

Association of Depression With Mortality in Older Adults Undergoing Transcatheter or Surgical Aortic Valve Replacement

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IMPORTANCE Depression is increasingly recognized as a risk factor for adverse outcomes in cardiovascular disease. However, little is known about depression in older adults undergoing transcatheter (TAVR) or surgical (SAVR) aortic valve replacement.

OBJECTIVE To determine the prevalence of depression and its association with all-cause mortality in older adults undergoing TAVR or SAVR.

DESIGN, SETTING, AND PARTICIPANTS This preplanned analysis of the Frailty Aortic Valve Replacement (FRAILTY-AVR) prospective cohort study included 14 centers in 3 countries from November 15, 2011, through April 7, 2016. Individuals 70 years or older who underwent TAVR or SAVR were enrolled. Depressive symptoms were evaluated using the Geriatric Depression Scale Short Form at baseline and follow-up.

MAIN OUTCOMES AND MEASURES All-cause mortality at 1 and 12 months after TAVR or SAVR. Logistic regression was used to determine the association of depression with mortality after adjusting for confounders such as frailty and cognitive impairment.

RESULTS Among 1035 older adults (427 men [41.3%] and 608 women [58.7%]) with a mean (SD) age of 81.4 (6.1) years, 326 (31.5%) had a positive result of screening for depression, whereas only 89 (8.6%) had depression documented in their clinical record. After adjusting for clinical and geriatric confounders, baseline depression was found to be associated with mortality at 1 month (odds ratio [OR], 2.20; 95% CI, 1.18-4.10) and at 12 months (OR, 1.532; 95% CI, 1.03-2.24). Persistent depression, defined as baseline depression that was still present 6 months after the procedure, was associated with a 3-fold increase in mortality at 12 months (OR, 2.98; 95% CI, 1.08-8.20).

CONCLUSIONS AND RELEVANCE One in 3 older adults undergoing TAVR or SAVR had depressive symptoms at baseline and a higher risk of short-term and midterm mortality. Patients with persistent depressive symptoms at follow-up had the highest risk of mortality.

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The point prevalence of major depressive disorders in the general population in the United States is estimated to be 7%, with a lifetime prevalence of 16%.¹ The prevalence reaches 45% in patients with coronary artery disease, afflicting 15 million in the United States.^{2,3} In addition to the negative effects of depression on mental health and quality of life, the American Heart Association has emphasized the relevance of depression as a risk factor for major adverse cardiovascular events after acute coronary syndromes.^{4,5} Previous studies^{6,7} have similarly shown that depression and anxiety are prevalent risk factors for adverse events after cardiac surgery, including surgical aortic valve replacement (SAVR) procedures, which is not surprising given the pathophysiologic overlap between aortic valve stenosis and coronary artery disease.⁸

Little is known about the role of depression in older adults undergoing transcatheter aortic valve replacement (TAVR), because to date no large-scale study has focused on mental health in this distinct patient population. Furthermore, none of the previous studies were able to adjust for frailty and cognitive impairment, which are critical confounders owing to their known association with depression and adverse outcomes.⁹ If depression is an independent risk factor after aortic valve replacement, targeted referrals for testing and therapy may be beneficial to improve patient-centered outcomes. Thus, we sought to determine the prevalence of depression and its association with all-cause mortality in a large representative cohort of older adults undergoing TAVR and SAVR.

