Association of ACEI/ARB and statin prescribing patterns with mortality after Transcatheter Aortic Valve Replacement (TAVR): Findings from real-world claims data

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Background Transcatheter aortic valve replacement (TAVR) has become the standard of care for most patients with severe aortic stenosis (AS), but the impact of medical therapy prescribing patterns on post-TAVR patients has not been thoroughly investigated.

Methods We analyzed Optum claims data from 9,012 adults who received TAVR for AS (January 2014-December 2018). Pharmacy claims data were used to identify patients who filled ACEI/ARB and/or statin prescriptions during the study's 90-day landmark period post-TAVR. Kaplan-Meier and adjusted Cox Proportional Hazards models were used to evaluate the association of prescribing patterns with mortality during the 3-year follow-up period. Subgroup analyses were performed to examine the impact of 11 potential confounders on the observed associations.

Results A significantly lower adjusted 3-year mortality was observed for patients with post-TAVR prescription for ACEI/ARBs (hazard ratio [HR] = 0.82, 95% confidence interval [CI] 0.74-0.91, $P = .0003$) and statins (HR = 0.85, 95% CI 0.77-0.94, $P = .0018$) compared to patients who did not fill prescriptions for these medications post-TAVR. Subgroup analyses revealed that the survival benefit associated with ACEI/ARB prescription was not affected by any of the potential confounding variables, except preoperative ACEI/ARB prescription was associated with significantly lower risk of mortality vs postoperative prescription only. No other subgroup variables had significant interactions associated with survival benefits, including preoperative use of statins.

Conclusions In this large-scale, real-world analysis of patients undergoing TAVR, the prescription of ACEI/ARB and statins was associated with a significantly lower risk of mortality at 3-years, especially in those where the medications were initiated preoperatively. (Am Heart J 2023;258:27–37.)

Keywords: Aortic stenosis; Transcatheter aortic valve replacement; Renin-angiotensin system inhibitor; ACEI/ARB; Statin

Aortic stenosis (AS) is a valvular heart disease commonly encountered in clinical practice that is increasingly prevalent in patients with advancing age.[1] Severe AS, for which aortic valve replacement (AVR) is often recommended,[2] is estimated to have an incidence of 4.4% per year in patients ≥65 years old.[3]

Over the last decade, transcatheter aortic valve replacement (TAVR) has evolved to become a valuable treatment option in a broad range of patients with severe symptomatic AS regardless of their surgical risk pro-

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file.[4,5] The medical management of patients pre- and post-TAVR is therefore important. The benefits of therapies such as renin-angiotensin system inhibitors (RASIs)[6,7] and statins[8-10] post-TAVR have been demonstrated in registry studies and several small clinical trials. However, large-scale, real-world studies are needed to explore the association of post-TAVR prescribing patterns with long-term post-TAVR outcomes, to examine if there are subgroups of patients who may benefit more from certain therapies, and to determine potential avenues for future prospective studies.

Using real-world claims data and a population level approach, this study explores the association of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) and/or statin prescriptions post-TAVR with 3-year mortality for a large United States (U.S.)-based study population.

Methods

Data source

This retrospective study utilized de-identified, patient-level health claims data from Optum® Clinformatics® Data Mart (OptumInsight, Inc., Eden Prairie, MN), a U.S.-based database that standardizes and integrates data for approximately 13 million annual lives covered by commercial health insurance or Medicare Advantage (C and D).[11] Optum® Clinformatics® Data Mart captures medical and pharmacy claims data from inpatient and outpatient settings, including hospital admission date, clinical diagnoses, procedure codes, hospital discharge date, and prescription pharmacy claims information.[11] It also provides health care plan enrollment information and reasons for disenrollment, including death.[11] Mortality data is available primarily via the database's Date of Death claims dataset, sourced from the Death Master File maintained by the U.S. Social Security Administration.[11,12] Patient data can be tracked across multiple health care providers, allowing for the longitudinal evaluation of clinical outcomes over time.

As this was a retrospective, observational study that utilized de-identified data for patients who met eligibility criteria, informed consent was not required from patients under an Institutional Review Board exemption status. All aspects of this study were conducted in compliance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996 regulations and the HIPAA Omnibus Rule of 2013.

Study Population

This study included 9,012 adults (≥18 years old) who received TAVR between January 2014 and December 2018, per Optum® Clinformatics® Data Mart data and met all additional study eligibility criteria. To ensure longitudinal completeness of baseline data, study participants must have been continuously enrolled in a commercial or Medicare Advantage plan, with both medical and pharmacy benefits, for a study baseline period of ≥6 months prior to hospital admission for TAVR. Study participants must have survived through the study landmark period of 90 days after hospital discharge post-TAVR. Patients with transapical access TAVRs or end-stage renal disease were excluded from the study (See Supplemental Materials for ICD-9/10 codes). Patients were censored if they left the health plan before the end of the 3-year follow-up period. Eight patients with missing region were excluded. Patients with missing race information ($n = 865$ [9.6%]) were imputed with mode (White), as White was the large majority.

