Temporal Trends and Outcomes of Transcatheter and Surgical Aortic Valve Replacement in Patients With Cardiac Amyloidosis and Severe Aortic Stenosis.

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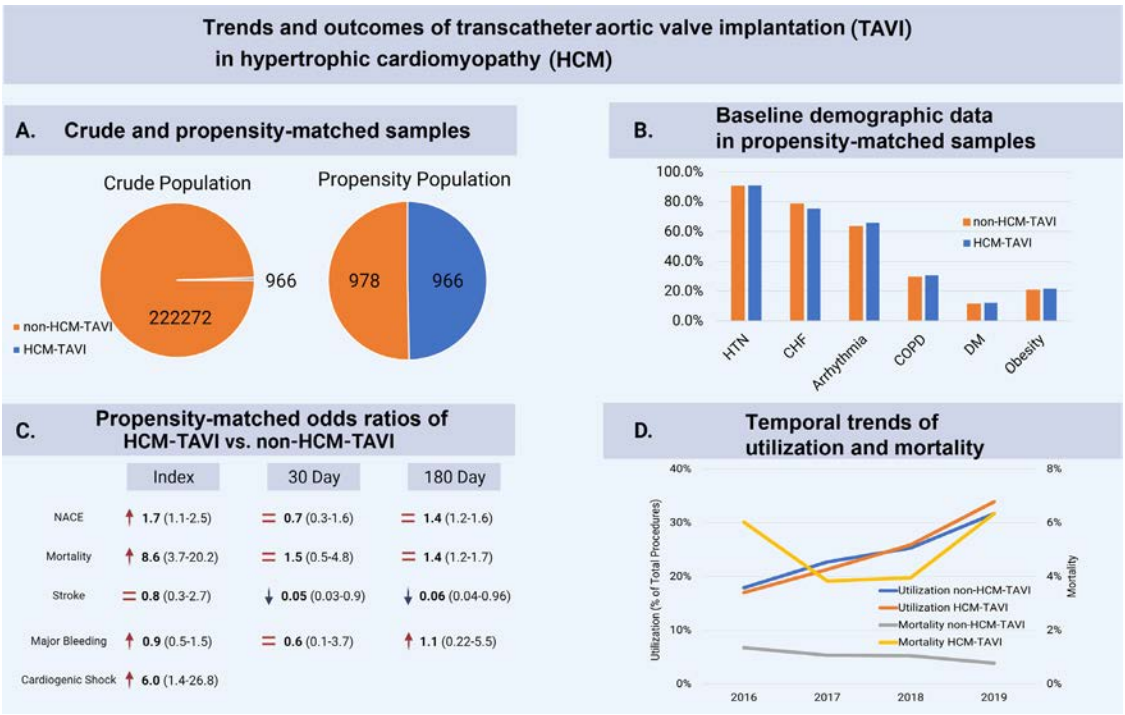

Figure 1. Central Illustration: Trends and Outcomes of Transcatheter Aortic Valve Implantation in Hypertrophic Cardiomyopathy

(18.6%) versus non−HCM-TAVI (2.9%).[3] In addition, we found that the risk of complications attenuated on follow-up, indicating that patients surviving the initial postprocedure cardiogenic shock might have favorable outcomes.

Our results highlight the need for clinicians to be aware of the complex hemodynamic interplay of TAVI in HCM. The immediate period after TAVI in these patients is the most critical and is associated with worse outcomes. Future studies are needed to determine the role of prophylactic septal alcohol ablation before TAVI.

Disclosures

The authors have no conflicts of interest to disclose.

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Temporal Trends and Outcomes of Transcatheter and Surgical Aortic Valve Replacement in Patients With Cardiac Amyloidosis and Severe Aortic Stenosis

Cardiac amyloidosis (CA) is an infiltrative/restrictive cardiomyopathy, caused by the deposition of misfolded amyloid fibrils in the form of immunoglobulin light-chain or transthyretin amyloid within the myocardium. To date, there is no treatment to reverse the process already present at diagnosis; however, new pharmacologic therapies have shown promise in slowing down disease progression.[1,2] Aortic stenosis (AS) is one of the most common valvopathy, in which treatment is centered around valvular replacement with either transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR). Without valvular intervention, severe symptomatic AS is associated with a poor prognosis and 50% mortality rate within 2 years of diagnosis. Studies have shown the prevalence of transthyretin amyloid deposits, ranging from 4% to 29%, in patients with severe AS undergoing valvular intervention.[3] With the increasing life expectancy of the general population, many patients with CA remain suitable candidates for aortic valve replacement. Therefore, we sought to describe the trends and outcomes of TAVI and SAVR in patients who were diagnosed with concomitant CA and severe AS.

