Propensity Matched Analysis Comparing Conscious Sedation Versus General Anesthesia in Transcatheter Aortic Valve Implantation

Wassim Mosleh, MD[a], Jeffrey F. Mather, MS[b], Mostafa R. Amer, MD[c], Brett Hiendlmayr, MD[d], Francis J. Kiernan, MD[d], and Raymond G. McKay, MD[d,*]

Conscious sedation (CS) has been increasingly utilized in transcatheter aortic valve implantation (TAVI). We aim to compare safety, efficacy, efficiency, and direct cost outcomes of patients who underwent TAVI with general anesthesia (GA) to those with CS. Records for all adult patients undergoing transfemoral TAVI at our institution between February 2012 and September 2018 were retrospectively screened. Patients were grouped by anesthesia treatment (GA or CS) and propensity matched. Safety (in-hospital and 30-day mortality, in-hospital and 30-day stroke, cardiac arrest, need for permanent pacemaker, and composite bleed/vascular adverse events), efficacy (follow-up echocardiographic findings), efficiency (procedure duration, fluoroscopy time, radiation dose, intensive care unit (ICU) stay, hospital length-of-stay, and discharge to home), and direct cost outcomes were compared. A total of 589 patients met our inclusion criteria. Propensity matching yielded 154 GA patients and 154 CS patients. There were no differences in the safety outcomes of in-hospital or 30-day mortality, in-hospital or 30-day stroke, cardiac arrest, and need for permanent pacemaker between GA and CS groups. There was a significant reduction in composite bleeding/vascular events in the CS group (8.4% vs 19.5%, $p < 0.01$). There were no differences in the follow-up echocardiograms with respect to aortic valve area, left ventricular ejection fraction, and incidence of moderate or severe aortic regurgitation. The CS group had shorter procedural fluoroscopy times and radiation dose, shorter length-of-stay and ICU stay, with similar procedural duration. CS patients were more likely to be discharged to home (59.7% vs 74.7%, $p < 0.01$). Total direct costs for CS were decreased in almost every departmental category, with a mean 10.4% reduction in overall direct costs ($p < 0.001$). In conclusion, TAVI with CS is associated with less bleeding and vascular events, lower procedural radiation exposure, reduced length of hospitalization and ICU stay, and lower direct costs in comparison with TAVI with GA. These outcomes occur without sacrificing procedural efficacy or safety. **(Am J Cardiol 2019;124:70−77)**

Transcatheter aortic valve implantation (TAVI) has been approved by the United States Food and Drug Administration as an alternative treatment for patients with severe symptomatic aortic stenosis who are deemed either extreme, high, or intermediate risk for surgical aortic valve replacement. The number of TAVI implantations in the US rose from 4,627 in 2012 to 24,808 in 2015,[1] an increase that underscores the need to better understand the risks and benefits of different periprocedural approaches. Recent developments in TAVI have hinged on reducing all aspects of its invasive nature including use of general anesthesia (GA), which induces a reversible and controlled loss of consciousness. In contrast to GA, conscious sedation (CS) focuses on the depression of awareness, whereby a patient's response to external stimuli becomes limited while allowing for the maintenance of an independently patent airway, the ability to respond to verbal stimuli, and faster recovery.[2] Multiple studies have shown the feasibility of CS without forgoing procedural success or safety.[3−5] Further studies have documented the superiority of CS over GA with respect to a reduction in procedure time, length of intensive care unit (ICU) stay, and overall patient length of hospitalization, with no effect on overall mortality.[2,4,6,7] Cost-effectiveness has not been fully addressed in these studies. In the present study, we aim to utilize propensity matching in a single-center to compare the safety, efficacy, efficiency, and cost associated with TAVI among those who underwent CS versus those who underwent GA.

Methods

This retrospective, observational study was conducted at Hartford Hospital, an 890 bed tertiary care urban medical center in Hartford, Connecticut. The Hartford Hospital Institutional Review Board (Assurance #FWA000000601) approved the study and certified that it met the criteria for a

[a]Division of Cardiology, University of Connecticut, Farmington, Connecticut; [b]Department of Research Administration, Hartford Hospital, Hartford, Connecticut; [c]Division of Primary Care Internal Medicine, University of Connecticut, Farmington, Connecticut; and [d]Division of Interventional Cardiology, Hartford Hospital, Hartford, Connecticut. Manuscript received February 3, 2019; revised manuscript received and accepted March 19, 2019.

See page 76 for disclosure information.

*Corresponding author: Tel: (860) 972-2975; fax: 860-545-3557.

E-mail address: raymond.mckay@hhchealth.org (R.G. McKay).

0002-9149/© 2019 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjcard.2019.03.042

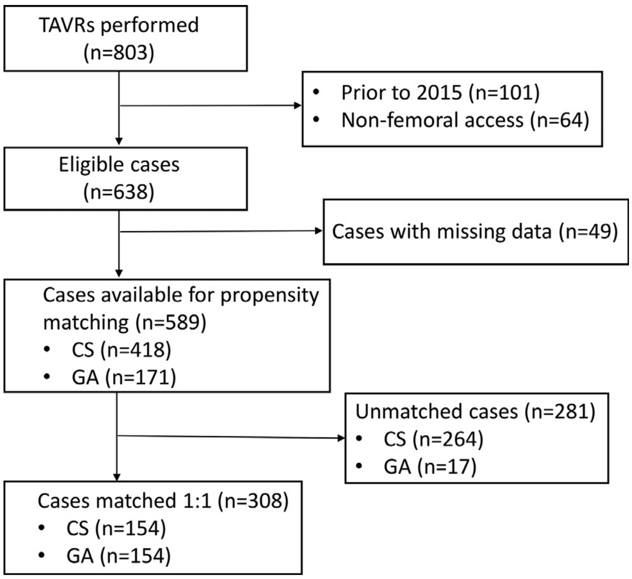

Figure 1. Consort diagram for patient selection. CS = conscious sedation; GA = general anesthesia; TAVI = transcatheter aortic valve implantation.

