Impact of Malnutrition on Outcomes Following Transcatheter Aortic Valve Implantation (from a National Cohort)

Sara Emami, MS, Sarah Rudasill, BA, Nikhil Bellamkonda, BS, Yas Sanaiha, MD, Mario Cale, BS, Josef Madrigal, BS, Nathaniel Christian-Miller, BS, and Peyman Benharash, MD*

Malnutrition is associated with increased mortality in open cardiac surgery, but its impact on transcatheter aortic valve implantation (TAVI) is unknown. This study utilized the National Readmissions Database to evaluate the impact of malnutrition on mortality, complications, length of stay (LOS), 30-day readmission, and total charges following TAVI. Adult patients undergoing isolated TAVI for severe aortic stenosis were identified using the 2011 to 2016 National Readmissions Database, which accounts for 56.6% of all US hospitalizations. The malnourished cohort included patients with nutritional neglect, cachexia, protein calorie malnutrition, postsurgical nonabsorption, weight loss, and underweight status. Multivariable models were utilized to evaluate the impact of malnutrition on selected outcomes. Of 105,603 patients, 5,280 (5%) were malnourished. Malnourished patients experienced greater mortality (10.4% vs 2.2%, p <0.001), postoperative complications (49.2% vs 22.6%, p <0.001), 30-day readmission rates (21.4 vs 14.9%, p <0.001), index hospitalization charges ($331,637 vs $208,082, p <0.001), and LOS (16.4 vs 6.2 days, p <0.001) relative to their nourished counterparts. On multivariable analysis, malnutrition remained a significant, independent predictor of increased index mortality (Adjusted odds ratio (AOR) = 2.68, p <0.001), complications (AOR = 2.09, p <0.001), and 30-day readmission rates (AOR = 1.34, p <0.001). Malnutrition was most significantly associated with infectious complications at index hospitalization (AOR = 3.88, p <0.001) and at 30-day readmission (AOR = 1.43, p <0.027). In conclusion, malnutrition is independently associated with increased mortality, complications, readmission, and resource utilization in patients undergoing TAVI. Preoperative risk stratification and malnutrition modification may improve outcomes in this vulnerable population. **(Am J Cardiol 2020;125:1096−1101)**

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative to open surgery for patients with severe symptomatic aortic stenosis.[1,2] A growing body of research suggests that TAVI is associated with decreased rates of acute kidney injury, atrial fibrillation, and transfusion requirements relative to surgical aortic valve replacement.[3] Malnutrition is especially prevalent in this high-risk population, with rates as high as 65% in adults >65 years.[4] Malnutrition in older adults undergoing open surgical procedures is associated with increased rates of mortality, readmission, and longer lengths of hospital stay (LOS) relative to their properly nourished counterparts.[5,6] However, few have examined the association between malnutrition and outcomes following less invasive procedures such as TAVI. A simple method for preoperative nutritional classification before TAVI may allow for better risk assessment and mitigation. The present study utilized a national cohort to investigate the independent impact of malnutrition on mortality, postoperative complications, discharge location, rates and causes of 30-day readmission, LOS, and total charges following TAVI.

Methods

All adult patients (>18 years) admitted for TAVI were identified using the 2011 to 2016 National Readmission Database. As part of the Healthcare Cost and Utilization Project maintained by the Agency for Healthcare Research and Quality, the National Readmission Database is an all-payer database that provides accurate national estimates for 36 million discharges per year, accounting for 56.6% of all US hospitalizations. Patients without a preoperative diagnosis of aortic stenosis, and those with endocarditis, a history of valve surgery, or a concurrent cardiac procedure, were excluded (Figure 1).

Malnutrition, as defined in the Healthcare Cost and Utilization Project, encompassed protein calorie malnutrition, cachexia, nutritional neglect, weight loss secondary to failure to thrive, underweight status, and postsurgical nonabsorption.[7] A patient was identified as malnourished if they had at least one of the above diagnoses. The International Classification of Diseases - 9/10 codes used to extract these diagnoses are shown in Table 1. The malnourished cohort was further stratified by admission status (elective vs nonelective). Patient and hospital characteristics, co-morbidities, and complications were derived from the database in

---

Division of Cardiac Surgery, Cardiovascular Outcomes Research Laboratories (CORELAB), David Geffen School of Medicine, University of California, Los Angeles, California. Manuscript received October 29, 2019; revised manuscript received and accepted December 18, 2019.

See page 1100 for disclosure information.

*Corresponding author: Tel: (310) 206-6717; fax: (310) 206-5901.
E-mail address: pbenharash@mednet.ucla.edu (P. Benharash).

