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Critical Care [ALERT]

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SPECIAL FEATURE

Management of the Cardiac Surgery Patient

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The goal of this review is to provide an evidence-based narrative for the management of post-operative patients who have coronary artery bypass graft (CABG) surgery and heart valve repair/replacement surgeries.

MECHANICAL VENTILATION/ACID-BASE DISORDERS

Most importantly, initial ventilator settings should include a respiratory rate set to 20-25 breaths/minute to allow for compensation for the metabolic acidosis that commonly accompanies the postoperative state, a normal tidal volume (6 mL/kg of ideal body weight), and positive end-expiratory pressure (PEEP) set at 5 cm H_2O to 8 cm H_2O. Early extubation (within six hours of surgery completion) improves outcomes with respect to morbidity and inpatient mortality. Prolonged mechanical ventilation (> 24 hours after surgery) is a quality metric for both heart valve and CABG surgery. Patient characteristics that influence the duration of mechanical ventilation after CABG include depressed level of consciousness related to anesthetics, acid-base disturbances, bleeding, and hypoxemia related to cardiac or non-cardiac etiologies.[1] However, patient characteristics do not account for the variability between institutions with respect to duration of mechanical ventilation after CABG.[2]

Postoperatively, decreases in sodium and increases in chloride levels, relative to presurgical levels, can be expected most likely because of a combination of antidiuretic hormone release and intravenous saline. Decreases in albumin and inorganic phosphate levels may be seen.[3] The anion gap or base excess (BE) has been used as a marker of the number of unmeasured anions in the blood, but neither predicts mortality in the critically ill.[4] Hyperlactatemia after cardiac surgery is frequent and is related to tissue hypoxia related to cardiac surgery (hypothermia/cardioplegia/cardiopulmonary bypass). In contrast to BE/anion gap, persistently elevated lactate levels beyond six hours after surgery are an independent marker of mortality.[5]

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POST-CARDIOTOMY HYPOTENSION

Cardiac tamponade, vasoplegic syndrome, global cardiac failure, or right ventricular (RV) failure are considerations in the hypotensive post-cardiotomy patient. Tamponade may occur up to 10 days after surgery and is more common with valvular surgery. The usual echocardiographic signs of tamponade may be absent on transthoracic echocardiogram (TTE), and small posterior collections (seen in 50% of all cases of tamponade) may lead to hemodynamic compromise.[6] Thus, a high clinical suspicion is mandatory, with a low threshold for obtaining a transesophageal echocardiogram (TEE). Although many patients receive vasoactive agents post-operatively, this practice varies widely.

A large retrospective cohort study assessed this practice nationally and found that, although more than 90% of patients received at least one vasoactive medication perioperatively, this practice declined to about 30% on postoperative day (POD) 1.[7] In this survey, although phenylephrine was the most common vasopressor used during hospitalization, norepinephrine use was more common on POD 1. Conditions that are associated with the use of vasopressors include arrhythmias, urgent or emergent surgery, congestive heart failure (CHF), and preoperative use of angiotensin-converting enzyme (ACE) inhibitors. Post-cardiotomy shock may manifest as failure to wean from cardiopulmonary bypass (CPB) or vasopressor-refractory hypotension (the vasoplegic syndrome).[8] The vasoplegic syndrome occurs in 8% of patients after CPB and is characterized by a low central venous pressure (CVP), a low pulmonary artery wedge pressure, low systemic vascular resistance (SVR), and a normal-high cardiac index (CI). Perioperative beta-blocker or ACE inhibitor use and longer CPB times predict a higher risk for the vasoplegic syndrome. Norepinephrine or epinephrine is the typical first-line agent, with vasopressin added as necessary while coming off CPB. Phenylephrine may be preferred in the setting of rapid atrial fibrillation. Epinephrine typically is used for low cardiac output states as documented on pulmonary artery catheter or TEE assessment. In a single randomized trial that compared norepinephrine and epinephrine as the vasopressor of choice in the setting of post-cardiotomy vasoplegic shock, epinephrine (but not norepinephrine) was associated with decrements in BE, new acidosis, and hyperlactatemia.[9]

