Frailty and Related Outcomes in Patients Undergoing Transcatheter Valve Therapies

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by

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Overview

As the population ages, understanding the relationship between frailty, a syndrome involving multisystem impairment in functional recovery, and outcomes is increasingly important to accurately predict healthcare utilization and adverse outcomes. The addition of frailty to risk models is also important to ensure adequate risk-adjustment. National guidelines strongly recommend an objective evaluation of frailty to optimize patient selection, but the range of available measures raises issues with consistency. In clinical practice, frailty is not often measured due to the lack of consensus surrounding frailty assessment tools, and there are divergent prevalence estimates and effect sizes reported across different studies. Furthermore, the prospective collection of information on frailty is time-consuming and may not always be feasible. In addition, registries may misrepresent frailty status and prevalence by focusing on a limited definition of frailty, not including all hospitals, and defining frailty according to a single point in time.

Administrative claims represent an alternative source of data by which frailty might be more easily assessed. In the first paper, we, therefore, focused on ICD-9 claims-based frailty index and aimed to show the role of frailty on long-term mortality in patients undergoing transcatheter valve therapies. However, we realized that based on ICD-9 based-claims may not comprehensively quantify frailty across all patients due to limited available number of codes. Since the transition to ICD-10 on October 1, 2015, which contains nearly 5-fold (from 14,000 to 70,000) the number of available claims, the increased granularity of claims data now permits a more comprehensive assessment of conditions associated with frailty and allows a more detailed longitudinal record of how frailty influences risk. Thus, in the second paper, we used an ICD-10 based frailty index to evaluate frailty and measure the impact of frailty on more outcomes (not only mortality) such as long hospital stay and readmission in patients undergoing transcatheter valve therapies.

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ORIGINAL ARTICLE

Impact of a Claims-Based Frailty Indicator on the Prediction of Long-Term Mortality After Transcatheter Aortic Valve Replacement in Medicare Beneficiaries

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BACKGROUND: Prospectively collected frailty markers are associated with an incremental 1-year mortality risk after transcatheter aortic valve replacement (TAVR) compared with comorbidities alone. Whether information on frailty markers captured retrospectively in administrative billing data is similarly predictive of long-term mortality after TAVR is unknown. We sought to characterize the prognostic importance of frailty factors as identified in healthcare billing records in comparison to validated measures of frailty for the prediction of long-term mortality after TAVR.

METHODS AND RESULTS: Adult patients undergoing TAVR between August 25, 2011, and September 29, 2015, were identified among Medicare fee-for-service beneficiaries. The Johns Hopkins Claims–based Frailty Indicator was used to identify frail patients. We used nested Cox regression models to identify claims-based predictors of mortality up to 4 years post-procedure. Four groups of variables, including cardiac risk factors, noncardiac risk factors, patient procedural risk factors, and nontraditional markers of frailty, were introduced sequentially, and their integrated discrimination improvement was assessed. A total of 52 338 TAVR patients from 558 clinical sites were identified, with a mean follow-up time period of 16 months. In total, 14 174 (27.1%) patients died within the study period. The mortality rate was 53.9% at 4 years post-TAVR. A total of 34 863 (66.6%) patients were defined as frail. The discrimination of each of the 4 models was 0.60 (95% CI, 0.59–60), 0.65 (95% CI, 0.64–0.65), 0.68 (95% CI, 0.67–0.68), and 0.70 (95% CI, 0.69–0.70), respectively. The addition of nontraditional frailty markers as identified in claims improved mortality prediction above and beyond traditional risk factors (integrated discrimination improvement: 0.019; $P<0.001$).

CONCLUSIONS: Risk prediction models that include frailty as identified in claims data can be used to predict long-term mortality risk after TAVR. Linkage to claims data may allow enhanced mortality risk prediction for studies that do not collect information on frailty.

Key Words fee-for-service plans ■ frailty ■ Medicare ■ risk factors ■ transcatheter aortic valve replacement

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WHAT IS KNOWN

- Frailty and disability play a key role in the identification of older patients' potential for improvement after transcatheter aortic valve replacement.

WHAT THE STUDY ADDS

- Our findings show that the inclusion of frailty and disability markers as identified in Medicare beneficiaries significantly improved the prediction of long-term mortality.
- These claims-based risk factors may allow for enhanced mortality prediction in the absence of prospectively collected data.

Severe calcific aortic valve stenosis is the most common cause of valve replacement in the elderly population in the United States.[1] Although surgical aortic valve replacement remains the preferred treatment for severe symptomatic aortic stenosis in patients at low surgical risk, current guidelines recommend transcatheter aortic valve replacement (TAVR) as an alternative treatment in patients at increased surgical risk based on several clinical trials showing equivalence or superiority to surgery for patients with extreme, high, and intermediate surgical risks.[2–8]

Risk stratification before TAVR is important when selecting those patients who will most likely benefit from the procedure. To date, clinical risk prediction models of 1-year mortality after TAVR have been developed using traditional risk scoring systems. These include the Society for Thoracic Surgery Predicted Risk of Mortality score[9,10] and the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE),[11] as well as other individual clinical risk predictors.[12–16] Prior studies have suggested that measurement of frailty can enhance the prediction of mortality after TAVR.[17–30] In addition, a relatively small, prospective study recently showed that adding frailty measurements to conventional risk scores improved the assessment of 1-year mortality risk after TAVR.[31]

However, the assessment of frailty in clinical practice can be challenging, and these factors are commonly not collected in the nationwide registries, such as the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. In the absence of prospectively collected data, the ability to identify these factors in billing records may allow for enhanced mortality prediction. To test this, we evaluated hospitalizations of patients undergoing TAVR in a Medicare inpatient database to determine whether the incorporation of claims-based measures of frailty might augment mortality prediction compared with using comorbidities alone.

METHODS

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

Study Population

The Centers for Medicare and Medicaid Services MedPAR files include administrative billing claims for all hospitalizations of Medicare fee-for-service beneficiaries and have been used to study national patterns of procedure utilization in the United States.[32–34] In the MedPAR database, hospitalizations of adult patients (≥18 years old) were included if they had at least 1 *International Classification of Diseases, Ninth Revision*, *Clinical Modification* code for either transfemoral (35.05) or transapical (35.06) TAVR performed between August 25, 2011, and September 29, 2015.

Cardiac and Noncardiac Covariates and Procedural Risk Factors

A total of 34 cardiac and noncardiac covariates and procedural risk factors were initially defined as possible risk factors for all-cause mortality after TAVR based on our clinical knowledge. Age, sex, race, chronic heart failure, smoking, peripheral vascular disease, diabetes mellitus, and a couple of well-known cardiac diseases were defined as cardiac risk factors. Other comorbidities, such chronic kidney, liver and obstructive pulmonary diseases, anemia, obesity, hypothyroidism, coagulopathy, and the Charlson comorbidity index, were defined as noncardiac risk factors. Procedural risk factors included emergency or urgent admission, transapical access, and preprocedural shock.

Frailty Index

There are several ways to measure claims-based frailty.[35,36] In this study, the Johns Hopkins Claims–based Frailty Indicator, a previously developed and both internally and externally validated index, was used to identify frailty.[37–40] This index includes 21 criteria identifiable in claims data, such as demographic variables and markers of physical and cognitive dysfunction, to identify patients meeting the Fried frailty phenotype.[41] This has been extensively validated and shown to predict poor health outcomes, including incidence of falls, worsening mobility, hospitalization, and death. Based on the Johns Hopkins Claims–based Frailty Indicator algorithm,[37] a score cutoff of ≥0.12 was used to identify frail patients (Table I in the Data Supplement).

Some variables included in the John Hopkins Claims–based Frailty Indicator, such as age, sex, and Charlson comorbidity index, overlap with variables commonly used for risk adjustment in TAVR patients. To examine the prognostic importance of frailty variables often omitted from risk adjustment, we classified a subgroup of variables in the frailty indicator as nontraditional frailty markers. These included impaired mobility, depression, Parkinson disease, any type of arthritis, cognitive impairment, paranoia, chronic skin ulcer, pneumonia, skin and soft tissue infections, mycoses, gout or other crystal-induced arthropathies, falls, musculosketal problems, and urinary tract infection.

All covariates were ascertained using secondary diagnosis codes that were coded as present on admission during the index hospitalization, as well as from principal and secondary diagnosis codes from all hospitalizations in the year before

the date of admission of the index hospitalization (Table II in the Data Supplement).