Outcomes, Covariates, & Subgroup Variables

The primary outcome was all-cause mortality. Post-TAVR medication prescription was defined as pharmacy claims data indicating ≥1 fill of an ACEI/ARB and/or statin prescription during the 90-day post-TAVR landmark period (See Supplemental Materials for NCD codes). Pre-TAVR medication prescription was defined as pharmacy claims data indicating ≥2 fills of an ACEI/ARB and/or statin prescription during the 6-month baseline period, with the criterion of ≥2 fills used to ensure that medications were not prescribed solely for an acute event. Pharmacy claims data for filled prescriptions were used as a proxy for written prescriptions as the latter are not directly measured by claims data. Prescription fills were not assumed to measure patient adherence or compliance, but were assumed to be a reasonable proxy for physician prescribing behavior. Note that use of prescription fills likely overestimates actual medication usage and underestimates prescribing patterns.

The Elixhauser comorbidity score, a well-validated risk adjustment methodology for mortality, served as a standardized method for measuring patient comorbidity based on diagnosis codes.[13]

In this analysis, the Elixhauser comorbidity score included congestive heart failure, cardiac arrhythmias, valvular disease, pulmonary circulation disorders, peripheral vascular disorders, hypertension (complicated and uncomplicated), paralysis, other neurological disorders, chronic pulmonary disease, diabetes uncomplicated, diabetes complicated, hypothyroidism, renal failure, liver disease, peptic ulcer disease excluding bleeding, HIV/AIDS, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis/collagen vascular diseases, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, blood loss-anemia, deficiency anemias, alcohol abuse, drug abuse, psychoses, and depression.[13] These diagnoses were defined using ICD-9/10 codes, available in the Supplemental Materials.

A set of 11 subgroup variables was selected to gauge potential confounding factors. Subgroup variables were selected based on their likelihood to confound associa-

tions between ACEI/ARB or statins and survival, namely, pre-TAVR ACEI/ARB or statin prescription, post-TAVR ACEI/ARB, statin, or beta blocker prescription, age (≤80 or >80 years), sex, and history of the following key comorbidities: diabetes, renal failure, myocardial infarction, heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), and coronary artery disease.

Statistical analyses

Patient demographic and risk characteristics at baseline, reported by post-TAVR medication prescription, were used to assess baseline differences between groups (Table I). Differences were evaluated by *t* tests for continuous characteristics and χ^2 test for binary characteristics. All outcome models were adjusted using the Elixhauser score and independently adjusted for key comorbidities known to be associated with mortality, specifically diabetes, hypertension, renal failure, coronary artery disease, history of myocardial infarction, and heart failure. Ejection fraction was not available in claims data, so we independently adjusted for history of systolic heart failure as an indicator of reduced ejection fraction. The complete list of baseline demographic and risk characteristics used for covariate adjustment of all outcome models are shown in Table I (See Supplemental Materials for ICD-9/10 codes).

For the primary analysis, an unadjusted Kaplan-Meier model was used to visualize 3-year mortality. A single, multivariable, adjusted Cox proportional hazards model (with covariates for post-TAVR use of each medication) was used to explore the association of post-TAVR medication prescription with 3-year mortality.

To assess any differences in medication survival benefit by subgroups and detect potential confounding factors, we replicated the main model after including the interaction of post-TAVR medication prescription with each subgroup variable. A separate covariate-adjusted Cox proportional hazards model was run for each medication and each subgroup variable to test for significance of the interaction. Unadjusted Kaplan-Meier curves were used for visualization.

Proportional hazards assumption testing was based on the supremum test in SAS. The only noteworthy violations were for the statin subgroup analysis, concerning interactions with age and prior statin use. Visual inspection of the stratified Kaplan-Meier curves indicated that any potential violation of the proportional hazards assumption did not meaningfully change the conclusion of non-significance for these subgroup analyses.

A *P*-value of <.05 was considered statistically significant for all analyses.

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Results

Study population

A total of 9,012 patients who underwent TAVR were analyzed in this study (Figure 1). Key characteristics of the total study population included a mean age of 80 ± 6.89 years, with 62% of patients ≥80 years old, 47% female, and 84% White (Table I).

After TAVR, 35% of patients were prescribed ACEI/ARBs (n = 3,172) and 52% (n = 4,697) were prescribed statins. Of those prescribed ACEI/ARBs after TAVR, 69% (n = 2,180) also had a prescription from pre-TAVR and 31% (n = 992) were newly prescribed. Of statin users, 73% (n = 3,435) had a continued prescription and 27% (n = 1,262) had a new prescription. Not all patients who were prescribed these medications prior to TAVR had a continued prescription; 24% of ACEI/ARB prescriptions (n = 679) and 13% of statin prescriptions (n = 497) were discontinued after TAVR. The majority of patients in both groups with a prescription immediately after TAVR (ie, the landmark period) continued to fill their medication prescription at 1-year post-TAVR: 84% of ACEI/ARB patients and 92% of statins patients (*Table S1*). The number of patients who were adherent to their ACEI/ARB prescription over the 3-years of the study period is shown in *Figure S1*, with adherence defined as a medication possession ratio of at least 80%.

