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SPECIAL FEATURE

Thrombocytopenia in the Critically Ill

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Dr. Radigan reports no financial relationships relevant to this field of study.

Thrombocytopenia, defined as a platelet count of < 150 x 10^9/L, is a common acquired condition in critically ill patients.[1] Approximately half of critically ill patients experience thrombocytopenia during the length of their ICU stay.[2] In nearly 10% of these patients, platelet counts reach a nadir of < 50 x 10^9/L. In one study, the incidence of mild (100-149 x 10^9/L), moderate (50-99 x 10^9/L), and severe (< 50 x 10^9/L) thrombocytopenia in the critically ill was 15.3%, 5.1%, and 1.6%, respectively.[3]

CLINICAL SIGNIFICANCE

Thrombocytopenia is not only a pathologic entity, but the severity of thrombocytopenia and the recovery time of the platelets often predicts outcome, including overall mortality of ICU patients.[1,4,5] Critically ill patients with moderate and severe thrombocytopenia demonstrate higher ICU and hospital mortality.[3] If the recovery is delayed beyond day four, several studies have demonstrated higher morbidity and mortality. In one study, the morality rate of critically ill patients who experienced persistent thrombocytopenia for 14 days was 66% compared to a mortality rate of 16% for patients who exhibited normal or recovered platelets.[6] Even when not associated with bleeding, thrombocytopenia often creates barriers to effective management of patients, including a hold or delay in necessary interventions, an increased number of prophylactic platelet transfusions, change or cessation of anticoagulation (especially in the setting of a concern for heparin-induced thrombocytopenia [HIT]), and a reduction in the intensity of anticoagulation for fear of complications.[7]

ETIOLOGY OF THROMBOCYTOPENIA IN THE ICU

Thrombocytopenia is most often multifactorial. The six major mechanisms that result in thrombocytopenia in the ICU include: hemodilution, increased platelet consumption, decreased platelet production, increased platelet sequestration, platelet destruction, and laboratory artifact of pseudothrombocytopenia.[8] *(See Table 1.)* Often, more than one of these mechanisms is responsible for thrombocytopenia in the critically ill. Pseudothrombocytopenia may occur because of clots in the tube or platelet aggregates in ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood.[9] Automated cell counters cannot recognize these aggregates. This phenomenon may be triggered

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in patients taking glycoprotein IIb/IIIa antagonists such as abciximab, tirofiban, and integrillin.[10] The timing of thrombocytopenia often is useful in determining etiology. Two different studies that included medical ICU patients revealed that platelet count usually decreases after admission, with a typical recovery after five days, which may reflect effective treatment of the primary disease process.[11,12] Generally, a slow and steady fall in platelets over five to seven days is more consistent with a consumptive coagulopathy or bone marrow failure.[7] If the platelets abruptly decrease within one to two days after an initial recovery, it is often immunologic or drug-related. When it occurs within a few hours of transfusion, there should be concern for bacterial contamination or passive alloimmunization.

DIAGNOSTIC APPROACH

To help determine whether the thrombocytopenia is acute or chronic, it is important to ask the patient or family about prior platelet counts, family history of bleeding disorders, the patient's history of bleeding disorders, medication exposures, exposure to particular infections, dietary practices (including veganism and vegetarianism), and other comorbidities, including hematological disorders, rheumatological diseases, or poor diet (including a history of bariatric surgery.) On physical exam, look for petechiae, purpura, ecchymosis, lymphadenopathy, splenomegaly, and hepatomegaly.