Outcomes

The primary outcome for this study was all-cause long-term mortality, determined through linkage of the MedPAR files to the Centers for Medicare and Medicaid Services denominator file which includes information on a patient's vital status. Time to death was calculated as the time between the date of procedure and date of death. Patients were censored if they were no longer enrolled in Medicare according to the denominator file as of December 31, 2015, which marked the end of the follow-up period. The study was approved by the institutional review board of Beth Israel Deaconess Medical Center with a waiver of informed consent for retrospective data analysis.

Statistical Analysis

Continuous variables are presented as means and SDs, and categorical variables are presented as counts and percentages. Covariates were compared between surviving and nonsurviving patients using χ^2 statistics and *t* tests. Kaplan-Meier plots were created to plot time to death with a 30-day landmark analysis, stratified by the number of nontraditional frailty markers included. The log-rank test was used to compare the survival distributions of each frailty scale.

Covariates with a P <0.1 in univariate Cox regression analysis were ultimately included in the model. Subsequently, nested multivariable Cox regression incorporating random hospital effects was performed using 4 sequential models to determine the incremental improvement in prediction of long-term mortality with the addition of 4 sets of covariates. The sequential models included variables associated with (1) cardiac risk factors, (2) noncardiac risk factors, (3) procedural risk factors, and (4) nontraditional frailty markers. Harrell's C statistic was used to assess model discrimination, and the improvement in discrimination with the addition of variables was assessed by the change in the C statistic and the DeLong test.[42] An integrated discrimination improvement test was used to assess discrimination improvement.[43] All statistical analyses were performed in STATA software, version 15.0 (Stata Corporation, College Station, TX) using a 2-tailed P value for significance of <0.05.

RESULTS

A total of 52 338 hospitalizations from 558 clinical sites involved receipt of TAVR during the study period. The baseline characteristics of patients are shown in Table 1. A total of 27 147 (51.9%) were men, and the mean age was 82.4±8.0 years. There were 34 863 (66.6%) patients who were identified as frail. Musculoskeletal problems (15.5%) and arthritis (13.9%) were the most prevalent nontraditional frailty markers.

Mortality

In total, 14 174 (27.1%) patients died within the study period, with a mean follow-up time of 16 months. The all-cause mortality rate was 3.6% in hospital, 5.1% at 30 days, 19.0% at 1 year, 30.1% at 2 years, 42.3% at 3 years, and 53.9% at 4 years post-TAVR. Kaplan-Meier curves showing overall mortality up to 4 years after TAVR stratified by the number of nontraditional frailty markers are shown in the Figure. Compared with those without any nontraditional frailty markers, the hazard ratio (HR) was 1.166 (95% CI, 1.122–1.211) for patients with 1 frailty marker, 1.417 (95% CI, 1.350–1.488) for those with 2 frailty markers, and 1.490 (95% CI, 1.383–1.610) for those with ≥3 frailty markers (P<0.001 for all). The predicted 4-year mortality was 57% for frail patients and 48% for nonfrail patients (HR=1.342; 95% CI, 1.293–1.393; P<0.001). In the 30-day landmark analysis, compared with those without any nontraditional frailty markers, the HR was 1.010 (95% CI, 0.925–1.144) for patients with 1 frailty marker, 1.185 (95% CI, 0.955–1.308) for those with 2 frailty markers, and 1.136 (95% CI, 0.935–1.380) for those with ≥3 frailty markers (P=0.135).

Discrimination Improvement and Model Covariates

In nested models, the discrimination of the first model including only cardiac risk factors was 0.60 (95% CI, 0.59–60). The addition of noncardiac risk factors in the second model resulted in a C statistic of 0.65 (95% CI, 0.64–0.65; integrated discrimination improvement=0.032; P<0.001 compared with the first model). With the incorporation of additional procedural characteristics in the third model, the C statistic was 0.68 (95% CI, 0.67–0.68; integrated discrimination improvement=0.019; P<0.001 compared with the second model). Finally, the inclusion of nontraditional frailty markers resulted in a C statistic of 0.70 (95% CI, 0.69–0.70; integrated discrimination improvement=0.019; P<0.001 compared with third model). Comparisons of the C statistics using the DeLong test were statistically significant (P<0.001) for each model (model 2 versus model 1, model 3 versus model 2, model 4 versus model 3; Table 2).

The HRs for the final covariates, determined from nested Cox regression analysis, are presented in Table 3. The covariates that were most strongly associated with increased long-term mortality were atrial fibrillation (HR: 1.394; 95% CI, 1.347–1.442; P<0.001), chronic heart failure (HR: 1.249; 95% CI, 1.195–1.304; P<0.001), dialysis (HR: 2.033; 95% CI, 1.844–2.411; P<0.001), liver disease (HR: 2.046; 95% CI, 1.905–2.197; P<0.001), emergency admission (HR: 1.298; 95% CI, 1.225–1.374; P<0.001), preprocedural shock (HR: 2.369; 95% CI, 2.201–2.549; P<0.001), pneumonia (HR: 1.883; 95% CI, 1.761–2.014), and chronic skin ulcer (HR: 1.670; 95% CI, 1.540–1.811). As shown in Table III in the Data Supplement, the claims-based pre-

Table 1. Characteristics of the Study Population Between Surviving and Dead Patients

	Overall n=52 338	Alive n=38 164 (72.9%)	Dead n=14 174 (27.1%)	*P* Value
Cardiac history				
Age, y (mean±SD)	82.4±8.0	82.2±7.8	82.9±8.3	<0.001
Men, no. of pts (%)	27 147 (51.9)	19 444 (50.1)	7703 (54.3)	<0.001
White race, no. of pts (%)	48 635 (92.9)	35 414 (92.8)	13 221 (93.3)	0.067
Chronic heart failure, no. of pts (%)	39 416 (75.3)	27 982 (73.3)	11 434 (80.7)	<0.001
Diabetes mellitus, no. of pts (%)	19 062 (36.4)	13 915 (36.5)	5147 (36.3)	0.15
Smoker, no. of pts (%)	16 679 (31.9)	12 667 (33.2)	4012 (28.3)	<0.001
Coronary artery disease without revascularization, no. of pts (%)	37 770 (72.2)	27 783 (72.8)	9987 (70.5)	<0.001
Prior myocardial infarction, no. of pts (%)	8419 (16.1)	6057 (15.9)	2362 (16.7)	0.028
Prior percutaneous coronary intervention, no. of pts (%)	11 465 (21.9)	8693 (22.8)	2772 (19.6)	<0.001
Prior valvular surgery, no. of pts (%)	855 (1.6)	649 (1.7)	206 (1.5)	0.047
Prior aortic surgery, no. of pts (%)	211 (0.4)	140 (0.4)	71 (0.5)	0.031
Prior coronary artery bypass graft surgery, no. of pts (%)	12 073 (23.1)	9133 (23.9)	2940 (20.7)	<0.001
Peripheral vascular disease, no. of pts (%)	5382 (10.3)	3853 (10.1)	1529 (10.8)	0.021
Atrial fibrillation, no. of pts (%)	24 567 (46.9)	16 671 (43.7)	7896 (55.7)	<0.001
Left bundle branch block, no. of pts (%)	5502 (10.5)	4323 (11.3)	1179 (8.3)	<0.001
Right bundle branch block, no. of pts (%)	2000 (3.8)	1555 (4.1)	445 (3.1)	<0.001
Cerebrovascular disease, no. of pts (%)	7230 (13.8)	5108 (13.4)	2122 (15.0)	<0.001
Tricuspid valve disorders, no. of pts (%)	4557 (8.7)	3177 (8.3)	1380 (9.7)	<0.001
Endocarditis, no. of pts (%)	45 (0.1)	23 (0.1)	22 (0.2)	0.001
Aortic aneurysm, no. of pts (%)	1876 (3.6)	1283 (3.4)	593 (4.2)	0.001
Noncardiac history				
Chronic kidney disease without dialysis, no. of pts (%)	21 071 (40.3)	14 113 (37.0)	6958 (49.1)	<0.001
Renal dialysis, no. of pts (%)	1269 (2.4)	714 (1.9)	555 (3.9)	<0.001
Liver disease, no. of pts (%)	1915 (3.7)	1042 (2.7)	873 (6.2)	<0.001
Chronic obstructive pulmonary disease, no. of pts (%)	17 566 (33.6)	12 226 (32.0)	5340 (37.7)	<0.001
Home O_2, no. of pts (%)	3551 (6.8)	2207 (5.8)	1344 (9.5)	<0.001
Hypothyroidism, no. of pts (%)	11 456 (21.9)	8311 (21.8)	3145 (22.2)	0.31
Coagulopathy, no. of pts (%)	10 285 (19.7)	6973 (18.3)	3312 (23.4)	<0.001
Obesity, no. of pts (%)	7852 (15.0)	6197 (16.2)	1655 (11.7)	<0.001
Anemia, no. of pts (%)	26 328 (50.3)	18 282 (47.9)	8046 (56.8)	<0.001
Charlson Comorbidity Index (mean±SD)	3.30±1.87	3.14±1.83	3.74±1.92	<0.001
Procedural characteristics				
Emergency admission, no. of pts (%)	3819 (7.3)	2396 (6.3)	1423 (10.0)	<0.001
Urgent admission, no. of pts (%)	7377 (14.1)	4927 (12.9)	2450 (17.3)	<0.001
Transapical, no. of pts (%)	8071 (15.4)	5218 (13.7)	2853 (20.1)	<0.001
Preprocedural shock, no. of pts (%)	1423 (2.7)	535 (1.4)	888 (6.3)	<0.001
Nontraditional frailty markers				
Impaired mobility, no. of pts (%)	314 (0.6)	212 (0.6)	102 (0.7)	0.031
Depression, no. of pts (%)	4243 (8.1)	3099 (8.1)	1144 (8.1)	0.85
Parkinson disease, no. of pts (%)	717 (1.4)	517 (1.4)	200 (1.4)	0.62
Arthritis (any type), no. of pts (%)	7290 (13.9)	5537 (14.5)	1753 (12.4)	<0.001

