Health Care Resource, Economic, and Readmission Implications After Acute Decompensated Aortic Stenosis−A Nationwide Study

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Acute decompensated aortic stenosis (ADAS) is common. The cumulative burden of ADAS from a clinical, health care resource, and financial perspective is unknown. This study sought to assess the national impact of ADAS compared with electively treated, stable patients with aortic stenosis (non-ADAS). Using the National Readmissions Database between 2016 and 2019, patients with ADAS and non-ADAS were identified using International Classification of Diseases, Tenth Revision codes. Patients with ADAS were propensity-matched to non-ADAS patients (1:2) using age, gender, and Charlson co-morbidity index. We compared in-hospital mortality, length of stay (LOS), health care−associated costs, and 90-day readmission data between the 2 cohorts. A total of 51,498 propensity-matched patients were included in this study: median age 75 years, 64% men. The in-hospital mortality for ADAS was higher than non-ADAS (2.8% vs 1.5%, p <0.0001). The LOS during the index admission was longer for ADAS (9 [5 to 13] vs 4 [2 to 6] days, p <0.0001). The health care−associated costs per patient was greater for ADAS ($55,450.0 [41,860.4 to 74,500.7] vs $43,405.7 [34,218.5 to 56,034.8], p <0.0001). Readmission to hospital within 90 days was more frequent in ADAS (21.1 vs 16.8%, p <0.001). The in-hospital mortality during readmission was higher with ADAS (3.9% vs 2.8%, p = 0.004). The readmission LOS was longer with ADAS (4 [2 to 7] vs 3 [2 to 6] days, p <0.0001). In conclusion, ADAS imposes a significant burden clinically and financially and on health care resources compared with non-ADAS during the index admission and 90-day follow-up. There is an urgent need to predict ADAS and optimize the timing of aortic valve replacement to reduce the incidence and the burden associated with ADAS. **(Am J Cardiol 2023;204:200−206)**

Keywords: acute decompensated aortic stenosis, acute heart failure, aortic stenosis, surgical aortic valve replacement, TAVI, transcatheter aortic valve replacement

The treatment for aortic stenosis (AS) is restricted to either surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR). Guideline-based indications depend on the severity of AS, symptoms, adverse impact on left ventricular function, or abnormal exercise response.[1,2] If patients do not satisfy these criteria, they are often followed up with regular clinical reviews and echocardiograms until they meet 1 of these indications. However, up to 1/3 of patients do not get a timely aortic valve replacement (AVR) and instead present with acute decompensated AS (ADAS).[3] Most centers perform urgent AVR during the index admission. Despite this, patients with ADAS have a higher mortality, more procedural complications, and greater hospital length of stay (LOS) than patients with stable AS who underwent elective AVR (non-ADAS).[4−6] Although these metrics are important, previous studies have not captured the full impact of ADAS, in particular, the outcomes with SAVR, financial burden, and impact on readmission and its implications. A more holistic understanding of ADAS will highlight the burden of this common yet poorly understood clinical entity, with the potential to guide resource allocation and further research. This study aimed to assess the impact of ADAS compared with non-ADAS from an economic, clinical, and health care provision perspective using a large "real-world" national database.

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See page 205 for Declaration of Competing Interest.

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Methods

The data for this study were obtained from a publicly available national inpatient database. The National Readmissions Database (NRD) in the United States is drawn from the State Inpatient Databases. Part of the Healthcare Cost and Utilization Project, the NRD obtains data from hospital billing information and discharge abstracts. The NRD includes the characteristics of the patients, type of the admission (elective or unplanned), readmission days after the discharge, and the International Classification of Diseases Clinical Modification codes. This study was considered exempt from institutional review board approval because the NRD contains deidentified patient information and is publicly available. KPP and HS had access to the data and take responsibility for its integrity and the data analysis.

