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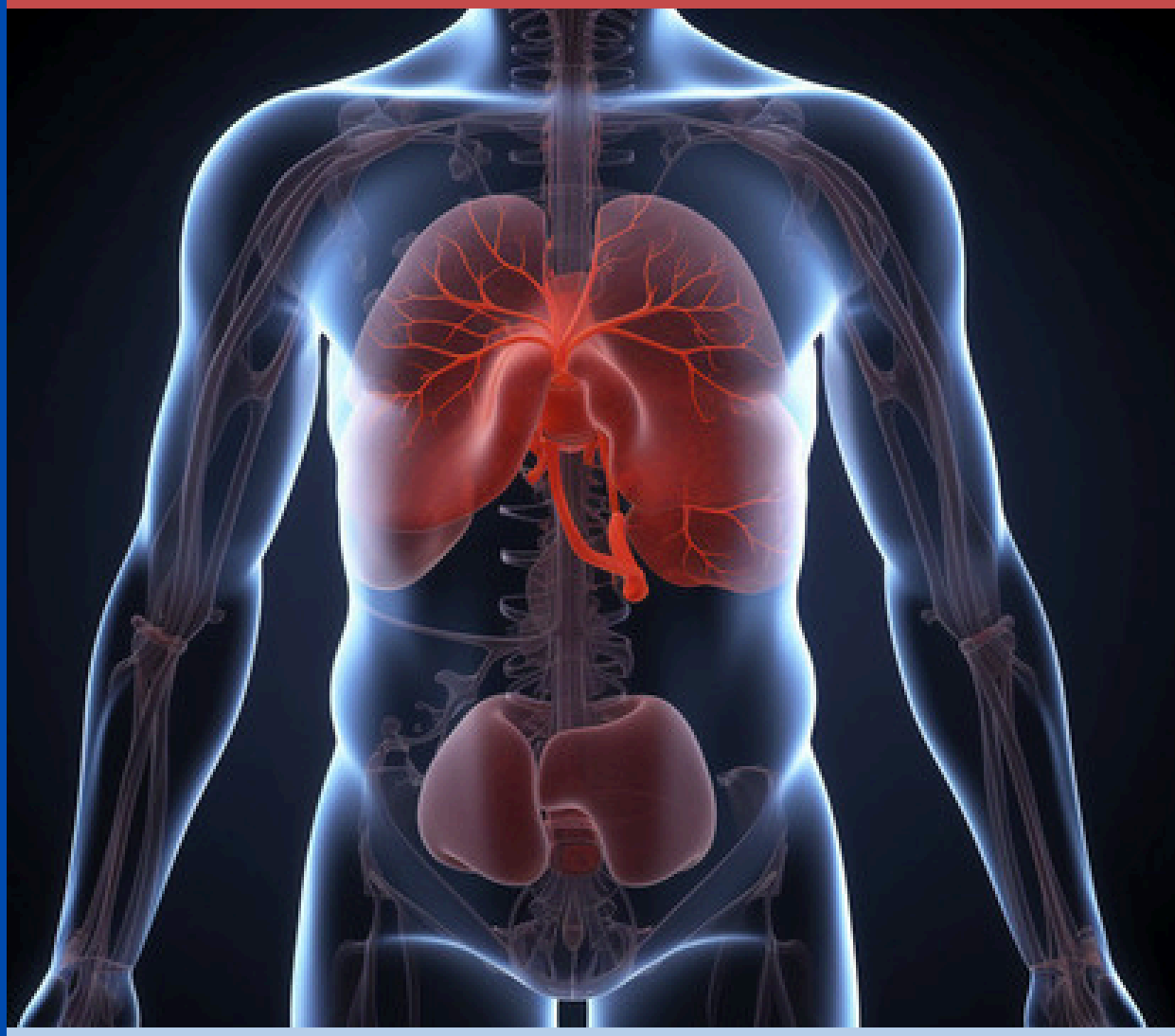
PULMONARY & CRITICAL CARE INSIDER



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VIEWPOINT

DUSTIN D. LINN, PHARMD, MBA, BCPS, BCCCP

Discordance between Oscillometric and Invasive Blood Pressure Measurements

Blood pressure monitoring is of importance for critically ill patients to prevent organ dysfunction and mortality. Mean arterial pressure (MAP) and systolic arterial pressure (SAP) were identified as having the blood pressure components having the strongest association with mortality (Khanna, 2023). Evidence has demonstrated that more than 90% of patients with distributive shock have at least one mean arterial pressure (MAP) reading less than 65 mmHg, a common blood pressure target in critically ill patients (Vincent, 2018). Furthermore, 62% of these patients spend at least two hours below a MAP threshold of 65 mmHg and 17.2% spend more than two hours below a threshold of 55 mmHg. (Khanna, 2023). In patients with sepsis, each 1 mmHg of time-weighted average MAP below 65 mmHg is associated with a 7% increase in the acute kidney injury, 3.7% increase in risk for myocardial injury, and 11.4% increase in the risk of death (Maheshwari, 2018). Ensuring patients maintain blood pressure above targets to ensure organ perfusion is essential. Therefore, it is ideal to have a safe and accurate blood pressure monitoring device to make certain these targets are met.