Mortality

A significant survival benefit was observed for patients with post-TAVR prescription of both medications, with lower adjusted 3-year mortality for those with ACEI/ARB prescription (HR = 0.82, 95% CI 0.74-0.91, P = .0003; Figure 2) and statin prescription (HR = 0.85, 95% CI 0.77-0.94, P = .0018; Figure 3), as compared to patients who did not have prescriptions for these medications after TAVR. In supplemental analyses, we did not observe a survival benefit with prescription of beta blockers (Figure S1).

For both medications, additional analyses were performed to evaluate potential confounding by examining interactions between post-TAVR medication prescription and subgroup variables for the association with survival benefit. For ACEI/ARB prescription, the interaction between pre-TAVR and post-TAVR prescription for the association with survival was significant (Figure 4), with the benefit limited to patients with continued medication prescription (HR = 0.65, 95% CI 0.54-0.78, P < .0001; Figure 5A) as compared to new prescription (HR = 0.98, 95% CI 0.84-1.14, P = .7721; Figure 5B).

Table I. Baseline demographic and risk characteristics for the total study population and by post-TAVR ACEI/ARB or statin prescription

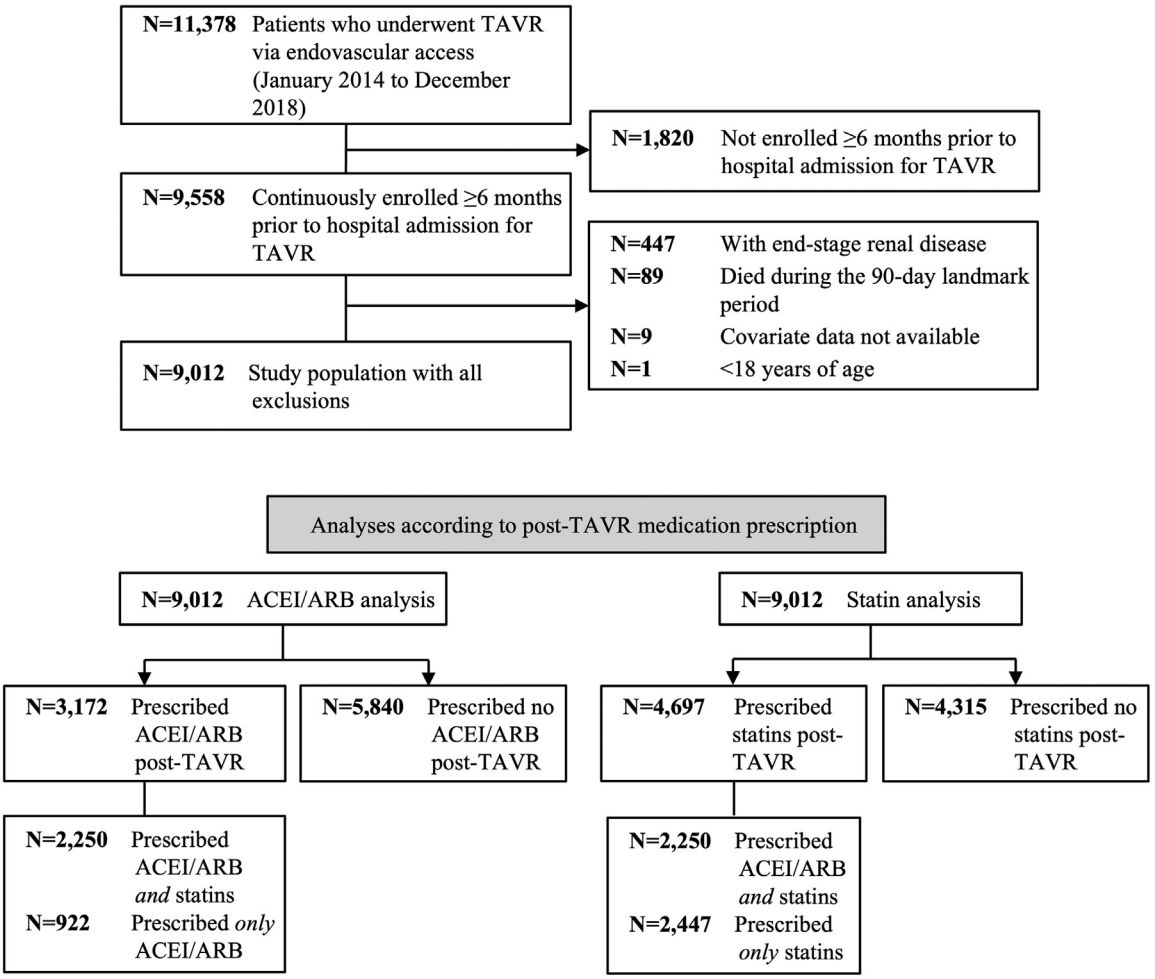
Patient Characteristics	Total population	By Post-TAVR ACEI/ARB Prescription			By Post-TAVR statin prescription		
		ACEI/ARB Not Prescribed Post-TAVR	ACEI/ARB Prescribed Post-TAVR	*P*-Value	Statins Not Prescribed Post-TAVR	Statins Prescribed Post-TAVR	*P*-Value
Demographic Characteristics							
# Patients (% of total)	9,012 (100%)	5,840 (64.80%)	3,172 (35.20%)	n/a	4,315 (47.88%)	4,697 (52.12%)	n/a
Age, mean (SD); in years	80 (6.89)	80.39 (6.70)	79.27 (7.18)	<.01*	80.68 (6.70)	79.36 (7.01)	<.01*
<80 years	3,395 (37.67%)	2,038 (34.90%)	1,357 (42.78%)	<.01*	1,423 (32.98%)	1,972 (41.98%)	<.01*
