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Project Title: **E-QUALITY - Elderly project for QUALITY of life post-transcatheter aortic valve implantation (TAVI)**

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Summary (250 words max single spaced):

Background: In the past decade, there has been increased use of Transcatheter Aortic Valve Implantation (TAVI) for the treatment of severe symptomatic aortic stenosis (AS) in those felt to be inoperable or high surgical risk. Much is known about safety and efficacy of this procedure, but health-related quality of life (HRQoL), cognitive, and frailty outcomes have been under studied. **Methods:** A retrospective chart review with prospective follow-up was completed for all Manitoba TAVI patients between September 1, 2012 and March 31, 2018. A detailed 30-day and 1-year clinical and HRQoL analysis, using both questionnaires and clinical assessment, were performed. **Results:** A total of 208 patients underwent a TAVI procedure, with 30-day and 1-year survivals of 98% and 89%, respectively. HRQoL improvements were evident: 30-days post-TAVI there were improvements in Kansas City Cardiomyopathy Questionnaire (KCCQ-12) social limitation (+31; p=0.014) and overall KCCQ-12 scores (+19; p=0.005). There were improvements in patients' cognition: Montreal Cognitive Assessment (MoCA) scores improved by 1.0 (p=0.003) and 1.3 (p=0.034) at 30-days and 1-year post-TAVI, respectively. Furthermore, frailty improvements were shown with improvements in handgrip strength at 1-year post-TAVI (+3.4kg; p<0.001). **Conclusion:** In this first account of the TAVI population in Manitoba, TAVI lead to statistically significant improvements in HRQoL, cognition, and frailty. Accumulating data on outcomes after TAVI allow for realistic expectations of life after TAVI, which can facilitate more fully informed decision making. This is essential for patients, families, and practitioners as they wade through complex options in the treatment of severe AS.

Student Signature

Primary Supervisor Signature

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E-QUALITY - Elderly project for QUALITY of life post-TAVI

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Introduction & Background

Aortic stenosis (AS) is a pathological progressive narrowing of the aortic valve (AV), with eventual consequences of left ventricular hypertrophy, increased left ventricular end-diastolic pressure, and left ventricular contractile dysfunction.[1] Over time, increasing severity of stenosis can lead to symptoms, after which patients experience a precipitous decline in survival and health-related quality of life (HRQoL).[1]

The primary etiology of AS is age-related degenerative changes of the AV. The prevalence of AS increases with age, with an estimated 3.4% of people above the age of 75 years suffering from severe AS (AV area $\leq$1.0 cm^2, $V_{max} \geq$4 m/s and/or AV mean gradient $\geq$40 mmHg).[2] Since the 1960's, the standard treatment option for severe symptomatic AS has been surgical aortic valve replacement (SAVR); this treatment may not be an option or not recommended for those with higher perioperative risks due to frailty or presence of multiple co-morbidities, all of which increase with age.[3, 4] With life expectancy on the rise and older adults becoming a rapidly growing demographic there is a growing aggregate of people suffering from severe AS.[5] In more recent years, transcatheter aortic valve implantation (TAVI) has emerged as a less invasive alternative treatment. TAVI is a percutaneous transcatheter procedure that allows implantation of a bioprosthetic valve into the aortic position.[6] The global rates of TAVI procedures have been on the rise since its inception in 2002.[3, 6] In large, multinational, randomized controlled trials, TAVI has been shown to have mortality benefit compared to medically managed severe AS, and non-inferior to SAVR in higher risk patients.[7-11]

In conjunction with feasibility and safety of TAVI, patient-centred outcomes are essential. Many patients are $\geq$80 years of age and their primary treatment goals may be improved quality rather than quantity of life.[12, 13] When interviewed, patients with severe AS reported significant symptom burden, including shortness of breath, fatigue, impairment in functional capabilities, reduced ability to participate in social outings, and declining self-image as a result.[14] Patients need to be equipped with realistic expectations of how TAVI will effect their present disease experience. Despite its importance, HRQoL after TAVI has been infrequently measured. In a survey completed by 250 TAVI centers within 38 different countries, assessment of quality of life occurred in only 25% of centers.[15] In Canada between 2013 and 2014, only 31.9% of patients underwent formal HRQoL assessments before their TAVI procedure, and only 12.4% after.[16] With the rapid expansion of TAVI, there is an urgent need to understand these fundamental outcomes as healthcare providers and patient-caregiver units contemplate the best management for this lethal disease

The purpose of this study was to gain a more granular understanding of the short-term (30 days) and long-term (1 year) outcomes of patients following a TAVI procedure in a single centre. In addition to the traditional hospital survival outcomes, we sought to quantify in-hospital complication rates, decision regret, and changes in HRQoL, frailty, and cognition.

Methods

Study Design

The undertaking of this project required two study arms*. Arm 1* was a retrospective chart review of all patients who received TAVI in Manitoba from September 1, 2012 to May 31, 2017. Data was used to complete the previously initiated Manitoba TAVI database. *Arm 2* was a concurrent prospective observation of patients presenting for TAVI or follow-up post-TAVI between June 1, 2017 to March 31, 2018. Their data was combined with existing data in the database to make our overall study population those who underwent TAVI between September 1, 2012 and March 31, 2018.

