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FASTTRACK CLINICAL RESEARCH
Valvular heart disease

Outcomes of transcatheter aortic valve replacement in patients with cardiogenic shock

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Abstract

Aims The safety and efficacy of transcatheter aortic valve replacement (TAVR) with contemporary balloon expandable transcatheter valves in patients with cardiogenic shock (CS) remain largely unknown. In this study, the TAVRs performed for CS between June 2015 and September 2022 using SAPIEN 3 and SAPIEN 3 Ultra bioprosthesis from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry were analysed.

Methods and results CS was defined as: (i) coding of CS within 24 h on Transcatheter Valve Therapy Registry form; and/or (ii) pre-procedural use of inotropes or mechanical circulatory support devices and/or (iii) cardiac arrest within 24 h prior to TAVR. The control group was comprised of all the other patients undergoing TAVR. Baseline characteristics, all-cause mortality, and major complications at 30-day and 1-year outcomes were reported. Landmark analysis was performed at 30 days post-TAVR. Cox-proportional multivariable analysis was performed to determine the predictors of all-cause mortality at 1 year. A total of 309 505 patients underwent TAVR with balloon-expandable valves during the study period. Of these, 5006 patients presented with CS prior to TAVR (1.6%). The mean Society of Thoracic Surgeons score was 10.76 ± 10.4. The valve was successfully implanted in 97.9% of patients. Technical success according to Valve Academic Research Consortium-3 criteria was 94.5%. In a propensity-matched analysis, CS was associated with higher in-hospital (9.9% vs. 2.7%), 30-day (12.9% vs. 4.9%), and 1-year (29.7% vs. 22.6%) mortality compared to the patients undergoing TAVR without CS. In the landmark analysis after 30 days, the risk of 1-year mortality was similar between the two groups [hazard ratio (HR) 1.07, 95% confidence interval (CI) 0.95–1.21]. Patients who were alive at 1 year noted significant improvements in functional class (Class I/II 89%) and quality of life (ΔKCCQ score +50). In the multivariable analysis, older age (HR 1.02, 95% CI 1.02–1.03), peripheral artery disease (HR 1.25, 95% CI 1.06–1.47), prior implantation of an implantable cardioverter-defibrillator (HR 1.37, 95% CI 1.07–1.77), patients on dialysis (HR 2.07, 95% CI 1.69–2.53), immunocompromised status (HR 1.33, 95% CI 1.05–1.69), New York Heart Association class III/IV symptoms (HR 1.50, 95% CI 1.06–2.12), lower aortic valve mean gradient, lower albumin levels, lower haemoglobin levels, and lower Kansas City Cardiomyopathy Questionnaire scores were independently associated with 1-year mortality.

Conclusion This large observational real-world study demonstrates that the TAVR is a safe and effective treatment for aortic stenosis patients presenting with CS. Patients who survived the first 30 days after TAVR had similar mortality rates to those who were not in CS.

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Structured Graphical Abstract

Key Question

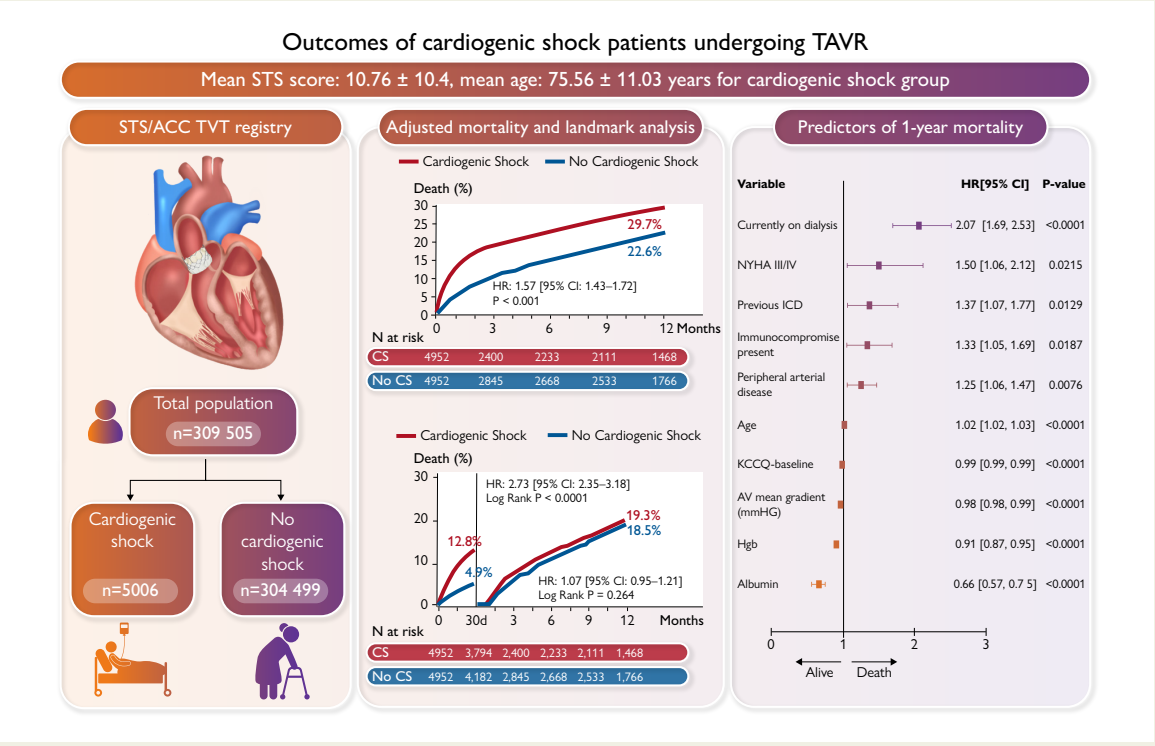
To assess the outcomes of transcatheter aortic valve replacement (TAVR) in patients with cardiogenic shock (CS) with contemporary balloon-expandable transcatheter valve platforms. Safety and efficacy of TAVR in this population remains largely unknown.

Key Finding

The valve was successfully implanted in 97.9% of patients. In a propensity-matched analysis, CS was associated with higher in-hospital, 30-day, and 1-year mortality compared to the patients undergoing TAVR without CS. In the landmark analysis after 30 days, the risk of 1-year mortality was similar between the two groups. Patients who were alive at 1 year noted significant improvements in functional class and quality of life.

Take Home Message

This large observational real-world study demonstrates that TAVR is a safe and effective treatment in patients with CS.



Outcomes of cardiogenic shock patients undergoing TAVR.

Keywords Cardiogenic shock • Transcatheter aortic valve replacement • Transcatheter aortic valve implantation • TAVI • TAVR • Aortic stenosis • Mortality

Introduction

Cardiogenic shock (CS) in the setting of severe aortic stenosis (AS) carries a poor prognosis. It leads to a vicious cycle of subendocardial ischaemia, reduced preload and increased afterload, ultimately resulting in acute decompensation and death.[1] Previous studies in AS patients with CS who underwent successful balloon aortic valvuloplasty (BAV) reported a 30-day mortality of 33%–47%,[2,3] 1-year mortality of 70%,[3] and 2-year mortality of 90%.[4] Therefore, conservative therapy leads to poor outcomes in these patients. Most patients in CS are denied surgical aortic valve replacement because of increased peri-operative risk of morbidity and mortality. Transcatheter aortic valve replacement (TAVR) has become an attractive alternative because of the less invasive nature of this procedure.

It is estimated that 1%–4% of the patients undergoing TAVR may present with CS.[5] Because of the low prevalence, prior single and multicentre studies have been limited by a small sample size. An earlier study from the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) Transcatheter Valve Therapy Registry (TVT-R-R) reported the outcomes of TAVR in 2220 patients in CS from 2014 to 2017.[5] However, many of these patients underwent TAVR with older generation valves, the primary endpoint was limited to 30-day outcomes, and only patients >65 years were included. Meanwhile, TAVR volumes continue to increase, operator volume and experience continue to grow, and newer device platforms have been introduced.[6] The safety and efficacy of TAVR with new generation transcatheter heart valves in patients with CS remains largely unknown. Accordingly, we

analysed the TVT-R-R data to report in-hospital, 30-day, and 1-year outcomes of TAVR with balloon-expandable bioprosthesis in patients with AS and CS in a contemporary real-world setting. We also report the predictors of 1-year mortality in this population.