Data were extracted from the NRD between 2016 and 2019. More recent data after 2019 were not included to avoid potential bias owing to the impact of COVID-19, which changed the usual clinical practice in many ways and therefore is likely to influence the trends and impact of ADAS. International Classification of Diseases, Tenth Revision codes were used to identify patients with AS treated with either SAVR or TAVR (Supplementary Table 1) and co-morbidities (Supplementary Table 2) and to calculate the Charlson co-morbidity index (Supplementary Table 3). Medically managed patients with AS were not included in this study. Patients aged ≥18 years were included in this study. Patients were stratified into 2 cohorts based on whether their admission was elective or unplanned—the latter formed the ADAS group. The NRD provides yearly data and cannot be used to follow-up patients after December 31. The 90-day data were only available for patients treated between January and September inclusive. Consequently, patients treated in October, November, and December were excluded from this analysis (Supplementary Figure 1).

For the assessment of the yearly prevalence and trends of ADAS compared with non-ADAS, all patients coded as such in the NRD were included. For the remainder of the analysis, a propensity-matched population in 1:2 of ADAS versus non-ADAS was selected.

Patients were not involved in the design or conduct of this study.

The study end points were assessed between ADAS and non-ADAS and analyzed according to the index admission and 90-day readmission. For both admissions, in-hospital mortality, hospital LOS, and health care−associated cost were adjusted for differences between different payers. The reasons for hospital readmission were divided into heart failure, bradyarrhythmias and conduction abnormalities, tachyarrhythmias, cerebrovascular accidents, acute coronary syndrome, vascular (arterial) related, other cardiovascular reasons, nontraumatic bleeding, noncardiac infection, malignancy-related, and other noncardiovascular reasons.

The obtained data are shown as median (interquartile range), number (%), odds ratio (OR), and 95% confidence interval (95% CI), β (95% CI), and hazard ratio (HR) (95% CI). Propensity matching was performed using age, gender, and Charlson co-morbidity index (nearest neighbor method 1:2, caliper 0.20). The yearly prevalence and trends of ADAS are shown as a percentage of the total number of AVRs performed for AS. The normality of continuous data was assessed using the Kolomogrov−Smirnov test. Baseline characteristics were compared between the ADAS and non-ADAS cohorts using the Mann−Whitney U test for nonparametric data and the chi-square test for binary data. The p-trends from 2016 to 2019 were evaluated using the Cochran−Armitage trend test. Logistic regression analysis was used for the evaluation of impact of ADAS on mortality. A multiple regression analysis was also used to derive β coefficients and 95% CI for the impact of ADAS on mortality, LOS, and hospital-associated costs during admission. For the regression analysis, the included variables were type of admission (i.e., ADAS or non-ADAS) and type of AVR because the stratified groups had been adjusted using propensity matching. Freedom from hospital readmission was compared between the ADAS and non-ADAS cohorts using the log-rank test and Cox hazard model. Kaplan−Meier curves were created for freedom from hospital readmission, comparing ADAS with non-ADAS cohorts among patients who underwent SAVR and TAVR separately. STATA version 15.1 (StataCorp, College Station, Texas) was used for all statistical analysis. A 2-sided p <0.05 was considered significant.

Results

Overall, 106,556 patients with AS were treated with AVR between 2016 and 2019 (Supplementary Figure 1). The proportion of patients with ADAS reduced from 18% to 15%, largely because more non-ADAS patients were treated, whereas the absolute number of patients with ADAS remained similar (4,268 vs 4,333 in 2016 vs 2019, respectively) (Figure 1). During the study period, patients with ADAS used an excess of approximately 25,000 hospital bed days and cost an excess of $71.8 million (Supplementary Table 4).

In the propensity-matched population, 51,498 patients were included in this study (age 75 [67 to 82] years, 32,754 men [63.6%]). The prevalence of coronary artery disease, heart failure, atrial fibrillation, previous percutaneous coronary intervention, previous coronary artery bypass grafting, and previous balloon aortic valvuloplasty were higher in the ADAS than the non-ADAS cohort (all p <0.0001). Although the prevalence of peripheral vascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and previous myocardial infarction was higher in the non-ADAS than the ADAS cohort (all p <0.0001) (Table 1). The majority of primary payers (80%) were Medicare/Medicaid (Supplementary Table 5).

