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SPECIAL FEATURE

Thrombocytopenia in the ICU

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

The term thrombocytopenia refers to platelet counts < 150,000/microL, with severe thrombocytopenia defined as a count < 50,000/microL. A normal platelet count is between 150,000 and 450,000/microL, but some healthy individuals have baseline counts outside that range. For this reason, low counts are not always a cause for alarm and repeat testing is warranted before acting on a value. Critically ill patients have thrombocytopenia for a variety of reasons and it is often a marker of physiological stress. Epidemiological studies have showed that ICU patients admitted with thrombocytopenia have higher severity of illness scores and more organ dysfunction.[1] In this review, I will discuss the topic of thrombocytopenia in the critically ill patient. While a detailed review of workup and management of thrombocytopenia is beyond the scope of this article, I will touch on key concepts and common disease states that all ICU clinicians should know.

PLATELET PRODUCTION

A healthy individual produces platelets on the order of 35,000-50,000/microL each day, but megakaryocyte production can ramp up considerably during times of increased demand. Platelets survive in the circulation for 8-10 days, and then are removed by the reticuloendothelial system in the liver and spleen. Disease processes that upset this balance can lead to thrombocytopenia. In general terms, these processes include decreased bone marrow production, immune-mediated destruction, consumption in thrombi, and splenic sequestration (as with portal hypertension and splenomegaly). Typically, bone marrow disorders that reduce platelet production will also reduce other hematologic cell lines, causing pancytopenia. Normally, one-third of the body's platelets reside in the spleen, in balance with the circulating pool. Conditions that increase splenic size or congestion will drop the platelet count without decreasing the total body platelet mass.

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EPIDEMIOLOGY

Thrombocytopenia is a common finding in ICU patients. Hui et al conducted a systematic review of 24 studies (n = 6894 patients) looking at the epidemiology and consequences of thrombocytopenia in ICU patients.[2] Patients were in medical, surgical, mixed, cardiac, and trauma ICUs. This insightful study showed several key themes. In general, the quality of evidence on this topic is fair. All 24 studies were observational, half were retrospective, most were single-center, most didn't account for loss to follow-up, some didn't specify ICU type, and the definition of "thrombocytopenia" differed between studies. In only two studies did researchers even have a protocol for re-verifying the platelet count.

Hui and colleagues found that the frequency of thrombocytopenia varied across studies. The prevalence of thrombocytopenia at ICU admission ranged from 8-68%. The incidence of developing new thrombocytopenia during the course of an ICU stay ranged from 13-44%. Nine studies reported risk factors for thrombocytopenia. The most common risk factors for the development of thrombocytopenia were sepsis, renal failure, shock, organ dysfunction, and high illness severity.

Hui et al found the rigor of studies looking at outcomes associated with thrombocytopenia in ICU patients to be mediocre. Of five studies reporting bleeding outcomes, only two used objective a priori definitions of "bleeding." Only one study looked at the risk of bleeding using multivariate methods to adjust for confounders and it found no association between thrombocytopenia and bleeding. Among the 16 studies examining mortality, only eight adjusted for confounders; six studies found thrombocytopenia was a risk factor for death, and two studies found no association. Two studies investigated the association between thrombocytopenia and antiplatelet medications: one found no association between aspirin and thrombocytopenia, and the other found that use of non-steroidal anti-inflammatory drugs was more common among thrombocytopenic patients (P = 0.012).[1]

RISKS OF THROMBOCYTOPENIA

Williamson et al examined risk factors and outcomes of ICU thrombocytopenia in a large and heterogeneous cohort of adult ICU patients.[3] Subjects came from a 16-bed medical/coronary unit and a 14-bed surgical/trauma unit in a tertiary hospital in Quebec. A total of 20,696 patients were included. They defined thrombocytopenia as < 100,000 platelets/microL. They used multivariate regression to adjust for demographics, comorbidities, severity of illness, and numerous other confounders. Thrombocytopenia at admission was *prevalent* in 13% of patients. Another 8% of patients developed *incident* thrombocytopenia during their ICU stay. Overall, they found an increased ICU length of stay for both prevalent and incident thrombocytopenia (4.0 days and 6.1 days, respectively) compared to patients without thrombocytopenia (3.4 days; $P < 0.001$ for both). Major bleeding was more common for both prevalent and incident thrombocytopenia (20.3% and 19.3%, respectively) compared to patients without thrombocytopenia (12.5%; $P <$ 0.001 for both). Prevalent and incident thrombocytopenia were associated with increased mortality (14.3% and 24.7%, respectively) compared to patients without thrombocytopenia (10.2%; $P <$ 0.001 for both). In subgroup analyses, it appeared thrombocytopenia had the greatest impact on mortality among patients with cancer, genitourinary, digestive, respiratory, vascular, and infectious diagnoses. It had less of an impact on neurologic and musculoskeletal diagnoses.