Vasopressin deficiency has been described after CPB.[10] Vasopressin also has been shown to actively induce dilation in the pulmonary vasculature under hypoxic conditions via a V1 receptor-mediated release of nitric oxide.[11] For these two reasons, vasopressin is used as an adjunct in the setting of vasoplegic shock as well as up front in the setting of pulmonary hypertension. Vasopressin infusions typically are dosed in the 4 IU/hour to 6 IU/hour range, which is higher than the 2 IU/hour to 3 IU/hour infusions typically used in the setting of septic shock. Dobutamine usually is added on in settings of RV or biventricular failure to maintain a cardiac index of > 2.1 L/minute/m^2. Methylene blue infusion has been used to reverse refractory vasoplegia, and its use has been associated with reduced mortality.[12,13] A single 5-gram dose of intravenous hydroxycobalamin may be attempted in methylene blue-refractory vasoplegic shock.[14]

Refractory hypotension may be related to pure RV failure in the setting of severe pulmonary hypertension (PH). TTE criteria of an impaired RV include right ventricular systolic pressure (RVSP) of > 50 mmHg, tricuspid annular plane systolic excursion (TAPSE) < 17 mm, and a tricuspid annular velocity of < 9 cm/second. RV failure may be exacerbated by hypoxia, acidosis, and/or hypercapnia; a PaO_2 of > 90 mmHg and a pH > 7.45 are reasonable targets in this setting.[15] One study compared inhaled nitric oxide (iNO) and inhaled prostacyclin to treat PH (pulmonary vascular resistance [PVR] > 200 dynes·sec/cm^5 and transpulmonary pressure gradient [TPG] > 10 mmHg) after valve replacement surgery for mitral stenosis.[16] Prostacyclin (10 µg/mL) was nebulized in line with the inspiratory limb of the ventilator circuit at a rate of 0.30 mL/min. Nitric oxide was maintained at 20 ppm, with the FiO_2 maintained at the lowest concentration possible. Both treatments were identical with respect to improvement in cardiac output and

reductions in mean pulmonary artery pressure, TPG, and PVR. Nebulized prostacyclin was easier to administer and less toxic.

Another study assessed the additive effects of inhaled iloprost and iNO in patients undergoing mitral, aortic, or tricuspid valve replacement/repair with or without CABG.[17] Patients were high risk and had preoperative left ventricular ejection fractions of < 35% and severe PH (RVSP > 50 mmHg and reduced RV systolic function). All patients were weaned from CPB on an epinephrine and dobutamine infusion to maintain a CI of > 2.1 L/min/m^2. Pulmonary vasodilators were added if there was evidence of continued RV failure (TAPSE < 10 mm, persistent CI < 2.1 L/min/m^2 despite vasopressors/inotropes, or need for high inotropic support [defined as epinephrine > 0.1 µg /kg/min and/or dobutamine > 10 µg /kg/min]). Inhaled iloprost (10 µg nebulized using a jet nebulizer every two hours) was added to iNO (10 ppm) if endpoints were not reached, and combined treatment had additive effects on PVR and RV systolic function. Milrinone and/or intravenous sildenafil may be added in these settings to allow weaning of these inhaled agents and facilitate extubation. Post-cardiotomy cardiac failure is defined as a systolic blood pressure (SBP) < 90 mmHg (or vasopressor support to maintain SBP > 90 mmHg) in addition to CI < 2.2, pulmonary artery wedge pressure (PAWP) > 15 mmHg, and evidence of end organ hypoperfusion. Mechanical support in this scenario may include intra-aortic balloon pump (IABP) placement. Ventricular assist devices (VADs), including right ventricular assist devices (RVADs) for right ventricular failure, left ventricular assist devices (LVADs), or biventricular assist devices (BiVADs) for biventricular failure, may be useful as escalating therapy for IABP-refractory shock.[18] Some centers prefer immediate transition to venous-arterial extracorporeal membrane oxygenation (VA-ECMO) rather than a stepwise progression from IABP to VAD to VA-ECMO. Alternatively, VADs (instead of VA-ECMO) may facilitate early extubation and ambulation while awaiting ventricular recovery.[19] Decision-making in this regard remains a surgeon- or institution-specific preference based on expertise and immediate availability.