Data from the National Inpatient Sample (NIS) database from 2012 to

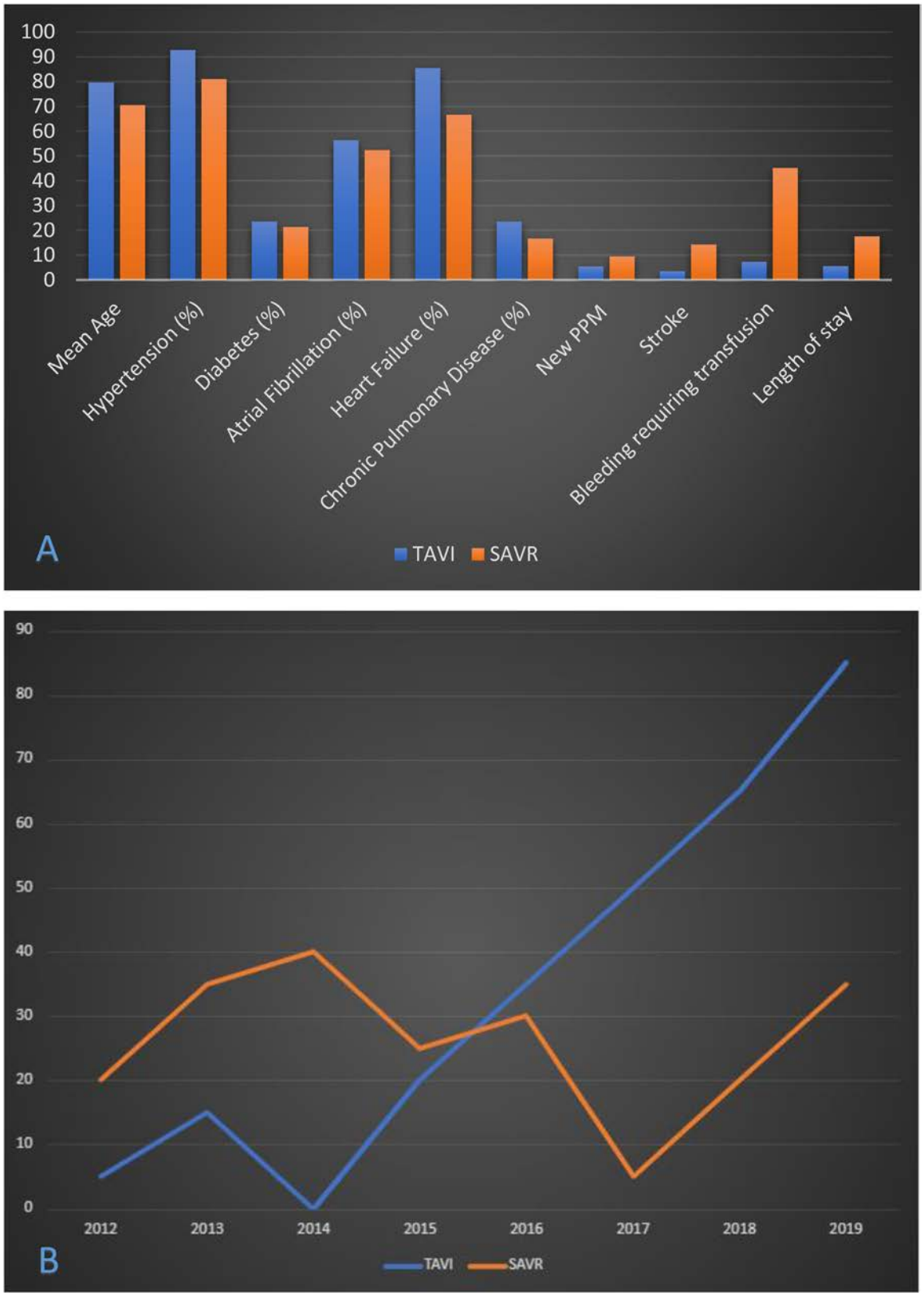

Figure 1. (*A*) Baseline characteristics and postprocedural complications after TAVI versus SAVR in patients with CA. (*B*) Trends in aortic valve intervention in patients with cardiac amyloidosis, 2012 to 2019.

