Journal of Clinical Anesthesia and Intensive Care

Martin et al., J Clin Anesth Intensive Care 2021; 2(1): 15-19.

Short Communication

The evolution of sedation for transcatheter aortic valve replacement

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Received date: November 22, 2020
Accepted date: February 22, 2021

Citation: Martin JA, Carlson RE, Tsai MH. The evolution of sedation for transcatheter aortic valve replacement. J Clin Anesth Intensive Care. 2021; 2(1): 15-19.

Abstract

U.S. health care spending grew 4.6 percent in 2018, reaching $3.6 trillion or $11,172 per person. For comparison, Switzerland the country with the second highest healthcare expenditure in the Organization for Economic Cooperation and Development (OECD) spent $7,280 per person. As a share of the nation's Gross Domestic Product in 2018, United States health spending accounted for 17.7 percent. A 2018 survey indicated that hospital Chief financial officers (CFOs) rank cost reduction opportunities as the most important priority for the upcoming year. Fast forward to 2020 and hospitals find themselves under even greater fiscal strain due to the consequences of the Covid-19 pandemic.

Introduction

Aortic stenosis is the most common valvular heart disease of the elderly, with an age-increasing prevalence of 1-2% of persons aged 75 years and up to 6% for those aged 85 and over [1]. From 1989 to 2009, there has been an increase in the rate of aortic valve surgery noted in those over 75 years of age [2]. Heart valve disorders are the 17th most expensive condition treated in U.S. hospitals with a cost of $5,151,000,000 annually [3].

With the recent adoption of minimally invasive techniques, Transcatheter Aortic Valve Replacements (TAVRs) are projected to grow from 125,000 in 2018 to 289,000 by 2025, a growth of 131% [4]. The costs of TAVR have been established for the entirety of a hospital stay and compared to Surgical aortic valve replacement (SAVR) at one year. TAVR was shown to be a cost-effective alternative to SAVR for patients with severe Aortic Stenosis at intermediate risk [5]. In a recent retrospective analysis at the University of Vermont, we found the type of anesthesia administered had a significant impact on TAVR case duration [6]. Specifically, TAVRs performed with monitored anesthesia care (MAC) were significantly shorter in duration (33 minutes) compared to those receiving general anesthesia (GA) which resulted in cost savings of $3,185 per case. At our institution, we perform approximately 220 TAVRs per year representing a cost savings of more than $600,000 annually. Beginning in April of 2021, we are starting a pilot program where patients will receive nurse lead sedation (NLS) in the absence of an anesthesiologist. For our institution and many others physician-prescribed, nurse-administered conscious sedation for TAVR is the next significant step towards achieving operational efficiency by improving scheduling and optimizing costs without compromising patient safety. Furthermore, it is imperative for national registries to define the specifics of sedation to advance our understanding of outcome data and to improve the analysis of clinical conditions surrounding procedural outcomes.

Evidence in Support of Sedation for TAVR

There is a growing body of literature suggesting that sedation for TAVR is feasible and cost effective. Toppen et al. showed a 25% reduction in direct costs with sedation, the majority of cost savings resulted from reduced ICU and room utilization [7]. Several studies have documented a decrease in the administration of vasopressors associated with sedation [8-11]. In studies assessing procedural times, sedation consistently reduces TAVR case duration [12-15]. Large observational

studies report no difference in intermediate outcomes comparing sedation with general anesthesia for TAVR. Brecker et al. used propensity score–matching to analyze the characteristics and outcomes of patients who underwent TAVR with either GA (n = 245) or non-GA (n = 245) in the international, CoreValve ADVANCE Study. No statistically significant differences existed between the non-GA and GA groups in all-cause mortality (25.4% *vs.* 23.9%, p=0.78), cardiovascular mortality (16.4% *vs.* 16.6%, p=0.92), or stroke (5.2% *vs.* 6.9%, p=0.57) through 2-year follow-up [12]. Oguri et al. analyzed clinical outcomes for GA (n=1377) and local anesthesia (n=949) in the FRANCE2 registry and found no significant differences between groups in the rates of 30-day survival (GA [91.4%] versus LA [89.3%]) [16]. Husser et al. analyzed all patients undergoing elective or urgent transfemoral TAVR in the Germany Aortic Valve Registry (GARY) from 2011 to 2014. 8,121 patients receiving conscious sedation with local anesthesia were compared with 8,422 patients receiving GA. No differences in 1-year mortality between groups in the entire population (16.5% *vs.* 16.9%; HR: 0.93; 95% CI: 0.85 to 1.02; p ¼ 0.140) and in the propensity-matched population (14.1% *vs.* 15.5%; HR: 0.90; 95% CI: 0.78 to 1.03; p ¼ 0.130) was noted [17]. Finally, Hyman et al. analyzed 120,080 patients in the Transcatheter Valve Therapy (TVT) Registry who underwent transfemoral TAVR between 2016 and 2019 and found sedation was associated with decreased in-hospital mortality (adjusted risk difference: 0.2%; p=0.010), 30-day mortality (adjusted risk difference: 0.5%; p<0.001), and shorter length of hospital stay (adjusted difference: 0.8 days; p<0.001) [18].