Hypotension associated with valve replacement surgery has unique considerations that are discussed briefly here. Excessive bleeding after aortic valve replacement must include consideration of bleeding from the aortotomy suture line. Left ventricular (LV) hypertrophy is almost universal in patients with a stenotic or regurgitant aortic valve. Therefore, maintenance of adequate preload for a hypertrophied LV with fluid loading is important, but it is imperative that afterload is not increased excessively since this may place undue stress on the aortotomy suture line. Most clinicians will strive to maintain an SBP < 140 mmHg to limit stress on the suture line. Intravenous nitroglycerin or nicardipine may be used for postoperative hypertension. Since the aortic valve is replaced close to the coronary ostia, malpositioning of the prosthesis may lead to coronary occlusion of either the left or, more commonly, the right coronary ostium resulting in refractory LV failure and/or refractory ventricular arrhythmias.[20]

Massive bleeding after mitral valve surgery can be the result of catastrophic atrioventricular groove disruption.[21] A severely calcified mitral valve requiring debridement is a risk factor. Elderly patients with a friable myocardium also are at risk. Although typically discovered during surgery, on occasion this may present in the immediate postoperative period. A rare complication of mitral valve replacement/repair that can lead to refractory shock is systolic anterior motion (SAM) of the anterior bioprosthetic mitral leaflet.[22] SAM leads to dynamic LV outflow tract obstruction, which may be exacerbated by a rapid heart rate and a small underfilled LV. Management includes beta-blockade to slow the heart rate, fluid therapy to increase preload, and a deliberate reduction in the dose of vasopressors/inotropes. Reoperation may be needed in severe cases.

In the setting of post-cardiotomy cardiac arrest due to ventricular fibrillation, published guidelines recommend three attempts at defibrillation prior to external chest compressions.[23] An attempt at pacing (if internal pacer wires are present) is recommended for those patients with extreme bradycardia or asystole. Pulseless electrical activity (PEA) arrests typically are managed with immediate resternotomy and internal cardiac massage with the presumption that either occult bleeding in the chest or tamponade is the most likely etiology. Other causes of PEA arrests in this scenario also must be excluded. At least one survey of clinicians reflected broad agreement with these guidelines, including emergent resternotomy and internal cardiac massage within five minutes of arrest if surgery occurred within the previous 24 hours.[24]

FLUID MANAGEMENT

Assessment of Resuscitation Endpoints

Endpoints for fluid resuscitation after cardiac surgery include mean arterial pressure > 65 mmHg, CVP 8 mmHg to 12 mmHg, optimized cardiac index > 2.2 L/min/m^2, and mixed venous oxygenation > 65 mmHg if a pulmonary artery catheter (PAC) is in place. None of the dynamic ultrasound parameters relating to the inferior vena cava (IVC) predict fluid responsiveness in mechanically ventilated patients post-CABG.[25] A single study of 40 patients assessed the utility of respirophasic carotid artery peak velocity

variation ([maximal velocity during one respiratory cycle - minimal velocity during one respiratory cycle]/average) as a predictor of fluid responsiveness in mechanically ventilated patients. A cutoff of 11% was 85% sensitive and 82% specific for fluid responsiveness.[26] Central venous oxygen saturation ($ScvO_2$) and mixed venous oxygen saturation (SvO_2) are used commonly as endpoints for resuscitation. Yazigi et al performed simultaneous measurements of $ScvO_2$ and SvO_2 prior to fluid therapy in patients with CI < 2.2 L/min/m^2 and pulmonary artery occlusion pressure (PAOP) < 12 mmHg and then after fluids had been administered to bring CI to > 2.5 L/min/m^2.[27] There was a large disagreement between values. The authors concluded that $ScvO_2$ could not be used as a substitute for SvO_2. This concept seems to apply to patients undergoing valvular surgery as well.[28] With respect to the use of resuscitation endpoints, anesthesiologists were more likely to use TEE, pulse pressure variation, and stroke volume variation in one survey of clinicians in the United States.[29] Central venous pressure and pulmonary artery occlusion pressures were used to indicate volume status by 73% and 53% of clinicians, respectively, in this survey.

