Frailty in patients undergoing transcatheter aortic valve replacement: from risk scores to frailty-based management

Andreas Tzoumas¹, Damianos G. Kokkinidis²,², Stefanos Giannopoulos³, George Giannakoulas⁴, Leonidas Palaiodimos²,⁵, Dimitrios V Avgerinos⁶, Polydoros N Kampaktsis⁷, Robert T. Faillace²

¹. Aristotle University of Thessaloniki, Thessaloniki, Greece; ². Department of Medicine, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, USA; ³. Division of Cardiology, Rocky Mountain Regional VA Medical Center, University of Colorado, Denver, USA; ⁴. First Cardiology Department, AHEPA University Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; ⁵. Division of Hospital Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, USA; ⁶. Department of Cardiothoracic Surgery, New York-Presbyterian/Weill Cornell Medical Center, New York, USA; ⁷. Division of Cardiology, New York University Langone Medical Center, New York, USA

✉ Correspondence to: damiankokki@gmail.com

https://doi.org/10.11909/j.issn.1671-5411.2021.06.002

Aortic stenosis (AS) is the most common valvular disease in the western countries and is associated with aging.¹,² Transcatheter aortic valve replacement (TAVR) now offers a therapeutic option for elderly patients who are deemed inoperable and is an excellent alternative for those who are considered high-risk for surgical valve replacement.³,⁴ However, mortality after TAVR is still high with one-year and two-year mortality rates of 24.3% and 33.9%, respectively.⁵ Thus, utilization of effective risk stratification tools before TAVR cannot be overstated.⁵–⁸ Currently, EUROSCORE II and the Society of Thoracic Surgery score are the recommended risk models to predict postoperative mortality in cardiac surgery, however, they were not designed to be used for TAVR patients.⁶,⁸ The main limitation in the implementation of these models is that they do not take into account frailty.⁹ Frailty assessment could not only offer incremental prognostic information but could also theoretically improve outcomes with preoperative or postoperative management and modification of specific frailty components.¹⁰,¹¹

PATHOGENESIS OF FRAILTY AND AORTIC STENOSIS

The pathogenesis of frailty is likely associated with age-related biologic changes that lead to multisystem impairment.¹²,¹³ Specifically, frailty has been related with dysregulation of the immune, endocrine and musculoskeletal systems,¹² with chronic inflammation and neuromuscular dysfunction considered key underlying mechanisms.¹⁴ In severe AS, left ventricular remodeling and diastolic heart failure predispose to reduced exercise capacity and increased episodes of hospitalization.¹⁵–¹⁷ Thus, the natural course of severe AS leads to immobility and a chronic inflammatory state induced by valvular pathology and the frequent hospitalizations.¹⁵,¹⁸,¹⁹ Importantly, TAVR patients are frequently considered inoperable or high risk for surgery, thus frailty is by definition more common in this population compared to surgical patients.

IMPACT OF FRAILTY ON MORTALITY AND QUALITY OF LIFE AFTER TAVR

Frailty has been associated with increased short-term and long-term mortality after TAVR. Afilalo, et al.¹⁰ evaluated seven different frailty scales in the FRAILTY-AVR study, a prospective multi-center cohort comprising 1,020 elderly patients (minimum age: 70 years) undergoing TAVR or surgical aortic valve replacement. Among the TAVR population subgroup, frailty as measured by all seven scales, was independently associated with increased one-year mortality. Essential Frailty Toolset (EFT) was
the strongest predictor of one-year mortality [adjusted odds ratio (OR) = 3.19, 95% CI: 2.03–5.02] (Figure 1). Additionally, five out of seven frailty scales significantly predicted thirty-day mortality in TAVR cohort. In another analysis of FRAILTY-AVR study comprising 400 TAVR patients, the prognostic value of sarcopenia was evaluated, which is one of the biological substrates of frailty. Sarcopenia was defined as low psoas muscle area by computed tomographic imaging and low chair-rise performance, and was associated with significantly increased one-year mortality after TAVR (OR = 11.30, 95% CI: 2.51–50.91).

