DOES TRANSCATHETER AORTIC VALVE REPLACEMENT PERFORMED IN A COMMUNITY HOSPITAL SETTING IMPROVE HEALTH RELATED QUALITY OF LIFE?

by

Dorothy M. Urschel

A capstone project submitted to the
School of Nursing
The State University of New York at Buffalo
In partial fulfillment of the requirements for the degree of Doctor of Nursing Practice

May, 2018
DNP Capstone Project Approval Form

This is to certify that

Dorothy Urschel

(Name of Student)

successfully defended his/her Capstone project entitled:

Does Transcatheter Aortic Valve Replacement (TAVR) Performed in a Community Hospital Setting Improve Health Related Quality of Life (HRQOL)?

on

April 20

, 2018

(Date)

Capstone Faculty Advisor

Sharon Hawner, PhD, RN

(Typed Name)

(Signature)

Committee Member 1*

(Typed Name)

(Signature)

Committee Member 2*

(Typed Name)

(Signature)

Committee Member 3*

(Typed Name)

(Signature)

*If applicable
Abstract

Problem. The efficacy of Transcatheter Aortic Valve Replacement (TAVR) for aortic stenosis (AS) has been established in multicenter randomized controlled trials, but its effectiveness in community hospital settings is less certain.

Objective. To improve our understanding of the Health Related Quality of Life (HRQOL) benefits of TAVR in a community hospital setting.

Background literature/Theoretical framework. Despite the overall success of TAVR approximately one-third of patients have disappointing HRQOL outcomes, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Methods. A one-group observational study of TAVR patients treated at St. Peter’s Hospital (Albany, NY) was done. To assess possible HRQOL benefits, preoperative, 1-month postoperative, and 1-year postoperative mean KCCQ scores were compared using repeated measures ANOVA. Bivariate correlations between preoperative mortality risk scores and the KCCQ scores were done. To control for confounding factors in this relationship, multiple linear regressions of KCCQ against six independent variables were also done.

Results. From 2013 to 2017, 188 patients underwent TAVR at St. Peter’s Hospital. Preoperative, 1-month, and 1-year postoperative mean KCCQ scores were 41.6, 67.8, and 89.1 respectively. This improvement was significant in ANOVA (p<0.001). Preoperative and 1-month postoperative KCCQ scores were negatively and significantly correlated with preoperative mortality scores (r = -0.27, p = 0.001, r = -0.16, p = 0.035). In regression models, mortality risk score was not a significant predictor of KCCQ scores.

Conclusions and Implications. Patients undergoing TAVR in a community hospital setting (St. Peter’s Hospital) experienced a significant improvement in HRQOL.
Acknowledgements

I would like to thank Sharon Hewner, PhD, RN, who served as my DNP Capstone Advisor for this project.

In addition, thank you to two St. Peter’s Hospital (Albany, NY) colleagues for their help extracting data from the hospital TAVR database:
Laurie Harbeck, MPH, Manager, Cardiac & Vascular Outcomes
Linsey Marchione, MA, Data Analyst.

Finally, I would like to thank two family members: my mother for her support and encouragement over the years, and H. Urschel for everything she brings to my life.
Nature of Project and Problem Identification.

Aortic stenosis (AS) is the most common heart valve disorder in the United States (Thaden, Nkomo, & Enriquez-Sarano, 2014). The natural history of symptomatic AS is characterized by progressive symptoms (dyspnea, angina, arrhythmia, fatigue, and syncope), disability, and death within several years (Thourani et al., 2015). Traditionally, surgical aortic valve replacement was the treatment of choice but many patients were too ill to undergo such a physiologically demanding operation (Thaden et al., 2014). More recently, a non-surgical treatment option, transcatheter aortic valve replacement (TAVR), has become available (Bourantas & Serruys, 2014). This newer treatment, being less invasive, can be offered to patients who are deemed too high risk for traditional open surgical valve replacement. Due to the invasiveness, novelty, and cost of this new treatment, the Centers for Medicare and Medicaid Services (CMS) has mandated that hospitals providing the treatment must do so within the structure of a formal program, and meet specified CMS standards (Jacques, 2012). This requirement applies to both academic and community hospitals.

Although the efficacy of TAVR has been established in multicenter randomized controlled trials (Kodali et al., 2012; Leon et al., 2016), there is little published literature from community hospital programs to support the more general effectiveness of the treatment. The major TAVR randomized controlled trials are considered explanatory, as opposed to pragmatic type trials. That is, the interventions were performed in a standardized fashion and under ideal circumstances (Schwartz & Lellouch, 2009). This poses several problems for the generalization of trial results to community hospitals. First, there is an underlying hospital selection bias that is often lurking within multicenter randomized controlled trials and this can compromise the external validity of the trial results (Rothwell, 2005). Academic and specialized centers are
typically over represented in explanatory multicenter trials. Second, most of the hospitals selected for the TAVR trials were high volume cardiac surgery centers. The well-known, but incompletely understood, volume outcome relationship in cardiac surgery can also influence the generalization of multicenter trial results to community hospitals, since community hospitals often have lower volumes than their academic hospital counterparts (Shahian & Normand, 2003).

Patients undergoing TAVR procedures for aortic stenosis are typically elderly, frail, and have limited life expectancies irrespective of treatment (Bourantas & Serruys, 2014). Therefore, treatment efficacy should not be assessed using survival alone (Arnold et al., 2014; Reynolds et al., 2011). Health related quality of life (HRQOL) is as important, or perhaps more important, than survival (Reynolds et al., 2011). In multicenter randomized trials, TAVR has been shown to improve HRQOL (Arnold et al., 2014; Reynolds et al., 2011). Within the intermediate to high risk patients with aortic stenosis who are considered for TAVR there are subsets that appear to derive the most, and the least, benefit in HRQOL (Arnold et al., 2014). One possible preoperative determinant of post TAVR HRQOL is the Society of Thoracic Surgeons (STS) mortality risk score (O'Brien et al., 2009). Arnold et al. (2014) found that patients with poor TAVR outcomes, defined using a composite measure of survival and HRQOL, had significantly (p=0.005) higher preoperative STS risk scores than patients who had good outcomes.

Since the HRQOL benefits of TAVR are related to subtleties in patient selection, and a host of poorly understood factors, it is not certain that favorable results from multicenter (and largely academic centers) randomized controlled trials can be generalized to community hospital settings (Arnold et al., 2014; Rothwell, 2005). For this reason there is a need for a TAVR HRQOL outcomes study, and also an analysis of possible aids to TAVR patient selection to optimize HRQOL life benefits, in a community hospital setting. The TAVR program at St.
Peter’s Hospital, a community hospital in Albany, NY, was established in 2013. The program’s results generally compare favorably to national benchmarks in standard outcomes such as 30-day operative mortality and length of stay, but the program’s performance in HRQOL has not been assessed. Taken together, the needs of the St. Peter’s Hospital TAVR program and the need for a community hospital based study of TAVR HRQOL effectiveness suggested the Capstone Project reported herein.

The purpose of this Capstone Project is to improve our understanding of the HRQOL that can be expected after TAVR procedures are performed in a community hospital setting, and how preoperative risk influences these anticipated benefits. The project is guided by the following research questions:

1. Do patients with intermediate to high operative risk aortic stenosis treated with TAVR in a community hospital setting (St. Peter’s Hospital, Albany, NY) experience an improvement in their HRQOL, as measured by the short form Kansas City Cardiomyopathy Questionnaire (KCCQ-12)?