Methods

Study population

Consecutive patients undergoing TAVR with contemporary balloon-expandable transcatheter heart valves [SAPIEN 3 and SAPIEN 3 Ultra (Edwards Lifesciences, Irvine, CA, USA)] in the USA, between 17 June 2015 and 30 September 2022, were evaluated in the current study. Patient eligibility for treatment with TAVR was determined by each site using their local heart team and standard of care procedures. All data were site-reported as per standards set by the STS/ACC TVT-R-R. As a requirement by the Centers for Medicare & Medicaid Services, the TVT-R-R includes all patients who undergo TAVR in the USA. The data are frequently audited for accuracy and represent a real-world population. Details of the TVT-R-R have been reported previously.[6] The study has been approved by a central institutional review board (Advarra) and granted a waiver of informed consent by the Duke University School of Medicine Institutional Review Board under the Common Rule 45 CFR 46.3. The analyses were performed on data downloaded by Edwards Lifesciences from the STS/ACC TVT-R-R. Since the data sharing agreement between Edwards Lifesciences and the STS/ACC is restricted to valve manufactured by Edwards Lifesciences only, this analysis was based only on the Edwards SAPIEN 3 and SAPIEN Ultra valves as previously.[7]

The primary group of interest included patients with CS who underwent TAVR. CS was defined as the (i) coding of CS within 24 h of procedure on the TVT-R form ($n = 1922$); and/or (ii) pre-procedural use of inotropes ($n = 3678$) or mechanical circulatory support (MCS) devices (intra-aortic balloon pump, $n = 411$; catheter-based assist device, $n = 364$); and/or (iii) cardiac arrest within 24 h prior to TAVR ($n = 371$). Detailed definitions of these categories are provided in the supplementary data. There was overlap in these groups as the same patient could be included in multiple categories, giving us a final study population of 5006 CS patients. The control group comprised patients undergoing TAVR without underlying CS. There were many patients who were labelled as 'elective' and 'CS' on the TVT-R forms but had TAVR on the same day of admission. These were assumed to be most likely mislabelled based on intra-procedural inotropes or coding errors. Therefore, we performed a sensitivity analysis after excluding the same day TAVR and 'elective status' patients. This confirmed that this specific group was not as sick and was probably mislabelled, as the mean STS score was in the intermediate category at 4.9, mean left ventricular ejection fraction (LVEF) was in the normal range (55%), and only 0.5% had moderate-severe mitral regurgitation (MR) (see Supplementary data online, *Table S1*). Some patients may have been same day transfers from outside hospitals; however, those numbers should be low and may not affect the overall results. Based on this analysis, we excluded these patients from the CS group and included them in the non-CS group. Supplementary data online, *Figures S1* and *S2* present the results of the whole cohort of 9499 patients prior to exclusion. The results are similar to the selected cohort but suggest a lower risk CS population because of possible mislabelling of same day elective TAVRs as CS.

Procedural and clinical outcomes

The primary outcome of interest was all-cause mortality at 1 year. Procedural characteristics, major complications, and in-hospital outcomes were reported. Implant success was defined as successful deployment of a single TAVR device in the proper anatomical location. Technical success (at exit from procedure room) was defined using the Valve Academic Research Consortium (VARC)-3 criteria as freedom from mortality, successful deployment of the device, and freedom from surgery or intervention related to the device or to a major vascular or access-related or cardiac structural complication.[8] Major adverse cardiac and cerebrovascular events including all-cause mortality, cardiac death, stroke, aortic valve reintervention, life-threatening bleeding, major vascular complication, new dialysis, new onset atrial fibrillation, percutaneous coronary intervention (PCI), permanent pacemaker (PPM), valve-related readmission, and any readmission were assessed at 30 days and 1 year post-TAVR. New York Heart Association (NYHA) functional class and quality of life (QoL) determined by the Kansas City Cardiomyopathy Questionnaire overall summary score (KCCQ OS) were also reported at 30 days and 1 year after TAVR. Landmark analysis was performed using 30 days post-TAVR as a landmark point.

Statistical analysis

Continuous variables were presented as mean (SD) or median [interquartile range (IQR)] and were compared between groups using the two-sample *t*-test or Wilcoxon rank sum test. Categorical variables were presented as frequencies and percentages and were compared using the χ^2 or Fisher's exact test. The 30-day and 1-year adverse event rates were based on Kaplan–Meier estimates, and all comparisons were made using the log-rank test. Patients who were lost to follow-up or withdrew were censored at the time of their last known alive status. A propensity score matching analysis was performed to adjust for differences in baseline characteristics and potential confounders that may lead to biased estimates of the CS vs. non-CS group comparison. The propensity score was calculated by logistic regression including the following baseline covariates: age, sex, body mass index, access site, prior PCI, prior coronary artery bypass graft (CABG) surgery, prior stroke, carotid stenosis, peripheral arterial disease (PAD), hypertension, diabetes, chronic lung disease (CLD), immunocompromise status, porcelain aorta, atrial fibrillation, creatinine level, haemoglobin level, estimated glomerular filtration rate, aortic valve mean gradient, LVEF, MR, tricuspid regurgitation (TR), NYHA functional class III/IV, 5-meter walk test, KCCQ OS score, currently on dialysis, prior PPM placement, previous implantable cardioverter-defibrillator (ICD) placement, aortic regurgitation (AR), prior transient ischaemic attack (TIA) or stroke, endocarditis, use of home oxygen, and STS score. Missing baseline data were imputed using the Markov–Chain Monte Carlo method prior to modelling. Missing values were imputed five times, and the mean propensity score within an individual was used for final matching. Supplementary data online, *Table S2* presents the percentage of patients with missing baseline characteristics values. Based on their propensity scores, each CS patient was matched to a non-CS patient 1:1 to create two balanced cohorts, using a greedy matching strategy with a calliper of width equal to 0.02 of the SD of the logit of the propensity score. Residual differences after propensity matching were assessed using absolute standardized differences of each covariate and displayed using a Love plot. Sensitivity analyses were performed to investigate the robustness of the results. The outcomes were assessed in an additional propensity score-matched cohort of patients labelled CS but were admitted on the same day as TAVR. This sensitivity analysis was performed without imputation. These patients were subsequently excluded from the 'CS' group and were incorporated into the 'non-CS' group as explained above. Univariate analysis was performed to determine the baseline characteristics that were predictive of 30-day and 1-year all-cause mortality. A multivariable Cox proportional hazard model with a stepwise selection method of significant predictors using entry and exit criterion of $P = 0.1$ was used to identify independent predictors of all-cause mortality at 30 days and 1 year in CS patients. Adjusted hazard ratios (HRs) were calculated for four pre-specified sub-groups using a multivariable Cox proportional hazard analysis adjusting for all the covariates used in the propensity score. Paired *t*-test was performed to analyse the change in KCCQ score and LVEF from baseline to 1 year in patients who had complete data at all the time points. All statistical analyses were performed using SAS, version 9.4 (SAS Institute), and statistical significance was set at a two-sided $P < 0.05$ without multiplicity adjustment.

Table 1 Unadjusted baseline characteristics for patients with and without cardiogenic shock

