

# The association between different anesthetic techniques and outcomes in patients undergoing transfemoral aortic valve replacement

## ABSTRACT

**Background:** There is an increasing number of patients undergoing transfemoral aortic valve replacement (TAVR) with sedation. There is limited data assessing the efficacy and safety of the different types of sedative drugs. The objective was to compare two sedation techniques with regard to the need for vasoactive support, respiratory support, rate of conversion to general anesthesia (GA), common perioperative morbidities, intensive care unit (ICU) stay, and in-hospital mortality.

**Methods:** A retrospective chart review study conducted among patients who underwent TAVR at a specialized cardiac center between January 2016 and December 2019. Data collection included patient diagnosis, preoperative comorbidities, intraoperative outcomes, and postoperative outcomes.

**Results:** A total of 289 patients received local anesthesia; 210 received propofol infusion and 79 received a mixed propofol-ketamine infusion (Ketofol). The average age was  $75.5 \pm 8.9$  years and 58.1% of the patients were females. Comparing propofol and ketofol groups, 31.2% and 34.2% of the patients required drug support, 7.6% and 6.3% required conversion to GA, 46.7% and 59.5% required respiratory support, respectively. These intraoperative outcomes were not significantly different between groups,  $P = 0.540$ ,  $P = 0.707$ , and  $P = 0.105$ , respectively. In-hospital 30-day mortality in propofol and ketofol groups were 1.9% and 3.8%, respectively,  $P = 0.396$ . In both groups, the median post-procedure coronary care unit stay was 26 hours while post-procedure hospital stay was 3 days.

**Conclusions:** There were no significant differences in perioperative or postoperative outcomes in TAVR patients receiving either propofol or ketofol. Propofol infusion, either alone or with ketamine, is reliable and safe, with minimal side effects.

**Key words:** Hemodynamic, ketamine, mortality, postoperative outcome, procedural sedation, propofol, respiratory depression, transcatheter aortic valve replacement

## Introduction


Transfemoral aortic valve replacement (TAVR) is a growing substitute for surgical aortic valve replacement.<sup>[1]</sup> The procedure involves replacing a diseased valve, most commonly

a stenotic aortic valve, with a catheter-deployed prosthetic substitute.<sup>[1]</sup> Even though TAVR was first conducted in 2001, the procedure did not receive full US Food and Drug Administration approval until 2011.<sup>[2]</sup>

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Initially, TAVR was exclusively conducted for high-risk surgical patients.<sup>[3]</sup> It is now gaining popularity as the primary treatment option for lesser risk patients as well.<sup>[4]</sup> In the wake of the increasing number of patients undergoing TAVR, there is a growing interest in defining the most suitable anesthetic management.<sup>[5-7]</sup> The choice between general anesthesia (GA) or local sedation, in the form of monitored anesthesia care (MAC), is still a matter of contention.<sup>[5-7]</sup>

Although both GA and MAC are both effective techniques of anesthesia in cases of TAVR, a handful of studies have reported that MAC not only reduces procedure time, but also lessens intensive care and overall hospital stay, reduces costs, and is associated with fewer injuries compared with GA.<sup>[5,8]</sup> The superiority of MAC was questioned by some investigators.<sup>[9]</sup> However, two recent meta-analyses showed significant reduction in the incidence of several complications including stroke and hospital mortality with sedation.<sup>[8,10]</sup>

Although there is an increasing number of patients undergoing TAVR with sedation, there is limited data in literature regarding the comparative efficacy and safety of the different types of sedative drugs and techniques currently being used in MAC. In this study, we aim to share our center experience after shifting to MAC for almost all patients undergoing TAVR. Additionally, to compare different sedation techniques with regard to the need for vasoactive support, respiratory support, rate of conversion to GA, common perioperative morbidities, ICU stay, and in-hospital mortality.