Methods

Study Design

The Frailty Aortic Valve Replacement (FRAILTY-AVR)^{10,11} prospective cohort study was designed to compare the value of various frailty scales to estimate mortality after TAVR and SAVR. Participating centers included the Jewish General Hospital and McGill University Health Center, McGill University, Montreal, Quebec, Canada; Institut de Cardiologie de Montréal, Centre Hospitalier de l'Université de Montréal, and Hôpital du Sacré-Coeur de Montréal, Université de Montréal, Montreal, Quebec, Canada; St Paul's Hospital, University of British Columbia, Vancouver, Canada; St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; St Boniface Hospital, University of Manitoba, Winnipeg, Canada; University of Ottawa Heart Institute, University of Ottawa, Ottawa, Ontario, Canada; Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada; Beth Israel Deaconess Medical Center and Massachusetts General Hospital, Harvard University, Boston, Massachusetts; Washington University School of Medicine, Washington University, St Louis, Missouri; and Institut Cardiovasculaire Paris Sud, Hôpital Privé Jacques Cartier, Massy, France. The 14 centers enrolled patients from November 15, 2011, through April 7, 2016. The research ethics boards at all participating centers approved this study, and patients signed an informed consent before being enrolled.

The methods and primary results of the FRAILTY-AVR study were recently reported¹⁰; in brief, patients completed a preprocedural assessment of frailty, disability, comorbidity, cogni-

Key Points

Question What is the prevalence of depression and its association with all-cause mortality among older adults undergoing aortic valve replacement?

Findings In this multicenter prospective cohort study, 326 of 1035 older adults undergoing transcatheter or surgical aortic valve replacement (31.5%) had evidence of depression at baseline and a higher risk of short-term and midterm mortality. Patients with depressive symptoms that persisted after the procedure had the highest risk of subsequent mortality.

Meaning Screening for depression may be justified during the baseline evaluation and follow-up of patients with severe aortic stenosis who are referred for aortic valve replacement.

tive function, and mood and subsequently completed a post-procedural telephone interview at 6 and 12 months. In this preplanned substudy, the prevalence, correlates, and prognostic association of depressive mood symptoms were examined.

Population

Patients who were at least 70 years of age with symptomatic aortic stenosis were included if they underwent TAVR or SAVR with or without concomitant coronary revascularization at one of our participating study centers. Patients were excluded if they had emergency surgery, clinical instability (defined as unstable vital signs or refractory ongoing symptoms), replacement of more than 1 heart valve, replacement of the aorta, severe neuropsychiatric impairment precluding informed consent, or a prohibitive language barrier.

Depression

Depressive symptoms were evaluated with the 5-item Geriatric Depression Scale Short Form (GDS-SF),¹² which captures satisfaction, boredom, helplessness, anhedonia, and worthlessness. A GDS-SF score of at least 2 of 5 is indicative of clinically relevant depression. The GDS-SF was administered at baseline and at the 6- and 12-month follow-up. The change in GDS-SF status from baseline to 6 months was classified for surviving patients as no depression at either time point, resolved depression, new depression, or persistent depression. The 5-item GDS-SF was previously validated in older adults with multiple cardiac and noncardiac comorbidities and found to be as effective as the 15-item version.¹³

Assessment of Frailty, Cognitive Function, and Other Covariates

Physical frailty was defined as a Short Physical Performance Battery (SPPB) score of 8 or less.¹⁴ The SPPB encompasses 5-m gait speed, time to complete 5 chair rises, and ability to complete standing balance positions, with each scored from 0 to 4 and summed, for a possible total of 12. Frailty was also evaluated with the Fried scale,¹⁵ which encompasses 5-m gait speed, handgrip strength, unintentional weight loss, inactivity, and exhaustion. The Fried scale is scored from 0 to 5, with a score of 3 or more indicating frailty. Cognitive impairment was defined as a Mini-Mental State Examination score of 23 or less.¹⁶

End Points

The primary end points were all-cause mortality at 1 and 12 months after the index procedure. Vital status was ascertained by contacting the patients or their family members by telephone, verifying hospital-level medical records, and linking our study database with administrative data sources. No patient was lost to or unavailable for follow-up for these end points.

Statistical Analysis

Continuous variables were summarized with the sample means and SDs. Differences between continuous variables across depression states were expressed as means with 95% CIs using the independent 2-tailed *t* test. Discrete categorical variables were summarized with counts and percentages. Differences between categorical variables across depression states were expressed as means with 95% CIs for the proportions. Univariate analysis was performed to assess the association of relevant covariates with the study end points.