Baseline characteristics[a]	Cardiogenic shock $n = 5006$	No cardiogenic shock $n = 304\,499$	*P*-value
Age (years)	75.56 ± 11.026 (5001)	78.99 ± 8.604 (304 422)	<0.0001
Male sex	64.52% (3229/5005)	58.46% (177 998/304 460)	<0.0001
Race			
White	88.7% (4442)	92.6% (281 831)	<0.0001
Black/African American	4.9% (245)	3.8% (11 494)	<0.0001
Other	3.2% (160)	1.8% (5362)	<0.0001
BMI (kg/m^2)	29.08 ± 14.937 (4991)	29.72 ± 12.330 (303 863)	0.003
STS score	10.76 ± 10.362 (4663)	4.88 ± 3.993 (297 192)	<0.0001
NYHA class III/IV	91.33% (4527/4957)	67.79% (204 767/302 081)	<0.0001
Hypertension	85.48% (4279/5006)	90.22% (274 622/304 403)	<0.0001
Diabetes	43.66% (2185/5005)	38.22% (116 299/304 299)	<0.0001
Currently on dialysis	10.97% (549/5004)	3.66% (11 121/304 218)	<0.0001
Chronic lung disease	38.67% (1926/4980)	31.91% (96 831/303 443)	<0.0001
Current/recent smoker (<1 year)	14.36% (601/4186)	7.72% (19 390/251 078)	<0.0001
Use of home oxygen	10.17% (509/5006)	7.19% (21 891/304 279)	<0.0001
Immunocompromised	8.0% (386/4824)	6.67% (19 457/291 511)	0.0003
Hostile chest	5.87% (294/5006)	4.37% (13 311/304 359)	<0.0001
Porcelain aorta	3.08% (154/5005)	1.82% (5545/304 271)	<0.0001
Atrial fibrillation/flutter	49.77% (2490/5003)	35.71% (108 649/304 291)	<0.0001
Prior stroke	12.07% (604/5005)	10.60% (32 261/304 359)	0.0008
PAD	26.03% (1303/5005)	23.02% (70 057/304 310)	<0.0001
Carotid stenosis	18.94% (775/4091)	19.97% (51 437/257 596)	0.1
Prior PCI	31.9% (1598/5003)	31.6% (94 653/299 709)	0.59
Prior CABG	18.68% (935/5005)	16.66% (50 700/304 317)	0.0001
Left main stenosis ≥50%	10.03% (469/4675)	6.67% (19 688/295 089)	<0.0001
Prior MI	36.89% (1845/5001)	19.04% (57 895/304 130)	<0.0001
< 30 days	48.59% (894/1840)	11.89% (6859/57 699)	<0.0001
≥ 30 days	51.41% (946/1840)	88.11% (50 840/57 699)	<0.0001
Permanent pacemaker	12.63% (632/5004)	11.28% (34 314/304 283)	0.003
Previous ICD	7.83% (392/5006)	2.8% (8519/304 187)	<0.0001
Baseline albumin	3.28 ± 0.60 (4416)	3.83 ± 0.50 (253 259)	<0.0001
Baseline creatinine	1.71 ± 1.501 (4984)	1.30 ± 1.105 (303 320)	<0.0001
Baseline haemoglobin	10.88 ± 2.071 (4987)	12.36 ± 2.002 (303 405)	<0.0001
Endocarditis	2.46% (123/5002)	0.62% (1876/304 291)	<0.0001
Prior BAV	7.81% (390/4995)	2.88% (8763/304 227)	<0.0001
Valve in valve	12.01% (601/5006)	3.33% (10 145/304 499)	<0.0001
Concomitant PCI	1.52% (76/5006)	0.33% (995/304 499)	<0.0001
Echocardiographic characteristics			
LVEF (%)	39.79 ± 17.641 (4975)	56.11 ± 12.321 (302 624)	<0.0001
Aortic valve area (cm^2)	0.695 ± 0.3189 (4639)	0.745 ± 0.2489 (296 402)	<0.0001

Continued

Table 1 *Continued*

Baseline characteristics[a]	Cardiogenic shock $n = 5006$	No cardiogenic shock $n = 304\,499$	*P*-value
AV mean gradient (mmHg)	40.77 ± 17.377 (4734)	42.04 ± 14.036 (299 696)	<0.0001
Aortic regurgitation (≥moderate)	28.61% (1418/4956)	16.15% (48 697/301 600)	<0.0001
Bicuspid aortic valve	8.93% (442/4950)	5.20% (15 748/302 596)	<0.0001
Mitral regurgitation (≥moderate)	45.21% (1954/4322)	24.90% (60 024/241 025)	<0.0001
Tricuspid regurgitation (≥moderate)	32.39% (1606/4958)	16.77% (50 571/301 604)	<0.0001

[a]Values are mean ± SD (*n*) or % (*n*).
AV, aortic valve; BAV, balloon aortic valvuloplasty; BMI, body mass index; STS, Society of Thoracic Surgeons; CABG, coronary artery bypass graft; ICD, implantable cardioverter-defibrillator; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; NYHA, New York Heart Association; PAD, peripheral arterial disease.

Results

Baseline characteristics

Of the 309 505 patients who underwent TAVR with balloon-expandable SAPIEN 3 (S3) and SAPIEN 3 Ultra (S3U) valves during the study period, 1.6% ($n = 5006$) presented with CS prior to the TAVR. Of the 5006 patients with CS, 12% ($n = 601$) underwent valve in valve (ViV), and 4405 patients underwent TAVR in native aortic valve. Two-thirds of the patients received S3 valve ($n = 3343$), and one-third had S3U ($n = 1663$) valves. The median (IQR) number of days from date of admission to the TAVR procedure was 5 (2–9) days. Complete follow-up for outcomes was available in 92.37% patients at 30 days and 76.35% patients at 1 year in the CS group. In the non-CS group, complete follow-up was available in 93.03% patients at 30 days and 76.86% patients at 1 year. Patients in CS group were younger, less likely females, and had a significantly higher mean STS score compared to those not in CS. *Table 1* shows the differences in baseline demographics, co-morbidities, and echocardiographic characteristics between the two groups. Overall, the CS group was much sicker with a higher prevalence of diabetes, atrial fibrillation, prior stroke, prior CABG, PAD, acute coronary syndrome (ACS), end-stage renal disease (ESRD), CLD, prior BAV, left main stenosis > 50%, or obstructive coronaryartery disease.

CS patients had a lower LVEF (39% vs. 56%), lower mean aortic gradient (40 mmHg vs. 42 mmHg), smaller effective aortic valve area (0.65 vs. 0.71 cm^2), higher frequency of bicuspid aortic valve (9% vs. 5%), ≥moderate AR (28% vs. 16%), and ≥ moderate MR (45% vs. 25%). Transfemoral access (93% vs. 95%) was less common with higher use of transapical and axillary access in CS patients. Following propensity matching using the variables listed in the methods section, the sample size was reduced to 4952 patients in both groups. After propensity matching, there were no or minimal differences between the baseline characteristics as shown in *Table 2* and Supplementary data online, *Figure S3*.

In-hospital and 30-day outcomes

Table 3 presents the procedural and in-hospital differences between the matched CS and non-CS groups. In-hospital mortality was significantly higher in patients with CS compared with no CS [9.9% vs. 2.7%; odds ratio (OR), 3.64, 95% confidence interval (CI) 3.02–4.39; $P < 0.0001$]. Cardiac death (5.9% vs. 1.5%), stroke (2.9% vs. 1.5%), new dialysis (3.5% vs. 1.1%), TIA, major vascular complication, life-threatening bleeding, new onset atrial fibrillation, and PCI were also significantly higher in the CS group compared to the non-CS group. There was no difference in aortic valve re-intervention, PPM rate, or periprocedural myocardial infarction (MI). Conversion to open cardiac surgery (0.73% vs. 0.38%) and coronary compression or obstruction rate (0.40% vs. 0.18%) were higher in CS patients compared with non-CS, whereas annular dissection, aortic dissection, device embolization, and perforation rates were similar. Patients in the CS group had a higher frequency of general anaesthesia use and longer procedure times. Implant success was high and numerically similar (97.9% vs. 98.9%) in both groups. Technical success as defined by VARC-3 criteria was achieved in 94.5% of the patients presenting with CS compared to 96.7% in the non-CS group ($P < 0.0001$). Median length of stay post-TAVR was more than double (5 vs. 2 days), and discharge to home was significantly lower (59% vs. 79%) in the CS group compared to the non-CS group. The rate of 30-day mortality (12.9% vs. 4.9%) and stroke (3.2% vs. 1.9%) was significantly higher in the CS group compared to the non-CS group ($P < 0.0001$). *Table 4* shows the differences between other outcomes. Overall, the trends were similar to the in-hospital outcomes.

One-year outcomes of transcatheter aortic valve replacement in cardiogenic shock

Table 4 shows the 1-year outcomes in the matched group. Adjusted 1-year mortality was significantly higher at 29.7% in the CS group compared to 22.6% in the non-CS group (HR, 1.57; 95% CI 1.43–1.72; $P < 0.001$) (*Figure 1*). The rates of stroke, life-threatening bleeding, major vascular complications, new dialysis, atrial fibrillation, and PCI were higher in the CS patients. The rates of PPM (9.3% vs. 9.1%), aortic valve re-intervention (0.83% vs. 0.54%), valve-related readmissions, and overall readmissions (39% vs. 38%) were similar in the CS and non-CS groups. In a landmark analysis after 30 days (*Figure 2*), all-cause mortality was similar between the CS and non-CS groups (19.3% vs. 18.5%, HR, 1.07; 95% CI 0.95–1.21; $P = 0.26$). Supplementary data online, *Table S3* provides the results of significant univariate predictors of all-cause mortality at 1 year.