A similarly-sized multicenter registry from Japan evaluated frailty using a semi-quantitative Clinical Frailty Scale (CFS), which categorized patients into five groups with increasing frailty grade (Table 1). Results showed that the CFS grade was associated with increasing thirty-day mortality risk and was assessed as an independent risk factor for one-year death rate [hazard ratio (HR) = 1.28, 95% CI: 1.10–1.49]. In this study, the CFS grade correlated with other markers of frailty such as body mass index < 20 kg/m², serum albumin < 3.5 mg/dL late gait speed and weak grip strength. Hence, although CFS is a semi-quantitative tool, it accurately reflected the physical component of frailty in TAVR patients and was useful in predicting mortality outcomes after TAVR. Moreover, two additional studies demonstrated that frailty assessment alone accurately predicted one-year mortality after TAVR and its additive

![Central illustration: essential frailty toolset in older adults undergoing aortic valve replacement](http://www.jgc301.com; jgc@jgc301.com)

**Figure 1  Essential frailty toolset.** Reprinted from Journal of the American College of Cardiology. Reference: Afilalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: the FRAILTY-AVR study. J Am Coll Cardiol 2017; 70: 689–700. DOI: 10.1016/j.jacc.2017.06.024 with permission from Elsevier. EFT: essential frailty toolset; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement.

| Groups | Condition/CFS stage | Description |
|--------|---------------------|-------------|
| Group 1| CFS 1               | Very fit: robust, active, energetic with regular exercise |
| Group 2| CFS 2               | Well: no symptomatic disease, occasional exercise, less fit than CFS 1 patients |
| Group 3| CFS 3               | Managing well: well-controlled medical problems, no regular exercise beyond routine walking |
| Group 4| CFS 4               | Vulnerable: independent, though common activity limitation due to medical problems, self-report of ‘slowness’ or ‘tiredness’ during the day |
| Group 5| CFS 5               | Mildly frail: more evident slowing, require help in high order instrumental activity of daily living |
| Group 6| CFS 6               | Moderately frail: require help with all outside and home-based activities |
| Group 7| CFS 7               | Severely frail: completely dependent on others for any activity of daily living, albeit stable |
| Group 8| CFS 8               | Very severely frail: completely dependent, close to end of life, vulnerable even to minor illness |
| Group 9| CFS 9               | Terminally ill: approaching to the end of life, or life expectancy < 6 months, even if not otherwise frail |

CFS: Clinical Frailty Scale.
value in conventional risk scores of one-year mortality.\[11,23\]

A similar relationship between frailty and short-term and long-term mortality has been replicated by two recent meta-analyses evaluating frailty status in 5,876 and 3,159 patients, respectively.\[24,25\] Frailty was associated with increased risk of one-year mortality (HR = 2.16, 95% CI: 1.57–3.00),\[24\] and increased early (≤ 30 days; HR = 2.35, 95% CI: 1.78–3.09) and late mortality (> 30 days; HR = 1.63, 95% CI: 1.34–1.97).\[25\] A recent retrospective cohort of 890 patients from the Alina Health System database demonstrated that along with other comorbidities, excessive frailty significantly increased the three-year mortality risk (HR = 2.48, 95% CI: 1.79–3.44).\[26\] Increasing evidence from additional studies demonstrated that the addition of frailty assessment in existing prediction risk models significantly improves discrimination for short-term and mid-term mortality rates following TAVR.\[27–29\] Specifically, a retrospective analysis of 266 frail TAVR patients demonstrated that frailty status was correlated with both periprocedural and late mortality, with higher frailty indexes associated with higher risk for one-year all-cause death.\[27\] Additionally, Stortecky, et al.\[28\] with a prospective cohort of 100 patients undergoing TAVR suggested that the addition of Multidimensional Geriatric Assessment-based information to global risk scores could further improve the risk prediction for all-cause mortality and major adverse cardiovascular and cerebral events at thirty-day and one-year after the index procedure. Details regarding impact of frailty on mortality in selected TAVR studies are presented in Table 2.