## Methods

**Design and setting:** The current study was a retrospective chart review study conducted at Prince Sultan Cardiac Center (PSCC). PSCC is a 174-bed specialized cardiac center located in the heart of Riyadh city (Saudi Arabia) serving both pediatric and adult patients. PSCC provides state-of-the-art comprehensive cardiovascular services to armed forces personnel, their families, and other eligible patients.

**Patient selection:** The current study targeted patients with severe symptomatic aortic stenosis who underwent TAVR at PSCC between January 2016 and December 2019. Exclusion criteria included patients who did not complete the TAVR, patients with pre-procedure plan for GA, and patients who received only boluses (ketamine or other drugs) but did not receive infusion.

**Data collection:** It was collected using a structured data collection sheet and abstracted from the cardiology and anesthesia data sheets. The collected data included the

following information: patient demographics, medical history, preoperative patient diagnosis, NYHA class, cardiac presentation, intraoperative data related to the TAVR device insertion, and postoperative outcomes. Patient demographics included age at diagnosis, gender, weight, body mass index, and surface area. Medical history included cardiovascular problems particularly hypertension, prior coronary artery bypass graft (CABG), prior percutaneous coronary intervention (PCI), and/or peripheral vascular disease (PVD); endocrine problems particularly diabetes mellitus including treatment (oral hypoglycemic drugs or insulin therapy), hypothyroidism, or hyperthyroidism; respiratory problems particularly smoking, previous diagnosis and/or treatment of chronic lung disease, bronchial asthma and/or oxygen home sleep apnea; neuropsychiatric disease particularly a previous stroke, transit ischemic attack (TIA), carotid stenosis, dementia, depression, psychosis, or anxiety disorder; ASA classification, and other comorbidity particularly renal disease, liver disease, and/or anemia. The patient's cardiac condition at the time of the TAVR procedure included atrial fibrillation at the time of TAVR; heart failure two weeks or less prior to the TAVR; New York Heart Association Classification of Cardiac Function (NYHA Class); the presence and degree of coronary artery disease (CAD) at the time of TAVR; and left ventricle ejection fraction (LVEF) percentage. Intraoperative data included the type of anesthesia or sedation at the start of the procedure as well as airway and vasoactive support were added; intraoperative complications; length of the procedure; conversion from local anesthesia with sedation (LAS) to GA. The study outcomes included postoperative in-hospital mortality, length of stay in the coronary care unit (CCU), overall hospital stay, and the need for permanent pacemaker (PPM).

**Anesthetic management:** Intraoperative management was nearly identical in all patients of the two study groups. Typically, upon reaching the operating room table, the patient is monitored using a five-lead electrocardiogram (ECG), a pulse oximeter, and near infra-red spectrometry (NIRS). An arterial line was then inserted in radial artery for invasive blood pressure monitoring and frequent blood gas analysis. Additionally, two wide bore intravenous cannulas were inserted, typically one in each upper limb, mainly for the purposes of sedation, the administration of fluids, and/or vasoactive support drugs. Before the start of the procedure, baseline vitals were obtained and an arterial blood gas analysis at room air settings conducted. As the patient was being draped, sedation started and titrated up to a Richmond Agitation Sedation Scale (RASS) value of 3. Additional central venous access was obtained through femoral venous cannulation conducted by the operating cardiologist. Conversion to GA was typically imposed by

one of the following criteria: intra-procedure cardiac arrest, hemodynamic instability, acute pulmonary edema, or bleeding requiring femoral artery exploration and/or vascular surgery. Vasoactive drugs were administered whenever required in order to maintain hemodynamic stability. Post TAVR, all patients were transferred to the CCU for recovery. In case oxygen therapy support is required, patients were transferred with face mask oxygen supply. Patients who required conversion to GA were transferred to the CCU whilst intubated and ventilated.

