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ORIGINAL RESEARCH

Use of Dexmedetomidine in Transfemoral Transcatheter Aortic Valve Implantation (tf-TAVI) Procedures

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ABSTRACT

Introduction: Dexmedetomidine is a highly selective alpha-2 adrenoreceptor agonist without any effect on the GABA receptor. Its sedative, anxiolytic, analgesic, and sympatholytic activities together with opioid-sparing effects make it suitable for short- and long-term sedation in the intensive care setting. We report our experience with dexmedetomidine use during transfemoral transcatheter aortic valve implantation (TAVI) procedure as an alternative to general anesthesia.

Methods: This is a retrospective analysis of high-risk patients undergoing dexmedetomidine infusion for the transfemoral TAVI procedure between July 2017 and October 2019. The primary outcome parameters were hemodynamic: heart rate (HR), mean arterial pressure (MAP); respiratory oxygen saturation (SpO_2), pH, partial pressure of arterial oxygen (PaO_2), partial pressure of arterial carbon dioxide ($PaCO_2$), and sedation level (Richmond Agitation-Sedation Scale, RASS). The frequency of conversion to general anesthesia and the need for sedative "rescue therapy" were secondary endpoints. We also reported the overall anesthetic management and the incidence of intra- and postoperative complications.

Results: Eighty-five patients were evaluated (age 81.58 ± 5.23 years, 36.5% men, 63.5% women). High comorbidity, according to the Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM). The patients' hemodynamic functions were kept normal. Complications such as cardiac arrest occurred in four patients; orotracheal intubation and cardiopulmonary resuscitation were necessary. Atrioventricular block occurred in nine patients. Respiratory parameters were maintained stable. Complications such as apnea, hypoventilation, and hypoxemia did not occur. All patients had RASS scores above or equal to 0 and − 1. No patient required rescue midazolam or fentanyl. No conversion to general anesthesia in patients sedated with dexmedetomidine was observed in the absence of hemodynamic complications caused by the surgical technique.

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Conclusion: In this series, sedation with dexmedetomidine for TAVI procedures with femoral access was proven effective and safe. Dexmedetomidine may be a valid alternative to general anesthesia in high-risk older patients undergoing transfemoral TAVI.

Keywords: Anesthesia; Aortic stenosis; Dexmedetomidine; Sedation; TAVI

Key Summary Points

In general tf-TAVI is performed under deep sedation with propofol and midazolam, through dosages which enable one to keep the patient calm but "contactable". However, the onset of considerable hypotension and desaturation and the need for absolute immobility to facilitate the surgical procedure often warrant a subsequent orotracheal intubation with general anesthesia
Dexmedetomidine is a highly selective alpha-2 agonist with sedative, analgesic properties
Dexmedetomidine can be used for cooperative sedation in which well-sedated patients can be awakened by stimulation for clinical assessment and cooperation whilst maintaining patients' spontaneous breathing
Key learning from this manuscript: Dexmedetomidine infusion during tf-TAVI preserves gas exchange, minimizes hemodynamic instability, guarantees the patients' immobility, allows TEE to be performed, and decreases the frequency of delirium. It allows early recognition of neurological complications and their immediate treatment

INTRODUCTION

Degenerative aortic stenosis represents the most frequent valvulopathy in western countries [1]. Its incidence increases with age, with a prevalence of about 8.1% in over 80-year-old people [2]. Surgical aortic valve replacement has represented the standard treatment for patients with severe symptomatic aortic stenosis. However, since 30% of patients are not eligible for surgical treatment because of comorbidities and short life expectancy [3], the recent development of transcatheter aortic valve implantation (TAVI) has emerged as a valid alternative for high-risk patients [4].

In general, TAVI is performed under deep sedation with propofol and midazolam, through dosages which enable one to keep the patient calm but still "contactable". However, the onset of considerable hypotension and desaturation and the need for absolute immobility to facilitate the surgical procedure often warrant a subsequent orotracheal intubation with general anesthesia.