waiver of the requirement to obtain informed consent. A consort diagram is illustrated in Figure 1. All consecutive adults (age > 18 years) who underwent elective or urgent TAVI procedure at Hartford Hospital from February 2012 to September 2018 and whose data were recorded in the STS/ACC TVT Registry (n = 803) were considered. Patients undergoing nonfemoral access and patients with TAVIs done before 2015 were excluded to minimize procedural and temporal confounders. From these patients, a cohort of 589 patients with no missing records were used to propensity-match patients grouped by the type of anesthesia, either GA or CS delivered at the initiation of the procedure. At our institution, following the introduction of CS, almost all subsequent patients were treated with CS, with the exception of cases requiring alternative vascular access and for those that required intraoperative transesophageal echocardiography (TEE) for valve sizing when their kidney function did not allow for safe use of preprocedure CT-angiography. The decision to utilize GA due to potential risk for airway compromise, based on Mallampati Classification, previous history of stroke, or assessment by the Alderte Scale or the American Society of Anesthesia classification, was made on an individual basis by a multidisciplinary Heart Team consisting of cardiologists, cardiac surgeons, and anesthesiologists.

As defined by the STS/ACC TVT Registry, GA is defined as “a drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation”, while CS is defined as “a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation.” Compared outcome measures included in-hospital and 30-day mortality, in-hospital and 30-day stroke, cardiac arrest, need for permanent pacemaker, composite bleeding/vascular event, delirium, discharge to home, hospital length-of-stay, procedural duration, ICU stay, and direct costs. Total direct cost for each patient was extracted from Allscripts EPSi software (Allscript, Raleigh, North Carolina). The costs included were only those accrued at the index admission, pre- and postoperatively. Total direct cost are the expenses directly related to patient care for each department specific charge code, excluding indirect cost associated with overhead or indirect charges. CS direct cost data is expressed as a percentage of the GA group. Additional variables are as defined in the STS/ACC TVT Registry data dictionary.[7] All outcomes reported by the site to the registry were done using Valve Academic Research Consortium definitions.[8,9] The STS/ACC TVT Registry Adverse Event Definitions were used for composite bleeding or vascular adverse events.

The Edwards Sapien valve (Edwards Life sciences, Irvine, California) was first used in February 2012, and the Medtronic CoreValve prosthesis (Medtronic, Minneapolis, Minnesota) was first used in February 2013. In August 2014, the Edwards Sapien XT was introduced, followed by the Medtronic CoreValve Evout R and Evolut PRO in September 2015. Shortly afterwards, in October 2015, the Edwards Sapien 3 was used. Valve choice was at the preference of the heart team. We restricted cases using transfemoral access only. In addition, we included only cases performed after 2014 as GA was used exclusively as the anesthesia choice until June 2015 when CS was introduced.

To control for confounding introduced by nonrandom patient-associated factors related to choice of anesthesia, a propensity score (PS) was developed to characterize the probability of receiving either GA or CS. The PS was created from a logistic regression analysis by modeling anesthesia type as the dependent variable. Covariates for the logistic regression for calculating the PS included the STS risk score, diabetes, preprocedure creatinine, and the previous 2-week NYHA class. Patients were matched 1:1 using nearest neighbor matching with a caliper of 0.1 SD of the PS. The quality of the matching was determined by assessing whether any variable or linear combination of variables were significantly unbalanced after matching using the model imbalance chi-square test. Overall model performance was measured using Nagelkerke’s R2, a measure of explained variance and the Hosmer-Lemeshow test.

Continuous variables are expressed as mean ± SD or median (interquartile range) and were compared with a Student’s *t* test or the Mann-Whitney *U* test, respectively. Categorical variables were analyzed using the chi-square test or Fisher’s exact test, as appropriate. Event rates were generated using the Kaplan-Meier method and log-rank tests were used for group comparisons. All effects were considered significant at $p < 0.05$. The statistical analyses were performed with SPSS 21.0 (SPSS, Chicago, Illinois). PS matching was performed using PS Matching for SPSS, version 3.0.4.

Results

Of the 803 patients undergoing TAVI procedures considered for screening, 589 met the inclusion and exclusion criteria with no missing records and were subject to propensity matching. After grouping of patients by the type of anesthesia, either GA or CS, with 1:1 matching, a total of 308 cases remained for analysis. The final study groups that were analyzed included a total of 154 patients in the GA group and 154 patients in the CS group, leaving 281 unmatched patients (Figure 1).

In the entire TAVI patient population (n = 803), a total of 366 (46%) patients received GA, 425 (53%) received CS, and 5 (1%) received a combination with conversion from CS to GA. When compared to the 308 matched patient cohort, the unmatched general population had a slightly increased proportion of patients with peripheral vascular disease, had fewer patients with diseased coronary vessels, and a lower incidence of heart failure 2 weeks before the TAVI procedure (Table 1). Patients in the CS and GA subgroups were well-matched based on assessed characteristics (Table 1). The overall balance test for the matching was not significant (p = 0.96) confirming no significant unbalance after matching. Due to the temporal differences in the introduction of TAVI valves, there were significant differences in types of devices used between the CS and GA matched groups, with a larger proportion of Edwards Sapien 3 valves and lower proportion of Medtronic Corevalve, Evolut R and Evolut PRO valves used in the CS group (Table 1).