2. To what extent are the changes in HRQOL related to severity of operative risk, as measured by the preoperative Society of Thoracic Surgeons (STS) mortality risk score?

**Review of Literature and Theoretical Framework.**

The efficacy of TAVR for patients with aortic stenosis has been studied in several randomized controlled trials and in several propensity matched non-randomized trials (Tam et al., 2017). Table 1 summarizes the major American randomized controlled trials (Adams et al., 2014; Kodali et al., 2012; Leon et al., 2010; Leon et al., 2016; Smith et al., 2011). There are two key results from these trials. First, in high risk AS patients TAVR significantly improves one-
year survival (70% vs. 50%) compared to standard medical treatment (which may include including balloon valvuloplasty) (Leon et al., 2010). Second, TAVR gives similar one-year (Adams et al., 2014; Smith et al., 2011) and two-year survivals (Kodali et al., 2012; Leon et al., 2016) to that obtained with surgical aortic valve replacement.

Table 1

Selected randomized controlled trials of TAVR compared to other treatments

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Sub-Population of AS Patients</th>
<th>Comparison Group</th>
<th>Major Findings for TAVR vs. Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leon (2010) STS score &gt; 10</td>
<td>Standard therapy</td>
<td>Better 1-year survival (70% vs. 50%)</td>
<td>Improved symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Higher stroke and vascular complications</td>
</tr>
<tr>
<td>Smith (2011) STS score &gt; 10</td>
<td>SAVR</td>
<td>Similar 30-day mortality and 1-year survival</td>
<td>Similar symptom improvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>More vascular complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Less major bleeding and atrial fibrillation</td>
</tr>
<tr>
<td>Kodali (2012) STS score &gt; 10</td>
<td>SAVR</td>
<td>Similar 2-year survival</td>
<td>Similar symptom improvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>More paravalvular leaks</td>
</tr>
<tr>
<td>Adams (2014) Estimateda 30-day mortality of 15 - 50%</td>
<td>SAVR</td>
<td>Better 1-year survival (86% vs. 81%)</td>
<td>No increased stroke rate</td>
</tr>
<tr>
<td>Leon (2016) STS score 4-8</td>
<td>SAVR</td>
<td>Similar 2-year survival</td>
<td>More vascular complications &amp; paravalvular leak</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Less major bleeding and atrial fibrillation</td>
</tr>
</tbody>
</table>

Note. TAVR = Transcatheter Aortic Valve Replacement; AS = Aortic Stenosis; STS = Society of Thoracic Surgeons; SAVR = Surgical Aortic Valve Replacement. Standard therapy is medical therapy, including balloon valvuloplasty, for patients at high risk for traditional surgical intervention.

a Experts’ estimate of operative risk. Mean STS score approximately 7.5.

The randomized and high quality observational trials have themselves been the subject of further analysis in the form of meta-analyses and systematic reviews (Cao et al., 2013; Carnero-Alcazar et al., 2017; Kondur et al., 2016; Tam et al., 2017). The primary trials have studied TAVR in different subpopulations of patients with aortic stenosis. This makes meta-analyses
difficult. Not surprisingly, the various meta-analyses yield slightly different conclusions depending on the inclusion criteria, specific populations included, and endpoints of interest. Nevertheless, general agreement exists on the following points. When compared to surgical aortic valve replacement, TAVR results in similar operative mortality, stroke rate, and one and two year survival. TAVR is less prone to major bleeding than surgical aortic valve replacement, but it has a greater incidence of major vascular complications, need for permanent pacemaker, and paravalvular regurgitation. Paravalvular regurgitation leads to cardiac symptoms and it also contributes to late deaths (Kodali et al., 2012).

Given the general frailty and limited life expectancy of patients considered for TAVR, considerations of quality of life are at least as important as duration of life (Deutsch et al., 2013). A systematic review of high quality evidence has concluded that TAVR improves HRQOL in patients with severe aortic stenosis (Kim et al., 2014). Improvement in physical or biological domains of HRQOL was most pronounced, with general health and psychological domains showing only modest improvement (Kim et al., 2014). Notable individual studies of HRQOL are summarized in Table 2 (Arnold et al., 2017; Osnabrugge et al., 2015; Reynolds et al., 2011; Reynolds et al., 2012). Of particular relevance is the data taken from the national TAVR registry, which show that approximately two thirds of TAVR patients experience a “favorable” HRQOL outcome (defined in this study as a KCCQ Overall Score of greater than 60, on a 0-100 range, and not more than a 10 point decline compared to baseline) (Arnold et al., 2017).
Table 2

*Selected studies of health related quality of life after TAVR*

<table>
<thead>
<tr>
<th>First Author (Year)</th>
<th>Type of Study</th>
<th>Sub-Population of Aortic Stenosis Patients</th>
<th>Major Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reynolds (2011)</td>
<td>RCT: TAVR vs. Standard</td>
<td>High risk</td>
<td>TAVR significantly improves HRQOL at 1, 6, and 12 months</td>
</tr>
<tr>
<td>Reynolds (2012)</td>
<td>RCT: TAVR vs. SAVR</td>
<td>High risk</td>
<td>TAVR &amp; SAVR provided similar HRQOL benefits (KCCQ-OS improved by 25-30 points)</td>
</tr>
<tr>
<td>Arnold (2017)</td>
<td>Observational: TVT national registry data on TAVR patients</td>
<td>Intermediate and high risk</td>
<td>Mean KCCQ-OS scores/changes: Baseline 42 points 1 month +28 points 1 year +32 points</td>
</tr>
<tr>
<td>Osnabrugge (2015)</td>
<td>Observational: Single arm study</td>
<td>Extreme risk</td>
<td>Mean KCCQ-OS changes: 1 month +24 points 1 year +27 points</td>
</tr>
</tbody>
</table>

*Note.* RCT = randomized controlled trial; TAVR = Transcatheter Aortic Valve Replacement; HRQOL = Health Related Quality of Life; SAVR = Surgical Aortic Valve Replacement; TVT = Transcatheter Valve Therapy; KCCQ-OS = Kansas City Cardiomyopathy Questionnaire Overall Score (0-100 range, higher values indicate better HRQOL). Intermediate/High risk denotes preoperative STS risk scores of 4-8 and > 8, respectively. Extreme risk defined as expectation of operative mortality or irreversible morbidity exceeds 50%. Standard therapy is medical therapy for patients at high risk for traditional surgical intervention.

The Kansas City Cardiomyopathy Questionnaire (KCCQ) is a validated 23-item questionnaire that quantifies physical limitations, symptoms, self-efficacy, social interference and quality of life in patients suffering from heart failure and related disorders (Green, Porter, Bresnahan, & Spertus, 2000). Its main advantage over more generic HRQOL survey instruments is that it specifically addresses the problems that people with heart disease experience. This survey instrument was used to assess HRQOL in the North American multicenter randomized controlled trials (Arnold et al., 2014; Reynolds et al., 2011). Currently, an abbreviated or short form version of the original KCCQ, the KCCQ-12, is used in CMS approved TAVR programs.
The newer short form version of the KCCQ is highly correlated with the original version, preserves the original’s psychometric properties, and is easier to administer (Spertus & Jones, 2015). Patients undergoing TAVR procedures at St. Peter’s Hospital complete the KCCQ-12 preoperatively, one month postoperatively, and at one year after the procedure. The survey results are prospectively entered into a standardized TAVR database, which is part of a national TAVR data registry. The national registry, termed the Transcatheter Valve Therapy (TVT) registry, is a joint venture of the Society of Thoracic Surgeons (STS) and the American College of Cardiology (Carroll et al., 2013). The relevant outcomes of interest in this Capstone Project are the one month and one year postoperative KCCQ-12 scores, which are compared to the preoperative (baseline) patient score.

