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Hospital Medicine

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Tighter Blood Pressure Control Post-Intracranial Hemorrhage May Decrease Recurrence

By Deborah J. DeWaay, MD, FACP

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Dr. DeWaay reports no financial relationships in this field of study

SYNOPSIS: Inadequate blood pressure control in intracranial hemorrhage (ICH) survivors was associated with recurrent ICH.

SOURCE: Biffi A, Anderson C, Battey T, Ayres A, Greenberg S, Viswanathan A, Rosand J. Association Between Blood Pressure Control and Risk of Recurrent Intracerebral Hemorrhage. *JAMA*. 2015; 314(9):904-912

Fifty percent of stroke related morbidity and mortality are related to intracerebral hemorrhage (ICH). ICH secondary to arteriolosclerosis usually occurs in the deep structures of the brain, such as the basal ganglia, thalami or brainstem. In contrast, ICH secondary to cerebral amyloid angiopathy tends to occur in the "lobar" or cortical-subcortical regions. Improving secondary prevention of ICH is important because a recurrent bleed is usually more devastating than the first occurrence.

This was a single-center longitudinal cohort study of patients with ICH. Patients were included in the study if they were diagnosed with an ICH confirmed by CT scan, had symptoms that began <24 hours prior to presentation, and were ≥ 18 years old over a 7 year period. Patients with an ICH that was secondary to trauma, had a conversion of an ischemic infarct, had a rupture of an aneurysm of arteriovenous malformation or tumor were excluded. A lobar ICH was defined as occurring in the cerebral cortex ± underlying white matter. An ICH that occurred in the basal ganglia, thalami or brainstem was labelled a nonlobar ICH. In order to determine if a patients' blood pressure was controlled and if any recurrent strokes occurred, all participants or caregivers were interviewed at 3, 6, 9, 12 months and every 6 months afterwards. In addition, the investigators obtained any new imaging and blood pressure readings were obtained from

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the patient, the electronic health record (EMR) and when necessary external medical records. Patients were excluded if more than one blood pressure reading was missing within a given 6 month period or if there was a discrepancy between the EMR medication record and the patient's self-reported list. In addition to interviewing the patient, caregivers and accessing the EMR for data on deaths and new strokes, the Social Security Death Index was also queried.

In order to analyze the relationship between blood pressure and recurrent ICH the authors generated 4-time varying exposures. The rates of ICH recurrence per 1000 person-years were computed and compared to the patients' blood pressure being adequately or inadequately controlled as determined by 4 blood pressure variables. First, authors used the American Heart Associate/American Stroke Association guidelines (AHA/ASA) and the patients' blood pressures to create a dichotomous variable. The goal for non-diabetics was less than 140/90. For diabetics the goal was less than 130/80. Second, the hypertension stage of the patient based on the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure 7 (JNC 7) criteria. Third and fourth, systolic and diastolic blood pressures were used as continuous variables respectively.

1145 of 2278 patients who were screened were enrolled: 505 lobar ICH and 640 nonlobar ICH. 102 of the lobar ICH patients had a recurrence. 44 of the nonlobar ICH patients had a recurrence. Adequate blood pressure control was defined by the AHA/ASA guidelines. 54.6% of patients achieved goal for at least 1 measurement during followup. 43.2% of patients consistently had controlled blood pressure at all available points. The rate of consistent blood pressure control was not significantly different between the two location types. There was no significant difference between type of antihypertensive used, number of antihypertensives and location of stroke recurrence (lobar vs. nonlobar).

A bivariable analysis showed that inadequate blood pressure was associated with recurrent lobar ICH (HR 3.19 [CI 1.42-7.16] p = .005]. This significant difference was also present with multivariate analysis. Lobar ICH rates were 49 per 1000 person-years with adequate blood-pressure control versus 84 per 1000 person-years in those without. In addition, a bivariable analysis showed that inadequate blood pressure was associated with recurrent non-lobar ICH (HR 3.99 [CI 1.16-13.76] p = .03]. Non-lobar ICH rates were 27 per 1000 person-years with adequate blood-pressure control versus 52 per 1000 person-years in those without. This significant difference was also present with multivariate analysis. Only 50% of participants had controlled blood pressure per the guidelines.

In conclusion, there appears to be an association between uncontrolled blood pressure and recurrent ICH irrespective of location. This association became stronger as the stage of hypertension, as defined per the JNC-7 guidelines, was more severe. These findings suggest that secondary prevention with controlled blood pressure maybe very important with this population. Limitations of this study include the authors' ability to capture the correct blood pressure. Also, it is a single centered study. Lastly, this study points to a possible association, not causality.

■ COMMENTARY

Although a randomized controlled trial is necessary to validate this study, the concept remains important. There is great variability in managing blood pressure control in a hospitalized patient. Additionally, little evidence shows tight blood pressure control as necessary except in certain populations such as severe kidney injury and heart failure, benefits patient outcomes. Patients with a history of intracerebral hemorrhage may be another population where tighter blood pressure control during hospitalization may be important. Discharge planning and coordination remain struggles in our current medical system. The challenge for hospitalists making sure the patient understands their medication regimen, and has followup with a primary care provider especially in times of high patient volume and short hospitalizations remains. Good discharge planning including close followup with a primary care provider, helping the patient understand their medication regimen and having a good blood pressure regimen will be even more important in the ICH patient population in order to give them the best chance of having good blood pressure control post-hospitalization. ■

ABSTRACT & COMMENTARY

Optimal Duration of Anticoagulation for Unprovoked Pulmonary Embolism

By Samuel Nadler, MD, PhD

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Dr. Nadler reports no relationships relevant to this field of study.

SYNOPSIS: Treatment for 24 months with oral anticoagulation for unprovoked, first-time pulmonary embolism was superior to treatment for 6 months only.