The association between frailty and quality of life (QoL) with TAVR was shown in a secondary analysis of the PARTNER trial, where frailty, as

### Table 2  Impact of frailty on mortality in selected studies.

| Study               | Number of patients | TAVR patients | Design                                      | Frailty scales                                                                                           | Outcome                                                                                                                                 |
|---------------------|--------------------|---------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Afilalo, et al\[10\]| 1,020              | 646           | Prospective multicenter cohort              | Fried, Fried+, SPPB, Rockwood, Bern, Columbia, EFT                                                                                                 | OR = 3.29\*, 95% CI: 1.73–6.26                                                                                                       |
| Shimura, et al\[22\]| 1,215              | 1,215         | Multicenter registry (OCEAN-TAVI)           | Clinical frailty scale stage                                                                          | HR = 1.42, 95% CI: 1.04–1.95                                                                                                        |
| Rogers, et al\[21\] | 544                | 544           | Prospective single-center cohort            | ≥ 3 out of 5: BMI < 20 kg/m\(^2\), Serum albumin < 3.5 g/dL, Katz index of independence in ADL score ≤ 4/6, Low grip strength, Slow 15-foot walk time | OR = 5.06, 95% CI: 1.36–18.8; NRI = 73%, 95% CI: 31–41.1 (after adding frailty to STS prediction model)                             |
| Schoenenberger, et al\[23\] | 330                | 330           | Prospective single-center cohort            | MMSE, TUG, MNA, BADL, IADL, MOBILITY DISABILITY                                                          | HR = 3.29, 95% CI: 1.98–5.47; LR chi-square test statistic = 38.27; C-statistic = 0.72, P< 0.001; LR chi-square test statistic = 28.71; C-statistic = 0.68, P< 0.001                                       |
| Tang, et al\[26\]   | 890                | 890           | Retrospective single-center cohort          | ≥ 3 out of 5: BMI < 20 kg/m\(^2\), Serum albumin < 3.5 g/dL, Katz index of independence in ADL score ≤ 4/6, Low grip strength, Slow 15-foot walk time | HR = 2.48, 95% CI: 1.79–3.44                                                                                                        |
| Steinvi, et al\[27\] | 498                | 498           | Retrospective single-center cohort          | ≥ 3 out of 5: BMI < 20 kg/m\(^2\), Serum albumin < 3.5 g/dL, Katz index of independence in ADL score ≤ 4/6, Low grip strength, 5-meter walk test | HR = 2.2, 95% CI: 1.25–3.96 (frailty status); HR = 2.0, 95% CI: 1.08–3.7 (for 3 frailty criteria); HR = 3.07, 95% CI: 1.4–6.7 (for 4-5 frailty criteria) |
sessed by the Kansas City Cardiomyopathy Questionnaire overall summary (KCCQ-OS) score was an independent predictor of death or poor QoL at one year after TAVR. Additionally, a substudy of Transcatheter Valve Therapy Registry among 6,151 patients with available 5-m walk test data revealed that patients with slower gait speed (an index of physical frailty) reported worse one-year KCCQ-OS compared to those with normal gait speed.

### FRAILTY AND POST-TAVR COMPLICATIONS

Data are conflicting regarding the relationship of frailty and postoperative adverse events (as defined by the Valve Academic Research Consortium-2 consensus guidelines). Shimura, et al. showed a significant relationship between escalating CFS grade and the incidence of postoperative vascular complications, acute kidney injury (AKI), life-threatening major bleeding and length of hospital and intensive care unit stays. The same group of authors in another secondary analysis of Optimized Catheter-Alvular Intervention-TAVR registry demonstrated an association between frailty and procedural complications, such as need for transfusion, AKI, bleeding and cardiac tamponade using serum albumin level of 3.5 g/dL as a cutoff to dichotomize patients in frail and non-frail. Finally, Puls, et al. in a prospective single center cohort of 300 patients concluded that the incidence of minor bleeding, transfusion requirement, stage 3 AKI and renal replacement therapy and prolonged hospitalization was