Statistical analysis: Categorical data were presented as frequencies and percentages while continuous data were presented as mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. Distribution normality was assessed using the Kolmogorov-Smirnov test. Variables were compared between the two study groups. Chi-square or Fisher's exact test, as appropriate, was used to examine differences in categorical variables while student's *t*-test or Mann Whitney, as appropriate, was used to examine differences in continuous variables. All *P* values were two-tailed. A *P* value < 0.05 was considered significant. The SPSS (Version 25.0. Armonk, NY: IBM Corp) was used for all statistical analyses.

## Results

A detailed review of patients' records showed that 401 patients who underwent TAVR at PSCC between January

2016 and December 2019 were initially identified. As shown in Figure 1, 61 out of the 401 patients were excluded, due to incomplete anesthesia-related data (*n* = 60) or aborted TAVR procedure (*n* = 1). As shown in Figures 1 and 2, the two types of anesthesia were identified; 321 (94.4%) patients received LAS while 19 (5.6%) patients received pre-planned GA. Those who had pre-planned GA were also excluded. Among the patients who received LAS, 210 (65.4%) patients primarily propofol infusion plus propofol top-up boluses, 79 (24.6%) received primarily ketofol infusion plus a mix of propofol and ketamine boluses (at a ratio of 4:1), 32 (10.0%) patients received only boluses (ketamine or other drugs) but did not receive infusion. Other bolus drugs included fentanyl, midazolam, or propofol. Due to the small number of patients who received boluses only, they were further excluded from the study. This left 289 patients to be included in the current analysis: 210 (72.7%) in the propofol group and 79 (27.3%) in the ketofol group. A flowchart of the study population and the types of anesthesia received are shown in Figures 1 and 2.

Table 1 summarizes the baseline demographic and clinical characteristics of the included patients. The average age was 75.5 ± 8.9 years and 58.1% of the patients were females. The median (and IQR) of body mass index was 29.7 (26.4–34.6). The most frequent comorbidities were hypertension (77.5%), diabetes (62.5%), diabetes on insulin (26.6%), prior PCI (21.8%), chronic lung disease (10.4%), renal disease (10.0%), prior CABG (9.3%), and hypothyroidism (9.0%). Approximately,

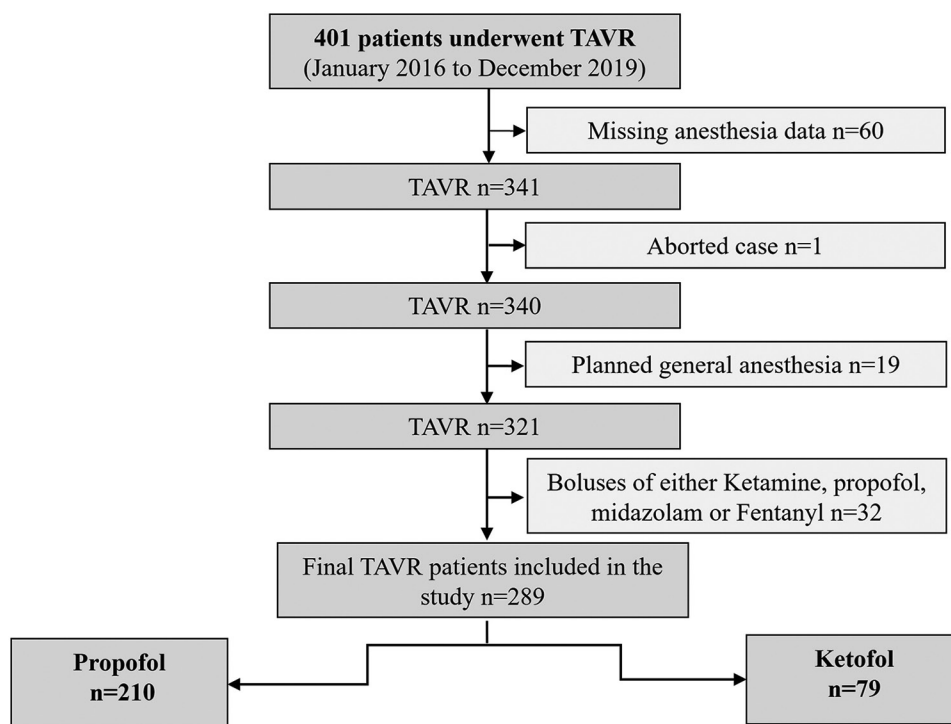
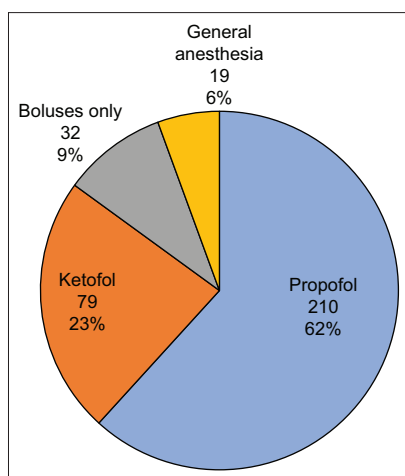