(*Continued*)

Table 1. Continued

	Overall n=52 338	Alive n=38 164 (72.9%)	Dead n=14 174 (27.1%)	*P* Value
Cognitive impairment, no. of pts (%)	4924 (9.4)	3381 (8.9)	1543 (10.9)	<0.001
Paranoia, no. of pts (%)	493 (0.9)	326 (0.9)	167 (1.2)	<0.001
Chronic skin ulcer, no. of pts (%)	1283 (2.5)	629 (1.6)	654 (4.6)	<0.001
Pneumonia, no. of pts (%)	1782 (3.5)	777 (2.0)	1005 (7.3)	<0.001
Falls, no. of pts (%)	60 (0.1)	36 (0.1)	24 (0.1)	0.20
Skin and soft tissue infections, no. of pts (%)	515 (1.0)	304 (0.8)	211 (1.5)	<0.001
Mycoses, no. of pts (%)	748 (1.4)	379 (1.0)	369 (2.6)	<0.001
Gout or other crystal-induced arthropathies, no. of pts (%)	3309 (6.3)	2387 (6.3)	922 (6.5)	0.30
Musculosketal problems, no. of pts (%)	8101 (15.5)	6244 (16.4)	1857 (13.1)	<0.001
Urinary tract infection, no. of pts (%)	4888 (9.3)	3032 (7.9)	1856 (13.1)	<0.001

dictors of long-term mortality used in the current study are similar to those defined in clinical studies.

DISCUSSION

In the present study, we show that administrative codes can be used to identify cardiac and noncardiac risk factors, procedural characteristics, and markers of frailty which likely rendered TAVR patients at high surgical risk. The majority of TAVR patients in the database were frail, and the incorporation of these factors into statistical models improved the prediction of long-term mortality in patients undergoing TAVR when combined with traditional risk factors. Furthermore, our results demonstrate that the rate of long-term mortality after TAVR gradually increases with an increasing number of recorded nontraditional frailty markers. These findings illustrate the impact of frailty on outcomes for patients undergoing TAVR.

Impact of Frailty on Long-Term Mortality

There is a paucity of clinical studies for patients with structural heart disease which include an assessment of risk factors for frailty. For instance, the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, the largest registry collecting patient characteristics and outcomes related to TAVR procedures in the United States, collects only a few frailty markers, such albumin, hemoglobin, and the 5-meter speed test.[44] However, it has been demonstrated that incorporating frailty improves the prediction of mortality after TAVR. Adding a frailty index improved the C statistic for discrimination of 1-year mortality of the Society for Thoracic Surgery Predicted Risk of Mortality score from 0.64 to 0.68 (P<0.001) and improved the discrimination of the logistic EuroSCORE from 0.67 to 0.72 (P<0.001).[31]

Afilalo et al[19] reported that the average prevalence of frailty in the TAVR population, based on assessments using 7 separate frailty scales, was 54% (37%–74%). Despite both its commonality and its importance, frailty scales are infrequently collected in routine clinical care.[45] In the absence of prospectively collected data on frailty, we show that prognostic information can be identified in claims data. Furthermore, we showed that including claims-based frailty alongside traditional risk

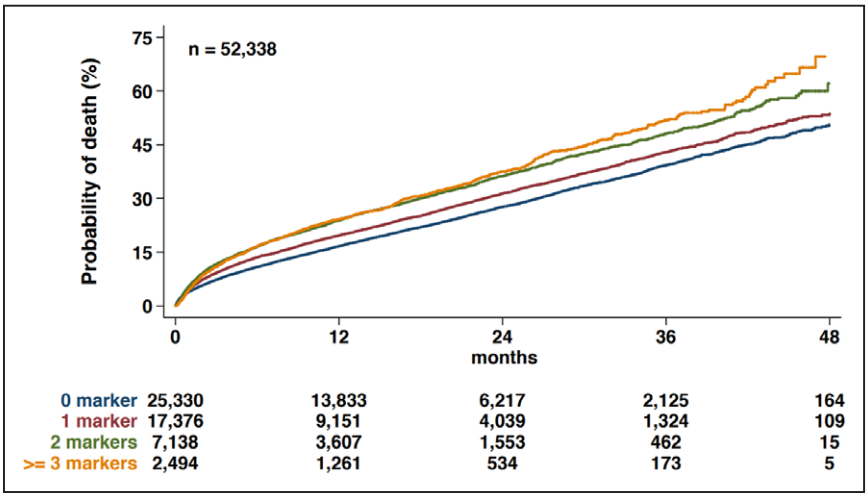

Figure. Kaplan-Meier curves for all-cause mortality according to presence of nontraditional frailty markers.

Table 2. Results of Multivariable Nested Cox Regression

	Hazard Ratio	95% CIs	*P* Value
Cardiac history			
Age (by year)	1.015	1.013–1.018	<0.001
Male	1.223	1.179–1.269	<0.001
Chronic heart failure	1.249	1.195–1.304	<0.001
Diabetes mellitus	1.047	1.009–1.086	0.013
Smoker	0.886	0.852–0.921	<0.001
Coronary artery disease without revascularization	0.924	0.887–0.962	<0.001
Prior percutaneous coronary intervention	0.930	0.889–0.972	0.001
Prior coronary artery bypass graft surgery	0.883	0.845–0.923	<0.001
Atrial fibrillation	1.394	1.347–1.442	<0.001
Left bundle branch block	0.893	0.841–0.948	<0.001
Right bundle branch block	0.840	0.763–0.924	0.004
Aortic aneurysm	1.141	1.046–1.244	0.003
Noncardiac history			
Chronic kidney disease without dialysis	1.378	1.330–1.427	<0.001
Renal dialysis	2.033	1.844–2.411	<0.001
Liver disease	2.046	1.905–2.197	<0.001
Chronic obstructive pulmonary disease	1.198	1.155–1.243	<0.001
Home O_2	1.556	1.466–1.652	<0.001
Coagulopathy	1.100	1.057–1.145	<0.001
Obesity	0.789	0.748–0.833	<0.001
Anemia	1.132	1.093–1.172	<0.001
Charlson Comorbidity Index	1.136	1.125–1.146	<0.001
Procedural characteristics			
Emergency admission	1.298	1.225–1.374	<0.001
Urgent admission	1.166	1.114–1.220	<0.001
Transapical	1.123	1.076–1.172	0.020
Preprocedural shock	2.369	2.201–2.549	<0.001
Nontraditional frailty markers			
Impaired mobility	1.240	1.015–1.516	0.035
Depression	1.067	1.003–1.135	0.038
Cognitive impairment	1.229	1.165–1.297	0.001
Paranoia	1.252	1.075–1.459	0.004
Chronic skin ulcer	1.670	1.540–1.811	<0.001
Pneumonia	1.883	1.761–2.014	<0.001
Skin and soft tissue infections	1.269	1.106–1.457	<0.001
Mycoses	1.446	1.301–1.607	<0.001
Urinary tract infection	1.279	1.215–1.345	<0.001

factors in statistical modeling significantly improved the discrimination of long-term mortality. However, in our landmark analysis, adding nontraditional frailty markers did not predict differences in perioperative mortality. These results suggest that the incorporation of frailty is more important for the prediction of long-term mortality than perioperative mortality. In addition, the improvement performance of adding frailty was similar in magnitude to adding procedural covariates which are well-known risk factors[10] in the TAVR population. We think that by merging claims-based frailty data with ongoing structural heart registries, we might enhance the ability to define patient risk and understand long-term outcomes, improve hospital benchmarking, and increase the completeness of data collection.