There were no significant differences between the 2 cohorts in regards to follow-up echocardiographic parameters including postprocedure, 30-day, and 1-year left ventricular ejection fraction, incidence of moderate or severe aortic regurgitation, and postprocedure valve area (Table 2). However, there was a statistically significant increase in AV Mean gradient in the CS group at 1 year. There were no differences in rates of in-hospital and 30-day mortality, in-hospital and 30-day stroke, cardiac arrest, and need for permanent pacemaker, between GA and CS groups (Table 3). There was a significant reduction in the CS group compared to the GA group with respect to composite bleeding/vascular events (Table 3, Figure 2). Postoperative delirium trended lower in the CS group, as did postoperative bleeding and hospital readmission.

There was no significant difference in GA versus CS cohorts with respect to procedure duration. However, the CS group required shorter fluoroscopy time, lower fluoroscopy dose-area-product, and fluoroscopy dose Air kerma. ICU stay was shorter in the CS group. In addition, hospital LOS was also lower in the CS group by 1 day. Finally, a higher percentage of patients in the CS group were discharged home. Hospital total direct costs for CS were decreased in almost every category, with a mean 10% reduction in direct overall costs ($p < 0.001$). The breakdown of costs in the CS cohort as a percentage of costs in the GA cohort for each category, along with the proportions of each cost category from the total cost is summarized in Table 4 and Figure 3.

Due to the baseline differences in valve types used between the 2 cohorts, we performed 2 additional sensitivity analyses. Because of differences in the relative percentages of balloon-expandable versus self-expanding prostheses in the CS and GA groups, we performed a cost analysis examining only the Sapien 3 valve that yielded a similar outcome of a 12% reduction in direct costs for the CS cohort (88% of GA direct cost, $p < 0.01$). In addition, given that 100% of the CS group had new generation valves (Sapient 3, Evolut R or Evolut PRO) compared to 65% of the GA group, we performed another sensitivity analysis, including valve-type as a variable in the propensity matching. This resulted in a significantly lower number of patients in each cohort (109 in each cohort) with each cohort receiving only Sapien 3, Evolut R or Evolut Pro valves, and with no significant differences in the distribution of balloon-expandable and self-expanding prostheses between the 2 study groups. This second analysis continued to show no significant differences between CS and GA with respect to any of the safety outcomes, and the difference in composite vascular/bleeding outcome was no longer significant (11.9% vs 14.7%, p = 0.550). CS patients continued to have a significantly lower fluoroscopy time (minutes, 22.5 ± 7.22 vs 25.38 ± 10.86, p = 0.025), lower fluoroscopy dose-area-product (Gy-cm2, 38,206 ± 33,085 vs 50,740 ± 52,624,p = 0.038), lower fluoroscopy dose Air kerma (Gy, 1,198 ± 1,250 vs 1,859 ± 1,453, $p < 0.001$), and an even larger reduction in hospital LOS (days, 7.00 ± 6.06 vs 9.68 ± 8.06, p = 0.006). The CS group no longer showed a higher AV gradient at 1-year follow-up, and instead showed a lower AV gradient at 30-day follow-up (mmHg, 8.71 ± 3.52 vs 10.85 ± 5.20, p = 0.001). Postprocedure, 30-day and 1-year follow-up aortic regurgitation were similar in both groups. Finally, CS still had a significant mean direct-cost reduction of 8.1% (p = 0.006).

Discussion

As TAVI use has become more widespread, the evolution of TAVI technology and the adoption of fast-track protocols have been examined in efforts to decrease procedural costs and improve clinical outcomes. One of these changes has been the increasing utilization of CS. In a study of a large TAVI population (n = 10,997) using the STS/ACC TVT Registry, a comparative effectiveness analysis was performed supporting the hypothesis that TAVI with CS is associated with superior clinical outcomes in comparison with TAVI with GA, without significantly sacrificing procedural efficacy or safety.[10] Similar outcomes have been reported by the German Aortic Valve Registry [11] and the French Aortic National CoreValve and Edwards 2 (FRANCE-2) Registry.[12] Because these studies have included patients treated between 2014 to 2015, 2011 to 2014, and 2010 to 2011, respectively, they may not be comparable with contemporary outcomes in patients referred for TAVI, given advancements in procedural techniques and in the specific TAVI valves implanted. Moreover, these reports advocated for future studies focusing on possible economic benefits, which they have not fully addressed. One study to date from the STS/ACC registry between 2012 and 2016 has analyzed cost differences between CS and GA anesthesia methods, although the study was limited by a small number of patients in the CS group.[13] Given that institutional costs may vary significantly, the present study adds to the current literature with its single-center experience of a larger cohort of CS patients. It also provides a more comprehensive comparison between GA and CS in regards to all factors including safety, efficacy, efficiency, and costeffectiveness.

