Chronic Conditions in Advanced Cardiac Disease: A Cluster Analysis of Transcatheter Aortic Valve Replacement (TAVR)-Treated Patients

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INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has revolutionized the care of older adults with symptomatic aortic stenosis, enabling treatment where once there was none.[1] One third of these high-risk patients remain severely symptomatic or die 1 year after treatment and half of all deaths are due to non-cardiac causes.[2] TAVR patients provide a unique opportunity to study multiple chronic conditions (MCC) for older adults with advanced cardiovascular disease (CVD). Here, we examine patterns of MCC present at the time of treatment and explore associations with short- and long-term patient-centered outcomes.

METHODS

Retrospective analysis of claims data from the OptumLabs® Data Warehouse (OLDW) includes de-identified claims data for privately insured and Medicare Advantage enrollees in a large, private, US health plan. The database contains longitudinal health information on enrollees, representing a diverse mixture of ages, ethnicities, and geographical regions across the USA. This study was deemed exempt from Institutional Review Board (IRB) review. The analytic cohort included all patients who underwent TAVR between January 1, 2011, and December 31, 2017, and were covered by an enrolling health plan at the time of treatment. For each patient we assessed the presence or absence of each of the 30 component comorbidity claims is described by Gagne et al.[3] during the 1 year prior to TAVR. Cluster analysis was performed using the R function *poLCA*, an expectation maximization algorithm that identifies the maximum likelihood estimates of the model parameters.[4] Each TAVR patient was assigned to the "best fit" class defined by the highest probability of membership. Associations were assessed between cluster membership and clinical outcomes. Mortality was assessed as a composite from the Social Security Administration's Death Master File, a discharge status of "expired," and an EMR-based deceased indicator.

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RESULTS

We identified 6910 TAVR patients for analysis. The average age was 80.2 years and 45% were women. Over one third (36%) of patients had ≥ 7 comorbidities documented in the year leading up to TAVR. Rates of re-hospitalization or death were 16% and 26% at 30 and 90 days, respectively. One-year mortality was 9%. Cluster analysis yielded six distinct comorbidity clusters (Fig. 1). The comorbidity clusters were minimal disease (Cluster 1, $n = 2232$, 32%), failure to thrive (Cluster 2, $n = 1249$, 18%), neuro/psych (Cluster 3, $n = 778$, 11%), malignancy/thrombosis (Cluster 4, $n = 1304$, 19%), metabolic syndrome (Cluster 5, $n = 885$, 12%), and high burden MCC (Cluster 6, $n = 452$, 7%).]–>

The relationship between cluster membership and outcomes is shown in the Table 1. Cluster 1 was the reference class. Membership in Cluster 4 and Cluster 6 was associated with 3-fold increased odds of prolonged LOS (OR 3.26, [95% CI 2.83–3.76] and OR 3.14, [95% CI, 2.55–3.86], respectively) compared to Cluster 1. Membership in Cluster 6 was associated with 3.5-fold higher rate of re-hospitalization or death following TAVR at 30 and 90 days (HR 3.54, [95% CI 2.85–4.40] and HR 3.54, [95% CI 3.00–4.18]) compared to Cluster 1. Membership in Cluster 6 was also associated with a fourfold increased risk of 1-year mortality compared to Cluster 1 [HR 4.13, CI (3.08–5.54)]. TAVR patients in Cluster 1 spent on average 46.4 more days alive outside of the hospital in the year following TAVR than did patients in Cluster 6.