0002-9149/© 2020 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjcard.2019.12.038

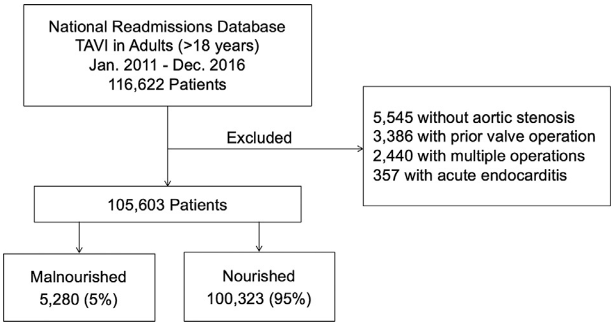

Figure 1. Consort diagram for patient selection. Of 116,622 adult patients undergoing TAVI, 105,603 met inclusion criteria and 5,280 (5%) were malnourished. TAVI = transcatheter aortic valve implantation.

Table 1
International Classification of Diseases (ICD) - 9/10 diagnosis codes for malnutrition

Malnutrition Type	ICD-9 Codes	ICD-10 Codes
Protein calorie malnutrition	260, 261, 262, 263.0, 263.1, 263.2, 263.8, 263.9	E40, E41, E43, E440, E441, E45, E46
Cachexia[*]	7994	R64
Nutritional neglect[†]	99584	T7401XA, T7601XA
Weight loss[‡]	78321, 7833, 7837	R634, R633, R627
Underweight[§]	78322, V850, V8551	R636, T7601XA, Z681, Z6851
Postsurgical Non-absorption	5793	K912

[*] Defined as involuntary weight loss of greater than 10% of baseline body weight characterized by atrophy of muscles and depletion of lean body mass.

[†] Defined as suspected or confirmed adult neglect, abuse, or other maltreatment leading to neglect in nutrition.

[‡] Defined as feeding difficulties, abnormal weight loss, and adult failure to thrive syndrome (progressive functional deterioration of a physical and cognitive nature at which an individual's ability to live with multisystem diseases, cope with ensuing problems, and manage his/her care are remarkably diminished).

[§] Defined as BMI ≤ 19.9.

Table 2
Patient and hospital characteristics by malnutrition status

Variable	Nourished (N = 100,322)	Malnourished (N = 5,280)	p Value
Women	46,883 (46.7%)	2,718 (51.5%)	<0.001
Age (years)	81.1 ± 8.3	81.7 ± 7.9	0.005
Nonelective admission	19,998 (21.1%)	2,120 (41.8%)	<0.001
Elixhauser Comorbidity Index	5.3 ± 1.7	5.9 ± 1.6	<0.001
Insurance			
Medicare	92,182 (91.9%)	4,946 (93.7%)	0.020
Medicaid	875 (0.9%)	40 (0.8%)	0.576
Private	5,280 (5.3%)	223 (4.2%)	0.04
Other	1,986 (2%)	72 (1.4%)	0.092
Co-morbidities			
Coronary artery disease	63,702 (65.1%)	2,585 (50.6%)	<0.001
Congestive heart failure	71,402 (72.5%)	4,163 (79.3%)	<0.001
Prior myocardial infarction	9,628 (10.2%)	341 (6.8%)	<0.001
Hypertension	72,971 (76.2%)	2,933 (57.8%)	<0.001
Peripheral vascular disease	22,615 (23.8%)	954 (19.1%)	<0.001
Smoker	19,955 (21%)	498 (10%)	<0.001
Diabetes mellitus	32,155 (33.5%)	941 (18.8%)	<0.001
Pulmonary hypertension	18,150 (19.1%)	1,052 (21%)	0.052
Chronic pulmonary disease	34,343 (36%)	1795 (35.7%)	0.804
Dialysis dependence	1,732 (1.8%)	102 (2.1%)	0.476
Chronic kidney disease	30,847 (32.2%)	1,604 (31.6%)	0.622
Anemia	3,717 (4.0%)	161 (3.3%)	0.118
Coagulopathy	15,983 (16.9%)	992 (19.8%)	0.001
Fluid and electrolyte disorders	1,848 (19.5%)	1,945 (38.5%)	<0.001
Liver disease	2,787 (3%)	248 (5%)	<0.001
Obesity	12,859 (13.6%)	251 (5%)	<0.001
Cancer	3,360 (3.6%)	224 (4.5%)	0.026
Hypothyroidism	16,764 (17.7%)	632 (12.7%)	<0.001
Substance use disorder	1,442 (1.5%)	91 (1.8%)	0.259
Hospital bed size			
Small	4,309 (4.3%)	175 (3.3%)	0.087
Medium	15,838 (15.8%)	667 (12.6%)	0.013
Large	80,175 (79.9%)	4,438 (84.1%)	0.002
Hospital teaching status			
Urban teaching	89,844 (89.6%)	4,838 (91.6%)	0.051
Urban Non-teaching	9,627 (9.6%)	414 (7.8%)	0.093
Rural	851 (0.8%)	28 (0.5%)	0.027

this study (Table 2). The Elixhauser index, a widely utilized estimate of patient co-morbidity, was calculated based on 30 common comorbidities.[8]