Figure 1: Study Flow Chart



**Figure 2: Different anesthetic techniques used in TAVR patients (N = 340).** Note: Propofol group included patients who received primarily propofol infusion plus propofol top-up boluses, Ketofol group included patients who received primarily ketofol infusion plus a mix of propofol and ketamine boluses (at a ratio of 4:1), boluses only group included patients who received only boluses of ketamine or other drugs but did not receive any infusion, and general anesthesia group included patients with pre-planned general anesthesia

37 (12.8%) of the patients were presented with heart failure within two weeks before TAVR and 4 (1.4%) were presented with fibrillation. The most frequent NYHA class was class III (58.5%), followed by class III (19.0%) and class IV (14.5%). The median (and IQR) of left ventricular (LV) ejection fraction was 55% (45%–60%). The most frequent CAD presentation was lack of angina (67.5%), stable angina (17.6%), unstable angina (8.7%), NSTEMI (5.5%), and lastly STEMI (0.7%). There was no significant difference in baseline demographic and clinical characteristics between the two groups, with the exception of higher prevalence of pre-TAVR heart failure presentation (22.8% versus 9.0%, 0.002) and presence of dementia (5.1% versus 0.5%, 0.021) in the ketofol group.

Table 2 shows the intraoperative data related to the TAVR device insertion among included patients. The main transcatheter heart valve used was the self-expandable (82.7%) valve while balloon expandable valve was used in only 17.3% of the patients. The majority (97.6%) of the implants were conducted successfully within 99 min on average. A total of 21 patients (7.3%) required conversion to GA. Almost one-third (32.1%) of the patients required drug support. This included mainly infusion (77.2%) and less extent boluses (45.7%). The most frequent complications were bleeding (5.5%) and packed red blood cells (PRBC) transfusion (5.8%), followed by temporary pacemaker (TPM) (3.1%), vascular intervention (2.4%), emergency PCI (2.1%), vascular stent (1.4%), para-valvular leak (1.0%), emergency CABG (0.3%), and cardiac tamponade (0.3%). The most frequent respiratory support at the end of the procedure was facemask or nasal

cannula (50.2%), followed by room air (44.3%) and lastly endotracheal intubation (5.5%). There was no significant difference in intraoperative data between the two groups, with the exception of higher prevalence of emergency PCI (5.1% versus 1.0%, 0.049) and immediate post-procedural moderate to severe para-valvular leak (3.8% versus 0.0%, 0.020) in the ketofol group.

Table 3 shows the intra-procedural outcomes among included patients. A total of 7 (2.4%) patients died, 4 (1.9%) in the propofol group and 3 (3.8%) in the ketofol. The median post-procedure CCU stay was 26 hours in both groups. The median post-procedure hospital stay was 3 days in both groups. PPM was implanted in 9 (3.1%) patients, 6 (2.9%) in the propofol group, and 3 (3.8%) in the ketofol group. There was no significant difference in the above study outcomes data between the two groups.

