.E. | Wald | df | Sig. | Exp(B) | 95% C.I.for EXP(B) Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| Type AVR procedure | 1.739 | .329 | 27.912 | 1 | .000 | 5.692 | 2.986 | 10.851 |
| STS with 2 categories | 1.227 | .352 | 12.140 | 1 | .000 | 3.412 | 1.711 | 6.805 |
| Constant | -1.560 | .293 | 28.268 | 1 | .000 | .210 | | |

*Legend.* AVR = Aortic Valve Replacement, STS = Society of Thoracic Surgeons.

### 4.9. Regression to Predict Follow-Up Complications

Similarly, a logistic regression analysis was conducted to investigate the predictors of follow up complications and the results are presented in Table 4.9. The predictor variables; STS category and type of AVR procedure, were entered. The model was significant ($\chi^2 = 11.83$, $p = 0.003$) but it classified correctly only those who did not have any complications. The Nagelkerke $R^2$ suggested that 10.6% of the variance in complications was explained by the predictors. The Hosmer and Lemeshow test had a p value of 0.837, which is not statistically significant; thus, the data did fit the model. The predictor type of procedure was significant (B = 1.785, P = 0.002). The odds ratio showed six times higher likelihood (Exp(B)=5.957) for having follow up complication after SAVR compared to TAVI. The STS category was also significant (B=1.112, P = 0.039). The estimated odds ratio showed three times (Exp(B)=3.040) higher likelihood for having a follow up complication if a patient was a high or intermediate risk patient in comparison to a low risk patient. Thus, patients who underwent SAVR and had

intermediate or high surgical risk were more likely to have complications at 30 days follow up than those who underwent TAVI or had low surgical risk.

Table 11

*Logistic Regression for Predicting Follow-up Complications (N = 233)*

| | B | S.E. | Wald | df | Sig. | Exp(B) | 95% C.I.for EXP(B) Lower | Upper |
|---|---|---|---|---|---|---|---|---|
| Type of AVR procedure | 1.785 | .587 | 9.231 | 1 | .002 | 5.957 | 1.884 | 18.836 |
| STS with 2 categories | 1.112 | .538 | 4.279 | 1 | .039 | 3.040 | 1.060 | 8.719 |
| Constant | -3.742 | .590 | 40.165 | 1 | .000 | .024 | | |

*Legend.* AVR = Aortic Valve Replacement , STS = Society of Thoracic Surgeons

# CHAPTER 5

# DISCUSSION

The purpose of this study was to identify the individual characteristics of patients undergoing AVR, procedural details, in-hospital and 30-day mortality and complications, and patient factors that were predictive of mortality, in-hospital and follow up complications at 30 days following the procedure in a sample of patients with severe AS.

At baseline, the TAVI group was significantly older, at higher surgical risk, had more frequent history of hypertension, peripheral artery disease, prior PCI or CABG and mild impairment in the GFR, but with smaller body surface area and BMI compared to the SAVR group. The findings of the study showed a low mortality rate overall and per AVR group, whereby only eight patients died by 30 days, four from each group. In terms of in-hospital complications, SAVR patients were more likely to develop new atrial fibrillation, but less likely to develop left BBB or paravalvular leak than TAVI patients. At follow up, SAVR patients had more readmissions that TAVI patients.

Multivariate analyses showed the type of procedure (SAVR vs. TAVI) and the STS risk score to predict the occurrence of in-hospital and follow up complications, with the SAVR patients and those at intermediate or high surgical risk more likely to develop complications in the hospital and at 30 days that the TAVI and low surgical risk patients. In the following sections, we compare this study's key findings with those of previous research, appraise their implications, and discuss the methodological strengths as well as limitations of the study.

### 5.1. Key Findings Compared to the Literature

First, compared to the findings of the literature, this study's key findings are consistent with those of some studies. In particular, the NOTION 2 Trial has reported similar findings. The mean age of patients enrolled in the NOTION 2 trial was 79 years of age, which is rather similar to the mean age of our sample of 79.49 years. In both studies, the male gender accounted for half of the study sample. In the NOTION 2 trial, the average STS score for the SAVR and TAVI groups was 3.1% (SD=1.7) and 2.9% (SD=1.6) respectively, reflecting a low STS scores in both groups. However, in our study the average STS score for the SAVR patients was 2.83% (SD=2.04), which reflects a low risk STS score while that for TAVI was 4.17% (SD=2.21), reflecting an intermediate risk STS score. The higher STS score in the TAVI group in this study may be accounted for by the older age and more comorbidity in this group, as noted by the higher frequency of hypertension, PCI and CABG.