Multivariable logistic regression models were used to estimate the association between depression and all-cause mortality. Models were adjusted for baseline covariates, including age, sex, physical frailty, cognitive impairment, the Society of Thoracic Surgeons (STS) predicted risk of mortality, and the type of procedure performed. Sensitivity analyses were performed to further adjust for individual covariates that were found to be significantly associated with depression. Survival curves were generated with the Kaplan-Meier method. Statistical analyses were performed with Rstudio software (version 0.99.491; <https://www.rstudio.com/>) and Stata software (version 14.1; StataCorp).

Results

Baseline Characteristics

Our cohort consisted of 1035 patients with a mean (SD) age of 81.4 (6.1) years, including 427 men (41.3%) and 608 women (58.7%). At baseline, 326 patients (31.5%) had positive results of screening for depression, whereas only 89 (8.6%) had a diagnosis of depression documented in their clinical record. Prevalent depression was elicited in 222 of 657 patients (33.8%) undergoing TAVR and 104 of 378 (27.5%) undergoing SAVR. Compared with patients without depression, those with depression were more likely to have diabetes (114 [35.0%] vs 175 [24.7%]), chronic kidney disease (154 [47.2%] vs 271 [38.2%]), hypertension (276 [84.7%] vs 543 [76.6%]), chronic obstructive pulmonary disease (74 [22.7%] vs 108 [15.2%]), cerebrovascular disease (69 [21.2%] vs 106 [15.0%]), and higher mean (SD) Society of Thoracic Surgeons–predicted risk of mortality (5.8% [4.2%] vs 5.1% [3.7%]) (Table 1). Moreover, compared with patients without depression, patients with depression were more likely to be frail according to the SPPB (180 [55.2%] vs 232 [32.7%]) and the Fried scale (248 [76.1%] vs 451 [63.6%]) and to be cognitively impaired (72 [22.1%] vs 108 [15.2%]). Baseline characteristics stratified by TAVR and SAVR are presented in eTables 1 and 2 in the Supplement.

Association of Depression With 1-Month Mortality

At 1 month, 24 deaths (7.4%) were observed in the group with depression compared with 21 deaths (3.0%) in the group without depression. On univariate analysis, the association between depression and 1-month mortality was statistically significant (unadjusted odds ratio [OR], 2.60; 95% CI, 1.43–4.75). An association with 1-month mortality was also observed for physical frailty (unadjusted OR, 5.15; 95% CI, 1.83–14.50) and cognitive impairment (unadjusted OR, 2.78; 95% CI, 1.48 to 5.23). On multivariable logistic regression, depression (adjusted OR, 2.20; 95% CI, 1.18–4.10) was the only independent patient-level variable prognostic factor of short-term mortality (Table 2). Separate analyses stratified by TAVR and SAVR revealed similar results and are presented in eTables 3 and 4 in the Supplement.

Association of Depression With 12-Month Mortality

At 12 months, 62 deaths (19.0%) were observed in the group with depression and 83 deaths (11.7%) were observed in the group without depression (Figure). The causes of the 145 deaths were cardiovascular in 45 (31.0%), noncardiovascular in 57 (39.3%), and unknown in 43 (29.7%), with no observed difference in cause of death based on depression status. On univariate analysis, the association between depression and 12-month mortality was statistically significant (unadjusted OR, 1.77; 95% CI, 1.24–2.54). On multivariable logistic regression, patient-level variables prognostic of all-cause mortality included depression (adjusted OR, 1.53; 95% CI, 1.03–2.24), cognitive impairment (adjusted OR, 2.31; 95% CI, 1.53–3.49), and physical frailty (adjusted OR, 2.37; 95% CI, 1.38–4.09) (Table 2). Separate analyses stratified by TAVR and SAVR revealed similar results and are presented in eTables 3 to 5 and eFigures 1 and 2 in the Supplement. The association of depression with 12-month mortality was not significantly modified by the presence of concomitant frailty, cognitive impairment, or coronary artery disease. In addition, the association was not attenuated by adjusting for individual comorbidities associated with depression or by considering frailty (SPPB score) as a continuous covariate (eTable 6 in the Supplement).