| Study             | Number of patients | TAVR patients | Design                  | Frailty scales                                                                 | Outcome                                      |
|-------------------|--------------------|---------------|-------------------------|--------------------------------------------------------------------------------|-----------------------------------------------|
| Stortecky, et al. | 100                | 100           | Prospective cohort      | Bern scale, BADL, IADL, MMSE, MNA, Poor mobility, TUG                           | OR = 8.33, 95% CI: 0.99–70.48                  |
| Hermiller, et al. | 2,482 (derivation cohort) | 2,482 (derivation cohort) | Secondary analysis of Core Valve Trial (NCT01240902) | 5MGS, Albumin, Assisted living, BADL, Falls, Grip strength, MMSE, Weight loss | HR = 1.60, 95% CI: 1.04–2.47 (Albumin < 3.3 g/dL); HR = 1.68, 95% CI: 1.05–2.69 (Assisted living); HR = 1.82, 95% CI: 1.17–2.82 (Katz ADL ≥ 2 deficits) |
| Green, et al.     | 244                | 244           | Secondary analysis of PARTNER trial (NCT00330894) | Albumin, Grip strength, Gait speed, Katz ADL                                    | HR = 2.5, 95% CI: 1.40–4.35                   |
| Arnold, et al.    | 8,039              | 8,039         | Observational cohort from the SITS/ACC TVT Registry | 5MGS                                                                           | OR = 1.11, 95% CI: 1.01–1.22                   |
| Puls, et al.      | 300                | 300           | Prospective single-center cohort | Katz ADL < 6                                                                   | HR = 2.67, 95% CI: 1.7–4.3                    |
| Van Mournik, et al.| 5,876 (9 studies) | 5,876 (9 studies) | Meta-analysis            | Different frailty scales among the included studies                            | HR = 2.16, 95% CI: 1.57–3.00                   |
| Anand, et al.     | 1,900              | 1,900         | Meta-analysis            | Four studies using objective frailty assessment                                | HR = 2.35, 95% CI: 1.78–3.09                  |
| Anand, et al.     | 3,159 (7 studies)  | 3,159 (7 studies) | Meta-analysis            | Seven studies using objective frailty assessment                                | HR = 1.63, 95% CI: 1.34–1.97                  |

*Presented as estimated using EFT in TAVR and surgical aortic valve replacement cohorts. Presented as estimated using EFT in TAVR cohort. Presented as frailty index combined with EUROSCORE. Presented as frailty index combined with SITS score. ADL: activities of daily living; BADL: basic activity of daily living; BMI: body mass index; CI: confidence interval; EFT: essential frailty toolset; HR: hazard ratio; IADL: instrumental activities of daily living; LR: likelihood ratio; MMSE: mini-mental state examination; MNA: mini-nutritional assessment; NCT: national clinical trial; NRI: net reclassification improvement; OCEAN-TAVI: Optimized Catheter-Alvular Intervention-TAVR; OR: odds ratio; PARTNER: placement of aortic transcatheter valves; SPPB: short physical performance battery; STS: Society of Thoracic Surgeons; TAVR: transcatheter aortic valve replacement; TUG: time up and go; TVT: transcatheter valve therapy registry; 5MGS: 5-m gait speed.
significantly greater in the subgroup of frail patients. On the other hand, Green, et al. did not identify significant associations between frailty markers and postprocedural stoke, vascular complications or major bleeding events in two secondary analyses of the PARTNER trial (NCT00530894). However, the small sample of frail patients in those studies was probably a limiting factor for detection of such associations. Proper selection of TAVR eligible patients can improve the postoperative outcomes. Similarly, Honda, et al. studying 150 patients undergoing TAVR suggested that although objective malnutrition status assessment could predict one-year mortality after TAVR, malnutrition was not associated with increased incidence of inhospital adverse events following TAVR. Furthermore, a retrospective study enrolling 157 patients undergoing preoperative chest computed tomography examinations to evaluate sarcopenia by measuring skeletal muscle index at two thoracic levels, demonstrated that skeletal muscle index was not associated with surgical complications (postoperative renal failure, stroke, bleeding) following TAVR. Considering the small datasets and the heterogeneous outcomes, more studies will be needed in the future to better characterize the ideal frailty components whose assessment can improve and predict outcomes in AS patients undergoing TAVR.

