# Intensive Care Unit Management of Transcatheter Aortic Valve Recipients

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#### Abstract

Severe aortic stenosis is an increasingly prevalent disease that continues to be associated with significant mortality. Transcatheter aortic valve replacements have been used as an alternative to surgical aortic valve replacement in high-risk patients with multiple comorbidities. In this review, we discuss postoperative considerations pertinent to the successful management of these complicated patients in the intensive care unit.

#### Keywords

transcatheter aortic valve replacement (TAVR), intensive care unit (ICU), critical care management, severe aortic stenosis, high-risk patients

# Introduction

The first human percutaneous transcatheter aortic valve was implanted in 2002 for severe, inoperable aortic stenosis (AS),<sup>1</sup> and since then, transcatheter aortic valve replacement (TAVR) has been increasingly utilized in the management of high-risk patients. AS increases in prevalence with advancing age<sup>2</sup> and is estimated to affect 2% to 9% of patients older than 65 years.<sup>3</sup> Once patients become symptomatic, AS can result in significant mortality if left untreated. Despite advances in surgical, anesthetic, and critical care management, there is a 16.4% in-hospital mortality rate in high-risk patients undergoing surgical aortic valve replacement (SAVR) as well as a high associated rate of prolonged length of stay in the intensive care unit (ICU) and perioperative morbidity.<sup>4,5</sup> As such, at least 30% of symptomatic patients with severe AS do not undergo traditional SAVR owing to pre-existing risk factors such as advanced age, left-ventricular (LV) dysfunction, coronary and peripheral artery disease, and pulmonary hypertension,<sup>6-9</sup> leaving percutaneous therapies as an attractive option.

TAVR, whether by the transfemoral (TF), transapical (TA), or transaortic (TAO) approach, offers a less-invasive technique for definitive management of severe AS that avoids complete sternotomy and cardiopulmonary bypass. The current first-generation valves in use are the self-expanding porcine pericardial tissue Medtronic CoreValve (MC; Medtronic, Minneapolis, MN) and the balloon-expandable bovine pericardial tissue Edwards SAPIEN (ES) and SAPIEN XT (Edwards Lifesciences Inc, Irvine, CA) valves.<sup>10</sup>

TF-TAVR is the least-invasive approach, and although general anesthesia has been standard in the United States, there is growing interest in performing this procedure with a combination of monitored anesthesia care and local or regional anesthesia.<sup>11,12</sup> Motloch et al<sup>13</sup> reported the results of 74 patients undergoing TAVR, of whom 33 underwent general anesthesia and 41 underwent local anesthesia with sedation. Despite the fact that patients who had local anesthesia with sedation had higher Society of Thoracic Surgery scores and New York Heart Association (NYHA) heart failure classifications, there was no difference in procedure-related 30-day mortality or complications. These patients also had earlier mobilization, shorter procedure times, and lower labor costs.

TA-TAVR requires a mini–left thoracotomy, and TAO-TAVR requires a partial J-sternotomy (or, rarely, a mini– right thoracotomy), and both require general anesthesia. Both TA and TAO techniques avoid manipulation of the iliofemoral vessels and aortic arch, which is desirable in patients with severe atherosclerotic disease, and both achieve better alignment of the valve delivery system with the aortic annulus. TAO-TAVR avoids LV apical injury, and there is generally less postoperative pain and impairment of respiratory dynamics observed following the partial J-sternotomy compared with the mini–left thoracotomy.<sup>6</sup>

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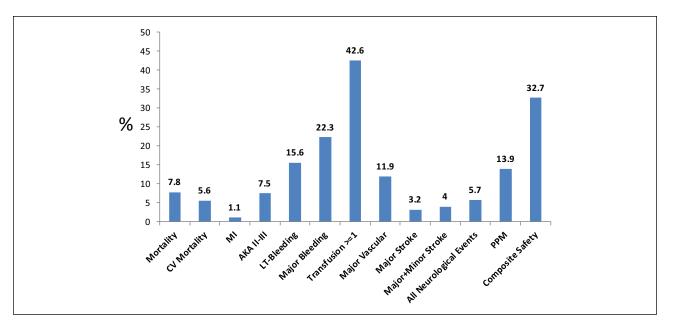


Figure 1. 30-Day event rates of major VARC-related outcomes.<sup>a</sup>

Abbreviations: VARC, Valve Academic Research Consortium; CV, cardiovascular; MI, myocardial infarction ≤72 hours after the procedure; AKI II-III, stage II to III acute kidney injury as defined by VARC; LT, life-threatening bleeding as defined by VARC; PPM, permanent pacemaker. <sup>a</sup>From Genereux et al.<sup>14</sup>

The greatest critical care challenges are high-risk patients with low ejection fractions (EFs < 25%), moderate-to-severe pulmonary hypertension, and low diffusing capacity of the lung for carbon monoxide undergoing either the TA or TAO approach.