Setting

This study was undertaken at St. Boniface General Hospital (SBGH); one of only 8 hospitals in Western Canada and the only one in the province of Manitoba which performs TAVI procedures.[16] SBGH is a tertiary healthcare facility in the city of Winnipeg. Ethics approval was granted by the University of Manitoba Research Ethics Board and the Research Review Committee from the St. Boniface Hospital. Permission was granted by the Health Research Ethics Board for data collection from patient records, and consent for any additional tests in the prospective arm were obtained on an individual basis.

TAVI Database

Information was gathered retrospectively via SBGH electronic patient records (EPR) and paper chart review. Prospective data collection periodically involved additional information from patient clinic visits. The database was created based on current Valve Academic Research Consortium (VARC)-2 clinical endpoints.[17] The database was kept secure on a password protected shared drive at SBGH. Data collected included patient demographics and comorbidities, echocardiogram parameters, procedure data, complications, discharge data, and follow-up data.

HRQoL, Frailty, and Cognition

Nine assessments were used to ascertain the effect of TAVI on HRQoL, frailty, and cognition. HRQoL was assessed by three tests: the EuroQol 5 Dimension (EQ-5D-3L), short form Kansas City Cardiomyopathy Questionnaire (KCCQ-12), and Patient Health Questionnaire (PHQ-9). Cognition was measured with the Montreal Cognitive Assessment (MoCA). Frailty was assessed with: the Katz Index of ADLs, the Canadian Study of Health and Aging Clinical Frailty Scale (CSHA-CFS), handgrip strength, 5-meter (5m) gait speed, and chair rises. Assessments were completed by the patient with the aid of a trained nurse at the TAVI clinic. This study looked at outcomes at baseline (pre-TAVI), 30-days post-TAVI, and 1-year post-TAVI.

HRQoL – While most people would agree quality of life is an important concept, there is a lack of a universally agreed upon definition.[18] At a minimum it is one's self perception of their own wellbeing: physically, mentally, and socially.[18, 19] HRQoL focuses on the impact of illness and treatments on one's wellbeing. The EQ-5D-3L is a two-part questionnaire (EQ-5D-3L descriptive system and the EuroQol visual analogue scale; EQ VAS). It is a general measure of HRQoL for a range of diseases.[20] The EQ-5D-3L descriptive system involves the patient rating five dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) on a three-point scale: no difficulty (1 point), some/moderate difficulty (2 points), extreme difficulty (3 points). A Canada specific value set was then used to derive a

single index score between 0 and 1, where 0 is dead and 1 is full health.[21] The EQ VAS involves the patient indicating their perception of their "health state today" as a percentage, where 0% is "worst imaginable health state" and 100% is "best imaginable health state." The EQ-5D-3L has been used extensively internationally, with evidence to support validity and reliability.[22, 23]

KCCQ describes HRQoL for those living with heart failure.[24] KCCQ has been validated for the AS population; of the triad of symptoms associated with AS, symptoms of heart failure are typically predominant, making the KCCQ an appropriate test.[25] The KCCQ has been shown to be more sensitive to change in patients with heart failure symptoms compared to other measures, including NYHA functional class, 6-minute walk test, and EQ-5D-3L.[26] KCCQ-12 is a shortened form of the original but with preserved specificity, sensitivity, and reliability.[27] The tool quantifies limitations in physical function, symptom burden (frequency, change over time, severity), quality of life, and socially; with a summary score there is a total of five scores. Each score has a range of 0 to 100, with higher numbers indicating better HRQoL. For ease of conceptualization, the KCCQ summary score has been correlated with New York Heart Association (NYHA) functional classification system: summary score >75 is approximately NYHA class I, 60 to 75 is approximately class II, 45 to 60 is approximately class III, and <45 approximately class IV.[28] The TAVI Quality Indicator Working Group recommends using both EQ-5D and KCCQ to assess quality of life in the TAVI population.[29]

To add to the assessment of mental wellbeing, the PHQ-9 was used.[30, 31] It is a screening tool of depression. It involves the patient stating frequency of nine experiences in the past two weeks. Scores are 0, 1, 2, or 3 for "not at all," "several days," "more than half the days," or "nearly every day," respectively. Possible score range is 0 to 27. A score of 10 or greater has been typically accepted as the cut-off for detecting major depressive disorders.[32] The PHQ-9 has been shown to be sensitive to changes in depression diagnostic status.[33]

Cognition – The MoCA assesses multiple cognitive domains including: short-term memory recall, visuospatial abilities, executive functioning, attention, concentration, and working memory, language, and orientation to time and place.[34] The MoCA is a validated tool with good internal consistency, high test-retest reliability, and superior sensitivity to other cognitive assessments, such as the Mini Mental Status Exam (MMSE).[34] The MoCA is scored out of 30, with less than 26 indicating cognitive impairment. It was used as the sole cognitive assessment tool, as diagnostic utility does not improve if combined with other tests.[35]

Frailty – Frailty was defined by an international consensus group as, "a medical syndrome with multiple causes and contributions that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death."[36] There has been much debate over the best way to define and assess frailty. We used multiple assessments. First, the Katz Index of ADLs quantifies one's ability to independently complete bathing, dressing, toileting, transferring, continence, and feeding.[37] We used the categorical approach to scoring, where 1 point was given for full independence with the task, for a final score ranging from 0 to 6. Second, the CSHA-CFS is a validated tool that uses clinical judgement to score the patient from 1 to 9, with 1 being very fit, 5 being mildly frail, and 9 being terminally ill.[38] The final three measures were physical tasks, used as indicators of physical ability and muscle strength. Handgrip strength of the dominant hand was measured using a dynamometer. Various cut-off values exist in the literature, but typically a grip strength of <30kg in men and <20kg in women is considered frail.[39] The 5m gait speed measured the time it took a person to walk 5 meters at their normal walking pace. If the person took longer than 6 seconds, they were said to be frail.[39] Gait speed is better than the NYHA functional class in assessing functional impairment in those with symptomatic AS.[40] The final

test was the chair rise test. It measured how long it took for the patient to stand from a seated position five times in a row with their arms crossed so only their lower body strength was engaged.