Automated oscillometric non-invasive blood pressure (oscNIBP) devices and invasive intraarterial catheters are the most common modalities used to measure blood pressure in critically ill patients. The reference method for arterial blood pressure in critically ill patients is by direct measurement with an arterial catheter. This catheter is most often placed in the radial artery. While the incidence of complications with arterial catheters seem to be rare, these complications may include temporary vascular occlusion, thrombosis, ischemia, hematoma formation, and infection (Nuttall, 2016). In contrast to providing a direct measurement, oscNIBP values are calculated. Oscillometric devices measure the amplitude of pressure changes in the occluding cuff as the cuff deflates from above the systolic pressure. Pulsations reach a maximum amplitude at an approximation of MAP and then diminish. The result is an “oscillometric envelope” from which systolic, diastolic, and mean pressures are calculated. OscNIBP devices are noninvasive, require no special training for placement, and may help reduce or eliminate the risk of complications from arterial catheters. However, oscNIBP monitoring devices may not always provide concordant measurements with arterial line measurements. This review will highlight literature describing this phenomenon of differences in oscNIBP and ABP measurements.

VIEWPOINT

DUSTIN D. LINN, PHARMD, MBA, BCPS, BCCCP

The largest study to compare invasive and noninvasive blood pressure monitoring evaluated 24,225 noncardiac surgery cases in which a radial arterial catheter was used to compare the difference between NIBP and intraarterial blood pressure. NIBP was likely to be higher than intraarterial blood pressure at lower blood pressures for mean, systolic, and diastolic pressures and lower than intraarterial blood pressure at higher pressures (Figure 1). Other studies have sought to evaluate the correlation between oscNIBP and intraarterial blood pressure in critically ill patients. Meidert, et al. conducted a prospective observational study of hypotensive patients in the emergency department equipped with an arterial catheter to investigate the accuracy of oscNIBP (Meidert, 2022). The study included 75 simultaneous oscNIBP and intraarterial blood pressure readings from 30 patients. Invasive mean MAP was 51 ± 8 mmHg while mean oscNIPB was 64 ± 15 mmHg, resulting in a mean of differences of 13 ± 15 mmHg (95% limits of agreement: -16 to 41 mmHg). In an error grid analysis, 42% of paired oscNIBP measurements differed from intraarterial measurements with high clinical relevance, meaning there would be practice differences when using one measurement over another (e.g., failure to recognize and initiate treatment for hypotension). Kaufmann, et al. prospectively collected oscNIBP and ABP values in critically ill ICU patients with and without norepinephrine administration (Kaufmann, 2020). Amongst 736 patients, there was little mean difference in blood pressure values, but large limits of agreement, suggesting significant imprecision. Around 1 in 4 patients had differences in blood pressure that may have led to at least low-risk treatment decision differences.

The question of discordant NIBP and ABP readings also must consider the potential for arterial pressure gradients in critically ill patients. This is a prudent consideration given that oscNIBP measurements are typically obtained from the brachial artery, while the more distal radial artery is the most frequent site of arterial cannulation due to its ease of accessibility. In healthy patients, SAP is higher in peripheral arteries compared to central arteries; however, this may be reversed in critically ill patients with higher central and lower peripheral pressures. The cause of this reversal is unclear, but may be related to risk factors such as small arterial diameter from vasoactive medications, endogenous plasma norepinephrine levels, decreased vascular elasticity with aging, or the phenomenon of wave reflection back to the central component that amplifies the disparity (Hasegawa, 2024). As such, radial arterial pressures may be lower than brachial pressures leading to differences in measurements.