Choice of Fluids for Resuscitation

Chloride-restricted intravenous fluids (IVFs) reduce the rate of stage 1 acute kidney injury (AKI) at 24 and 48 hours compared with chloride-liberal IVFs.[30] The use of 5% albumin is frequent, albeit controversial. A recently published study has elevated the debate on albumin use in the resuscitation of cardiac surgery patients. The HAS-FLAIR study was a "pre/post" intervention study in a single center wherein 50 patients undergoing cardiac surgery were resuscitated only with crystalloids, and a subsequent 50 patients were given two initial treatments with 100 mL of 20% albumin (total of 200 mL) followed by crystalloid if necessary.[31] Interventions were targeted to correct hypotension or hypovolemia or optimize cardiac index in the first 24 hours after surgery. The use of 20% albumin bolus therapy led to an overall smaller use of fluids, a decreased median overall dose of norepinephrine, and a shorter median time to cessation of norepinephrine. The lack of randomized trials in this setting makes specific recommendations regarding fluid choice difficult.

TREATMENT OF BLEEDING AND COAGULOPATHY

Excessive bleeding has been described as > 200 mL/hour total output, 1,000 mL in the first 24 hours, or excessive oozing during surgery or the immediate postoperative period.[32] Typically, this relates to post-CPB coagulopathy and/or the use of antiplatelet drugs preoperatively. Other risk factors for excessive bleeding include advanced age, prolonged cardiopulmonary bypass, presence of heart failure, chronic kidney disease, chronic obstructive pulmonary disease, and preoperative anticoagulation.[33] Heparin typically is administered during surgery and reversed postoperatively with protamine (1 mg for every 100 units of heparin administered). Tranexamic acid is an antifibrinolytic agent typically used intraoperatively. On occasion, both these agents may be indicated in the scenarios of excessive postoperative bleeding.

Coagulation parameters may be monitored using the prothrombin and partial thromboplastin times, platelet counts, and thromboelastography (TEG) or rotational thromboelastometry (ROTEM).[34] First, TEG or ROTEM allows an understanding of how quickly a clot forms (the R time for TEG; coagulation time for ROTEM). These values indicate a lack of factors in the coagulation cascade and so abnormalities can be treated with either fresh frozen plasma (FFP) or prothrombin complex concentrate (PCC). The next variable that is assessed is the strength of the clot once formed (the maximum amplitude [MA] for TEG; maximum clot formation [MCF] for ROTEM). These values indicate the extent of fibrin cross-binding and the contribution of platelets to the strength of the clot formed. Newer versions of TEG and ROTEM are able to specify whether a deficiency in platelets or fibrin cross-linking is the reason for reduced clot strength, thereby guiding whether a platelet transfusion, cryoprecipitate, or both may be indicated. Finally, these assays assess how quickly the clot is lysed (lysis at 30 and 60 minutes [LY30/LY60] for TEG; the lysis index [LI30] for ROTEM). These are markers of intrinsic fibrinolysis; they are more useful intraoperatively, but early lysis of a clot may inform decision-making with respect to administration of tranexamic acid postoperatively as well. A TEG-based strategy does seem to reduce the need for allogeneic blood products and coagulation factors in cardiac surgery patients.[34]

In the absence of TEG/ROTEM, a prolonged activated coagulation time (ACT) would inform decisions to treat with protamine (typically 25 mg for an ACT between 120 and 150 seconds and 50 mg if > 150 seconds). Bleeding in the setting of low fibrinogen levels (typically < 150 mg/dL) would trigger transfusion with cryoprecipitate, since each unit of cryoprecipitate is expected to raise the fibrinogen level by 10 mg/dL. Alternatively, FFP or PCC may be used in this setting. One retrospective study that assessed the use of PCC or FFP in CABG patients suggests that PCC may be more effective than FFP in reducing the need for transfusion after CABG.[35] If platelet transfusions are indicated by TEG/ROTEM results or for a critical value of thrombocytopenia, a "six pack" of platelets (1 unit of apheresis platelets) typically will raise platelet counts by approximately 30,000/μL.