The primary outcome was mortality at index hospitalization. Secondary outcomes included postoperative complications, discharge location, rates of 30 and 90 day readmission, LOS, and total charges at index hospitalization. Mortality, LOS, and hospital charges were also tabulated at 30 and 90 day readmission. A composite variable for complications considered neurological (included intracerebral hemorrhage, acute ischemia, and stroke), cardiovascular (cardiac arrest, ventricular tachycardia, and ventricular fibrillation), respiratory (pneumonia, pneumothorax, pulmonary edema, pulmonary collapse, empyema, prolonged ventilation, and tracheostomy), renal (acute kidney injury), and infectious complications (sepsis, septicemia, wound infection, and mediastinitis). Of those patients readmitted within 30 days of TAVI, the primary reason for readmission was categorized using the Diagnosis Related Group codes.

Using Patrick Royston's module for trend analysis, trends of malnutrition in TAVI patients were analyzed over the study period by using survey weighted estimates.[9] Patient characteristics were analyzed by malnutrition status. The adjusted Wald test was used to compare continuous variables, while Pearson's chi-squared was utilized for categorical variables. Multivariable logistic regression models were used to analyze the independent impact of malnutrition on categorical outcomes, while multivariable linear regression models were used for continuous variables such as LOS and total charges. Model fit was evaluated by comparing C-statistics and Akaike information criterion for categorical outcomes, and adjusted R-squared and Akaike information criterion values for continuous ones. Covariates included in the multivariable models were clinically relevant factors found to have a p ≤0.2 on univariate analysis. Statistical significance was considered as p value <0.05. All statistical analyses were performed using STATA 15.1 (StataCorp LP, College Station, Texas). This study was deemed exempt by the Institutional Review Board at the University of California, Los Angeles.

Results

An estimated 116,622 adult patients underwent TAVI for severe aortic stenosis during the study period. After application of exclusion criteria (Figure 1), 105,603 patients remained, of which 5,280 (5%) were considered malnourished. Over the course of the study period, the proportion of patients undergoing TAVI significantly increased, as did the proportion of TAVI patients with malnutrition (PTREND <0.001; Figure 2).

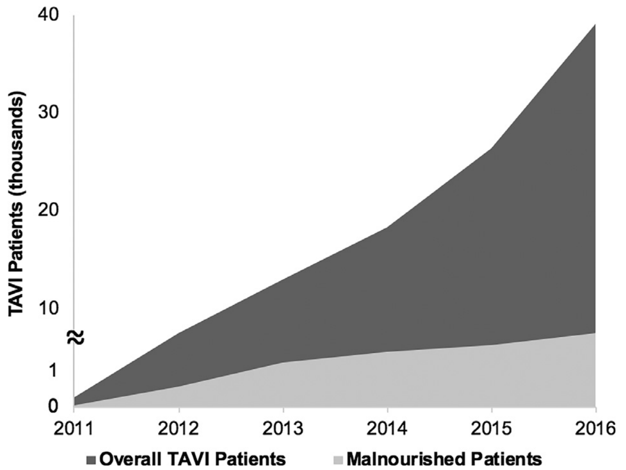

Figure 2. National temporal trends in TAVI patients and the malnourished cohort. While the proportion of patients undergoing TAVI significantly increased throughout the study period from 1.3% to 32.6% (PTREND <0.001), the proportion of malnourished patients increased as well with a mean of 5% (PTREND <0.001). TAVI = transcatheter aortic valve implantation.

On an average, malnourished patients were older and more likely to be female, insured by Medicare, admitted nonelectively, and have a higher Elixhauser Comorbidity Index compared with their nourished counterparts (Table 2). Malnourished patients had significantly higher rates of preexisting congestive heart failure and fluid and electrolyte disorders, but lower rates of coronary artery disease, previous myocardial infarction, and hypertension among others (Table 2).

Malnourished patients experienced higher rates of mortality (10.4% vs 2.2%, p <0.001) and postoperative complications (49.2% vs 22.6%, p <0.001) at index hospitalization (Table 3). After subgroup analysis of complications, malnourished patients demonstrated higher rates of respiratory, cardiovascular, infectious, renal, and neurologic complications. Malnourished patients also experienced increased discharge to a skilled nursing facility. At index hospitalization, malnourished patients were, on average, in the hospital 10 days longer than their nourished peers. Furthermore, hospitals experienced, on average, an increase of $123,555 in charges when caring for malnourished patients compared with nourished patients (Table 3).