VIEWPOINT

DUSTIN D. LINN, PHARMD, MBA, BCPS, BCCCP

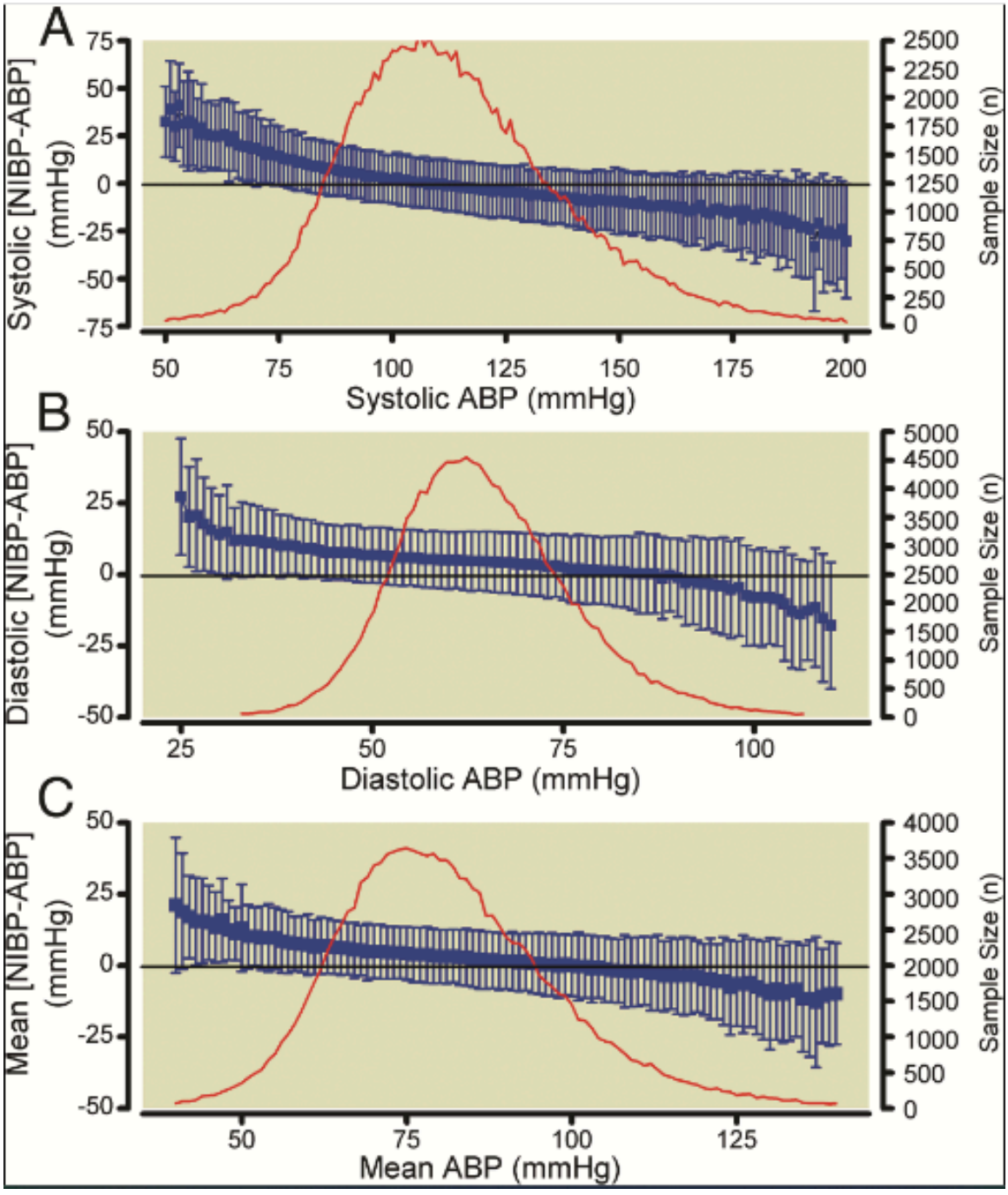


Figure 1 (retrieved from Invasive and concomitant noninvasive intraoperative blood pressure monitoring: observed differences in measurements and associated therapeutic interventions, 2011)

"Difference between oscillometric cuff and radial artery catheter measurements of blood pressure. Averaged difference (± SD) between simultaneous noninvasive (NIBP) and invasive radial artery (ABP) systolic (A), diastolic (B), and mean (C) blood pressure measurements in 24,225 adult patients during noncardiac surgery and anesthesia as well as total sample size of data pairs for each ABP value (bell-shaped curve and right-side Y-axis)" (Wax, 2011) Gradients between the central and peripheral arterial circulation have been identified most often in certain subgroups of patients.

VIEWPOINT

DUSTIN D. LINN, PHARMD, MBA, BCPS, BCCCP

Gradients between the central and peripheral arterial circulation have been identified most often in certain subgroups of patients. Gradients where radial blood pressure has underestimated central blood pressure, typically at the femoral site, have been demonstrated to be greatest in patients undergoing liver transplant surgery, in the immediate period following weaning from cardiopulmonary bypass, and in critically ill patients with refractory shock (Ahmad, 2017; Kim, 2022; Wisanusattra, 2022). Differences in MAP at the radial site were lower than at the femoral site in these studies by a mean of 5.7 mmHg, 9.8 mmHg, and 7.6 mmHg, respectively. A recent meta-analysis sought to compare central and peripheral arterial blood pressure gradients in critically ill patients and found mean gradients of 3.5 mmHg in MAP (95% CI, 2.1-4.8 mmHg), 8.0 mmHg in systolic arterial pressure (95% CI, 3.9-12.0 mmHg), and 1.1 mmHg in diastolic arterial pressure (95% CI, -0.1-2.4 mmHg) (Hasegawa, 2024). The authors concluded that the significance of these changes is unclear and that clinical practice preferring the use of peripheral arterial catheters need not change. However, given that gradients may be highest in critically ill patients with refractory shock, this may explain some of the findings demonstrating significantly lower oscNIBP values in patients with shock and low blood pressure.

In conclusion, oscNIBP values may overestimate blood pressure, particularly at low blood pressure values. This difference may be, in part, related to central-to-peripheral blood pressure gradients that occur in critically ill patients. While blood pressure is just one component of the cardiovascular system responsible for ensuring end-organ perfusion, maintaining blood pressure at accepted targets with reliable blood pressure monitoring tools may help prevent organ hypoperfusion and untoward outcomes.

VIEWPOINT:
HOME NONINVASIVE VENTILATION

BY BHARAT BAJANTRI, MD.

When should we initiate NIV for chronic hypercapnic respiratory failure – inpatient or outpatient?

Chronic hypercapnic respiratory failure (CHRF) due to chronic obstructive pulmonary disease (COPD) significantly increases the risk of hospitalizations and mortality. According to the American Thoracic Society (ATS) guidelines, home nocturnal noninvasive ventilation (NIV) has been shown to reduce these risks, particularly for patients suffering from hypercapnia (elevated carbon dioxide levels) post-discharge. Approximately 20% of patients hospitalized with COPD are rehospitalized within one month, and the figure rises to 40% for those with hypercapnic respiratory failure, with the highest risk of rehospitalization occurring within the first two days after discharge.

In clinical trials, Kohnlein et al. demonstrated that the use of home noninvasive ventilation (NIV) in patients with chronic hypercapnic respiratory failure (CHRF) and elevated PaCO2 levels (above 52 mm Hg) significantly reduced the one-year mortality rate, from 33% to 10%. Similarly, Murphy and colleagues found that for patients with persistent hypercapnia two to four weeks after discharge, home NIV lowered the combined risk of rehospitalization or death from 80.4% to 63.4%. Both trials involved patients being acclimated and titrated to NIV in a hospital setting before transitioning to home therapy.