Regardless of the presentation, it is always important to repeat the complete blood count with smear. This is especially important when pseudothrombocytopenia is suspected, but it should be performed using a non-EDTA anticoagulant such as heparin or citrate.[7] EDTA can induce clumping or platelet rosettes around white blood cells, which then causes the platelets to be counted as leukocytes. Regardless, it is critical to consider an immunologic cause of thrombocytopenia whenever platelet counts decrease within 24-48 hours several days after ICU admission. Although drug-related platelet nadir may be < 10,000/uL, platelet nadir for HIT typically is 20,000 uL to 50,000 uL.[5] If the onset of the thrombocytopenia started prior to ICU admission and fits the appropriate scenario, consider evaluation for autoimmune diseases, HIV, and liver disease, including hepatic enzymes, synthetic function, and hepatitis panel. If a consumptive coagulopathy is confirmed in the setting of thrombocytopenia, disseminated intravascular coagulation (DIC) is a major concern and further supported by decreasing serum fibrinogen levels and increasing thrombin time (TT), prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrin degradation products.[9] When microangiopathic changes are confirmed on smear, it is important to entertain the diagnosis of thrombotic thrombocytopenic purpura (TTP), Shiga toxin-mediated hemolytic uremic syndrome (ST-HUS), or other syndromes of thrombotic microangiopathy. To narrow the differential and aid in diagnosis, it is important to note whether the thrombocytopenia occurs in isolation or with associated anemia or leukopenia. Pancytopenia also must be worked up further, especially with the concern for myelodysplastic syndrome. If TTP, ST-HUS, HIT, or an acute hematologic malignancy is suspected, it is a medical emergency and warrants an immediate hematology consult.

TREATMENT

Although there is usually no role for prophylactic platelet transfusions to decrease bleeding risk in critically ill patients, many consider it reasonable to prophylactically transfuse platelets in patients with severe sepsis at a threshold of $\leq 10 \times 10^9$/L or at $< 20 \times 10^9$/L in particularly high-risk patients.[13,14] If a patient is undergoing an invasive intervention, there are criteria for minimum platelet counts that have been defined and supported mainly by expert opinion rather than randomized, controlled trials.[15] Of course, these are only suggested guidelines and may be adjusted by each individual patient scenario, including consideration for platelet function, history of bleeding, medications, liver and renal function, and/or in the setting of sepsis. Table 2 summarizes recommendations for prophylactic platelet transfusions before invasive procedures. Additional treatment guidelines are outlined below.

Thrombocytopenia with abnormal coagulation profiles. Thrombocytopenia with an abnormal coagulation profile is seen most commonly with septic DIC. DIC is a disease process characterized by systemic activation of the coagulation cascade that results in disseminated fibrin formation and is confirmed by abnormal elevation of the PT and aPTT, decreased fibrinogen and platelets, and schistocytes on smear.[5] Since fibrinogen is an acute phase reactant, fibrinogen levels

Table 1: Major Mechanisms of Thrombocytopenia in the Critically Ill

Hemodilution	• Infusion of fluids • Transfusion of red blood cells and plasma
Increased platelet consumption	• Major bleeding • Massive tissue trauma • Sepsis • Disseminated intravascular coagulation • Diabetic ketoacidosis • HELLP syndrome • Malaria • Thrombosis (pulmonary embolism, heparin-induced thrombocytopenia) • Intravascular devices including hemofiltration, extracorporeal membrane oxygenation, and cardiac assist devices • Thrombotic microvascular disorders
Decreased platelet production	• Intoxication • Bone marrow disorder including acute leukemia, myelodysplasia, metastatic bone marrow infiltration, hemophagocytosis, or graft failure after stem cell transplant • Irradiation or chemotherapy • Viral infections • Chronic liver disease
Increased platelet sequestration	• Hepatosplenomegaly • Hypothermia
Increased platelet destruction	• Autoantibody mediated, including immune thrombocytopenia, drug-dependent antibodies, or alloantibodies in post-transfusion purpura • Severe infection including viruses • Heparin-induced thrombocytopenia (early onset) • Antiphospholipid syndrome • Thrombotic thrombocytopenic purpura
Pseudothrombocytopenia	• Clotting in the blood sample • EDTA-induced platelet clumping • GPIIB/IIIa inhibitor induced pseudothrombocytopenia • Platelet rosetting with leukocytes

Thiele T, et al. Thrombocytopenia in the intensive care unit—diagnostic approach and management. *Semin Hematol* 2013;50: 239-250.