**FRAILTY-GUIDED MANAGEMENT IN THE PERI-TAVR SETTING AND FUTURE DIRECTIONS**

Frailty evaluation provides prognostic information that is additive to existing risk scores. However, it could also provide the basis for therapeutic interventions that could improve outcomes. Experience gained from interventional studies involved frail patients has shown that frailty is potentially reversible. Regular exercise intervention and physical activity may reduce frailty, especially in individuals at greater risk for disability. Additionally, nutritional supplementation and follow-up after discharge in malnourished independent, geriatric patients significantly benefits QoL. To maximize benefits, frailty and disability can be successfully treated using an interdisciplinary multifaceted treatment strategy addressing simultaneously multiple frailty components.

Although these interventions have not been studied adequately in the TAVR population, existing evidence suggests that the early implementation of cardiac rehabilitation program following TAVR enhances patients’ exercise tolerance and functional status as well as QoL. Proponents of frailty assessment in TAVR in fact support frailty assessment at baseline and after TAVR to allow for the detection of functional changes in the elderly. Further studies have demonstrated significant benefits regarding functional and emotional status of post-TAVR patients who followed multicomponent rehabilitation programs including early mobilization, physical therapy and psychological support. A multidisciplinary approach to these patients requires the collaboration of the Heart Valve team with extracardiac specialties including nutritionists, physiotherapists, occupational therapists and psychologists, as soon as the frailty is identified in the preoperative phase. Considering the results of Mamane, et al. evaluation of sarcopenia, which can be objectively assessed with a limited computed tomography scan or bioelectrical impedance testing along with a clinical muscle test, may provide additional benefits in patients prior to TAVR. The reason is that sarcopenic patients can be effectively managed with intensive nutritional supplementation and exercise to increase their functional reserve for TAVR.

These results will be confirmed by the ongoing PERFORM-TAVR trial (NCT03522454) where the investigators evaluate a multi-faceted intervention in 250 frail participants with Short Physical Performance Battery score ≤ 8. The intervention consists of a protein-rich oral nutritional supplement for four weeks before-TAVR and a home-based exercise program for twelve weeks post-TAVR. Similarly, results from two ongoing trials (TAVR-FRAILTY/NCT02597985, TAVR-Prehab/NCT03107897) evaluating the efficacy of rehabilitation prior to TAVR are eagerly anticipated.
outcomes following TAVR, there is not a single, consensus tool to evaluate frailty in clinical practice.\cite{35} The 2017 ACC/AHA guidelines for the management of patients with heart valve disease recommend the use of Katz Activities of Daily Living (ADL) to categorize patients to none, mild, or moderate to severe frailty status.\cite{54} However, they recognize that alternative frailty scores may be acceptable to evaluate frailty stage.\cite{54} Expert Consensus Decision Pathway for TAVR recommend six-minute walking test and dependence on ADL for physical functioning evaluation; Mini Mental State Exam to address cognitive function; screening for depression with history followed by a validated tool such as the Center for Epidemiologic Studies Depression Scale; and addressing risk for malnutrition (body mass index < 20 kg/m\(^2\), ten-pound weight loss in past year, serum albumin < 3.5 mg/dL or score ≤ 11 on Mini Nutritional Assessment).\cite{55} Additionally, the role of the Heart Valve team consisting of a multidisciplinary group of experts in different cardiology subspecialties in collaboration with the referral physician and cardiac surgeon is considered critical for effective frailty assessment and risk stratification of TAVR patients.\cite{55} The 2019 Canadian Cardiovascular Society TAVI position statement supports the use of the EFT and the KCCQ for frailty and QoL assessment, respectively.\cite{56} However, the wide and heterogenous definition of frailty hinders the comparability of the plethora of frailty tools. Future research into the biological basis of frailty will enable a better understanding of this clinical syndrome and its subsequent standardized, objective incorporation in clinical practice. We propose the incorporation of frailty assessment in clinical practice using EFT or CFS as an initial screening test for patients undergoing TAVR along with further diagnostic and therapeutic considerations to address the key components of frailty (Figure 2).