Similar to the NOTION trial (Søndergaard et al., 2016), in our study, patients who underwent TAVI had a relatively shorter length of stay of an average of 2.16 days than SAVR patients, whose length of stay averaged 7.11 days. Yet, the average length of stay in the NOTION trial was rather higher than that in our study; where the length of stay in the TAVI group in the NOTION trial was 8.9 days while that in the SAVR group was 12.9 days. It is worth noting that the NOTION-2 trial was done in 2009 and patient recruitment took place between 2009 and 2013. Ever since, the minimalist TAVI approach has been adopted. The minimalist approach includes same-day admission for a procedure performed in a hybrid operating room or cardiac catheterization laboratory, avoidance of invasive lines (e.g., central venous and urinary catheters), local anesthesia only or with light procedural sedation administered by an anesthesiologist, percutaneous

access and closure, and removal of the temporary pacemaker at the end of the procedure. The minimalist concept was further extended to the post-procedure phase, with a focus on rapid reconditioning, active mobilization after four hours, and accelerated return to baseline function and activities of daily living driven by a nursing protocol (Lauck et al., 2020). All these changes led to a shorter length of stay in TAVI patients over the years, as reflected in our study in the TAVI group.

The primary outcome measure, a composite of all-cause mortality, stroke, or myocardial infarction in-hospital and at 30 days, was not statistically different between TAVI and SAVR groups in both our study and the NOTION trial. In the NOTION trial, 30 day all-cause mortality was five patients in the SAVR group versus three in the TAVI group, whereas in our study only one patient passed away in the TAVI group at 30 days. Again, this difference may be accounted for by advances and more practice with the TAVI procedure.

The reported complications in all trials (PARTNER (Leon et al., 2016; Mack et al., 2019; Smith et al., 2011). and NOTION trials (Søndergaard et al., 2016).) were similar to those in our study, using the VARC-2 criteria. The only difference between the trials and our study were outside the VARC-2 criteria, namely pleural effusions, pericardial effusions and pneumonia, which were not significantly different between the two groups. These particular complications were not noted in the Notion and PARTNER trials, where the investigators only reported re-hospitalizations without describing the cause of readmission. Regarding arrhythmias post AVR, in the NOTION and our study, cumulative rates of new onset atrial fibrillation remained significantly lower in the TAVI group (0.8% in our study while NOTION trial reported 22.7%) compared to the SAVR group (42.9% in our study while the NOTION trial reported

60.2%). Atrial fibrillation (AF) is recognized as a common complication of open cardiac surgery, with a reported incidence of up to 65% (Filardo et al., 2010). While early investigators dismissed postoperative AF as benign, transient, self-limited and of no consequence, more recent research documented associations of AF with several adverse outcomes, including increased length of stay (overall and in intensive care), risk of stroke, need for a permanent pacemaker, and more importantly in-hospital and long-term mortality (Filardo et al., 2010). The lower risk for AF in patients who undergo TAVI thus put them at an advantage in terms of morbidity and mortality.

Recent studies showed that TAVI can induce cardiac conduction abnormalities, the most frequent one being left bundle-branch block (LBBB). The incidence of TAVI-induced LBBB has been reported to vary between 7% and 83% and appears to depend on the device being used (Houthuizen et al., 2012). In our study, development of new onset LBBB was rather frequent among TAVI patients where it happened in 14.4% of the cases, versus none in the SAVR group. The clinical significance of the LBBB, especially in the setting of possible acute myocardial infarction, necessitates examining patients for this complication following the TAVI procedure. Moreover, several studies have shown the frequency of pacemaker implantation in patients who undergo TAVI, in particular the NOTION 2 trial, in which the rate of pacemaker implantation was 34.1% for TAVI patients in comparison to 1.6% for the SAVR patients. Our study showed that the rate for pacemaker implantation for the TAVI group was higher (2.5%) than that of the SAVR group (0.8%) but the difference was not statistically significant. Again this difference in findings can be accounted for by the time when the NOTION trial was conducted (2009-2013). Ever since TAVI was found to be associated with arrhythmias necessitating pacemaker implantation, trials were conducted to study the impact of the

new pacemaker implantation on patient outcomes and how to decrease the rate of conduction abnormalities. Available evidence suggests that various electrical, anatomical, and procedural factors may explain the higher rate of conduction abnormalities necessitating pacemaker in TAVI patients and tackles those that are avoidable (Rosendael et al., 2018). Predictors of new pacemaker implantation include: 1) pre-existing damage of the conduction system, such as the RBBB, 2) the presence and distribution of calcifications underneath the aortic annulus plane that affect the interventricular septum (landing zone), and 3) implantation depth into the left ventricular outflow tract (LVOT) that were strongly associated with increased risk of pacemaker implantation after TAVI, regardless of the prosthesis used (self-expandable or balloon expandable). Therefore, after identification of these factors, particularly the procedural ones, the operator at the center where the study was conducted adopted the MIDAS (Minimizing Depth according to the Membranous Septum) technique. This technique aims for a pre-release depth of the prosthesis in relation to the non-coronary cusp that is no longer than the length of the patient's membranous septum -- but also no higher than 1 mm, to minimize risk of device embolization (Jilaihawi et al., 2019). This technique might have influenced our pacemaker rate, making it lower than that in other trials.