80 years	5,617 (62.33%)	3,802 (65.10%)	1,815 (57.22%)		2,892 (67.02%)	2,725 (58.02%)	
Female	4,192 (46.52%)	2,665 (45.63%)	1,527 (48.14%)	.02*	2,086 (48.34%)	2,106 (44.84%)	<.01*
White	7,540 (83.67%)	4,970 (85.10%)	2,570 (81.02%)	<.01*	3,715 (86.10%)	3,825 (81.43%)	<.01*
Patient region							
Midwest	2,265 (25.13%)	1,574 (26.95%)	691 (21.78%)	<.01*	1,241 (28.76%)	1,024 (21.80%)	<.01*
Northeast	1,678 (18.62%)	1,177 (20.15%)	501 (15.79%)	<.01*	839 (19.44%)	839 (17.86%)	.05
South	2,980 (33.07%)	1,876 (32.12%)	1,104 (34.80%)	<.01*	1,339 (31.03%)	1,641 (34.94%)	<.01*
West	2,089 (23.18%)	1,213 (20.77%)	876 (27.62%)	<.01*	896 (20.76%)	1,193 (25.40%)	<.01*
Medicare Advantage (vs Commercial)	8,428 (93.52%)	5,500 (94.18%)	2,928 (92.31%)	<.01*	4,099 (94.99%)	4,329 (92.17%)	<.01*
Baseline risk characteristics							
Elixhauser Comorbidity Score, mean (SD)	8.10 (3.18)	8.10 (3.26)	8.11 (3.01)	.90	7.95 (3.18)	8.24 (3.17)	<.01*
Comorbidities							
Diabetes	4,045 (44.88%)	2,440 (41.78%)	1,605 (50.60%)	<.01*	1,713 (39.70%)	2,332 (49.65%)	<.01*
Hypertension	8,511 (94.44%)	5,420 (92.81%)	3,091 (97.45%)	<.01*	4,024 (93.26%)	4,487 (95.53%)	<.01*
Renal Failure	3,261 (36.19%)	2,158 (36.95%)	1,103 (34.77%)	.04*	1,490 (34.53%)	1,771 (37.70%)	<.01*
Coronary Artery Disease	7,799 (86.54%)	5,046 (86.40%)	2,753 (86.79%)	.61	3,602 (83.48%)	4,197 (89.35%)	<.01*
History of Myocardial Infarction	1,537 (17.06%)	993 (17%)	544 (17.15%)	.86	652 (15.11%)	885 (18.84%)	<.01*
Heart Failure							
HFrEF	2,381 (26.42%)	1,515 (25.94%)	866 (27.30%)	.16	1,133 (26.26%)	1,248 (26.57%)	.74
HFpEF	2,050 (22.75%)	1,343 (23%)	707 (22.29%)	.44	971 (22.50%)	1,079 (22.97%)	.60

Categorical characteristics are reported as n (%)

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; SD, standard deviation; TAVR, transcatheter aortic valve replacement

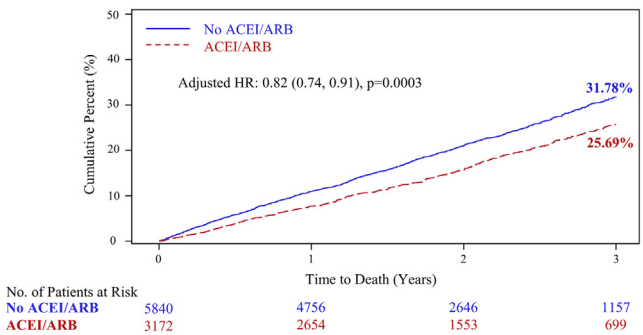
* indicates $P < .05$ for baseline group difference based on X^2 and *t* tests as appropriate