Perioperative packed red blood cell (PRBC) transfusions may increase morbidity and mortality in CABG patients, and guidelines recommend restrictive transfusion with a hemoglobin threshold of 7 g/dL.[33,36] Transfusion to hemoglobin above 10 g/dL is not recommended. The TRACS randomized controlled trial showed that among patients undergoing cardiac surgery, a transfusion trigger of 9.1 g/dL was non-inferior to 10.5 g/dL with respect to 30-day all-cause mortality and severe morbidity.[37] The number of PRBC units transfused was an independent risk factor for death or complications at 30 days. Subsequently, results of the TRICS III trial support recommendations for an even more restrictive strategy.[38] This trial randomized patients undergoing cardiac surgery to transfusion with a hemoglobin trigger of < 7.5 g/dL or < 9.5 g/dL anytime from induction of anesthesia. All patients were at moderate to high risk of death related to surgery. The restrictive strategy was noninferior to the liberal strategy with respect to relevant outcomes (death, stroke, new-onset renal failure, and myocardial infarction). Less blood was transfused in the restrictive strategy group. As in non-cardiac surgery settings, a lower threshold appears to be better, and a trigger of 7.5 g/dL seems reasonable in cardiac surgery patients cared for in the intensive care unit (ICU). Some clinicians target higher hemoglobin levels for patients with critical end organ ischemia (history of stroke, carotid stenosis, or gut ischemia), choosing thresholds closer to 10 g/dL. This practice is supported by Level C evidence.[33]

ACUTE KIDNEY INJURY

Postoperative acute kidney injury (AKI) relates to the usual culprits in severely ill patients: hypovolemia/hypotension (pre-renal), drug-related adverse effects, and congestion relating to fluid/volume overload (intra-renal). AKI is defined as an increase in the serum creatinine by > 0.3 mg/dL within 48 hours of surgery or urine volume < 0.5 mL/kg for at least six hours.[39] The presence of AKI or chronic kidney disease (CKD) prior to surgery is an independent risk factor for mortality after surgery.[40] Since CVP relates to the risk of AKI in patients with congestive heart failure, venous congestion also may relate to AKI post-cardiotomy.

A recent study attempted to relate quantitative assessment of portal vein pulsatility and renal venous congestion using Doppler interrogation to outcomes post-cardiotomy.[41] Portal venous flow (as in any other vein) typically is non-pulsatile. With increasing intrahepatic congestion, pulsatile flow is conducted from the right heart down the IVC, into the hepatic vein, and then via the sinusoids into the portal vein. Portal vein pulsatile flow > 50% predicted AKI with a hazard ratio of 2.09 for any AKI and 5.12 for severe AKI. Similarly, high right-sided pressures induced congestion in the renal medulla and cortex, increasing resistance to arterial blood flow through the kidney. Severe alterations to normal intra-renal flow as assessed by pulse wave Doppler were associated with increased risk for AKI. The management of AKI post-cardiotomy and after hypotension has resolved rests on diuresis to allow decongestion. Whether decongestion as guided by ultrasound-related targets improves outcomes remains unknown.

MANAGEMENT OF ARRHYTHMIAS

Atrial Fibrillation

Atrial fibrillation (AF) typically occurs between POD 2 and POD 6, with a peak incidence on POD 2.[42] A higher intraoperative fluid balance, valve replacement surgery, higher intraoperative core temperature, age, cardiopulmonary bypass time > 120 minutes, and high-dose inotropes are predictors of AF after cardiac surgery.[43,44] Treating hypokalemia and hypomagnesemia is imperative in the management of AF. Beta-blockers and calcium channel blockers may be used as first-line agents if blood pressure and left ventricular function are not prohibitive. These agents should not be used in the setting of severe pulmonary hypertension.[45]

Amiodarone infusions remain the "workhorse" of the management of de novo AF (for both rate and rhythm control). The pharmacological characteristics of amiodarone make it best suited in settings of heart failure and hypotension, commonly seen post cardiac surgery.[46] Amiodarone infusions typically begin with a 150-mg bolus delivered over 10 minutes, followed by a continuous infusion of 1 mg/min for six hours and then 0.5 mg/min for 18 hours to complete the "three bag regimen" for a total loading dose of ~ 1,000 mg. If necessary, repeat boluses of 150 mg may be administered over 10-30 minutes, but typically not exceeding six to eight (total bolus dose of 1,350 mg) in a 24-hour period. If indicated for ongoing rhythm and/or rate control, a total loading dose of 10 grams is typical, which may be given orally or intravenously depending on whether the patient's gut is functional. The major adverse effect of amiodarone is hypotension, which may be averted by slowing the infusion rate; it is important to note that total daily doses of > 2.1 g also have been associated with hypotension. Electrical cardioversion is more successful in scenarios of short duration AF and is indicated in the hemodynamically unstable patient. An initial biphasic shock at 100 J typically is selected, with escalation to 200 J if unsuccessful.