Figure 3 shows the 1-year mortality Kaplan–Meier curves, and Supplementary data online, *Table S4* shows the adjusted HRs for pre-

Table 2 Adjusted baseline characteristics for patients with and without cardiogenic shock

Baseline characteristics[a]	Cardiogenic shock n = 4952	No cardiogenic shock n = 4952	P-value
Age (years)	75.62 ± 10.913 (4948)	75.80 ± 11.153 (4951)	0.4
Male sex	64.61% (3199/4951)	64.17% (3177/4951)	0.64
Race			
White	88.8% (4395/4952)	88.3% (4373/4952)	0.49
Black/African American	5.0% (245/4952)	7.1% (351/4952)	<0.0001
Other	3.1% (157/4952)	2.2% (110/4952)	0.004
BMI (kg/m^2)	29.09 ± 14.995 (4937)	28.93 ± 11.255 (4934)	0.54
STS score	10.25 ± 9.095 (4609)	9.97 ± 10.517 (4789)	0.16
NYHA class III/IV	91.23% (4474/4904)	90.96% (4475/4920)	0.63
Hypertension	85.60% (4239/4952)	86.13% (4265/4952)	0.45
Diabetes	43.71% (2164/4951)	45.03% (2229/4950)	0.19
Currently on dialysis	10.85% (537/4950)	11.40% (564/4948)	0.38
Chronic lung disease	38.75% (1909/4926)	39.58% (1951/4929)	0.4
Current/recent smoker (<1 year)	14.38% (595/4138)	11.56% (488/4220)	0.0001
Use of home oxygen	10.18% (504/4952)	10.12% (501/4951)	0.92
Immunocompromised	7.97% (380/4770)	8.54% (408/4870)	0.31
Hostile chest	5.84% (289/4952)	6.12% (303/4951)	0.55
Porcelain aorta	3.09% (153/4951)	3.32% (164/4944)	0.52
Atrial fibrillation/flutter	49.71% (2460/4949)	50.16% (2482/4948)	0.65
Prior stroke	12.0% (594/4951)	12.24% (606/4951)	0.71
PAD	26.10% (1292/4951)	26.95% (1334/4950)	0.34
Carotid stenosis	18.96% (768/4051)	19.0% (778/4094)	0.96
Previous PCI	32.1% (1586/4949)	32.5% (1609/4947)	0.61
Prior CABG	18.68% (925/4951)	18.80% (930/4947)	0.88
Left main stenosis ≥50%	9.99% (462/4625)	8.84% (424/4798)	0.055
Prior MI	36.89% (1825/4947)	28.67% (1418/4946)	<0.0001
< 30 days	48.30% (879/1820)	25.14% (356/1416)	<0.0001
≥ 30 days	51.70% (941/1820)	74.86% (1060/1416)	<0.0001
Permanent pacemaker	12.71% (629/4950)	12.66% (626/4946)	0.94
Previous ICD	7.88% (390/4952)	8.56% (424/4951)	0.21
Baseline albumin	3.28 ± 0.60 (4364)	3.53 ± 0.59 (4225)	<0.0001
Baseline creatinine	1.70 ± 1.504 (4930)	1.80 ± 1.704 (4929)	0.002
Baseline haemoglobin	10.90 ± 2.067 (4933)	10.87 ± 2.068 (4932)	0.48
Endocarditis	2.38% (118/4948)	2.22% (110/4946)	0.59
Prior BAV	7.67% (379/4942)	7.18% (355/4947)	0.35
Valve in valve	11.85% (587/4952)	7.43% (368/4952)	<0.0001
Concomitant PCI	1.51% (75/4952)	0.67% (33/4952)	<0.0001
Echocardiographic characteristics			
LVEF (%)	39.94 ± 17.619 (4922)	39.90 ± 16.282 (4929)	0.91
Aortic valve area (cm^2)	0.696 ± 0.3198 (4593)	0.705 ± 0.2741 (4754)	0.12

Continued

Table 2 *Continued*

Baseline characteristics[a]	Cardiogenic shock $n = 4952$	No cardiogenic shock $n = 4952$	*P*-value
AV mean gradient (mmHg)	40.75 ± 17.390 (4687)	40.73 ± 15.991 (4816)	0.95
Aortic regurgitation (≥moderate)	28.41% (1393/4903)	27.78% (1363/4906)	0.49
Bicuspid aortic valve	8.96% (439/4898)	6.24% (307/4918)	<0.0001
Mitral regurgitation (≥moderate)	45.1% (1927/4277)	48.2% (2015/4176)	0.003
Tricuspid regurgitation (≥moderate)	32.15% (1577/4905)	32.08% (1578/4919)	0.94

[a]Values are mean ± SD (*n*) or % (*n*).
AV, aortic valve; BAV, balloon aortic valvuloplasty; BMI, body mass index; STS, Society of Thoracic Surgeons; CABG, coronary artery bypass graft; ICD, implantable cardioverter-defibrillator; PCI, percutaneous coronary intervention; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; NYHA, New York Heart Association; PAD, peripheral arterial disease.

specified subgroups within the CS patients. Patients with ≥ moderate MR prior to TAVR had a significantly increased risk of 1-year mortality compared to those with ≤ moderate MR (34.0% vs. 27.6%; $P < 0.001$) (*Figure 3A*). After adjustment, ≥moderate MR was not a significant predictor of 1-year mortality (adjusted HR 1.07; 95% CI 0.93–1.22; $P = 0.34$). When the CS population was stratified by LVEF, we noted the lowest all-cause mortality in patients with LVEF >40%. There was no difference in all-cause mortality between patients with LVEF <20% and 20%–40% ($P = 0.96$) (*Figure 3B*). After multivariate adjustment, LVEF prior to TAVR was not associated with 1-year mortality. Patients who underwent TAVR for native vs. ViV showed a trend towards higher 1-year mortality (HR 1.2; 95% CI, 0.98–1.44; $P = 0.072$), which became significant after multivariate adjustment (adjusted HR 1.26; 95% CI 1.03–1.56; $P = 0.028$) (*Figure 3C*). *Figure 3D* shows the 1-year outcomes of the CS subgroups. Combined use of MCS and inotropes was associated with the highest mortality followed by MCS only group. Those on inotropes alone, had cardiac arrest within 24 h or were entered as CS on the TVT-R form had similar 1-year mortality. On stratifying the CS patients by median number of days from admission to TAVR, we found that early TAVR (≤ 5 days) was associated with lower 30-day (11.6% vs. 14.3%, $P = 0.02$) and 1-year mortality (26.5% vs. 33.3%, $P < 0.0001$) compared to those who had TAVR after 5 days from admission. After adjusting for covariates, early TAVR showed a trend towards lower 1-year mortality but was not significant (HR, 0.91; 95% CI 0.81–1.03; $P = 0.149$).

Multivariate predictors of 30-day and 1-year mortality

Figure 4A shows the multivariate predictors of 30-day mortality after TAVR in CS. Age, lower mean gradient, lower albumin levels, lower KCCQ scores, ESRD, PPM rate, PAD, and use of MCS prior to TAVR were independently associated with increased 30-day mortality. *Figure 4B* shows the multivariable predictors of all-cause mortality at 1 year in patients with CS undergoing TAVR. Age (adjusted HR, 1.02; 95% CI 1.02–1.03), ESRD (adjusted HR, 2.07; 95% CI 1.69–2.53), immunocompromised status (adjusted HR, 1.33; 95% CI 1.05–1.69), previous ICD (adjusted HR, 1.37; 95% CI 1.07–1.77), and PAD (adjusted HR, 1.25; 95% CI 1.06–1.47) were independently associated with increased mortality at 1-year in CS patients, whereas higher aortic mean gradient (adjusted HR, 0.98; 95% CI 0.98–0.99), higher albumin (adjusted HR, 0.66; 95% CI 0.57–0.75), and higher haemoglobin (adjusted HR, 0.91; 95% CI 0.87–0.95) were associated with lower 1-year mortality.

Echocardiographic and functional outcomes

At discharge, mean gradient (10 mmHg) and rate of moderate or severe paravalvular leak (PVL) (0.9%) were similar in CS and non-CS groups (see Supplementary data online, *Table S5*). At 30-day follow-up, mean LVEF improved from baseline in CS patients (39% to 46%), and mean gradients and rate of moderate/severe PVL (1.4%) stayed stable. Patients who survived to 1 year noted further improvement in LVEF to 52% with similar mean gradients and PVL rates (0.93%). In a paired analysis of patients who had echocardiographic data at baseline, 30 days, and 1 year, change in LVEF was similar amongst CS (Δ mean LVEF 6.5%) and non-CS groups (Δ mean LVEF 6.7%, $P = 0.54$) at 30 days. At 1 year, CS patients (Δ mean LVEF 11.9%) were noted to have a higher improved EF compared to non-CS patients (Δ mean LVEF 10.0%, $P = 0.002$). There was a significant improvement in NYHA class from baseline to 30 days and 1 year (see Supplementary data online, *Figure S4*) with 88% of patients in NYHA class I/II at 1 year. Similarly, KCCQ OS scores improved significantly from 28 at baseline to 80 at 1 year (see Supplementary data online, *Figure S5*).