With this background, we report our 2-year experience with dexmedetomidine sedation for patients undergoing tf-TAVI procedures. Dexmedetomidine has sedative, anxiolytic, hypnotic, analgesic properties and sympatholytic activities. It reduces the activity of neurons in the locus coeruleus while maintaining their reactivity. Therefore, it is an attractive alternative to traditional sedatives such as propofol and benzodiazepine [5]. It interacts with the adrenoceptors present in the periphery (α_{2A}), in the brain (α_{2B}), and in the spinal cord (α_{2C}), having a highly selective α_2-adrenergic receptor agonist activity without any effect on the GABA receptor. It induces narcosis without respiratory depression [6, 7]. Dexmedetomidine induces dose-dependent effects, ranging from minimal to deep sedation. Moreover, except at doses that cause very deep sedation or general anesthesia, the sedation is reversible. The patient can be easily roused to a lucent state, but when left undisturbed will fall back into a state very similar to natural sleep. These are unique properties among the sedative medications in common use.

Dexmedetomidine does not impair the respiratory drive per se and seldom causes apnea.

In this study, we hypothesized that owing to its unique characteristics dexmedetomidine can be used as the only drug for sedation in patients undergoing tf-TAVI procedures.

METHODS

In this retrospective analysis we included a consecutive series of patients who underwent anesthesia with dexmedetomidine infusion for a transcatheter aortic valve implantation procedure between July 2017 and October 2019 at San Michele Hospital, Maddaloni, Caserta, Italy. Patients included were (1) aged over 60 years old, (2) had severe symptomatic aortic stenosis, (3) American Society of Anesthesiologists (ASA) score above or equal to 4, (4) Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score above or equal to 10% and Euro score above or equal to 20%, and (5) contraindication to open surgical repair. Patients known to have poor outcomes include those with severe kyphoscoliosis restricting lung function and operative exposure; significant previous mediastinal radiotherapy with myocardium damage from radiation; porcelain aorta. Ascending aorta calcium prevents clamping, cannulation, and difficulty constructing a proximal anastomosis. The risk of embolic stroke increases significantly; significant cirrhosis, with associated malnutrition, potential to develop multiorgan failure, and bleeding risk [8] (Table 1). Patients were excluded if a reasonable quality or duration of life (more than 1 year) is considered unlikely because of comorbidities. Besides comorbidities, older age "per se" raises several anesthetic concerns related to the frailty [9] (Table 1). In our practice, the individual surgical risk was assessed through the STS-PROM score and Euro score. All patients had an STS-PROM score risk above or equal to 10% and Euro score above or equal to 20% [10]. Appropriate patient selection and screening are important for success and for avoiding complications. All patient received a careful medical history, they were informed about the risk and complications related to the procedure, and signed informed consent. The anesthetic risk was defined by ASA score, always above or equal to 4 [11]. Patients were commonly monitored with five-electrode ECG, pulse oxymetry, and urinary catheter [12]. A large-bore (18-g) peripheral intravenous access line was usually inserted at the very beginning. All patients received 5 L of oxygen per minute via face mask after insertion of the radial artery catheter to respond rapidly to changes in hemodynamics. The central venous catheter (internal jugular vein) was placed using ultrasound guidance under local anesthesia to administer vasopressors and inotropic support in accordance with standard guidelines [13]. Dexmedetomidine infusion was started at the rate 0.8 μg/kg/h (loading dose) immediately before placement of the radial artery catheter, followed, after 30 min, by a maintenance infusion of 0.5 μg/kg/h to obtain a targeted level of sedation. Arterial blood gas measurements were performed at baseline and repeated 5 mins after heparin administration for activated clotting time (ACT) dose. Dopamine infusion started in all patients at 3 μg/kg/min; then before balloon valvuloplasty, the dosage was increased up to 5 μg/kg/min. Hemodynamic stability was the main objective of anesthetic management during TAVI [14]. The procedures were performed in a hybrid operation theater. X-ray fluoroscopy and transthoracic echo were used to assess the results of balloon valvuloplasty and the position of the prosthetic valve. However, when valve calcification is mild and fluoroscopy imaging is difficult, TEE was performed by passing the probe through a hole in a non-invasive ventilation (NIV) face mask on deep sedation [15]. All patients were admitted to the intensive care unit (ICU) for 24 h after the procedure for monitoring. The primary outcomes in this study were hemodynamic: heart rate (HR), mean arterial blood pressure (MAP); respiratory: oxygen saturation (SpO_2), pH, partial pressure of arterial oxygen (PaO_2), $PaCO_2$ (partial pressure of arterial carbon dioxide), sedation level (Richmond Agitation-Sedation Scale, RASS). The frequency of conversion to general anesthesia and the need for sedative "rescue therapy" were secondary endpoints. We also reported intra- and postoperative complications. All the