Pacemaker Management

Epicardial wires typically are placed on the surface of the right atrium and the right ventricle, and, by convention, the former emerges on the right side of the sternum and the latter on the left. The major indication for pacing is complete heart block and bradycardia without reliable atrioventricular (AV) node

conduction. With dual chamber pacing wires in place, the pacemaker function can be used to pace the atrium using the normal AV node to conduct to the ventricle in the setting of sinus bradycardia, for example. In this scenario, the pacemaker senses the atrium and, if no depolarization is detected, a pacing spike is delivered at the set rate. If a rate above a preset rate is sensed, no spike is delivered (AAI mode: Atrium paced, Atrium sensed, response to sensing: Inhibited). The DDD mode (Dual chambers paced, Dual chambers sensed, response to sensing: Dual paced and inhibited as required) is the most commonly used pacemaker mode. This mode allows a "set it and forget it" approach and is useful in all indications for pacing. In essence, this mode allows a takeover of the cardiac conduction system, sensing for an atrial depolarization below the set sensing rate, and delivering an atrial pacing spike if none is detected. A ventricular spike is delivered if ventricular depolarization is not detected at the prespecified end of the PR interval. The pacemaker is not triggered ("inhibited") if intrinsic atrial activity is detected above a prespecified rate.[47] ■

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REFERENCES

The complete list of references is available online: http://bit.ly/3pacPYd

ABSTRACT & COMMENTARY

Pressure Support Compared to T-Piece Trial: What Is the Optimal Strategy?

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SYNOPSIS: Post-hoc analysis of a multicenter, randomized clinical trial among adults receiving at least 24 hours of mechanical ventilation who were ready for ventilator weaning revealed that the use of pressure support significantly increased the proportion of patients successfully extubated compared to T-piece.

SOURCE: Thille AW, Coudroy R, Nay MA, et al. Pressure-support ventilation vs T-piece during spontaneous breathing trials before extubation among patients at high risk of extubation failure: A post-hoc analysis of a clinical trial. *Chest* 2020;158:1446-1455.

Although T-piece still is the most frequently performed trial prior to extubation, guidelines suggest that an initial spontaneous breathing trial (SBT) should be conducted using pressure support ventilation (PSV) rather than a T-piece trial. This guideline was based on a large randomized controlled trial (RCT) that showed the proportion of patients who were extubated successfully 72 hours after an initial SBT was higher with PSV than with T-piece. Since this trial was thought to include mostly patients at low risk for extubation failure, Thille and colleagues performed a post-hoc analysis of a multicenter RCT from April 2017 to January 2018 among 641 adults who were intubated more than 24 hours, were ready for extubation after successful SBT, and deemed high risk for extubation failure in 30 intensive care units (ICUs) in France. The initial SBT was performed using PSV or T-piece according to either the physician's or center's decision. The primary outcome was the proportion of patients who were extubated successfully 72 hours after the initial SBT and not reintubated. High-risk patients were identified as patients older than 65 years of age or with underlying cardiac or respiratory disease. The underlying chronic cardiac diseases included left ventricular dysfunction (defined by left ventricular ejection fraction less than or equal to 45%), a history of cardiogenic pulmonary edema, documented ischemic heart disease, or permanent atrial fibrillation. The underlying chronic lung diseases included chronic obstructive pulmonary disease (COPD), obesity-hypoventilation syndrome, or restrictive pulmonary disease. The exclusion criteria were long-term treatment with noninvasive ventilation (NIV) at home, contraindication to NIV, underlying neuromuscular disease, traumatic brain injury leading to intubation, patients with unplanned extubation (accidental or self-extubation), or patients with a do-not-reintubate order at the time of extubation.