The present study demonstrates that the use of CS compared to GA did not compromise procedural safety with

Table 1
Baseline characteristics of the unmatched and propensity-matched cohorts

Variable	Unmatched (n = 281)	GA (n = 154)	CS (n = 154)	p Value
Age (years)	81.36 ± 8.31	80.31 ± 9.31	82.06 ± 7.41	0.068
Female	355 (45%)	65 (42%)	82 (53%)	0.052
BSA (m^2)	1.89 ± 0.27	1.93 ± 0.28	1.86 ± 0.25	0.021
BMI (kg/m^2)	28.35 ± 6.76	29.87 ± 7.67	27.24 ± 5.28	0.001
Race (White)	769 (97%)	149 (97%)	148 (96%)	0.759
Hypertension	728 (91%)	142 (92%)	138 (90%)	0.428
Diabetes mellitus	280 (35%)	54 (35%)	45 (29%)	0.272
Smoker (current or within 1 year)	46 (6%)	10 (6%)	4 (3%)	0.101
Previous MI	208 (26%)	39 (25%)	38 (25%)	0.895
Previous PCI	207 (26%)	37 (24%)	36 (23%)	0.893
Previous CABG	161 (20%)	25 (16%)	30 (19%)	0.457
Atrial fibrillation or flutter	619 (77%)	114 (74%)	107 (70%)	0.603
Peripheral artery disease	204 (25%)	30 (19%)	26 (17%)	0.555
Previous stroke	88 (11%)	10 (6%)	19 (12%)	0.079
Previous TIA	54 (7%)	5 (3%)	11 (7%)	0.123
Chronic lung disease		#N/A	#N/A	0.545
No chronic lung disease	315 (40%)	52 (35%)	59 (39%)	
Mild chronic lung disease	158 (20%)	30 (20%)	36 (24%)	
Moderate chronic lung disease	127 (16%)	30 (20%)	23 (15%)	
Severe chronic lung disease	182 (23%)	36 (24%)	32 (21%)	
End stage renal disease	23 (3%)	3 (2%)	4 (3%)	0.702
Previous aortic balloon valvuloplasty	29 (4%)	3 (2%)	5 (3%)	0.474
Previous surgical aortic valve replacement	35 (4%)	12 (8%)	7 (5%)	0.236
Creatinine (mg/dl)	1.33 ± 1.18	1.34 ± 1.10	1.24 ± 1.14	0.422
Hemoglobin (g/dl)	11.52 ± 1.97	11.46 ± 1.72	11.50 ± 1.71	0.855
Albumin (g/dl)	3.73 ± 0.48	3.60 ± 0.53	3.75 ± 0.43	0.009
FEV1 (% predicted)	69.65 ± 24.55	67.45 ± 22.24	68.81 ± 24.21	0.617
DLCO (% predicted)	71.02 ± 22.15	71.54 ± 22.54	72.42 ± 22.94	0.760
STS risk score (%)	10.89 ± 7.95	10.95 ± 8.41	10.34 ± 7.59	0.504
Low risk	13 (2%)	0 (0%)	4 (3%)	
Intermediate risk	135 (17%)	18 (12%)	33 (21%)	
High risk	390 (49%)	93 (60%)	83 (54%)	
Inoperable/extreme risk	257 (32%)	43 (28%)	34 (22%)	
KCCQ12	47.46 ± 24.54	41.66 ± 22.44	45.92 ± 24.28	0.128
AV annulus size (mm)	24.39 ± 2.65	24.43 ± 2.71	24.27 ± 2.56	0.595
MV regurgitation		#N/A	#N/A	0.900
None	18 (4%)	4 (6%)	5 (6%)	
Trace/trivial	68 (16%)	9 (14%)	12 (14%)	
Mild	188 (43%)	24 (38%)	39 (46%)	
Moderate	140 (32%)	22 (35%)	24 (28%)	
Severe	20 (5%)	4 (6%)	5 (6%)	
Aortic regurgitation		#N/A	#N/A	0.661
None	162 (21%)	32 (21%)	25 (17%)	
Trace/trivial	147 (19%)	24 (16%)	30 (20%)	
Mild	335 (43%)	68 (45%)	65 (43%)	
Moderate	117 (15%)	24 (16%)	24 (16%)	
Severe	22 (3%)	4 (3%)	7 (5%)	
AV peak velocity (m/s)	4.16 ± 0.67	4.17 ± 0.75	4.12 ± 0.68	0.552
LV internaldiastolic dimension (cm)	4.49 ± 0.76	4.53 ± 0.85	4.46 ± 0.76	0.405
AV area (cm^2)	0.69 ± 0.25	0.71 ± 0.38	0.69 ± 0.19	0.574
Number narrowed coronary arteries		#N/A916	#N/A	0.162
None	324 (41%)	24 (16%)	37 (24%)	
1	161 (20%)	23 (15%)	30 (19%)	
2 or 3	304 (39%)	104 (67%)	86 (57%)	
Left main ≥50%	78 (10%)	12 (8%)	15 (10%)	0.546
Proximal LAD ≥70%	154 (19%)	20 (13%)	33 (21%)	0.050
AV Peak Gradient (mmHg)	71.52 ± 22.54	74.18 ± 24.04	68.72 ± 20.69	0.061
NYHA Class (within 2 weeks)		#N/A	#N/A	0.999
I	58 (7%)	3 (2%)	3 (2%)	
II-III	559 (71%)	109 (69%)	107 (69%)	
IV	170 (22%)	45 (29%)	44 (29%)	

(*continued*)

Table 1 (*Continued*)