Among the ADAS cohort, 7,645 patients (44.3%) were treated with TAVR (age 82 [75 to 87] years; 56% men) and 9,613 (55.7%) were treated with SAVR (70 [63 to 76] years; 70% men). Among the non-ADAS cohort, 18,688 (54.7%) were treated with TAVR (age 80 [74 to 86] years; 58% men) and 15,461 (45.3%) were treated with SAVR (69 [62 to 75] years; 71% men) (Supplementary Table 6). The in-hospital mortality was higher in patients with ADAS

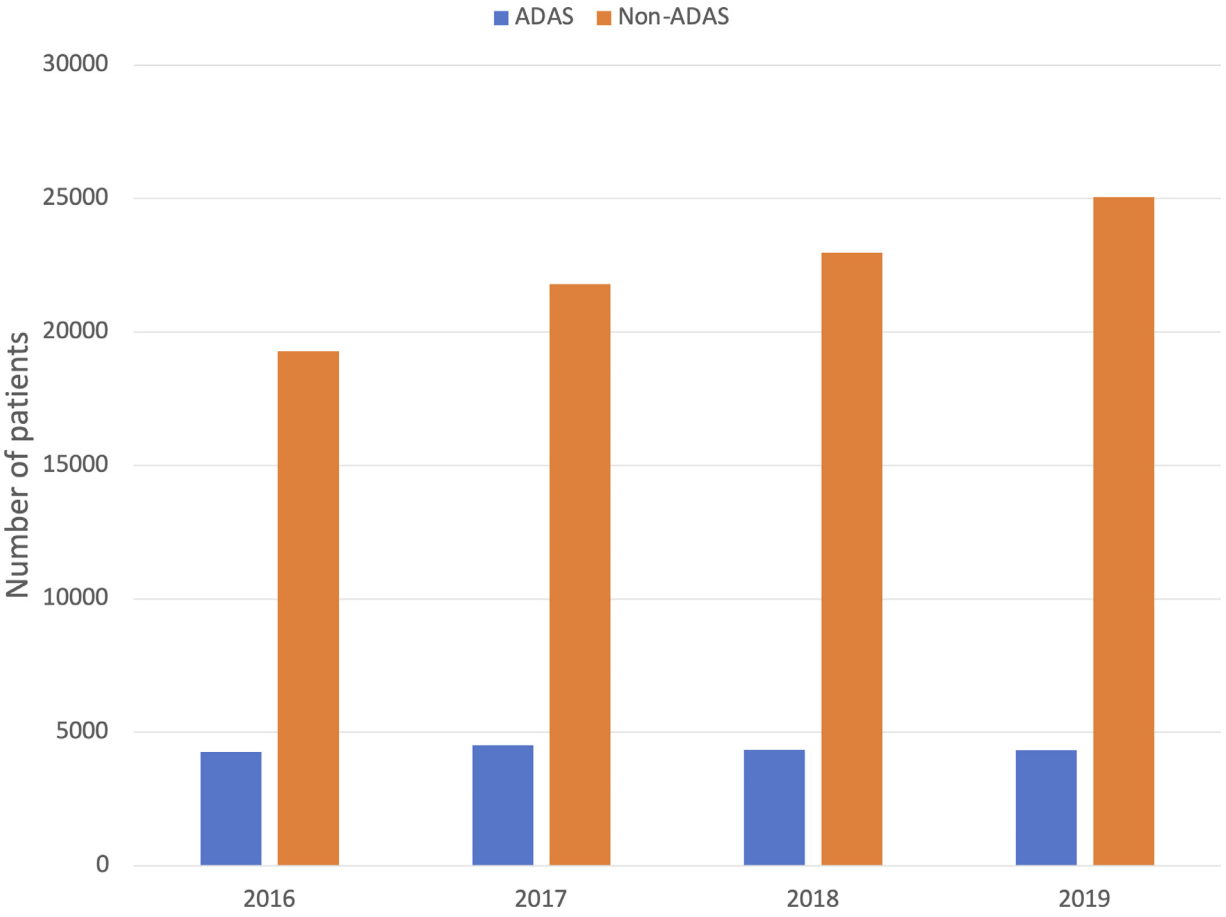

Figure 1. Number of patients treated with ADAS and with stable, electively treated aortic stenosis (non-ADAS).