## Discussion

Medications typically used for procedural sedation include propofol, ketamine, fentanyl, and midazolam. They can be administered in different combinations, through either infusion or bolus techniques. Propofol's pharmacokinetic profile carries the known risks of cardiac depression and needs careful monitoring, particularly in patients with significant aortic stenosis.<sup>[11]</sup> Ironically, many centers use propofol infusion in sedation for TAVR. To the author's knowledge, this is the first study describing mixed ketamine-propofol (ketofol) use in TAVR. The results of this study show equivalent outcomes with propofol and ketofol infusions. There were no significant differences in the need for respiratory and circulatory support during the procedure. Additionally, overall hospital stay, ICU stay, and in-hospital mortality were similar in both groups.

Propofol in the current study was used in 62% of the TAVR patients while ketofol was used in 23% of the TAVR patients. Similarly, a large survey of the perioperative care for TAVR patients in European centers showed that MAC was performed in 44% of the patients. Propofol was used in more than 55% of the patients while ketamine was used only in 10% of the patients.<sup>[12]</sup> The infusion of a mixture of propofol and ketamine (ketofol) for sedation has been investigated in few studies, with mixed findings. The earliest report by Frizelle and colleagues suggested a better hemodynamic profile of ketofol compared with propofol for sedation during spinal anesthesia.<sup>[13]</sup> However, Kogan and colleagues observed a drop in mean arterial pressure (MAP) >20% or a decrease in oxygen saturation >5% in 6% and 5% of pediatric patients (respectively) during cardiac catheterization.<sup>[14]</sup>

**Table 1: Baseline demographic and clinical characteristics of TAVR patients who received local anesthesia (n=289)**

Variables	All patients (n=289)	Propofol (n=210)	Ketofol (n=79)	P
Age, years*	75.5±8.9	75.6±8.8	75.5±9.4	0.954
Gender				
Male	168 (58.1%)	126 (60.0%)	42 (53.2%)	0.294
Female	121 (41.9%)	84 (40.0%)	37 (46.8%)	
Weight, kg*	77.5±16.2	78.0±17.0	76.3±13.6	0.364