Figure 1



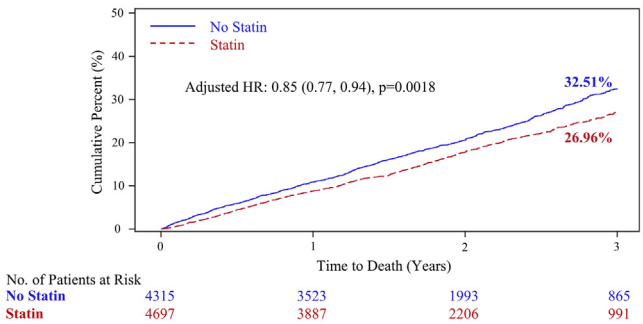
Consort diagram and schematic of analyses according to post-TAVR medication prescription. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; TAVR, transcatheter aortic valve replacement

Figure 2



Association of post-TAVR ACEI/ARB prescription with 3-year mortality. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HR, hazard ratio; TAVR, transcatheter aortic valve replacement

Figure 3



Association of post-TAVR statin prescription with 3-year mortality. Abbreviation: HR, hazard ratio; TAVR, transcatheter aortic valve replacement

No significant differences were detected for any of the other potential confounders. Interestingly, the beneficial impact of ACEI/ARB prescription on mortality was present irrespective of the patients' left ventricular systolic function or baseline heart failure type (ie, HFrEF and HFpEF). Patients who were adherent to ACEI/ARB prescription showed a greater mortality benefit than those who were not (Figure S1). For statin users, no interactions with subgroup variables were significant, indicating that the association between statins prescription and mortality was not statistically different based on any of the potential confounders (Figure 6). In contrast to the finding for ACEI/ARBs, the survival benefit of statins prescription did not vary significantly based on continued medication prescription (HR = 0.92, 95% CI 0.75-1.13, P = .4127; Figure 7A) vs new prescription (HR = 0.93, 95% CI 0.80-1.07, P = .3125; Figure 7B).

Discussion

This large-scale, real-world landmark analysis indicates a potential survival benefit of prescribing ACEI/ARBs and statins after TAVR. It also suggests the importance of medication prescription continuation for patients who were prescribed ACEI/ARBs prior to TAVR. While previous work has demonstrated the association between ACEI/ARB[6,7] and/or statin[8-10] use and reduced mortality post-TAVR, these findings add to previous work by observing that the association with improved survival holds in a large, diverse cohort of patients, including elderly and high-risk patients who cannot usually be involved in clinical trials. Also, to our knowledge, this is the first time that the survival benefit of ACEI/ARB has been observed to be specific to a subgroup of patients with continued prescription.

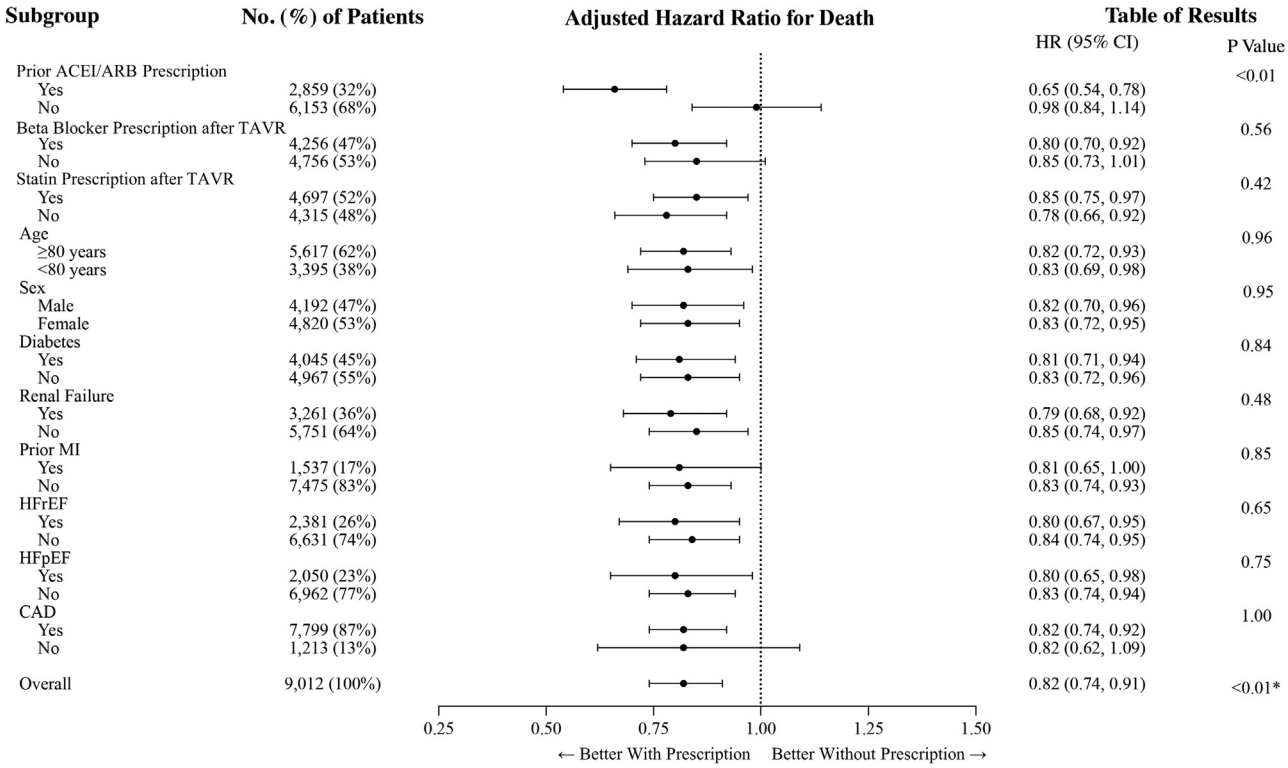
Use of claims data offers several advantages for health care outcomes research, including access to large and diverse sample sizes, lack of selection bias, longitudinal follow-up, and the potential for performing robust multivariable modeling.[14,15] This study combines a larger study population (9,012 patients who underwent TAVR over a 4-year period) with a longer follow-up period (3 years) than previous studies.[16] In addition, our study is the first to explore the question of whether the survival benefit for patients prescribed ACEI/ARBs and statins post-TAVR applies to both continued and new prescriptions of these medications.