In addition to adverse clinical outcomes, thrombocytopenia has other consequences.[4] First, fear of bleeding may dissuade clinicians from performing necessary interventions or procedures. Second, thrombocytopenia may prompt platelet transfusion, which has been associated with infectious and noninfectious complications and an increased risk of death in certain populations, such as liver transplant patients.[5] Furthermore, thrombocytopenia often leads to additional investigations and tests (e.g., heparin-induced thrombocytopenia (HIT) panel).

Table. Common Causes of Thrombocytopenia in ICU Patients		
Cause	**Other Possible Findings**	**Comment**
Drugs	Fever, thrombosis (HIT)	See text
Infections	Fever, lymphadenopathy	#1 cause in ICU patients; viral, bacterial, parasitic
Liver disease	Hepatosplenomegaly	May be initial presentation of liver disease
Rheumatologic	Thrombosis (APS)	See "APS" below
Post-trauma/surgery	Typical nadir at post-op day 4	Consumption is proportional to intraoperative tissue and blood loss
Pregnancy		5% of pregnant woman develop mild gestational thrombocytopenia which resolves after delivery; if count is < 70,000/microL, consider other causes such as preeclampsia, TTP, or HELLP
Nutrient deficiency (e.g., B12, folate, copper)	Neurologic symptoms	Consider if history of bariatric surgery or restricted diet
Myelodysplasia	Other cytopenias	
Aplastic anemia	Other cytopenias	
DIC	Fever, thrombosis	Clots usually venous; most common with infection and malignancy
Bone marrow infiltration (e.g., leukemia, lymphoma)	Lymphadenopathy, other cytopenias	
Paroxysmal nocturnal hemoglobinuria	Thrombosis, hemolytic anemia, cytopenias	Clots of intrabdominal and cerebral veins
TTP-HUS	Neurologic symptoms, hemolytic anemia, renal insufficiency, thrombosis	Clots of small vessels; plasma exchange may be life-saving; many patients present only with anemia and thrombocytopenia
Antiphospholipid syndrome	Thrombosis, history of recurrent pregnancy loss, lupus anticoagulant	Clots either venous and arterial; can occur in isolation or with other processes (SLE, infection, cancer, medications)
Congenital thrombocytopenia		May see large platelets on smear; usually diagnosed in childhood
APS = antiphospholipid syndrome; HIT = heparin-induced thrombocytopenia; TTP-HUS = thrombotic thrombocytopenic purpura-hemolytic uremic syndrome; SLE = systemic lupus erythematosis; DIC = disseminated intravascular coagulation; HELLP = hemolysis, elevated liver enzymes, low platelets		

When to worry about bleeding? The absolute platelet count is not a good predictor of bleeding risk. Rather, one should consider all factors that increase bleeding risk. Accordingly, the literature does not advocate a specific threshold for transfusing patients. Prior bleeding at a certain platelet count is a better predictor in a given patient, and clinical judgment is useful in this regard. A minimum count of 50,000/microL for surgical procedures seems wise. Severe spontaneous bleeding is likely with counts < 10,000/microL. One exception is patients with idiopathic thrombocytopenic purpura (ITP), who rarely have severe spontaneous bleeding even with very low counts.

APPROACH TO ICU THROMBOCYTOPENIA

When a critically ill patient has thrombocytopenia, the differential is broad (*see Table*). Always repeat the test to confirm it's true, review the peripheral smear (to exclude clumping or lab artifact), and assess other hematologic parameters. If the drop occurs after admission to the hospital, it's likely from infection or drugs. A new reduction is more concerning than a chronic low count, as it suggests an active process. Other abnormal hematologic labs should prompt a diligent workup for a serious diagnosis.

The differential for a thrombocytopenic patient who is actively bleeding or has purpura depends on whether he has other symptoms. If the patient lacks evidence of systemic illness and other hematologic labs are normal, the likely diagnosis is either immune thrombocytopenia (ITP) or drug-induced thrombocytopenia. If the patient has other symptoms, however, the differential is broad (*see Table*). Depending on clinical judgment, consider coagulation studies, liver function tests, cultures, and bone marrow aspiration. Getting a detailed history is key, including past platelet counts, new medications, bleeding history, and family history. Examination should focus on lymphadenopathy and hepatosplenomegaly.