Both the original KCCQ and the short form KCCQ-12 have a range, or overall score (OS), of 0 to 100, with higher scores indicating better HRQOL (Spertus & Jones, 2015). To aid clinicians’ interpretations of the overall score, the KCCQ-OS has been categorized as very poor (KCCQ-OS <25), poor (KCCQ-OS 25–49), fair (KCCQ-OS 50–74), and good (KCCQ-OS ≥75) health related quality of life (Arnold et al., 2013). Changes in the KCCQ-OS of 5, 10, and 20 points correspond to small, moderate or large clinical improvements, respectively (Spertus et al., 2005). In the context of TAVR procedures, a one year KCCQ-OS ≥60, which is roughly equivalent to New York Heart Association class I–II symptoms, is deemed a favorable outcome (Arnold et al., 2013). Typically, a decrease of ≥ 10 points in the KCCQ-OS score from baseline to 1 year is considered a poor outcome (Arnold et al., 2014).

The STS preoperative valve surgery risk model predicts the risk of operative mortality after adult cardiac valve surgery (O'Brien et al., 2009). In patients with aortic stenosis, those with intermediate (risk score of 4.0 – 8.0) and high (risk score greater than 8.0) risk are
considered for TAVR. All patients being assessed for possible TAVR at St. Peter’s Hospital undergo risk assessment and the preoperative risk scores are prospectively entered into the TAVR database. In the Placement of Aortic Transcatheter Valve (PARTNER) multicenter trial, preoperative mortality risk scores influenced postoperative HRQOL but other preoperative predictors of post TAVR HRQOL were also identified (Arnold et al., 2014). Some of these other predictors overlap with the STS risk assessment instrument in terms of their domains of focus. Relevant predictors from the PARTNER trial are detailed in the methods section.

An appropriate theoretical model for research on HRQOL was proposed by Ferrans, Zerwic, Wilbur, and Larson (2005). It in turn is a modification of a theory proposed by Wilson and Cleary (1995). In Ferrans’ theory there are four main determinants of quality of life: biological function, symptoms, functional status, and general health perceptions (Ferrans, Zerwic, Wilbur, & Larson, 2005). In addition, characteristics of the individual and characteristics of the environment influence the four determinants, and these characteristics also directly influence quality of life. A graphical representation of the theory is given in Figure 1.
Biological function, which includes the physiological processes that are essential to life, is the most fundamental determinant of health status (Wilson & Cleary, 1995). Abnormalities of biological function influence the other three determinants of quality of life - symptoms, functional status, and general health perceptions – in addition to directly affecting overall quality of life (Ferrans et al., 2005). Typically the most direct goal of medical interventions, such as TAVR, is to improve outcomes in the biological function domain.

The next determinant, symptoms, include a patient’s perception of an abnormal physical, emotional, or cognitive state (Wilson & Cleary, 1995). Symptoms often arise from an alteration of biological function, but they are often surprisingly independent of biological function. Two
individuals with similar states of biological function may differ profoundly in the severity of their symptoms. In this way, symptoms are a determinant of HRQOL that is distinct from biological function.

Functional status, which assesses the ability to perform certain tasks, is affected by both biological function and symptoms. Once again, this determinant is not necessarily highly correlated with the previously discussed determinants. Four sub-domains of functioning are physical, social, role, and psychological (Wilson & Cleary, 1995).

The final determinant is general health perceptions. This is an extremely subjective concept and is not a simple summation of the preceding determinants (Ferrans et al., 2005). It permits an individual to summarize their perception of health independent of biological function, symptoms, and functional status.

Characteristics of the individual are demographic, developmental, psychological, and biological factors that affect health outcomes (Ferrans et al., 2005). Demographic characteristics include gender, age, and ethnicity. Psychological factors include cognitive processes which influence perceptions, motivation, and beliefs. In the context of characteristics of the individual, biological factors are essentially genetically based characteristics. Note that many of the characteristics of the individual are either difficult, or impossible, to modify.

Characteristics of the environment are physical or social (Ferrans et al., 2005). Examples of physical characteristics include factors such as neighborhood pollution, walking environment, public transportation, personal security, living conditions, and access to healthy food choices. Examples of social characteristics include the influence of family members and prevalent cultural views of health and healthcare.
We can link the individual questions in the KCCQ-12 (provided in Appendix A) to one or more domains of the Ferrans theory. For simplicity, in Table 3 only one domain from the theory is listed for each question.

Table 3

*Linking KCCQ-12 items to Ferrans theory domains*

<table>
<thead>
<tr>
<th>KCCQ-12 Item number</th>
<th>Nature of Question</th>
<th>Ferrans Domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a, 1b, 1c</td>
<td>Daily activities</td>
<td>Functional Status</td>
</tr>
<tr>
<td>2</td>
<td>Feet swelling</td>
<td>Biological Function</td>
</tr>
<tr>
<td>3</td>
<td>Fatigue</td>
<td>Symptoms</td>
</tr>
<tr>
<td>4</td>
<td>Shortness of breath</td>
<td>Symptoms</td>
</tr>
<tr>
<td>5</td>
<td>Sleeping in a chair</td>
<td>Symptoms</td>
</tr>
<tr>
<td>6</td>
<td>Enjoyment in life</td>
<td>General Health Perceptions</td>
</tr>
<tr>
<td>7</td>
<td>Satisfaction with life</td>
<td>General Health Perceptions</td>
</tr>
<tr>
<td>8a, 8b, 8c</td>
<td>Lifestyle impact</td>
<td>Functional Status</td>
</tr>
</tbody>
</table>

*Note.* KCCQ = Kansas City Cardiomyopathy Questionnaire.

In summary, the literature, mostly derived from multicenter RCTs, shows that TAVR yields similar outcomes to surgical aortic valve replacement, and approximately two-thirds of patients experience a good long term HRQOL outcome. KCCQ is a valid HRQOL survey instrument suitable for AS patients, and its multidimensional assessment can be informed by Ferrans’ theoretical model. Pre-operative prediction of long term post-TAVR HRQOL is imprecise, and there is some suggestion that the STS mortality risk score may be useful in this regard (although its designed purpose is to predict operative mortality as opposed to HRQOL).
With this background established, we now address the methodological approach to answering our research questions.

**Methods.**

**Design.**

This Capstone Project’s statement of purpose, literature review, and theoretical framework argued for a one group observational design to examine HRQOL after TAVR performed in a community hospital setting. The design is one group since there is no comparison group, such as patients treated by standard medical therapy or surgical aortic valve replacement. That type of comparison has been done in multicenter randomized controlled trials of TAVR efficacy. In this Capstone Project, comparisons are of the “within group” type; baseline (preoperative), one month, and one year KCCQ-12 data give three dependent groups. The observational design involves retrospective examination of existing data. The relevant data was prospectively collected and deposited into a dedicated TAVR database at St. Peter’s Hospital. The study population consists of every patient entered into the database from 2013 until the fourth quarter of 2017.