The echocardiographic findings post AVR were similar to those reported in the literature, which include the PARTNER trials and NOTION trials. Trans-aortic mean gradients, the difference in pressure between the left ventricle (LV) and aorta during systole (Baumgartner et al., 2009), were significantly lower in the TAVI group than the SAVR group, which can be the result of patient prosthesis mismatch (PPM). Prosthesis-patient mismatch develops when the effective orifice area (EOA) of the inserted

prosthetic valve is comparably too small in relation to body size of the patient. Its main hemodynamic consequence is a higher trans-aortic gradient on the LVOT, which affects the long-term mortality of patients (Takagi et al., 2016). According to the SURTAVI trial, rates of PPM were significantly lower after TAVI than after SAVR across all groups of indexed annulus size, reflecting better hemodynamic performance of transcatheter versus surgical valves, irrespective of the propensity to develop PPM (Head et al., 2019). Rates of PPM are lower in TAVI most likely owing to valve-sizing differences and the ability of transcatheter valves to expand to the anatomical annulus size, which is not possible with a fixed-size surgical sewing ring. Larger valve areas with TAVI would be expected to decrease the incidence of PPM, which might result in better late clinical outcomes (Leon et al., 2016).

Another echocardiographic finding that was significant after AVR was the rate of PVL, which was higher in the TAVI group at each time point compared with SAVR. TAVI was associated with higher mild, mild to moderate, moderate and even severe PVL than the SAVR group, which is in parallel with the findings of the PARTNER trials and NOTION trials. Yet, the improvement in mild PVL is expected whereby clinical trials demonstrated an improvement in the severity of PVL over time, especially with a self-expandable bio-prosthesis, presumably because of the ongoing remodeling at the interface of the bio-prosthesis and native annulus, as well as the neo-endothelialization of the stented region of the bio-prosthesis (Søndergaard et al., 2016).

It is worth noting that mortality, and a number of complications such as bleeding, vascular complications and acute kidney injury were not significantly different between the two groups; this may be explained by the age and STS difference between them. So, although one would expect more complications from surgery than a

less invasive procedure, the TAVI group were older, with higher surgical risk and more co-morbidities than the SAVR group. The overall frequency of some complications such as infection, bleeding and vascular complications was very small in both groups, thus reflecting quality care and skilled operators.

All trials, PARTNER (Leon et al., 2016; Mack et al., 2019; Smith et al., 2011) and NOTION (Søndergaard et al., 2016), did not examine predictors of mortality or complications. In our study, once significant differences were detected in complications during hospitalization and at 30-day follow up, a logistic regression was conducted to determine the predictors of these complications. Based on the literature review and our simplified conceptual figure (Figure 3), three predictors could impact the outcomes of patients; the demographic variables, clinical variables and procedural variables. Taking into consideration that the STS score is a meticulous score that includes both clinical and demographic variables, we decided to enter the STS category and the type of procedure as predictors into the regression. Yet, since our sample included a small number of high-risk patients, the high risk and intermediate STS categories were merged and compared to the low risk STS category. Both variables were significant predictors of both in-hospital and 30-day complications. In both in-hospital and at 30-day follow up, patients undergoing SAVR were almost six times more likely to develop complications than the patients undergoing TAVI. Moreover, patients who were considered intermediate/high risk patients were three times more likely to develop complications than patients who were considered low risk patients. These findings are expected from a clinical point of view, and support current practice of assessing STS in these AVR patients in deciding the optimal treatment modality as well as following up on complications that may occur in these patients.

## 5.2. Implications

The findings of this study have implications relevant to nursing education, practice and policy making in the context of assessment of outcomes in patients undergoing AVR. In general, older adults, who constitute the majority of patients presenting with AS, are more frail and susceptible to adverse outcomes such as delayed recovery and prolonged LOS postoperatively due to complications (Kaye et al., 2009; Bjorkelund et al., 2011). The cardiology clinical nurse specialist (CNS) can identify the quality indicators for this patient population and assess those who are at a higher risk for complications and implement care plans that monitor and detect complications early on, to decrease the patients' length of stay and improve their quality of care.

At the nursing education level, nurses can improve the quality of care by increasing their relevant knowledge while individualizing patient care. Specifically, in this study, the type AVR was demonstrated to have statistically significant correlation with conduction abnormalities whether atrial fibrillation or left bundle branch block requiring pacemaker intervention. This may call nurses' attention to increase telemetry monitoring and become more attuned to nursing skills including EKG interpretation, especially during the post-procedure phase. Moreover, this study showed that the type of AVR has a different impact on echocardiographic parameters and valve function, hence nurses should be more knowledgeable regarding the impact of such parameters on outcomes of patients and the necessity of monitoring patients regularly. Hence, the cardiology CNS can utilize his/her expertise and specialization to provide consultation services to the nursing staff to ensure that nurses are skilled in ECG interpretation, and collaborate with other health care professionals in providing quality evidence-based

care. Moreover, the CNS should guide, teach, and design education programs for nurses to promote continuing education in the management of this patient population.

At the nursing practice level, it is worth noting that the key findings of this study are mostly related to factors that are essentially non-modifiable, for example, patient age, STS score, medical history as well as procedural factors. Nonetheless, the findings may still have practice implications on how to care for this patient population. Nursing care focuses mainly on patient monitoring and assessment; in these patients, nurses ought to be skilled in identifying dysrhythmias, such as atrial fibrillation and bundle branch block. The cardiology CNS can coach nurses to ensure they monitor patients and identify adverse events in a timely manner. More importantly, the cardiology CNS should ensure that care to patients is being provided based on evidence.

