Published in final edited form as:

Am J Med. 2020 October ; 133(10): 1219–1222. doi:10.1016/j.amjmed.2020.01.041.

Cognition, Frailty, and Functional Outcomes of Transcatheter Aortic Valve Replacement

Meera Kapadia, BSE^a, Sandra M. Shi, MD^{b,c}, Jonathan Afilalo, MD, MSc^d, Jeffrey J. Popma, MD^e, Roger J. Laham, MD^e, Kimberly Guibone, NP^e, Dae Hyun Kim, MD, MPH, ScD^{b,c}

^aUniversity of Arizona College of Medicine, Tucson, AZ, USA

^bDivision of Gerontology, Beth Israel Deaconess Medical Center, Boston, MA, USA

^cMarcus Institute for Aging Research, Hebrew SeniorLife, Boston, MA, USA

^dDivision of Cardiology, Jewish General Hospital, Montreal, Quebec, Canada

^eDivision of Cardiology, Beth Israel Deaconess Medical Center, Boston, MA, USA

Abstract

Background: Cognitive impairment and frailty are highly prevalent in older adults undergoing transcatheter aortic valve replacement. This study aimed to investigate the relationship of cognitive impairment and frailty with functional recovery after transcatheter aortic valve replacement.

Methods: This was a single-center prospective cohort study of 142 patients who were 70 years old and underwent transcatheter aortic valve replacement for aortic stenosis. Before transcatheter aortic valve replacement, cognitive impairment was defined as Mini-Mental State Examination score <24 points (range: 0–30) and moderate-to-severe frailty was defined as a deficit-accumulation frailty index 0.35 (range: 0–1). The functional status composite score, the number of 22 daily and physical tasks that a patient could perform independently, measured at baseline and 1, 3, 6, 9, and 12 months postoperatively were analyzed using linear mixed-effects model.

Correspondence: Dae Hyun Kim, MD, MPH, ScD. 1200 Centre Street, Boston, MA, 02131; Tel: 617-971-8320; Fax: 617-971-5339; daehyunkim@hsl.harvard.edu.

Credit Author Statement

Conceptualization; JA, JP, RL, DK

Data curation; JA, KG, DK

Formal analysis; MK, SS, DK

Funding acquisition; JA, DK Investigation; DK

Methodology; DK

Project administration; DK

Resources; DK

Software; DK

Supervision; DK

Visualization; SS, DK

Roles/Writing – original draft; MK, SS, DK Writing – review & editing. All Authors

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Conflict of interest: Dr. Popma reports receiving grants to his institution from Medtronic, Boston Scientific, and Edwards Lifesciences, and serves on advisory boards for Boston Scientific and Edwards Lifesciences. Ms. Guibone is a consultant to Medtronic, Inc. The other authors have no disclosures.

Results: The mean age was 84.2 years, with 74 women (51.8%). Patients with moderate-to-severe frailty and cognitive impairment (n=27, 19.0%) had the lowest functional status at baseline and throughout 12 months, while patients with mild or no frailty and no cognitive impairment (n=48, 33.8%) had the best functional status. Patients with cognitive impairment alone (n=19, 13.4%) had better functional status at baseline than those with moderate-to-severe frailty alone (n=48, 33.8%), but their functional status scores merged and remained similar during the follow-up.

Conclusions: Preoperative cognitive function plays a vital role in functional recovery after transcatheter aortic valve replacement, regardless of baseline frailty status. Impaired cognition may increase functional decline in the absence of frailty, whereas intact cognition may mitigate the detrimental effects of frailty. Cognitive assessment should be routinely performed before transcatheter aortic valve replacement.

Keywords

cognitive function; frailty; functional status; transcatheter aortic valve replacement

BACKGROUND

Transcatheter aortic valve replacement (has become an established treatment option for older adults with symptomatic severe aortic stenosis. A recent analysis of the Society of Thoracic Surgeons/Transcatheter Valve Therapy registry showed that in-hospital mortality after transcatheter aortic valve replacement has decreased, yet 1 in every 3 patients die or remain symptomatic.^{1,2} While several studies identified frailty as a strong predictor of poor outcome, the role of cognitive impairment—which affects a third of patients—is less well studied.³ Particularly, how cognitive function interacts with frailty is unclear. This study aimed to determine the association of cognitive function and frailty with functional recovery after transcatheter aortic valve replacement.

METHODS

We conducted a single-center prospective cohort study of 143 patients who were 70 years old, undergoing transcatheter aortic valve replacement for severe aortic stenosis, and followed for 12 months at an academic medical center in February 2014–June 2017. Exclusion criteria were (a) emergent surgery, (b) clinical instability precluding pre-operative assessment, (c) severe neuropsychiatric impairment (Mini-Mental State Examination [MMSE] score <15 points or active psychosis), (d) non English speaking. Study design and procedures are detailed elsewhere.⁴ After excluding one patient with missing MMSE data, this analysis includes 142 patients. The institutional review board approved this study and written informed consent was obtained.