A non-bleeding ICU patient admitted with chronic isolated asymptomatic thrombocytopenia likely has ITP, liver disease, HIV infection, or a myelodysplastic syndrome. The most common cause of new onset thrombocytopenia in ICU patients is sepsis, accounting for approximately half of cases.[6] After sepsis, the most common causes are liver disease (hypersplenism), disseminated intravascular coagulation (DIC), primary hematologic disorders, medications, massive transfusion, and alcoholism.

When to worry about clotting? A few rare thrombocytopenia conditions are associated with increased risk of thrombosis. These include HIT, antiphospholipid antibody syndrome, disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS), and paroxysmal nocturnal hemoglobinuria. Treatment of each generally focuses on the underlying problem (e.g., stopping heparin, anticoagulation, treating infection, plasma exchange, etc.). In general, appropriate use of anticoagulants or thromboprophylaxis should not be withheld if the platelet count if > 50,000/microL, especially if the patient is at high risk (e.g., postoperative).

PLATELET COUNT TRENDING

Platelet count courses vary among different ICU patient populations.[7] For surgical patients, platelet counts frequently dip on days 1-4 as a result of perioperative consumption. The magnitude of the drop reflects the extent of tissue trauma and blood loss. Thereafter, platelet counts rise on days 5-7, and peak at day 14. The reactive count seen at 2 weeks is a downstream response to the acute consumption and subsequent thrombopoietin surge during surgery. If the recovery is blunted after 4 days in a postoperative patient, consider the presence of continuing critical illness. A new drop after day 4 suggests an acute pathology such as infection or drug-induced bone marrow suppression.

For medical ICU patients, the platelet course depends on the underlying disease state and is useful for prognostic purposes. Akca et al performed a prospective observational study of 1449 patients from 40 ICUs in 16 countries.[8] Thrombocytopenia was defined as < 150,000/microL. Platelet counts and other measures of organ dysfunction were measured daily. In general, platelet counts dropped significantly in the first days of acute illness, reaching a nadir on day 4. Among survivors, the platelet count returned to its admission value by the end of week 1 and subsequently rose higher than its admission value by day 9. In non-survivors, the platelet count also returned to its admission value at week 1, but then plateaued and there was no subsequent increase. In other words, thrombocytopenia at any time is associated with increased ICU mortality, but prolonged thrombocytopenia with a blunted platelet recovery confers additional risk of death.

Moreau et al looked at hospital mortality among 1077 ICU patients in nine ICUs who subsequently spent > 5 days in the unit.[9] All had normal admission platelet counts. At ICU admission, there was no difference in platelet counts between survivors and non-survivors. Like Akca, they found that platelet counts reached a nadir on day 4. After adjusting for severity of illness and other factors, they determined that a 30% decline in platelet count during the first 4 days strongly and independently predicted hospital mortality. Taken together, these two studies suggest that a severe platelet drop in the first 4 days and/or a blunted recovery response are both poor prognostic indicators.

DRUG-INDUCED THROMBOCYTOPENIA

Any drug can cause thrombocytopenia via platelet-reactive antibodies. However, certain culprits are commonly implicated. These include heparin, sulfonamides, beta-lactams, piperacillin, vancomycin, rifampin, carbamazepine, phenytoin, and quinine. Thrombocytopenia will develop within hours of exposure if the patient has been previously exposed, or within 2 weeks if it is a new drug. Upon drug removal, the thrombocytopenia usually resolves within 1 week.

HIT is a potentially lethal condition in which anti-platelet antibodies activate the platelets, thereby both depleting the platelet supply but also increasing the risk of thrombosis. Clots can be either venous or arterial, with venous being more common. Thrombosis occurs in up to half of individuals. Onset is usually 5-10 days after heparin initiation. Rapid early onset of HIT (within 24 hours) can occur if the patient was exposed to heparin in the past 3 months. Upon drug removal, the thrombocytopenia resolves within 1 week. However, the antibodies can persist for 2-3 months. Rarely, "delayed-onset HIT" can occur (with or without thrombosis) several days after heparin is withdrawn because the patients have very high HIT antibody titers. In one series, it occurred a median of 9 days after the drug was stopped.[10] The probability of HIT as a cause for a low platelet count can be estimated using the validated "4Ts Score" (Thrombocytopenia, Timing, Thrombosis, and oThers).[11] A score < 4 can essentially exclude HIT with a negative predictive value of 99.8%. Patients with a presumptive HIT diagnosis should have immediate heparin discontinuation and administration of a non-heparin anticoagulant (unless there is a bleeding risk). A HIT antibody test should be sent. Readers interested

in learning more about this condition are referred to an excellent review by Lee et al.[12]