versus non-ADAS: 2.8% versus 1.5%, respectively (OR [95% CI] 1.8 [1.6 to 2.1], p <0.0001). Mortality was similar among different centers according to bed capacity in the non-ADAS population (p = 0.75). However, in the ADAS population, a trend in higher mortality was observed among smaller compared with larger bed capacity centers (p = 0.01) (Supplementary Table 7). The LOS during the index admission was longer for patients with ADAS than

Table 1
Baseline characteristics of the study population

Characteristic	All patients (n=51,498)	ADAS (n=17,282)	Non-ADAS (n=34,216)	P-value
Demographics				
Age, years	75 (67-82)	75 (67-82)	75 (67-82)	0.28
Male sex	32,754 (64)	11,002 (64)	21,752 (64)	0.84
Co-morbidities				
Charlson co-morbidity index, points	2 (1-3)	2 (1-3)	2 (1-3)	0.21
Coronary artery disease	8,732 (17)	3,617 (21)	5,115 (15)	<0.0001
Heart failure	28,953 (56)	10,290 (60)	18,663 (55)	<0.0001
Peripheral artery disease	12,613 (25)	3,682 (21)	8,931 (26)	<0.0001
Diabetes mellitus	169 (0.3)	39 (0.2)	130 (0.4)	0.004
Chronic obstructive pulmonary disease	13,318 (26)	4,205 (24)	9,113 (27)	<0.0001
Chronic kidney disease	14,835 (29)	4,780 (28)	10,055 (29)	<0.0001
Atrial fibrillation	13,461 (26)	4,827 (28)	8,634 (25)	<0.0001
Previous myocardial infarction	5,012 (10)	1,438 (8)	3,574 (11)	<0.0001
Previous percutaneous coronary intervention	870 (1.7)	552 (3.2)	318 (0.9)	<0.0001
Previous coronary artery bypass grafting	10,365 (20)	4,858 (28)	5,507 (16)	<0.0001
Previous balloon aortic valvuloplasty	1,026 (2.0)	413 (2.4)	613 (1.8)	<0.0001
Previous cerebrovascular accident	1,572 (3.2)	550 (3.2)	1,022 (3.0)	0.22

Baseline characteristics of the study population, comparing patients with acute decompensated aortic stenosis (ADAS) to patients with stable, electively treated aortic stenosis (non-ADAS). Data is expressed as median (IQR) or number (%).