Variable	Unmatched (n = 281)	GA (n = 154)	CS (n = 154)	p Value
Device type		#N/A	#N/A	<0.01
Edwards Sapien	46(6%)	1 (1%)	0	
Edwards Sapien XT	33(4%)	18 (12%)	0	
Edwards Sapien 3	448 (57%)	74 (48%)	122 (81%)	
Medtronic corevalve	88 (11%)	30 (19%)	0	
Medtronic Evolut R	120 (15%)	26 (17%)	22 (15%)	
Medtronic Evolut Pro	50 (6%)	5 (3%)	6 (4%)	
Contrast volume (ml)	105.67 ± 50.13	98.95 ± 49.05	100.30 ± 42.80	0.797
Fluoroscopy time (min)	25.94 ± 13.85	27.63 ± 11.03	22.26 ± 7.53	<0.01
Fluoroscopy dose DAP (mGycm^2)	50,101 ± 73,376	52,432 ± 60,710	34,883 ± 31,257	0.002
Fluoroscopy dose air kerma (mGy)	1,748 ± 1,683	2,215 ± 1,614	1,277 ± 1,200	<0.01

Values are number (%), mean ± SD, or median (quartiles). p Value is for GA and CS group comparison.

AV = aortic valve; BMI = Basal Metabolic Index; BSA = body surface area; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CTA = computer tamography with angiography; CS = conscious sedation; DAP = dose area product; DLCO = diffusing capacity of the lungs for carbon monoxide; FEV1 = forced expiratory volume in the first second; GA = general anesthesia; INR = international normalized ratio; KCCQ 12 = Kansas City Cardiomyopathy Questionnaire 12; LAD = Left anterior descending artery; LV = left ventricle; MI = myocardial infarction; MV = mitral valve; Non-STEMI = non ST segment elevation myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RV = right ventricle; STS = society of thoracic surgeons; TEE = tranesophageal echocardiogram; TIA = transient ischemic attack; TTE = transthoracic echocardiogram.

similar rates of in-hospital and 30-day death and stroke, cardiac arrest, and need for permanent pacemaker. Moreover, the CS group was safer in terms of lower combined vascular and bleeding complications. This finding is in agreement with a report by Toppen et al where there were less bleeding events overall in the CS cohort,[13] but in contrast to a study by Brecker et al where they observed no differences in any of the bleeding events and significantly more major vascular complications in the CS group.[14] In this latter study, there was a higher incidence of surgical cut-down as the initial strategy in the GA group, which was considered a complication in the CS group if utilized.

One of the main theoretical concerns of using CS over GA is a higher incidence of paravalvular leakage and an increased need for permanent pacemaker implantations.[12,14,15] In part, these adverse outcomes may be related to decreased use of intraprocedural TEE with decreased ability to assess aortic regurgitation and decreased optimal

Table 2
Comparison of follow-up echocardiographic data of the propensity-matched cohorts

Variable	GA (n = 154)	CS (n = 154)	p Value
LVEF (%)#N/A			
Preprocedure	53.46 ± 17.24	54.34 ± 15.19	0.638
30-day	55.57 ± 13.13	55.76 ± 12.26	0.899
1 year	54.44 ± 14.27	56.26 ± 12.80	0.531
AV mean gradient (mmHg)			
Preprocedure	43.50 ± 14.55	41.56 ± 13.36	0.232
Postprocedure	7.67 ± 7.87	6.76 ± 13.98	0.667
30-day	9.76 ± 5.04	10.32 ± 5.17	0.366
1-year	9.52 ± 4.74	12.29 ± 7.64	0.030
Postprocedure aortic regurgitation			0.064
None	60.00 (40%)	64.00 (42%)	
Trace/trivial	35.00 (23%)	50.00 (32%)	
Mild	45.00 (30%)	37.00 (24%)	
Moderate	10.00 (7%)	3.00 (2%)	
Severe	0.00 (0%)	0.00 (0%)	
30-day aortic regurgitation			0.187
None	62.00 (44%)	66.00 (48%)	
Trace/trivial	25.00 (18%)	28.00 (20%)	
Mild	39.00 (27%)	38.00 (28%)	
Moderate	16.00 (11%)	6.00 (4%)	
Severe	0.00 (0%)	0.00 (0%)	
1 year aortic regurgitation			0.225
None	28.00 (45%)	18.00 (51%)	
Trace/trivial	14.00 (23%)	8.00 (23%)	
Mild	13.00 (21%)	9.00 (26%)	
Moderate	7.00 (11%)	0.00 (0%)	
Severe	0.00 (0%)	0.00 (0%)	

Values are number (%), mean ± SD, or median (quartiles).

AV = aortic valve; CS = conscious sedation; ECHO = echocardiogram; GA = general anesthesia; LVEF = left ventricle ejection fraction.

Table 3
In-hospital and 30-day outcomes between the propensity-matched general anesthesia (GA) and conscious sedation (CS) cohorts

Variable	GA (n = 154)	CS (n = 154)	p Value
In-hospital outcomes			
Death	2 (0.7%)	0 (0%)	0.156
Stroke	4 (2.6%)	3 (1.9%)	0.702
Cardiac arrest	4 (2.6%)	2 (1.3%)	0.684
Conduction disturbance requiring pacemaker	31 (20.1%)	20 (13.0%)	0.092
Bleed/vascular*	30 (19.5%)	13 (8.4%)	0.005
Delirium	21 (13.6%)	13 (8.4%)	0.146
Procedural duration, min	78.5 (65-107)	77.0 (65-92)	0.226
LOS (days)	6.0 (4.0-12.3)	5.0 (3.0-9.3)	0.001
ICU (hours)	24.2 (0-44.3)	20.0 (0-28.5)	0.003
Discharge home	92 (59.7%)	115 (74.7%)	0.005
30 day outcomes			
Mortality	2 (1.3%)	3 (1.9%)	0.652
Stroke	4 (2.6%)	3 (1.9%)	0.702
Hospital readmission	50 (32.5%)	35 (22.7%)	0.056

Values are number (%), mean ± SD, or median (quartiles).