SUMMARY

Thrombocytopenia in ICU patients is a common finding with numerous potential causes. Common risk factors include sepsis, renal failure, shock, organ dysfunction, and high illness severity. Surgical ICU patients frequently exhibit thrombocytopenia postoperatively, but a delayed recovery or acute platelet drop merits close scrutiny. Studies looking at outcomes suggest that mortality among thrombocytopenic patients is not due primarily to bleeding. ■

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ABSTRACT & COMMENTARY

Should Patients with Acute Respiratory Failure be Extubated at Night?

By David J. Pierson, MD, Editor

SYNOPSIS: In this retrospective study of extubation outcomes in five ICUs at a single medical center, patients extubated at night had no increase in adverse events and their mortality rates and lengths of ICU stay were lower. However, these results were likely affected by the high proportion of post-cardiac-surgery patients in the nighttime extubation group.

SOURCE: Tischenkel BR, et al. Daytime versus nighttime extubations: A comparison of reintubation, length of stay, and mortality. *J Intensive Care Med* 2014; Apr 24. [Epub ahead of print.]

This is a retrospective study of extubation outcomes in the five ICUs of Montefiore Medical Center in New York during a recent 23-month period. Institution-wide, respiratory therapist-driven weaning and extubation protocols (incorporating physician input for marginal data or clinician concern) and 24/7 intensivist ICU presence were in place at the time of the study. Once patients were clinically improved, with spontaneous respiratory rate and required inspired oxygen fraction and positive end-expiratory pressure requirements in an acceptable range, and were hemodynamically stable with manageable respiratory secretions and acceptable arterial blood gas results, they underwent a 30-minute spontaneous breathing trial with added pressure support to keep their tidal volumes at least 5 mL/kg ideal body weight. If the results of this trial were satisfactory according to standardized objective and subjective criteria, the patients were extubated. Outcomes with respect to the need for reintubation, hospital length of stay, and mortality were compared for patients extubated between 7 p.m. and 7 a.m. (coinciding with shift changes for nurses, respiratory therapists, and intensivists) vs those extubated during the day.

More than twice as many patients (n = 1555) had been extubated during daytime hours as during the night (n = 685). Reintubation occurred twice as frequently among patients extubated during the day (7.7%) as among those extubated at night (3.8%; odds ratio 0.5; $P = 0.01$). Total hospital length of stay was significantly shorter for patients extubated at night ($P = 0.002$; actual data not provided), despite adjustment for demographic factors, Elixhauser Comorbidity Measure, and other variables. Although

Table. A Reasonable Approach to Whether a Patient with Acute Respiratory Failure Should Be Extubated during Nighttime Hours	
Extubation at Night Reasonable	**Extubation at Night Ill-Advised**
In-house intensivist coverage present	No in-house nighttime intensivist coverage
Need for mechanical ventilation primarily due to anesthesia for surgery	Need for mechanical ventilation primarily due to acute respiratory failure
No severe comorbidities, especially underlying respiratory disease	Longer duration of mechanical ventilation (e.g., more than 48-72 hours)
Excessive or hard-to-clear respiratory secretions absent	Marginal weaning and/or extubation criteria; marginal results from spontaneous breathing trial
Normal mental status	Serious or multiple underlying comorbidities
Mechanical ventilation for less than 24 hours	Previous failed extubation attempts
	Difficult intubation
	Excessive or hard-to-clear respiratory secretions
	Decreased level of consciousness

it was not statistically significant, there was a trend toward lower mortality among patients extubated at night. The authors conclude that a practice of delaying extubation until morning in patients who meet weaning and extubation criteria during the night is not supported by their results, and that patients should be extubated as soon as these criteria are met.

■ COMMENTARY

A number of recent studies pertain to the context and findings of the current report. First, outcomes for patients admitted at night have been shown to be worse in comparison with patients admitted during daytime hours, at least in some institutions. The risk for medical errors is higher at night. And adding the in-unit presence of a qualified intensivist has been shown to improve patient outcomes. These findings suggest that the results of critical care during the night may not be as good as those during the day, at least in some settings.