Discussion

This large real-world observational study demonstrates that TAVR with contemporary balloon expandable S3 and S3U valves is a safe and effective treatment option for patients presenting with CS. The rate of in-hospital and 30-day mortality after TAVR in patients with CS was 9.9% and 12.9%, which is considerably lower than the reported mortality of 35%–70% in conservatively managed patients.[2–4,9] The 30-day landmark analysis showed no difference in mortality between the propensity-matched CS and non-CS groups suggesting a good long-term prognosis if patients survive the initial post-procedural stay. Additionally, the majority of survivors were doing well at 1 year with significant improvements in NYHA functional class and QoL assessed by KCCQ OS scores. The rate of major and minor complications post-TAVR was low, and procedural success was high despite the presence of CS. Lastly, we found that older age, lower mean gradient, lower albumin, ESRD, immunocompromised state, prior ICD, and PAD were

Table 3 Adjusted procedural and in-hospital outcomes for patients with and without cardiogenic shock

Outcomes[a]	Cardiogenic shock $n = 4952$	No cardiogenic shock $n = 4952$	Odds ratio (95% CI)**	*P*-value
Procedural outcomes				
Access			NA	0.09
Transfemoral	93.27% (4617/4950)	92.43% (4576/4951)		
Non-transfemoral	6.72% (333/4950)	7.57% (375/4951)		
Access type			NA	0.05
Percutaneous	89.74% (4323/4817)	89.19% (4289/4809)		
Cutdown	8.28% (399/4817)	8.44% (406/4809)		
Mini thoracotomy	1.12% (54/4817)	1.37% (66/4809)		
Mini sternotomy	0.44% (21/4817)	0.79% (38/4809)		
Procedure indication			NA	<0.0001
Aortic stenosis	87.79% (4343/4947)	92.42% (4571/4946)		
Aortic regurgitation	4.63% (229/4947)	1.76% (87/4946)		
Mixed AS/AR	2.69% (133/4947)	2.55% (126/4946)		
Failed bioprosthetic surgical valves	4.89% (242/4947)	3.28% (162/4946)		
Valve size			NA	0.08
20 mm	3.41% (169/4951)	2.83% (140/4947)		
23 mm	29.41% (1456/4951)	27.77% (1374/4947)		
26 mm	40.29% (1995/4951)	41.44% (2050/4947)		
29 mm	26.88% (1331/4951)	27.96% (1383/4947)		
General anaesthesia	58.79% (2907/4945)	49.11% (2427/4942)	1.20 [1.15, 1.24]	<0.0001
Procedure time, min (IQR)	83.00 [59.00, 120.00]	76.00 [57.00, 104.00]	NA	<0.0001
Contrast volume (ml, median)	75.00 [49.00, 119.50]	76.00 [50.00, 115.00]	NA	0.19
Implant success	97.86% (4844/4950)	98.89% (4892/4947)	0.99 [0.98, 0.99]	<0.0001
Technical success[b]	94.5% (4673/4945)	96.7% (4773/4935)	0.98 [0.97, 0.99]	<0.0001
Procedure complications				
Conversion to open heart surgery	0.73% (36/4951)	0.38% (19/4944)	1.89 [1.09, 3.29]	0.02
Coronary compression or obstruction	0.40% (20/4952)	0.18% (9/4952)	2.22 [1.01, 4.88]	0.04
Annular dissection	0.32% (16/4952)	0.14% (7/4952)	2.29 [0.94, 5.55]	0.06
Aortic dissection	0.24% (12/4952)	0.26% (13/4952)	0.92 [0.42, 2.02]	0.84
Device embolization	0.18% (9/4952)	0.08% (4/4952)	2.25 [0.69, 7.30]	0.17
Perforation	0.99% (49/4952)	0.75% (37/4952)	1.32 [0.87, 2.03]	0.19
Index hospitalization				
Length of stay	5.00 [2.00, 9.00]	2.00 [1.00, 5.00]	NA	<0.0001
ICU stay (h)	44.8 [20.15, 102.15]	24.0 [0.90, 46.0]	NA	<0.0001
Discharge location				
Home	59.55% (2949/4952)	79.28% (3926/4952)	NA	<0.0001
Extended care/rehab	19.1% (946/4952)	11.09% (549/4952)	NA	<0.0001
Nursing home	8.32% (412/4952)	5.51% (273/4952)	NA	<0.0001
Hospice	0.77% (38/4952)	0.30% (15/4952)	NA	0.002

Continued

Table 3 *Continued*

Outcomes[a]	Cardiogenic shock *n* = 4952	No cardiogenic shock *n* = 4952	Odds ratio (95% CI)**	*P*-value
In-hospital				
All-cause mortality	9.94% (492/4952)	2.73% (135/4952)	3.64 [3.02, 4.39]	<0.0001
Cardiac death	5.92% (293/4952)	1.49% (74/4952)	3.96 [3.08, 5.09]	<0.0001
Stroke	2.89% (143/4952)	1.45% (72/4952)	1.99 [1.50, 2.63]	<0.0001
All-cause mortality or stroke	12.22% (605/4952)	3.96% (196/4952)	3.09 [2.64, 3.61]	<0.0001
Aortic valve re-intervention	0.24% (12/4952)	0.14% (7/4952 (0.14	1.71 [0.68, 4.35]	0.25
New dialysis	3.53% (175/4952)	1.11% (55/4952)	3.18 [2.36, 4.30]	<0.0001
TIA	0.26% (13/4952)	0.08% (4/4952)	3.25 [1.06, 9.96]	0.03
Major vascular complication	2.32% (115/4952)	1.31% (65/4952)	1.77 [1.31, 2.39]	0.0002
Life-threatening bleeding	2.46% (122/4952)	0.65% (32/4952)	3.81 [2.59, 5.62]	<0.0001
Atrial fibrillation (new onset)	3.84% (157/4084)	1.59% (67/4224)	2.42 [1.83, 3.22]	<0.0001
PCI	1.51% (75/4952)	0.67% (33/4952)	2.27 [1.51, 3.42]	<0.0001
Permanent pacemaker	7.19% (356/4952)	7.03% (348/4952)	1.02 [0.89, 1.18]	0.75
Peri-procedural MI	0.20% (10/4952)	0.16% (8/4952)	1.25 [0.49, 3.16]	0.64

[a]Values are mean ± SD (*n*), % (*n*), or median [IQR]; odds ratio for procedural and in-hospital outcomes.
[b]Technical success defined using VARC-3 criteria.
AS, aortic stenosis; AR, aortic regurgitation; ICU, intensive care unit; IQR, interquartile range; TIA, transient ischaemic attack; PCI, percutaneous coronary intervention; MI, myocardial infarction.

independent predictors of higher 1-year mortality in CS patients undergoing TAVR (*Structured Graphical Abstract*).

This is the largest study to date exploring the outcomes of TAVR in patients presenting with CS in the contemporary era of third- and fourth-generation transcatheter heart valves. A previous analysis from TVT-R-R[5] reported the outcomes of TAVR in CS patients. However, that study included patients from 2014 to 2017 when older generation TAVR valves were being used, had a smaller sample size, high-risk patients were used as the comparison group, and the primary analysis was restricted to 30-day outcomes. In addition, TAVR numbers were growing, but it was not ubiquitous as low-risk indication was not approved. Our study expands this previous analysis by using more contemporary data (2015–22), a larger sample size of 5006 patients, only including the latest third- and fourth-generation balloon-expandable valve platforms, and using 1-year mortality as the primary outcome of interest. We used propensity score matching to identify if 'shock' itself was associated with worse outcomes. Propensity matching helped identify a high-risk group comparable in terms of co-morbidities and demographics thus providing a reasonable comparison. We found that the 30-day and 1-year mortality in the current analysis was lower than previously reported, which may reflect a better selection of patients undergoing TAVR, better procedural outcomes with the latest generation SAPIEN valves, and increasing operator experience and volume. Another key finding of the current study is that there was no difference in mortality between the CS and matched non-CS groups after the 30-day landmark analysis, compared to the previous analysis[5] that showed higher mortality after 30 days. Another study reported plateauing of mortality after 90 days from TAVR; however, it was limited by a small sample size of 180 patients.[10] Thus, our landmark analysis suggests that mortality after 30 days is secondary to the patients' co-morbidities and risk factors rather than CS prior to TAVR. It is critical to identify strategies to manage the shock component post-TAVR to achieve better long-term outcomes.

CS patients undergoing TAVR had significantly higher in-hospital, 30-day, and 1-year mortality compared to the matched non-CS patients. One-year mortality in the present study was 29%, which is lower than the previously reported mortality rate of 35%–50% after TAVR in CS.[5,10] In comparison, mortality was 50% in AS patients who were not surgical candidates and were managed medically,[9] 70% in patients who underwent BAV only for CS,[3] 50% in CS patients presenting with acute MI,[11] and 35%–55% in CS patients with severe MR undergoing transcatheter edge-to-edge repair.[12] These studies provide a reasonable indirect comparison suggesting that TAVR in CS may have better outcomes than these groups. If AS is the primary cause of obstructive CS resulting in low cardiac output and systemic perfusion, treating the cause can lead to rapid improvement in the clinical status of the patient. These patients are usually too sick for surgical intervention, so TAVR may be the only feasible option. As TAVR has become safer and more streamlined, earlier and faster intervention to relive obstructive shock in these patients may continue to improve outcomes.