Although TAVR is less invasive than a surgical AVR, there remain many challenges in the post-procedure management of these complex patients. Advanced age and multiple comorbidities render these patients susceptible to a number of significant complications. Figure 1 displays 30-day post-procedure complication data from a recent meta-analysis utilizing the Valve Academic Research Consortium definitions.<sup>14</sup> Optimal ICU management identifies these complications early and provides supportive and critical care to minimize additional end-organ injury.

# **Neurological Considerations**

# Stroke and Transient Ischemic Attack

Neurological symptoms may be a result of hypoperfusion, but early neurological events are more likely to be a result of embolization of calcium, debris, or microthrombi. Transcranial Doppler studies have shown that most strokes occur during balloon aortic valvuloplasty, catheter manipulation across the stenotic valve, and valve manipulation.<sup>15-17</sup> Given the risk of neurological events, formal neurological evaluation should be performed in the perioperative period.

The PARTNER trial data<sup>9</sup> revealed the risk of a neurological event to be 2 times higher in the TAVR group

compared with the SAVR group (5.5% vs 2.4% at 30 days, 8.3% vs 4.3% at 1 year), but the rate of major stroke (defined as Modified Rankin score  $\geq 2$  and demonstrates clinical disability<sup>18</sup>) was not significantly different between the 2 groups.<sup>19</sup> Other studies have shown that strokes occur in 9% of TAVR patients postoperatively, 5% of which were major strokes and 3% of which were transient ischemic attacks.<sup>20</sup> These events most frequently occur in the first week postoperatively, and the highest risk is within the initial 24 hours.<sup>19,21</sup> Moreover, postoperative diffusionweighted magnetic resonance imaging scans have demonstrated "clinically silent" acute ischemic changes throughout the brain in 68% to 90% of TAVR patients, significantly more than in SAVR patients.<sup>19,22</sup> Though we believe that these events are "clinically silent," the actual long-term ramifications will become evident with time.

Beginning with the PARTNER II trial and SAPIEN XT valve and continuing with the current S3 valve study protocol, all patients undergo formal examination by a neurologist preoperatively and postoperatively. The examination utilizes the Modified Rankin Scale and National Institutes of Health Stroke Scale (NIHSS) along with the Barthel index if there is a history of a prior cerebrovascular accident or transient ischemic attack. A baseline formal neurological assessment is obtained preoperatively, followed by another 24 hours post-TAVR. Other formal neurological assessments occur at discharge and at 30 days, 6 months, and 1 year postoperatively. An annual examination is conducted for the first 5 years postoperatively.

# Postoperative Pain

Adequate postoperative pain management is necessary to facilitate early patient mobilization and this is particularly important in elderly patients because it reduces the incidence of delirium and respiratory dysfunction. Patients receiving TF-TAVR generally do not have significant pain, and local anesthetic infiltration at the access site can be helpful. Multimodal pain management techniques, including neuraxial techniques, have been used extensively in the TA- and TAO-TAVR patients. When a thoracotomy is required, epidural analgesia is helpful in managing postoperative pain and may be particularly beneficial in TA-TAVR patients with chronic obstructive pulmonary disease.<sup>5</sup>

Use of a multimodal pain management approach is the standard of care for these elderly and frail patients. Nonopioid adjuncts such as intravenous acetaminophen, intravenous lidocaine infusion, and gabapentin are quite effective. Toradol should be used with extreme caution in this patient population because there is a high prevalence of pre-existing chronic kidney disease (CKD), which leads to an increased risk of significant renal dysfunction after TAVR. When opioids are required for moderate to severe pain, lower doses should be tried first and attention must be paid to the drug's mode of clearance and side effect profile. Tramadol may be considered because it has a better side-effect profile than other opioids, although it has been known to cause delirium.<sup>23</sup> A bowel regimen should be initiated with all opioids.