Predictors of All-Cause Mortality After TAVR

Predictive models for in-hospital and 30-day mortality have provided moderate discrimination in the Transcatheter Valve Therapy registry (C statistic: 0.67 in the training data set; 0.66 in the validation sample)[10] and the France-2 Registry (C statistic: 0.67 in the training sample; 0.59 in the validation sample).[16] The primary advantage of our analysis of MedPAR data is the inclusion of a large, generalized population with the ability to track mortality for the long term. Although we do not have all the necessary variables to calculate traditional surgical risk scores, such as the Society for Thoracic Surgery Predicted Risk of Mortality or logistic EuroSCORE, the final model derived from MedPAR data had reasonable discrimination (C statistic=0.70), and the claims-based predictors of long-term mortality used in the current study are similar to those defined in clinical studies (Table III in the Data Supplement).

Limitations

There are several limitations to the present study. The indications and criteria for patient selection for TAVR are not available, and administrative coding may misclassify some comorbidities and complications compared with prospective collection using standard clinical trial definitions. In addition, because the study population was limited to Medicare beneficiaries, we did not have information on all patients <65 years of age who might have undergone TAVR in the United States, and those patients <65 years who were included in the study may not be representative of younger patients overall.

Conclusions

Our findings show that risk prediction models that include frailty as identified in claims data can be used to more accurately predict long-term mortality risk after TAVR. Linkage to claims data may allow enhanced mortality risk prediction for studies that do not collect information on frailty.

Table 3. Comparison of the C Statistics in Each Model

	C Statistic (95% CI)	IDI	IDI (*P* Value)	DeLong (*P* Value)
Model 1 (cardiac risk factors)	0.60 (0.59–0.60)	…	…	…
Model 2 (model 1+noncardiac risk factors)	0.65 (0.64–0.65)	0.032*	<0.001*	<0.001*
Model 3 (model 2+procedural characteristics)	0.68 (0.67–0.68)	0.019†	<0.001†	<0.001†
Model 4 (model 3+nontraditional frailty markers)	0.70 (0.69–0.70)	0.019‡	<0.001‡	<0.001‡

IDI indicates integrated discrimination improvement.
*Model 2 vs model 1.
†Model 3 vs model 2.
‡Model 4 vs model 3.

ARTICLE INFORMATION

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CLINICAL RESEARCH
Valvular heart disease

Frailty and related outcomes in patients undergoing transcatheter valve therapies in a nationwide cohort

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Aims We sought to identify the prevalence and related outcomes of frail individuals undergoing transcatheter mitral valve repair and transcatheter aortic valve replacement (TAVR).

Methods and results Patients aged 65 and older were included in the study if they had at least one procedural code for transcatheter mitral valve repair or TAVR between 1 January 2016 and 31 December 2016 in the Centers for Medicare and Medicaid Services Medicare Provider and Review database. The Hospital Frailty Risk Score, an International Classification of Diseases, Tenth Revision (ICD-10) claims-based score, was used to identify frailty and the primary outcome was all-cause 1-year mortality. A total of 3746 (11.6%) patients underwent transcatheter mitral valve repair and 28 531 (88.4%) underwent TAVR. In the transcatheter mitral valve repair and TAVR populations, respectively, there were 1903 (50.8%) and 14 938 (52.4%) patients defined as low risk for frailty (score <5), 1476 (39.4%) and 11 268 (39.5%) defined as intermediate risk (score 5–15), and 367 (9.8%) and 2325 (8.1%) defined as high risk (score >15). One-year mortality was 12.8% in low-risk patients, 29.7% in intermediate-risk patients, and 40.9% in high-risk patients undergoing transcatheter mitral valve repair (log rank $P < 0.001$). In patients undergoing TAVR, 1-year mortality rates were 7.6% in low-risk patients, 17.6% in intermediate-risk patients, and 30.1% in high-risk patients (log rank $P < 0.001$).

Conclusions This study successfully identified individuals at greater risk of short- and long-term mortality after undergoing transcatheter valve therapies in an elderly population in the USA using the ICD-10 claims-based Hospital Frailty Risk Score.

Keywords Claims data • Frailty • Transcatheter valve therapies

Introduction

Frailty is conceptually defined as a multisystem clinical syndrome that results in a decreased physiological reserve and an increased vulnerability to stressors.[1] Regardless of definition, frailty is a key factor in identifying older patients' potential for improvement after transcatheter valve therapies.[2] Prior studies have shown that both short- and long-term mortality rates are significantly higher after transcatheter mitral valve repair and transcatheter aortic valve replacement (TAVR) in frail patients.[3–9] National guidelines strongly recommend an objective evaluation of frailty to optimize patient selection, but the range of available measures raises issues with consistency.[10,11] In clinical practice, frailty is not often measured due to the lack of consensus surrounding frailty assessment tools,[12] and there are divergent

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prevalence estimates and effect sizes reported across different studies.[4,13]

Since 2012, the transcatheter valve therapy (TVT) registry has reported the outcomes of patients undergoing procedures including TAVR and transcatheter mitral valve repair in the USA.[14] This robust registry allows for transparent analysis of patient outcomes after these procedures. However, the prospective collection of information on frailty is time-consuming and may not always be feasible. In addition, registries may misrepresent frailty status and prevalence by focusing on a limited definition of frailty, not including all hospitals, and defining frailty according to a single point in time. Administrative claims represent an alternative source of data by which frailty might be more easily assessed.[15,16] However, prior claims-based classification systems may have been insufficiently granular to adequately characterize complex conditions such as frailty. The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), which was introduced in many countries including the USA in 2015, greatly increased the number of codes that are available for use. Recently, an ICD-10-based frailty score has been developed and validated among the elderly population in the UK.[17] No studies have yet evaluated whether the ICD-10-CM-based Hospital Frailty Risk Score can be used to evaluate frailty among patients undergoing valvular heart disease interventions. Therefore, in this study, we sought to identify the prevalence of frailty based on the recently validated ICD-10-based Hospital Frailty Risk Score, and measure the impact of frailty on outcomes of individuals undergoing TAVR or transcatheter mitral valve repair using data from the US Centers for Medicare and Medicaid Services (CMS) Medicare Provider Analysis and Review (MedPAR) data, which contains a longitudinal record of patient hospitalizations.

Materials and methods

Study population

The CMS MedPAR database utilized for this study is a 100% sample of administrative billing claims for inpatient hospitalizations, and has been used previously to study national patterns of procedure utilization in the USA.[18,19] Patients aged 65 and older were included in the study if they had at least one procedural code for transcatheter mitral valve repair (ICD-10-CM code 02UG3JZ) or TAVR (ICD-10-CM codes 02RF38H or 02RF38Z), between 1 January 2016 and 31 December 2016.

Covariates

Baseline covariates were ascertained using secondary diagnosis codes that were coded as 'present on admission' during the index hospitalization (i.e. the hospitalization for the initial procedure), as well as from principal and secondary diagnosis codes from all hospitalizations at least 3 months prior to the date of admission for the index hospitalization in each patient (from 1 October 2015 to 1 October 2016). Elixhauser (see Supplementary material online, *Table S1*) and Charlson (see Supplementary material online, *Table S2*) comorbidity indices, both of which are validated summary comorbidity measures that have been previously shown to predict mortality in the Medicare population,[20,21] were measured for each patient.