At the policy making level, the cardiology CNS should collaborate with members of the interdisciplinary team to identify patient care problems and set priorities, implement, and evaluate processes in clinical cardiology, evaluate current policies and adherence to international guidelines by monitoring clinical indicators. Clinical pathways and order sets can be developed to standardize patient care based on empirical evidence, identify variances in care, and evaluate patients' outcomes accordingly. This also implies that the cardiology CNS has to serve as a researcher by conducting, utilizing, and disseminating multidisciplinary research to ensure high quality and appropriate patient care.

When it comes to ethical decision making, the cardiology CNSs have a decisive role in solving moral issues with ethical decision making skills, clinical expertise & leadership. Ethical dilemmas occur when obligations appear to require the person to choose adopting two options that are ethically troubling. Therefore, this can cause moral

distress and uncertainty for the patients. In some cases, the patient's age does not make him a candidate for TAVI and the patient has to be guided to accept his other option, SAVR, even if it is more invasive. In other cases, the patient's mental capacity and health status do not make him a candidate for either AVR approach, and thus he/she should get palliative care. The cardiology CNS aims to empower the patient to make rational, informed decisions about his or her health by providing education, counseling and care to these patients and their families. The CNS can moderate patient/family conferences with the medical team to discuss these issues in order to facilitate decision-making.

### 5.3. Strengths

This study has several strengths, including developing a structured approach in identifying and organizing variables, adopting a stepwise process in data analyses, and providing the first evidence on the outcomes of patients with AVR in Lebanon.

The first and principal challenge that this study had to deal with was how multiple variables could be reasonably identified. To address this challenge, a systematically structured approach was used. The Clinical Pathway Model (Figure 1) and the Predictors and Outcomes of TAVI vs SAVR Conceptual Model (Figure 2) were developed as the underlying framework to classify and organize the variables in a simplified conceptual model (Figure 3) to guide the statistical analysis.

In addition, this study is one of the few studies that included patients from all STS risk categories, similar to the NOTION trial. Other trials, such as the PARTNER trials, compared patient groups who were either from low, intermediate or high STS categories.

### 5.4. Limitations

One of the methodological limitations is the study's sample. This study included subjects who were carefully screened and selected for the AVR procedures. Patients with previous or concomitant valvular diseases were excluded from this study, so outcomes in those patients cannot be extrapolated from this study. Moreover, because this study used a single study center's clinical data, the sample only represented this center's population. Therefore, this study's findings cannot be generalized to the Lebanese population of patients with AS who undergo AVR.

Limitations of this study include also its retrospective design, and the inability to account for variables such as frailty and NYHA that may be important confounders but were not documented in the medical records, as well as missing data that could have added more outcomes to our study such as variables that enable calculation of the PPM. Furthermore, the limited sample size may also have caused some associations to be statistically not significant.

Conventional models of risk following cardiac surgery such as the STS score are not calibrated to accurately predict the outcomes in older adults and do not currently include frailty parameters. In some studies, compared with STS risk score alone, frailty status was a significant predictor of 1-year mortality after TAVI procedure (Rogers et al., 2018). Therefore, frailty assessment should be part of the pre-procedural assessment and should be documented and included in future studies to further improve patient outcomes after AVR.

Another limitation is the short-term follow up period, which could explain the lack of difference in mortality. Recommendations for future research include using

multi-center databases, a prospective approach, applying more rigorous data collection techniques and following up the patients over at least one year.

In conclusion, patients who undergo AVR are prone to develop complications that differ by type of procedure performed. Recommendations from these findings include training nurses in identification of these complications, as well as inclusion of other relevant in the medical records of these patients, as well as future prospective studies with long term follow up to more accurately establish the prognosis of this patient population.

# APPENDIX 1

# COMPARING PATIENT OUTCOMES OF TAVI VS. SAVR: DATA COLLECTION FORM

## Data Collection Form

### A. DEMOGRAPHICS

| | | | | | |
|---|---|---|---|---|---|
| Gender | ○ Male ○ Female | Age | | MRN | |
| Admission Date | | STS Score (%) | | Procedure | |

### B. MEDICAL HISTORY AND RISK FACTORS

| | | | | | | |
|---|---|---|---|---|---|---|
| Smoking | ○ No ○ Yes | BMI (kg/m²) | ○ <18.5 | ○ 18.5-24.9 | ○ 25-29.9 | ○ >30 |
| **Comorbidities** | ○ Hypertension | ○ Diabetes, on | ○ Oral | ○ Insulin | ○ Other | ○ COPD |
| | ○ Dyslipidemia | ○ eGFR ml/min | ○ >60 | ○ 30-59 | ○ <29 | ○ PAD |
| | ○ Stroke | ○ Carotid Stenosis | ○ Right | ○ Left | Both | |
| | ○ TIA | ○ Heart Failure | ○ HFpEF | ○ HFrEF | | |
| **Cardiac Srgx** | ○ PCI | ○ ICD | ○ CRTD | ○ PPM | | |
| Bundle Branch Block | ○ Left | ○ Right | | | | |
| Atrial Fibrillation | ○ Yes | ○ No | | | | |