Longitudinal Changes in Depressive Symptoms

When comparing paired depression scores at baseline with those at 6 months after the procedure (excluding patients who did not survive to the 6-month assessment), patients were grouped into the following 4 categories: 460 (59.2%) had no depression at either time point, 143 (18.4%) had resolved depression, 86 (11.1%) had new depression, and 88 (11.3%) had persistent depression. Of these categories, persistent depression at 6 months was most strongly associated with subsequent mortality (adjusted OR, 2.98; 95% CI, 1.08–8.20) (Table 3). Patients with persistent depression, compared with those with resolved depression, had higher mean (SD) baseline GDS-SF scores (3.0 [1.0] vs 2.6 [0.8]) but no notable differences in baseline frailty, cognition, comorbidity burden, left ventricular ejection fraction, aortic stenosis severity, or New York Heart Association class, with 82.3% of patients having minimal New York Heart Association I to II limitations at 6 months (eTable 7 in the Supplement).

Table 1. Baseline Characteristics by Depression Status

| Characteristic | Patients With Depression (n = 326) | Patients Without Depression (n = 709) | Mean Difference (95% CI) ^a |
|--|------------------------------------|---------------------------------------|---------------------------------------|
| Age, mean (SD), y | 81.2 (6.3) | 81.5 (6.1) | -0.22 (-1.03 to 0.59) |
| Female, No. (%) | 146 (44.8) | 281 (39.6) | 0.05 (-0.02 to 0.11) |
| BMI, mean (SD) | 27.7 (5.6) | 27.2 (5.4) | 0.46 (-0.26 to 1.18) |
| Atrial fibrillation, No. (%) | 119 (36.5) | 224 (31.6) | 0.05 (-0.01 to 0.11) |
| Hypertension, No. (%) | 276 (84.7) | 543 (76.6) | 0.08 (0.03 to 0.13) |
| Dyslipidemia, No. (%) | 230 (70.6) | 480 (67.7) | 0.03 (-0.03 to 0.09) |
| Diabetes, No. (%) | 114 (35.0) | 175 (24.7) | 0.10 (0.04 to 0.16) |
| Coronary artery disease, No. (%) | 195 (59.8) | 440 (62.0) | -0.02 (-0.09 to 0.04) |
| Cerebrovascular disease, No. (%) | 69 (21.2) | 106 (15.0) | 0.06 (0.01 to 0.11) |
| Peripheral arterial disease, No. (%) | 45 (13.8) | 118 (16.6) | -0.03 (-0.08 to 0.02) |
| COPD, No. (%) | 74 (22.7) | 108 (15.2) | 0.08 (0.03 to 0.13) |
| Chronic kidney disease, No. (%) | 154 (47.2) | 271 (38.2) | 0.09 (0.03 to 0.15) |
| GFR, mean (SD), mL/min/1.73 m ² | 59.7 (19.5) | 63.0 (17.6) | -3.25 (-5.64 to -0.86) |
| Hemoglobin level, mean (SD), g/dL | 11.9 (1.7) | 12.4 (1.7) | -4.87 (-7.11 to -2.63) |
| Mean aortic gradient, mean (SD), mm Hg | 44.1 (14.5) | 46.4 (16.1) | -2.27 (-4.32 to -0.22) |
| LVEF, mean (SD), % | 55.8 (12.8) | 56.0 (12.4) | 0.06 (-1.56 to 1.68) |
| Geriatrics domain | | | |
| SPPB score, mean (SD) ^b | 5.7 (3.4) | 7.0 (3.1) | -1.38 (-1.80 to -0.96) |
| SPPB score ≤8, No. (%) ^b | 180 (55.2) | 232 (32.7) | 0.12 (0.06 to 0.18) |
| Fried score, mean (SD) ^c | 2.6 (1.4) | 1.8 (1.3) | 0.77 (0.60 to 0.95) |
| Fried score ≥3, No. (%) ^c | 248 (76.1) | 451 (63.6) | 0.22 (0.16 to 0.29) |
| Cognitive impairment, No. (%) | 72 (22.1) | 108 (15.2) | 0.07 (0.02 to 0.12) |
| ADL disability, No. (%) | 121 (37.1) | 137 (19.3) | 0.18 (0.12 to 0.23) |
| Surgical characteristics, No. (%) | | | |
| TAVR | 222 (68.1) | 435 (61.4) | 0.07 (0.01 to 0.13) |
| SAVR | 104 (31.9) | 274 (38.6) | -0.07 (-0.13 to -0.01) |
| STS predicted mortality, mean (SD), % | 5.8 (4.2) | 5.1 (3.7) | 0.71 (0.21 to 1.22) |
| Mortality, No. (%) | | | |
| 1 mo | 24 (7.4) | 21 (3.0) | 0.04 (0.01 to 0.07) |
| 6 mo | 43 (13.2) | 58 (8.2) | 0.05 (0.01 to 0.09) |
| 12 mo | 62 (19.0) | 83 (11.7) | 0.07 (0.03 to 0.12) |