Before transcatheter aortic valve replacement a research nurse or a trained research assistant conducted a comprehensive assessment, including assessments of medical history, Society of Thoracic Surgeons predicted risk of mortality (STS-PROM), New York Heart Association (NYHA) class, self-reported functional status, cognitive function, and physical performance. Cognitive impairment was defined as MMSE score (range: 0–30) <24 points. A deficit-

accumulation frailty index was calculated from comprehensive assessment (range: 0–1) (bit.ly/cgafi), with 0.35 representing moderate-to-severe frailty. The primary outcome was a functional status composite score (range: 0–22 points; higher scores indicate better function), defined as the number of 22 daily and physical tasks that a patient could perform independently. Functional status was assessed at baseline and 1, 3, 6, 9, and 12 months postoperatively via telephone interview or mailed questionnaire. As a secondary outcome, poor outcome was defined as death or decline in functional status with NYHA class 3–4 at within a shorter time frame of 6 months.

We compared baseline characteristics between patients with and without cognitive impairment using 2 sample t test or Fisher's exact test. We examined the change in functional status using a randomintercept linear mixed-effects regression that modeled the composite functional status score as a function of cognitive impairment, moderate-to-severe frailty, indicators for follow-up time, and their interaction terms. For the secondary outcome, we used logistic regression to estimate the odds ratio (OR) and 95% confidence interval (CI) of poor outcome associated with 1-point increase in MMSE and with cognitive impairment and moderate-to-severe frailty. All regression models adjusted for age, sex, and STS-PROM. Analyses were performed in Stata 14 and a 2-sided p-value<0.05 was considered statistically significant.

RESULTS

The study population (n=142) had a mean age of 84.2 years (standard deviation, 6.0), 73 women (51.4%), and 140 white race (98.6%). Compared to patients with no cognitive impairment, patients with cognitive impairment had significantly lower mean MMSE (21.0 vs 26.9), higher mean Frailty Index (0.41 vs 0.36), and higher prevalence of activity-of-daily living disability (30.4% vs 9.4%).

At 6 months, poor outcome occurred in 24.3% (n=33) of 136 patients with available data. Higher MMSE score was associated with 16% lower odds of poor outcome (per 1-point increase: OR, 0.84; 95% CI, 0.75–0.96). Among patients with mild or no frailty (Frailty Index<0.35), presence of cognitive impairment did not increase the risk of poor outcome (MMSE 24–30 vs <24: 15.7% vs 16.9%; adjusted OR, 1.10; 95% CI, 0.24–5.04) (Figure 1). Among those with moderate-to-severe frailty (Frailty Index ≥0.35), cognitive impairment seems to increase the risk of poor outcome (MMSE 24–30 vs <24: 21.8% vs 44.3%; adjusted OR, 2.85; 95% CI, 0.96–8.42).

Over 12 months (Figure 2), patients (n=27, 19.0%) with moderate-to-severe frailty (Frailty Index ≥0.35) and cognitive impairment (MMSE<24) had the lowest functional status at baseline and throughout the follow-up, whereas patients (n=48, 33.8%) with mild or no frailty (Frailty Index<0.35) and no cognitive impairment (MMSE 24–30) had the best functional status. Patients with cognitive impairment alone (n=19, 13.4%) had better functional status at baseline than those with moderate-to-severe frailty alone (n=48, 33.8%), but their functional status scores merged and remained similar during the follow-up.

DISCUSSION

This study shows that both cognitive impairment and moderate-to-severe frailty are strong predictors of functional status trajectory over 12 months after transcatheter aortic valve replacement. Our results suggest that impaired cognition may increase functional decline in the absence of moderate-to-severe frailty, whereas intact cognition may mitigate the detrimental effects of moderate-to-severe frailty.

Our results corroborate and extend existing literature that preoperative cognitive function is important in functional recovery after surgical procedures. It is known that cognitive impairment is the strongest risk factor for postoperative delirium, which plays a vital role in engagement in rehabilitation and postoperative care.⁵ Our study is the first to consider the interaction of cognitive impairment with preexisting frailty in the context of transcatheter aortic valve replacement. Despite the relatively lower stress of transcatheter aortic valve replacement and thus lower incidence of delirium, transcatheter aortic valve replacement patients have diminished ability to recovery from delirium.⁶ Thus the prevention of delirium and its deleterious effects is all the more vital in this vulnerable population.

Although our findings based on a single-center cohort has limited generalizability, the prospectively collected and granular longitudinal data on functional status in our study offers unique insights into the determinants of functional recovery after transcatheter aortic valve replacement. In the current practice, a formal cognitive assessment is not routinely performed before transcatheter aortic valve replacement. Our findings support routine cognitive assessment as part of shared decision-making and perioperative care planning about transcatheter aortic valve replacement.

Funding sources:

Harvard Catalyst and National Institutes of Health (KL2TR001100-01, UL1TR001102, 2T35AG038027, T32AG023480, P30AG031679, P30AG048785). The funding sources did not have any role in study design; collection, analysis, and interpretation of data; writing the report; and decision to submit the article for publication.