### C. ECHOCARDIOGRAM FINDINGS

| | | | | | |
|---|---|---|---|---|---|
| LV Ejection Fraction (%) | | AV Area (cm²) | | MG (mmHg) | |
| Aortic Insufficiency | ○ None | ○ Trace/Trivial | ○ 1+/Mild | ○ 2+/ Moderate | ○ 3-4+/Severe |
| Valve Morphology | ○ Unicuspid | ○ Bicuspid | ○ Tricuspid | ○ Quadracuspid | |

### D. PROCEDURE INFORMATION

**TAVI**

| | | | | | |
|---|---|---|---|---|---|
| Time (min) | | Anesthesia | ○ Local | ○ General | |
| Valve Brand | | Access Site | ○ Femoral | ○ Axillary | ○ Subclavian |
| Successful Implantation | ○ No ○ Yes | Inotropes | ○ No ○ Yes | Post MG (mmHg) | |

**SAVR**

| | | | | | |
|---|---|---|---|---|---|
| Time (min) | | Cross Clamp Time | | Valve Brand | |
| Successful implantation | ○ No ○ Yes | Inotropes | ○ No ○ Yes | Post MG (mmHg) | |

### E. PROCEDURAL COMPLICATIONS

| | | | | |
|---|---|---|---|---|
| **Complication** | ○ No | ○ Yes | Transfusions | |
| **Cardiac** | ○ Atrial Fibrillation<br>○ Unplanned | ○ Pacemaker Intervention | ○ Tamponade<br>○ New LBBB | ○ Myocardial Infarction<br>○ New RBBB |
| **Device** | ○ Thrombosis | ○ Embolization<br>○ Migration | | |
| **Neuro** | ○ Stroke<br>○ TIA | | **Vascular** | ○ Minor<br>○ Major |
| **Bleeding** | ○ Fatal | ○ Major | ○ Minor | |

| F. POST PROCEDURE LABS AND FINDINGS | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| LVEF (%): | | PVL | ○ No | ○ Mild | ○ Mild/Moderate | ○ Moderate | ○ Severe | | | |
| **G. POST PROCEDURAL COMPLICATIONS** | | | | | | | | | | |
| **Cardiac** | ○ Atrial Fibrillation<br>○ Endocarditis<br>○ Unplanned | | ○ Pacemaker Intervention | | ○ Tamponade | | ○ Myocardial Infarction<br>○ New LBBB<br>○ New RBBB | | | |
| **Device** | ○ Thrombosis | | ○ Embolization<br>○ Migration | | **Renal** | | ○ Acute Kidney Injury<br>○ New need for Dialysis | | | |
| **Neuro** | ○ Hemorrhagic Stroke | | ○ Ischemic Stroke | | **Vascular** | | ○ Minor<br>○ Major | | | |
| **Bleeding** | ○ Fatal | | ○ Major | | ○ Minor | | | | | |
| **H. DISCHARGE** | | | | | | | | | | |
| Date | | Days in CCU | | Status | ○ Alive | ○ Deceased | | | | |
| ➢ **If Deceased, Primary Cause of Death:** | ○ Cardiac | ○ Non-cardiac | | | | | | | | |
| **I. 30 DAY FOLLOW UP** | | | | | | | | | | |
| Date | | Status | ○ Alive | ○ Deceased | | | | | | |
| ➢ **If Deceased, primary cause of death:** | ○ Cardiac | ○ Non-cardiac | | | | | | | | |
| **Cardiac** | ○ Atrial Fibrillation<br>○ Endocarditis<br>○ Unplanned | | ○ Pacemaker Intervention | | ○ Tamponade<br>○ New RBBB | | ○ Myocardial Infarction<br>○ New LBBB | | | |
| **Device** | ○ Thrombosis | | ○ Embolization<br>○ Migration | | **Renal** | | ○ Acute Kidney Injury<br>○ New need for Dialysis | | | |
| **Neuro** | ○ Hemorrhagic Stroke | | ○ Ischemic Stroke | | **Vascular** | | ○ Minor<br>○ Major | | | |
| **Bleeding** | ○ Fatal | | ○ Major | | ○ Minor | | | | | |

# APPENDIX 2

# COMPARING PATIENT OUTCOMES OF TAVI VS. SAVR: CODE MANUAL

| # | Variable | Definition | Note |
|---|---|---|---|
| **Pre-Procedural Phase** | | | |
| Demographics | | | |
| 1 | Gender | AVR patient's gender | M/F |
| 2 | Admission Date | Date of admission of AVR patient to the hospital | dd/mm/yyyy |
| 3 | Age | Age of AVR patient at the time of the procedure | years |
| 4 | STS Score | STS score of AVR patient | % |
| 5 | MRN | Medical Record Number assigned to the AVR patients medical chart | 0- |
| 6 | Procedure | Type of AVR the patient is undergoing | SAVR or TAVI |
| Medical History and Risk Factors | | | |
| Comorbidities | | | |
| 7 | Smoking | AVR patient's smoking status at the time of the procedure | Yes/No |
| 8 | BMI | The body mass index (BMI) for measuring body fat based on height and weight prior to the date of the AVR procedure. BMI = Weight (kg) / Height$^2$($m^2$) | $Kg/m^2$ |
| 9 | Hypertension | History of hypertension defined by any one of the following: history of hypertension diagnosed and treated with medication, diet, and/or exercise | Yes/No |
| 10 | Diabetes | History of diabetes diagnosed and/or treated by a healthcare provider. Management includes oral medication or insulin or both. | Yes/No |
| 11 | Dyslipidemia | History of dyslipidemia and/or treated with medications or lifestyle modifications | Yes/No |
| 12 | eGFR | Estimated glomerular filtration rate documented by pre-procedural blood tests. | mL/minute |