One study of 135 patients showed that epidural analgesia provided better analgesia after TA-TAVR and was associated with decreased respiratory complications and improved short-term and 1-year mortality.<sup>24</sup> Paravertebral nerve block catheters may cause less hypotension than thoracic epidural analgesia, with similar efficacy in post-thoracotomy patients.<sup>25</sup> However, the risk of holding clopidogrel (or other antiplatelet therapy) must be weighed against the benefits of epidural analgesia or paravertebral nerve block catheters. Intercostal nerve blocks with a long-acting local anesthetic agent are another alternative in high-risk patients who need dual antiplatelet therapy in the immediate postprocedure period.

#### Delirium

Advanced age is a well-known risk factor for ICU delirium, which has been associated with increased morbidity and mortality, long-term cognitive dysfunction, prolonged mechanical ventilation, and increased length of stay.<sup>26,27</sup> Other risk factors for delirium following cardiac surgery include atrial fibrillation, renal failure, history of stroke or transient ischemic attack, and mechanical ventilation,<sup>26,28</sup> all of which are common in the TAVR population. Whereas hyperactive delirium may be more easily diagnosed, hypoactive delirium—characterized by a decreased level of consciousness, inattention, disordered thinking—or a mixed delirium with elements of both agitation and hypoactive delirium is more frequently underrecognized. In fact, hypoactive delirium is not only more common, but is also associated with higher mortality rates.<sup>27,29</sup> Increased use of tools such as the Confusion Assessment Method for the ICU (CAM-ICU) aids in earlier diagnosis and treatment of delirium.<sup>30,31</sup>

Delirium remains difficult to manage but preventive measures should be taken. Frequent reorientation, minimizing lines to facilitate early mobilization, promoting normal sleep-wake cycles, and early discharge from the ICU are all helpful in preventing delirium. In patients requiring sedation, use of the Richmond Agitation-Sedation Scale (RASS)<sup>31</sup> minimizes the amount of sedatives used, reduces delirium and facilitates earlier extubation. Dexmedetomidine, a selective  $\alpha$ -2 agonist, has gained increasing popularity for its opioid- and benzodiazepine-sparing qualities. The use of dexmedetomidine may help prevent delirium<sup>27,32</sup> and may possibly aid in promoting a regular sleep cycle.<sup>33</sup>

When maintaining RASS-targeted light-to-moderate sedation, dexmedetomidine was noninferior to propofol and midazolam and reduced the amount of time on mechanical ventilation.<sup>34</sup> However, patients on dexmedetomidine did experience more adverse events, such as hypotension and bradycardia. Low-dose risperidone<sup>35</sup> and low-dose ketamine<sup>36</sup> on induction of anesthesia have also been shown to provide delirium prophylaxis in the cardiac surgical population. Antipsychotics have commonly been used for both the treatment and prophylaxis of acute delirium, though they do prolong the QT interval and may predispose patients to arrhythmias.

## Cardiac Considerations

#### Hemodynamics

After the severely stenotic lesion is corrected, many patients will exhibit improved hemodynamics with increased LVEF and cardiac output. Patients with AS experience chronic pressure overload, which is followed by LV hypertrophy and diastolic dysfunction. As such, these patients benefit from adequate preload and filling volumes as well as maintenance of sinus rhythm.

Vasodilators such as sodium nitroprusside and nicardipine are helpful in the management of both postoperative hypertension and elevated systemic vascular resistance, which is frequently present in elderly patients with significant peripheral vascular disease. In patients with preserved LV systolic function, significant hypertension may occur following correction of the stenotic lesion. Control of hypertension for post-procedural hemostatic concerns must be balanced against ensuring adequate end-organ perfusion pressure in the setting of long-standing moderate to severe hypertension.

Pulmonary artery catheter (PAC) monitoring data were required for patients receiving TAVRs in the PARTNER and PARTNER II studies. For high-risk patients, generally defined as those with a LVEF <25% or moderate to severe pulmonary hypertension, PAC monitoring for 24 to 48 hours is generally advisable. These patients may exhibit hemodynamic variability from new-onset right-ventricular or LV systolic dysfunction, exacerbation of pulmonary hypertension, or hypotension related to decreased vascular tone (from preoperative antihypertensives, epidural analgesia, etc). Frequently, the PAC is discontinued in the immediate post-procedure period in low- to medium-risk patients undergoing TF-TAVR.

Patients with preoperative severe LV systolic dysfunction—often manifested by low-flow, low-gradient AS are at high risk for postoperative LV dysfunction and may require postoperative inotropic support.<sup>25</sup> As with general cardiothoracic postoperative ICU care, trending and appropriately treating hemodynamic parameters and other variables, including cardiac index, central venous pressure, systemic vascular resistance, mixed venous oxygen saturation, and lactate and urine output, are essential to optimizing patient outcomes.