Body mass index, kg/m <sup>2</sup> *	29.7 (26.4-34.6)	30.1 (26.4-34.6)	29.4 (26.4-3.1)	0.861
Body surface area, m <sup>2</sup> *	1.8±0.20	1.8±0.21	1.8±0.17	0.829
History				
Hypertension	224 (77.5%)	165 (78.6%)	56 (74.7%)	0.480
Diabetes	181 (62.5%)	126 (60.0%)	55 (69.6%)	0.132
Diabetes on insulin	87 (26.6%)	56 (26.7%)	21 (26.6%)	0.988
Smoker	15 (5.2%)	8 (3.8%)	7 (8.9%)	0.084
Chronic lung disease	30 (10.4%)	19 (9.0%)	11 (13.9%)	0.226
Bronchial Asthma	13 (4.5%)	10 (4.8%)	3 (3.8%)	>0.99 <sup>s</sup>
PVD	1 (0.3%)	1 (0.5%)	0 (0.0%)	>0.99 <sup>s</sup>
Renal disease	29 (10.0%)	18 (8.6%)	11 (13.9%)	0.191
Liver disease	5 (1.7%)	3 (1.4%)	2 (2.5%)	0.617 <sup>s</sup>
Hypothyroidism	26 (9.0%)	19 (9.0%)	7 (8.9)	0.961
Hyperthyroidism	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Anemia	13 (4.5%)	7 (3.3%)	6 (7.6%)	0.119
Prior CABG	27 (9.3%)	21 (10.0%)	6 (7.6%)	0.531
Prior PCI	63 (21.8%)	45 (21.4%)	18 (22.8%)	0.803
Previous stroke	22 (7.6%)	17 (8.1%)	5 (6.3%)	0.614
TIA	3 (1.0%)	1 (0.5%)	2 (2.5%)	0.182 <sup>s</sup>
Carotid stenosis	6 (2.1%)	5 (2.4%)	1 (1.3%)	>0.99 <sup>s</sup>
Home oxygen	6 (2.1%)	4 (1.9%)	2 (2.5%)	0.666 <sup>s</sup>
Sleep apnea	5 (1.7%)	3 (1.4%)	2 (2.5%)	0.617 <sup>s</sup>
Dementia	5 (1.7%)	1 (0.5%)	4 (5.1%)	0.021 <sup>s</sup>
Depression	3 (1.0%)	2 (1.0%)	1 (1.3%)	>0.99 <sup>s</sup>
Psychosis	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Anxiety	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
ASA Class 3	319 (100%)	210 (100%)	79 (100%)	>0.99
Presentation				
Atrial Fibrillation	4 (1.4%)	3 (1.4%)	1 (1.3%)	>0.99 <sup>s</sup>
Heart failure within 2 weeks before TAVR	37 (12.8%)	19 (9.0%)	18 (22.8%)	<b>0.002</b>
NYHA Class				
Class I	23 (8.0%)	19 (9.0%)	4 (5.1%)	0.656
Class II	55 (19.0%)	41 (19.5%)	14 (17.7%)	
Class III	169 (58.5%)	121 (57.6%)	48 (60.8%)	
Class IV	42 (14.5%)	29 (13.8%)	13 (16.5%)	
CAD presentation				
No angina	195 (67.5%)	142 (67.6%)	53 (67.1%)	0.459
Stable angina	51 (17.6%)	35 (16.7%)	16 (20.3%)	
Unstable angina	25 (8.7%)	21 (10.0%)	4 (5.1%)	
STEMI	2 (0.7%)	2 (1.0%)	0 (0.0%)	
NSTEMI	16 (5.5%)	10 (4.8%)	6 (7.6%)	
LV ejection fraction, %*	55 (45-60)	55 (45-60)	55 (45-60)	0.294