Table 1 Inclusion and exclusion criteria

Inclusion criteria
Quantification of risk with a Euro score above or equal to 20% and Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) above or equal to 10%
Severe symptomatic aortic stenosis
Contraindications to open surgical repair. Patients known to have poor outcomes include those with:
Severe kyphoscoliosis restricting lung function and operative exposure
Significant previous mediastinal radiotherapy with damaged myocardium from radiation
Porcelain aorta. Ascending aorta calcium prevents clamping, cannulation, and difficulty constructing a proximal anastomosis. The risk of embolic stroke increases significantly
Significant cirrhosis, with associated malnutrition, potential to develop multiorgan failure, and bleeding risk
Exclusion criteria
Aortic valve is congenital bicuspid or unicuspid. Secure placement of the valve becomes technically difficult because of abnormal anatomy
Mechanical aortic valve currently in situ
Recent myocardial infarction less than 1 month before TAVI, with coronary artery disease requiring open surgery
Severe mitral regurgitation (see below)
Severe pulmonary hypertension
Mixed aortic valve disease with predominant aortic regurgitation
Endocarditis or evidence of intracardiac thrombus or mass
Recent cerebrovascular accident within 6 months of the procedure
End-stage renal failure requiring chronic dialysis (see below)
Incapacitating dementia or neurodegenerative disease
Patient frailty
Severe respiratory disease
Life expectancy less than 12 months due to non-cardiac comorbidity

parameters were measured at the entrance to the hybrid room (T_0), at the half-way point (T_1), and at the end (T_2). The study included 85 high-risk surgical patients with "critical aortic stenosis".

The mean age of patients was 81.58 ± 5.23 years. Thirty-four patients were men (36.5%) and 51 were women (63.5%).

Summarized data are presented as absolute numbers, percentages, and means. All analyses were performed using SPSS statistical software.

This retrospective analysis is based on data from medical records for the evaluation of patients undergoing sedation with dexmedetomidine in tf-TAVI, a standard clinical therapy, and so ethics committee approval was not required. All patients provided written informed consent for participation and the

trials were conducted in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and the provisions of the 2008 Declaration of Helsinki. Patient approval for the publication was obtained.

RESULTS

The patients' hemodynamic functions were maintained stable (Table 2). Complications such as cardiac arrest occurred in four patients; orotracheal intubation and cardiopulmonary resuscitation were necessary for problems related to surgery technique. Atrioventricular block occurred in nine patients.

The patients' respiratory functions were maintained stable (Table 2). Complications such as apnea, hypoventilation, and hypoxemia did not occur.

All patients had a RASS scores above or equal to 0 and − 1.

In this cohort, no patient required rescue midazolam or fentanyl.

No conversion to general anesthesia in patients sedated with dexmedetomidine was observed in the absence of hemodynamic, respiratory, and neurological complications.

The total hospital mortality rate was 0%. All patients, after 5 ± 2 days of treatment, left the hospital in a good neurological condition (GSC 15).

DISCUSSION

Dexmedetomidine is suitable for short- and longer-term sedation in the intensive care setting. It is associated with a shorter time to extubation than midazolam and propofol, and a shorter duration of mechanical ventilation than midazolam. Patient receiving dexmedetomidine are also easier to rouse, more cooperative, and better able to communicate than patients receiving midazolam or propofol [16].