In this cohort of CS patients undergoing TAVR, we found multiple risk factors that were independently associated with all-cause mortality at 1 year. None of the procedural or shock-related factors were predictive of long-term mortality consistent with the 30-day landmark analysis. For example MI within 30 days of TAVR was not associated with 30-day or 1-year mortality in patients with CS undergoing TAVR. ESRD had the highest hazards of all the risk factors with a two-fold increase in risk of 1-year mortality. This is consistent with previous studies that reported a 1-year mortality of 37% in ESRD patients without CS.[13] Thus, careful discussions and shared decision-making should happen in ESRD

Table 4 Adjusted 30-day and 1-year outcomes for patients with and without cardiogenic shock

Outcomes[a]	Cardiogenic shock $n = 4952$	No cardiogenic shock $n = 4952$	Hazard ratio (95% CI)	*P*-value
30-day outcomes				
All-cause mortality	12.87% (608)	4.93% (232)	2.73 [2.35–3.18]	<0.0001
Cardiac death	6.90% (323)	2.05% (97)	3.43 [2.73–4.30]	<0.0001
Stroke	3.26% (154)	1.85% (89)	1.76 [1.36–2.29]	<0.0001
All-cause mortality/stroke	15.24% (725)	6.34% (301)	2.51 [2.19–2.87]	<0.0001
Aortic valve reintervention	0.36% (16)	0.16% (8)	2.06 [0.88–4.81]	0.09
Life-threatening bleeding	2.89% (127)	1.14% (52)	2.56 [1.86–3.54]	<0.0001
Major vascular complication	2.49% (120)	1.50% (73)	1.66 [1.24–2.22]	0.0005
New dialysis	3.80% (178)	1.40% (66)	2.77 [2.09–3.67]	<0.0001
New onset atrial fibrillation	4.06% (159)	1.73% (71)	2.36 [1.79–3.12]	<0.0001
PCI	1.68% (81)	0.74% (36)	2.28 [1.54–3.37]	<0.0001
Permanent pacemaker	8.05% (381)	8.07% (389)	0.98 [0.85–1.13]	0.83
Valve-related readmission	0.72% (31)	0.50% (23)	1.42 [0.83–2.43]	0.20
Any readmission	11.9% (507)	11.03% (499)	1.08 [0.95–1.22]	0.25
1-year outcomes				
All-cause mortality	29.70% (1126)	22.64% (800)	1.57 [1.43–1.72]	<0.0001
Cardiac death	11.34% (446)	5.78% (205)	2.35 [1.99–2.77]	<0.0001
Stroke	4.29% (178)	3.11% (124)	1.50 [1.20–1.89]	0.0004
All-cause mortality and stroke	31.85% (1238)	24.16% (871)	1.58 [1.45–1.72]	<0.0001
Aortic valve reintervention	0.83% (28)	0.54% (18)	1.71 [0.95–3.09]	0.07
Life-threatening bleeding	4.03% (157)	1.73% (69)	2.44 [1.84–3.24]	<0.0001
Major vascular complication	2.66% (124)	1.84% (82)	1.54 [1.17–2.04]	0.002
New dialysis	4.39% (193)	2.18% (87)	2.32 [1.80–2.99]	<0.0001
New onset atrial fibrillation	4.60% (172)	2.14% (82)	2.24 [1.72–2.92]	<0.0001
PCI	2.36% (98)	2.11% (72)	1.45 [1.07–1.96]	0.02
Permanent pacemaker	9.26% (411)	9.08% (418)	1.00 [0.87–1.15]	0.99
Valve-related readmission	2.89% (84)	2.32% (74)	1.28 [0.94–1.76]	0.12
Any re-admission	39.31% (1205)	37.78% (1290)	1.07 [0.99–1.16]	0.09

[a]Values are mean ± SD (*n*) or % (*n*).
PCI, percutaneous coronary intervention.

patients presenting with CS. Significant MR, significant TR, and LVEF were associated with 1-year mortality in the univariate analysis but became non-significant after multivariate adjustment. This signifies that the acute outcomes may be affected by other valvular disorders, but co-morbidities tend to determine the long-term outcomes.[14] There was no difference in 1-year mortality between those with LVEF <20% or 20%–40%, suggesting that very low EF should not be the only variable used in offering or denying TAVR in the setting of CS. In patients who survived, EF improved significantly during follow-up, and valvular regurgitation lesions improved. Patients undergoing ViV had a significantly lower 1-year mortality compared to those undergoing TAVR for native AS. Urgent and emergent TAVR can be performed with minimal or no contrast use because of the presence of a previous bioprosthetic valve, thus offering a quick bailout compared to patients with native AS. The median time from date of admission to TAVR in CS patients in the current study was 5 days reflecting some delay in intervention in these sick patients. To investigate this further, we examined if early TAVR would be associated with better outcomes in CS. TAVR within the first 5 days of admission was significantly associated with lower 1-year mortality in univariate analysis; however, there was only a trend towards lower mortality after adjusting for co-morbidities and risk factors. Thus, it could be hypothesized that early work-up, consultation with the heart valve team, and intervention may benefit patients presenting in CS.

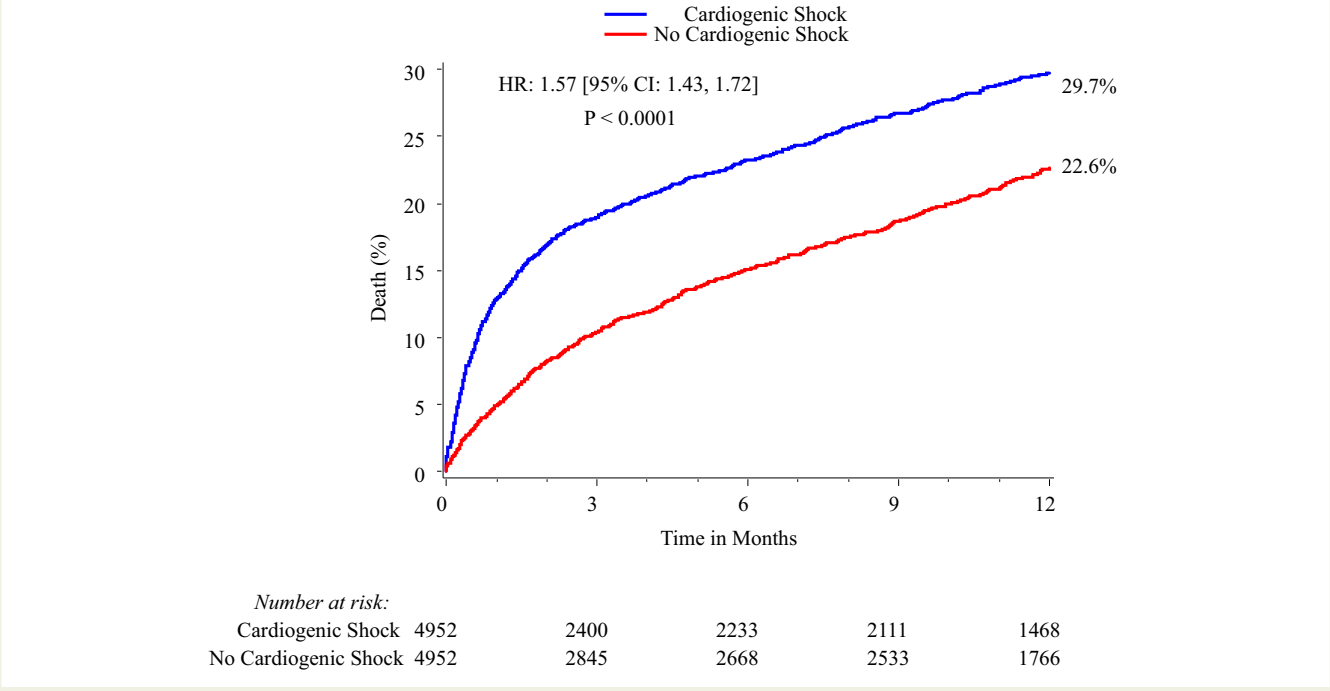


Figure 1 One-year all-cause mortality in propensity-matched cardiogenic shock and non-cardiogenic shock groups.