CS = conscious sedation; GA = general anesthesia; ICU = intensive care unit; LOS = length of stay.

* Bleed/vascular: the composite outcome of bleed/vascular adverse events as defined by the STS/ACC TVT Registry's adverse event definitions v2.0.

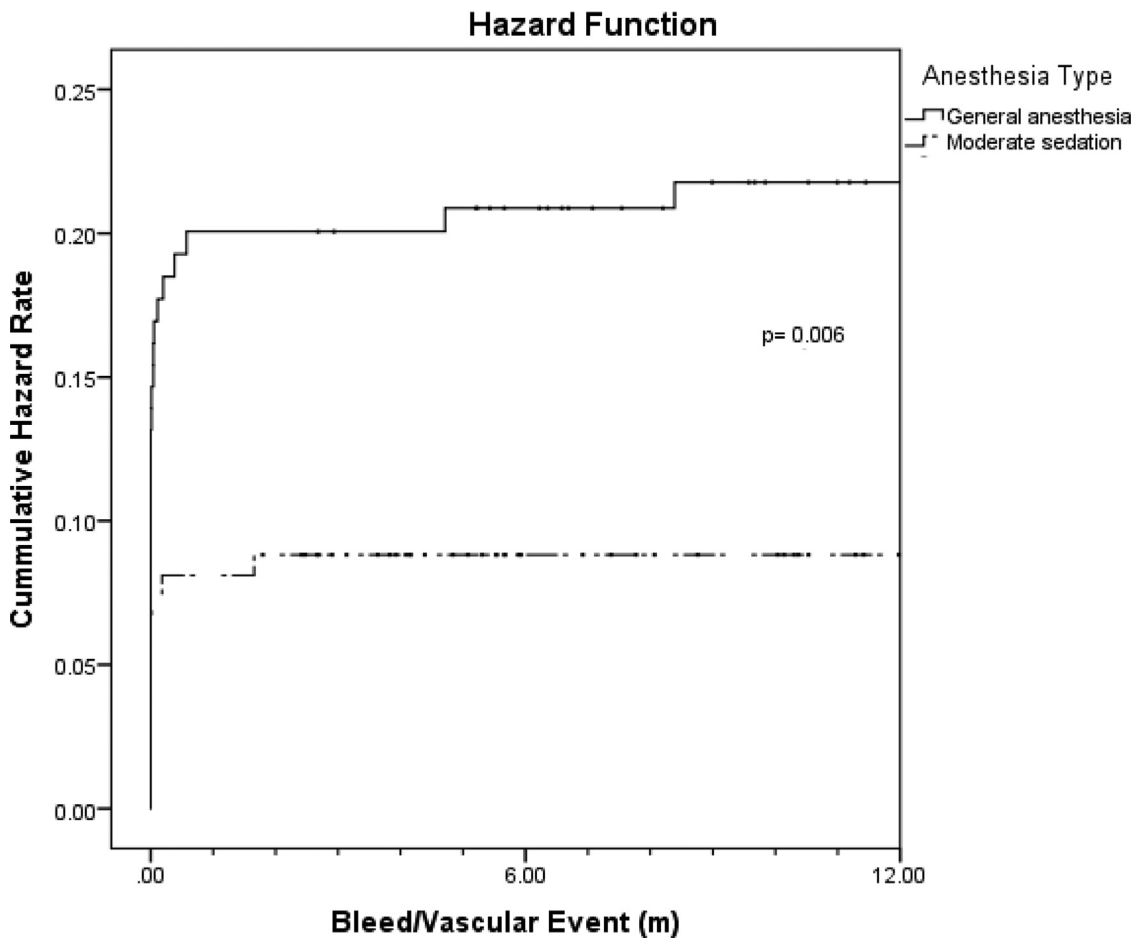

Figure 2. Illustration of the cumulative hazard function of the composite bleeding and vascular events in the conscious sedation (CS) group compared to the general anesthesia (GA) group over time in months (m) (19.5% vs CS 8.4%, p < 0.01).

positioning of the TAVI prosthesis in the aortic annulus.[16] In contrast to previous studies, and in agreement with study by Husser et al,[11] the present study found no differences in postprocedure, 30-day and 1-year moderate/severe aortic regurgitation and no difference in need for in-hospital pacemaker implantation between the 2 anesthesia strategies, arguing against the absolute need for routine TEE during the procedure.

Table 4
Cost analysis

Direct cost category	% of GA direct cost	p Value	% of total cost GA	% of total cost CS
Anesthesia	103.9%	0.552	0.8%	1.0%
Laboratory	76.4%	0.132	2.1%	1.3%
ICU/SDU	52.9%	0.001	7.9%	4.7%
Operating room	46.4%	0.001	3.3%	1.7%
Pharmacy	53.4%	<0.001	1.5%	0.9%
Radiology	73.5%	0.081	0.5%	0.4%
Cardiology	98.6%	0.307	75.9%	83.5%
Rehab	68.6%	<0.001	0.3%	0.2%
Nursing	73.9%	0.021	1.0%	0.8%
Respiratory care	40.7%	0.012	1.4%	0.6%
Other*	78.5%	0.235	7.3%	6.9%
Total	89.6%	<0.001	100.0%	100.0%

CS = conscious sedation; GA = general anesthesia; ICU = intensive care unit; SDU = step down unit.