Abbreviations: ADL, activities of daily living; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; SAVR, surgical aortic valve replacement; SPPB, Short Physical Performance Battery; STS, Society of Thoracic Surgeons; TAVR, transcatheter AVR.

SI conversion factor: To convert hemoglobin to grams per liter, multiply by 10.0.

^a Represents the difference between the group with depression and the group without depression (unity).

^b Scores range from 0 to 12, with a score of 8 or less indicative of frailty.

^c Scores range from 0 to 5, with a score of 3 or more indicative of frailty.

Discussion

This study is the first, to our knowledge, to investigate the interplay among depression, frailty, and mortality in older adults undergoing TAVR and SAVR. Our study suggests that depression is underdiagnosed and affects as many as 1 in 3 patients in this context. When present, depression is associated with an increased risk of short-term and midterm mortality after adjusting for clinical and geriatric risk factors. The association between baseline depression and 12-month mortality was modulated by intercurrent changes in depressive symptoms, such that patients with persistent depression were at significantly higher risk than were those with resolved depression. The extent to which this risk resulted from a persistent mood disorder or a marker of poor underlying health status may have varied among individual patients. Depressed patients were more likely to be frail and cognitively impaired, reaffirming the overlap between these geriatric syndromes.

Our prospective multicenter study adds to the emerging body of evidence on depression in older adults undergoing heart valve surgery. Oterhals et al¹⁷ conducted a single-center

retrospective study of 912 patients who had undergone SAVR and found that self-reported depression and anxiety were correlated with worse physical functioning after surgery. Faria et al¹⁸ conducted a prospective study of 52 patients undergoing SAVR with a mean (SD) age of 68 (10) years and reported a 52% prevalence of depression postoperatively and an association with surgical complications and length of stay. Ho et al¹⁹ conducted a prospective study of 648 patients undergoing valve surgery and reported a 29% prevalence of depression preoperatively and an association with 6-month mortality (OR, 1.90; 95% CI, 1.07-3.40). Compared with these studies, ours was the only one to include patients undergoing TAVR, administer a validated depression scale at multiple points, and adjust for cognitive function and physical frailty.

More evidence is available regarding depression in patients with coronary artery disease. The Depression Effects on Coronary Artery Disease Events (DECADE) study included a prospective cohort of 2390 patients and established depression as an independent risk factor for all-cause mortality; in that cohort, Pelletier et al²⁰ found that patients with coronary artery disease who had depression were 3-fold more likely to experience a fatal outcome during 9 years. The association