Decision Regret

Decision regret implies remorse surrounding a decision made. It is potentially an indicator of the quality of a health decision.[41] The Decision Regret Scale (DRS) was utilized 12 to 24 months after TAVI. The DRS is a 5-item scale, where each statement is rated on a Likert scale. The final score is a percentage, with 0% meaning no regret and 100% meaning high regret. The DRS has been previously validated, with outcomes shown to be strongly correlated with decision conflict and decision satisfaction.[41] Although no cut-offs have been agreed upon for clinically significant decision regret, in a systematic review of 59 studies the mean score after various treatment and screening decisions was 16.5 out of 100.[42] This test was only initiated as of June 2017.

Statistical Analysis of Database

Categorical data is presented as percentage and frequencies and continuous data is presented as median with 1st and 3rd quartiles. Median was chosen for summary statistics as the data for most continuous variables were somewhat skewed and median is more representative of the "typical" patient. The sample size was based on the number of individuals with available data. Long term survival up to 3 years was visualized with a Kaplan Meier curve.

Median values with 1st and 3rd quartile range were presented for HRQoL, frailty, and cognitive questionnaires and clinical assessments at baseline, 30-days post-TAVI, and 1-year post-TAVI. 30-day and 1-year post-TAVI results were compared to baseline and median degree of change was reported. Patients acted as their own controls to mitigate confounders of patients' comorbidities contributing to symptomatology.[43] A paired analysis, using a paired T-Test or Signed Rank Test where appropriate, was used to determine whether change after TAVI was statistically different. A p-value of 0.05 or less was considered statistically significant. Patient scores were excluded if they were missing baseline data. MoCA scores were excluded if the patient was blind, deaf, or had a significant language barrier. Physical test scores were excluded if the patient was not physically able to complete them (handgrip strength, 5-metre gait speed, chair rises). All analysis was performed using SAS version 9.3.

There is no universally accepted rule in determining the sample size required to appropriately run a multivariable linear regression model, however using power calculation software (G*Power version 3.1.9.2) it was determined that a sample size of 92 follow-up patients would be required for moderate effect sizes to be detected in a linear regression model containing 5 tested predictors with an alpha of 0.05 and a power of 80%.

Role of BScMed Student

The BScMed student played a vital role in bringing the Manitoba TAVI database up to date via filling in missing data going back to the first TAVI patient and adding new patient data as people were seen in clinic or in hospital. She filled out data abstraction forms and transcribed information into the electronic database. She also reviewed previously entered data and audited completed clinical test documents to ensure correctness in scoring. During the first summer, the student observed many clinic visits to gain an understanding of how the tests are performed. She also advised on introduction of new assessments, including the Decision Regret Scale.

Results

Baseline Characteristics

A total of 208 patients underwent a TAVI procedure in Manitoba between September 1, 2012 and March 31, 2018. Patient demographics are described in Table 1. The median age was 84 years old. There was a high prevalence of comorbidities. Many patients had significant symptom burden according to the NYHA functional classification: 78% of our population were either NYHA class III or IV. The median Society of Thoracic Surgery (STS) score, which predicts risk of mortality, was 3.9%. Although a STS score of <4% is alone considered low surgical risk, there is indication for TAVI in the setting of frailty, multiple comorbidities, anatomical features, and advanced age.[44] Of the studied patients, the majority were consider very old adults ($\geq$80 years old), 27.2% previously underwent a coronary artery bypass grafting (CABG), 16% had a severely calcified aorta known as a porcelain aorta, 23.9% had a Katz Index of ADLs score of <6, and 51.3% had a slow 5m gait speed (>6 seconds).

Baseline echocardiogram measurements are described in Table 1. The median AV area was 0.73 cm^2, AV mean gradient was 39 mmHg, AV peak gradient was 66.4 mmHg, and peak velocity (V_{max}) was 4.08 m/s. Most met the echocardiographic parameters for severe AS, while some had low flow, low gradient AS (those with left ventricular dysfunction) and considered severe after confirmation with dobutamine stress echocardiogram.

Procedural Data

Procedural data is reported in Table 2. Most patients underwent TAVI as an elective out-patient (197 patients; 94.7%), while the remaining were in-patients who required TAVI urgently (11 patients; 5.3%). Transfemoral was the access site for most patients (189 patients; 94%), with the remaining either transapical (10 patients; 5.0%) or more recently transaortic (2 patients; 1.0%). Types of valves varied: 164 people (78.9%) received a balloon expandable Edwards valve, either SAPIEN 3 (39 patients; 18.8%) or SAPIEN XT (125 patients; 60.1%), and 44 patients (21.2%) received Medtronic CoreValve Evolut R self-expanding valve. The final anesthesia for 121 patients (60.5%) was conscious sedation, and for 79 patients (39.5%) was general anesthesia (conscious sedation became more favoured over time). Of the 79 reported general anesthesia cases, 53 were from prior to the first use of conscious sedation in March 2015.