| | | | |
|---|---|---|---|
| 13 | Stroke | History of stroke defined as an acute episode of focal or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction, where the neurological dysfunction lasts for greater than 24 hours. | Yes/No |
| 14 | TIA | History of transient ischemic attack defined as a transient episode of focal neurological dysfunction caused by brain, spinal cord, or retinal ischemia, without acute infarction, where the neurological dysfunction resolves within 24 hours. | Yes/No |
| 15 | Carotid Stenosis | History of any significant carotid stenosis more than 50% in the right, left or both carotids | Yes/No |
| 16 | COPD | History of chronic obstructive pulmonary disease prior to procedure. | Yes/No |
| 17 | PAD | History of peripheral artery disease which includes upper and lower extremity, renal, mesenteric, and abdominal aortic systems. This can include:<br>1. Claudication, either with exertion or at rest,<br>2. Amputation for arterial vascular insufficiency,<br>3. Vascular reconstruction, bypass surgery, or percutaneous intervention to the extremities (excluding dialysis fistulas and vein stripping),<br>4. Documented abdominal aortic aneurysm with or without repair, 5. Positive noninvasive test (e.g., ankle brachial index =< 0.9, ultrasound, magnetic resonance or computed tomography imaging of > 50% diameter stenosis in any peripheral artery, i.e., renal, subclavian, femoral, iliac) or angiographic imaging. | Yes/No |
| 18 | Heart Failure | History of diagnosis of heart failure with preserved ejection fraction (HFpEF) or reduced ejection fraction (HFrEF). | HFpEF/HFrEF |
| | | Cardiac Procedures and ECG | |
| 19 | PCI | History of percutaneous coronary intervention (PCI) prior to the date of the procedure. | Yes/No |
| 20 | ICD | History of implantable cardioverter defibrillator (ICD) implantation prior to the date of procedure | Yes/No |
| 21 | CRTD | History of cardiac resynchronization therapy-defibrillator implantation prior to the date of procedure. | Yes/No |

| | | | |
|---|---|---|---|
| 22 | BAV | History of balloon aortic valvuloplasty (BAV) prior to the date of procedure. | Yes/No |
| 23 | PPM | History of permanent pacemaker implantation prior the procedure. | Yes/No |
| 24 | Bundle Branch Block | History of bundle branch block and shown on ECG prior to the procedure, either left bundle branch block or right bundle branch block. | Yes/No |
| 25 | Atrial Fibrillation | History of atrial fibrillation, diagnosed on ECG prior to the procedure. | Yes/No |
| | | Echocardiography Findings | |
| 26 | LVEF | The left ventricular ejection fraction (LVEF) is the indicates the percentage of blood pumped out of the left ventricle at the end of contraction. If a percentage rate if reported such as 50-55%, report a whole number representing the mean such as 53% | % |
| 27 | AV Area | Aortic valve area calculation is an indirect method of determining the area of the aortic valve. | $Cm^2$ |
| 28 | MG | This indicates the mean pressure gradient across the aortic valve. | mmHg |
| 29 | Aortic Insufficiency | Any echocardiographic evidence of aortic valve insufficiency/regurgitation according to grade. | Grade |
| 30 | Valve morphology | Aortic valve morphology indicating normal tricuspid leaflets or congenital malformation resulting in bicuspid valve, unicuspid or quadracuspid | Morphology |
| | | **Procedural Phase** | |
| | | Procedure Information | |
| | | TAVI | |
| 31 | Time | Time from start of procedure til the end. | Minutes |
| 32 | Anesthesia | Type of anesthesia administered during procedure. | Local/General |
| 33 | Valve Brand | Bio-prosthetic valve brand used during the procedure. | Edwards/Medtronic/ Boston Scientific/ Abbott |
| 34 | Access Site | Access site used during the procedure. | Femoral/ Axillary/ Subclavian |
| 35 | Successful implantation | Valve implantation done successfully. | Yes/No |