* Other: assessment center, dialysis, central sterile, electrophysiology, emergency room, GI endoscopy, IV therapy, medical supplies, medical service, dental clinic, palliative care, orthopedics, pulmonary lab, speech therapy, surgical service, and vascular lab.

In this study, the use of CS was associated with reduced hospital and ICU length of stay and a significant reduction in fluoroscopy time and radiation exposure despite similar procedure durations. These results may have been related to less hemodynamic instability and a lower requirement for vasoactive medications associated with GA, with an overall lower level of patient acuity. The reduced time spent in the hospital and ICU are vital as it has been independently proven to lower the risk of hospital-acquired infections and mortality.[17]

While previous large registry-based studies suggested that the use of CS with a less complicated postprocedural course may result in a significant reduction in health care expenses, this hypothesis has not been fully validated. In our study, we have demonstrated that time-efficiency also translated to costeffectiveness as CS also showed significant decrease in almost every cost category, with an average 10% reduction in direct overall costs. This is in agreement with Toppen et al,[13] although the cost saving was greater, at >25%. Respiratory care and pharmacy costs showed the largest reductions with the introduction of CS.

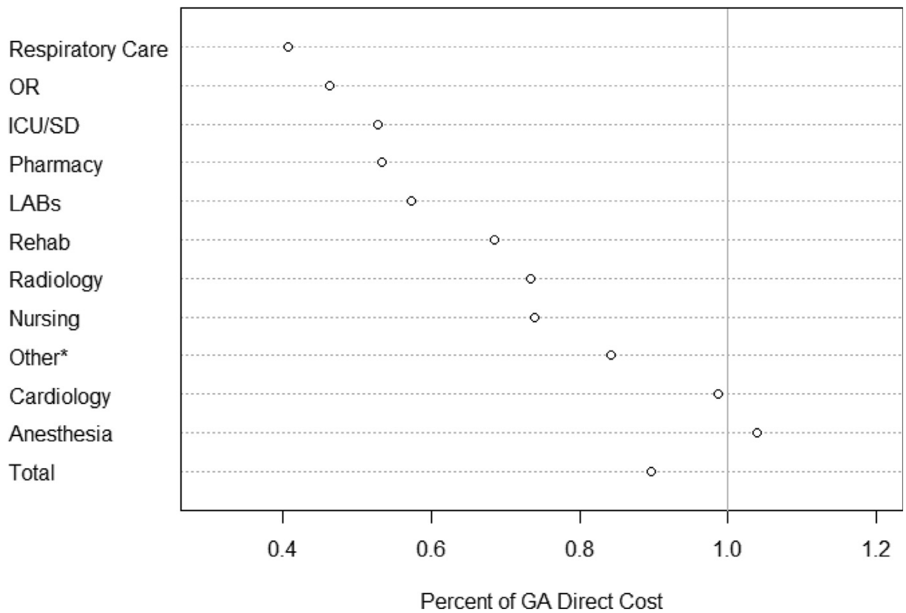

Figure 3. The breakdown of costs in the conscious sedation (CS) cohort as a percentage of costs in the general anesthesia (GA) cohort for each category.

However, laboratory, operating room, radiology, cardiology, rehabilitation, and nursing costs all showed significant reductions with CS. Anesthesia costs in contrast did not differ significantly. While costs may vary from 1 institution to another, our study offers promising economic outcomes for utilization of CS in TAVI procedures.

In addition to a reduction in in-hospital direct costs, the economic benefits of CS may extend to less financial penalties incurred by the postdischarge Medicare Post-Acute Care Transfers (PACT) policy.[18] Post-Acute Care Transfer reduces hospital reimbursement when a TAVI patient is transferred to another health-care facility after staying fewer days than the national average as measured by CMS. In the present study, a higher percentage of TAVI patients were discharged to home. Higher rates of discharge to home may indicate that more patients are functionally capable of self-care postoperatively, without the need for transfer to inpatient rehabilitation or skilled nursing facilities.

In comparison to previous reports, the present study describes outcomes in contemporary patients referred for TAVI, with a large percentage of patients receiving either the Edwards Sapien 3 or Medtronic Evolut prostheses. Secondary sensitivity analyses have confirmed similar CS cost reduction with the Sapien 3 valve alone, and have confirmed conclusions on safety, efficacy, efficiency, and direct cost reduction in an analysis of only latest generation Sapien 3, Evolut R and Evolut PRO prostheses. Our study is the largest to date to report cost-effectiveness outcomes comparing GA versus CS approaches in TAVI patients.

As a single center, observational study with a relatively small sample size, there remains a need for an adequately powered, multi-center, randomized controlled trial for validation. While propensity matching is a recognized approach to reduce selection bias in observational studies, we cannot discount the influence of residual bias. Our study had a temporal inclusion of patients spanning a period of 4 years, where GA was done earlier at our institution, and therefore procedural advancements and proceduralist skills may have been better in the CS cohort. Finally, we did not account for inflation during the 4-year period in the cost analysis.

In summary, this study supports the hypothesis that TAVI with CS is associated with lower direct costs in comparison with GA. This finding comes without sacrificing procedural efficacy or safety, encouraging the use of CS in future TAVIs.

Disclosures

There are no relationships with industry.