In-hospital complications are described in Table 2. The most common post-procedural complication was implantation of a new permanent pacemaker with 27 cases (13%). Vascular complications occurred in 8 cases (3.9%), involving either peripheral artery stenting or other vascular intervention. There were 3 reports (1.4%) of access site bleed and 8 reports (3.9%) of access site hematomas. Other bleeding included 1 documented gastrointestinal bleed (0.5%). Blood transfusions were required in 3 cases (1.4%) for various reasons. Cardiac arrest occurred in 9 cases (4.3%), due to either ventricular fibrillation (4 patients; 1.9%) or hypotension (5 patients; 2.4%). Of the 208 people, 1 had a transient ischemic attack (0.5%), and 3 had a stroke (1.4%). The strokes occurred between 0 and 17 days post-TAVI. Death prior to discharge occurred in 6 cases (2.9%); 2 deaths occurred within 24 hours of the procedure, with one person sustaining likely aortic annular rupture or LV perforation and the other person decompensating rapidly after cardiac arrest and cardiopulmonary resuscitation; the 4 other deaths occurred after decompensation in the intensive cardiac care unit over a period of 8 days to 5 weeks after the TAVI procedure. Most patients experienced no major complications and stayed in hospital for a median length of time of 5 days. A total of 97.1% of patients survived to

discharge. Of the total population, 93.7% were discharged to their own home and 3.4% to another care facility.

Short and Long-Term Survival

Kaplan Meier Curves were created to estimate survival (Figure 1). 30-day survival was 98%, 1-year survival was 89%, 2-year survival was 80%, and 3-year survival was 71%.

HRQoL, Frailty, and Cognition

Results of questionnaires and clinical assessments are described in Table 3 and analyzed for significant change after TAVI as shown in Table 4. Since the inception of the TAVI program at SBGH, there have been continually evolving standards of clinical care, leading to variability of what tests were performed. Some tests have been done since the beginning (frailty testing and MoCA), while the KCCQ-12 was initiated in April 2017, accounting for the variable number of patients who completed each.

HRQoL - Prior to their TAVI procedure, baseline KCCQ-12 scores demonstrated that most patients had a low HRQoL, with median scores ranging from 31.5 to 50 out of 100 between the 5 categories. After TAVI, KCCQ-12 showed 30-day improvements in social limitation score (+31 points; p=0.014) and overall summary score (+19 points; p=0.005; Figure 2A). Other KCCQ-12 categories (symptom frequency, physical limitation, quality of life) did not reach statistical significance. The EQ VAS showed a statistically significant improvement of 10% at 30 days (p<0.001) and 6% at 1 year (p=0.046), see Figure 2B. The EQ-5D-3L index score at 30 days increased 0.05 points (p=0.046). The EQ-5D-3L index scores at 1 year did not show statistically significant change. The PHQ-9 scores were low at baseline (absence of detected depressive symptoms); scores remained low after TAVI.

There were improvements in patients' cognition (Figure 2C): median MoCA scores improved by 1.0 point at 30 days (p=0.003). This improvement was durable up to 1 year, with 1.3-point improvement compared to pre-TAVI (p=0.034).

Frailty improvements were shown with increased handgrip strength 1 year after TAVI (+3.4kg; p<0.001; Figure 2D). Longer recovery rates could account for no detectable change at 30 days.[45] Baseline Katz Index of ADLs showed the majority of people were completely independent, making the median score already at maximum score of 6 out of 6. CSHA-CFS scores 30-days after TAVI conveyed a median decline of less than a full point; this is of uncertain clinical significance, but likely due to deconditioning before the procedure and in-hospital stay post-TAVI. CSHA-CFS score 1 year after TAVI, and 5m gait speed post-TAVI did not show change of significance. For the chair rise test, there was a 1.0 second improvement 30-days post-TAVI, this is of uncertain clinical significance, but values are trending toward improvement.

Decision Regret

A total of 37 patients completed a DRS 12 to 23 months post-TAVI. Overall, decision regret was low, with 21 patients (57%) having 0% regret. Our population had 31 people (84%) with less decision regret than the average screening and treatment procedures (<16.5%).[42] Of the remainder, 5 people (13.5%) scored between 20 and 25%, and 1 person (2.7%) scored 95%. A chart review of the individual with high regret showed no indication of complication with the

procedure, only a medical consult indicating the patient did not perceive improvement with their symptoms.

Discussion

This study lead to novel findings on the outcomes after TAVI. TAVI has been largely reserved for those patients who have been deemed prohibitive or high surgical risk. Most patients in Manitoba who underwent TAVI were octogenarians with multiple comorbidities. TAVI is an invasive and costly procedure, but with potential for increasing quantity and quality of life. Weighing futility versus benefit with TAVI is not a straightforward process.[46] This study did not look specifically at futility; improvements in predicting poor outcome after TAVI have been reported elsewhere.[47, 48] Our study endeavored to evaluate HRQoL, frailty, and cognition outcomes after TAVI in Manitoba, as measurable potential benefits from the procedure.