The St. Peter’s Hospital TAVR database is based on the national TVT database (Carroll et al., 2013). Given the prospective nature of data collection, and the need to meet national database collection standards, high quality data was expected. Since the data needed for the Capstone Project was already collected, there was no need to design methods and procedures for data collection. Instead, the analogous procedure to data collection that applied here was a process of data extraction, reformatting, and cleaning (Barton & Peat, 2014). Only a relatively
A small amount of data from an individual subject’s data was needed for the Capstone Project, so the extraction process was very selective.

**Variables.**

The key dependent variables in the Capstone Project are KCCQ-12 Overall Scores at baseline (preoperative), one month and one year post TAVR. The independent variables are the preoperative STS mortality risk score and selected variables identified in the PARTNER trial. Table 4 lists some of the most significant predictors of HRQOL from the PARTNER trial, which are also available (or have proxies) in the St. Peter’s Hospital TAVR database.

Table 4

Selected preoperative predictors of composite (survival and HRQOL) outcome after TAVR in the PARTNER Trial

<table>
<thead>
<tr>
<th>Possible Predictor</th>
<th>Acceptable Outcome Group</th>
<th>Poor Outcome Group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS risk score&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.4 (4.5)</td>
<td>11.9 (4.1)</td>
<td>0.005</td>
</tr>
<tr>
<td>6-min walk test (m)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>123.9 (122.2)</td>
<td>84.0 (104.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean aortic gradient (mmHg)</td>
<td>45.1 (14.3)</td>
<td>41.2 (14.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.29 (0.46)</td>
<td>1.36 (0.51)</td>
<td>0.002</td>
</tr>
<tr>
<td>Major arrhythmia (%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>47.5</td>
<td>57.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oxygen dependence (%)</td>
<td>9.3</td>
<td>14.3</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Note.** HRQOL = health related quality of life; TAVR = Transcatheter Aortic Valve Replacement; PARTNER = Placement of Aortic Transcatheter Valve; STS = Society of Thoracic Surgeons. Values in parentheses, following a mean, are standard deviations. p values are from univariate comparisons of means and proportions.

<sup>a</sup> Patients in the PARTNER trial were high risk (STS scores > 8).

<sup>b</sup> In the current national TAVR database, 5-metre walk time has replaced the 6-min walk test.

<sup>c</sup> Defined as atrial fibrillation or flutter, supraventricular tachycardia, ventricular arrhythmias, or high-degree atrioventricular block.
The relevant research question in this Capstone Project, in terms of the dependent and independent variables, pertains to the relationship of preoperative STS scores to one month and one year postoperative KCCQ-12 scores, and the influence of other preoperative predictors on this relationship, in patients undergoing TAVR at St. Peter’s Hospital.

**Statistical Methods.**

The statistical methodology is presented in the context of the following specific operationalized forms of the previously stated research questions:

1. Do patients’ KCCQ-12 Overall Scores at one month and one year after undergoing TAVR improve compared to baseline scores?

2a. What is the correlation between preoperative STS mortality risk scores and preoperative, one month, and one year postoperative KCCQ-12 Overall Scores?

2b. Is preoperative STS mortality risk score an important determinant of KCCQ-12 Overall Scores after controlling for other preoperative determinants of post TAVR HRQOL identified in the PARTNER Trial (aortic gradient, serum creatinine, 5-meter walk time, major arrhythmia, and home oxygen dependence)?

For the first question, a repeated measures ANOVA was performed (Polit, 2010). That showed if the three KCCQ means were significantly different, but it did not specify the exact relationships that contributed to any difference. For that, pairwise Bonferroni post hoc tests were done (Barton & Peat, 2014).

For the second question bivariate Pearson correlations between STS risk scores and KCCQ-12 Overall Scores were performed (Polit, 2010). Correlation analysis is simple but does not control for possible confounding variables. Multiple linear regressions was used to control
for other possible determinants of KCCQ-12 Overall Score. The independent or explanatory variables for the regression, previously outlined in Table 4, were selected based on the analysis of the PARTNER trial (Arnold et al., 2014). That analysis assessed many more possible predictors than listed in Table 4, but it was not feasible to duplicate the PARTNER modeling using the St. Peter’s Hospital data set; the sample sizes were dramatically different. Given a sample size of under 200 patients in the St. Peter’s Hospital database, compared to over 2,000 patients in the PARTNER study, a more parsimonious regression model was required (Barton & Peat, 2014). Therefore, only six of the most significant independent variables from the PARTNER trial - STS risk score, 6-minute walk test, mean aortic gradient, serum creatinine, presence of major arrhythmia, and home oxygen dependence - were used to inform the regression model. Finally, the 6-minute walk test (distance measured) used in the PARTNER trial was replaced by the 5-metre walk time (time measured), which is the analogous metric used in the current national TVT database. All statistical analysis was done with IBM SPSS Statistics for Windows Version 24 software (IBM Corp., Armonk, N.Y., USA).

Results.

From 2013 to 2017, 188 patients with intermediate and high risk AS underwent TAVR at St. Peter’s Hospital. Mean age of the population was 83 (SD 7.5) years, and 57% were female. Mean STS mortality risk score was 7.85 (SD 4.56). In hospital mortality and 30-day mortality were 2.2% and 3.1%, respectively. One year follow up data is not available for patients who underwent TAVR in 2017, but that group of patients still contributes to other important aspects of the dataset. For example, one month postoperative follow up, which includes the one month KCCQ, is available for most of the 2017 patients. Apart from the incomplete one year follow up
problem, missing values were not a major issue. For most variables, the missing value percentage was under 10% and appeared to be random. For the one year KCCQ, there were 127 candidate patients. Of these 127 patients, 98 had completed the one year KCCQ survey. The reason for non-completion in the remaining 29 cases include early death (4), late death (18), lost to follow up (5), and unknown (missing values) (2).

Preoperative, one month, and one year postoperative mean (95% CI) KCCQ scores were 41.6 (36.2, 46.9), 67.8 (62.4, 73.1), and 89.1 (84.7, 93.4), respectively (Figure 2). Kolmogorov-Smirnov tests of normality for preoperative, one month, and one year KCCQ scores yielded test statistics of 0.067 (p=0.062), 0.097 (p<0.001), and 0.293 (p<0.001). That is, the one month and one year scores failed the normality assumed in ANOVA analysis. In both cases the samples were negative (left) skewed, with this being especially pronounced in the one year group. This distributional finding is to be expected since the scores are, roughly speaking, improving over time. Fortunately, ANOVA is robust to violations of normality when the sample size is reasonably large, as it was in this study (Barton & Peat, 2014).

Mauchly’s test was done to assess the sphericity (equal variance) assumption inherent in repeated measures ANOVA analysis. Mauchly’s test did not show that the assumption of sphericity had been violated ($\chi^2 = .683, p = 0.711$). Therefore, standard repeated measures ANOVA (without a Greenhouse-Geisser, or similar, correction) was carried out. The progressive increase (improvement) in mean KCCQ scores was significant in ANOVA analysis ($F(2, 168) = 117.5, p<0.001$). All pairwise Bonferroni comparisons of groups were also significant (p<0.001 for all comparisons). At one year post-TAVR, 92.9% of patients completing the survey had KCCQ scores greater than 60, which is a threshold commonly associated with a good HRQOL outcome (Arnold et al., 2013).
Figure 2. Mean KCCQ values over time.