#### Pulmonary Hypertension

Severe pulmonary hypertension (secondary to left-sided heart disease) and AS do not commonly coincide, but the combination has been associated with sudden cardiac death.<sup>37</sup> Whereas TAVR may significantly decrease pulmonary artery systolic pressures,<sup>38</sup> pre-existing severe pulmonary hypertension increases the risk of 30-day and 1-year mortality and the risk of right heart failure. In patients with severe pulmonary hypertension, a pulmonary vasodilator (ie, inhaled prostacyclin or nitric oxide) can be used both intraoperatively and to facilitate ventilator weaning. In patients with continued pulmonary vasodilator requirements, initiating sildenafil is frequently beneficial.

In a study from the FRANCE 2 registry, Lucon et al<sup>39</sup> reported on the results of 2435 patients with baseline pulmonary hypertension undergoing TAVR. The patients were divided into 3 groups: group I, mild PH (systolic PA pressures < 40 mm Hg); group II, mild to moderate PH (40-59 mm Hg), and group III, severe PH (>60 mm Hg). The authors found mild to moderate and severe PH to be independent risk factors for all-cause mortality, with a higher 1-year mortality in groups II and III. Interestingly, in survivors, NYHA functional class improved in all groups.

PAC-derived intracardiac filling pressures and cardiac output should guide post-procedure volume administration and use of inotropes and systemic vascular resistance– altering agents. Frequently, these patients will have permanent pacemakers, and adjustments should be made to their settings to optimize the patient's hemodynamics. Newonset atrial fibrillation should be aggressively treated with early electrical cardioversion in patients with a decreasing cardiac index or increasing pulmonary artery pressures.

#### Myocardial Ischemia

Myocardial ischemia or infarction is not uncommon given the hypertrophied myocardium that develops in severe AS and the nature of the TAVR procedure, which includes periods of rapid ventricular pacing (during valve deployment) and severe hypotension, calcium embolization during valve deployment, and possible coronary obstruction by the valve. Traditional cardiac biomarkers may be difficult to interpret in the perioperative setting because elevated troponin levels are not unusual after TAVR.<sup>26,40</sup> The prognostic value of elevated cardiac troponin T (cTnT) levels was recently demonstrated in a study of 198 TF-TAVR patients.<sup>41</sup> Preoperatively, patients with severe AS were found to have significantly elevated cTnT levels, which increased 7-fold post-procedure, peaking on day 3. The degree of increase was predicted by baseline renal function, duration of intra-procedure rapid ventricular pacing, and preoperative baseline cTnT levels. The authors found pre-procedure and post-procedure cTnT levels to be predictive of 1-year mortality.

Because of the expected increase in cTnT levels, echocardiography should be used to evaluate any suspected change in ventricular function, including assessment for new wall motion abnormalities. New-onset left bundle branch block or other ECG rhythm changes may also negatively affect post-procedure ventricular function. Typically, apical akinesis is seen following TA-TAVR, which likely explains the difficult postoperative course experienced by patients with low LVEF following TA-TAVR.

Other, rare complications that may cause hemodynamic instability include tamponade, valve embolization, and annular or aortic root rupture.<sup>42</sup> As always, transesophageal or transthoracic echocardiography should be rapidly used for definitive diagnosis. Formal echocardiographic evaluation should be performed in all patients prior to discharge from the ICU.

#### Aortic Insufficiency

In a noncompliant left ventricle, increases in LV end-diastolic pressure caused by aortic insufficiency (AI) can result in ventricular dysfunction. It is important to ascertain the degree of AI present at the end of the procedure because even mild AI has been associated with increased late mortality.<sup>43</sup> Makkar et al<sup>44</sup> showed a nonsignificant trend toward higher cardiac mortality, but not all-cause mortality, in patients with moderate to severe AI at 2 years. Some degree of paravalvular leak occurs in 85% of patients post-TAVR<sup>9</sup> and is usually mild to moderate in severity. Most AI is paravalvular and is generally caused by inadequate inflation of the prosthesis or by calcium deposits preventing proper valve seating.<sup>9</sup> Attempts can be made to re-balloon the stent and valve<sup>42</sup> when severe paravalvular leak is present. Moderate to severe AI is present in 12% of patients at 30 days and in 7% at 1 year.<sup>7,10</sup> If significant central AI is present, valve-in-valve deployment of a new transcatheter aortic valve must be considered.<sup>45</sup>