**CONCLUSIONS**

Frailty is a major risk factor for mortality and functional decline following TAVR and should be a standard evaluation in the heart valve clinic. Baseline and follow-up frailty-guided management could provide additional support to patients and improve outcomes. Useful information from ongoing trials and properly designed future prospective cohorts will provide evidence regarding the appropriate interventions in frail TAVR patients in the preoperative and postoperative period with an ultimate goal to improve survival and functional status. Future efforts should also focus on standardizing frailty assessment, given the large spectrum of current frailty scales and tools.

**ACKNOWLEDGMENTS**

All authors had no conflicts of interest to disclose.

---

**Figure 2** Recommended frailty-based clinical management pathway of elderly TAVR patients. BMI: body mass index; CFS: clinical frailty scale; CT: computed tomography; EFT: essential frailty toolset; GDS: geriatric depression scale; MNA: mini-nutritional assessment; SPPB: short physical performance battery; TAVR: transcatheter aortic valve replacement.
REFERENCES

[1] Nakano VT, Gardin JM, Skelton TN, et al. Burden of valvular heart disease: a population-based study. Lancet 2006; 368: 1005–1011.

[2] Osnabrugge RL, Mylotte D, Head SJ, et al. Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. J Am Coll Cardiol 2013; 62: 1002–1012.

[3] Hinterbuchner L, Strohmer B, Hammener M, et al. Frailty scoring in transcatheter aortic valve replacement patients. Eur J Cardiovasc Nurs 2016; 15: 384–397.

[4] Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011; 364: 2187–2198.

[5] Kodali SK, Williams MR, Smith CR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med 2012; 366: 1686–1695.

[6] Arangalage D, Cimadevilla C, Alkhoder S, et al. Agreement between the new EuroSCORE II, the Logistic EuroSCORE and the Society of Thoracic Surgeons score: implications for transcatheter aortic valve implantation. Arch Cardiovasc Dis 2014; 107: 353–360.

[7] Watanabe Y, Hayashida K, Leferve T, et al. Is EuroSCORE II better than EuroSCORE in predicting mortality after transcatheter aortic valve implantation? Catheter Cardiovasc Interv 2013; 81: 1053–1060.

[8] Durand E, Borz B, Godin M, et al. Performance analysis of EuroSCORE II compared to the original logistic EuroSCORE and STS scores for predicting 30-day mortality after transcatheter aortic valve replacement. Am J Cardiol 2013; 111: 891–897.

[9] Piankova P, Afilalo J. Prevalence and prognostic implications of frailty in transcatheter aortic valve replacement. Cardiol Clin 2020; 38: 75–87.

[10] Afifalo J, Lauck S, Kim DH, et al. Frailty in older adults undergoing aortic valve replacement: the FRAILTY-AVR study. J Am Coll Cardiol 2017; 70: 689–700.

[11] Rogers T, Alraies MC, Moussa Pacha H, et al. Clinical frailty as an outcome predictor after transcatheter aortic valve implantation. Am J Cardiol 2018; 121: 850–855.

[12] Chen MA. Frailty and cardiovascular disease: potential role of gait speed in surgical risk stratification in older adults. J Geriatr Cardiol 2015; 12: 44–56.

[13] Thongprayout C, Cheungpasitporn W, Kashani K. The impact of frailty on mortality after transcatheter aortic valve replacement. Ann Transl Med 2017; 5: 144.

[14] Leng S, Chaves P, Koenig K, et al. Serum interleukin-6 and hemoglobin as physiological correlates in the geriatric syndrome of frailty: a pilot study. J Am Geriatr Soc 2002; 50: 1268–1271.

[15] Ha FJ, Bissland K, Mandrawa C, et al. Frailty in patients with aortic stenosis awaiting intervention. Intern Med J 2021; 51: 319–326.

[16] Rosenhek R, Zilberszac R, Schemper M, et al. Natural history of very severe aortic stenosis. Circulation 2010; 121: 151–156.

[17] Kampaktsis PN, Kokkinidis DG, Wong SC, et al. The role and clinical implications of diastolic dysfunction in aortic stenosis. Heart 2017; 103: 1481–1487.