In addition, malnourished patients experienced greater readmission rates. Malnourished patients were more likely to be readmitted within 30 days after TAVI (21.4% vs 14.9%, p <0.001) with greater mortality rates, LOS, and charges (Table 3). Of surviving patients, malnourished patients were more often readmitted within 30 days for respiratory (14.1% vs 10.3%, p = 0.0114) or infectious (15.2% vs 11.6%, p = 0.0362) complications. Moreover, malnourished patients experienced greater mortality rates, LOS, and charges within 90 days of readmission (Table 3).

Table 3
Univariate analysis of the effect of malnutrition on postoperative outcomes

Outcome	Nourished (N = 100,322)	Malnourished (N = 5,280)	p Value
Index mortality	2,199 (2.2%)	548 (10.4%)	<0.001
Any complication	21,381 (22.6%)	2,485 (49.2%)	<0.001
Postoperative complications			
Acute kidney injury	9,343 (10%)	1,202 (24.3%)	<0.001
Cardiovascular	5,094 (5.4%)	522 (10.5%)	<0.001
Infectious	975 (1%)	424 (8.5%)	<0.001
Neurological	1,807 (1.9%)	238 (4.8%)	<0.001
Respiratory	8,561 (9.1%)	1,466 (29.2%)	<0.001
Index LOS (days)	6.2 ± 0.6	16.4 ± 1.4	<0.001
Index charges	$208,082 ± $84,456	$331,637 ± $84,589	<0.001
Discharge to facility	53,014 (52.8%)	3,613 (68.4%)	<0.001
Readmission within 30 Days	13,495 (14.9%)	1,018 (21.4%)	<0.001
Readmission within 90 Days	17,662 (24.6%)	1,256 (34%)	<0.001
30 day readmission			
Mortality	583 (4.3%)	96 (9.4%)	<0.001
LOS (days)	5.9 ± 6.5	7.9 ± 9	<0.001
Charges	$55,305 ± $28,309	$69,198 ± $23,417	0.002
Reasons for readmission at 30 days			
Infectious	1,492 (11.6%)	151 (15.2%)	0.036
Respiratory	1,324 (10.3%)	140 (14.1%)	0.011
Cardiovascular	5,190 (40.3%)	296 (29.9%)	<0.001
90 day readmission			
Mortality	482 (6%)	76 (12%)	<0.001
LOS (days)	6.2 ± 7	7.5 ± 7.3	0.002
Charges	57,109 ± 84,488	67,917 ± 84,240	0.025

LOS = length of stay.

A multivariable model adjusted for baseline differences among groups (C = 0.79 for mortality). After accounting for patient and hospital characteristics, malnutrition was independently associated with increased mortality, complications, LOS, and charges, as well as 30- and 90-day readmission rates (Table 4). Furthermore, malnutrition was associated with increased odds of postoperative complications in every category analyzed in this study (Figure 3). At 30 days, malnutrition was associated with greater resource utilization but not mortality (Table 4). Malnourished patients were frequently readmitted within 30 days for respiratory and infectious reasons when compared with readmitted nourished patients (Table 4). At 90 days, malnutrition was associated with increased mortality, LOS, and hospital charges (Table 4).

Table 4
Multivariable analysis demonstrating the impact of malnutrition on postoperative outcomes (Reference is Nourished Peers)

Outcome	Adjusted odds ratio [95% CI]	p Value
Index mortality	2.67 [2.14−3.33]	<0.001
Any complication	2.09 [1.86−2.34]	<0.001
Index LOS	2.66 [2.51−2.82]	<0.001
Index charges	1.35 [1.30−1.40]	<0.001
Discharge to facility	1.51 [1.28−1.78]	<0.001
30 day readmission	1.34 [1.16−1.54]	<0.001
90 day readmission	1.34 [1.17−1.54]	<0.001
30 day readmission		
Mortality	1.15 [1.06−1.24]	0.309
LOS	1.19 [1.09−1.29]	0.001
Total charges	1.16 [1.04−1.28]	0.005
Reasons for readmission at 30 days		
Infectious	1.43 [1.04−1.97]	0.027
Respiratory	1.35 [1.02−1.80]	0.038
Cardiovascular	0.62 [0.49−0.79]	<0.001
90 day readmission		
Mortality	2.12 [1.46−3.09]	<0.001
LOS	1.10 [1.00−1.19]	0.033
Total charges	1.18 [1.06−1.32]	0.004

LOS = length of stay.