Dworakowski et al<sup>46</sup> recently studied 2440 patients undergoing TAVR. Among them, 53% received a balloonexpandable device and 47% received a self-expanding device; 68% underwent a TF approach, whereas the remaining 32% needed a surgical (either TA, TAO, or subclavian) approach. AI occurred in 68% of the patients studied and was graded as mild in 57% of the cases and moderate to severe in 10%. A large aortic annulus, high pre-procedural TAO gradient, and the use of a self-expanding valve were found to be independent predictors of moderate to severe AI. Moreover, they observed an association between moderate to severe AI and increased mortality; interestingly, the association was only significant for the balloon-expandable device.

#### Arrhythmias and Conduction Abnormalities

In the PARTNER trial, more patients required permanent pacemaker placement following TAVR than SAVR (7.3% vs 3.4%) for complete atrioventricular block and severe bradycardia.<sup>47</sup> Patients receiving CoreValve as opposed to Sapien were more likely to require a permanent pacemaker (19.2%-42.5% vs 1.8%-8.5%).<sup>69</sup> The increased need for a permanent pacemaker seen after CoreValve insertion is thought to be a result of its larger profile and deeper intraventricular insertion, resulting in anatomical compression of the conduction system.

More recent studies have estimated that 33% to 65% of TAVR patients require permanent pacemaker placement because of conduction abnormalities.<sup>26,48,49</sup> A pre-existing conduction abnormality, particularly a right bundle branch block, is associated with the need for pacemaker post-TAVR.<sup>47,49</sup> A small study of 27 patients found that patients who developed new conduction abnormalities post-TAVR did not experience the improvement in LVEF observed in patients without conduction abnormalities.<sup>50</sup>

Recently, Jilaihawi et al<sup>51</sup> examined the outcomes in high-risk and octogenarian patients undergoing surgical AVR, MC, and ES TAVR. The ES TAVR included both TF and TA approaches. Their meta-analysis consisted of 5024 TAVR patients (ES-3222 and MC-1802). The only significant difference (P value <.0001) in complications between the 2 TAVR groups was the need for pacemaker placement after the procedure—24.5% for the MC group versus 5.9% for the ES group.

About one-quarter of PARTNER trial patients had preexisting atrial fibrillation.<sup>20</sup> In those patients without a history of atrial fibrillation, an enlarged left atrium and the TA approach were found to be risk factors for new onset atrial fibrillation, which was seen in 31.9% at 48 hours postoperatively in one study.<sup>52</sup> There was an increased risk of stroke but no increased mortality risk associated with atrial fibrillation.<sup>10</sup> Given the risk of new arrhythmia or conduction abnormality, continuous telemetry monitoring should be done until discharge.

#### Mitral Regurgitation

Mitral regurgitation (MR) often accompanies severe AS. The optimal management of MR in the setting of traditional, open surgical AVR continues to be studied. The 2014 AHA/ACC (American Heart Association/American College of Cardiology) Guideline for the management of patients with valvular heart disease<sup>53</sup> gives a class I recommendation for mitral valve repair or replacement in the setting of chronic, severe primary MR and planned AVR; the recommendation is class IIa for chronic, moderate primary MR. In the setting of planned AVR and chronic, severe secondary MR, the recommendation is IIa. When the concomitant diagnosis is chronic, moderate secondary MR, a IIb recommendation is given.

In the TAVR literature, the incidence of associated moderate to severe MR ranges from 20% to 50% and the effect on post-TAVR outcomes has only recently been elucidated. Toggweiler et al<sup>54</sup> reported the results of 478 patients with associated MR undergoing TAVR. Though they found moderate or severe MR to be associated with an increased early mortality, no association was seen with late mortality. Reduction in MR severity was seen in 55% of patients at 1 year of follow-up and was predicted by high TAO gradients, functional as opposed to structural MR, and absence of atrial fibrillation and pulmonary hypertension.

#### Heart Failure

Many TAVR patients have pre-existing moderate to severe LV systolic dysfunction and class III or IV NYHA symptoms. Postoperatively, inotropic support should be initiated to support clinical signs of heart failure as opposed to the use of vasopressors. Cardiac index parameters, when available, should be utilized in guiding supportive therapy and volume resuscitation. Patients who have continued their angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker therapy preoperatively often present with an elevated cardiac index and low blood pressure postoperatively. Typically, these patients respond well to the use of a low-dose vasopressin infusion.