Despite these promising results, the American Thoracic Society (ATS) guidelines recommend starting home NIV in an outpatient setting several weeks after discharge, primarily due to concerns about potential overuse and the possibility of unnecessarily extended hospital stays. The guidelines suggest that some patients may experience spontaneous resolution of hypercapnia, making it preferable to reassess their condition at a follow-up appointment.

However, delays in initiating home NIV—often caused by challenges such as scheduling outpatient appointments and navigating insurance requirements—leave patients at risk of rehospitalization during the critical post-discharge period. Starting home NIV while the patient is still hospitalized could mitigate this risk and offer more thorough education and training, which would be difficult to provide during a single outpatient session.

VIEWPOINT:
HOME NONINVASIVE VENTILATION

BY BHARAT BAJANTRI, MD.

Critics have noted that up to 25% of control group participants in prior studies saw their hypercapnia resolve spontaneously after three months, leading some to argue that these patients had acute rather than chronic hypercapnia. Nevertheless, research by Struik et al. showed that 95% of patients with PaCO2 levels above 60 mm Hg upon discharge saw no more than an 8 mm Hg reduction in PaCO2 over the following year. This suggests that patients with persistent hypercapnia (PaCO2 > 60 mm Hg after 48 hours) are unlikely to see their levels drop below the 52 mm Hg threshold typically used in randomized controlled trials (RCTs), supporting the early initiation of home NIV for these individuals.

Additionally, recent data from insurance claims indicate that starting home NIV early is associated with lower mortality rates and reduced Medicare expenditures. Patients diagnosed with CHRF and prescribed home NIV within 15 days experienced an average cost reduction of $3,412, with an additional $2,072 saved if NIV was prescribed within the first seven days.

VIEWPOINT:
HOME NONINVASIVE VENTILATION

BY BHARAT BAJANTRI, MD.

Clinical Interpretation:

While the American Thoracic Society (ATS) guidelines advise against initiating home noninvasive ventilation (NIV) immediately upon discharge, emerging evidence suggests that doing so could provide significant benefits for select patients. Early initiation of home NIV has been shown to reduce rehospitalizations and improve outcomes, particularly during the vulnerable post-discharge period.

My Practice Approach:

Qualifying Patients During Hospitalization: I will prioritize initiating home NIV for patients with chronic hypercapnia secondary to COPD who experience recurrent hospital admissions. Specifically, if their PaCO2 remains elevated above 60 mm Hg for at least 48 hours following the resolution of acute hypercapnic respiratory failure, they will be considered for home NIV upon discharge.

Post-Discharge Evaluation: For patients who do not meet the criteria for immediate initiation of home NIV, I will reassess their PaCO2 levels during their post-hospitalization outpatient visit. If chronic hypercapnia is confirmed, and they meet the clinical criteria, I will then recommend home NIV to optimize their long-term outcomes. This dual approach—addressing eligible patients both at discharge and during follow-up—may help tailor therapy to those most likely to benefit, reducing the risk of rehospitalization and improving their quality of life.

ORIGINAL STUDY SUMMARIES:
SAFETY AND EFFICACY OF REDUCED-DOSE VERSUS FULL-DOSE ALTEPLASE FOR ACUTE PULMONARY EMBOLISM

BY BHARAT BAJANTRI, MD

100 mg tPA vs 50 mg tPA for Acute Pulmonary Embolism

The primary aim of this observational study was to evaluate the safety and short-term efficacy of “full-dose” alteplase (100 mg) versus “reduced-dose” alteplase (50 mg) using propensity scoring methods to account for differences among patients. Researchers analyzed electronic health records from 16 hospitals, identifying a total of 284 adult patients with pulmonary embolism (PE) who received alteplase between 2012 and 2020: 98 patients were in the full-dose group, and 186 in the reduced-dose group.

The incidence of major extracranial bleeding was approximately 3%, while intracranial bleeding occurred in about 1%. Notably, major bleeding was more prevalent in the full-dose group compared to the reduced-dose group. The authors observed that many patients experiencing significant bleeding had supratherapeutic heparin levels or had undergone recent invasive procedures. When assessing efficacy—measured by early resolution of physiological impairments related to PE, as well as ICU and hospital length of stay and mortality rates—results were comparable between both dosing regimens. These findings align with previous prospective studies, reinforcing the established equipoise for both full- and reduced-dose systemic thrombolysis.
Clinical interpretation: The risk of intracranial hemorrhage due to alteplase in prospective RCTs is low especially with doses less than 100 mg, the risk < 1%, however the studies are underpowered.

The initial dosing of thrombolytics, particularly tissue plasminogen activator (tPA) for pulmonary embolism (PE), draws from protocols established for stroke (maximum dose of 90 mg) and myocardial infarction (maximum dose of 100 mg). However, there are compelling reasons to consider significantly lower doses for PE treatment.

- In cases of PE, the entire infused dose of alteplase is delivered directly to the pulmonary arteries, in contrast to myocardial infarction, where only about 5% of blood flow reaches the coronary arteries. This targeted delivery is crucial, especially given that alteplase has a half-life of approximately 4 minutes, enabling each molecule to circulate through the lungs about five times on average.