It would be incorrect to assume futility of TAVI can be determined by age alone. A large study of 24,025 people was undertaken using the American national registry (STS/ACC TVT) to compare outcomes of nonagenarians versus those younger than 90 years old.[45] They found the nonagenarians had lower 30-day KCCQ scores, but after 1 year there were no differences between the two groups. Authors concluded even with extreme age, TAVI offers similar improvements in HRQoL. Through patient interviews, the reasons for improved HRQoL have been hypothesized as a combination of factors, including decreased burden of physical symptoms, and added peace of mind with improved life expectancy.[49] Just as severe symptomatic AS is limiting in a multitude of ways, TAVI can provide benefits on multiple levels: decreased breathlessness, decreased fatigue, which consequentially can lead to a fuller life of increased social participation and more positive outlook.[14, 49] In interviews, one person reported TAVI improved them enough to be considered for hip replacement surgery; in that regard the HRQoL improvements of TAVI can be compounded with increasing the possibility for other quality of life improving interventions.[49]

In our population, significant improvements in HRQoL were observed at 30-days, with KCCQ-12 summary score increasing by 19 points to a median value of 89.5 out of 100, a score corresponding to NYHA class I.[28] KCCQ-12 changes of 5 or more points have been shown to be clinically important, so the improvements seen here represent clinically significant improvement in HRQoL.[26, 27] This adds to previous studies which reported improvements in HRQoL after TAVI compared to baseline.[50-52]

There were improvements in measured cognition as detected by the MoCA at both 30-days and 1 year. This is promising in light of research suggesting many octogenarians have incremental annual decline in MoCA performance.[53] Studies on change in cognition after TAVI are limited, and the few available have mixed results.[54, 55] By not stratifying our baseline values, a ceiling effect may have been present as those with high scores pre-TAVI did no have much room for improvement. Nevertheless, our results add to this small body of pre-existing literature.

Our population had improved grip strength 1 year after TAVI. Grip strength is a measure of physical function, a hallmark of the frailty syndrome, and a risk factor for the development of disability.[56] Other frailty measures we used were unable to detect a statistical change after TAVI, but it is important to note a lack of decline in scores. Frailty has been shown to be predictive of outcome after TAVI.[47, 57] To our knowledge, this is one of the first studies to show improvement in frailty as a result of TAVI.

Not everyone experiences successful outcomes post-TAVI, and there is a range of levels of improvement and time to improvement. If there is a major complication, like debilitating stroke or death, people can be left worse than their baseline. The in-hospital death and complication rates in this study were low overall, but still present. The most common complication was implantation of new pacemaker (13%). The incidence of new pacemaker reported in the STS/ACC TVT registry from 2013 to 2015 was 11.8%.[58] In our cohort in-hospital stroke rate was 1.4%. In-hospital stroke rates have been reported for other sites: 2.9% in the STS/ACC TVT registry, 3.4% in the German registry, and 2.1% in the Canadian quality report.[16, 58, 59] Our in-hospital death rate was 2.9%. It was also 2.9% in 2015 in America according to the STS/ACC TVT registry.[58]

The 30-day and 1-year mortality rates, estimated by the Kaplan Meier Curve, were 98% and 89%, respectively. This approximates what has been previously reported in randomized control trials.[7, 8, 60, 61] It is interesting to parallel this with the SAVR population from the same site, keeping in mind they are an operable cohort versus the surgically risky TAVI cohort. Patients ≥80 years of age who underwent SAVR at SBGH between 1995 to 2014, had survival rates of 93.6% and 83.8%, 30-days and 1-year post-SAVR, respectively.[62].

Limitations

There were limitations to the study. First, as an observational study there was no control for selection bias and there was no comparison group (a group with severe symptomatic AS who were medically managed). However, randomization could be considered as unethical due to the two large multicentre studies, as well as several other prospective cohort studies, demonstrating an association with improved mortality in patients undergoing a TAVI. [7-11] As an observational study, data was occasionally missing. Second, all questionnaires and clinical assessments were not done for every person at every time point. Assessments were not completed post-TAVI for those who died or were too sick to attend clinic, meaning the study cohort was bias toward those who benefited from the procedure. Additionally, there was variability on time before TAVI baseline tests were completed, and 30-days and 1-year post-TAVI test dates were not always exactly 30-days and 1-year post-TAVI. There were a number of potential contributing factors, including changing clinical follow-up standards and with one-third of people living rurally, there could have been transportation difficulties. Thirdly, tests were completed by multiple nurses in the TAVI clinic, and it is possible there could be slight variations between how each performed the tests. We endeavored to mitigate this through test observation and supplemental electronic reading provided to clinic nurses by a researcher. Finally, there were limitations to individual tests. Handgrip strength could have been underestimated if the patient suffered from conditions effecting the hand like arthritis or carpal tunnel syndrome. KCCQ-12 and EQ-5D-3L could not have included all factors effecting quality of life (patient expectations, coping, and negative affect).[18] Additionally, tests could not exclude effects of other events in patients' lives. HRQoL questionnaires would be sensitive to fatigue related to severe anemia or a new malignancy, breathlessness related to severe lung disease, and depression due to recent traumatic life events. We hoped to lessen this by having patients act as their own control.