Patients who have been living with NYHA class III or IV heart failure often have baseline systolic blood pressures ranging from 85 to 95 mm Hg. These baseline parameters should be used as a guide for postoperative hemodynamic goals with regard to blood pressure management.

## Suicide Left Ventricle

A unique clinical phenomenon seen after TAVR has been described as the "suicide left ventricle."55 Patients with small LV end-diastolic diameters, a preserved EF, significant LV septal hypertrophy, high aortic valve gradients, and small overall LV mass are at high risk for developing this clinical syndrome, which is quite similar to that seen in hypertrophic cardiomyopathy patients. After valve deployment, there is a marked reduction in ventricular afterload, producing improvements in ventricular myocardial energetics. Valvuloarterial impedance (Z) and meridional wall stress are both dramatically reduced,<sup>56</sup> allowing a reduction in myocardial oxygen consumption and enhanced coronary blood flow; this combination of factors causes improved ventricular contractility. Extremely high LV outflow tract gradients are generated, with a reduced cardiac output, leading to hypotension and shock. The treatment for suicide left ventricle is similar to that of hypertrophic cardiomyopathy-removal of exogenous inotropes, suppression of endogenous catecholamines, fluid administration, and vasopressor use as clinically indicated.

## Hematological Considerations

#### Antiplatelet Therapy

Dual antiplatelet therapy with aspirin and clopidogrel should be started on postoperative day 1<sup>7,10,16,44</sup> and can be transitioned to aspirin alone at 6 months, though further studies are needed to better define a standard regimen. If warfarin is otherwise indicated, continuing warfarin with aspirin alone is preferred because triple therapy is associated with increased bleeding complications.<sup>57</sup> If the patient had recent coronary stent placement or any other indication for antiplatelet therapy, warfarin and clopidogrel should be prescribed. As with any other patient receiving neuraxial analgesia, aspirin therapy is safe, but ADP receptor blockers like clopidogrel should not be administered until 2 hours after the removal of an epidural or paravertebral catheter, per American Society for Regional Anesthesia guidelines.<sup>58</sup>

#### Table I. Bleeding: VARC Consensus End Points After TAVR.

Life-threatening or disabling bleeding Fatal bleeding, or
Bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, or pericardial necessitating
pericardiocentesis, or intramuscular, with compartment syndrome, or
Bleeding causing hypovolemic shock or severe hypotension requiring vasopressors or surgery, or
Overt source of bleeding with drop in hemoglobin $\geq$ 5 g/dL or whole blood or packed red blood cells (RBCs) transfusion $\geq$ 4 units
Major bleeding
Overt bleeding either associated with a drop in the hemoglobin level of at least 3.0 g/dL or requiring transfusion of 2 to 3 units of whole blood/RBC and
Does not meet criteria of life-threatening or disabling bleeding
Minor bleeding
Any bleeding worthy of clinical mention (eg, access site hematoma) that does not qualify as life-threatening,

Abbreviations: VARC, Valve Academic Research Consortium; TAVR, transcatheter aortic valve replacement.

#### Anemia and Hemorrhage

disabling, or major

Preoperative anemia is common in the TAVR patient population and has been correlated with an increased incidence of post-procedure blood transfusion. Binder et al<sup>59</sup> prospectively studied 373 TAVR, 270 TF-TAVR, and 103 TA-TAVR patients. Transfusion rates were 11% in the TF-TAVR group, versus 47% in the TA-TAVR group. Low baseline hemoglobin, female sex, low body mass index, and decreased renal function were found to be independent predictors for blood transfusion. Table 1 contains the Valve Academic Research Consortium–defined bleeding end points following TAVR.

Among the 657 patients in the operable high-risk cohort of the PARTNER I trial, major bleeding complication rates were 23% in the SAVR group, 11% in the TF-TAVR group, and 9% in the TA-TAVR. A significantly higher 30-day rate of transfusion was found in the SAVR (18%) as compared with the TF-TAVR (7%) or TA-TAVR (5%) groups. For all groups, major bleeding complication was found to be the strongest predictor of 1-year mortality. The authors do note that the incidence of major bleeding complications has decreased from 15% to 20% in the early literature to rates as low as 1% in recent studies reporting 30-day major bleeding complications following percutaneous TF-TAVR.<sup>60</sup>

Individual transfusion decisions should be based on the patient's past medical history and comorbidities. Mixed venous oxygen saturation should be optimized in the early postoperative period to allow maximum oxygen delivery to organs at risk for peri-procedural injury. Further studies are needed to define transfusion thresholds and guidelines in this often elderly and extremely frail population.