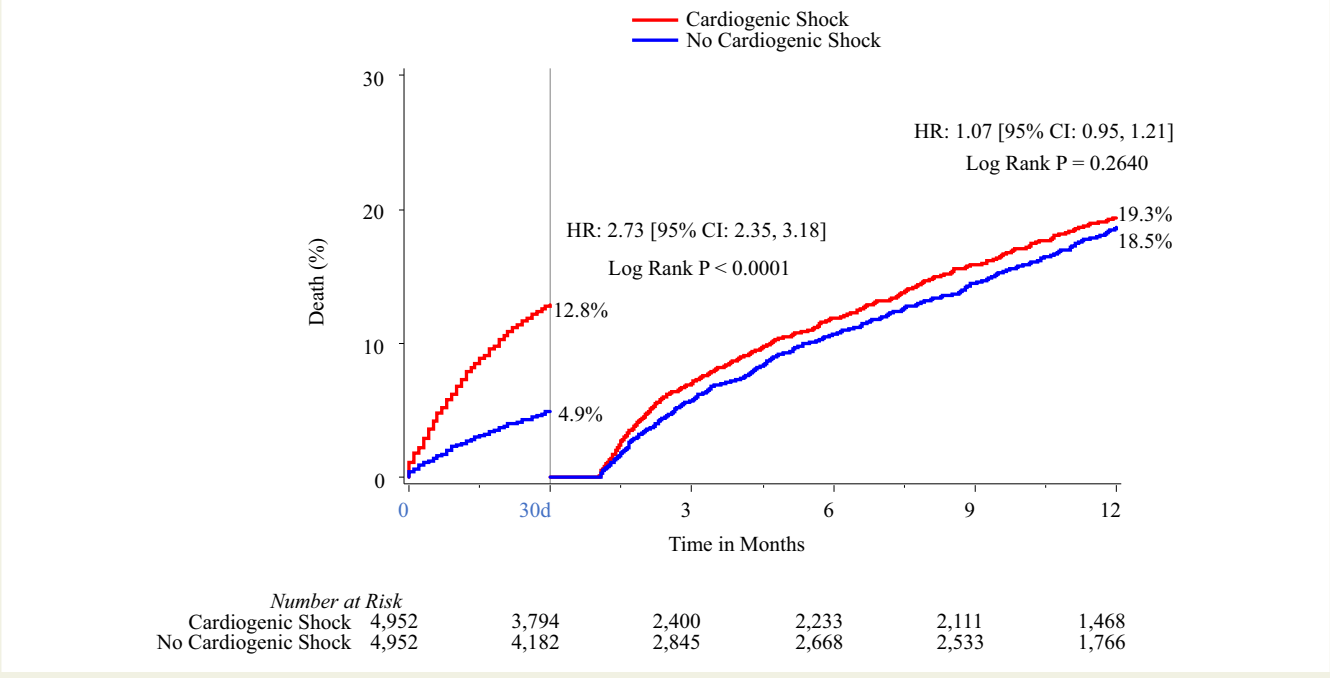


Figure 2 Thirty-day landmark analysis of propensity-matched cardiogenic shock and non-cardiogenic shock groups through 1 year CS.

Among all the CS patients who underwent TAVR, approximately 60% were discharged home, 20% went to an inpatient rehabilitation unit, and 8% were discharged to a nursing home. This is reassuring and reflects the need to include TAVR early in the treatment algorithm for the management of severe AS and CS. Once the obstructive component from AS is relieved, the majority of patients recover and rehabilitate almost completely to be discharged home. Patients who survived and followed at 1 year noted a significant improvement in their NYHA functional class with 88% reporting class I or II status. In addition, there was a marked improvement in their QoL as assessed by KCCQ scores which increased by 40 points from baseline to 30 days and 50 points from baseline to 1 year. This implies that not only majority of

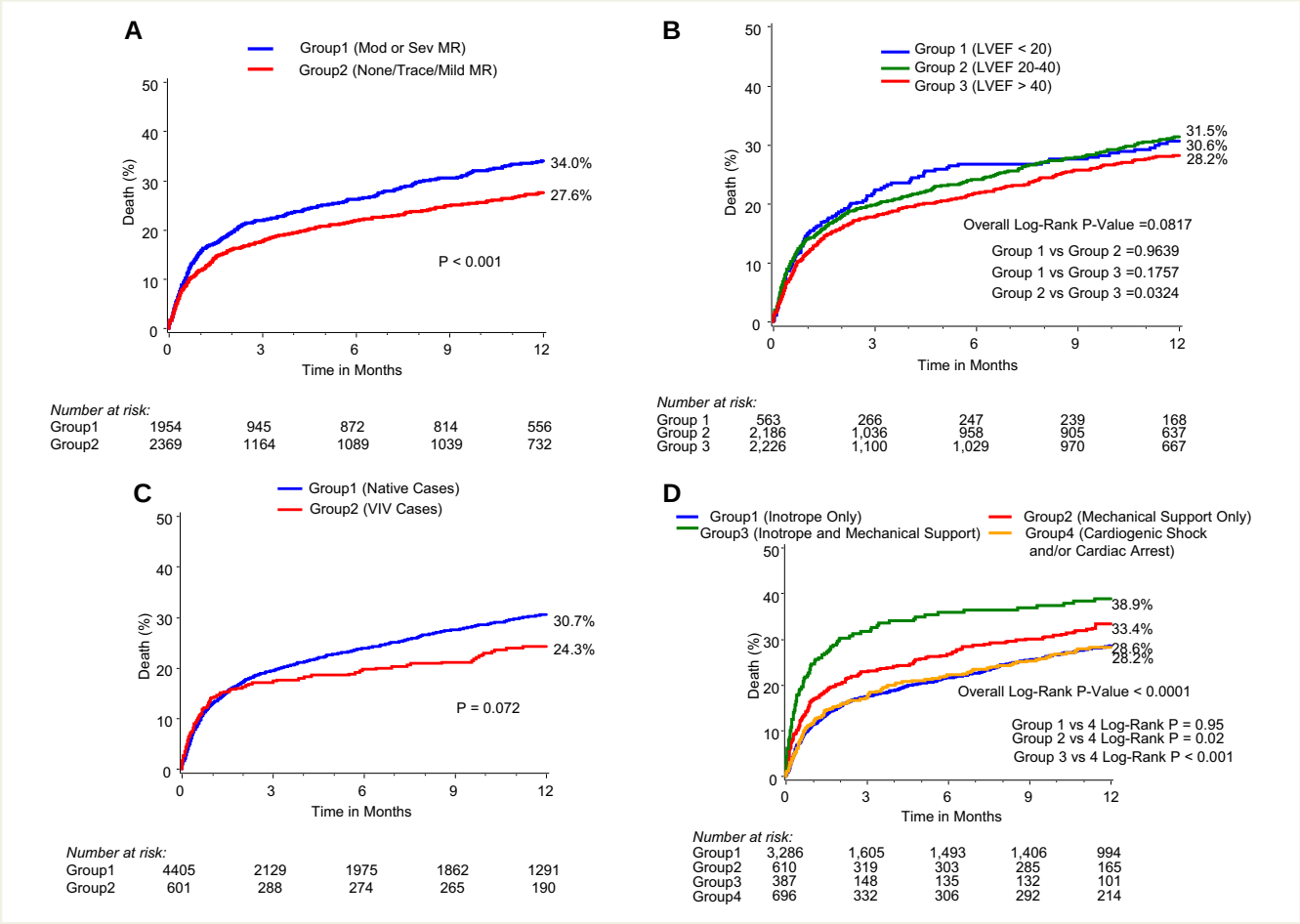


Figure 3 One-year all-cause mortality for pre-specified subgroups in the cardiogenic shock group. (*A*) ≥Moderate mitral regurgitation vs. ≤ mild/trace/none mitral regurgitation. (*B*) Left ventricular ejection fraction <20% vs. 20%–40% vs. > 40%. (*C*) Native cases vs. valve-in-valve. (*D*) Pre-procedure inotropes only, vs. mechanical circulatory support only vs. mechanical circulatory support and inotropes vs. coding of CS on TVT-R form/cardiac arrest.

the patients were alive at 1 year, but they were doing quite well based on NYHA functional class and QoL KCCQ OS score improvements. Cardiac deaths accounted for 50% of all deaths at 30 days and 38% at 1 year signifying that majority of these patients die from non-cardiac comorbidities.