Conclusion

In this first account of the TAVI population in Manitoba, mortality was comparable to previously reported randomized control trials and TAVI lead to statistically significant improvements in HRQoL, cognition, and frailty, with low decision regret overall. Accumulating data on outcomes after TAVI allow for realistic expectations of life after TAVI, which can facilitate informed

decision making. This is essential for patients, families, and practitioners as they wade through complex options in the treatment of severe symptomatic AS.

Future Directions

Completion of the Manitoba TAVI database represents a step toward a possible national TAVI registry in Canada, like the American STS/ACC TVT registry.[63] Benefits of a national registry include ease of post-market surveillance of valves, consistencies in outcomes reported, and rich source of data for future observational studies.[63] Currently, the most recent information available for Canada is the Canadian Cardiovascular National Quality Report from 2016, which includes data of TAVI procedures during 2013-2014.[29] A national registry would be a major undertaking, but the future will hopefully bring improved medical information technology infrastructure to mitigate burdens of current data collection methods.[63]

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Appendix

Table 1. Baseline characteristics of patients and echocardiographic findings

Characteristic	TAVI Patients (N=208)
Age	84 (80 - 88)
Sex (Female)	101 (48.6%)
Living situation	
Winnipeg	137 (66.2%)
Non-Winnipeg	70 (33.8%)
Body mass index (kg/m^2)	27.9 (25.1 - 31.6)
Risk scores	
STS Score (%)	3.9% (2.5% - 5.5%)
EuroSCORE (%)	3.9% (2.3% - 6.8%)
NYHA classification	
1	10 (5.0%)
2	33 (16.5%)
3	124 (62.0%)
4	33 (16.5%)
Comorbidities	
Hypertension	167 (82.3%)
Dyslipidemia	146 (71.9%)
Diabetes	62 (30.5%)
Permanent pacemaker	12 (7.7%)
Previous myocardial infarction	35 (17.2%)
Previous stroke	31 (15.4%)
Pulmonary hypertension	42 (21.3%)
Chronic lung disease	42 (20.8%)
Dialysis	1 (0.5%)
Atrial fibrillation	66 (32.7%)
Congestive heart failure	84 (42.0%)
High risk characteristics	
Previous CABG	55 (27.2%)
Porcelain aorta	23 (16.0%)
Baseline Katz < 6	33 (23.9%)
5m gait speed > 6 sec	59 (51.3%)
Echo Parameters	
LVEF ≥50%	169 (83.3%)
LV dysfunction (LVEF <50%)	34 (16.7%)
AV mean gradient (mmHg)	39.0 (31.7 - 49.5)
AV peak gradient (mmHg)	66.4 (52.9 - 83.0)
AV peak velocity (m/s)	4.08 (3.64 - 4.55)
AVA (cm^2)	0.73 (0.63 - 0.85)
Aortic regurgitation	
None	69 (35.6%)
Trivial	15 (7.7%)
Mild	82 (42.3%)
Moderate	26 (13.4%)
Severe	2 (1.0%)

Continuous variables expressed as median (quartile 1 - quartile 3); Categorical variables expressed as N (%). Summary statistics based on non-missing values in clinical database.

Table 2. Procedural data including in-hospital complications, length of stay in hospital after TAVI, and patient disposition

Characteristic	TAVI Patients (N=208)
Urgency	
Elective out-patient	197 (94.7%)
Urgent in-patient	11 (5.3%)
Anesthesia	
Conscious sedation	121 (60.5%)
General	79 (39.5%)
Valve Sheath Access	
Transfemoral	189 (94.0%)
Transapical	10 (5.0%)
Transaortic	2 (1.0%)
Valve type	
Edwards SAPIEN XT	125 (60.1%)
Edwards SAPIEN 3	39 (18.8%)
CoreValve Evolute R	44 (21.2%)
In-hospital complications	
Periprocedural vascular complications	8 (3.9%)
Peripheral artery stent	4 (1.9%)
Other vascular surgery/intervention	4 (1.9%)
Myocardial infarction	0 (0.0%)
Pacemaker implantation	27 (13.0%)
New atrial fibrillation	6 (2.9%)
Cardiac arrest	
Ventricular fibrillation	4 (1.9%)
Hypotension	5 (2.4%)
Transient ischemic accident	1 (0.5%)
Stroke	3 (1.4%)
Infection at access site	0 (0.0%)
Bleeding at access site	3 (1.4%)
Hematoma at access site	8 (3.9%)
Retroperitoneal bleed	0 (0.0%)
GI bleed	1 (0.5%)
GU bleed	0 (0.0%)
Blood transfusion	3 (1.4%)
Dialysis	0 (0.0%)
Hospital Length of Stay	5 (3 - 8)
Disposition	
Died in-hospital	6 (2.9%)
Discharged home	194 (93.7%)
Other acute care	5 (2.4%)
Extended care/rehab	1 (0.5%)
Hospice	1 (0.5%)

Continuous variables expressed as median (quartile 1 - quartile 3); Categorical variables expressed as N (%). Summary statistics based on non-missing values in clinical database