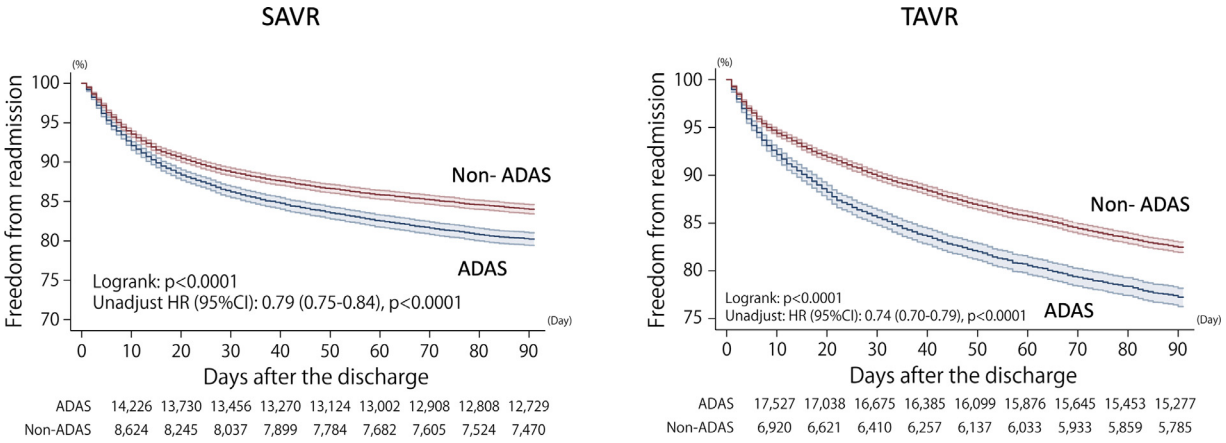

Figure 2. Kaplan−Meier curves for freedom from hospital readmission among SAVR *(left)* and TAVR *(right)* patients, comparing acute decompensated aortic stenosis (ADAS in *blue*) to patients with stable, electively treated aortic stenosis (non-ADAS in *red*).

non-ADAS: 9 (5 to 13) versus 4 (2 to 6) days, p <0.0001; (β [95% CI] 5.1 [5.0 to 5.2], p <0.0001) than non-ADAS. The adjusted health care−associated cost per patient was higher in ADAS versus non-ADAS: $55,450.00 ($41,860 to $74,501) versus $43,406 ($34,219 to $56,035); p <0.0001 ($\beta$ [95% CI] $14,851.0 [$14,276.0 to $15,426.4], p <0.0001) (Supplementary Table 5).

Of the patients who survived to hospital discharge during the index admission (ADAS: 16,777 and non-ADAS: 33,644), readmission to hospital within 90 days was more frequent in ADAS versus non-ADAS (21% vs 17%, respectively, log-rank p <0.001). This was the case, regardless of whether patients were treated with SAVR or TAVR (Figure 2).

The data on causes for readmission were missing for 0.6% and 0.3% of the ADAS and non-ADAS cohorts, respectively. Cardiovascular causes for readmission accounted for 43.5% of readmission in the ADAS cohort and 44.3% in the non-ADAS cohort (Table 2). Noncardiovascular causes accounted for 56.5% of readmissions in the ADAS cohort and 55.7%. Readmission for heart failure was more frequent in ADAS versus non-ADAS (3.4% vs 2.1%, respectively, p <0.001).

Patients with ADAS had a higher in-hospital mortality during readmission than non-ADAS patients (3.9% vs 2.8%, respectively, p = 0.004) (OR [95% CI] 1.42 [1.12 to 1.79], p = 0.003). The LOS was longer for patients with ADAS during their readmission than non-ADAS patients (4 [2 to 7] days vs 3 [2 to 6] days, respectively, p <0.0001). The adjusted cost per patient for hospital readmission within 90 days was similar between ADAS and non-ADAS ($9,828 [$5,461 to $18,381] vs $9,603 [$5,509 to $17,471], p = 0.26).

Discussion

In this study, we assessed the cumulative impact of ADAS from a clinical, health care provision, and financial perspective using a large national payer dataset. We demonstrate 4 key findings for patients with ADAS in comparison with non-ADAS. First, patients with ADAS have a 1.8-fold higher risk of adjusted in-hospital mortality that remained

Table 2
Causes of hospital readmission

Reason for readmission	ADAS (n= 3538)*	Non-ADAS (n=5653)*	P value
Cardiac causes for readmission			
Heart failure	575 (16)	692 (12)	<0.0001
Bradyarrhythmia or conduction abnormality	108 (3.1)	254 (4.5)	0.001
Tachyarrhythmia	244 (6.9)	447 (7.9)	0.08
Stroke	115 (3.2)	231 (4.1)	0.04
Acute coronary syndrome	92 (2.6)	120 (2.1)	0.15
Vascular (arterial) related	160 (4.5)	275 (4.9)	0.48
Other cardiovascular reasons	242 (6.8)	492 (8.7)	0.001
Non-cardiac causes for readmission			
Non-traumatic bleeding	111 (3.1)	201 (3.6)	0.31
Non-cardiac Infection	570 (16)	927 (16)	0.75
Malignancy related	48 (1.4)	123 (2.2)	0.005
Other non-cardiovascular reasons	1274 (36)	1896 (34)	0.02

Causes of hospital readmission compared between patients with acute decompensated aortic stenosis (ADAS) and patients with aortic stenosis and stable or no symptoms (non-ADAS).