Values are presented as number and percentage unless mentioned otherwise, \* mean±standard deviation or median (interquartile range). <sup>s</sup>P-values were derived from Fisher exact test. Abbreviations: PVD, peripheral vascular disease; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; TIA, transient ischemic attack; ASA, American Society of Anesthesiologist; TAVR, transcatheter aortic valve replacement; NYHA, New-York heart Association; CAD, coronary artery disease; STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; LV, left ventricle

Additionally, ketofol has been shown in a clinical trial design to be less favorable than etomidate for induction of anesthesia in patients with LV dysfunction undergoing coronary artery

bypass graft surgery.<sup>[15]</sup> On the other hand, ketofol has been compared with propofol in patients undergoing TAVR with good outcomes.<sup>[16,17]</sup> Ketofol in TAVR had a better safety

**Table 2: Intraoperative outcomes among TAVR patients who received local anesthesia (n=289)**

	All patients (n=289)	Propofol (n=210)	Ketofol (n=79)	P
Transcatheter heart valve used				
Balloon expandable	50 (17.3%)	39 (18.6%)	11 (13.9%)	0.352
Self-expandable	239 (82.7%)	171 (81.4%)	68 (86.1%)	
Implant success	282 (97.6%)	205 (97.6%)	77 (97.5%)	0.941
Procedure time (average)	99	96	107.5	0.709
Conversion to GA	21 (7.3%)	16 (7.6%)	5 (6.3%)	0.707
Drug support				
No support	195 (67.9%)	143 (68.8%)	52 (65.8%)	0.540
Support needed	94 (32.1%)	67 (31.2%)	27 (34.2%)	
Infusion	50 (17.4%)	35 (16.8%)	15 (19.0%)	
Boluses	21 (7.3%)	17 (8.2%)	4 (5.1%)	
Both	21 (7.3%)	13 (6.3%)	8 (10.1%)	
Emergency PCI	6 (2.1%)	2 (1.0%)	4 (5.1%)	<b>0.049*</b>
Emergency CABG	1 (0.3%)	0 (0.0%)	1 (1.3%)	0.273*
Cardiac Tamponade	1 (0.3%)	0 (0.0%)	1 (1.3%)	0.273*
Para-valvular leak	3 (1.0%)	0 (0.0%)	3 (3.8%)	<b>0.020*</b>
PRBC transfusion	13 (5.8%)	9 (5.4%)	4 (6.7%)	0.749*
Vascular stent	4 (1.4%)	3 (1.4%)	1 (1.3%)	>0.999*
Vascular intervention	7 (2.4%)	7 (3.3%)	0 (0.0%)	0.196*
Bleeding	16 (5.5%)	13 (6.2%)	3 (3.8%)	0.570*
TPM	8 (3.1%)	7 (3.7%)	1 (1.4%)	0.450
Respiratory support at end of procedure				
Room air	128 (44.3%)	101 (48.1%)	27 (34.1%)	0.105
Facemask or NC	145 (50.2%)	98 (46.7%)	47 (59.5%)	
On ETT	16 (5.5%)	11 (5.2%)	5 (6.3%)	

Values are presented as number and percentage. \*P-values were derived from Fisher exact test. Abbreviations: GA, General anesthesia, PCI, Percutaneous coronary intervention; CABG, Coronary arteries bypass graft; PRBC, Packed red blood cells; TPM, temporary pacemaker; NC, Nasal cannula; ETT, Endotracheal tube

**Table 3: Postoperative outcomes among TAVR patients who received local anesthesia (n=289)**

Variables	All patients (n=289)	Propofol (n=210)	Ketofol (n=79)	P
In-hospital mortality	7 (2.4%)	4 (1.9%)	3 (3.8%)	0.396
Post-procedure CCU stay, hours*	26 (23-50)	26 (24-49.5)	26 (23-52)	0.818
Post-procedure hospital stay, days*	3 (2-5)	3 (2-5)	3 (2-5)	0.371
PPM	9 (3.1%)	6 (2.9%)	3 (3.8%)	0.709

Values are presented as number and percentage unless mentioned otherwise, \*median (interquartile range). Abbreviations: PPM, permanent pacemaker; CCU, coronary care unit

profile with minimal respiratory compromise and more stable hemodynamics<sup>[16]</sup> as well as less nausea and vomiting and shorter recovery period.<sup>[17]</sup> There is a general concept in procedural sedation that a combination of sedatives may permit the use of lower doses of individual agents, thereby reducing their hemodynamic and respiratory effects.<sup>[18]</sup>

Although propofol is known to have a hypotensive effect,<sup>[11]</sup> there was no significant difference in the need of vasoactive support between propofol and ketofol in the current study. This may be related to the small dose of propofol used in the current study, which was around 10–20 mg/h. The hemodynamic effects of propofol during TAVR compared to other sedative drugs has been examined before.<sup>[19-24]</sup> The drug was generally safe specially when smaller dose is used. For example, propofol and dexmedetomidine were compared in two studies in TAVR patients, with no

significant differences in intraoperative use of vasoactive drugs, in-hospital outcomes, and 30-day outcomes.<sup>[19,21]</sup> On the contrary, propofol in a relatively higher dose and with a concomitant infusion of remifentanyl or fentanyl boluses was associated with higher catecholamine use compared with dexmedetomidine in TAVR patients.<sup>[22]</sup> Similarly, propofol infusion in quite high dose required more vasopressors than remifentanyl infusion in TAVR patients.<sup>[23]</sup>