However, although the prediction of successful weaning and extubation are not perfect, many studies have shown improved success rates (including getting patients extubated sooner) with the use of evidence-based criteria and standardized protocols. Numerous studies have shown associations between shorter durations of mechanical ventilation and improved ICU and hospital outcomes, and it is well established that ventilator-associated pneumonia and other ventilator-associated complications are strongly related to the duration of endotracheal intubation. Thus, it is reasonable to reconsider the traditional approach of many intensivists not to extubate patients recovering from acute respiratory failure during the nighttime hours.

On the surface, this study would appear to refute that time-honored, cautious approach. However, despite the authors' attempts to reduce confounding by diagnosis, severity of illness, and other factors, I am concerned by the differences between the patients who were extubated at night and those extubated during the day in this study. More than half of all the study patients (1171 of 2240) were managed in a cardiac surgery ICU (CSICU), and patients in these units comprised 81.8% of all those who were extubated at night. As the authors state, in their CSICUs, "a protocol is set in place so that patients are to be extubated within 6 hours of the end of their surgery." They acknowledge that patients undergoing elective cardiac surgical procedures, which typically begin in the morning, "would undergo extubation during the study's defined nighttime hours (after 7 p.m.)," and, in fact, the CSICUs had a disproportionate number of extubations between 7 p.m. and 10 p.m. compared to the other units.

Patients ventilated after cardiac surgery have acute respiratory failure mainly due to anesthesia, and studies have shown improved outcomes with early extubation in such patients. Retrospective studies are inherently limited in terms of establishing causal relationships, and despite the authors' statistical adjustments, I think their inability to associate nighttime extubation with any unfavorable consequences could be due to the marked differences between the patients who were extubated at night vs during the day.

However, this study shines useful light on the long-standing debate as to whether extubation should be deferred until the next morning when a patient first meets criteria during the evening or nighttime hours. The table provides a reasonable approach to this question. It is based more on experience and common sense than on explicit published evidence, but is generally consistent with the results of this study and others in the literature. ■

ABSTRACT & COMMENTARY

What Factors Contribute the Most to Decrements in Post-ICU Physical Function in Acute Lung Injury Survivors?

By Linda L. Chlan, RN, PhD, FAAN

Dean's Distinguished Professor of Symptom Management Research, The Ohio State University, College of Nursing

Dr. Chlan reports that she receives grant/research support from Hospira.

SYNOPSIS: Mean daily doses of up to 40 mg of prednisone equivalents and lengthy ICU stays were associated with impaired physical outcomes in patients who survived acute lung injury.

SOURCE: Needham D, et al. Risk factors for physical impairment after acute lung injury in a national, multicenter study. *Am J Respir Crit Care Med* 2014;189:1214-1224.

Patients with acute lung injury (ALI) who survive lengthy ICU stays are at risk for a plethora of adverse outcomes, including impaired and prolonged recovery of physical functioning. Many times, medications such as corticosteroids and neuromuscular blocking agents, administered to treat patients with ALI, contribute to these decrements. Needham et al sought to tease out the complex interplay of corticosteroids on patient outcomes and how that might influence any physical limitations in those patients who survived ALI. The purpose of this observational, secondary data analysis was to pool data from ALI patients from 12 hospital sites co-enrolled in two ARDSNet studies to evaluate 6- and 12-month physical outcomes and a number of risk factors in those who survived their ICU stays. Three physical outcomes measures were selected as markers of long-term outcomes from a list of seven measures included in the original data set: 1) manual muscle testing for extremity strength using the MRC sum score, 2) the 6-minute walk test (6MWT) for physical functioning, and 3) the SF-36 physical function (PF) scale as a measure of quality of life.

The study sample consisted of 203 ALI patients with a mean age of 48 (± 15) years, 49% male, and a mean APACHE III score of 85 ± 25. ALI patients received mechanical ventilation for a mean of 11 (± 9) days, had ICU stays of 14 (± 11) days, while 27% received neuromuscular blocking agents and 43% received corticosteroids, with a mean daily dose of the latter of 52 (± 81) mg (prednisone equivalents). At 6 months, 8% of patients had ICU-acquired weakness by the MRC sum score, with percent predicted values on the 6MWT of 65% (± 22) and 61% (± 36) on the SF-36PF. Between the 6- and 12-month assessment points, there were small improvements in the physical outcomes included in this study. Several multiple regression models were run, adjusting for age, gender, comorbidities, and baseline functional status.