Dexmedetomidine is used during drug-induced sleep endoscopy (DISE). It provides greater hemodynamic stability and less respiratory depression than propofol [17].

Table 2 Results

Patients evaluated	85
Age (years)	81.58 (± 5.23)
Weight (kg)	72.75 (± 13.35)
Height (cm)	158.87 (± 6.54)
Hemodynamic parameters	
HR (bpm)	
T_0	71.55 (± 10.28)
T_1	72.52 (± 10.99)
T_2	73.63 (± 10.89)
MAP (mmHg)	
T_0	91.96 (± 11.12)
T_1	86.58 (± 10.76)
T_2	90.53 (± 11.75)
Respiratory parameters	
SpO_2 (%)	
T_0	97.46 (± 1.11)
T_1	98.38 (± 0.51)
T_2	99.13 (± 0.38)
PaO_2 (mmHg)	
T_0	97.46 (± 12.74)
T_1	162.79 (± 63.42)
T_2	139.14 (± 44.53)
$PaCO_2$ (mmHg)	
T_0	39.04 (± 5.69)
T_1	40.21 (± 5.65)
T_2	39.15 (± 6.16)
pH	
T_0	7.39 (± 0.32)
T_1	7.41 (± 0.34)
T_2	7.40 (± 0.35)

HR heart rate, *MAP* mean arterial pressure, SpO_2 oxygen saturation, PaO_2 partial pressure of arterial oxygen, $PaCO_2$ partial pressure of arterial carbon dioxide

On this basis, we used dexmedetomidine during tf-TAVI. It guarantees cooperative sedation, the patients' immobility, and an adequate level of sedation while maintaining patients' spontaneous breathing [18].

Sedation with dexmedetomidine has the advantage not only of avoiding orotracheal intubation but also the advantage of early postoperative recovery in patients who already have comorbidities.

Advantages also can include rapid assessment of any neurological complications including delirium, injury, and stroke, caused by calcification or air embolization, dissection, or hypotension. It allows one to avoid the cardiac depressant effects of anesthetic drugs and results in a decrease in periprocedural hemodynamic instability [19, 20]. Hypotension and bradycardia are side effects of anesthetic drugs that may lead to reduced vital organ perfusion, putting the patient at risk of permanent neurological deficits, myocardial ischemia, and renal impairment [21, 22]. These effects are absent or minimal with dexmedetomidine infusion.

CONCLUSIONS

Percutaneous aortic valve implantation can be successfully conducted with dexmedetomidine sedation. Dexmedetomidine preserves gas exchange, minimizes hemodynamic instability, decreases frequency of delirium, and provides a deep level of sedation without respiratory depression and with reduced ICU and hospital stay. It offers a unique ability to supply sedation and analgesia without respiratory depression. It is a new agent with a wide safety margin, excellent sedative capacity, and moderate analgesic properties. It does not increase the rate of postoperative complications. In conclusion, dexmedetomidine sedation can be an interesting alternative for sedation of patients undergoing transfemoral TAVI. As the patient is conscious and contactable, it allows early recognition of neurological complications and their immediate treatment.

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Compliance with Ethics Guidelines. This retrospective analysis is based on data from medical records for the evaluation of patients undergoing sedation with dexmedetomidine in tf-TAVI, a standard clinical therapy, and so ethics committee approval was not required. All patients provided written informed consent for participation and the trials were conducted in accordance with the International Conference on Harmonisation Good Clinical Practice guidelines and the provisions of the 2008 Declaration of Helsinki. Patient approval for the publication was obtained.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Izquierdo-Gómez MM, Hernández-Betancor I, García-Niebla J, Marí-López B, Laynez-Cerdeña I, Lacalzada-Almeida J. Valve calcification in aortic stenosis: etiology and diagnostic imaging techniques. Biomed Res Int. 2017;2017:5178631.