ORIGINAL STUDY SUMMARIES:
SAFETY AND EFFICACY OF REDUCED-DOSE VERSUS FULL-DOSE ALTEPLASE FOR ACUTE PULMONARY EMBOLISM

BY BHARAT BAJANTRI, MD

- Moreover, PE is characterized by complete blockage due solely to clot formation, unlike coronary artery issues that often involve a combination of plaque buildup and acute thrombus. The greater the proportion of the obstruction caused by the clot, the more effective thrombolysis will be, indicating that a lower dose of alteplase can still achieve successful treatment outcomes.
- It's important to recognize that achieving complete clot dissolution is not necessary for improving patient outcomes; even a partial reduction in obstruction can lead to significant clinical benefits. In many situations, reopening certain pulmonary arteries while leaving others occluded can yield favorable health results.

A critical complication of acute pulmonary embolism is the rapid increase in right ventricular (RV) afterload, which can lead to sudden death or acute RV failure and shock. Therefore, the volume and distribution of the embolism, along with the functional reserve of the right ventricle, are crucial determinants of outcomes in acute PE. Additionally, many patients have significant underlying conditions—such as cancer, major trauma, or recent surgery—adding to the heterogeneity of acute PE presentations and underscoring the need for individualized treatment. This variability suggests that a fixed dosing approach for thrombolytics may not be ideal given the differing balances of fibrinolysis and fibrin generation among patients.

For those with confirmed PE who exhibit clinical deterioration, a systemic dose of 50 mg alteplase should be strongly considered, as it has been shown to provide similar efficacy to full-dose alteplase with a lower risk of hemorrhagic complications. If the initial response is inadequate, additional doses can be administered as needed. In patients who are not in a peri-arrest state, intermittent administration of reduced doses—ranging from 10 to 50 mg of alteplase—or slow infusion techniques, often employed by interventional radiology, may also be viable options.

Regardless of hemodynamic status, the traditional approach of administering a full 100 mg of alteplase upfront may soon become obsolete, particularly as emerging evidence suggests that reduced-dose alteplase offers similar efficacy with a lower bleeding risk profile. The ongoing PEITHO 3 trial aims to provide clearer guidance on the optimal choice between full-dose and reduced-dose alteplase for patients with submassive, intermediate-risk pulmonary embolism.

ORIGINAL STUDY SUMMARIES AND PERSPECTIVE: THE PEXIVAS TRIAL

BY BHARAT BAJANTRI, MD

Finally, the first RCT: Plasmaphersis versus steroids for ANCA Vasculitis and DAH. But do we really know more than what we did before?

The PEXIVAS trial (Plasma Exchange and Glucocorticoids in Severe Antineutrophil Cytoplasmic Antibody–Associated Vasculitis) stands as the largest study focused on antineutrophil cytoplasmic antibody–associated vasculitis (AAV) and notably the first to include participants with diffuse alveolar hemorrhage (DAH) requiring mechanical ventilation. This trial aimed to evaluate treatment effects and outcomes for AAV patients, both with and without DAH.

At the trial's outset, DAH was identified based on chest imaging showing bilateral pulmonary infiltrates, with no alternative explanations such as volume overload or infection. Additionally, participants were required to exhibit at least one of the following criteria: 1) bronchoscopy evidence of DAH, characterized by progressively bloody bronchoalveolar lavage returns; 2) hemoptysis; 3) unexplained anemia with hemoglobin levels below 10 g/dl or a decrease of over 1 g/dl; or 4) elevated DLCO on pulmonary function tests. Patients were classified as having severe DAH if their oxygen saturation was less than 85% on room air or if they were on mechanical ventilation.

End-stage kidney disease was defined as the necessity for dialysis for a minimum of 12 consecutive weeks or the requirement for kidney transplantation. Serious infections were characterized as infectious syndromes necessitating hospitalization or intravenous antimicrobial treatment.

Conducted between 2010 and 2016, the PEXIVAS trial was a large randomized controlled trial (RCT) involving 704 participants, with follow-up continuing until July 2017. All patients received immunosuppressive induction therapy with either cyclophosphamide or rituximab, following plasma exchange if they were assigned to either of the first two groups. The intravenous methylprednisolone dosage ranged from 1 to 3 grams over three days, determined at the discretion of the treatment team.

ORIGINAL STUDY SUMMARIES AND PERSPECTIVE: THE PEXIVAS TRIAL

BY BHARAT BAJANTRI, MD

Oral glucocorticoids were initiated with prednisolone at a dose of 1 mg/kg/day, potentially increasing to 5 mg/kg/day over varying periods, resulting in a 50% reduction in cumulative glucocorticoid exposure within the first six months for those on the reduced-dose regimen compared to the standard-dose group. All patients received consistent glucocorticoid dosing from six to twelve months, with further adjustments made at the physician's discretion.

The study consisted of four groups:

- Group 1: Plasma exchange (7 sessions) + Standard steroid dose
- Group 2: Plasma exchange (7 sessions) + Reduced steroid dose
- Group 3: Standard steroid dose only
- Group 4: Reduced steroid dose only

Outcomes revealed that 99 patients died, and 138 developed kidney failure. Importantly, plasma exchange did not significantly impact mortality or the incidence of kidney failure. Moreover, there was no notable difference in outcomes between the two steroid dosing groups regarding mortality or kidney failure rates; however, the reduced steroid dose group experienced fewer serious infections.

ORIGINAL STUDY SUMMARIES AND PERSPECTIVE: THE PEXIVAS TRIAL

BY BHARAT BAJANTRI, MD

The authors concluded that the findings do not endorse the routine use of plasma exchange for all patients with severe vasculitis. They emphasized that the reduced-dose steroid regimen is equally effective and safer than the standard-dose regimen, with implications for cost savings and enhanced patient safety in future vasculitis treatments.