may be normal. DIC occurs most often in the setting of sepsis/systemic inflammatory response syndrome and often is associated with a very poor prognosis, especially when platelet counts fail to recover. Treatment includes addressing the underlying cause and supportive care, including transfusion of blood products as clinically indicated. Thrombocytopenia with abnormal coagulation profiles also may occur in the setting of severe liver impairment because of a lack of synthesis of coagulation factors and in association with coinciding splenomegaly and liver disease.[5]

Table 2: Minimum Platelet Counts for Common ICU Procedures

Procedure	Minimum Platelet Count (x 10^9/L)
Central venous catheter insertion	20
Elective lumbar puncture	50
Emergency lumbar puncture	20
Bronchoscopy	20
Bronchoscopy with biopsy	50
Gastrointestinal endoscopy with biopsy	20
Transjugular liver puncture	10
Thoracentesis	50

Greinacher A, Selleng S. How I evaluate and treat thrombocytopenia in the intensive care unit patient. *Blood* 2016;128:3032-3042.

Thrombocytopenia with microangiopathic hemolytic anemia (MAHA). MAHA is non-immune hemolysis that results from intravascular red blood cell fragmentation that produces schistocytes. Syndromes of microangiopathic thrombocytopenia, including TTP and ST-HUS, commonly present with MAHA, thrombocytopenia, and organ injury.

TTP is a prothrombotic thrombocytopenic disorder in which microangiopathic hemolytic anemia may be complicated by renal failure, neurologic disorders, fever, or other organ involvement.[16] It is caused by a hereditary deficiency or acquired antibodies to the von Willebrand factor-cleaving protease ADAMTS13. Low levels of ADAMTS13 lead to large von Willebrand factor multimeres in which platelets bind. This dysregulation causes microvascular thrombosis and further destruction of red blood cells.[17] TTP may complicate the course of stem cell transplant or autoimmune disease. It is rarely drug-mediated but may be prompted by non-dose-related idiosyncratic, immunologic reactions or a toxic dose-related reaction. Known culprits include quinine, quetiapine, gemcitabine, clopidogrel, ticlopidine, mitomycin C, calcineurin inhibitors, and chemotherapeutic agents.[18] When drug-induced, the most important treatment is to stop the offending agent immediately. TTP also may occur postoperatively.[19] Since anemia, thrombocytopenia, fever, renal failure, and mental status changes are common complications in a postoperative course, there is often significant delay in diagnosis of postoperative TTP. Non-immune-mediated postoperative TTP also may occur early after surgery because of increased ADAMSTS13 consumption, as opposed to the later presentation of immune-mediated

postoperative TTP in which anti-ADAMTS13 antibodies lead to decreased ADAMTS13 levels. Early plasma exchange is critical for optimal treatment of TTP. Coinciding corticosteroids and rituximab may decrease the number of plasma exchange treatments needed for remission.[8] Platelets should not be transfused in this setting.

ST-HUS is caused by an enteric infection with a Shiga toxin-secreting strain of *Escherichia coli* or *Shigella dysenteriae*.[16] Excessive platelet activation leads to the formation of thrombi in the microcirculation, which leads to platelet consumption and subsequent thrombocytopenia. Clinicians can halt this process by using the monoclonal humanized anti-C5 antibody, eculizumab.[20] Although this treatment is promising, its efficacy remains questionable.[21] Additional systemic disorders that may present with MAHA and thrombocytopenia include DIC, systemic infection, systemic malignancy, pregnancy-related syndromes, solid organ transplant, and hematopoietic cell transplant.[5] In addition, MAHA and thrombocytopenia may be present in the setting of coinciding systemic rheumatic disease and severe hypertension.[5]

Thrombocytopenia in combination with thrombosis. If thrombocytopenia develops in the setting of venous or arterial thromboses, the differential diagnosis narrows to HIT, antiphospholipid syndrome (APS), and other systemic disorders as discussed below. HIT is a life-threatening heparin-mediated, prothrombotic disorder caused by an autoantibody against platelet factor 4 (PF4) after complex formation with heparin. Typically, the platelet count falls more than half, usually nadiring between 50-80 x 10^9/L and may occur with catastrophic arterial and venous thrombosis.[22] The probability of HIT in an ICU patient may be estimated using the 4Ts score (Thrombocytopenia, Timing, Thrombosis, and oThers).[23] The reader is encouraged to look up the reference for more details in terms of calculating the score.[24]