Our results align with those of earlier studies that demonstrate lower mortality for patients who received ACEI/ARBS[6,7] or statins[8-10] post-TAVR as compared to patients who did not use these medications. While the physiology underlying this relationship is not yet known, previous work demonstrated the potential of RASIs to attenuate cardiac remodeling in patients with aortic stenosis and proposed their theoretical role in limiting post-AVR myocardial fibrotic changes that may increase cardiovascular morbidity and overall mortality.[17-19] Statins have been observed to reduce the incidence of ischemic events[20] and to exert beneficial pleiotropic effects including reductions in inflammation[21] and infections[8] that may explain the mechanism of their positive effects on mortality.

We did not observe an association of survival benefit with prescription of beta blockers post-TAVR, which is in agreement with a previous multi-center study from the Placement of Aortic Transcatheter Valve (PARTNER) I trial that showed no significant improvements in mortality with beta blocker use at one-year post-TAVR in high-risk patients.[22] The lack of survival benefit with beta blockers could also be due to variabilities in heart rate at discharge, as patients with low heart rate have been shown to have less survival benefit from beta blockers.[23] In addition, the pleiotropic effects of ACEI/ARB on hypertension, renal function, and myocardial fibrosis and remodeling may potentially underly the observed differences.

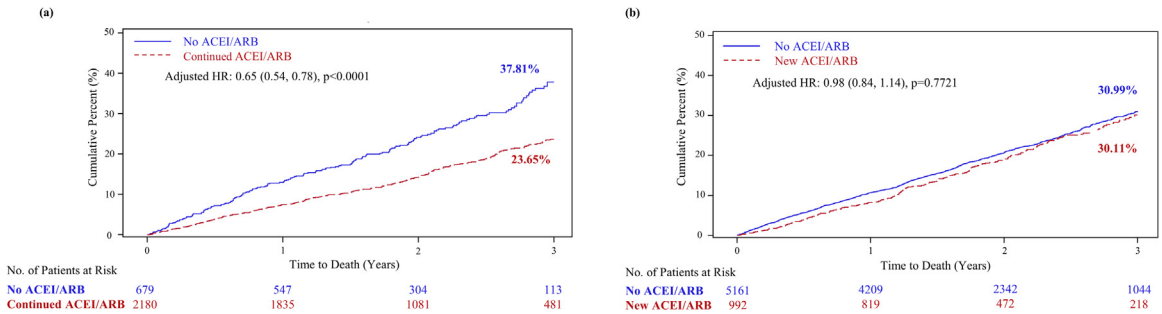
Another potential contributor to the association observed in earlier studies may be the impact of mortality