Definition of frailty

To identify frail individuals, we calculated the Hospital Frailty Risk Score for each individual. This score was recently developed and validated in a large, older (≥75 years) population in the UK, and is based on diagnoses associated with high resource use.[17] It has not been used to describe frailty in the USA. For each patient, we calculated the Hospital Frailty Risk Score based on 109 ICD-10 diagnostic codes (the first three characters) from all hospitalizations occurring at least 3 months prior to the date of admission for the index hospitalization or using secondary diagnosis codes that were coded as 'present on admission' during the index hospitalization in each patient. The full list of diagnoses is shown in Supplementary material online, *Table S3*. We categorized individuals into risk categories based on their calculated Hospital Frailty Risk Score. Individuals were categorized as low (<5), intermediate (5–15), and high risk (>15) for frailty based on previously published cut-points, and patients in the intermediate-risk and high-risk categories were defined as frail.[17]

Outcomes

The primary outcome was all-cause 1-year mortality, determined through linkage of the MedPAR files to the Medicare Beneficiary Summary File, which includes vital status information. Time to death was calculated as the time period between the date of the index procedure and the date of death. Additionally, we identified long hospital stays (defined as >10 days in hospital), and 30-day mortality. Furthermore, we determined the number of rehospitalizations (defined as '0', '1', and '≥2'); all-cause rehospitalization rates within 1 year; and rehospitalizations due to acute myocardial infarction, acute heart failure, acute kidney failure, stroke or transient ischaemic attack, and acute post-haemorrhagic anaemia as secondary outcomes in patients discharged alive from the index procedure. Transfers to other hospitals were linked to a single index hospitalization. Time to rehospitalization was calculated as the time period between the date of discharge from the index hospitalization and the date of admission for the first subsequent hospitalization. Patients were censored if they were no longer enrolled in Medicare according to the denominator file as of 31 December 2016, which marked the end of the follow-up period for time to rehospitalization.

Statistical analysis

Continuous variables are presented as means and standard deviations or medians and inter-quartile ranges, and categorical variables are presented as counts and percentages. Restricted cubic spline curves with five knots were used to show the non-linear associations between the Hospital Frailty Risk Score and 1-year mortality. Multivariable Cox regression models were used to determine the impact of frailty (continuous and categorical) on all-cause 1-year mortality. Competing risk Cox regression analyses were used to show the performance of frailty in all-cause rehospitalization and each subgroup of rehospitalization, and to show cumulative incidence rates of rehospitalization, since mortality was a competing risk for rehospitalization. Patients who died within the study period (before 31 December 2016) represented a competing risk since they could not be rehospitalized after the date of death. Since different measures of comorbidity may be collinear with the frailty score, we used variance inflation factors (VIF) to test whether there are collinearities among the Hospital Frailty Risk Score, Elixhauser and Charlson comorbidity indices. Models were adjusted for age, sex, and Elixhauser and Charlson comorbidity indices. Multivariable Cox regression models were used to investigate the interaction between the Hospital Frailty Risk Score and transcatheter valve therapies. Harrell's c-statistic was used to assess model discrimination, and the improvement in discrimination with the addition of the Hospital Frailty Risk Score was assessed by the change in the c-statistic and the DeLong test.[22] An integrated discrimination improvement (IDI) test was also used to assess discrimination improvement.[23] Unadjusted cumulative incidence curves were created to plot

Table 1 List of ICD-10 codes, their prevalence in each group, and the number of points that each variable contributes to the creation of the Hospital Frailty Risk Score in patients undergoing transcatheter mitral valve repair and transcatheter aortic valve replacement

		Transcatheter mitral valve repair, *n* = 3746, *n* (%)	Transcatheter aortic valve replacement, *n* = 28 531, *n* (%)	Points
G81	Hemiplegia	31 (0.8)	365 (1.3)	4.4
G30	Alzheimer's disease	23 (0.6)	312 (1.1)	4.0
I69	Sequelae of cerebrovascular disease (secondary codes)	96 (2.6)	993 (3.5)	3.7
R29	Other symptoms and signs involving the nervous and musculoskeletal systems (R29.6 Tendency to fall)	53 (1.4)	534 (1.9)	3.6
N39	Other disorders of urinary system (includes urinary tract infection and urinary incontinence)	410 (10.9)	3080 (10.8)	3.2
F05	Delirium, not induced by alcohol and other psychoactive substances	49 (1.3)	479 (1.7)	3.2
W19	Unspecified fall	6 (0.2)	34 (0.1)	3.2
S00	Superficial injury of head	24 (0.6)	161 (0.6)	3.2
R31	Unspecified haematuria	162 (4.3)	924 (3.2)	3.0
B96	Other bacterial agents as the cause of diseases classified to other chapters (secondary code)	163 (4.4)	1186 (4.2)	2.9
R41	Other symptoms and signs involving cognitive functions and awareness	102 (2.7)	891 (3.1)	2.7
R26	Abnormalities of gait and mobility	212 (5.7)	1559 (5.5)	2.6
I67	Other cerebrovascular diseases	30 (0.8)	319 (1.1)	2.6
R56	Convulsions, not elsewhere classified	20 (0.5)	141 (0.5)	2.6
R40	Somnolence, stupor, and coma	11 (0.3)	124 (0.4)	2.5
T83	Complications of genitourinary prosthetic devices, implants, and grafts	35 (0.9)	200 (0.7)	2.4
S06	Intracranial injury	7 (0.2)	99 (0.3)	2.4
S42	Fracture of shoulder and upper arm	9 (0.2)	73 (0.3)	2.3
E87	Other disorders of fluid, electrolyte, and acid-base balance	1176 (31.4)	7677 (26.9)	2.3
M25	Other joint disorders, not elsewhere classified	78 (2.1)	547 (1.9)	2.3
E86	Volume depletion	245 (6.5)	1558 (5.5)	2.3
R54	Senility	149 (4.0)	1523 (5.3)	2.2
F03	Unspecified dementia	162 (4.3)	1595 (5.6)	2.1
W18	Other fall on same level	1 (<1)	19 (0.1)	2.1
Z75	Problems related to medical facilities and other health care	4 (0.1)	12 (<1)	2.0
F01	Vascular dementia	5 (0.1)	124 (0.4)	2.0
S80	Superficial injury of lower leg	10 (0.3)	84 (0.3)	2.0
L03	Cellulitis	114 (3.0)	699 (2.4)	2.0

The score presents the top 28 codes, each of which contributes ≥2 points. (All covariates are presented in Supplementary material online, *Table S3*.)

time to event, stratified by risk category. All statistical analyses were performed in STATA version 15.0 (Stata Corporation, College Station, TX, USA) or SAS version 9.4 (SAS Institute, Cary, NC, USA) using a two-tailed alpha <0.05 to define statistical significance.

Results

Overall results and frailty

A total of 32 986 patients treated with TAVR or transcatheter mitral valve repair were identified during the study period. After excluding 709 patients aged <65 years, a total of 32 277 patients were ultimately included in the analytic sample. Of these, 3746 underwent transcatheter mitral valve repair and 28 531 underwent TAVR. The prevalence of the 28 ICD-10 codes contributing the largest point totals (minimum two points) towards the Hospital Frailty Risk Score are presented in *Table 1* (all covariates are presented in Supplementary material online, *Table S3*). 'Other disorders of fluid, electrolyte and acid-base balance' (31.4% and 26.9%), and 'other disorders of urinary system' including urinary tract infection and urinary incontinence (10.9% and 10.8%), were the most frequently diagnosed codes in both the transcatheter mitral valve repair and TAVR groups, respectively. Baseline characteristics of patients are presented in *Table 2*. The mean age of TVT recipients was 80.1 ± 8.9 years in the group undergoing transcatheter mitral valve repair, and in 81.5 ± 8.1 in the group undergoing TAVR. The majority of patients were male in both transcatheter mitral valve repair (51.8%) and TAVR (53.6%) groups.

There were 1903 (50.8%) and 14 938 (52.4%) patients defined as low risk using a cut-point score of <5; while 1476 (39.4%) and 11 268

Table 2 Characteristics of patients after transcatheter mitral valve repair and transcatheter aortic valve replacement

	Transcatheter mitral valve repair (*n* = 3746)	Transcatheter aortic valve replacement (*n* = 28 531)
Age, mean (SD)	80.1 (8.9)	81.5 (8.1)
Male, no. of pts	1941 (51.8%)	15 304 (53.6%)
Charlson Index, mean (SD)	2.9 (1.9)	3.1 (2.0)
Elixhauser Comorbidity Index, mean (SD)	5.7 (1.9)	5.8 (1.9)
Hospital Frailty Index, mean (SD)	6.6 (6.1)	6.3 (5.7)
Hospital Frailty Risk Category		
Low risk (<5), no. of pts	1903 (50.8%)	14 938 (52.4%)
Intermediate risk (5–15), no. of pts	1476 (39.4%)	11 268 (39.5%)
High risk (>15), no. of pts	367 (9.8%)	2325 (8.1%)
Frail (≥5 Hospital Frailty Index), no. of pts	1843 (49.2)	13 593 (47.6%)

(39.5%) were defined as intermediate risk (5–15), and 367 (9.8%) and 2325 (8.1%) were defined as high risk (>15) in the transcatheter mitral valve and TAVR populations, respectively. The mean Hospital Frailty Risk Score was 6.6 ± 6.1 in the transcatheter mitral valve repair population and 6.3 ± 5.7 in the TAVR population.