REFERENCES

1. Grover FL, Vemulapalli S, Carroll JD, et al. 2016 Annual Report of The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. *J Am Coll Cardiol*. 2017;69(10):1215–1230. doi:10.1016/j.jacc.2016.11.033 [PubMed: 27956264]
2. Baron SJ, Arnold SV., Wang K, et al. Health status benefits of transcatheter vs surgical aortic valve replacement in patients with severe aortic stenosis at intermediate surgical risk: Results from the PARTNER 2 randomized clinical trial. *JAMA Cardiol*. 2017;2(8):837–845. doi:10.1001/jamacardio.2017.2039 [PubMed: 28658491]
3. Luan Erfe BM, Erfe JM, Brovman EY, Boehme J, Bader AM, Urman RD. Postoperative Outcomes in SAVR/transcatheter aortic valve replacement Patients With Cognitive Impairment: A Systematic Review. *Semin Thorac Cardiovasc Surg*. 2019;31(3):370–380. doi:10.1053/j.semtcvs.2018.11.017 [PubMed: 30529383]
4. Kim DH, Afilalo J, Shi SM, et al. Evaluation of Changes in Functional Status in the Year after Aortic Valve Replacement. *JAMA Intern Med*. 2019;179(3):383–391. doi:10.1001/jamainternmed.2018.6738 [PubMed: 30715097]
5. Jones RN, Marcantonio ER, Saczynski JS, et al. Preoperative Cognitive Performance Dominates Risk for Delirium among Older Adults. *J Geriatr Psychiatry Neurol*. 2016;29(6):320–327. doi:10.1177/0891988716666380 [PubMed: 27647793]

6. Shi SM, Sung M, Afilalo J, et al. Delirium Incidence and Functional Outcomes After Transcatheter and Surgical Aortic Valve Replacement. *J Am Geriatr Soc.* 2019;1–9. doi:10.1111/jgs.15867

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Clinical Significance

- Both cognitive impairment and frailty are associated with poor functional recovery after TAVR.
- Cognitive impairment in the absence of significant frailty increases the risk of functional decline.
- Better cognition provides a protective effect against functional decline in the presence of significant frailty

Figure 1. Cognitive Impairment, Frailty, and Risk of Death or Functional Decline with Severe Symptoms at 6 Months After Transcatheter Aortic Valve Replacement

The risk of death or functional decline with severe symptoms, defined as New York Heart Association class 3–4, at 6 months was shown according to the presence of cognitive impairment (MMSE<24) and moderate-to-severe frailty (frailty index ≥0.35). The estimates were adjusted for age, sex, and Society of Thoracic Surgeons predicted risk of mortality.

No at Risk	0	1	3	6	9	12
MMSE 24-30, FI < 0.35	48	48	46	41	42	41
MMSE < 24, FI < 0.35	19	18	15	12	10	10
MMSE 24-30, FI ≥ 0.35	48	45	41	40	37	36
MMSE < 24, FI ≥ 0.35	27	25	21	19	17	17

Figure 2. Cognitive Impairment, Frailty, and Change in Functional Status Over 12 Months After Transcatheter Aortic Valve Replacement

The mean (node) and 95% confidence interval (CI) of the functional status composite score (range: 0–22, higher values indicating better function) was plotted by the presence of cognitive impairment and moderate-to-severe frailty at baseline. The results were adjusted for age, sex, and Society of Thoracic Surgeons predicted risk of mortality

Table 1.

Characteristics of transcatheter aortic valve replacement Patients by Cognitive Function

Characteristics	Cognitive Impairment (N=46)	No Cognitive Impairment (N=96)	P value
Age, years, mean $\pm$ SD	83.1 $\pm$ 6.0	84.7 $\pm$ 5.9	0.12
Male, n (%)	23 (50.0)	50 (52.1)	0.86
Non-white race, n (%)	1 (2.2)	1 (1.0)	0.55
NYHA class 3–4, n (%)	41 (89.1)	84 (87.5)	1.00
Aortic valve area, cm ² , mean $\pm$ SD	0.7 $\pm$ 0.2	0.7 $\pm$ 0.2	0.73
STS predicted risk of mortality, %, mean $\pm$ SD	5.5 $\pm$ 2.5	6.0 $\pm$ 3.1	0.34
Charlson comorbidity index, mean $\pm$ SD	3.9 $\pm$ 2.1	3.4 $\pm$ 2.4	0.22
MMSE, mean $\pm$ SD	21.0 $\pm$ 2.1	26.9 $\pm$ 1.6	<0.001
Frailty index (range, 0–1), mean $\pm$ SD	0.41 $\pm$ 0.12	0.36 $\pm$ 0.10	0.004
ADL disability, n (%)	14 (30.4)	9 (9.4)	0.003
IADL disability, n (%)	38 (82.6)	75 (78.1)	0.66

Note: Abbreviations: ADL, activities of daily living; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; NYHA, New York Heart Association; SD, standard deviation; STS, Society of Thoracic Surgeons; transcatheter aortic valve replacement, transcatheter aortic valve replacement