Preoperative and one month postoperative KCCQ scores were negatively and significantly correlated with preoperative STS risk scores ($r = -0.27$, $p = 0.001$, $r = -0.16$, $p = 0.035$, respectively) (Figures 3 and 4), but one year postoperative KCCQ scores were not correlated with STS risk scores ($r = -0.62$, $p = 0.543$). In the regression models detailed below, STS risk score was not a significant predictor of pre, one month, or one year KCCQ.
Figure 3. Scatterplot and correlation of STS risk score and preoperative KCCQ.
Regression models of the following form were used:

\[ KCCQ = b_0 + b_1 \times \text{STS score} + b_2 \times \text{aortic gradient} + b_3 \times \text{creatinine} + b_4 \times \text{5-metre walk time} + b_5 \times \text{major arrhythmia} + b_6 \times \text{home O}_2\text{ dependence} + \epsilon. \]

The regressions were carried out on the original dataset, and also on datasets created by SPSS’s multiple imputation (5 iterations) algorithm (Patrician, 2002). In the regressions on the original datasets, cases which did not have complete data for each variable were excluded. For the imputed datasets, each regression used data from all 188 patients. The regression results were
robust across the datasets, with no change in the independent variables which were found to be significant. For this reason, only the regression results on the original, unaltered, dataset are presented (Table 5).

Table 5

Regression beta coefficients with corresponding t statistics and significance values

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Preop KCCQ</th>
<th>1-month KCCQ</th>
<th>1-year KCCQ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>beta</td>
<td>t</td>
<td>p</td>
</tr>
<tr>
<td>Constant</td>
<td>72.184</td>
<td>84.042</td>
<td>88.023</td>
</tr>
<tr>
<td>STS risk score</td>
<td>-.406</td>
<td>-.843</td>
<td>.401</td>
</tr>
<tr>
<td>Aortic gradient</td>
<td>.249</td>
<td>1.927</td>
<td>.056</td>
</tr>
<tr>
<td>Creatinine</td>
<td>-.858</td>
<td>-.272</td>
<td>.786</td>
</tr>
<tr>
<td>5-metre walk time</td>
<td>-2.933</td>
<td>-5.324</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Home O$_2$</td>
<td>-10.262</td>
<td>-1.134</td>
<td>.259</td>
</tr>
</tbody>
</table>

Note. Statistically significant regression coefficients are highlighted with boldface.

a N= 129.  b N = 134.  c N=75.

In the preoperative KCCQ regression, the 5-metre walk time (p<0.001) and the presence of a major arrhythmia (p=0.01) were significant predictors of poor baseline HRQOL. In the one month postoperative KCCQ regression, elevated creatinine (p=0.047) and prolonged 5-metre walk time (p=0.001) were significant predictors of poor early postoperative HRQOL. At one year, the aortic gradient (p=0.039) was a significant predictor of favorable postoperative HRQOL (although a large aortic valve gradient indicates severe aortic stenosis, it also indicates preserved left ventricular function).
Discussion and Implications.

The first research question in this study asked if patients with intermediate to high operative risk aortic stenosis treated with TAVR in a community hospital setting (St. Peter’s Hospital, Albany, NY) experienced an improvement in their HRQOL, as measured by the short form Kansas City Cardiomyopathy Questionnaire. We can confidently answer this question in the affirmative. The improvement in HRQOL after TAVR was statistically significant. Perhaps more importantly, the magnitude of benefit was clinically significant. Mean KCCQ improved by approximately 47 points, from 42 to 89. This result is similar to that reported from the TVT national TAVR registry (Arnold et al., 2017), where the preoperative mean KCCQ was 42 and the one year improvement was 32 points. It also compares favorably to the 25-30 point improvement reported Reynolds et al. (2012), and the 27 point improvement reported by Osnabrugge et al. (2015).

Changes in KCCQ score of 5, 10, and 20 points are typically thought to correspond to small, moderate or large clinical improvements, respectively (Spertus et al., 2005). In the context of TAVR procedures, a 1-year KCCQ score greater than 60, which is roughly equivalent to New York Heart Association class I–II symptoms, is deemed a favorable outcome (Arnold et al., 2013). By this criterion, for St. Peter’s Hospital TAVR patients who reached one year follow up, 93% have had favorable HRQOL outcomes.

One possible preoperative determinant of post TAVR HRQOL is the STS mortality risk score (O'Brien et al., 2009). The possible correlation between the mortality risk score and HRQOL, as measured by the KCCQ-12 overall score, is the subject of research question 2a. Arnold et al. (2014) found that patients with poor TAVR outcomes, defined using a composite measure of survival and HRQOL, had significantly (p=0.005) higher preoperative STS risk
scores than patients who had good outcomes. For this reason we examined the relationship between preoperative STS risk scores and HRQOL, as measured by the KCCQ. Although STS risk scores were negatively and significantly correlated with preoperative and one month postoperative KCCQ scores, there was no significant correlation with one year KCCQ scores. High STS risk scores are an indicator of poor overall health so it is not surprising that high scores are associated with poor preoperative HRQOL, and to a lesser extent, early postoperative HRQOL. Although the STS mortality risk score is a valid predictor of operative mortality (its designed purpose), our results cast doubt on its usefulness as a predictor of long term post TAVR HRQOL.

Regression analysis was done to control for possible confounding variables in the STS risk score – KCCQ correlation; this was our approach to research question 2b. Our choice of regression independent variables was influenced by the findings of the PARTNER multicenter trial (Arnold et al., 2014). Importantly, we did not use our data to dictate the nature of the regression model. The regression results show that once confounding variables are controlled for, preoperative STS risk score is a remarkably poor predictor of HRQOL. This casts doubt on the importance of our previously noted significant negative correlations between STS risk score and preoperative and one month KCCQ scores.

The regression results revealed several other interesting findings, which are broadly consistent with those reported in the PARTNER trial (Arnold et al., 2014). Given the relatively small sample size in our study, we suggest caution in over interpreting these ancillary findings. Nevertheless, it is not surprising that prolonged 5-metre walk times and a history of major arrhythmia were associated with poor preoperative HRQOL. Similarly, it is physiologically plausible that prolonged 5-metre walk times and impaired renal function (elevated serum
creatinine) are predictive of poor one month postoperative HRQOL. More interesting is the finding that an elevated preoperative aortic valve gradient, which can be associated with preserved left ventricular function, was predictive of favorable one year postoperative HRQOL. This is consistent with the findings of many studies of valvular heart disease, where left ventricular function is a strong determinant of long term outcome after surgical intervention (O'Brien et al., 2009). In particular, the finding is consistent with that reported by Arnold et al. (2017) in their study based on the national TAVR database.

Taken together with evidence from randomized controlled trials, the current research results can inform the clinical practice of advanced practice registered nurses (APRNs) at St. Peter’s Hospital. Reassuringly, the findings from this research at a community hospital are broadly similar to those reported from multicenter RCTs. This should give APRNs at other community hospitals confidence in the knowledge that the multicenter RCT results may well generalize to community hospital TAVR programs. The current research serves as an example of how local research can augment evidence-based recommendations derived from multicenter RCTs, and help guide local practice. One specific example of this is the finding that a large aortic gradient was positively associated with a favorable one year HRQOL outcome after TAVR. Patients with aortic stenosis considering TAVR at St. Peter’s Hospital can be reassured that the severity of their aortic gradient, taken in isolation, does not preclude a good HRQOL outcome.