#### **Pulmonary Considerations**

#### Fast-Track Care

Fast-track cardiac care with early ventilator weaning is now standard in routine postoperative management. Decreases in time to extubation, mechanical ventilation– associated complications, and ICU length of stay have resulted without any significant difference in risk of mortality, myocardial infarction, or reintubation.<sup>16,61,62</sup> Patients undergoing TAVR are traditionally higher surgical risk than the average cardiac surgical patient, but TF-TAVR patients are increasingly fast-tracked given the minimally invasive approach. Frequently, low- to medium-risk TF-TAVR patients may be extubated after the procedure, prior to transport to the ICU.

#### Chronic Lung Disease

The effect of chronic lung disease (CLD) on outcomes in the PARTNER I trial<sup>63</sup> has recently been reported. All patients (2553 total) who underwent TAVR in the initial trial and continued access registry were evaluated, and 1108 patients had CLD. Among all patients, those with CLD had a higher 1-year mortality than those without CLD. Interestingly, in the nonoperable cohort, the death rate was lower after TAVR when compared with standard medical therapy. Poor mobility (as defined by a 6-Minute Walk Test <50 m) and oxygen-dependent CLD were identified as independent predictors of mortality.

After extubation, patients with significant pulmonary comorbidities need frequent evaluation because increased work of breathing and hypoxia may exacerbate any myocardial ischemia, particularly in high-risk patients with significant ventricular hypertrophy and coronary artery disease. ICU management should ensure optimal postoperative pain control to reduce splinting and the associated exacerbation of atelectasis. Pulmonary edema can be treated with noninvasive positive pressure ventilation. Pleural effusions should be drained and pre-existing pulmonary disease medically managed when indicated. Early mobilization and pulmonary toilet are essential to successful post-procedure ICU management and rapid ICU discharge.

#### **Renal Considerations**

Post-TAVR renal impairment was reported in <3% of patients in the original PARTNER trial<sup>64</sup>; however, other studies have reported a higher incidence of renal impairment in patients with and without pre-existing renal

**Table 2.** Acute Kidney Injury: Valve Academic Research

 Consortium Definition.

Change in serum creatinine (at 72 hours) compared with baseline	
Stage I	Increase in serum creatinine to 150% to 200% (1.5-2.0 × baseline value) or increase of >0.3 mg/dL (>26.4 mmol/L)
Stage 2	Increase in serum creatinine to 200% to 300% (2.0-3.0 × baseline value) or increase of >0.3 mg/dL (>26.4 mmol/L) but <4.0 mg/dL (<354 mmol/L)
Stage 3 <sup>a</sup>	Increase in serum creatinine to $\geq$ 300% (>3 times increase compared with baseline) or serum creatinine of $\geq$ 4.0 mg/dL ( $\geq$ 354 mmol/L), with acute increase of $\geq$ 0.5 mg/dL (44 mmol/L)

<sup>a</sup>Patients receiving renal replacement therapy were considered to meet stage 3 criteria, irrespective of other criteria.

impairment.<sup>65</sup> A recent analysis examining 13 studies with more than 1900 patients found that acute kidney injury (AKI) occurred in 8.3% to 57% of patients following TAVI (Table 2).<sup>66</sup> Factors noted to be associated with AKI include blood transfusion, TA approach, preoperative creatinine (Cr) >1.1 mg/dL, peripheral vascular disease, hypertension, and bleeding.<sup>66,67</sup>

Development of AKI is associated with a significant increase in both 30-day and late mortality,<sup>68,69</sup> and the need for renal replacement therapy (dialysis) post-TAVR confers a 10% increase in mortality rate.<sup>66</sup> AKI is often multifactorial, with preoperative CKD being the most significant risk factor for AKI on CKD. AKI may also result from hypotension during the procedure, long periods of rapid ventricular pacing, calcium emboli, medications, and contrast-induced nephropathy.

With regard to contrast-induced nephropathy, recent studies have shown that the actual dose of contrast agent used is not related to development of AKI.<sup>66,68</sup> Clinically, prevention of contrast-induced nephropathy continues to be poorly understood, and current recommendations include maintaining adequate hydration with an isotonic crystalloid, avoiding concurrent nephrotoxic agents (if possible) and minimizing the amount of contrast administered.<sup>70</sup> Hemodynamics, ventilation status, and mixed venous oxygen saturations should be optimized until the serum Cr has peaked and returned toward the baseline preoperative value. AKI will typically cause the serum Cr to peak 3 to 7 days after the insult.

