**MSCI Research Project Proposal**

*The impact of frailty in patients undergoing trans-catheter aortic valve replacement.*

**Credit**: 2.0

**Mentor:** XXXX

**Background:** Transcatheter aortic valve replacement (TAVR) is a novel treatment of severe aortic stenosis (AS) for patients who are high risk or prohibitive risk for conventional surgical aortic valve replacement (SAVR).[1](#_ENREF_1),[2](#_ENREF_2) It is not well understood which patients will benefit from TAVR and which patients will suffer a major adverse outcomes including stroke, major bleeding, and death.[3](#_ENREF_3) The purpose of our research program is to optimize patient selection prior to TAVR by identifying the patients most likely to benefit and those least likely to benefit from TAVR. TAVR is primarily used in elderly patients who cannot undergo surgery – the mean age of TAVR patients in clinical trials is 82 years.[1](#_ENREF_1),[2](#_ENREF_2) Risk prediction in elderly patients is complex and requires a multidimensional approach incorporating psychosocial factors such as functional status and nutrition.[4](#_ENREF_4),[5](#_ENREF_5) Frailty is a well described syndrome that incorporates these psychosocial factors into a scale incorporating five domains – shrinking, slowness, weakness, exhaustion, and low physical activity.[6](#_ENREF_6) The presence of frailty predicts post-operative complications in older surgical patients[7](#_ENREF_7) and is associated with post-operative mortality in patients undergoing cardiac surgery.[8](#_ENREF_8) Whether frail patients are at increased risk for major adverse outcomes compared to non-frail patients after TAVR is unknown.[9-11](#_ENREF_9)

**Purpose/Aims:** To assess the impact of frailty on risk for adverse outcomes (bleeding, vascular injury, stroke, re-admission, and death), hospital length of stay, and discharge destination following TAVR.

**Methods:** We will collect data retrospectively on a cohort of 287 patients who have undergone TAVR at Northwestern Memorial Hospital from 2010 to 2014. An IRB has been approved (IRB ID# STU00090016) to obtain patient demographics, clinical data, and procedural outcomes by chart review. We will complete the statistical analyses described below using SPSS and STATA software.

**Analytic Plan:** For the purposes of the abstract and manuscript data analyses, we will compare categorical variables using chi square and Fischer’s exact tests. We will compare continuous variables with independent samples t-tests and one way ANOVA. Additionally, we will use univariate and multivariate logistic regression models to identify predictors of adverse outcomes and discharge destination. We will use linear regression modeling to identify predictors of hospital length of stay. Cox proportional hazards modeling will be used in an exploratory analysis to study to impact of frailty on all-cause mortality following TAVR.

**Products:** At the conclusion of this research project I will complete the following items and submit to Dr. XXX for review.

1. A six page grant application for funding to support a program of research into the role of frailty in trans-catheter aortic valve replacement.
2. An abstract submission to a national meeting in the field of Interventional Cardiology. We will aim for submission to one of the following annual meetings (TCT, SCAI, ACC, or AHA). This abstract will focus on preliminary data studying the association between frailty status and discharge destination following TAVR.
3. A full length original manuscript submission to a peer reviewed journal in the field of Interventional Cardiology. This manuscript will describe our findings related to the impact of frailty status on adverse outcomes, hospital length of stay, and discharge destination following TAVR.

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**2.** Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ, Investigators PT. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *The New England journal of medicine* 2011;364:2187-2198.

**3.** Lindman BR, Alexander KP, O'Gara PT, Afilalo J. Futility, benefit, and transcatheter aortic valve replacement. *JACC Cardiovascular interventions* 2014;7:707-716.

**4.** Fukuse T, Satoda N, Hijiya K, Fujinaga T. Importance of a comprehensive geriatric assessment in prediction of complications following thoracic surgery in elderly patients. *Chest* 2005;127:886-891.

**5.** Singh M, Stewart R, White H. Importance of frailty in patients with cardiovascular disease. *European heart journal* 2014;35:1726-1731.

**6.** Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA, Cardiovascular Health Study Collaborative Research G. Frailty in older adults: evidence for a phenotype. *The journals of gerontology Series A, Biological sciences and medical sciences* 2001;56:M146-156.

**7.** Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, Takenaga R, Devgan L, Holzmueller CG, Tian J, Fried LP. Frailty as a predictor of surgical outcomes in older patients. *Journal of the American College of Surgeons* 2010;210:901-908.

**8.** Afilalo J, Alexander KP, Mack MJ, Maurer MS, Green P, Allen LA, Popma JJ, Ferrucci L, Forman DE. Frailty assessment in the cardiovascular care of older adults. *Journal of the American College of Cardiology* 2014;63:747-762.

**9.** Yamamoto M, Hayashida K, Watanabe Y, Mouillet G, Hovasse T, Chevalier B, Oguri A, Dubois-Rande JL, Morice MC, Lefevre T, Teiger E. Effect of Body Mass Index <20 kg/m(2) on Events in Patients Who Underwent Transcatheter Aortic Valve Replacement. *The American journal of cardiology* 2015;115:227-233.

**10.** Green P, Woglom AE, Genereux P, Daneault B, Paradis JM, Schnell S, Hawkey M, Maurer MS, Kirtane AJ, Kodali S, Moses JW, Leon MB, Smith CR, Williams M. The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. *JACC Cardiovascular interventions* 2012;5:974-981.

**11.** Stortecky S, Schoenenberger AW, Moser A, Kalesan B, Juni P, Carrel T, Bischoff S, Schoenenberger CM, Stuck AE, Windecker S, Wenaweser P. Evaluation of multidimensional geriatric assessment as a predictor of mortality and cardiovascular events after transcatheter aortic valve implantation. *JACC Cardiovascular interventions* 2012;5:489-496.