Clinical Implications

The trial supports the benefits of using a reduced steroid dose toward the end of the treatment course for responding patients, helping to mitigate the toxicities and infection risks associated with long-term steroid use. However, the precise dosing strategy for real-world application remains ambiguous. Despite the substantial sample size of the PEXIVAS trial, only 191 patients had DAH (including 61 with severe DAH and 29 on mechanical ventilation), leading to limited statistically significant events such as mortality differences and ventilator-free days. A key limitation is the absence of mandatory bronchoscopy for DAH diagnosis, which could have expedited enrollment and treatment across multiple sites, as most patients with DAH do not present with hemoptysis.

While this evidence is not robust enough to establish definitive treatment protocols, it represents the only available RCT on the subject. Future trials may provide more comprehensive data; in the meantime, I would still consider plasmapheresis for my most critically ill AAV patients with DAH, likely followed by rituximab treatment.

ORIGINAL STUDY SUMMARIES:
"MANAGEMENT OF RESPIRATORY FAILURE IN HEMORRHAGIC SHOCK"

BY PAYAL SHUKLA, MD

Management of Respiratory Failure in Hemorrhagic Shock Summary

Respiratory Failure in hemorrhagic shock is caused by multiple mechanisms. There is little evidence from clinical trials to guide care of this complication. This article summarizes the pathophysiology and management strategies based on the mechanism of the respiratory failure presented in the focused review: Management of Respiratory Failure in Hemorrhagic Shock (Davis, 2024).

Pathophysiology of Respiratory Failure in Hemorrhagic Shock

Respiratory failure in hemorrhagic shock arises through several interconnected mechanisms, though clinical evidence is sparse to guide the management of this complex condition. This discussion provides an overview of the pathophysiology and management strategies, focusing on the underlying causes of respiratory failure.

Hemorrhagic shock leads to respiratory failure primarily through reduced diaphragmatic blood flow and decreased cerebral perfusion. Severe blood loss results in diaphragmatic fatigue, weakening its ability to contract effectively, thereby compromising respiratory function. Concurrently, hypoperfusion of the brain can cause obtundation, diminished airway reflexes, and relaxation of the pharyngeal muscles, which may narrow and obstruct the upper airway. This can lead to irregular breathing patterns and, eventually, apnea, often preceding circulatory arrest.

Impact on CO_2 and Hemodynamics

Hemorrhagic shock also affects the partial pressure of CO_2 in systemic arterial blood ($PaCO_2$). While mild to moderate blood loss typically induces tachypnea and respiratory alkalosis, severe hemorrhagic shock can paradoxically lead to normal or elevated $PaCO_2$ levels despite rapid breathing. This occurs because reduced cardiac output limits CO_2 delivery to the alveoli for exhalation, increasing dead space ventilation. Consequently, end-tidal CO_2 levels decrease, signaling severe shock and potentially indicating the need for massive transfusion. Normally, the $PaCO_2$ is within 5 mm Hg of end-tidal CO_2, but in hemorrhagic shock, a $PaCO_2$ that exceeds end-tidal CO_2 by 10 mm Hg or more predicts a higher risk of mortality.

This condition can create a vicious cycle: rising PaCO2 stimulates ineffective hyperventilation, increasing metabolic CO2 production. As hypercapnia progresses, acidemia develops, worsening coagulopathy and causing systemic vasodilation alongside pulmonary vasoconstriction. Hemorrhage also diminishes oxygen saturation in hemoglobin, as peripheral tissues extract more oxygen to sustain metabolism. Severe hemorrhage further impairs pulmonary surfactant production, reducing lung compliance and leading to atelectasis. Regular monitoring of potassium and ionized calcium levels after every fourth unit of packed red blood cells (approximately one cooler) is essential, as maintaining calcium levels can significantly impact survival.

Management of Shock

When vasopressors are required to maintain venous return and ensure adequate cerebral and coronary perfusion, norepinephrine is the preferred agent. Patients with significant blood loss often have elevated endogenous catecholamine levels, so vasopressors might be administered as a bolus before induction for intubation. Reduced doses of induction agents are recommended, as all sedatives—including Propofol, Etomidate, and Ketamine—can cause hypotension in severely hemorrhagic patients. Neuromuscular blocking agents may also inhibit spontaneous negative pressure inspirations, contributing further to hypotension. End-tidal CO2 monitoring should be performed to detect decreases in cardiac output, and clinicians should anticipate the possibility of pulseless electrical activity (PEA) during intubation, checking peripheral pulses immediately after endotracheal intubation. The risk of arrest is particularly high in patients with pre-intubation systolic blood pressure exceeding 90 mm Hg.

Management of Respiratory Failure

Airway Management

Securing a patent airway is the priority in managing respiratory failure. For unconscious patients, maneuvers such as neck extension, mandible thrusting, and the use of nasopharyngeal or oral airways can relieve obstructions. Continuous pulse oximetry is recommended to monitor oxygen saturation, and supplemental oxygen should be provided. Preoxygenation is crucial if intubation is anticipated. In cases where respiratory effort is inadequate, bag-mask ventilation may be necessary, with a focus on maintaining the lowest possible mean airway pressure to prevent worsening hypovolemia.