Multiple studies have demonstrated an improvement in renal function following TAVR. Bagur et  $al^{69}$  found a significant increase in post-TAVR estimated glomerular filtration rate in 60% of their patients. These findings were very similar to data reported by Saia et  $al^{71}$  and Elhmidi et  $al^{68}$  where improvements in GFR were seen in 58% and 59% of the post-TAVR patients, respectively.

# **Vascular Considerations**

Vascular complications are one of the more frequent sources of perioperative morbidity and occur most frequently with the TF approach. Vascular injury is related to the large-caliber sheaths used and atherosclerotic nature of the vessels.<sup>72,73</sup> Major vascular complications (including aortic dissection, perforation, rupture, or bleeding requiring significant blood transfusions or intervention) occurred in 2% to 26% of patients with the TF approach and 5% to 7% with the TA approach.<sup>9</sup> In a small study comparing patients undergoing TAO and TA approaches, the TAO group had lower rates of both vascular complications and bleeding.<sup>74</sup>

In patients with hemodynamic instability, bleeding, retroperitoneal hemorrhage, and lower-extremity ischemia should be considered and evaluated with physical exam, non-contrast computed tomography, or urgent surgical exploration. The differential diagnosis involving major vascular complications should include access site hematoma, vascular dissection, vascular perforation, gastrointestinal bleeding, retroperitoneal bleeding, and pericardial bleeding.

# Endocrine and Nutrition Considerations

## Risk Factors and Glycemic Control

Within the cardiac surgery population, surrogate markers for malnutrition, such as low serum albumin level and low body mass index, place patients at higher risk for in-hospital and long-term mortality.<sup>16,75,76</sup> Targeting moderate glycemic control (glucose levels 120-180 mg/dL) has been recommended because it decreases the incidence of postoperative morbidity (particularly deep sternal wound infections) and mortality associated with acute hyperglycemia while minimizing the risk of hypoglycemia.<sup>77,78</sup> Implementing an insulin infusion protocol can be helpful in maintaining stable glucose levels, especially in patients requiring epinephrine infusions.

## Enteral Nutrition

The optimal timing of early enteral nutrition in critically ill patients remains an unanswered question.<sup>79</sup> There have been no randomized trials published to date on TAVR patients and post-procedure nutrition. Currently, American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)<sup>51</sup> guidelines recommend starting enteral nutrition for all appropriate patients within 24 to 48 hours of admission to the ICU. A recent review article on enteral nutrition in the acute phase of critical illness<sup>80</sup> highlights the uncertainty surrounding this topic. After reviewing the literature, one

of the authors' recommendations for clinical practice is to allow hypocaloric enteral feeding in the acute phase of critical illness for up to 7 days in previously well-nourished patients.

There is a deficit in the ICU nutrition literature regarding the management of moderately to severely malnourished patients. Future high-risk TAVR patients should be studied to further our knowledge of this complex clinical conundrum. For now, use of prealbumin levels and metabolic cart profiles provide guidance for nutrition supplementation in the chronic, critically ill post-TAVR patient.

#### Frailty

Frailty status has emerged in the medical literature as an important indicator of overall health and physiological reserve. Frailty, measured in the TAVR population by assessing gait speed, grip strength, serum albumin, and activities of daily living, is known to affect outcomes of older patients with heart disease<sup>81</sup> and those undergoing general surgery.<sup>82</sup> Green et al<sup>76</sup> reported on 159 patients in whom frailty status was assessed and who subsequently underwent TAVR. They found frailty status to be independently associated with 1-year mortality.

#### Summary

The prevalence of severe AS will continue to increase as medical management of chronic disease improves, and TAVR will be increasingly utilized in the management of these often elderly, high-risk patients. When compared with high-risk SAVR patients at 2 years, TAVR patients had a similar mortality rate (33.9% in TAVR vs 35% in SAVR) and equal improvement in symptoms and hemodynamics.<sup>43</sup> When compared with standard therapy (including balloon valvuloplasty), there were lower rates of death at 2 years (43.4% vs 68%) and rehospitalization (35% vs 72.5%) and improved functional status.<sup>44</sup> For our patients to experience these benefits, critical care practitioners must have a thorough understanding of the potential complications following TAVR. This knowledge, coupled with early diagnosis and appropriate therapeutic intervention, will allow us to improve TAVR outcomes through excellent ICU management.

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