Figure 4



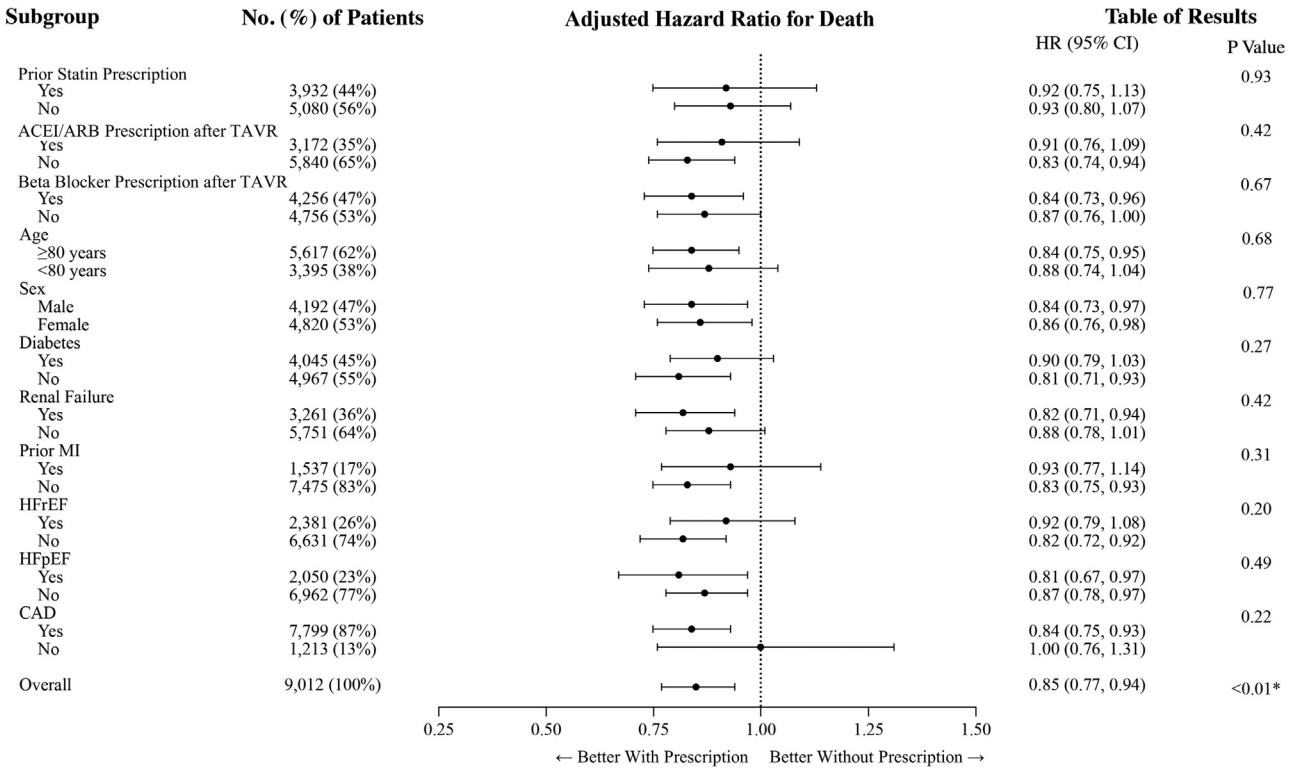
Subgroup analyses for patients with post-TAVR ACEI/ARB prescription. The *P*-value is from the test statistic for the interaction between the medication prescription and the subgroup variables, unless otherwise noted. * *P*-value for medication prescription overall. Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CI, confidence interval; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; MI, myocardial infarction; TAVR, transcatheter aortic valve replacement

Figure 5



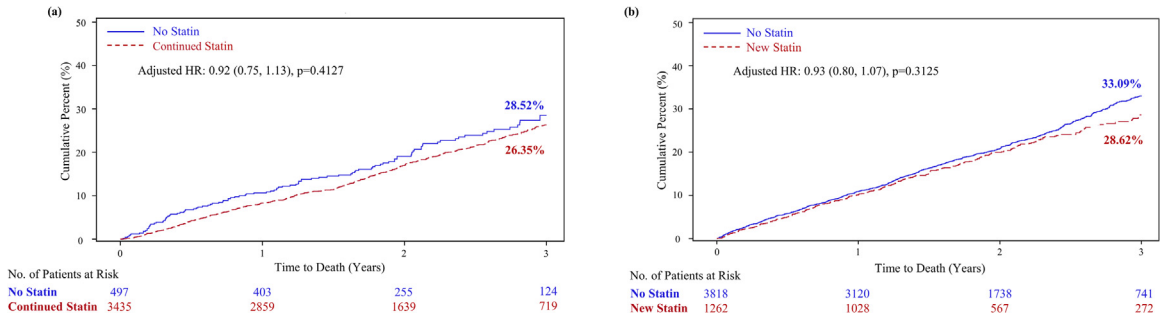
Subgroup analyses of continued and new ACEI/ARB prescriptions. **a.** Association of post-TAVR ACEI/ARB prescription with 3-year mortality for patients who had been prescribed ACEI/ARBs pre-TAVR (continued prescription) **b.** Association of post-TAVR ACEI/ARB prescription with 3-year mortality for patients who had not been prescribed ACEI/ARBs pre-TAVR (new prescription)**.** Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; HR, hazard ratio; TAVR, transcatheter aortic valve replacement

Figure 6



Subgroup analyses for patients with post-TAVR statin prescription. The p-value is from the test statistic for the interaction between the medication prescription and the subgroup variables, unless otherwise noted. * p-value for medication prescription overall. Abbreviations: CAD, coronary artery disease; CI, confidence interval; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HR, hazard ratio; MI, myocardial infarction; TAVR, transcatheter aortic valve replacement

Figure 7



Subgroup analyses of continued and new statin prescriptions. A. Association of post-TAVR statin prescription with 3-year mortality for patients who had been prescribed statins pre-TAVR (continued prescription). B. Association of post-TAVR statin prescription with 3-year mortality for patients who had not been prescribed statins pre-TAVR (new prescription). Abbreviation: HR, hazard ratio; TAVR, transcatheter aortic valve replacement

during the early postoperative period (often due to procedural or perioperative complications) on the assessment of patients' medication prescription in the months after TAVR. We sought to address this issue by performing a landmark analysis limited to patients who survived a 90-day landmark period between hospital discharge after TAVR and the start of the study's 3-year follow-up period. This approach excluded 89 patients (1%) who were similar in baseline demographics and risk to the overall study population (Table S2) and whose death was likely related to causes other than prescribing patterns (eg, TAVR complications).