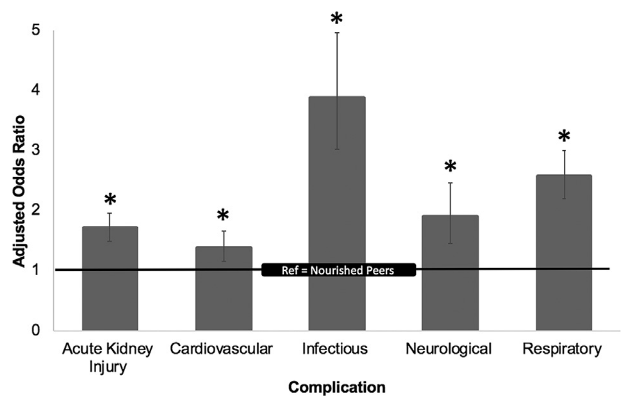

Figure 3. Adjusted odds ratio for postoperative complications for malnourished patients at index hospitalization. After adjustment, malnourished patients were more likely to experience acute kidney injury, and cardiovascular, infectious, neurological, and respiratory complications following TAVI. * indicates significance at p <0.001. TAVI = transcatheter aortic valve implantation.

When stratified by admission type, malnourished patients with elective admission had higher rates of index mortality, complications, 30 and 90 day readmissions, longer index LOS, and greater charges compared with their nourished counterparts (Figure 4). Elective patients with malnutrition had increased odds of index mortality, complications, and LOS compared with nonelective admission patients. Furthermore, electively admitted malnourished patients had higher odds of developing acute kidney injury or infectious, neurologic, or respiratory complications following TAVI relative to the elective malnourished cohort (Figure 5).

Discussion

TAVI has emerged as an alternative valve implantation procedure for the elderly and frail. Given the adverse impact of malnutrition on open surgical procedures, this study evaluated its predictive value in patients undergoing the less invasive TAVI. We examined a national cohort of malnourished patients who, relative to properly nourished patients, had significantly higher rates of mortality, longer hospital stays, increased rates of acute kidney injury, and more frequent pulmonary, cardiovascular, and infectious complications. Malnutrition was also associated with greater 30- and 90-day readmission rates, as well as an average of $123,555 more in index hospitalization

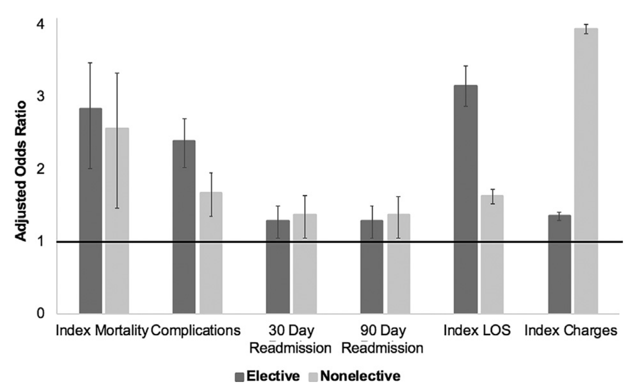

Figure 4. Adjusted odds ratio for outcomes in malnourished patients by admission status. Reference is nourished peers in respective subcohorts.

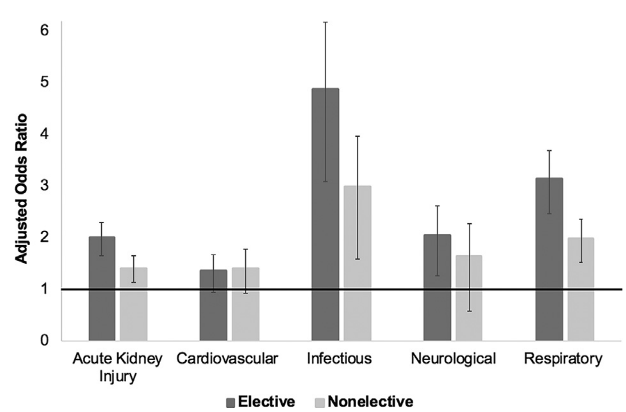

Figure 5. Adjusted odds ratio for complications in malnourished patients by admission status. Reference is nourished peers in respective subcohorts.

expenditures. These results may aid in patient selection and preoperative optimization given the significant impact of malnutrition in a less invasive procedure like TAVI.