Outcomes

All outcomes including long length of stay, crude 30-day mortality rate, 1-year mortality rate, and rehospitalization rates for all prespecified subgroups were consistently and significantly greater in higher Hospital Frailty Risk Score categories for patients undergoing both transcatheter mitral valve repair and TAVR (*Table 3*). The distribution of the Hospital Frailty Risk Score in the transcatheter mitral valve repair and TAVR populations are presented in *Take home figure*. The 1-year mortality rate increased with increasing values of the score in patients undergoing transcatheter mitral valve repair and TAVR (*Take home figure*). In Kaplan–Meier analysis (*Figure 1*), the 1-year mortality rate was 12.8% in the low-risk group, 29.7% in the intermediate-risk group, and 40.9% in the high-risk group for patients undergoing transcatheter mitral valve repair (log rank $P < 0.001$ for comparison between categories). In patients undergoing TAVR, 1-year mortality rates were 7.6% in the low-risk group, 17.6% in the intermediate-risk group, and 30.1% in the high-risk group (*P*-values <0.001 by log-rank test). Kaplan–Meier estimates for time to rehospitalization in transcatheter mitral valve repair and TAVR patients are also presented in Supplementary material online, *Figure S1* and *S2*, respectively.

The c-statistic for all-cause 1-year mortality without the Hospital Frailty Risk Score was 0.65 for mitral valve repair and 0.66 for TAVR. After adding the Hospital Frailty Risk Score, the c-statistics improved to 0.70 and 0.71, respectively (DeLong *P*-value <0.001 for both). Furthermore, the IDI after addition of the frailty score was 0.033 ($P < 0.001$) for mitral valve repair and 0.024 ($P < 0.001$) for TAVR. The c-statistic for all-cause 1-year mortality using only the Hospital Frailty Risk Score (unadjusted) was 0.67 for mitral valve repair and 0.67 for TAVR.

There was no meaningful collinearity (mean VIF = 1.70) among the Hospital Frailty Risk Score (VIF = 1.16), Elixhauser comorbidity index (2.0) and Charlson comorbidity index (1.95). In multivariable Cox regression analyses, after adjusting for age, gender, and Elixhauser and Charlson comorbidity indices, increasing Hospital Frailty Risk Score (1 point increase) was associated with increasing all-cause mortality (HR: 1.060 for transcatheter mitral valve repair and HR: 1.062 for TAVR) and rehospitalizations (HR: 1.061 for both procedures). These associations were also present when frailty was categorized into low, intermediate, and high-risk categories for both the transcatheter mitral valve repair and TAVR groups (*Table 4*). There was no interaction between Hospital Frailty Risk Score and transcatheter valve therapies on all defined outcomes (*Table 4*).

Discussion

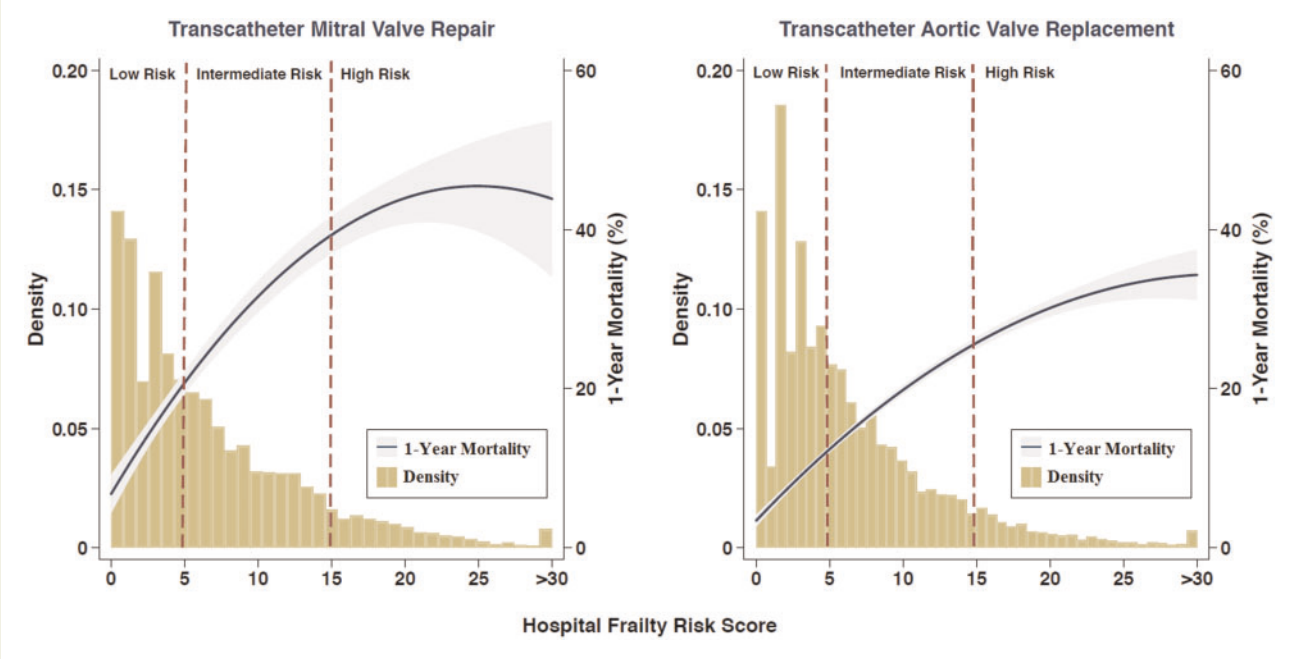
This nationwide cohort study demonstrates that almost half of patients undergoing transcatheter valve therapies in the USA have intermediate or high frailty levels, according to a frailty scoring system recently derived and validated in administrative claims data. The addition of the ICD-10-based Hospital Frailty Risk Score effectively stratified patients undergoing valvular interventions based on their risk of multiple patient-oriented endpoints, including short- and long-term mortality, long length of stay, and all-cause rehospitalization, and provided predictive information significantly above commonly used claims-based comorbidity assessments. Our study adds to the existing literature suggesting that frailty is an important predictor of outcomes for patients with valvular heart disease who are scheduled to undergo catheter-based interventions. It also demonstrates that a novel ICD-10-based frailty score developed in a patient population over the age of 75 years in the UK can provide accurate prognostic information on patient frailty in a younger (≥65 years) population undergoing transcatheter valve therapies in the USA.

Our study expands on similar findings demonstrating that adding frailty to summary measures of comorbidities can improve the discrimination of 1-year mortality in the TAVR population.[24] However, the assessment of frailty and its exact prevalence remains unclear due to substantial disagreement among 35 existing frailty scales, including commonly used scales such those by Fried and Rockwood.[25] For example, the rate of disagreement among seven of these scales ranged between 35% and 74% in the largest prospective study to date

Table 3 Outcomes of patients after transcatheter mitral valve repair and transcatheter aortic valve replacement

	Transcatheter mitral valve repair ($n = 3746$)				Transcatheter aortic valve replacement ($n = 28\,531$)			
	Low risk ($n = 1903$)	Intermediate risk ($n = 1476$)	High risk ($n = 367$)	*P*-value	Low risk ($n = 14\,938$)	Intermediate risk ($n = 11\,268$)	High risk ($n = 2325$)	*P*-value
Long length of stay, no. of pts (%)	40 (2.1)	210 (14.2)	119 (32.4)	<0.001	404 (2.7)	1727 (15.3)	629 (27.1)	<0.001
30-day mortality, no. of pts (%)	20 (1.1)	99 (6.7)	44 (12.0)	<0.001	143 (1.0)	418 (3.7)	169 (7.3)	<0.001
1-year mortality, no. of pts (%)[a]	244 (12.8)	439 (29.7)	150 (40.9)	<0.001	1142 (7.6)	1978 (17.6)	701 (30.1)	<0.001
	$n = 3674$ (alive at discharge, index procedure)				n = 28 111 (alive at discharge, index procedure)			
	Low risk ($n = 1899$)	Intermediate risk ($n = 1431$)	High risk ($n = 344$)		Low risk ($n = 14\,861$)	Intermediate risk ($n = 10\,991$)	High risk ($n = 2229$)	
No. of rehospitalizations, *n* (%)				<0.001				<0.001
0	1305 (68.7)	740 (51.7)	133 (38.7)		10 481 (70.5)	5909 (53.8)	819 (36.7)	
1	312 (16.4)	338 (23.6)	91 (26.5)		2487 (16.7)	2558 (23.3)	687 (30.8)	
≥2	282 (14.8)	353 (24.7)	120 (34.9)		1893 (12.7)	2524 (23.0)	723 (32.4)	
All-cause rehospitalization (within 1-year), no. of pts, (%)[a]	594 (47.9)	691 (72.9)	211 (81.3)	<0.001	4380 (47.7)	5082 (68.5)	1410 (85.3)	<0.001
Rehospitalization (within 1-year) due to								
Acute myocardial infarction, no. of pts, (%)[a]	25 (2.4)	35 (3.6)	16 (8.3)	<0.001	218 (2.5)	336 (3.8)	104 (11.0)	<0.001
Acute heart failure, no. of pts, (%)[a]	277 (19.4)	350 (36.3)	117 (54.7)	<0.001	1037 (10.3)	1598 (21.6)	486 (36.8)	<0.001
Acute renal failure, no. of pts, (%)[a]	217 (16.7)	296 (36.6)	100 (51.3)	<0.001	1029 (11.0)	1498 (22.8)	447 (42.9)	<0.001
Transient ischaemic attack or stroke, no. of pts, (%)[a]	36 (2.0)	36 (3.5)	21 (4.7)	<0.001	262 (2.6)	338 (3.6)	111 (12.1)	<0.001
Acute post-haemorrhagic anaemia, no. of pts, (%)[a]	108 (7.7)	117 (10.1)	28 (12.7)	<0.001	735 (8.0)	863 (10.6)	189 (15.4)	<0.001