In-hospital mortality in the current study was 2.4%, with no statistically significant difference between propofol and ketofol groups. The mortality was similar to previous studies and indicated that both propofol and ketofol sedation were safe in terms of the limited post-operative intensive care stay, overall hospital stay, and percentage of in-hospital mortality.<sup>[19]</sup> Similarly, Chen and colleagues found no difference in postoperative ICU stay or in-hospital mortality

in TAVR patients using different sedation regimens, including fentanyl, propofol, dexmedetomidine, and a mixture of propofol and dexmedetomidine.<sup>[20]</sup>

The percentage of patients in the current study who were on room air at the end of the procedure was 48% in the propofol group and 34% in the ketofol group, with insignificant statistical difference. The current finding was inconsistent with the data that showed better preservation of respiratory functions with ketamine.<sup>[24]</sup> Moreover, Mayer and colleagues found that the respiratory function of propofol was worse with higher carbon dioxide levels compared with dexmedetomidine in TAVR patients.<sup>[22]</sup> While it is difficult to explain the current findings, it is worth mentioning that the doses of propofol infusion and all sedation drugs in the current study were determined by titration, rather than the application of bispectral index monitor (BIS) or other electroencephalogram (EEG) processing monitoring systems.

Approximately 7.3% of the patients in the current study required conversion to GA, with no statistically significant difference between propofol and ketofol groups. This is clearly lower than other studies that showed rates as high as 17%.<sup>[25]</sup> Conversion in the current study occurred as a consequence of procedure-related cardio-pulmonary instability due to intra-procedure events, rather than problems due to the sedation technique or sedative drugs used. No conversion was necessitated by respiratory complications. Cardio-pulmonary causes of conversion in the current study included cardiac arrest, acute pulmonary edema, bleeding requiring femoral artery exploration or vascular surgery.

Unexpectedly, the current study showed higher incidence of para-valvular leakage with the ketofol group (3.8%) compared to none in the propofol group. This finding may be related to the relatively small number of patients included in the ketofol group. This should not be confused with earlier reports of higher incidence of para-valvular leakage in patients undergoing TAVR under sedation as compared to those under GA.<sup>[9,26]</sup>

Currently, more centers are adopting a minimalistic approach for TAVR sedation,<sup>[27]</sup> aiming for earlier recovery to normal daily functions and next-day discharge.<sup>[28]</sup> Delayed recovery of cognitive functions after TAVR is estimated at 4.5%.<sup>[29]</sup> Literature suggests ketamine, alone or combined with other sedatives, may play a role within this context.<sup>[30]</sup> However, further studies are still needed to confirm the ketamine role.

Few limitations of the current study are acknowledged. The retrospective observational design may raise concerns

about completeness of the recorded data. The single-center experience may limit the generalizability of the findings. The choice of sedation was not randomized, and ketamine choice was mainly dependent on individual preference. Yet, we believe that sharing our experience is important for building evidence, especially with limited number of studies covering different sedation agents. Additionally, a prospective multi-center study targeting a specific sedation agent for particular TAVR patient groups is highly recommended.

In conclusion, the current study showed the wide array of drugs/drug combinations used for the sedation in TAVR patients. Propofol infusion, either alone or with ketamine, is reliable and safe, with minimal side effects. In-hospital mortality was similar to previous studies and conversion rate from sedation to GA was even lower than similar studies. The current experience showed no significant differences in perioperative or postoperative outcomes between TAVR patients receiving either propofol or ketofol.

#### Ethical approval

The study obtained the ethical approval from the Ethics and Research Committee of the PSCC (approval no. R20006). The need to obtain informed consent was waived due to the retrospective nature of the study.

#### Authors' contributions

XX conceived the study idea. CC and AA were involved in the study design, analysis plan, and data collection. VV critically reviewed the manuscript. All authors interpreted the data analysis, contributed to the first draft of the manuscript, and critically revised the manuscript. All authors contributed to the drafting and editing of the final manuscript and have provided their permission to publish the manuscript. All authors agree to take responsibility for the work.

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#### Conflicts of interest

There are no conflicts of interest.

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