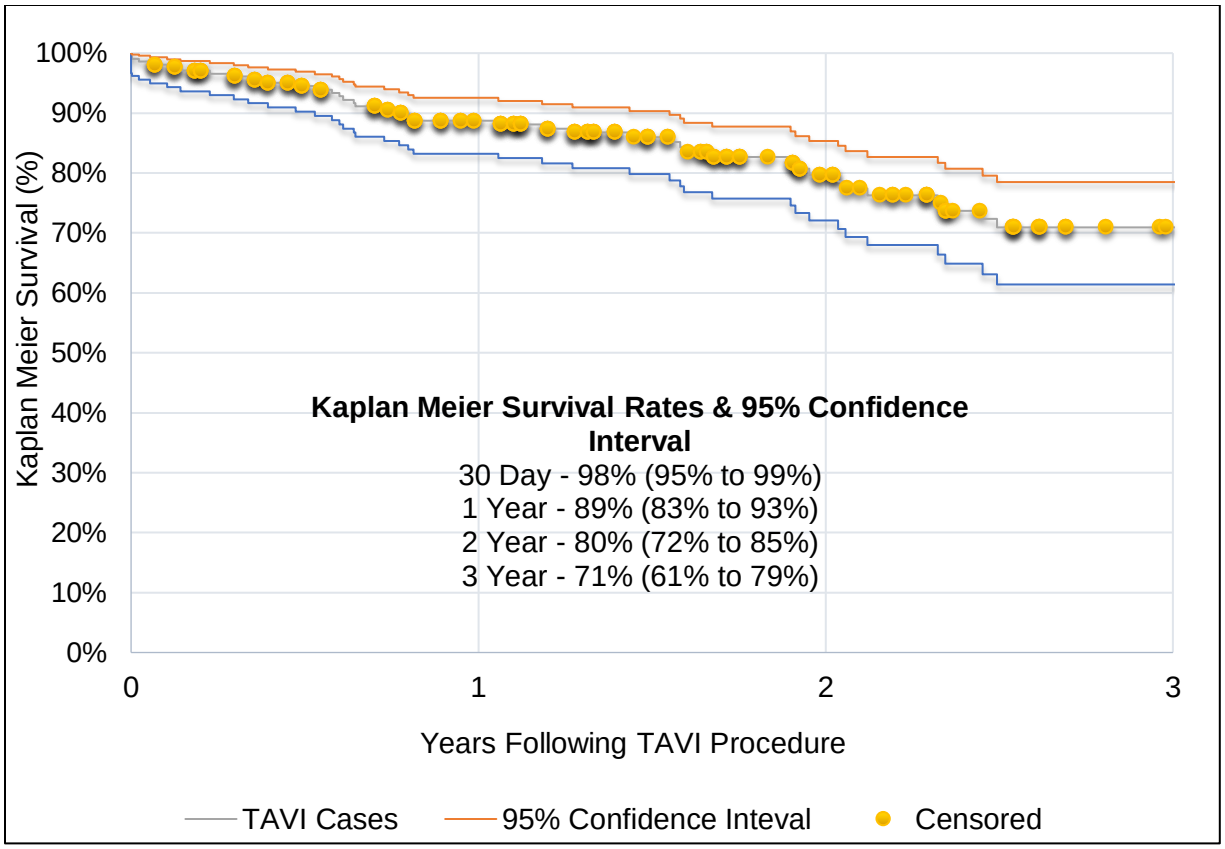

Figure 1. Kaplan Meier Curve estimating survival following TAVI procedures performed in Manitoba between September 1, 2012 and March 31, 2018

Table 3. Scores of questionnaires and clinical assessments

Test	Baseline		30-Days Post-TAVI		1-Year Post-TAVI	
	N	Summary	N	Summary	N	Summary
EQ-5D-3L						
Index score	54	0.74 (0.66 - 0.83)	46	0.78 (0.70 - 0.84)	11	0.78 (0.66 - 0.84)
EQ VAS (%)	95	65 (50 to 80)	84	80 (70 to 90)	49	80 (70 to 90)
KCCQ-12						
Symptom frequency	28	48 (30 to 67)	34	92 (67 to 100)	48	88 (74 to 98)
Physical limitation	27	50 (25 to 75)	34	92 (67 to 100)	51	75 (50 to 92)
Social limitation	27	50 (25 to 75)	33	92 (75 to 100)	50	92 (75 to 100)
Quality of life	28	31.5 (21 to 69)	34	88 (63 to 100)	49	100 (75 to 100)
Overall summary	28	48.5 (30 to 67)	34	89.5 (67 to 96)	51	88 (72 to 93)
Katz Index ADL (/6)	138	6 (6 to 6)	84	6 (6 to 6)	52	6 (5 to 6)
PHQ-9 (/27)	37	2 (1 to 5)	79	2 (0 to 4)	50	2 (0 to 4)
MoCA (/30)	152	23.5 (21 to 26)	82	25 (21 to 28)	49	26 (23 to 27)
CSHA-CFS (/9)	155	4 (4 to 5)	85	4 (3 to 4)	52	4 (3 to 5)
Handgrip strength (kg)	115	22 (16 to 30)	82	21 (17 to 30)	51	26 (17.3 to 32.6)
5m gait speed (s)	115	6.1 (4.8 to 7.4)	82	5.5 (4.6 to 6.5)	50	5.6 (4.8 to 7.4)
Chair rise (s)	118	16.7 (12.6 to 22.2)	69	14.3 (11.4 to 18)	37	15.1 (10.4 to 20.0)

Continuous variables expressed as median (quartile 1 - quartile 3); Categorical variables expressed as N (%). Summary statistics based on non-missing values in clinical database