The authors reported that corticosteroid dosages had a non-linear relationship to the three main outcomes of interest, with a change in slope occurring at a mean daily dose of 40 mg prednisone equivalents. Overall, corticosteroid doses up to 40 mg/day, prednisone equivalents, and ICU length of stay were significantly associated with decrements in the physical outcome measures. In patients who did not receive any corticosteroids, there was a significant decrement in all three of the physical measures of 1.33-4.59% in muscle strength, 6MWT, and SF-36PF. For each 10 mg/day increase in mean prednisone equivalents, up to 40 mg, there was a decrease in 6MWT and SF-36PF results. Interestingly, there were no significant changes in the physical measures for dose increases above 40 mg prednisone equivalents. To complicate the puzzling findings even further, an interaction between corticosteroid dose and ICU length of stay indicated that the corticosteroid prednisone equivalent doses had a negative effect on physical outcomes in those patients with a shorter ICU stay. The authors reported the results of several post hoc analyses that did not influence the main findings, including no impact of daily doses of sedative and opioid medications.

■ COMMENTARY

The findings from the observational study by Needham and colleagues provide more evidence of the decrements in physical outcomes in critically ill patients who experience lengthy ICU stays and mechanical ventilatory support due to ALI. However, the reader needs to keep in mind that association does not imply causation. Therefore, one cannot state that corticosteroids and lengthy ICU stays cause

decrements in physical function.

The relationship between corticosteroid dose and physical function is complex. The investigators of this study posit that ICU-acquired weakness and other physical function decrements are so common among the critically ill with lengthy ICU stays that it may be difficult to detect any influences specially attributed just to the receipt of specific medications, such as corticosteroids. Similar to minimizing doses of sedative and opioid medications, a judicious approach may be warranted with the dosing and duration of corticosteroids used in the ICU. The findings from this study add more evidence to the detrimental influence of prolonged bed rest and immobility on the physical function of patients who survive ALI. ■

CME QUESTIONS

1. Which of the following is true about acute thrombocytopenia in medical ICU patients?
a. The most common cause is medications.
b. The absolute platelet count is a good predictor of bleeding risk.
c. Before undertaking a workup for thrombocytopenia, the count should always be repeated and the peripheral smear directly reviewed.
d. Acute thrombocytopenia is seen in < 10% of medical ICU patients.
e. All of the above

2. Which of the following is *false* about platelet counts in ICU patients?
a. Surgical patients commonly have an acute drop after surgery, with a nadir at day 4.
b. The magnitude of the platelet drop in a postoperative patient is proportional to intraoperative blood loss and tissue injury.
c. Severe thrombocytopenia in ICU patients is associated with a high risk of death, and the cause of death is usually bleeding.
d. The finding of persistent thrombocytopenia (i.e., a blunted recovery) is associated with increased mortality.
e. None of the above

3. Which of the following was found in the study comparing daytime and nighttime extubations in patients who had required mechanical ventilation?
a. Reintubations were more frequent after nighttime extubation.
b. Patients extubated at night were more seriously ill than those extubated during the day.
c. Hospital length of stay was greater in patients extubated at night.
d. All of the above
e. None of the above

4. Which of the following is the most reasonable explanation for the finding that patients extubated at night had better outcomes than those extubated during the day?
a. Staffing was better at night.
b. Different weaning criteria and extubation protocols were used at night.
c. More patients extubated at night were ventilated after cardiac surgery.
d. All of the above
e. None of the above

5. Findings from the study by Needham and colleagues indicate which of the following in regard to corticosteroids?
a. The higher the dose of corticosteroids, the more protective they are to physical outcomes.
b. Higher doses of steroids cause decrements in muscle strength.
c. Corticosteroids up to 40 mg/day may impact physical outcomes.
d. Lengthy ICU stays require the administration of corticosteroids.
e. All of the above

6. Which of the following statements is true in regard to length of ICU stay in patients included in the study by Needham and colleagues?
a. Receipt of neuromuscular blocking agents was a predictor of lengthy ICU stays.
b. Lengthy ICU stay was associated with decreases in physical function measures.
c. Patients who required dialysis had the longest ICU stays.
d. Lengthy ICU stays cause a decrease in quality of life.
e. All of the above