The findings of our research can bring a local perspective to nursing education in the TAVR program at St. Peter’s Hospital. For example, the importance of collecting complete preoperative, one month, and one year data is highlighted by this data’s critical importance to the current research. Similarly, applying Ferrans’ theoretical framework to the KCCQ-12
questionnaire helps our nursing staff see how the survey instrument really addresses HRQOL in a multi-domain manner. Finally, this research brings a concreteness to the sometimes abstract findings of multicenter RCTs that inform evidence-based practice; our nurses and APRNs can see comparable research findings unfolding in their own patient population.

APRNs play a key role in the St. Peter’s Hospital TAVR program. They are active in the TAVR clinic, in-patient care, and post discharge follow up. In addition to their clinical practice roles, there is also an opportunity for nurse practitioners (NPs) to engage in clinical research (as this Capstone Project demonstrates). The DNP qualified NP, and those engaged in a DNP program, are particularly well suited to the type of clinical research typified by the current project. A knowledge of evidence-based medicine, survey instrument theory, applied statistics, and an ability to systematically review the literature, are all key DNP skills that can be applied to clinical research. By having a DNP prepared NP (or a DNP candidate) involved in the St. Peter’s Hospital TAVR program a virtuous cycle of research and clinical practice reinforce each other. The combination of local clinical research against a background of evidence-based practice provides a positive influence on clinical practice, and promotes intellectual engagement of the nursing providers.

The current research study has both strengths and limitations. One strength is the prospective nature of the data collection, and the discipline imposed by our participation in the national TAVR database. Nevertheless, this is not sufficient to guarantee high quality data. Review of data from the national database has shown it to be of inferior quality to that obtained in multicenter RCTs (Arnold et al., 2017). The St. Peter’s Hospital database, when compared to the national database, shows similar levels of missing values and patients lost to follow up (Arnold et al., 2017). Patients lost to follow up at one year is a particularly troubling problem in
the national database. It is possible that missing data at one year may bias results, and present an overly optimistic picture of improvement in HRQOL. Given the nature of AS, and the age and poor health of the TAVR patient population, death before one year follow up is not infrequent. For this reason, the PARTNER trial used a hybrid HRQOL-survival outcome (Arnold et al., 2014). This may be preferable to a pure HRQOL outcome measure.

Another limitation of this research is the relatively small sample size. The sample size did not adversely influence the question of HRQOL improvement after TAVR, which was a very robust finding, but it did limit the usefulness of the regression models’ findings. Perhaps a larger sample size would have revealed other significant predictors of KKCQ scores, in addition to those identified. Another limitation relates to the question of study generalizability. That one particular community hospital had post-TAVR HRQOL improvements consistent with those of large multicenter trials does not necessarily mean that other community hospitals would fare as well. Nevertheless, it is an encouraging result for the viability of TAVR performed in community hospitals.

Conclusions.

Patients undergoing TAVR in a community hospital setting (St. Peter’s Hospital, Albany, NY) experienced a significant and clinically meaningful improvement in HRQOL. STS mortality risk score is a poor predictor of long term postoperative HRQOL outcome. Advance practice nurses in community hospitals can use local clinical research findings to inform their clinical practice, and aid in the counselling and education of patients with aortic stenosis.
References


Reynolds, M. R., Magnuson, E. A., Wang, K., Thourani, V. H., Williams, M., Zajarias, A., . . . Cohen, D. J. (2012). Health-Related Quality of Life After Transcatheter or Surgical Aortic Valve Replacement in High-Risk Patients With Severe Aortic Stenosis: Results From the PARTNER (Placement of AoRTic TraNscathetER Valve) Trial (Cohort A). *Journal of the American College of Cardiology, 60*(6), 548-558. doi:https://doi.org/10.1016/j.jacc.2012.03.075

Rothwell, P. M. (2005). External validity of randomised controlled trials: “To whom do the results of this trial apply?”. *The Lancet, 365*(9453), 82-93. doi:https://doi.org/10.1016/S0140-6736(04)17670-8


Appendix A

Kansas City Cardiomyopathy Questionnaire (KCCQ-12)

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the answer that best applies to you.

1. Heart failure affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by heart failure (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Extremely Limited</th>
<th>Quite a bit Limited</th>
<th>Moderately Limited</th>
<th>Slightly Limited</th>
<th>Not at all Limited</th>
<th>Limited for other reasons or did not do the activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Showering/bathing</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>b. Walking 1 block on level ground</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>c. Hurrying or jogging (as if to catch a bus)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

2. Over the past 2 weeks, how many times did you have swelling in your feet, ankles or legs when you woke up in the morning?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Every morning</th>
<th>3 or more times per week but not every day</th>
<th>1-2 times per week</th>
<th>Less than once a week</th>
<th>Never over the past 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

3. Over the past 2 weeks, on average, how many times has fatigue limited your ability to do what you wanted?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>All of the time</th>
<th>Several times per day</th>
<th>At least once a day</th>
<th>3 or more times per week but not every day</th>
<th>1-2 times per week</th>
<th>Less than once a week</th>
<th>Never over the past 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

4. Over the past 2 weeks, on average, how many times has shortness of breath limited your ability to do what you wanted?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>All of the time</th>
<th>Several times per day</th>
<th>At least once a day</th>
<th>3 or more times per week but not every day</th>
<th>1-2 times per week</th>
<th>Less than once a week</th>
<th>Never over the past 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>
5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of shortness of breath?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every night</td>
<td>0</td>
</tr>
<tr>
<td>3 or more times per week but not every day</td>
<td>1</td>
</tr>
<tr>
<td>1-2 times per week</td>
<td>2</td>
</tr>
<tr>
<td>Less than once a week</td>
<td>3</td>
</tr>
<tr>
<td>Never over the past 2 weeks</td>
<td>4</td>
</tr>
</tbody>
</table>

6. Over the past 2 weeks, how much has your heart failure limited your enjoyment of life?

<table>
<thead>
<tr>
<th>Limitation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>It has extremely limited my enjoyment of life</td>
<td>0</td>
</tr>
<tr>
<td>It has limited my enjoyment of life quite a bit</td>
<td>1</td>
</tr>
<tr>
<td>It has moderately limited my enjoyment of life</td>
<td>2</td>
</tr>
<tr>
<td>It has slightly limited my enjoyment of life</td>
<td>3</td>
</tr>
<tr>
<td>It has not limited my enjoyment of life at all</td>
<td>4</td>
</tr>
</tbody>
</table>

7. If you had to spend the rest of your life with your heart failure the way it is right now, how would you feel about this?

<table>
<thead>
<tr>
<th>Satisfaction</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all satisfied</td>
<td>0</td>
</tr>
<tr>
<td>Mostly dissatisfied</td>
<td>1</td>
</tr>
<tr>
<td>Somewhat satisfied</td>
<td>2</td>
</tr>
<tr>
<td>Mostly satisfied</td>
<td>3</td>
</tr>
<tr>
<td>Completely satisfied</td>
<td>4</td>
</tr>
</tbody>
</table>

8. How much does your heart failure affect your lifestyle? Please indicate how your heart failure may have limited your participation in the following activities over the past 2 weeks.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Severely Limited</th>
<th>Limited quite a bit</th>
<th>Moderately limited</th>
<th>Slightly limited</th>
<th>Did not limit at all</th>
<th>Does not apply or did not do for other reasons</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Hobbies, recreational activities</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>b. Working or doing household chores</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>c. Visiting family or friends out of your home</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

Reproduced with permission from CV Outcomes, Inc.
Appendix B - IRB Approvals

NOTICE OF IRB EXEMPT APPROVAL

To: Dorothy Urschel
Re: IRB# 17-1206-2

Does Transcatheter Aortic Valve Replacement Performed in a Community Hospital Setting Improve Health Related Quality of Life?