ORIGINAL STUDY SUMMARIES:
"MANAGEMENT OF RESPIRATORY FAILURE IN HEMORRHAGIC SHOCK"

BY PAYAL SHUKLA, MD

Support During Endotracheal Intubation

Frequent or continuous blood pressure monitoring is vital during intubation. Resuscitation with blood products and balanced crystalloids can help sustain venous return and cardiac output, but over-resuscitation before bleeding is controlled should be avoided. Vasopressors like norepinephrine are useful in increasing venous return and maintaining perfusion pressure, particularly during anesthesia induction. Given the heightened risk of hemodynamic collapse post-intubation, vasopressors should be immediately available. If possible, delayed sequence ventilation might be employed to minimize significant hemodynamic fluctuations. In cases of severe hypovolemia, where there is no imminent risk of respiratory arrest, intubation should be postponed until after initial volume resuscitation.

Positive Pressure Ventilation

Positive pressure ventilation can further reduce venous return and cardiac output by increasing intrathoracic pressure, a particularly harmful effect in hypovolemic patients. Therefore, it is essential to use the minimum necessary mean airway pressure during ventilation. In bag-mask ventilation, the lowest possible mean airway pressure should be utilized. Tidal volumes should not exceed functional residual capacity, and techniques that increase mean airway pressure—such as large tidal volumes, high plateau pressures, and elevated respiratory rates—should be avoided. Even minimal positive end-expiratory pressure (PEEP) can be detrimental, with studies showing fatal outcomes at PEEP levels of 5 cmH2O in animal models of hemorrhagic shock.

Physiologic Approach to Management

A balanced approach prioritizes airway management while simultaneously addressing circulation. Basic non-invasive maneuvers should precede intubation unless immediate respiratory support is required. In cases of severe hypovolemia, initial volume resuscitation should be prioritized before intubation. The resuscitation process, hemorrhage control, and airway management must be carefully coordinated to optimize patient outcomes.

ORIGINAL STUDY SUMMARIES:
"MANAGEMENT OF RESPIRATORY FAILURE IN HEMORRHAGIC SHOCK"

BY PAYAL SHUKLA, MD

Conclusion

Managing respiratory failure in hemorrhagic shock demands a thorough understanding of the underlying pathophysiological changes and a careful balance between providing respiratory support and maintaining hemodynamic stability. By adhering to a physiologic approach, employing careful airway management, and cautiously utilizing positive pressure ventilation, clinicians can enhance outcomes for patients experiencing this life-threatening condition.

To manage respiratory failure in hemorrhagic shock, clinicians should understand that hypoperfusion worsens dead space ventilation, prioritize airway patency and use the minimum amount of mean airway pressure and PEEP and respiratory frequency. Hypercapnia should be treated with fluid resuscitation rather than increasing minute ventilation.

SNAPSHOTS

Blood is precious! Save it when you can!

Pharmacotherapy for Reducing RBC Transfusion for Patients in the ICU: A Systematic Review and Network Meta-Analysis

This study aimed to explore effective treatment strategies to minimize the need for red blood cell (RBC) transfusions in ICU patients by comparing various therapies. A network meta-analysis was conducted using data from 75 randomized controlled trials, covering 15,091 patients. These trials were selected from 117 eligible studies found in MEDLINE, CENTRAL, and Embase databases up to July 2023.

The treatments evaluated included erythropoiesis-stimulating agents (Epo), iron, combination therapy with iron and Epo, hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHI), vitamin D3 (VD3), and placebo/no treatment. The analysis revealed that combining iron and Epo significantly reduced the need for RBC transfusions compared to placebo or no treatment (risk ratio [RR]: 0.60; 95% confidence interval [CI], 0.49–0.74), with a moderate confidence rating.

Monotherapy with either Epo (RR: 0.81; CI, 0.63–1.04) or iron (RR: 0.83; CI, 0.70–0.98) also showed some potential for reducing transfusion requirements, though these results were less certain, with low confidence ratings. Importantly, combination therapy did not appear to raise the risk of venous thromboembolism (VTE) or infection. Epo alone showed a slight, non-significant increase in the risk of infection, while iron monotherapy did not elevate the risks of VTE or infection. Due to insufficient data, the effects of VD3 and HIF-PHI remained unclear.

Clinical Interpretation: In conclusion, the combination of iron and Epo appears to be the most effective and potentially safer option for lowering RBC transfusion needs in ICU patients, with fewer associated risks. This trial would make me consider ordering iron and Epo in patients who have anemia in the ICU but have Hemoglobin > 7 and not actively bleeding.

SNAPSHOT & PERSPECTIVE

By: Patricia Rich, MD, Morgan Crites, NP-C

Finally! New treatment Paradigm for Limited Stage Small Cell Lung Cancer?

Small cell lung cancer accounts for about 15 % of the lung cancer patient population. It is strongly associated with current and former smokers. It has a fast growth rate with rapid doubling time and tends to metastasize early.