Is Registry Data Sufficient?

Critics of the literature examining the impact of anesthetic technique on TAVR outcomes are quick to point out the methodological flaws inherent to observational studies. Selection bias is certainly a problem in the elderly, frail TAVR population, especially when there is an absence of criteria guiding the selection of anesthetic technique. A prime example of selection bias is found in the study by Husser et al. where the GA group was found to have a higher rate of bleeding, vascular complications, post procedure cardiopulmonary resuscitation and low output syndrome [17]. After secondary analysis with propensity matching (which attempts to adjust for known confounders), these complications persisted in significance. It is nonsensical to conclude that GA is associated with an increased risk of vascular complications and bleeding in the TAVR population. Nevertheless, registry data allows users to document the observed incidence of a given outcome and to generate hypotheses for further study.

Chronological biases are inherent to many registry studies [19]. The majority of TAVR programs began with GA to minimize patient discomfort and movement, allow for a controlled response to unanticipated complications and accommodate long procedure times. As individual expertise and institutional familiarity increases, a transition to the use of sedation commonly follows. In the French Registry study, sedation for TAVR increased from 14% in January 2010 to 59% in October 2011 [16]. Similarly, in 2017, the National Cardiovascular Data Registry of the United States documented an increasing use of sedation over each successive quarter from April of 2014 to April of 2015 [18]. Contributing to the issue of chronologic bias is the continuous improvement in valve design and decreasing size of the delivery device. Any improved outcomes stemming from recent technological advancements would be confounders in registry data comparing general anesthesia versus sedation over time. The only way to definitively compare patient outcomes by anesthetic modality and firmly establish patient selection criteria is through randomized controlled clinical trials.

Pitfalls of Sedation

There are several drawbacks of sedation for TAVR procedures, from the lack of ability to control patient movement and respiratory function to the absence of transesophageal echocardiography (TEE). The benefits of intra-procedure TEE guidance include the rapid diagnosis of potential catastrophic complications and assessment of post implantation paravalvular regurgitation (PVR). Functionally, the causes of refractory hypotension post-TAVR deployment amenable to rapid diagnosis with TEE include: 1) significant aortic or mitral regurgitation; 2) acute changes in ventricular function; 3) coronary artery occlusion; 4) landing zone trauma or ventricular perforation; and 5) pericardial effusion or tamponade [20,21]. PVR post TAVR is associated with increased late mortality emphasizing the need for accurate assessment and timely intervention [22-24]. Further, the need to convert from sedation to general anesthesia has been reported to be between 5% and 6% in large registry studies [25,26]. It is worth noting that conversion rates as high as 17% have been reported [27]. In this study, published in 2011 the most common event necessitating conversion to GA was a vascular access complication, the remainder of adverse events (e.g., uncooperative patient, pericardial effusion and cardiopulmonary resuscitation), combined for a 5% conversion rate. Future studies need to identify patient and procedural specific risk factors associated with the need to convert from sedation to general anesthesia.

Definition of Sedation

While there is evidence supporting safety of sedation for TAVR there remains a challenge in defining sedation across the large registries including the STS/ACC TVT, CoreValve Advance Study, FRANCE2, and the Gary [12,16-18]. Sedation can range from local anesthesia only at the puncture site to conscious sedation administered by nurses at the discretion of the operating physician and Monitored Anesthesia Care (MAC), a specific anesthesia service involving a qualified anesthesia provider for airway management and hemodynamic monitoring prepared to convert to general anesthesia as necessary [28]. The American Society of Anesthesiologists (ASA) Committee on Standards and Practice Parameters defines a continuum of depth of sedation/analgesia. The ASA sedation continuum is broken into 4 levels, with minimal sedation, moderate sedation (conscious sedation), deep sedation, and general anesthesia. A patient receiving conscious sedation as defined by the ASA provides a purposeful response to verbal or tactile stimulation with adequate spontaneous ventilation without airway intervention [29]. While registries indicate a patient received "conscious sedation" or simply "sedation," it is impossible to define the level of patient arousal required to achieve the reported outcomes. Explicitly describing the type of sedation as well as providers responsible for its administration will be necessary to evaluate efficacy.