[18] Papanastasiou CA, Kokkinidis DG, Kampaktsis PN, et al. The prognostic role of late gadolinium enhancement in aortic stenosis: a systematic review and meta-analysis. JACC Cardiovasc Imaging 2020; 13: 385–392.

[19] Papanastasiou CA, Kokkinidis DG, Jonsalagadda AK, et al. Meta-analysis of transthoracic echocardiography versus cardiac magnetic resonance for the assessment of aortic regurgitation after transcatheter aortic valve implantation. Am J Cardiol 2019; 124: 1246–1251.

[20] Mamane S, Mullie L, Lok Ok Choo W, et al. Sarcopenia in older adults undergoing transcatheter aortic valve replacement. J Am Coll Cardiol 2019; 74: 3178–3180.

[21] Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173: 489–495.

[22] Shimura T, Yamamoto M, Kano S, et al. Impact of the clinical frailty scale on outcomes after transcatheter aortic valve replacement. Circulation 2017; 135: 2013–2024.

[23] Schoenenerberger AW, Moser A, Bertschi D, et al. Improvement of risk prediction after transcatheter aortic valve replacement by combining frailty with conventional risk scores. JACC Cardiovasc Interv 2018; 11: 395–403.

[24] van Mourik MS, Velu JF, Lanting VR, et al. Preoperative frailty parameters as predictors for outcomes after transcatheter aortic valve implantation: a systematic review and meta-analysis. Neth Heart J 2020; 28: 280–292.

[25] Anand A, Harley C, Visvanathan A, et al. The relationship between preoperative frailty and outcomes following transcatheter aortic valve implantation: a systematic review and meta-analysis. Eur Heart J Qual Care Clin Outcomes 2017; 3: 123–132.

[26] Tang L, Sorajja P, Mooney M, et al. Transcatheter aortic valve replacement in patients with severe comorbidities: a retrospective cohort study. Catheter Cardiovasc Interv 2021; 97: E253–E262.

[27] Stevinil A, Buchanan KD, Kiramijyan S, et al. Utility of an additive frailty tests index score for mortality risk assessment following transcatheter aortic valve replacement. Am J Heart 2018; 200: 11–16.

[28] Stortecky S, Schoenenerberger AW, Moser A, et al. Evaluation of multidimensional geriatric assessment as a predictor of mortality and cardiovascular events after transcatheter aortic valve implantation. JACC Cardiovasc Interv 2012; 5: 489–496.

[29] Hermiller JB Jr, Yakubov SJ, Reardon MJ, et al. Predicting early and late mortality after transcatheter aortic valve replacement. J Am Coll Cardiol 2016; 68: 343–352.

[30] Green P, Arnold SV, Cohen DJ, et al. Relation of frailty to outcomes after transcatheter aortic valve replacement (from the PARTNER trial). Am J Cardiol 2015; 116: 264–269.

[31] Arnold SV, Spertus JA, Vemulpalli S, et al. Quality-of-life outcomes after transcatheter aortic valve replacement in an unselected population: a report from the STS/ACC Transcatheter Valve Therapy Registry. JAMA Cardiol 2017; 2: 409–416.

[32] Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 2013; 145: 6–23.

[33] Yamamoto M, Shimura T, Kano S, et al. Prognostic value of hypoalbuminemia after transcatheter aortic valve implantation (from the Japanese Multicenter OCEAN-TAVI Registry). Am J Cardiol 2017; 119: 770–777.
References

Puls M, Sobisiak B, Bleckmann A, et al. Impact of frailty on short- and long-term morbidity and mortality after transcatheter aortic valve implantation: risk assessment by Katz Index of activities of daily living. *EuroIntervention* 2014; 10: 609–619.

Green P, Woglon AE, Genereux P, et al. The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. *JACC Cardiovasc Interv* 2012; 5: 974–981.

Honda Y, Yamawaki M, Shigemitsu S, et al. Prognostic value of objective nutritional status after transcatheter aortic valve replacement. *J Cardiol* 2019; 73: 401–407.