This study has important implications in the current era. With the growth of TAVR worldwide, increasing operator experience, better devices, and extension of indication into low-risk groups, it is important to remember that TAVR was originally evaluated and approved in patients who were at prohibitive risk of surgery in the PARTNER trial.[9] TAVR led to a 20-point absolute reduction in all-cause mortality with a number needed to treat of 5 in that cohort. The rate of 1-year mortality in the current study is similar to the TAVR arm in the original trial; however, CS patients who are usually much sicker were not included in that trial. All TAVR trials to-date have excluded CS, and it is extremely difficult to conduct a randomized trial in AS patients with CS, so observational studies such as the current one can help guide treatment recommendations. The current European and US guidelines appropriately mention that TAVR should be offered to patients only if their expected survival from other co-morbidities is >1 year. Considering that 70% of the patients who present with CS prior to TAVR were alive at 1 year, CS by itself should not be considered a prohibitive factor. Other co-morbidities and risk factors predictive of higher mortality in this group can help select the appropriate patients for intervention. BAV has been evaluated extensively in the past for CS patients to facilitate recovery or to serve as a bridge to definite therapy in the future. However, studies have shown that the short-term and long-term mortality post-successful valvuloplasty remains very high.[2–4] Our study shows that TAVR in CS patients was found to be safe with a low risk of major peri-procedural complications, highly effective with a close to 98% successful implant rate and low PVL rate, and was associated with >90% in-hospital survival in a traditionally morbid condition. As the peri-procedural risk of TAVR and BAV is similar, it seems that definitive therapy in terms of TAVR is more beneficial than BAV alone. Overall, this study confirms the safety and efficacy of TAVR in patients with CS and suggests that TAVR with new generation balloon-expandable valves may be offered to most patients who are anatomically suitable candidates, as long as active medical conditions such as sepsis, pneumonia, haemorrhage, cancer, or other issues preclude them from recovery or deriving any benefit.

Limitations

There are several limitations of the study. This is an observational study with the possibility of selection bias as the sickest patients may not be

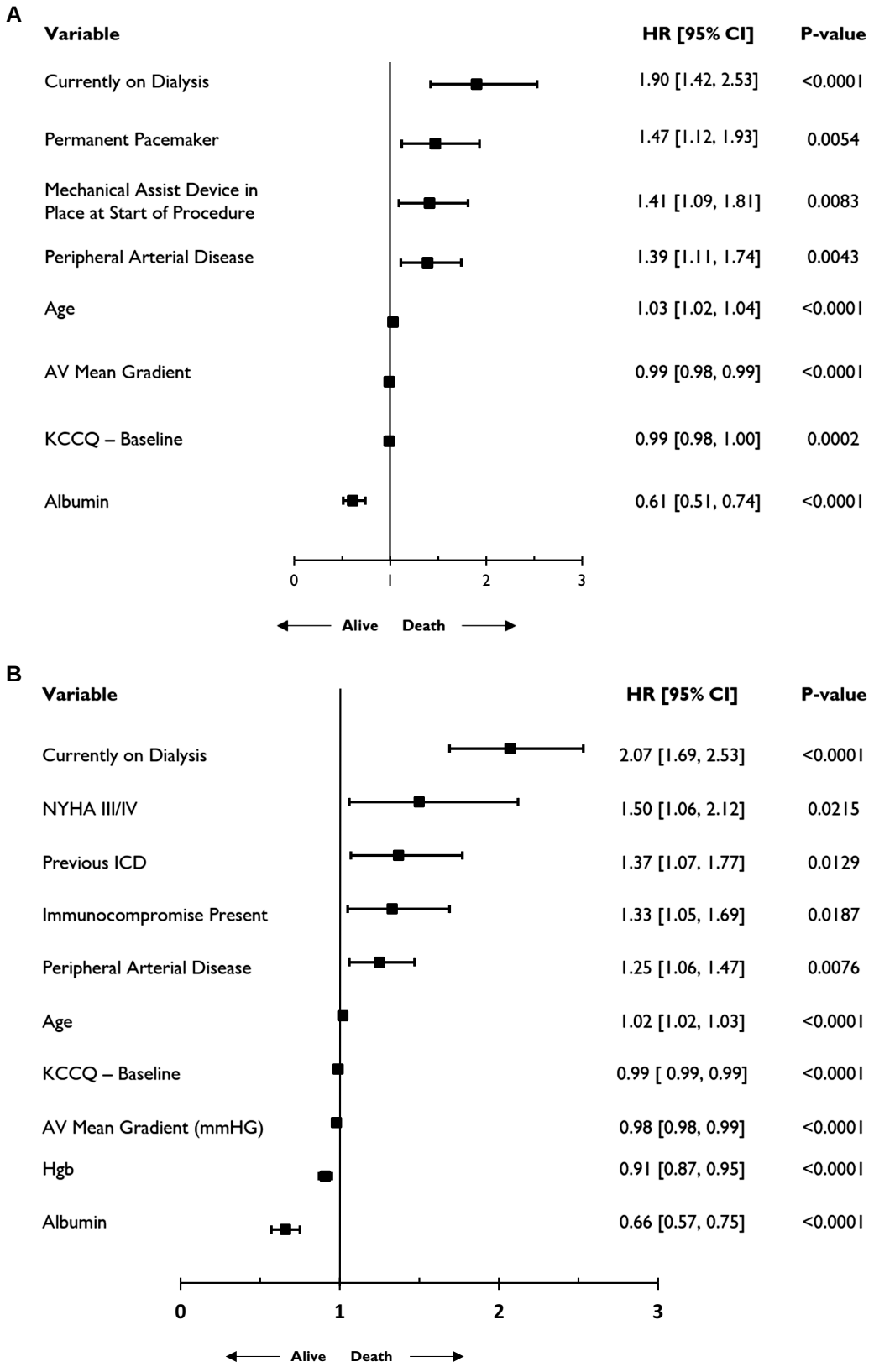


Figure 4 Multivariate predictors of all-cause mortality in patients with cardiogenic shock. (*A*) Multivariate predictors of all-cause mortality at 30 days in patients with cardiogenic shock. (*B*) Multivariate predictors of all-cause mortality at 1 year in patients with cardiogenic shock. AV, aortic valve; BL, baseline; HGB, haemoglobin; VIV, valve-in-valve; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction.

offered TAVR due to futility. All the data are site-reported. This may lead to data entry and coding errors as the TVT-R-R definition of CS may not apply to all cases. The mortality rate of those that were entered as CS on TVT-R forms was similar to the CS patients on inotropes alone, suggesting that coding of CS by the sites was accurate in identifying patients with CS. As there is lack of haemodynamic data or lactate levels, we included the best possible measures in the definition of CS. The recently published Society for Cardiovascular Angiography and Interventions shock stage classification defines classic CS (stage C) as a patient who manifests with hypoperfusion and who requires one intervention (pharmacological or mechanical) beyond volume resuscitation. These patients typically present with relative hypotension (but hypotension is not required).[15] Based on this, use of positive inotropes or MCS device prior to TAVR would classify patients as CS and were included the CS definition. Furthermore, we excluded same-day elective TAVR procedures who may have been inadvertently labelled as CS as explained in the 'Methods' section (see Supplementary data online, *Table S1*). PCI was performed in 30% of the CS patients who presented with MI within 30 days of TAVR as per the operator discretion. As the registry did not collect data on completeness of revascularization, its effect on outcomes cannot be determined. This study only included balloon-expandable valves, so the outcomes cannot be extrapolated to self-expanding valves. The follow-up is based on the TVT-R-R only as Medicare linkage is not available currently. Complete 1-year follow-up was available in 76% patients, which is similar to the previously published TVT-R-R-based studies.[7,12,16] Although there was no significant difference in the missingness of data between the CS and non-CS groups, we cannot be certain that this did not affect the overall results. All patients were censored at the time of last follow-up. Lastly, multiple testing may have increased the risk of type I error.

Conclusions

This large observational real-world study demonstrates that TAVR can be performed safely and successfully in patients with CS with current generation balloon expandable S3 and S3U valves. Despite the high mortality associated with CS, > 90% of the patients survived the initial hospitalization, and the majority of these patients were alive at 1 year with a significant improvement in their QoL and functional status. Patients who survived the first 30 days after TAVR had similar mortality rates to those who were not in CS. TAVR should be considered as a definitive treatment in most patients in CS if they are anatomically suitable candidates and do not have prohibitive co-morbidities that would curtail long-term survival. Future efforts should be focused on timing and peri-TAVR management of shock to further improve outcomes.

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Supplementary data

Supplementary data are available at *European Heart Journal* online.

Declarations

Disclosure of Interest

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Data Availability

The analysed *data underlying this article are available in the article and in its* online supplementary data.

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Ethical Approval

Ethical approval was not required. The study has been approved by a central institutional review board (Advarra) and granted a waiver of informed consent by the Duke University School of Medicine Institutional Review Board under the Common Rule 45 CFR 46.3.

Pre-registered Clinical Trial Number

Not applicable.

Disclaimer

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