Table 1
Demographic information, baseline co-morbidities and outcomes in patients with CA and severe AS undergoing TAVI and SAVR

Variables	SAVR (n=210)	TAVI (n=275)	Overall (n=485)
Female	35.7%	30.9%	33.0%
Age (years ± SD)	70.6 ± 10.1	79.9 ± 7.5	75.8 ± 9.8
LOS	17.6 ± 18.9	5.6 ± 5.3	10.8 ± 14.4
Total inflation adjusted Cost (US$)	96374 ± 113,100	60,771 ± 27801	77584 ± 82273
Race			
White	88.9%	84.9%	86.5%
Black	5.6%	11.3%	9.0%
Hispanic	2.8%	0.0%	1.1%
Asian	0.0%	1.9%	1.1%
Others	2.8%	1.9%	2.2%
Insurance			
Medicare	73.8%	96.4%	86.6%
Medicaid	2.4%	0%	1.0%
Private	23.8%	3.6%	12.4%
Location			
Rural	0	3.6%	2.1%
Urban non-teaching	7.1%	3.6%	5.2%
Urban teaching	62.9%	92.7%	92.8%
Hospital region			
Northeast	16.7%	43.6%	32.0%
Midwest	38.1%	16.4%	25.8%
South	21.4%	25.5%	23.7%
West	23.8%	14.5%	18.6%
Median Household income			
$1 - $38,999	11.9%	14.5%	13.4%
$39,000 - $47,999	19.0%	20.0%	19.6%
$48,000 - $62,999	31.0%	29.1%	29.9%
$63,000 or more	38.1%	36.4%	37.1%
Disposition			
Discharged home	19.0%	60.0%	42.3%
Skill Nursing facility	42.9%	14.5%	26.8%
Home Health Care	35.7%	18.2%	25.8%
Baseline co-morbidities			
Congestive Heart Failure	66.7%	85.5%	77.3%
Hypertension	81%	92.7%	87.6%
Diabetes Mellitus	21.4%	23.6%	22.7%
Chronic Kidney Disease	47.6%	49.1%	48.5%
Obesity	19%	5.5%	11.3%
Peripheral Vascular Disease	23.8%	20%	21.6%
Coronary Artery Disease	61.9%	58.2%	59.8%
Atrial Fibrillation	52.4%	56.4%	54.6%
Chronic pulmonary disease	16.7%	23.6%	20.6%
Pulmonary vascular disease	21.4%	23.6%	22.7%
Hypothyroidism	28.6%	14.5%	20.6%
Liver	4.8%	3.6%	4.1%
Cancer	7.1%	7.3%	7.2%
Anemia	4.8%	7.3%	6.2%
Rheumatological disease	11.9%	5.5%	8.2%
Coagulopathy	59.5%	18.2%	36.1%
Prior Coronary Artery Bypass Graft	4.8%	5.5%	5.2%
Prior Myocardial Infarction	2.4%	5.5%	4.1%
Prior Percutaneous Coronary Intervention	4.8%	16.4%	11.3%
Prior stroke	21.4%	23.6%	22.7%
Outcomes			
Stroke	14.3%	3.6%	8.2%
Pacemaker implantation	9.5%	5.5%	7.2%
Bleeding requiring transfusion	45.2%	7.3%	23.7%
Died during hospitalization	2.4%	7.3%	5.2%
Extracorporeal Membrane Oxygenation	2.4%	0%	1%
Intra-Aortic Balloon Pump	7.1%	0	3.1%
Acute kidney injury	26.2%	20.0%	22.7%
Acute kidney injury leading to Hemodialysis	4.8%	5.5%	5.2%

2019 was used to identify hospitalizations with International Classification of Diseases, Ninth Revision and International classification of Diseases, Tenth Revision procedural codes for TAVI and SAVR in patients with CA. The outcomes of interest were length of stay, cost of hospitalization, and postprocedural complications. Others variables reviewed included age, gender, hypertension, diabetes, atrial fibrillation, congestive heart failure, peripheral vascular disease, chronic pulmonary disease, pulmonary vascular disease, renal disease, liver disease, cancer, rheumatologist disease, hypothyroidism, coagulopathy, history of previous myocardial infarction, coronary artery bypass surgery, cerebral vascular accident, permanent pacemaker implantation, acute kidney injury, renal disease on hemodialysis, and transplant history. Categoric variables were reported as percentages and continuous variable as mean and SD. The NIS is a publicly available database with deidentified patient information; therefore, this study was determined to be exempt from institutional review board approval.