Table 2. Multivariable Models for Baseline Depression and Mortality

| Variable | OR (95% CI) | |
|-------------------------------------|------------------|------------------|
| | 1-mo Mortality | 12-mo Mortality |
| Depression (GDS-SF score ≥ 2) | 2.20 (1.18-4.10) | 1.53 (1.03-2.24) |
| Physical frailty | 2.89 (0.99-8.47) | 2.37 (1.38-4.09) |
| Cognitive impairment | 1.89 (0.97-3.68) | 2.31 (1.53-3.49) |
| Age, per year | 1.05 (0.98-1.12) | 1.04 (1.00-1.08) |
| Female sex | 1.43 (0.76-2.69) | 0.89 (0.60-1.31) |
| STS predicted mortality per 1% | 1.04 (0.97-1.12) | 1.09 (1.04-1.14) |
| Procedure | | |
| Femoral TAVR | 1 [Reference] | 1 [Reference] |
| Nonfemoral TAVR | 2.80 (1.34-5.84) | 1.65 (1.02-2.67) |
| Isolated SAVR | 1.15 (0.35-3.81) | 0.40 (1.16-0.98) |
| Combined SAVR and CABG | 1.33 (0.45-3.97) | 1.12 (0.62-2.03) |

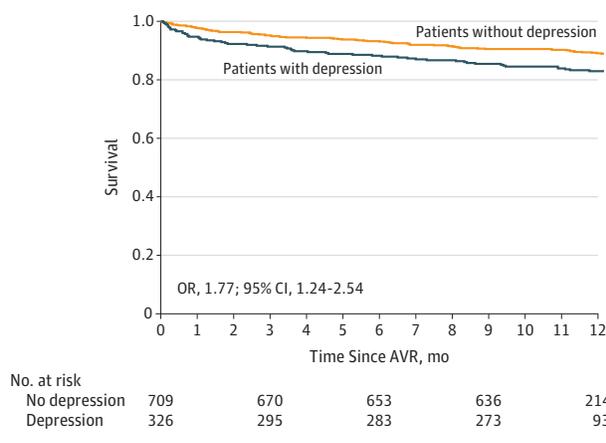
Abbreviations: CABG, coronary artery bypass grafting surgery; GDS-SF, Geriatric Depression Scale Short Form; OR, odds ratio; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement.

Table 3. Multivariable Model for Change in Depression and Mortality

| Variable | 12-mo Mortality, OR (95% CI) |
|-------------------------------------|------------------------------|
| Change in depression status at 6 mo | |
| No depression at either point | 1 [Reference] |
| Resolved depression | 1.57 (0.55-4.46) |
| New depression | 2.47 (0.90-6.78) |
| Persistent depression | 2.98 (1.08-8.20) |
| Physical frailty | 3.59 (1.03-12.46) |
| Cognitive impairment | 0.79 (0.30-2.08) |
| Age per 1-y increase | 1.02 (0.95-1.10) |
| Female sex | 0.57 (0.26-1.25) |
| STS predicted mortality, per 1% | 1.09 (1.01-1.17) |
| Procedure | |
| Femoral TAVR | 1 [Reference] |
| Nonfemoral TAVR | 1.17 (0.46-2.97) |
| Isolated SAVR | 0.27 (0.03-2.16) |
| Combined SAVR and CABG | 0.41 (0.09-1.95) |

Abbreviations: CABG, coronary artery bypass grafting surgery; OR, odds ratio; SAVR, surgical aortic valve replacement; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement.

Figure. Kaplan-Meier Survival Curves by Baseline Depression Status



At 12 months, 62 deaths (19.0%) were observed among 326 patients with depression and 83 deaths (11.7%) were observed in 709 patients without depression. AVR indicates aortic valve replacement; OR, odds ratio.

between depression and mortality is multifactorial. Depression is associated with nonadherence to medication therapy, poor social support, sedentary lifestyle, and cigarette smoking,^{21,22} all of which are risk factors for the development and progression of cardiovascular disease. Depression and cardiovascular disease are associated with higher levels of circulating inflammatory markers that can accelerate atherosclerosis and aggravate endothelial dysfunction through nitric oxide-dependent and -independent mechanisms.^{23,24} Depression is associated with perturbed serotonin metabolism in the brain and in circulating platelets, which can promote platelet activation, degranulation, aggregation, and atherothrombosis.^{25,26}