Currently, multiple well-established assessment tools are used to identify malnutrition in clinical practice, including the Malnutrition Universal Screening Tool,[10] Nutrition Risk Screening 2002,[11] Mini Nutritional Assessment[12] and its Short Form,[13] and Subjective Global Assessment.[14] However, these assessment tools can be subjective, complex, and time-consuming. A previous multicenter investigation identified a number of adverse outcomes in patients who underwent TAVI using the Mini Nutritional Assessment-Short Form score.[15] However, in our study, malnutrition was defined as a composite of diagnoses based on the National Readmission Database data dictionary. This definition holds several advantages over existing methodology. First, our study allows for a more generalizable, national-level analysis without subjective variation in survey administration. Second, this method utilizes a composite definition from co-morbidities coded in the medical record, significantly reducing the time required by survey methods. Third, this definition can be generated preoperatively to allow for risk stratification and possible mitigation of postoperative risks, including infection. Importantly, our methodology generated findings consistent with the existing literature, but also expanded on adverse events independently predicted by malnutrition within the TAVI population.[15]

Preoperative malnutrition portends significantly worse postoperative morbidity and mortality. Malnutrition has been shown to attenuate the patient's immune response, leading to delayed wound healing in surgical patients.[6,16,17] Further evidence suggests that preoperative malnutrition spurs T cell anergy and yields a dysfunctional immune response that predisposes to infection and protein catabolism.[18] Our findings in malnourished TAVI patients are consistent with previous studies in open surgery.[19−22] Malnutrition is often a modifiable risk factor that could prompt nutritional intervention.[23] Immunonutrition is one such preoperative intervention that may enhance the bodily response to infection. Nutritional supplements such as arginine and omega-3 fatty acids have been associated with reduced rates of infection, wound complications, and lengths of stay in malnourished surgical patients.[24] The potential of this preoperative intervention warrants further investigation in the TAVI population.

Beyond the index hospitalization, our results also demonstrate malnutrition to be associated with higher readmission rates following TAVI. Within 30 days, 19.3% of malnourished patients were readmitted, notably due to infectious causes. It is remarkable that malnourished TAVI patients have a readmission rate comparable to that of malnourished open general surgery counterparts, as Havens et al found that 18.9% of malnourished general surgery patients were readmitted within 30 days.[25] Furthermore, the higher rate of readmission for infection observed in the malnourished cohort is consistent with animal and human models that have linked malnutrition to immune suppression.[26,27] These readmission rates are unlikely due to differences in discharge location, as our study was consistent with previous literature in finding that malnourished patients were more likely to be transferred to a skilled nursing facility.[15]

Prolonged recovery time and higher readmission rates contribute to the significant economic impact of malnutrition. Our results indicate that malnutrition is associated with an increase in hospital-based charges due to adverse outcomes, prolonged LOS, and increased readmission. Since hospitals are reimbursed based on diagnosis-related groups, proper documentation of malnutrition is encouraged to ensure adequate hospital reimbursement. In a cohort of gastroenterology patients, identification of the appropriate diagnosis-related group category for malnutrition resulted in 8.3% increase in total hospital reimbursement.[28] These results highlight the importance of correct identification and documentation of malnutrition as a potential to increase hospital reimbursement while improving patient outcomes.

This study had several important limitations. There is no single definition of malnutrition; thus our study may underrepresent the true extent of the malnourished population. Given that this was a retrospective study, we are limited in understanding the unique etiology of each malnourished presentation. It is difficult to distinguish whether the patient had a preexisting chronic malnutrition diagnosis, became malnourished preoperatively during the hospital stay, or became malnourished as a result of the procedure. Furthermore, we were unable to assess the severity of a patient's malnutrition diagnosis. Lastly, the National Readmissions Database does not include sufficient data to calculate or extract the Society of Thoracic Surgeons risk score. Given that these traditional surgical risk scores typically do not include frailty or malnutrition, future studies should explore the impact of including frailty in these risk scoring systems.

In conclusion, this study confirms and further illustrates the consequences of malnutrition on TAVI patients. Malnutrition independently predicts adverse events following TAVI, including higher rates of mortality, complications, and 30- and 90-day readmission, along with increased resource utilization. Our findings support the use of coding-based assessment of malnutrition and its incorporation in risk assessment tools and policy generation.

Author Contributions

Sara Emami: Methodology, formal analysis, writing − original draft; **Sarah Rudasill**: Conceptualization, writing − original draft and review/editing; **Nikhil Bellamkonda**: Writing − original draft and review/editing; **Yas Sanaiha**: Conceptualization, methodology, data curation; **Mario Cale**: Conceptualization, writing − review and editing; **Josef Madrigal**: Methodology, writing − review and editing; **Nathaniel Christian-Miller**: Formal analysis, writing − review and editing; **Peyman Benharash**: Supervision, writing − review and editing, project administration.

Disclosures

The authors have no conflicts of interest to disclose.