A presumptive diagnosis of HIT is based solely on clinical findings and platelet counts until laboratory results are available.[7] Commonly, the immunoassay is the initial test of choice. It is highly sensitive (> 99%) and often available within most institutions for a rapid turnaround time but also demonstrates poor specificity.[23] Although this test is helpful in specific scenarios, more testing, such as a functional assay and/or the evaluation of serologic features (detection of IgG antibodies, quantification of the antibody level or optical density, or use of high heparin concentrations to dissociate or compete with binding of antibodies to PF4/H complexes), sometimes is necessary.[24] One functional assay, the serotonin release assay, exhibits high specificity and positive predictive values, but is limited to major commercial laboratories or referral laboratories at academic medical centers. When HIT is suspected strongly, heparin must be stopped immediately, and a therapeutic dose of a non-heparin anticoagulant should be started. Platelets should not be transfused in HIT. APS typically presents with immune-mediated thrombocytopenia, arterial and/or venous thrombosis, and pregnancy loss. Blood tests typically are positive for antiphospholipid antibodies and/or lupus anticoagulant.[25] It often presents with other autoimmune diseases, including lupus. In the ICU, it is critical to be aware of "catastrophic" APS, which presents with a more rapid and severe onset, often resulting in multi-organ failure. Treatment is early and appropriate anticoagulation, platelet inhibition (such as aspirin), corticosteroids, plasma exchange/immunoadsorption, and IV immunoglobulin.[26] Long-term treatments often include cyclophosphamide or rituximab. Eculizumab often is used to block complement activation. Additional systemic disorders that may present with thrombosis and thrombocytopenia include cancer-associated DIC or massive clot thrombocytopenia.

Toxin- and medication-related thrombocytopenia. Chronic intoxication of substances such as alcohol also causes thrombocytopenia from impaired megakaryopoiesis and often occurs concurrently with splenomegaly and liver cirrhosis, which can further aggravate thrombocytopenia.[27,28] Other acute intoxications include acetaminophen, which may cause thrombocytopenia, along with therapeutic doses of anticonvulsant drugs such as valproate, carbamazepine, phenobarbital, or phenytoin.[8] Discussion of herbal medications with the patient or family members also is critical, especially in the setting of unknown etiology.

Drug-related thrombocytopenia in the critically ill may be non-immune, drug-induced thrombocytopenia (DTP) or drug-induced immune thrombocytopenia (DITP). Adverse drug reactions caused by drug-dependent, antibody-mediated platelet destruction are responsible for almost 20% of all hospitalized patients with thrombocytopenia.[29] The most common culprits of drug-related thrombocytopenia in the ICU are new medications, as opposed to a patient's daily list of medications. Common offending agents include trimethoprim/sulfamethoxazole, penicillin, vancomycin, ibuprofen, ceftriaxone, rifampin, abciximab, and mirtazapine.[30] Commonly, non-immune culprits are histamine (H2) antagonists or nonsteroidal anti-inflammatory drugs. Notably, unfractionated heparin may cause a non-immunologic fall of platelets within the first days of initiating the medication. As for DITP, an abrupt platelet fall to < 5 x 10^9/L with mucocutaneous bleeding is typical.[8] The drug often has been started five to 10 days prior to the platelet fall. If the patient has been sensitized by a previous exposure to the drug, the onset of thrombocytopenia may be more rapid. If DTP or DITP is suspected, the offending medication should be stopped immediately. Typically, the platelets will increase steadily after five half-lives of the drug, which usually occurs within three to five days. When DITP is associated with severe bleeding, IV immunoglobulin and platelet transfusion are common treatment strategies.[31]