[a]Percentages represent Kaplan–Meier cumulative event probability (Kaplan–Meier curves for rehospitalizations are presented in Supplementary material online, *Figures S1* and *S2*).



Take home figure The distribution of the Hospital Frailty Risk Score and its association with 1-year mortality in the transcatheter mitral valve repair and transcatheter aortic valve replacement populations using restricted cubic spline plots. The vertical red dashed lines show thresholds for categorizing patients as low frailty risk (score <5), intermediate frailty risk (score 5–15), or high frailty risk (score >15). Since there were very few patients with a Hospital Frailty Risk Score of >30, those patients are classified into a single group.

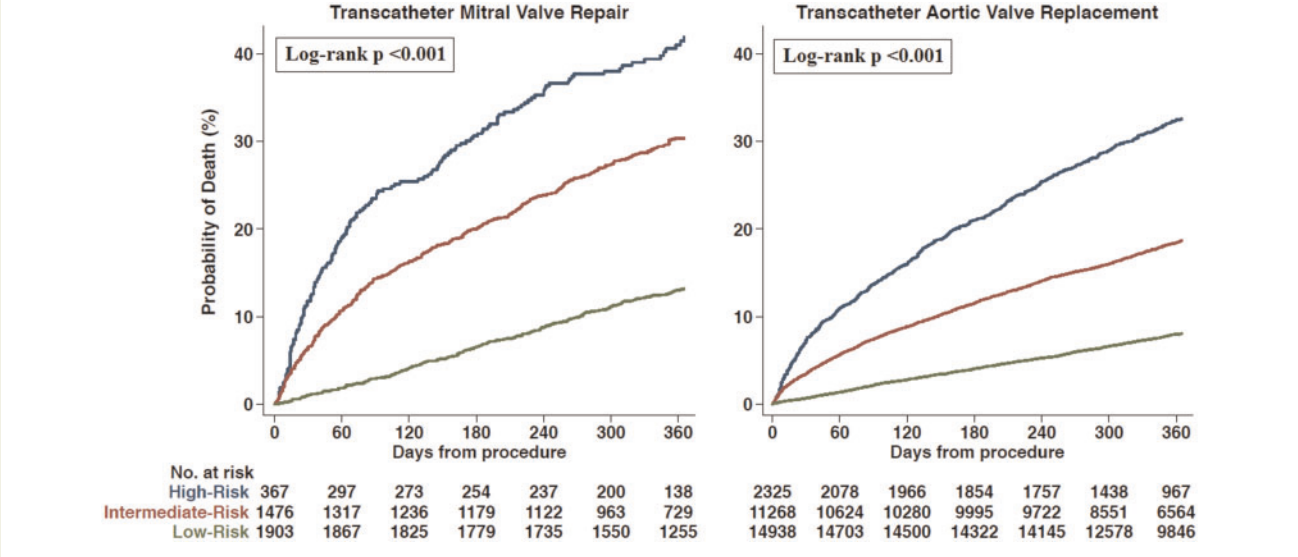


Figure 1 Unadjusted Kaplan–Meier curves for all-cause mortality in the transcatheter mitral valve repair and transcatheter aortic valve replacement populations.

specifically designed to investigate frailty in older patients undergoing TAVR.[4] This range of estimates illustrates the challenge of using any one frailty scale to diagnose an individual as frail. Furthermore, prior studies suggest that in order to be used as a measure that captures the dynamic nature of frailty, a continuous or ordinal scoring system might be better than a dichotomous one (frail vs. non-frail).[26] This idea is supported by our study findings, which demonstrate a graded increase in the risk of adverse events across most of the frailty-score

Table 4 Results of Cox multivariable regression models (adjusted for age, gender, Elixhauser and Charlson comorbidity indices)

	Transcatheter mitral valve repair		Transcatheter aortic valve replacement		*P*-value for interaction
	Hazard ratio (95% CIs)	*P*-value	Hazard ratio (95% CIs)	*P*-value	
All-cause mortality					
Hospital Frailty Risk Score	1.060 (1.050–1.070)	<0.001	1.062 (1.058–1.067)	<0.001	0.258
Hospital Frailty Risk Category		<0.001		<0.001	
Intermediate risk (5–15)	2.257 (1.858–2.743)	<0.001	1.931 (1.762–2.117)	<0.001	
High risk (>15)	3.192 (2.437–4.180)	<0.001	3.644 (3.214–4.132)	<0.001	
Rehospitalization for any cause					
Hospital Frailty Risk Score	1.061 (1.053–1.069)	<0.001	1.061 (1.058–1.064)	<0.001	0.151
Hospital Frailty Risk Category		<0.001		<0.001	
Intermediate risk (5–15)	1.714 (1.526–1.924)	<0.001	1.648 (1.579–1.719)	<0.001	
High risk (>15)	2.722 (2.306–3.214)	<0.001	2.920 (2.739–3.112)	<0.001	
Rehospitalization due to acute myocardial infarction (I21, at subsequent index)					
Hospital Frailty Risk Score	1.050 (1.001–1.101)	0.047	1.079 (1.063–1.095)	<0.001	0.192
Hospital Frailty Risk Category		<0.001		<0.001	
Intermediate risk (5–15)	2.031 (1.183–3.486)	<0.001	2.158 (1.800–2.587)	<0.001	
High risk (>15)	4.483 (2.257–8.904)	<0.001	4.250 (3.305–5.465)	<0.001	
Rehospitalization due to acute renal failure (N17, at subsequent index)					
Hospital Frailty Risk Score	1.073 (1.057–1.088)	<0.001	1.072 (1.064–1.079)	<0.001	0.355
Hospital Frailty Risk Category		<0.001		<0.001	
Intermediate risk (5–15)	1.907 (1.585–2.295)	<0.001	1.813 (1.667–1.971)	<0.001	
High risk (>15)	3.391 (2.639–4.351)	<0.001	3.473 (3.085–3.910)	<0.001	
Rehospitalization due to acute heart failure (I5021, I5031, I5041, I5023, I5033, I5043 at subsequent index)					
Hospital Frailty Risk Score	1.058 (1.044–1.072)	<0.001	1.068 (1.062–1.075)	<0.001	0.160
Hospital Frailty Risk Category		<0.001		<0.001	
Intermediate risk (5–15)	1.738 (1.471–2.054)	<0.001	1.892 (1.742–2.054)	<0.001	
High risk (>15)	2.869 (2.279–3.613)	<0.001	3.509 (3.128–3.936)	<0.001	
Rehospitalization due to stroke or TIA (I63 and G45, at subsequent index)					
Hospital Frailty Risk Score	1.065 (1.021–1.110)	0.003	1.074 (1.059–1.089)	<0.001	0.821
Hospital Frailty Risk Category		0.035		<0.001	
Intermediate risk (5–15)	1.511 (0.927–2.462)	0.097	1.918 (1.619–2.274)	<0.001	
High risk (>15)	4.546 (2.534–8.161)	<0.001	4.061 (3.204–5.146)	<0.001	
Rehospitalization due to acute post-haemorrhagic anaemia (D62, at subsequent index)					
Hospital Frailty Risk Score	1.043 (1.015–1.071)	0.002	1.043 (1.032–1.058)	<0.001	0.806
Hospital Frailty Risk Category		0.001		<0.001	
Intermediate risk (5–15)	1.620 (1.228–2.137)	0.001	1.636 (1.474–1.816)	<0.001	
High risk (>15)	2.049 (1.325–3.168)	0.001	2.266 (1.914–2.683)	<0.001	

For each outcome, two separate (continuous and categorical scale) models were built (low-risk group handled as a reference for category groups; hazard ratio = 1).

spectrum. In addition to the association between frailty and long-term mortality, the current study demonstrates a strong association between frailty and long-term rehospitalizations. Thus, identifying frail patients and stratifying risk categories using the Hospital Frailty Risk Score may also help physicians inform patients and families about the incidence of potential outcomes during the follow-up period. In addition, patients identified as having higher frailty risk could be targeted for strategies such as more intensive follow-up in an effort to prevent costly readmissions.