Date: December 12, 2017

This is to inform you that St. Peter's Health Partners Institutional Review Board (IRB) reviewed your proposed research study on December 11, 2017. We have determined that it meets the criteria for an exempt study and is approved. This determination was made based on the exempt criteria put forth by the federal regulations as defined in 45 CFR 46.101(b).

Since this study is exempt, no further IRB reports will be required by St. Peter's Health Partners IRB unless you make changes in the protocol or procedures.

If you have any questions, please feel free to contact the IRB office using the contact information below.

Signed Tuesday, December 12, 2017 8:30:10 AM ET by Lombardi, Thomas Pharm.D, FASHP
Thomas Lombardi, Pharm.D, FASHP
Chairperson, IRB

St. Peter's Health Partners Institutional Review Board
315 South Manning Boulevard, Albany, NY 12208
Phone 518-525-6273
www.sphp.com/institutional-review-board

SPHP IRB Federal Registration #:
FWA00004388/IRB00003258
January 11, 2018

Dear Dorothy Urschel,

On 1/11/2018, the University at Buffalo IRB reviewed the following submission:

<table>
<thead>
<tr>
<th>Type of Review:</th>
<th>Initial Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title of Study:</td>
<td>Does Transcatheter Aortic Valve Replacement Performed in a Community Hospital Setting Improve Health Related Quality of Life?</td>
</tr>
<tr>
<td>Investigator:</td>
<td>Dorothy Urschel</td>
</tr>
<tr>
<td>IRB ID:</td>
<td>STUDY000021115</td>
</tr>
<tr>
<td>Funding:</td>
<td>None</td>
</tr>
<tr>
<td>Grant ID:</td>
<td>None</td>
</tr>
<tr>
<td>END, IDE, or HDE:</td>
<td>None</td>
</tr>
<tr>
<td>Documents Reviewed:</td>
<td>HRP-503-Urschel_Capstone_IRB UB.pdf, Category: IRB Protocol</td>
</tr>
</tbody>
</table>

The study materials for the project referenced above were reviewed and approved by the SUNY University at Buffalo IRB (UBIRB) by Non-Committee Review. The UBIRB has determined on 1/11/2018 that the research is Exempt according to 45 CFR Part 46.101. There is no expiration date.

In conducting this study, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the Click system.

This UBIRB determination is given with the understanding that the proposed study design will be followed. If modifications are needed that significantly alter the purpose, design, or data collected, then those changes should be submitted to the IRB to determine if the modifications alter the research such that the criteria for an exempt determination are no longer met. You can create a modification by navigating to the active study in Click IRB and selecting ‘Create Modification / CR’. Otherwise, this study no longer needs to be reviewed by the IRB.

For more information on exemption criteria and categories, see the IRB Toolkit Worksheet: Exempt Determination (HRP-312). If you have any questions about this determination, please contact the IRB.

The UBIRB has approved the HIPAA Partial Waiver to permit you to receive personal health information as specified in section (1). The Partial Waiver Form has met the required elements of the federal regulations of HIPAA.
As principal investigator for this study involving human participants, you have responsibilities to the SUNY University at Buffalo IRB (UBIRB) as follows:

1. Ensuring that no subjects are enrolled prior to the IRB approval date.
2. Ensuring that the UBIRB is notified of all reportable information in accordance with the New Information SOP (HRP-024).
3. Ensuring that the protocol is followed as approved by UBIRB including minor changes which can be made if they do no impact the exempt determination.
4. Ensuring that the study is conducted in compliance with all UBIRB decisions, conditions, and requirements.
5. Bearing responsibility for all actions of the staff and sub-investigators with regard to the protocol.
6. Bearing responsibility for securing any other required approvals before research begins.

If you have questions, please contact the UBIRB at 716-888-4888 or ub-irb@buffalo.edu. Please include the project title and number in all correspondence with the UBIRB.
Appendix C – Permissions to Reproduce
Should any provision of this Agreement be held by a court of competent jurisdiction to be illegal, invalid, or unenforceable, that provision shall be deemed amended to achieve as nearly as possible the same economic effect as the original provision, and the legality, validity and enforceability of the remaining provisions of this Agreement shall not be affected or impaired thereby.

The failure of either party to enforce any term or condition of this Agreement shall not constitute a waiver of either party's right to enforce each and every term and condition of this Agreement. No breach under this agreement shall be deemed waived or excused by either party unless such waiver or consent is in writing signed by the party granting such waiver or consent. The waiver by or consent of a party to a breach of any provision of this Agreement shall not operate or be construed as a waiver of or consent to any other or subsequent breach by such other party.

This Agreement may not be assigned (including by operation of law or otherwise) by you without WILEY's prior written consent.

Any fee required for this permission shall be non-refundable after thirty (30) days from receipt by the CCC.

These terms and conditions together with CCC's Billing and Payment terms and conditions (which are incorporated herein) form the entire agreement between you and WILEY concerning this licensing transaction and (in the absence of fraud) supersedes all prior agreements and representations of the parties, oral or written. This Agreement may not be amended except in writing signed by both parties. This Agreement shall be binding upon and inure to the benefit of the parties' successors, legal representatives, and assigns.

In the event of any conflict between your obligations established by these terms and conditions and those established by CCC's Billing and Payment terms and conditions, these terms and conditions shall prevail.

WILEY expressly reserves all rights not specifically granted in the combination of (i) the license details provided by you and accepted in the course of this licensing transaction, (ii) these terms and conditions and (iii) CCC's Billing and Payment terms and conditions.

This Agreement will be void if the Type of Use, Format, Circulation, or Requestor Type was misstated during the licensing process.

This Agreement shall be governed by and construed in accordance with the laws of the State of New York, USA, without regards to such state's conflict of law rules. Any legal action, suit or proceeding arising out of or relating to these Terms and Conditions or the breach thereof shall be instituted in a court of competent jurisdiction in New York County in the State of New York in the United States of America and each party hereby consents and submits to the personal jurisdiction of such court, waives any objection to venue in such court and consents to service of process by registered or certified mail, return receipt requested, at the last known address of each party.

WILEY OPEN ACCESS TERMS AND CONDITIONS

Wiley Publishes Open Access Articles in fully Open Access Journals and in Subscription journals offering Online Open. Although most of the fully Open Access journals publish open access articles under the terms of the Creative Commons Attribution (CC BY) License only, the subscription journals and a few of the Open Access Journals offer a choice of Creative Commons Licenses. The license type is clearly identified on the article.

The Creative Commons Attribution License

The Creative Commons Attribution License (CC BY) allows users to copy, distribute and transmit an article, adapt the article and make commercial use of the article. The CC BY license permits commercial and non-commercial use.

Creative Commons Attribution Non-Commercial License

The Creative Commons Attribution Non-Commercial (CC BY-NC) license permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes (see below).

Creative Commons Attribution Non-Commercial NoDerivs License

The Creative Commons Attribution Non-Commercial NoDerivs License (CC BY-NC-ND) permits use, distribution and reproduction in any medium, provided the original work is
Permission to reproduce KCCQ-12 questionnaire as an appendix of a dissertation

Dorothy Urschel <durschel@buffalo.edu>  
Mar 20 (6 days ago)  

I am a doctoral student (DNP) in the School of Nursing at the University at Buffalo. I am writing a paper entitled:  
Does Transcatheter Aortic Valve Replacement (TAVR) Performed in a Community Hospital Setting Improve Health Related Quality of Life (HRQOL)?  