| | | | |
|---|---|---|---|
| 36 | Inotropes | Inotropes used during procedure for hemodynamic support (such as levophed) | Yes/No |
| 37 | Post MG | Post implantation aortic mean pressure gradient. | mmHg |
| | | SAVR | |
| 38 | Time | Time from start of procedure til the end. | Minutes |
| 39 | Valve Brand | Valve brand used during the procedure. | Labcor/ St Jude/ |
| 40 | Successful implantation | Valve implantation done successfully. | Yes/No |
| 41 | Inotropes | Inotropes used during procedure for hemodynamic support (such as levophed) | Yes/No |
| 42 | Post MG | Post implantation aortic mean pressure gradient. | mmHg |
| | | **Procedural Complications** | |
| 43 | Complication | Indicate whether the patient underwent complication during the procedure. | Yes/No |
| 44 | Cardiac | A. Atrial Fibrillation<br>New-onset atrial fibrillation<br><br>B. Bundle Branch Block<br>Implant-related new or worsened cardiac conduction disturbance (either left bundle branch block or right bundle branch block)<br><br>C. Pacemaker Insertion<br>New permanent pacemaker implantation<br><br>D. Myocardial Infarction<br>New ischemic symptoms (e.g. chest pain or shortness of breath), or new ischemic signs (e.g. ventricular arrhythmias, new or worsening heart failure, new ST-segment changes, hemodynamic instability, new pathological Q-waves in at least two contiguous leads, imaging evidence of new loss of viable myocardium or new wall motion abnormality) AND<br>Elevated cardiac biomarkers (preferable CK-MB) within 72 h after the index procedure, consisting of at least one sample post-procedure with a peak value exceeding 15× as the upper reference limit for troponin or 5× for CK-MB. If cardiac biomarkers are increased at baseline (.99th percentile), a further increase in at least | Yes/No<br><br>Yes/No<br><br>Yes/No<br><br>Yes/No |

| | | | |
|---|---|---|---|
| | | 50% post-procedure is required AND the peak value must exceed the previously stated limit.<br><br>E. <u>Cardiac Tamponade</u><br>Evidence of a new pericardial effusion associated with hemodynamic instability and clearly related to the TAVI procedure | |
| 45 | Device | A. <u>Thrombosis</u><br>Any thrombus attached to or near an implanted valve that occludes part of the blood flow path, interferes with valve function, or is sufficiently large to warrant treatment.<br><br>B. <u>Embolization</u><br>The valve prosthesis moves during or after deployment such that it loses contact with the aortic annulus<br><br>C. <u>Migration</u><br>After initial correct positioning, the valve prosthesis moves upwards or downwards, within the aortic annulus from its initial position, with or without consequences | |
| 46 | Neuro | Acute episode of a focal or global neurological deficit with at least one of the following: change in the level of consciousness, hemiplegia, hemiparesis, numbness, or sensory loss affecting one side of the body, dysphasia or aphasia, hemianopia, or other neurological signs or symptoms consistent with stroke<br><br>A. <u>Stroke:</u><br>Duration of a focal or global neurological deficit ≥24 h<br>*or*<br>24 hours if available neuroimaging documents a new hemorrhage or infarct;<br>*or*<br>the neurological deficit results in death<br><br>**<u>Ischemic:</u>** an acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of the central nervous system tissue<br>**<u>Hemorrhagic</u>**: an acute episode of focal or global cerebral or spinal dysfunction caused by intra-parenchymal, | Yes/ No |

| | | | |
|---|---|---|---|
| | | intraventricular, or subarachnoid hemorrhage<br><br>B. <u>Transient Ischemic Attack (TIA)</u><br>Duration of a focal or global neurological deficit less than 24 hours, any variable neuroimaging does not demonstrate a new hemorrhage or infarct<br><br>Confirmation of the diagnosis by at least one of the following:<br>1. Neurologist or neurosurgical specialist<br>2. Neuroimaging procedure (CT scan or brain MRI), but stroke may be diagnosed on clinical grounds alone | Yes/ No |
| 47 | Vascular | <u>Major</u><br>• Any aortic dissection, aortic rupture, annulus rupture, left ventricle perforation, or new apical aneurysm/pseudo-aneurysm<br>*or*<br>• Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudo-aneurysm, hematoma, irreversible nerve injury, compartment syndrome, percutaneous closure device failure) leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment<br>*or*<br>• Distal embolization (non-cerebral) from a vascular source requiring surgery or resulting in amputation or irreversible end-organ damage<br>*or*<br>• The use of unplanned endovascular or surgical intervention associated with death, major bleeding, visceral ischemia or neurological impairment<br>*or*<br>• Any new ipsilateral lower extremity ischemia documented by patient symptoms, physical exam, and/or decreased or absent blood flow on lower extremity angiogram<br>*or*<br>• Surgery for access site-related nerve injury | Yes/ No |

| | | | |
|---|---|---|---|
| | | *or*<br>• Permanent access site-related nerve injury<br><br><u>Minor</u><br>• Access site or access-related vascular injury (dissection, stenosis, perforation, rupture, arterio-venous fistula, pseudo-aneurysms, hematomas, percutaneous closure device failure) not leading to death, life-threatening or major bleeding, visceral ischemia, or neurological impairment<br>*or*<br>• Distal embolization treated with embolectomy and/or thrombectomy and not resulting in amputation or irreversible end-organ damage<br>*or*<br>• Any unplanned endovascular stenting or unplanned surgical intervention not meeting the criteria for a major vascular complication<br>*or*<br>• Vascular repair or the need for vascular repair (via surgery, ultrasound-guided compression, transcatheter embolization, or stent-graft) | |