In patients with chronic heart failure, a meta-analysis of 27 studies²⁷ reported a pooled prevalence of depression of 33% in women and 26% in men, comparable to our observed prevalence of 31.5%. The prevalence was significantly lower when

stringent diagnostic criteria were applied by mental health professionals. The potential for questionnaire instruments to overdiagnose depression underscores the potential overlap between symptoms of chronic heart failure and those of a major depressive disorder, including emotional (loss of interest, thoughts of death) and somatic (low energy levels, sleep disturbance) symptoms. Therefore, clinicians should be cautious not to rely solely on questionnaire instruments to diagnose depression. Notwithstanding the diagnostic challenges, the meta-analysis²⁷ showed that depression was independently associated with a 2-fold increase in the risk of all-cause mortality.

The clinical implications of our findings support active screening for depression before and after aortic valve procedures to identify patients who may benefit from further psychiatric evaluation for the diagnosis and treatment of a depressive disorder. This 2-tiered approach is in line with the American Heart Association recommendation to screen for depression with a brief questionnaire and, when the finding is positive, to confirm the diagnosis with a comprehensive expert evaluation.²⁸ Once confirmed, targeted therapies such as cognitive behavioral therapy, exercise therapy, and antidepressants may be of benefit, with sertraline and citalopram having an established safety record in patients with cardiac disease and cardiac rehabilitation having a favorable effect on depression after SAVR.²⁹

Beyond the disabling consequences on patient survival and quality of life, depression imparts a large economic, public health, and caregiver burden,³⁰ warranting careful consideration by health care clinicians and stakeholders. Clinicians should be vigilant to the evolution of depressive symptoms after surgery, because new or persistent symptoms herald a greater risk of mortality. Although previous studies focusing on quality of life after TAVR and SAVR^{31,32} reported that mental health, on aggregate, improved in the ensuing months

after the procedure, our study identified a vulnerable subset of patients in whom depressive symptoms did not improve but rather persisted or deteriorated and portended a higher risk of death.

Limitations

Interpretation of these results should be considered in light of the following limitations. First, although the GDS-SF is a validated instrument to screen for depression (sensitivity of 94% and specificity of 82%),^{10,12} confirmatory testing with formal psychiatric evaluation was not systematically performed in this study, leading to a possible risk of misclassification for depression status. Nevertheless, our objective evaluation of depression at multiple time points was preferable to use of self-reported or clinically documented depression in previous studies. Second, the use of antidepressants and referral to psychiatric specialists was not recorded and may have influenced the prevalence and prognosis of depression. In keeping with this hypothesis, patients with persistent (potentially untreated) depression had worse outcomes compared with those who had resolved (potentially treated) depression. Third, despite our best efforts to adjust for relevant covariates, depressed patients had a higher prevalence of clinical risk factors that may have caused a component of residual confounding; however, sensitivity analysis adjusting for additional covariates did not significantly attenuate the effects, and our

study is the first, to our knowledge, to have adjusted for frailty and cognitive impairment, which are 2 of the most critical confounders.

Conclusions

Our analysis from the FRAILTY-AVR study demonstrates that depression is highly prevalent among patients with aortic stenosis undergoing TAVR and SAVR and appears to be associated with a heightened risk of all-cause mortality. These findings underscore the importance of screening for depression during the baseline evaluation and reevaluating changes in depression status during follow-up. Screening for depressive symptoms can be efficiently performed with brief objective tools such as the GDS-SF, which are more prognostic than self-reported depression but less robust than structured interviews conducted by mental health professionals. Professional evaluation is useful to confirm the diagnosis and ensure that apparent depressive symptoms are not confounded by heart failure symptoms or poor general health status. Given the prognostic implications and diagnostic challenges, coordinated care involving cardiovascular and psychogeriatric specialists is indicated to provide optimal management to patients undergoing TAVR and SAVR who exhibit depressive symptoms.

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