Our results have several important clinical implications for the current and, potentially, future pharmacotherapeutic management of patients pre- and post-TAVR. As this study demonstrates, a notable proportion of patients are not prescribed ACEI/ARB or statins post-TAVR, though we note that in this study, filled prescriptions were used as a proxy for written prescriptions. Prescription discontinuation is highest for patients prescribed ACEI/ARB (24%), which is particularly troubling given the importance of longitudinal use found here specifically for patients who were prescribed ACEI/ARB pre-TAVR. A similar, approximately 10%, decline in RASI prescriptions between hospital admission and discharge for TAVR was noted in previous work regarding prescribing practices for RASIs post-TAVR.[24] There may be several reasons for this decline in prescriptions. Previous work found that patients who received a new pacemaker or developed acute kidney injury after TAVR were less likely to receive a RASI prescription post-TAVR.[24] These or other medical contraindications to ACEI/ARB continuation such as hyperkalemia or low blood pressure may impact outcomes. Managing providers may feel that prescribing ACEI/ARBs or statins for patients post-TAVR is no longer medically warranted or beneficial, or patients may believe their cardiac disease has been treated with TAVR and as a result, self-discontinue medical therapy.

While previous work has demonstrated the benefit of pre-TAVR ACEI/ARB use on post-TAVR survival,[25] our study reveals that the survival benefit associated with prescription of ACEI/ARB (with or without statins) post-TAVR is dependent upon prescription of these medications pre-TAVR. Prospective studies are needed to evaluate the causality of this association and to further explore a potential survival benefit (and other possible clinical benefits) of ACEI/ARB and statins. Topics warranting investigation include whether this prophylactic ACEI/ARB regimen should be prescribed to all patients pre-TAVR or only those with particular medical indications and what the optimal therapeutic duration and dosing for such a regimen might be.[26] Patients placed on ACEI/ARB after TAVR, not previously on the medication prior to TAVR, may have their blood pressure lowered too much.[22] Results from prospective studies could have important implications for the prescribing practices and medical management of patients post-TAVR, as well as for the development of clinical practice guidelines.

Our study has several limitations. First, all studies that utilize administrative data to study clinical events have inherent challenges, including the potential for unmeasured confounding. Specifically, we recognize that outcomes measured over a 3-year period are likely to be influenced by factors other than medication continuity during this period. The study's analyses are risk-adjusted for patient characteristics observed in claims data, but may still be impacted by other unmeasured factors. Notably, there were no significant differences detected across 11 potential confounders in the statins group and only one confounder that showed a difference in the ACEI/ARB group (pre-TAVR ACEI/ARB prescription), though these subgroup variables do not constitute an exhaustive list of potential confounders. For example, socioeconomic status and health behavior were not available in claims data and could not be examined.

Second, while this study shows that patients prescribed ACE/ARB or statins post-TAVR have a lower mortality, we cannot know if this is due to an effect of the medication or a reduction in major cardiovascular events or stroke. Additional analysis of our study population showed that 10.3% of patients in both subgroups (with and without ACEI/ARB) developed new renal failure and 3.3% developed new hypertension during hospitalization. Adjustment for these in the model showed similar results as the main analysis (Table S3), therefore these risk factors did not explain the observed association between ACEI/ARB prescription and lower mortality.

Third, the study population was limited to patients in the Optum® Clinformatics® Data Mart and thus does not represent all patients in the U.S. who underwent TAVR during the study period. However, the UnitedHealthcare system, from which these claims are drawn, covers a large portion of the U.S. and can reasonably be assumed to be geographically representative of the country. Further, the 9,012 patients in our cohort have longitudinal data on medication fills over the 5 years of the study period, which is a remarkably rich source of information.

Fourth, while the study's goal was to measure the impact of physician prescribing behavior after TAVR on mortality, pharmacy claims data for filled prescriptions were used as a proxy for written prescriptions as the latter are not directly measured by claims data. In addition, although this study did not assume patient adherence, supplemental analysis of our study data found that the benefit of post-TAVR ACEI/ARB prescription appears to be even larger for those who are adherent (Figure S2). Adherence was based on a medication possession ratio of at least 80%. Thus, the degree of association between prescription and mortality may be even larger for adherent patients than found in the current study. Finally, while

our analysis adjusts for the influence of prescription of other medications, it does not explicitly measure the independent impact of switching therapies.

Conclusions

This study's real-world landmark analysis demonstrates an association between prescription of ACEI/ARBs and/or statins following TAVR for AS and improved patient survival while revealing the importance of continued ACEI/ARB prescription for those taking it pre-TAVR. Our study highlights the importance of pharmacotherapeutic management of patients for whom TAVR is anticipated or performed.

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Conflict of interest

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2022.12.012.

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