The initial SBT was accomplished with PSV (7 cm H_2O in median without positive end-expiratory pressure [PEEP]) in 243 patients (38%) and with a T-piece in 398 patients (62%). The amount of patients who were extubated after the first attempt at SBT was 77% (186/283) in the PSV group and 63% (249/398) in the T-piece group ($P = 0.0002$). Sixty-seven percent (162/243) of patients in the PSV group remained successfully extubated 72 hours after initial SBT, compared to 56% (223/398) of patients in the T-piece group (absolute difference 10.6%; 95% confidence

interval [CI], 2.8 to 28.1; *P* = 0.0076). Reintubation rates within the subsequent 72 hours did not differ significantly between the PSV and T-piece groups (13% vs. 10%, respectively, *P* = 0.4259). First attempt SBT with PSV was independently associated with successful extubation (adjusted odds ratio (OR), 1.60; 95% CI, 1.30 to 2.18; *P* = 0.0061).

■ COMMENTARY

Approximately 10% to 15% of all mechanically ventilated patients who are extubated will fail, and higher numbers are expected for those at particularly increased risk.[1] SBT may be performed using T-piece (no inspiratory pressure augmentation) or using PSV (generally limited to 5 cm H_2O to 8 cm H_2O or automatic tube compensation). There has been controversy regarding which method is optimal.

Many argue that patients who demonstrate an ability to breathe while receiving no inspiratory pressure augmentation convincingly prove readiness to wean. Those who disagree stress that patients who otherwise may be extubated safely will fail an SBT without pressure augmentation but will pass with pressure support. In a systematic review and meta-analysis of 31 trials, it has been shown that patients undergoing SBTs using PSV vs. T-piece appear to be 6% (95% CI, 2% to 10%) more likely to be extubated successfully.[2] The most recent international practice guidelines published in 2017 made a conditional recommendation (moderate quality of evidence) that the initial SBT be conducted with inspiratory pressure augmentation (5 cm H_2O to 8 cm H_2O) rather than without (T-piece or continuous positive airway pressure [CPAP]) for patients who are acutely hospitalized and ventilated for more than 24 hours.[3] Shortly after these recommendations, Subirà and colleagues conducted a randomized clinical trial among 1,153 adults deemed ready for weaning after at least 24 hours of mechanical ventilation in 18 ICUs.[4] They found that significantly higher rates of successful extubation occurred using an SBT consisting of 30 minutes of PSV than with two hours of T-piece ventilation. Unfortunately, there was concern that this trial included a majority of patients who were low risk for extubation failure. The current study, therefore, focused on high-risk patients.

It is important to point out that this study was a post-hoc analysis of a multicenter trial. Patient characteristics were similar between the two groups, except that the PSV group had a lower body mass index (BMI). The PSV trials were conducted using a pressure-support level of 7.0 cm H_2O, a PEEP level of 0 cm H_2O, and an FiO_2 of 30%. The T-piece trials were conducted using an additional oxygen flow of 4 L/min. In addition, the PSV trials were longer than the T-piece trials (60 minutes vs. 50 minutes). This is in contrast to the Subirà article, in which PSV trials were substantially shorter than the T-piece trials.[4] Among the 30 participating centers, six centers always performed SBT using PSV (114 patients, 18%), 11 centers always performed SBT using T-piece (229 patients, 36%), and 13 centers used PSV or T-piece (298 patients, 46%). Even though the physician had the opportunity to choose the type of SBT, the proportion of patients successfully extubated 72 hours after initial SBT was lower in the 11 centers that always performed T-piece trials compared to the six centers that always performed SBTs using PSV and the 13 centers that could also use PSV for SBTs (*P* = 0.0014). Since the proportion of patients who remained extubated 72 hours after the initial SBT was significantly higher in centers that only performed PSV trials compared to centers that only performed T-piece trials, the potential effect of bias is diminished to some extent.

The previously mentioned study by Subirà and colleagues had attending physicians decide on the extubation strategy (e.g., whether to reconnect the patient to the ventilator for one hour before extubation, or whether to administer NIV or high-flow nasal cannula after extubation).[4] The physicians were not blinded, and more patients were provided with prophylactic high-flow nasal oxygen or NIV in the PSV SBT group (24.7% vs. 18.7%), which may have affected the results. It is an added benefit to the literature that the postextubation plan of care was randomized in this trial. Although the original study showed that NIV immediately after extubation decreased reintubation rates significantly in patients who were at high risk of extubation failure, the proportion of patients who received NIV after extubation was identical in the two groups.