We identified 485 hospitalizations: a total of 275 for TAVI (56.7%) and 210 for SAVR (43.3%). Patients undergoing TAVI were significantly older (mean age 79.9 years vs 70.6 years) and had more co-morbidities, including hypertension (92.7% vs 81%), heart failure (85.5% vs 66.7%; p = 0.026), and permanent pacemaker (7.3% vs 2.4%) (Figure 1). Incidence of stroke was significantly lower in patients undergoing TAVI than SAVR (3.6% vs 14.3%). Postoperative bleeding requiring a transfusion was also lower in patients with TAVI (7.3% vs 45.2%). The mortality rate was 7.3% during hospitalization for patients with TAVI and 2.4% for SAVR. Mechanical support, including extracorporeal membrane oxygenation and intra-aortic balloon pump, were used in 2.4% and 7.1% in patients with SAVR respectively, whereas neither were required in patients with TAVI. Patients undergoing TAVI had significantly reduced length of stay in comparison with SAVR (5.6 ± 5.3 days vs 17.6 ± 18.9 days). The total cost of stay was also lower in the TAVI cohort ($60,771 ± 27,801 vs $96,374 ± 113,100). Routine discharges were more common with TAVI procedure at 60% versus 19% in SAVR arm (Table 1).

To the best of our knowledge, this study is the first and largest to describe the trends and clinical outcomes of TAVI and SAVR in patients with CA and AS. There are very few studies evaluating therapeutic management of AS in patients with CA. Previous studies reported an elevated risk and mortality associated with AVR in patients with CA that were thought to be secondary to the fragility of amyloid infiltrated myocardium. Recent studies with better screening tools for CA showed better outcomes with valvular intervention.[1,4] However, none of them have described the trends in this unique patient population.

The reduced risk of stroke observed in the TAVI arm is most likely related to improvement in valve size selection and advancement in TAVI devices, use of cardioembolic prevention devices, and improvement in operator experience.[5,6] The results are consistent with the study by Kapadia et al[6], which showed lower risk of stroke with TAVI than SAVR because of procedural technique. More patients were able to be routinely discharged home with a shorter length of stay and lower cost of procedure with TAVI. Patients with TAVI had higher absolute mortality, likely from older population with higher co-morbidities undergoing the transcutaneous procedure, than the patients with SAVR. Although TAVI was performed in higher risk population, patients had less complications, with lower cost and length of stay, proving that it should be considered as the treatment modality of choice in patients with concomitant diagnosis of CA and AS. Randomized controlled trials with longer follow-up and higher-powered study are needed to determine future clinical guidelines and mortality differences among these patients.

Our study draws strength from the use of the NIS database, overcoming bias associated with data from single-center and small regional hospitals. There is a potential for unknown confounders. Second, the NIS database data collection is dependent on accurate entry of diagnoses and procedural codes. Third, distinction between the various types of CA could not be made. Finally, absolute comparison in these 2 cohorts of TAVI and SAVR was not possible because the patient population in both the groups were fundamentally different. Nevertheless, we have identified a high-risk population, in whom a transcutaneous approach is beneficial.

In conclusion, length of stay, cost of hospitalization, and postprocedural complications in terms of stroke and postoperative bleeding requiring transfusion were markedly lower in patients undergoing TAVI, suggesting TAVI should be considered as the treatment modality of choice in patients with dual diagnosis of CA and severe AS.

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Mortality Risk in Patients With Pulmonary Embolism With Pleural Effusion

Previous investigations have frequently reported the presence of pleural effusion in patients with acute pulmonary embolism (PE).[1,2] Although retained not specific, the presence of pleural effusion may complicate and/or delay the diagnosis of acute PE. Moreover, data regarding the prognostic impact of pleural effusion in such patients have been poorly investigated by previous reports. We systematically reviewed the available information and performed a meta-analysis of data from the available cohort studies to estimate the prognostic role of pleural effusion and its related early mortality in patients diagnosed with acute PE.