Table 4. Analysis of questionnaire/assessment scores 30-days and 1-year after TAVI. Time points compared to baseline

Questionnaire/Assessment	30-Days Mean Change vs Baseline			1-Year Mean Change vs Baseline		
	N	Summary	P-Value	N	Summary	P-Value
EQ-5D-3L						
Index Score	40	0.05 (-0.04 to 0.11)	0.046	6	0.11 (-0.07 to 0.27)	0.438
EQ VAS (%)	65	10 (-5 to 20)	<0.001	22	6 (-6 to 25)	0.046
KCCQ-12						
Symptom frequency	15	0 (-12 to 42)	0.385	-	-	-
Physical limitation	14	19 (0 to 34)	0.110	-	-	-
Social limitation	14	31 (17 to 62)	0.014	-	-	-
Quality of life	15	17 (0 to 38)	0.065	-	-	-
Overall summary	15	19 (9 to 31)	0.005	-	-	-
Katz Index ADL (/6)	79	0 (0 to 0)	0.573	40	0 (-0.5 to 0)	0.086
PHQ-9 (/27)	23	1 (-1 to 2)	0.586	10	-1 (-3 to 1)	0.379
MoCA (/30)	80	1 (-1 to 3)	0.003	42	1.3 (-1 to 4)	0.034
CSHA-CFS (/9)	81	-0.5 (-1 to 0)	<0.001	42	0 (-1 to 1)	0.727
Handgrip strength (kg)	73	-0.7 (-2 to 3)	0.947	27	3.4 (1.4 to 5)	<0.001
5m gait speed (s)	75	-0.3 (-1.5 to 0.9)	0.162	28	-0.7 (-1.9 to 0.4)	0.059
Chair rise (s)	62	-1.0 (-4.7 to 1.4)	0.029	24	-1.7 (-11.0 to 2.7)	0.133

Continuous variables expressed as median (quartile 1 - quartile 3); Categorical variables expressed as N (%). Summary statistics based on non-missing values in clinical database

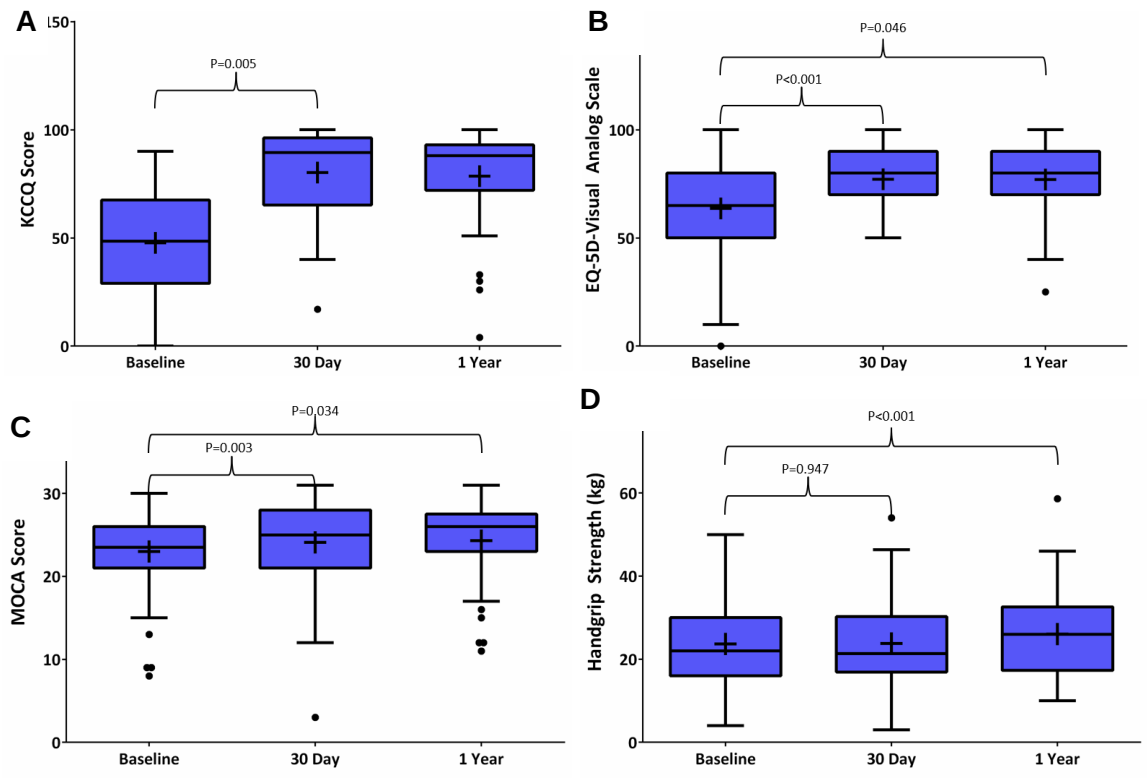

Figure 2. Measured scores of TAVI patients between September 2012 and March 2018 at baseline (pre-TAVI), 30-days post-TAVI, and 1-year post-TAVI. p-values calculated using Signed Rank Test for observations where measurements available at both time points. (**A**) KCCQ-12 summary scores, (**B**) EQ VAS scores, (**C**) MoCA scores, and (**D**) handgrip strength