Although it also is important to note that Thille's data further support SBT with PSV, the question remains whether all patients will benefit from the same strategy. Interestingly, Thille and his group had equally distributed the patients with underlying chronic cardiac disease or lung disease between the PSV and T-piece groups. Unfortunately, it is not clear how many patients were known to have COPD and the severity of that COPD. One would consider that a patient with more severe emphysematous changes, a quite compliant state, may not respond to a PSV of 8 cm H_2O the same as a patient with mild COPD without emphysematous changes. Although a trial published by Pellegrini and colleagues did not particularly address patients with emphysema, it revealed that T-piece almost doubled the time to liberation in the difficult/prolonged-weaning COPD subgroup, although it did not influence the overall or 48-hour reintubation rates.[5] Even though underlying chronic cardiac disease also was distributed equally, the details regarding heart failure were not known. Small amounts of pressure support and PEEP

may have significant hemodynamic effects and may reduce the work of breathing.[6] Removal of this support after extubation may result in rapid deterioration of left ventricular function leading to pulmonary edema. Although trials overall are pointing to PSV as an ideal weaning mode, T-piece trials still may be considered in patients with impaired cardiac function or severe emphysematous COPD since it is possible that this mode may unmask the need for further optimization prior to extubation.

This study supports the practice of SBT using PSV since it may hasten extubation without the increased risk of reintubation, especially in patients who are at high risk of extubation failure. Prior to applying this strategy to all patients in the ICU, a larger prospective RCT may be warranted to confirm these findings since this trial was a post-hoc analysis. Interestingly, Thille and colleagues are conducting an investigator-initiated, multicenter RCT comparing T-piece to PSV for SBTs in critically ill patients at high risk of reintubation.[7] This trial promises to give further clarity to this controversy. ■

REFERENCES

1. Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 2013;187:1294-1302.
2. Burns KEA, Soliman I, Adhikari NKJ, et al. Trials directly comparing alternative spontaneous breathing trial techniques: A systematic review and meta-analysis. *Crit Care* 2017;21:127.
3. Schmidt GA, Girard TD, Kress JP, et al. Official Executive Summary of an American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: Liberation from mechanical ventilation in critically ill adults. *Am J Respir Crit Care Med* 2017;195:115-119.
4. Subira C, Hernandez G, Vazquez A, et al. Effect of pressure support vs T-piece ventilation strategies during spontaneous breathing trials on successful extubation among patients receiving mechanical ventilation: A randomized clinical trial. *JAMA* 2019;321:2175-2182.
5. Santos Pellegrini JA, Boniatti MM, Boniatti VC, et al. Pressure-support ventilation or T-piece spontaneous breathing trials for patients with chronic obstructive pulmonary disease - A randomized controlled trial. *PLoS One* 2018;13:e0202404.
6. Kuhn BT, Bradley LA, Dempsey TM, et al. Management of mechanical ventilation in decompensated heart failure. *J Cardiovasc Dev Dis* 2016;3.
7. Thille AW, Coudroy R, Gacouin A, et al. T-piece versus pressure-support ventilation for spontaneous breathing trials before extubation in patients at high risk of reintubation: Protocol for a multicentre, randomised controlled trial (TIP-EX). *BMJ Open* 2020;10:e042619.

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.

CME/CE QUESTIONS

1. **Which of the following is contraindicated in the post-cardiotomy patient with atrial fibrillation and severe pulmonary hypertension?**
   a. Amiodarone for rate control
   b. Cardioversion for the hypotensive patient
   c. Beta-blockade for rate control
   d. Inhaled nitric oxide for right ventricular failure
2. **When interpreting thromboelastography results in the post-cardiotomy patients, which one of the following indicates the correct pairing for therapeutic intervention?**
   a. Prolonged R time and fresh frozen plasma
   b. Increased maximum amplitude and vitamin K
   c. Increased lysis time and cryoprecipitate
   d. Increased activated coagulation time and protamine
3. **In the study by Thille et al, what type of spontaneous breathing trial significantly increased the proportion of high-risk patients successfully extubated within the following 72 hours?**
   a. Pressure support ventilation without positive end-expiratory pressure (PEEP)
   b. T-piece
   c. Synchronized intermittent mandatory ventilation
   d. PEEP levels of 10 cm H_2O