2. Carabello BA, Paulus WJ. Aortic stenosis. Lancet. 2009;373:956–66.

3. Fusari M, Bona V, Muratori M, et al. Transcatheter vs surgical aortic valve replacement: a retrospective analysis assessing clinical effectiveness and safety. J Cardiovasc Med. 2012;13:229–41.

4. Compagnone M, Moretti C, Marcelli C, et al. Surgical risk scores applied to transcatheter aortic valve implantation: friends or foes? Short-term and long-term outcomes from a single-center registry. J Invasive Cardiol. 2019;31(10):E282–E288.

5. Chen K, Lu Z, Xin Y, Cai Y, Chen Y, Pan S. Alpha-2 agonists for long-term sedation during mechanical ventilation in critically ill patients. Cochrane Database Syst Rev. 2015;1:CD010269.

6. Paris A, Tonner PH. Dexmedetomidine in anaesthesia. Curr Opin Anaesthesiol. 2005;18:412–8.

7. Huupponen E, Maksimow A, Lapinlampi P, et al. Electroencephalogram spindle activity during dexmedetomidine sedation and physiological sleep. Acta Anaesthesiol Scand. 2008;52(2):289–94.

8. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur J Cardiothorac Surg. 2017;52(4):616–64.

9. Franco A, Gerli C, Ruggeri L, Monaco F. Anaesthetic management of transcatheter aortic valve implantation. Ann Card Anaesth. 2012;15(1):54–63.

10. MacMahon S, Meikle R. Anaesthesia for transthoracic aortic valve implantation (TAVI) in aortic stenosis. ATOTW 348. 2017. https://www.wfsahq.org/components/com_virtual_library/media/aa5ab7d8d943d44782e077031fa2b43f-348-TAVI.pdf.

11. Vavuranakis M, Kalogeras K, Kolokathis AM, et al. Antithrombotic therapy in TAVI. J Geriatr Cardiol. 2018;15(1):66–75.

12. Covello RD, Ruggieri L, Landoni G, et al. Transcatheter implantation of an aortic valve: anesthesiological management. Minerva Anestesiol. 2010;76:100–8.

13. Dobson G, Chong M, Chow L, et al. Guidelines to the practice of anesthesia-revised edition 2018. Can J Anesth. 2018;65:76–104.

14. Patrick-Mayr N, Gunther-Wiesner MD, et al. Dexmedetomidine versus propofol-opioid sedation in transcatheter aortic valve implantation patients: a retrospective analysis of periprocedural gas exchange and hemodynamic support. Can J Anesth. 2018;65:647–57.

15. Guarracino F, Cabrini L, Baldassarri R, et al. Non-invasive ventilation-aided transoesophageal echocardiography in high-risk patients: a pilot study. Eur J Echocardiogr. 2010;11:554–6.

16. Keating GM. Dexmedetomidine: a review of its use for sedation in the intensive care setting. Drug. 2015;75(10):1119–30.

17. Chang ET, Certal V, Song SA, et al. Dexmedetomidine versus propofol during drug-induced sleep endoscopy and sedation: a systematic review. Sleep Breath. 2017;21(3):727–35.

18. Alfieri A, Passavanti MB, Di Franco S, et al. Dexmedetomidine in the management of awake fiberoptic intubation. Open Anesth J. 2019;13:1–5. https://doi.org/10.2174/2589645801913010001.

19. Wiegerinck EM, Boerlage-van Dijk K, Koch KT, et al. Towards minimally invasiveness: transcatheter aortic valve implantation under local analgesia exclusively. Int J Cardiol. 2014;176(3):1050–2.

20. Aitkenhead AR. Injuries associated with anaesthesia. A global perspective global perspective. Br J Anaesth. 2005;95(1):95–109.

21. Morris RW, Watterson LM, Westhorpe RN, Webb RK. Crisis management during anaesthesia: hypotension. Qual Saf Health Care. 2005;14(3):e11.

22. Watterson LM, Morris RW, Westhorpe RN, Williamson JA. Crisis management during anaesthesia: bradycardia. Qual Saf Health Care. 2005;14(3):e9.