| | | | |
|---|---|---|---|
| 48 | Bleeding | <u>Fatal</u><br>Fatal bleeding is bleeding that directly causes death with no other explainable cause.<br>Bleeding that is contributory but not directly causal to death is not classified as fatal bleeding but may be categorized as other forms of bleeding.<br>Bleeding that leads to cessation of antithrombotic or other therapies may be contributory but again would not be classified as fatal bleeding. Bleeding associated with trauma or with surgery may be fatal, depending on whether it was determined to be directly causal or not.<br><br>• Bleeding in a critical organ, such as intracranial, intra-spinal, intraocular, or pericardial necessitating pericardiocentesis, or intramuscular with compartment syndrome (BARC type 3b and 3c)<br>*or*<br>• Bleeding causing hypovolaemic shock or severe hypotension requiring vasopressors or surgery (BARC type 3b)<br>*or*<br>• Overt source of bleeding with drop in hemoglobin ≥5 g/dL or whole blood or packed red blood cells (RBCs) transfusion ≥4 units (BARC type 3b)<br><br><u>Major</u><br>• Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0 g/dL or requiring transfusion of two or three units of whole blood/RBC, or causing hospitalization or permanent injury, or requiring surgery<br>*and*<br>• Does not meet criteria of life-threatening or disabling bleeding<br><u>Minor</u><br>The bleeding must require diagnostic studies, hospitalization, or treatment by a healthcare professional.<br>In particular, the bleeding must meet at least | Yes/No<br><br>Yes/ No<br><br>Yes/No |

| | | | |
|---|---|---|---|
| | | one of the following criteria:<br>• First, it requires intervention, defined as a healthcare professional– guided medical treatment or percutaneous intervention to stop or treat bleeding, including temporarily or permanently discontinuing a medication or study drug. Examples include, but are not limited to, coiling, compression, use of reversal agents such as vitamin K or protamine, local injections to reduce oozing, or a temporary/permanent cessation of antiplatelet, anti-thrombin, or fibrinolytic therapy<br>*Or*<br>• The bleeding leads to hospitalization or an increased level of care, defined as leading to or prolonging hospitalization or transfer to a hospital unit capable of providing a higher level of care<br>*Or*<br>• the bleeding prompts evaluation, defined as leading to an unscheduled visit to a healthcare professional resulting in diagnostic testing (laboratory or imaging). Examples include, but are not limited to, hematocrit testing, hemoccult testing, endoscopy, colonoscopy, computed tomography scanning, or urinalysis | |
| Post Procedural Findings | | | |
| 49 | PVL | Grade of paravalvular leak/aortic regurgitation shown on echocardiogram. | None, mild, mild/moderate, moderate, severe |
| 50 | LVEF | Post procedural LVEF | % |
| **Post Procedural Complications<br>All complications were defined above, only new ones will be defined** | | | |
| 51 | Endocarditis | • Fulfilment of the Duke endocarditis criteria<br>*Or*<br>• Evidence of abscess, paravalvular leak, pus, or vegetation confirmed as secondary to infection by histological or bacteriological studies during a re-operation | Yes/ No |

| | | | |
|---|---|---|---|
| 52 | Renal | Acute Kidney Injury (AKI)<br><br>AKI can also be diagnosed according to urine output measures<br><br>Stage 1<br>• Increase in serum creatinine to 150–199% (1.5–1.99 × increase compared with baseline) OR increase of ≥0.3 mg/dL (≥26.4 mmol/L)<br>*Or*<br>• Urine output <0.5 mL/kg/h for >6 but <12 hours<br><br>Stage 2<br>• Increase in serum creatinine to 200–299% (2.0–2.99 × increase compared with baseline)<br>*Or*<br>• Urine output <0.5 mL/kg/h for >12 but <24 hours<br><br>Stage 3<br>• Increase in serum creatinine to ≥300% (.3 × increase compared with baseline) OR serum creatinine of ≥4.0 mg/dL (≥354 mmol/L) with an acute increase of at least 0.5 mg/dL (44 mmol/L)<br>*Or*<br>• Urine output <0.3 ml/kg/h for ≥24 hours<br>*Or*<br>• Anuria for ≥12 hours<br><br>New Need for Dialysis<br>This indicates that the patient has not recovered from AKI and started on hemodialysis. | Yes/No<br><br>Yes/No |
| **Discharge** | | | |
| 53 | Date | Date of discharge from hospital | dd/mm/yyy |
| 54 | Days in CCU | Length of stay of patient in the Coronary Care Unit (CCU) | days |
| 55 | Status | Status of patient | Alive/ Deceased |
| 56 | Primary cause of death | Cardiac | Yes/No |

| | | | |
|---|---|---|---|
| | | • Death due to proximate cardiac cause (e.g. myocardial infarction, cardiac tamponade, worsening heart failure).<br>• Death caused by non-coronary vascular conditions such as neurological events, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular disease.<br>• All procedure-related deaths, including those related to a complication of the procedure or treatment for a complication of the procedure.<br>• All valve-related deaths including structural or non-structural valve dysfunction or other valve-related adverse events.<br><br><u>Non-Cardiac</u><br>Any death in which the primary cause of death is clearly related to another condition (e.g. trauma, cancer, suicide) | Yes/No |
| **30 Day Follow Up<br>Same Codes as before** | | | |

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