The research uses KCCQ-12 data from the TAVR database at St. Peter’s Hospital, Albany.  I would like to reproduce the KCCQ-12 questionnaire in an appendix of the paper.  

Thanks,  
Dorothy Urschel

Stan Kaufman <stan.kauffman@gmail.com>  
Mar 20 (6 days ago)  

Hello Dorothy, thanks for your interest. Are you referring to the Heart Failure Disease Management Program at Albany Medical Center? Is Rebecca Wagner in charge of the program you reference? This program uses the KCCQ, not the KCCQ-12. As far as I can see, we have not licensed the KCCQ-12 to anyone at U of Buffalo or Albany Med Ctr. Please provide more information so that we can identify what you mean. Thanks again for your interest.  

Stan Kaufman MD

Dorothy Urschel <durschel@buffalo.edu>  
Mar 22 (4 days ago)  

Hello Stan,  

I am the VP of the Cardiac and Vascular service line at St Peters Health Partners (a hospital down the road from Albany Medical Center)  
I am currently a DNP-Student at University at Buffalo --  
At St Peters--we currently license the registry for TAVR and within this registry we utilize the KCCQ-12 through the NY state Data registry. As above I am requesting to "reproduce" the questionnaire as part of the appendix of my final project for my doctoral studies.  
I hope this makes sense.  
I would be happy to discuss by telephone if that is easier.  

Many thanks in advance.

Dorothy Urschel <durschel@buffalo.edu>  
Mar 22 (4 days ago)  

Sorry I should clarify-  
We utilize NYState and the STS/AAC TVT- TAVR registry-  
Dorothy
Hello Dorothy, if your paper merely uses data collected through the STS/AAC registry, then there is no problem with your inclusion of the questionnaire in an appendix in your paper. You shouldn't have access to the scoring algorithms since the STS/AAC registry handles all the calculations for participating sites. Even if you were a direct licensee, though, you could not include/publish the scoring algorithms in your paper. But the questionnaire text is fine. I hope that works for you. Thanks again for your interest.

Best, Stan

Thanks perfect Stan!
Appreciate you getting back to me so promptly.
Best regards

Dorothy
Appendix D – UB School of Nursing Research Day (April 20, 2018) Poster

Does Transcatheter Aortic Valve Replacement (TAVR) Performed in a Community Hospital Setting Improve Health Related Quality of Life (HRQOL)?

Dorothy Urschel, MS, RN, MBA, FNP-BC, ACNP-BC, DNP Candidate University at Buffalo

Introduction

Aortic stenosis (AS) is the most common heart valve disorder in the US. Its natural history is characterized by progressive symptoms (dyspnea, angina, arthralgia, fatigue, and syncope), severity, and death within several years. Although surgical aortic valve replacement has been the treatment of choice, many patients remain in its underuse such as question.

Here we report, a non-surgical treatment option, transcatheter aortic valve replacement (TAVR), has become available. The efficacy of TAVR for AS has been established in multi-center RCTs, but its effectiveness in community hospital settings is less certain.

HRQOL is a multi-dimensional concept that includes domains related to physical, mental, emotional, and social functioning.

Despite the overall success of TAVR, approximately 20% to 40% of patients have disappointing HRQOL outcomes, as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ).

Objective & Research Questions

The objective of the project is to improve our understanding of the HRQOL benefits of TAVR in a community hospital setting, and how preoperative risk influences these benefits.

The research questions are:

1. Do patients with intermediate to high operative risk aortic stenosis treated with TAVR in a community hospital setting experience an improvement in their HRQOL, as measured by the short form Kansas City Cardiomyopathy Questionnaire (KCCQ-12)?

2. To what extent are the changes in HRQOL related to severity of operative risk, as measured by the preoperative Society of Thoracic Surgeons (STS) mortality risk score?

Theoretical Model

A Model of Heart Failure Pathogenesis of SF-36

Methods

A retrospective observational study of TAVR patients treated at St. Peter's Hospital was done, using existing, prospectively collected data from the hospital's TAVR database. To assess possible HRQOL benefits, preoperative, 1-month, and 1-year postoperative mean KCCQ scores were computed using repeated measures ANOVA with post hoc Bonferroni tests.

Bivariate correlations between preoperative STS mortality risk scores and the KCCQ scores were done. To control for confounding factors in this relationship, multiple linear regressions of KCCQ scores were done using STS risk score, early death, survival time, ejection fraction, and major amyloma as independent variables.

The statistical regression model (followed by RCT data) was as follows:

KCCQ score = b0 + b1 STS score + b2 aortic gradient + b3 post-operative mortality + b4 ejection fraction + b5 survival time + b6 major amyloma + b7 home exp.)

Results

From 2013 to 2017, 185 patients underwent TAVR at St. Peter's Hospital.

Preservavit 1-month and 1-year postoperative score (65.9 vs. 59.7, 82.4, 73.1, and 91.6 vs. 84.7, 83.4, respectively). This progressive improvement was significant in ANOVA analysis (F, 505) = 170.7, p < 0.001 and was also for all pairwise Bonferroni comparisons (p < 0.05).

All 1, 2, 50% of patients had KCCQ scores greater than 45, in each hospital, with a median survival time of 27.1 months to death.

Preoperative and 1-month postoperative KCCQ scores were significantly correlated with preoperative STS risk scores (r = 0.71, p = 0.005).

1-year postoperative HRQOL scores were not correlated with STS risk scores (r = -0.02, p = 0.45).

Discussion

The improvement in KCCQ scores for TAVR was statistically significant. Perhaps more importantly, the magnitude of benefit was clinically significant. Changes in KCCQ score of 5, 10, and 20 points are generally thought to represent small, moderate, or large clinical improvements, respectively.

The mean 1-year KCCQ improvement of 4 points is comparable to that reported in surgical RCTs. Similarly, the population of patients treated with TAVR is comparable to that reported in RCTs.

Our interest in the STS risk score as a possible predictor of post-TAVR HRQOL comes from a RCT which found that patients with poor TAVR outcomes, defined using a composite measure of survival and HRQOL, had significantly higher preoperative STS risk scores than those without outcomes. Although the STS mortality risk score is a valid predictor of operative mortality (as designed purpose), our results showed that, once confounding variables are controlled for, preoperative STS risk score is a poor predictor of post-TAVR HRQOL.

Conclusion & Practice Implications

Patients undergoing TAVR in a community hospital setting (St. Peter's Hospital) experience a significant improvement in HRQOL.

The HRQOL improvements were comparable to those reported from multi-center RCTs.

APRN's at St. Peter's Hospital can treat AS patients, with confidence. If expected HRQOL benefits of TAVR.

STS risk score is a poor predictor of long-term postoperative HRQOL outcomes.

For the patients with unique clinical characteristics, APRNs can provide resources based on other clinical research, that a good HRQOL outcome is possible with TAVR.

Prospective databases, such as the TAVR database, provide an opportunity for clinical practitioners to conduct research. Practice, and let research inform clinical practice at the level.

Acknowledgements

1. Shannon Cramer, PhD, RN served as the DNP capstone

2. St. Peter's Hospital TAVR database managers