* Causes of readmission were missing for 0.6% of the ADAS population and 0.3% of the non-ADAS population. Data is presented as number (percentage).

higher during hospital readmission. Second, readmissions were higher in patients with ADAS, in particular, there was an increased number of heart failure hospitalizations despite having their AS treated. Third, patients with ADAS used up more than double the inpatient admission duration at their index admission and continued to have more hospital inpatient bed days during readmission. Fourth, each patient with ADAS incurred an additional adjusted cost of almost $15,000 during their index admission.

Our data show that annual AVRs are increasing, predominantly driven by an increase in elective AVR. Consequently, the proportion of patients with ADAS is decreasing, despite a stagnant incidence. Although speculative, this could suggest that despite an increase in capacity for AVR, patients with AS continue to decompensate. This highlights 2 crucial issues regarding (1) the undertreatment of AS and (2) the optimum timing of valve replacement in AS. Between 43% and 48% of patients with AS with an indication for AVR did not have it, mainly because of older age, co-morbidities, and low-gradient AS phenotypes.[7,8] Management by cardiac specialists, in particular, those with expertise in valvular heart disease, may facilitate an increased likelihood for AVR.[9] Although we have made advances in lowering the thresholds for AVR,[10,11] further refinement is still required. Studies exploring the safety and efficacy of AVR in moderate and asymptomatic AS (NCT03042104, NCT04204915, NCT03094143, NCT02661451, NCT05149755) may broaden the treatment indications and potentially reduce ADAS. In addition, many centers and health care systems have long waitlists for AVR. The rates of mortality and ADAS increase with increased wait times.[12–14] With an increasing population, health care systems need to increase their capacity for AVR.

ADAS has gained recognition with several centers and registries, highlighting the issue. The findings are striking—ADAS is associated with increased short- and long-term mortality.[5,6,15] A meta-analysis calculated an HR for mortality: in-hospital: 2.09, 95% CI 1.39 to 3.14; at 30 days after TAVR: 2.29, 95% CI 1.69 to 3.10; and at 1 year after TAVR: 1.96, 95% CI 1.55 to 2.49.[4] Our findings for in-hospital mortality and during hospital readmission are consistent with this. The majority of patients with ADAS underwent SAVR. This is a surprising finding given that patients with ADAS are sicker and SAVR is more invasive. The rationale for treatment choice is not available to us. Although speculative, in line with guidelines at the time,[16] intermediate and possibly some high-risk patients may have undergone SAVR compared with current treatment decisions. Mortality was also higher in smaller compared with higher volume centers for the ADAS population but not for the non-ADAS population. This may reflect the greater experience or advanced cardiopulmonary support that maybe offered at higher volume centers. Further studies need to investigate the reasons behind this discrepancy in mortality. Strategies that reduce mortality need to be urgently explored for patients with ADAS. Perhaps the treatment of patients with ADAS needs to be centralized to high-volume centers with better outcomes. Studies have also showed a signal toward a better survival among patients with ADAS who are treated early. Among patients with AS in cardiogenic shock, balloon aortic valvuloplasty within 48 hours was associated with a lower mortality at 1 year than >48 hours (59% vs 90%, p = 0.01).[17,18] A total of 2 retrospective observational studies on patients with ADAS found that delayed treatment with TAVR was associated with an increased mortality at 1 and 2 years.[19,20] In theory, earlier treatment reduces the duration of left ventricular outflow obstruction and its consequent adverse impact on the heart, tissue hypoperfusion—especially the kidneys and brain—and reduces the risk of further cardiac decompensation. A small, prospective, pilot study assessed the impact of quicker treatment with TAVR in ADAS and demonstrated a signal toward reduced mortality and acute kidney injury.[21] Larger studies are required to confirm whether time to treatment improves clinical outcomes.