The study was performed in accordance with the Preferred Report Items for Systematic Reviews and Meta-analyses guidelines (Supplementary File 1). For this purpose, MEDLINE and Scopus databases were systematically searched for articles published in English language, from inception through May 1, 2022, using the following medical subject heading terms: "Pulmonary Embolism [Title/Abstract] AND pleural effusion [Title/Abstract] OR." Inclusion criteria were: (1) studies enrolling subjects with a confirmed diagnosis of acute PE, (2) stratifying the population as survivors and nonsurvivors, and (3) providing the results for early (in-hospital or 30-day) mortality as hazard ratio (HR) and relative 95% confidence interval (CI); conversely, case reports, review articles, editorials/letters, and case series with less than 10 participants, randomized controlled trials, and studies including duplicate populations, if any. References from the included studies were screened to potentially identify other investigations meeting the inclusion criteria. Two investigators independently extracted data (MZ and GR) and a third reviewer checked data (ST). Ethical approval and informed consent were not required as the study did not directly enroll human subjects. The quality of the included studies was graded using the Newcastle−Ottawa quality assessment scale.

Data were pooled using a random effects model, pooling the adjusted HR with the related 95% CI related to the mortality risk in PE patients with pleural effusion. Heterogeneity among studies was assessed using Higgins and Thomson I^2 statistic, where I^2 values correspond to the following levels of heterogeneity: low (<25%), moderate (25% to 75%), and high (>75%). The presence of potential publication bias was verified by visual inspection of the funnel plot. Due to the low number of the included studies (<10), small-study bias was not examined because our analysis was underpowered to detect such bias. A predefined sensitivity analysis (leave-one-out analysis) was performed, removing 1 study at the time, to evaluate the stability of our results. All meta-analyses were conducted using Comprehensive Meta-Analysis Software, version 3 (Biostat, New Jersey).

Initial search resulted in 1,669 articles. After removing duplicates (n = 632) and applying our inclusion criteria, only 4 studies[3−6] with 2,186 patients (mean age 63.0 years, 1,201 men) were included in the analysis. The general characteristics of patients enrolled are showed in Table 1. Pleural effusion was presents in 807 of patients with PE(36.9%). On pooled analysis, pleural effusion was found to be significantly associated with higher risk of death in the short-term period (HR 2.42, 95% CI 1.85 to 3.18, p <0.0001, $I^2 = 0\%$) (Figure 1). Visual inspection of the relative funnel plot did not reveal significant evidence of publication bias (Supplementary File 2). Moreover, sensitivity analysis yielded consistent results.

Our analysis, for the first time in medical literature, comprehensively evaluated the prognostic role of pleural effusion in patients with PE, suggesting some important implications for daily

Table 1
General characteristics of the patients enrolled

Author	Patients enrolled N	Mean age (years)	Males N, (%)	NS N (%)	Hypotension In patients with pleural effusion	Syncope (overall) N (%)	Cancer (overall) N (%)	Immobilization (overall) N (%)	HT N (%)	CAD N (%)	COPD N (%)	DM N (%)	HF N (%)	NOS
Yildizeli et al. [3]	570	68	278 (48.8)	74 (12.9)	NR	NR	NR	NR	259 (45.4)	104 (18.2)	157 (27.5)	95 (16.7)	87 (15.3)	7
Zhang et al. [4]	635	58.3	366 (57.6)	49 (7.7)	24 (61.5)	45 (12.5)	70 (19.3)	126 (34.8)	NR	NR	103 (28.5)	NR	23 (6.4)	8
Zhou et al. [5]	518	61.4	341 (65.8)	19 (3.6)	NR	NR	NR	NR	NR	NR	NR	NR	NR	7
Kiris et al. [6]	463	64.6	216 (46.6)	96 (20.7)	47 (39.0)	13 (2.8)	66 (14.2)	NR	192 (41.6)	58 (12.5)	40 (8.6)	95 (20.5)	30 (6.4)	8

NS = non-survivors; HT = arterial hypertension; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; HF = heart failure: NOS = Newcastle−Ottawa quality assessment scale; NR = not reported.