Transfusion-related thrombocytopenia. Post-transfusion purpura is an extremely rare disorder of previously pregnant women that occurs approximately seven to 14 days after allogeneic blood transfusion in which the platelet count falls to < 10 x 10^9/L.[7] During their previous pregnancy, the women are pre-immunized against a platelet blood group, most commonly human platelet antigen (HPA)-1a. Transfusion of HPA-1a-positive cellular blood products (red blood cell concentrates or platelets) triggers a response from memory B cells, which enhances the production of alloantibodies, subsequently destroying the autologous (antigen-negative) platelets. Preferred treatment is high-dose immunoglobulin G 1 g/kg per day for two consecutive days or 400-500 mg/kg per day for five days.[32]

Passive alloimmune thrombocytopenia, with platelet counts typically < 20 x 10^9/L, is caused by transfusion of plasma or red blood cells that contain high-titer platelet-specific antibodies.[7] Although the platelet-specific antibodies may be detected in the donor's plasma and on the recipient's platelets, it is not detectable in the recipient's plasma. This finding suggests that nearly 100% of the transfused alloantibodies bind immediately after transfusion. It is critical that these cases undergo further review to prevent other patients from developing the syndrome.

Additional causes of thrombocytopenia. In the setting of trauma, patients often experienced trauma-induced coagulopathy and hemodilution because of massive transfusion of other blood products. Although the optimal ratio for transfusion of blood products is highly controversial, studies support a survival benefit in patients who receive early plasma and platelet transfusions along with red blood cells.[33] Thrombocytopenia usually is a manifestation of the pancytopenia caused by marrow suppression. Less commonly, the thrombocytopenia occurs in isolation as a previously unrecognized comorbidity such as myelodysplastic syndrome, acute leukemia, infiltration of bone marrow from other malignancies, or infection.

SUMMARY

Not only is thrombocytopenia common in critically ill patients, but it also is associated with a worse prognosis. It is critical to find the cause, and then pursue the appropriate treatment strategy. ■

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ABSTRACT & COMMENTARY

Functional Outcomes After Receiving Life-sustaining Therapy in the ICU

By Betty Tran, MD, MSc, Editor

SYNOPSIS: Among patients who have spent at least three days in an ICU and required even brief mechanical ventilation and/or vasopressor support, almost half are dead and only one-third return to their baseline at six months. Several factors present on the first day of admission are associated with not returning to baseline status.

SOURCE: Detsky ME, et al. Six-month morbidity and mortality among ICU patients receiving life-sustaining therapy: A prospective cohort study. *Ann Am Thorac Soc* 2017 Jun 16. doi: 10.1513/AnnalsATS.201611-875OC. [Epub ahead of print].

Limited data are available concerning long-term outcomes of a general ICU population that could inform ICU discussions with patients and surrogates regarding expectations and prognosis. In this prospective cohort study of five ICUs (three medical, two surgical) within the University of Pennsylvania Health System, Detsky et al aimed to describe patients' survival and functional (physical and cognitive) outcomes at six months following an ICU admission of at least three days during which they received life-sustaining therapy in the form of mechanical ventilation for > 48 hours and/or vasopressors for > 24 hours within their first six days in the ICU.

Of 473 patients who met inclusion criteria, 303 ultimately consented to participate. Median age was 62 years (interquartile range, 53-71), 57.1% were male, and 37% were non-white. Prior to their ICU stay, 94.1% of patients resided at home, 28.4% were employed, and 68.0% demonstrated normal baseline function, defined as living at home with no self-reported deficits in cognition or abilities to ambulate up 10 stairs and toilet independently. ICU admission diagnoses were most common for respiratory failure (27.4%), sepsis (21.8%), and non-emergency surgery (17.8%).