1. Grover FL, Vemulapalli S, Carroll JD, Edwards FH, Mack MJ, Thourani VH, Brindis RG, Shahian DM, Ruiz CE, Jacobs JP, Hanzel G, Bavaria JE, Tuzcu EM, Peterson ED, Fitzgerald S, Kourtis M, Michaels J, Christensen B, Seward WF, Hewitt K, Holmes DR Jr., Registry SAT. 2016 Annual report of The Society of Thoracic Surgeons/American College of Cardiology transcatheter valve therapy registry. *J Am Coll Cardiol* 2017;69:1215–1230.
2. Frohlich GM, Lansky AJ, Webb J, Roffi M, Toggweiler S, Reinthaler M, Wang D, Hutchinson N, Wendler O, Hildick-Smith D, Meier P. Local versus general anesthesia for transcatheter aortic valve implantation (TAVR)—systematic review and meta-analysis. *BMC Med* 2014;12:41.
3. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S, Investigators PT. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363: 1597–1607.
4. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ, Investigators PT. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–2198.

5. Babaliaros V, Devireddy C, Lerakis S, Leonardi R, Iturra SA, Mavromatis K, Leshnower BG, Guyton RA, Kanitkar M, Keegan P, Simone A, Stewart JP, Ghasemzadeh N, Block P, Thourani VH. Comparison of transfemoral transcatheter aortic valve replacement performed in the catheterization laboratory (minimalist approach) versus hybrid operating room (standard approach): outcomes and cost analysis. *JACC Cardiovasc Interv* 2014;7:898–904.
6. He W, Huang RR, Shi QY, Liu XB, Wang JA, Yan M. Bispectral index-guided sedation in transfemoral transcatheter aortic valve implantation: a retrospective control study. *J Zhejiang Univ Sci B* 2017;18:353–359.
7. Carroll JD, Edwards FH, Marinac-Dabic D, Brindis RG, Grover FL, Peterson ED, Tuzcu EM, Shahian DM, Rumsfeld JS, Shewan CM, Hewitt K, Holmes DR Jr., Mack MJ. The STS-ACC transcatheter valve therapy national registry: a new partnership and infrastructure for the introduction and surveillance of medical devices and therapies. *J Am Coll Cardiol* 2013;62:1026–1034.
8. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB, Valve Academic Research C. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *J Thorac Cardiovasc Surg* 2013;145:6–23.
9. Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, Krucoff MW, Mack M, Mehran R, Miller C, Morel MA, Petersen J, Popma JJ, Takkenberg JJ, Vahanian A, van Es GA, Vranckx P, Webb JG, Windecker S, Serruys PW. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. *Eur Heart J* 2011;32:205–217.
10. Hyman MC, Vemulapalli S, Szeto WY, Stebbins A, Patel PA, Matsouaka RA, Herrmann HC, Anwaruddin S, Kobayashi T, Desai ND, Vallabhajosyula P, McCarthy FH, Li R, Bavaria JE, Giri J. Conscious sedation versus general anesthesia for transcatheter aortic valve replacement: insights from the National cardiovascular data registry society of thoracic surgeons/American College of cardiology transcatheter valve therapy registry. *Circulation* 2017;136:2132–2140.
11. Husser O, Fujita B, Hengstenberg C, Frerker C, Beckmann A, Mollmann H, Walther T, Bekeredjian R, Bohm M, Pellegrini C, Bleiziffer S, Lange R, Mohr F, Hamm CW, Bauer T, Ensminger S, Board GE. Conscious Sedation versus general anesthesia in transcatheter aortic valve replacement: The German Aortic Valve Registry. *JACC Cardiovasc Interv* 2018;11:567–578.
12. Oguri A, Yamamoto M, Mouillet G, Gilard M, Laskar M, Eltchaninoff H, Fajadet J, Iung B, Donzeau-Gouge P, Leprince P, Leguerrier A, Prat A, Lievre M, Chevreul K, Dubois-Rande JL, Chopard R, Van Belle E, Otsuka T, Teiger E, Investigators FR. Clinical outcomes and safety of transfemoral aortic valve implantation under general versus local anesthesia: subanalysis of the French Aortic National CoreValve and Edwards 2 registry. *Circ Cardiovasc Interv* 2014;7:602–610.
13. Toppen W, Johansen D, Sareh S, Fernandez J, Satou N, Patel KD, Kwon M, Suh W, Aksoy O, Shemin RJ, Benharash P. Improved costs and outcomes with conscious sedation vs general anesthesia in TAVR patients: Time to wake up? *PLoS One* 2017;12:e0173777.
14. Brecker SJ, Bleiziffer S, Bosmans J, Gerckens U, Tamburino C, Wenaweser P, Linke A, Investigators AS. Impact of anesthesia type on outcomes of transcatheter aortic valve implantation (from the Multicenter ADVANCE Study). *Am J Cardiol* 2016;117:1332–1338.
15. Maas EH, Pieters BM, Van de Velde M, Rex S. General or local anesthesia for TAVI? A systematic review of the literature and meta-analysis. *Curr Pharm Des* 2016;22:1868–1878.
16. Hahn RT, Little SH, Monaghan MJ, Kodali SK, Williams M, Leon MB, Gillam LD. Recommendations for comprehensive intraprocedural echocardiographic imaging during TAVR. *JACC Cardiovasc Imaging* 2015;8:261–287.
17. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K, Investigators EIGo. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* 2009;302:2323–2329.
18. H.R. 2015—Balanced Budget Act of 1997. https://www.congress.gov/bill/105th-congress/house-bill/2015.