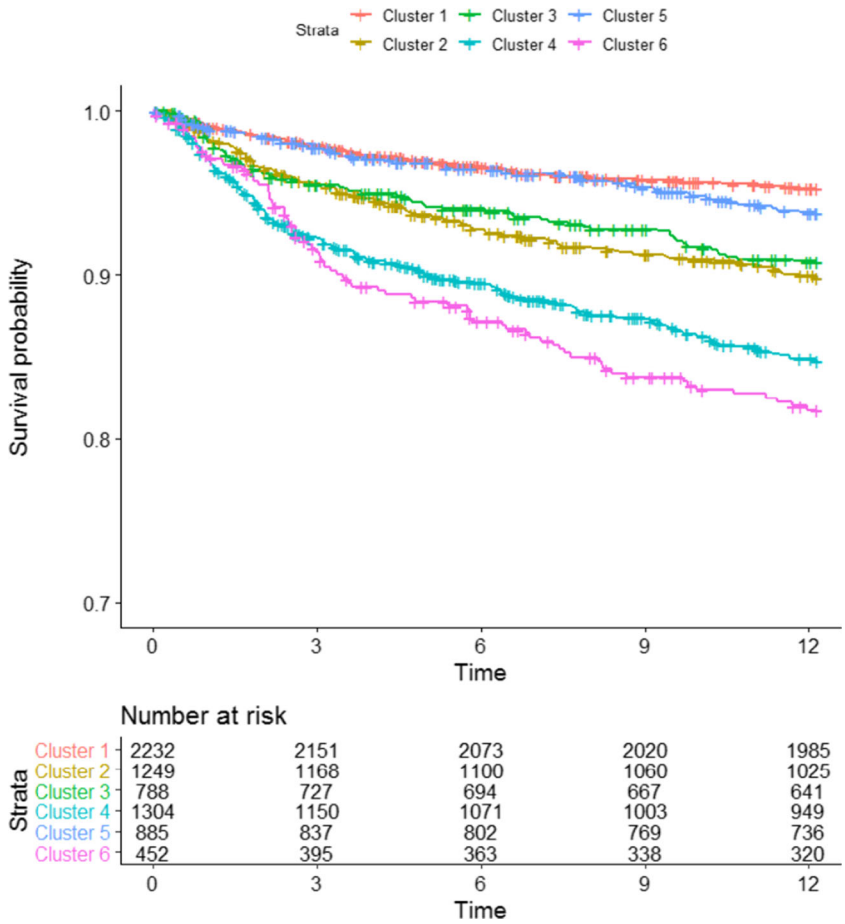

Fig. 1 Survival curves for patients treated with TAVR according to comorbidity cluster. Comorbidities were assessed according to Gagne et al.[24] Reference is Cluster 1 (minimal disease cluster)

DISCUSSION

The primary finding from this study is that cluster analysis yields novel patterns of MCC for patients with severe AS treated with TAVR and that MCC is associated with less favorable outcomes following treatment. Prognostically significant comorbid conditions not routinely captured through standard risk assessment or post-marketing surveillance efforts[5] are common and associated with worse outcomes. These observations are relevant in the context of decision-making for older adults with advanced cardiac disease, as it is increasingly clear that some patients do not benefit from treatment in terms of decreased symptom burden or mortality because of competing risks from comorbid conditions.[6] Patients with MCC who are unlikely to do well may benefit from a broader perspective of appropriate care since it is likely that prognosis following TAVR is substantially affected by these conditions. The magnitude and significance of comorbid conditions

Table 1 Cluster membership and outcomes

Cluster		Prolonged LOS (> 4 days)		Re-hospitalization or death at 30 Days		Re-hospitalization or death at 90 days		1-year mortality	
	N	Rate	OR	Rate	HR	Rate	HR	Rate	HR
1	2232	31.5%	–	9.4%	–	16.9%	–	4.6%	–
2	1249	39.6%	1.42 (1.23–1.64)	19.5%	2.17 (1.80–2.61)	31.5%	2.04 (1.77–2.35)	9.8%	2.19 (1.69–2.85)
3	788	37.7%	1.32 (1.11–1.56)	13.7%	1.50 (1.19–1.90)	25.8%	1.60 (1.35–1.90)	8.8%	1.98 (1.46–2.69)
4	1304	60.0%	3.26 (2.83–3.76)	19.0%	2.12 (1.76–2.54)	32.2%	2.09 (1.81–2.40)	14.4%	3.42 (2.69–4.35)
5	885	34.8%	1.16 (0.98–1.37)	14.6%	1.58 (1.27–1.96)	24.0%	1.47 (1.24–1.74)	5.9%	1.30 (0.93–1.82)
6	452	59.1%	3.14 (2.55–3.86)	29.6%	3.54 (2.85–4.40)	48.7%	3.54 (3.00–4.18)	17.3%	4.13 (3.08–5.54)

Cluster-specific outcomes. Unadjusted event rates are shown for each outcome stratified by cluster phenotype. The reference is Cluster 1. HR indicates hazard ratio. LOS is length of stay. OR is odds ratio. 95% confidence intervals are presented

require additional study and should be considered when designing care for high-risk patients considering this procedure.

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Compliance with Ethical Standards:

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

REFERENCES

1. **Leon MB**, **Smith CR**, **Mack M**, **et al.** Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363(17):1597–1607. https://doi.org/10.1056/NEJMoa1008232
2. **Xiong T-Y**, **Liao Y-B**, **Zhao Z-G**, **et al.** Causes of Death Following Transcatheter Aortic Valve Replacement: A Systematic Review and Meta-Analysis. J Am Heart Assoc 2015;4(9):e002096. https://doi.org/10.1161/JAHA.115.002096
3. **Gagne JJ**, **Glynn RJ**, **Avorn J**, **Levin R**, **Schneeweiss S**. A combined comorbidity score predicted mortality in elderly patients better than existing scores. J Clin Epidemiol 2011;64(7):749–759. https://doi.org/10.1016/j.jclinepi.2010.10.004
4. **Lewis J.** Package ' poLCA .' https://cran.r-project.org/web/packages/poLCA/poLCA.pdf. Published 2016.
5. **Holmes DR**, **Brennan JM**, **Rumsfeld JS**, et al. Clinical outcomes at 1 year following transcatheter aortic valve replacement. JAMA. 2015;313(10):1019–1028. https://doi.org/10.1001/jama.2015.1474
6. **Forman DE**, **Maurer MS**, **Boyd C**, et al. Multimorbidity in Older Adults With Cardiovascular Disease. J Am Coll Cardiol 2018;71(19):2149–2161. https://doi.org/10.1016/j.jacc.2018.03.022