Previous studies have demonstrated the value of using administrative data in the assessment of frailty based on ICD-9 codes.[9,15,16,27] Now, the use of ICD-10 codes routinely used in current administrative databases provides hospitals with a systematic method to prospectively screen for frailty risk. The Hospital Frailty Risk Score developed and validated in the UK performs at least as well as or better than existing frailty measures or risk stratification tools.[17] Recently, this score was also externally validated to predict outcomes including long length of stay, 30-day rehospitalization and

1-year mortality in elderly patients from Canada.[28] In addition, administrative data include a longitudinal record and demonstrate how the frailty phenotype influences risk indirectly, as evidenced by multiple hospitalizations for conditions related to elevated medical risk rather than geriatric-specific risk (e.g. falls, failure to thrive, etc.). Claims data represent an inexpensive alternative source of data in the absence of prospectively collected information on frailty, which is often not routinely collected in the course of care. The ubiquity of claims data may make it a useful alternative to clinical risk scoring systems in determining procedural outcomes.

There are several potential benefits to routinely identifying older people at risk of adverse clinical outcomes after transcatheter valve therapies. First, we believe that by merging claims-based frailty data with ongoing registries of transcatheter valve therapies, we might enhance the ability to define patient risk and understand long-term outcomes, improve hospital and physician benchmarking, and increase the completeness of data collection by incorporating variables that were not previously being collected. In addition, the score could be applied to hospital information systems prospectively, potentially removing the inter-operator variability and implementation burden associated with manual scoring systems. A uniform and easily implemented method of identifying frail patients can help highlight the magnitude of the challenge associated with their care, enable services to evolve and provide frailty-attuned care, and improve patient- and facility-level outcomes. Identifying frailty in patients with valvular heart disease may also assist physicians in determining appropriateness of treatment and in discussing a patient's prognosis with the patient and family members.

There are notable limitations to the current study. Physiological measures of frailty are not captured in administrative claims data, and thus the claims-based definition of frailty may not comprehensively quantify frailty for all patients. It is also unclear whether the frailty risk score is a truly a measurement of frailty or simply another comorbidity index. The indications and criteria for patient selection are not available, and administrative coding may misclassify some comorbidities and complications compared with prospective collection using standard clinical trial definitions. Future studies could validate the variables used in the frailty score in a small sample of patients undergoing valve therapies. Claims codes also do not always capture the severity of a given condition or its change post-procedure, and we are not able to determine the cause of death. Additionally, because the study population was limited to Medicare beneficiaries, we did not have information on all patients who might have undergone transcatheter valve therapies in the USA. Since the model's discrimination is still modest, the true clinical utility of this score is still unclear, and should be assessed prospectively. Because ICD-10 codes have only been used in the USA since October 2015, we selected a relatively short 3 month lookback period for frailty assessment. As more data become available, longer historical periods for frailty assessment may be useful. Such data would allow for more rigorous assessments regarding changing frailty scores over time—either increases due to accumulation of deficits, or decreases to successful treatment of reversible conditions. Future analyses examining longitudinal changes in frailty and its impact of outcomes are warranted. Also, due to the level of granularity in the claims data, we did not have the variables necessary to calculate traditional risk scores such as the EuroSCORE[29] or STS-PROM[30] score.

Conclusions

The Hospital Frailty Risk Score, which is readily available and relatively inexpensive to implement, provides hospitals and health systems with a systematic way to identify frailty in patients undergoing transcatheter valve therapies. The score effectively classifies patients at high risk for adverse events including mortality, rehospitalizations and long length of stay. Use of a claims-based frailty score may facilitate the prospective assessment of frailty among patients undergoing transcatheter valve therapies.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Summary

The majority of transcatheter valvular disease patients were frail, and the incorporation of these factors into statistical models improved the prediction of long-term mortality in patients undergoing transcatheter valvular therapies when combined with the traditional risk factors. These findings illustrate the impact of frailty on outcomes for patients undergoing transcatheter valvular therapies.

Discussion

There are several potential benefits to routinely identifying older people at risk of adverse clinical outcomes after transcatheter valve therapies. First, we believe that by merging claims-based frailty data with ongoing registries of transcatheter valve therapies, we might enhance the ability to define patient risk and understand long-term outcomes, improve hospital and physician benchmarking, and increase the completeness of data collection by incorporating variables that were not previously being collected. In addition, the score could be applied to hospital information systems prospectively, potentially removing the inter operator variability and implementation burden associated with manual scoring systems. A uniform and easily implemented method of identifying frail patients can help highlight the magnitude of the challenge associated with their care, enable services to evolve and provide frailty-attuned care, and improve patient- and facility-level outcomes. Identifying frailty in patients with valvular heart disease may also assist physicians in determining appropriateness of treatment and in discussing a patient's prognosis with the patient and family members.

Limitations

Our both studies have a few limitations. First, administrative codes may not capture the severity of a given condition or its alteration post-procedure. Second, our analysis was limited to Medicare beneficiaries, and may therefore have limited generalizability outside of this

population. Third, as the claims-based frailty indices was developed to identify clusters of healthcare utilization, it may not be useful to identify "phenotypic frailty" and the degree to which "phenotypic frailty" confers an increased risk of healthcare utilization above that of comorbidities alone is unknown. The indications and criteria for patient selection are not available, and administrative coding may misclassify some comorbidities and complications compared with prospective collection using standard clinical trial definitions. Claims codes also do not always capture the severity of a given condition or its change post-procedure, and we are not able to determine the cause of death.

Perspectives

As more data become available, longer historical periods for frailty assessment may be useful. Such data would allow for more rigorous assessments regarding changing frailty scores over time-either increases due to accumulation of deficits or decreases to successful treatment of reversible conditions. Future analyses examining longitudinal changes in frailty and its impact of outcomes are warranted.

Notably, among Medicare Fee-for-service beneficiaries, acute myocardial infarction (AMI), heart failure (HF), and pneumonia are among the top causes of hospitalization. [1] In addition, 1 in 5 Medicare patients hospitalized for these conditions is readmitted to a hospital within 30 days of discharge. [2] As a result, the Centers for Medicare and Medicaid Services (CMS) has increasingly focused policy efforts on improving care for these conditions by publicly reporting hospital-level mortality and readmission rates. [3-6] In addition, these measures have been incorporated into value-based programs, including the mandatory Hospital Value-Based Purchasing (HVBP) program, which financially rewards or penalizes hospitals based on their relative performance on 30-day risk-adjusted mortality rates for AMI, HF and pneumonia,[7] and

the Hospital Readmissions Reduction Program (HRRP), which financially penalizes hospitals with higher-than-expected 30-day risk-adjusted readmission rates. [8]

Using hospital-level readmission and mortality rates as measures of care quality requires accurate risk adjustment to account for differences in patient populations among hospitals. However, current risk-adjustment models used by the HVBP and HRRP do not account for frailty, as we showed that an important marker of patient complexity that contributes to the risk of adverse outcomes in several populations. [9] Whether the addition of a claims-based frailty metric to traditional comorbidity-based risk adjustment models for AMI, HF, and pneumonia more accurately predicts 30-day mortality and readmission rates is unknown and may have important implications for hospitals that participate in CMS value-based programs and tend to care for frail populations.

Therefore, future studies should address two questions. First, does patient frailty, as identified by administrative claims, predict adverse outcomes for Medicare beneficiaries hospitalized with AMI, HF, and pneumonia? Second, does the addition of frailty to traditional comorbidity-based risk adjustment models improve the prediction of 30-day mortality and readmission for these conditions?

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