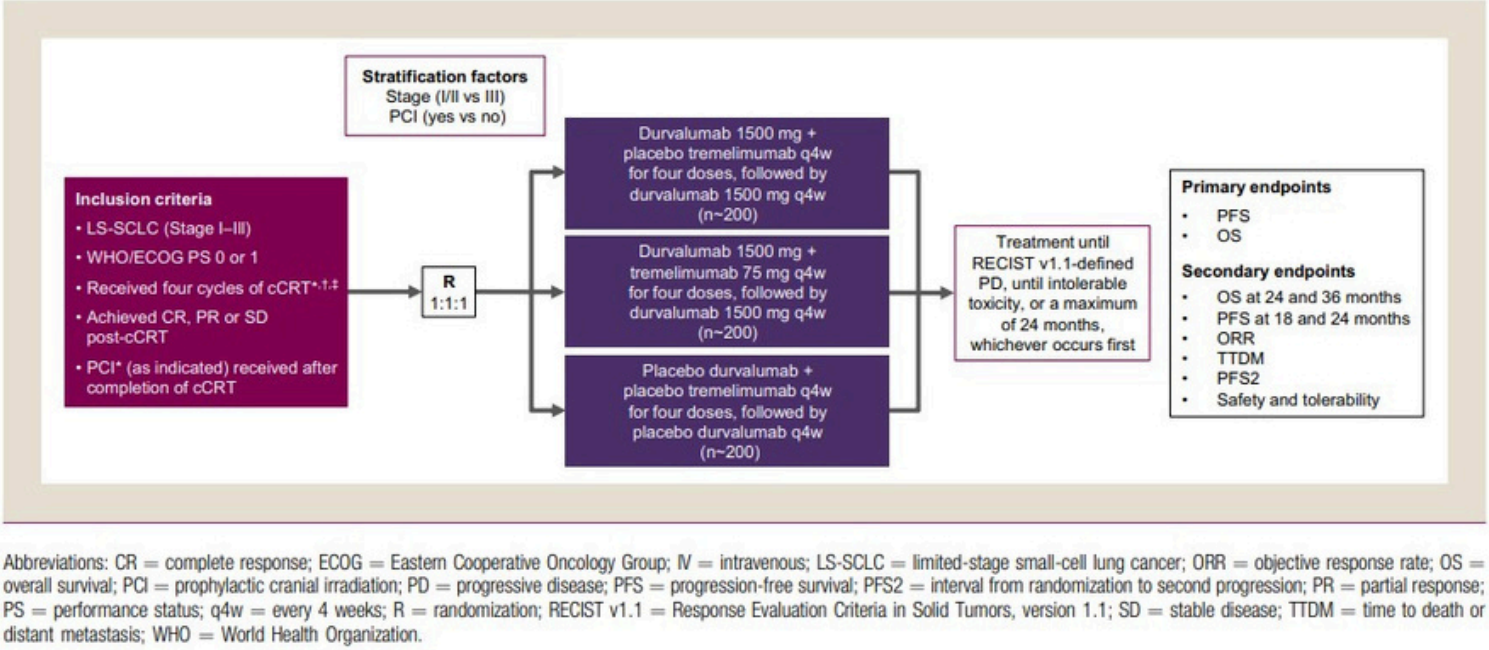
Although both the American Joint Committee on Cancer (AJCC) and the International Association for the Study of Lung Cancer (IASLC) recommend using the Tumor (T), Node (N), and Metastases (M) staging system, patients are typically staged as either limited-stage (LS) or extensive-stage (ES) disease (Vallières, 2009).

Limited stage small cell lung cancer (LS-SCLC) has historically been treated with platinum base chemotherapy and concurrent radiation (cCRT) (Evans, 1985). This standard of care treatment has not changed much in decades (Blackhall, 2023). The PACIFIC trial showed that adding immunotherapy after chemoradiation in patients with locally advanced non-small cell lung cancer resulted in significant improvement in progression free survival (PFS) and overall survival (OS) (Antonia, 2018).
The question is, can the same benefit be achieved in small cell lung cancer?

The Adriatic trial presented this year at ASCO's (American Society of Clinical Oncology) annual meeting is the first phase III trial to show benefit from adding immunotherapy as consolidation after concurrent chemotherapy and radiation in patients with LS-SCLC. The trial was designed as a phase 3, randomized, double-blind, placebo –controlled study. Eligible patients included stage I-III(LS-SCLC) who had not progressed after completing cCRT. Prophylactic brain irradiation was allowed. The patients were randomized to 1 of 3 arms: **see Figure 1.**

SNAPSHOT & PERSPECTIVE

By: Patricia Rich, MD, Morgan Crites, NP-C



Abbreviations: CR = complete response; ECOG = Eastern Cooperative Oncology Group; IV = intravenous; LS-SCLC = limited-stage small-cell lung cancer; ORR = objective response rate; OS = overall survival; PCI = prophylactic cranial irradiation; PD = progressive disease; PFS = progression-free survival; PFS2 = interval from randomization to second progression; PR = partial response; PS = performance status; q4w = every 4 weeks; R = randomization; RECIST v1.1 = Response Evaluation Criteria in Solid Tumors, version 1.1; SD = stable disease; TTDM = time to death or distant metastasis; WHO = World Health Organization.

Figure 1: Retrieved from Design and Rationale for a Phase III, Randomized, Placebo-controlled Trial of Durvalumab With or Without Tremelimumab After Concurrent Chemoradiotherapy for Patients With Limited-stage Small-cell Lung Cancer: The ADRIATIC Study, 2020

Two arms (arms 1 and 3) were reported in the interim analysis as the tremelimumab arm continues to be blinded. The median overall survival (OS) with durvalumab was 55.9 months (about 4 and a half years) versus 33.4 months (about 3 years) with placebo (HR (Hazard Ratio) 0.73). The median progression free survival (PFS) was 16.6 months with durvalumab versus 9.2 months with placebo (HR 0.76). The median improvement in OS with the addition of consolidation durvalumab was almost 2 years longer than the placebo group (22 months). The toxicities were similar in both groups with the addition of some of the known potential adverse effects of immunotherapy treatments (Spigel, 2024).

It will be interesting to review the data when the arm with tremelimumab is unblinded.
If the data holds and we can cure more earlier stage small cell lung cancer patients, this will be a game changer in the treatment of LS-SCLC.

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