Of the 303 enrolled patients, 72 (23.8%) died in the hospital, 21 (6.9%) were discharged to inpatient hospice, and 58 (17.5%) died between hospital discharge and the six-month follow-up. Of the surviving 173 patients at six months, 82.8% had returned to their original residence, 81.9% could toilet independently, 71.3% could ambulate 10 stairs independently, and 62.4% reportedly exhibited normal cognition. Surgical ICU patients experienced better survival and morbidity outcomes compared to medical ICU patients. Of the original 303 enrolled patients, 293 had complete data for six-month physical and cognitive outcomes and baseline characteristics, and were included in an analysis to identify predictors of return to baseline function. Of these, 91 (31.1%) returned to baseline at six months. Normal function prior to ICU admission was not associated significantly with increased likelihood to return to baseline. Independent predictors of not returning to baseline function included older age, being a medical (as opposed to a surgical) patient, non-white race, higher APACHE III score, hospitalization in the prior year, and a history of cancer, liver disease, neurologic condition, or any type of transplant.

■ COMMENTARY

This is a comprehensive cohort study that uncovered several important findings. First, six-month mortality among patients with ICU stays requiring life-sustaining therapy is quite high at 43%. Although hospitalization in the prior year was an independent predictor of poor return to baseline function in the multivariable model, it is notable that most patients (94.1%) resided at home, and 68% reported normal baseline function prior to their ICU hospitalization. Thus, an ICU hospitalization requiring life-sustaining therapy is a defining moment. A similar pattern has been observed in multiple studies focused on outcomes after hospitalization for severe sepsis.[1,2]

Second, the multivariable model presented is unique in its use of return to baseline status as an outcome that is important in ICU survivorship. Third, although six-month mortality is high, most patients who survive to six months are at home and functioning normally, albeit with cognitive impairments outnumbering physical ones. These findings are intriguing when viewed in the context of studies that have found that among patients on

prolonged mechanical ventilation, only 9% are at home and independently functioning at the one-year mark.[3] To the extent that functional status is an important component of quality of life for patients, data from the Detsky et al study are informative, although the results do not mitigate the complexity of real-time decisions in the ICU, especially when the decision involves whether to continue aggressive care (and possibly tracheostomy and G-tube placement) vs. pursue comfort care/hospice. For patients requiring life-sustaining ICU support, even briefly as defined by this study, these data suggest that mortality is high, but if they survive, the majority can return home and achieve some degree of normal function by six months. However, based on data from other studies, if patients continue to remain dependent on mechanical ventilation for a longer period, at some point a threshold is crossed such that their chances of functional independence decline drastically. It is interesting to note that surrogate ratings overall were more pessimistic than reports from patients in the study. Although independent risk factors for return to baseline are presented, they have yet to be validated as part of an accurate scoring system for predicting the outcome of return to baseline. Currently, data from this study are probably most helpful as part of patient and/or surrogate discussions regarding what to expect in terms of recovery, even after brief, but intense, ICU stays. ■

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ABSTRACT & COMMENTARY

Failure to Wean From the Ventilator: Is Pleural Effusion the Culprit?

By Betty Tran, MD, MSc, Editor

SYNOPSIS: The authors of a multicenter, prospective cohort study did not find an association between the presence of moderate or large pleural effusion and ventilator weaning failure.

SOURCE: Dres M, et al. Prevalence and impact on weaning of pleural effusion at the time of liberation from mechanical ventilation. A multicenter prospective observational study. *Anesthesiology* 2017;126:1107-1115.

Rates of ventilator weaning failure after a single spontaneous breathing trial (SBT) are reported between 26-42%.[1] There may be multiple contributors, but weaning failure ultimately is the result of excessive load on the respiratory system that exceeds the capacity of the respiratory muscles and/or poor gas exchange. To the extent that pleural effusion can both increase the load on the respiratory system by impairing lung mechanics and disrupt gas exchange, theoretically, it can affect weaning outcome.