Nemec U, Heidinger B, Sokas C, et al. Diagnosing sarcopenia on thoracic computed tomography: quantitative assessment of skeletal muscle mass in patients undergoing transcatheter aortic valve replacement. *Acad Radiol* 2017; 24: 1154–1161.

Ng TP, Feng L, Nyunt MS, et al. Nutritional, physical, cognitive, and combination interventions and frailty reversal among older adults: a randomized controlled trial. *Am J Med* 2015; 128: 1225–1236.

Verghese J, Mahoney J, Ambrose AE, et al. Effect of cognitive remediation on gait in sedentary seniors. *J Gerontol A Biol Sci Med Sci* 2010; 65: 1338–1343.

Binder EF, Schectman KB, Ehsani AA, et al. Effects of exercise training on frailty in community-dwelling older adults: results of a randomized, controlled trial. *J Am Geriatr Soc* 2002; 50: 1921–1928.

Cesari M, Vellas B, Hsu FC, et al. A physical activity intervention to treat the frailty syndrome in older persons-results from the LIFE-P study. *J Gerontol A Biol Sci Med Sci* 2015; 70: 216–222.

Giné-Garriga M, Guerra M, Pages E, et al. The effect of functional circuit training on physical frailty in frail older adults: a randomized controlled trial. *J Aging Phys Act* 2010; 18: 401–412.

Gariballa S, Forster S. Dietary supplementation and quality of life of older patients: a randomized, double-blind, placebo-controlled trial. *J Am Geriatr Soc* 2007; 55: 2030–2034.

Pedersen JL, Pedersen PU, Damsgaard EM. Early nutritional follow-up after discharge prevents deterioration of ADL functions in malnourished, independent, geriatric patients who live alone: a randomized clinical trial. *J Nutr Health Aging* 2016; 20: 845–853.

Cameron ID, Fairhall N, Langron C, et al. A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial. *BMC Med* 2013; 11: 65.

Bibas L, Levi M, Bendayan M, et al. Therapeutic interventions for frail elderly patients: part I. Published randomized trials. *Prog Cardiovasc Dis* 2014; 57: 134–143.

Gill TM, Baker DI, Gottschalk M, et al. A program to prevent functional decline in physically frail, elderly persons who live at home. *N Engl J Med* 2002; 347: 1068–1074.

Kokkinidis DG, Armstrong EJ, Giri J. Balancing weight loss and sarcopenia in elderly patients with peripheral artery disease. *J Am Heart Assoc* 2019; 8: e013200.

Ribeiro GS, Melo RD, Deresz LF, et al. Cardiac rehabilitation programme after transcatheter aortic valve implantation versus surgical aortic valve replacement: systematic review and meta-analysis. *Eur J Prev Cardiol* 2017; 24: 688–697.

Völler H, Salzwedel A, Nitardy A, et al. Effect of cardiac rehabilitation on functional and emotional status in patients after transcatheter aortic-valve implantation. *Eur J Prev Cardiol* 2015; 22: 568–574.

Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. *J Gerontol* 1994; 49: M85–M94.

Puri R, Jung B, Cohen DJ, et al. TAVI or no TAVI: identifying patients unlikely to benefit from transcatheter aortic valve implantation. *Eur Heart J* 2016; 37: 2217–2225.

Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017; 135: e1159–e1195.

Otto CM, Kumbhani DJ, Alexander KP, et al. 2017 ACC expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2017; 69: 1313–1346.

Asgar AW, Ouzounian M, Adams C, et al. 2019 Canadian cardiovascular society position statement for transcatheter aortic valve implantation. *Can J Cardiol* 2019; 35: 1437–1448.

Please cite this article as: Tzoumas A, Kokkinidis DG, Giannopoulos S, Giannakoulas G, Palaiodimos L, Avgerinos DV, Kampaktis PN, Faillace RT. Frailty in patients undergoing transcatheter aortic valve replacement: from risk scores to frailty-based management. *J Geriatr Cardiol* 2021; 18(6): 479–486. DOI: 10.11909/j.issn.1671-5411.2021.06.002