Data regarding hospital readmissions with ADAS are scarce and only reported by a single study.[22] Within 90 days of AVR, hospital readmissions were higher with ADAS, particularly, for heart failure, despite having had the AS treated. In our propensity-matched population, cardiovascular co-morbidities, including heart failure at baseline, were more prevalent in the ADAS cohort and may have contributed to increased heart failure readmissions. This raises 3 important implications; first, the impact of ADAS extends both in terms of symptoms and prognosis even after treatment with AVR. Second, this suggests the importance of cardiac remodeling and dysfunction and other cardiovascular co-morbidities in patients with AS. Cardiac remodeling and dysfunction can be captured using an echocardiography-based staging system. Data from the PARTNER 2 trial (equivalent to non-ADAS patients) showed that 33.6% of patients had stage 3 or 4 disease.[23] Comparatively, among an ADAS population, stage 3 or 4 disease was identified in 51.9% of the patients.[24] Although both studies were derived from different populations of AS, making direct comparison challenging, it does suggest that patients with ADAS may have more advanced cardiac remodeling and damage than non-ADAS patients. Third, a majority of readmissions were for noncardiovascular causes, both in the ADAS and non-ADAS cohorts, reflecting the multimorbid nature of such patients.

In terms of health care resource use, patients with ADAS are known to occupy more bed days than non-ADAS patients.[5,6,15] Our study confirms these findings at a national level and extends these by highlighting the increased LOS during readmission. Expediting investigations and treatment in ADAS can safely reduce the LOS. In a different health care system, a pilot study has demonstrated this, effectively halving the LOS and doubling the capacity to treat patients with ADAS without an increase in procedural complications.[21] This may reduce waitlist times and potentially reduce the incidence of ADAS. However, this small study needs to be replicated in a multicenter setting.

To the best of our knowledge, for the first time, our findings have illustrated the financial impact of ADAS. Over the 4-year study period, ADAS cost an extra $71.8 million annually. Each patient with ADAS incurs a cost of approximately $15,000 more than a non-ADAS patient. Costs during readmission were similar between both cohorts. However, the overall increased financial burden of ADAS is clear.

The results of our study need to be interpreted in the context of the retrospective observational study design based on a cohort from the United States. The NRD does not

provide details regarding cause of death or mortality rates other than in-hospital data. Although long-term mortality has been reported by others, the cause of mortality remains unknown, especially in this multimorbid population. In addition, the presentations and symptom burden of patients with ADAS are unknown. Although requiring an urgent inpatient AVR would indicate significant AS, the reason for decompensation cannot be identified and therefore ADAS in this case is implied rather than confirmed. Other useful parameters are not documented by the database, such as imaging, decisions regarding choice of treatment (SAVR vs TAVR), medications, and serologic results. The NRD, like other databases, is reliant on discharge abstracts and coding and therefore subject to coding errors. However, the strength of this study comes from the large number of "real-world" patients included, which represent a national population. We also used robust statistical methods to reduce the risk of selection bias.

In conclusion, ADAS contributes a significant clinical impact on patients, including inpatient mortality, uses more health care resources, has a greater financial burden, and is associated with more readmissions than electively treated stable patients with AS. The optimization of timing for AVR to reduce ADAS and clinical pathways to improve outcomes for patients with ADAS are urgently needed to help improve outcomes in these patients.

Declaration of Competing Interest

Drs. Patel and Mullen have an unrestricted grant from Edwards Lifesciences. The remaining authors have no competing interests to declare.

Data availability statement

Data for this study were obtained from the National Readmissions Database and are freely available online.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.07.081.

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