To determine whether the presence of pleural effusion affects ventilator weaning success or failure, Dres et al prospectively enrolled intubated patients on mechanical ventilation for at least 24 hours who met criteria for a first SBT in three ICUs (one medical, two medical/surgical) in Paris. SBTs were performed on pressure support ventilation at 7 cm H_2O and zero positive end-expiratory pressure or a T-piece for 30 minutes. SBT failure was predefined and present if any one of the following were met: pulse oximetry (SpO_2) < 90% on an FiO_2 of > 50%, respiratory distress (respiratory rate > 35 or increased by > 50%, cyanosis, agitation), systolic blood pressure > 180 mmHg, cardiac arrhythmia, or respiratory acidosis with pH < 7.32 with $PaCO_2$ > 50 mmHg. Weaning failure was defined as a failed SBT or if the patient required reintubation or noninvasive ventilation (NIV) within 48 hours of extubation. NIV used prophylactically for patients at risk for extubation failure (e.g., hypercapnia during SBT) was not counted as weaning failure. Pleural effusions were assessed via bedside ultrasound after completion of the SBT and classified according to the British Thoracic Society classification as small, moderate, or large and quantified by volume.[2,3] Ultrasound images from additional patients were performed separately to assess for interobserver and intraobserver reproducibility. The primary endpoint was the prevalence of pleural effusion (none to small vs. moderate to large) in patients with weaning failure vs. success.

A total of 136 patients were enrolled in the study; most were receiving mechanical ventilation for acute respiratory failure or shock for a median of six days (interquartile range, 3-11 days). Pleural effusion was present in 51 patients. Overall, 18 patients had a moderate to large pleural effusion and 118 had a small or no pleural effusion. Overall, interobserver agreement for visual estimation of pleural effusion was found to range from kappa = 0.70-0.89, and intraobserver agreement ranged from

kappa = 0.69-0.70. Not surprisingly, moderate to large pleural effusions were more frequent in patients with chronic renal failure, with septic or hemorrhagic shock as the primary reason for mechanical ventilation, and in those presenting with higher weight gain between ICU admission and first SBT.

Among the 136 patients enrolled, 91 had a successful SBT and were extubated; 10 of these patients ultimately required reintubation within 48 hours. Overall, 57 patients were considered weaning failures. The prevalence and volume of pleural effusion were similar in both the weaning success and weaning failure groups. In addition, the extubation failure rate, total duration of mechanical ventilation, and ICU length of stay were similar in both the group of patients who had none to small pleural effusion and the group with moderate to large pleural effusion.

■ COMMENTARY

When patients fail SBTs, we are forced to contemplate what interventions could be performed to improve their chances of weaning success. Pleural effusions are common in critically ill patients; although the current study reports a prevalence of 37%, some series cite rates of > 60%.[4] In an effort to do something, we consider a thoracentesis in the hopes of improving a patient's ability to wean from the ventilator. However, results from this study suggest that even moderate to large pleural effusions are not associated significantly with weaning success or failure. Although small in scope with few patients exhibiting moderate to large pleural effusions, this is the first multicenter, observational study on this topic. Its use of bedside ultrasound to detect and quantify pleural effusion is more accurate than use of chest radiographs, as seen in prior studies, and reproducibility between and within observers was moderate. Overall, this study highlights an important theme that is often seen in medicine: Even though biologic mechanisms exist and appear feasible, they may not produce a significant clinical effect. Although pleural effusion can affect respiratory dynamics by decreasing compliance, induce hypoxia via ventilation-perfusion mismatch and shunting, and increase cardiac filling pressures, these mechanisms do not appear to affect weaning failure. When reviewing possible causes for ventilator weaning failure, other etiologies besides pleural effusion probably should be considered first. ■

REFERENCES

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CME/CE QUESTIONS

1. **Approximately what percentage of critically ill patients experience thrombocytopenia during the length of their ICU stay?**
   a. 25%
   b. 50%
   c. 75%
   d. 99%

2. **In the article by Detsky et al, approximately what percentage of patients died within six months of an ICU hospitalization requiring life-sustaining therapy?**
   a. 5%
   b. 25%
   c. 50%
   d. 75%

3. **Which of the following statements is true regarding pleural effusion in the ICU?**
   a. The prevalence of moderate to large pleural effusions was similar in patients with weaning success and weaning failure.
   b. Pleural effusion was detected in 10% of ICU patients.
   c. Patients with no to small pleural effusion were more likely to experience chronic renal failure.
   d. Patients with moderate to large pleural effusion experienced longer durations of mechanical ventilation and ICU length of stay.