1. Thyregod HGH, Steinbrüchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, Chang Y, Franzen OW, Engstrøm T, Clemmensen P, Hansen PB, Andersen LW, Olsen PS, Søndergaard L. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the All-Comers NOTION Randomized

Clinical Trial. *J Am Coll Cardiol* 2015;65:2184–2194. Available at: https://www.sciencedirect.com/science/article/pii/S0735109715008190?via%3Dihub. Accessed October 4, 2019.
2. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Davidson MJ, Svensson LG, Akin J. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet* 2015;385:2477–2484. Available at: https://www.sciencedirect.com/science/article/pii/S0140673615603087?via%3Dihub. Accessed October 4, 2019.
3. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Sondergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PWJC, Kappetein AP. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321–1331.
4. Fávaro-Moreira NC, Krausch-Hofmann S, Matthys C, Vereecken C, Vanhauwaert E, Declercq A, Bekkering GE, Duyck J. Risk factors for malnutrition in older adults: a systematic review of the literature based on Longitudinal Data. *Adv Nutr* 2016;7:507–522. Available at: https://academic.oup.com/advances/article/7/3/507/4653577. Accessed October 4, 2019.
5. Van Stijn MFM, Korkic-Halilovic I, Bakker MSM, Van Der Ploeg T, Van Leeuwen PAM, Houdijk APJ. Preoperative nutrition status and postoperative outcome in elderly general surgery patients: a systematic review. *J Parenter Enter Nutr* 2013;37:37–43.
6. Haydock DA, Hill GL. Impaired wound healing in surgical patients with varying degrees of malnutrition. *J Parenter Enter Nutr* 1986;10:550–554. Available at: http://doi.wiley.com/10.1177/0148607186010006550. Accessed October 4, 2019.
7. Fingar KR, Weiss AJ, Barrett ML, Elixhauser A, Steiner CA, Guenter P, Brown MH. All-cause readmissions following hospital stays for patients with malnutrition, 2013: Statistical Brief #218. *Healthcare Cost and Utilization Project* 2016. Available at: https://www.hcup-us.ahrq.gov/reports/statbriefs/sb218-Malnutrition-Readmissions-2013.jsp?utm_source=AHRQ&utm_medium=EN1&utm_term&utm_content=1&utm_campaign=AHRQ_EN1_18_2017. Accessed June 18, 2019.
8. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8–27. Available at: http://www.ncbi.nlm.nih.gov/pubmed/9431328. Accessed October 4, 2019.
9. Royston P. *PTREND: Stata Module for Trend Analysis for Proportions*. Available at: https://econpapers.repec.org/software/bocbocode/s426101.htm. Accessed October 16, 2019.
10. Elia M. Screening for malnutrition: a multidisciplinary responsibility. Development and use of the Malnutrition Universal Screening Tool ('MUST') for adults. *Redditch:BAPEN* 2003. Available at: https://www.bapen.org.uk/pdfs/must/must_full.pdf. Accessed October 16, 2019.
11. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. *Clin Nutr* 2003;22:321–336. Available at: https://www.sciencedirect.com/science/article/pii/S0261561402002145?via%3Dihub. Accessed October 16, 2019.
12. Guigoz Y, Vellas B, Garry PJ. Assessing the nutritional status of the elderly: the mini nutritional assessment as part of the geriatric evaluation. *Nutr Rev* 2009;54:S59–S65. Available at: https://academic.oup.com/nutritionreviews/article-lookup/doi/10.1111/j.1753-4887.1996.tb03793.x. Accessed October 16, 2019.
13. Kaiser MJ, Bauer JM, Ramsch C, Uter W, Guigoz Y, Cederholm T, Thomas DR, Anthony P, Charlton KE, Maggio M, Tsai AC, Grathwohl D, Vellas B, Sieber CC, MNA-International Group.. Validation of the Mini Nutritional Assessment Short-Form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging* 2009;13:782–788. Available at: http://www.ncbi.nlm.nih.gov/pubmed/19812868. Accessed October 16, 2019.
14. Detsky A, McLaughlin Baker J, Johnston N, Whittaker S, Mendelson R, Jeejeebhoy K. What is subjective global assessment of nutritional status? *J Parenter Enter Nutr* 1987;11:8–13. Available at: http://doi.wiley.com/10.1177/014860718701100108. Accessed October 16, 2019.