Minimalist TAVR

A minimalist approach has been established at high volume centers striving to improve both safety and efficiency while decreasing cost to TAVR. There is no consensus definition of the "minimalist TAVR" and the term has been used to define minimal

sedation during TAVR or the development and implementation of a pathway including pre-, intra-, and post-procedure care [30]. Most minimalist TAVR pathways developed at high volume single centers decrease time to discharge while streamlining the peri-procedure management. Babaliaros et al. first studied the minimalist approach using conscious sedation in the catheterization lab for 142 patients and found no difference between the minimalist and standard approach in mortality at 30 days (0 *vs.* 6%), 30 day stroke/ TIA event rate (4.3 *vs.* 1.4% p=0.35), similar rates of moderate to severe paravalvular leak, reduced procedure time (150+/- 48 min vs 218 +/- 56 min p<0.001), time to discharge (3 days *vs.* 5 days), and cost (45,485 +/- 14297 *vs.* 55,377+/- 22587, p<0.001) [31]. The Vancouver 3M (Multidisciplinary, Multimodality but Minimalist) TAVR study expanded the Vancouver Clinical Pathway across thirteen small, medium and large volume TAVR centers. The 3M approach consisted of local anesthesia only (30%) or local with minimal sedation (69%), minimal lines with prompt removal, early mobilization and goal for next day discharge. Of 411 enrolled patients, next day discharge was achieved in 80.1% of patients with all-cause mortality or stroke at 30 days of 2.9% (confidence interval 1.7% to 5.1%) and conversion to general anesthesia in 1.5% of patients with similar rates across small, medium, and large volume TAVR centers [32]. Meta-analysis by Villablanca et al. analyzed 26 studies including 10,572 patients comparing local anesthesia with conscious sedation to general anesthesia. Overall, there was lower 30-day mortality (RR 0.73 95% CI 0.57-0.93 P=0.01), shorter procedure and fluoroscopy times, shorter ICU and hospital stays for conscious sedation [33]. More recently, Butala et al. utilized the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry, capturing data from TAVR procedures across the country between January 2016 and March 2019 in 120,080 patients observing an increase in conscious sedation from 33% to 64% and found decreased hospital mortality (adjusted risk difference 0.2% p=0.010), 30 day morality (adjusted risk difference 0.5%, p<0.001) and shorter length of stay 0.8 days P<0.001. While 17% of U.S. centers continue to exclusively use general anesthesia, conscious sedation has grown into the most common anesthetic practice for TAVR across the US and repeatedly demonstrated decreased procedural times, length of hospital stays and mortality benefit [34].

Embracing Nursing Administered Sedation for TAVR

Lauck et al. recent editorial in Structural Heart brought up the question of "who should lead TAVR anesthesia?" directing the focus to ensuring goals of a safe procedure while leveraging nursing expertise and competency [35]. Physician directed sedation without an anesthesiologist present became common for cardiac procedures in the 1990s. This change was spurred by the dramatic increase in percutaneous invasive cardiac procedures and a lack of anesthesiologist availability to meet the demand in a changing landscape of perioperative responsibilities [36-38]. Kezerashvili et. al. demonstrated the safety, efficacy, and cost effectiveness of nurse administered sedation for cardiac procedures by implementing a protocol including patient selection, institutional sedation policies, and plans for procedural complications based on ASA standards of practice for the non-anesthesiologist [39,40]. Patients selected for nursing administered sedation underwent 9,558 cardiac procedures including electrophysiology, cardiac catheterization, permanent pacemaker placement and TEE with serious complications (death or significant hemodynamic instability) in 0.1% of patients. The team reported $5,365,691 cost savings over a decade [39]. Focusing specifically on TAVR sedation, Keegan et al. completed a 5-year review of a minimalist TAVR protocol comparing anesthesia lead sedation (ALS) to nursing lead sedation (NLS). The team followed a strict protocol for selecting NLS patients based on increased risk of TAVR including issues of access or coronary obstruction along with challenges to sedation including obesity, respiratory disease, ASA Score >4 or Mallampati >2. Both groups had comparable survival to discharge (98.3% NLS *vs.* 100% ALS p=0.05), procedural success at discharge by echocardiographic assessment, and one year death/ readmission rate. NLS had shorter length of procedure and ICU stay when compared to ALS [41]. While the conversion rate from sedation to general anesthesia was 2.2% in the NLS group as compared to 0.8% in the ALS group this remains within the previously reported conversion rate by anesthesiologists [31]. TAVR procedure complications as opposed to sedation challenges caused the majority of conversions to GA.

Clearly, the immediate availability of an anesthesiologist to assist with complications remains a necessity to support a NLS program for TAVR. The transition from ALS to NLS is reinforced by the historical context where procedural nurses have an established record of safely administering sedation for cardiac procedures. Anesthesiologists must remain a leader in the development of procedural sedation protocols including patient selection, sedation policies, strategy for management of complications, and institutional knowledge to ensure ongoing procedural efficacy and safety in patients undergoing TAVR. The transition to NLS improves quality by reducing staffing costs, increasing flexibility in scheduling, decreasing procedural times and hospital length of stay while maintaining outcomes.

Conclusion

One must acknowledge that the question is not should sedation be administered to all patients undergoing TAVR rather, can it be done safely in a subset of TAVR patients to maximize resource allocation and generate cost savings. Overall, the opportunity for NLS for TAVR in a well-selected patient population appears to be safe, feasible and cost effective. It is quite possible the next great advancement in TAVR quality is the dissemination and widespread adoption of established NLS protocols.

Acknowledgement

The authors declare no conflict of interest. All the authors involved in the design, preparation of the manuscript.

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