15. Goldfarb M, Lauck S, Webb JG, Asgar AW, Perrault LP, Piazza N, Martucci G, Lachapelle K, Noiseux N, Kim DH, Popma JJ, Lefèvre T, Labinaz M, Lamy A, Peterson MD, Arora RC, Morais JA, Morin J-F, Rudski LG, Afilalo J. Malnutrition and mortality in frail and non-frail older adults undergoing aortic valve replacement. *Circulation* 2018;138:2202–2211. Available at: https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.033887. Accessed June 23, 2019.
16. Butterworth CE. The skeleton in the hospital closet. *Nutr Today* 1974;9:4–8. Available at: http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00017285-201607000-00006. Accessed October 16, 2019.
17. Keusch GT. The history of nutrition: malnutrition, infection and immunity. *J Nutr* 2003;133:336S–340S. Available at: https://academic.oup.com/jn/article/133/1/336S/4687573. Accessed October 16, 2019.
18. Mira JC, Brakenridge SC, Moldawer LL, Moore FA. Persistent inflammation, immunosuppression and catabolism syndrome. *Crit Care Clin* 2017;33:245–258.
19. Chermesh I, Hajos J, Mashiach T, Bozhko M, Shani L, Nir R-R, Bolotin G. Malnutrition in cardiac surgery: food for thought. *Eur J Prev Cardiol* 2014;21:475–483. Available at: http://journals.sagepub.com/doi/10.1177/2047487312452969. Accessed October 16, 2019.
20. Torre M La, Ziparo V, Nigri G, Cavallini M, Balducci G, Ramacciato G. Malnutrition and pancreatic surgery: prevalence and outcomes. *J Surg Oncol* 2013;107:702–708. Available at: http://doi.wiley.com/10.1002/jso.23304. Accessed June 23, 2019.
21. Tobert CM, Hamilton-Reeves JM, Norian LA, Hung C, Brooks NA, Holzbeierlein JM, Downs TM, Robertson DP, Grossman R, Nepple KG. Emerging impact of malnutrition on surgical patients: literature review and potential implications for cystectomy in bladder cancer. *J Urol* 2017;198:511–519. Available at: http://www.ncbi.nlm.nih.gov/pubmed/28286066. Accessed June 23, 2019.
22. Merli M, Nicolini G, Angeloni S, Riggio O. Malnutrition is a risk factor in cirrhotic patients undergoing surgery. *Nutrition* 2002;18:978–986. Available at: https://www.sciencedirect.com/science/article/pii/S089990070200984X. Accessed October 16, 2019.
23. Stoppe C, Goetzenich A, Whitman G, Ohkuma R, Brown T, Hatzakorzian R, Kristof A, Meybohm P, Mechanick J, Evans A, Yeh D, McDonald B, Chourdakis M, Jones P, Barton R, Tripathi R, Elke G, Liakopoulos O, Agarwala R, Lomivorotov V, Nesterova E, Marx G, Benstoem C, Lemieux M, Heyland DK. Role of nutrition support in adult cardiac surgery: a consensus statement from an International Multidisciplinary Expert Group on Nutrition in Cardiac Surgery. *Crit Care* 2017;21:131.. Available at: http://www.ncbi.nlm.nih.gov/pubmed/28583157. Accessed October 19, 2019.
24. Marik PE, Zaloga GP. Immunonutrition in high-risk surgical patients. *J Parenter Enter Nutr* 2010;34:378–386. Available at: http://doi.wiley.com/10.1177/0148607110362692. Accessed December 2, 2019.
25. Havens JM, Columbus AB, Seshadri AJ, Olufajo OA, Mogensen KM, Rawn JD, Salim A, Christopher KB. Malnutrition at intensive care unit admission predicts mortality in emergency general surgery patients. *J Parenter Enter Nutr* 2016;42:014860711667659. Available at: http://doi.wiley.com/10.1177/0148607116676592. Accessed October 16, 2019.
26. Schaible UE, Kaufmann SHE. Malnutrition and infection: complex mechanisms and global impacts. *PLoS Med* 2007;4:e115.. Available at: https://dx.plos.org/10.1371/journal.pmed.0040115. Accessed October 16, 2019.
27. Fock RA, Vinolo MAR, de Moura Sá Rocha V, de Sá Rocha LC, Borelli P. Protein-energy malnutrition decreases the expression of TLR-4/MD-2 and CD14 receptors in peritoneal macrophages and reduces the synthesis of TNF-α in response to lipopolysaccharide (LPS) in mice. *Cytokine* 2007;40:105–114. Available at: https://www.sciencedirect.com/science/article/pii/S104346660700381X?via%3Dihub. Accessed October 16, 2019.
28. Ockenga J, Freudenreich M, Zakonsky R, Norman K, Pirlich M, Lochs H. Nutritional assessment and management in hospitalised patients: Implication for DRG-based reimbursement and health care quality. *Clin Nutr* 2005;24:913–919. Available at: https://www.sciencedirect.com/science/article/pii/S0261561405000907?via%3Dihub. Accessed October 17, 2019.