SOURCE: Couturaud F, et al. Six months vs extended oral anticoagulation after a first episode of pulmonary embolism: The PADIS-PE randomized clinical trial. *JAMA* 2015;314:31-40.

Long-term treatment of pulmonary embolism (PE) with oral anticoagulant therapy is the standard of care, but the duration of therapy has not been well established. Based largely on a single, non-blinded study, the American College of Chest Physicians (ACCP) recommended that an unprovoked PE be treated with at least 3 months of oral anticoagulant therapy (Evidence: Grade 1B) with an extended course of treatment if the bleeding risk is low to moderate (Evidence: Grade 2B); similarly, the European Society of Cardiology recently recommended at least 3 months of therapy (Evidence: Class I, Level A) with extended therapy in patients with low bleeding risk (Evidence: Class IIa, Level B).[1,2]

The PADIS-PE study is a randomized, double-blind trial of adult patients with a first episode of unprovoked PE that seeks to better define the appropriate duration of therapy. In this study, 371 patients with radiographically confirmed PE who had already completed 6 months of therapy with a vitamin K antagonist were randomized to an additional 18 months of therapy or placebo. Unprovoked PE was defined by the absence of any reversible risk factor within 3 months of the PE, such as surgery, trauma, and bed rest, for more than 72 hours and the absence of active cancer within the last 2 years. Patients were excluded if they had previously experienced a deep vein thrombosis (DVT) or PE, had an independent indication for anticoagulation, had bleeding during the initial 6 months of therapy, had known thrombophilia, increased bleeding risk, platelets < 100,000, were expecting major surgery in the upcoming 18 months, or had a life expectancy of < 18 months. The primary outcome was a composite of recurrent venous thromboembolism or major bleeding within the 18-month trial period. This outcome was reassessed 24 months after the treatment period was completed.

During the 18-month trial period, treatment with warfarin reduced the primary endpoint significantly (HR, 0.22; CI, 0.01-1.20; $P = 0.001$.). This effect was due to a reduction in the rate of recurrent venous thromboembolism in the treatment group compared with the placebo group (1.7% vs 13.5%, HR 0.15, $P < 0.001$), while there was a non-significant increase in bleeding in the warfarin group (2.2% vs 0.5%, HR 3.96, $P = 0.22$). Overall, there was no difference in mortality during this period between the two groups (1.1% vs 1.1%, HR 1.32, $P = 0.78$). In the subsequent 24-month period, while not anticoagulated, the effects of prior treatment were largely lost. The overall rate of recurrent thromboembolism was similar in the former treatment and placebo groups (17.9% vs 22.1%, HR 0.69, $P = 0.14$), as was the bleeding risk (3.5% vs 3%, HR 1.12, $P = 0.85$). Mortality was similar in the two groups (9.1% vs 3.6%; HR 1.51; $P = 0.45$).

■ COMMENTARY

Previous professional guidelines have recommended "extended" courses of anticoagulation, but the optimal duration of therapy was ill-defined. The PADIS-PE study provides strong evidence that 24 months of vitamin K antagonism is superior to 6 months for the treatment of first-time, unprovoked PE. At the end of the 24-month therapeutic trial, patients were further monitored off therapy (median 41 months total). Interestingly during this period, the overall rates of recurrence of PE in the warfarin and placebo groups became statistically similar, as the warfarin group had 25 additional events while the placebo group experienced only 14 additional episodes of venous thromboembolism. This implies that the underlying cause of the PE, while unknown, had not resolved. This is further supported by the observation in this and other studies that the form of recurrence was similar to the index event. Additionally, the rate of recurrence was almost twice as high in the group that stopped therapy compared with the placebo group, implying that a rebound effect may increase the risk of clot after discontinuation of therapy. Therapy well beyond 24 months, even lifelong, might be beneficial.

As described above, recommendations regarding treatment of PE also vary based on the likelihood of

bleeding complications. This study included patients with low, moderate, and high risks of bleeding based on ACCP scoring. These factors include advanced age, previous bleeding, cancer, renal failure, liver failure, diabetes, previous stroke, poor anticoagulant control, frequent falls, and alcohol abuse. This study included 45.7% and 40.7% of patients at high risk (more than two risk factors) in the warfarin and placebo groups, respectively. Unfortunately, no subgroup analysis was performed, but a benefit was demonstrated despite inclusion of this proportion of high-risk patients.

The questions remain: What is the optimal length of treatment, and is there a way to prospectively determine who would benefit from extended anticoagulation? The PROLONG study stratified patients with unprovoked DVT after at least 3 months of treatment based on D-dimer levels and compared rates of recurrence in individuals with normal levels to individuals with elevated levels with or without extended treatment.[3] Remarkably, the lowest level of recurrence was in patients with elevated D-dimer levels who then received extended treatment. The HR for recurrence in patients with elevated D-dimer levels without vs with treatment was 5.36 (P = 0.007). As in the PADIS-PE trial, extended anticoagulation was clearly beneficial. Elevated D-dimer levels indicated elevated risk for recurrence and benefit of extended anticoagulation, but normal D-dimer levels did not preclude patients from benefiting from extended anticoagulation. Future development of biomarkers may assist in determining benefit of extended anticoagulation, but current studies suggest that lifelong anticoagulation after unprovoked PE is beneficial. ■

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Idarucizumab: A Promising New Drug that Reverses the Anticoagulant Effects of Dabigatran

By Dana Leifer, MD

Source: Idarucizumab for Dabigatran Reversal. Charles V. Pollack, Jr., M.D., et. al. *N Engl J Med*. 2015; 373: 511-20

Several new oral anticoagulants are changing the approach to anticoagulation for patients with nonvalvular atrial fibrillation and deep venous thrombosis/pulmonary emboli. These drugs, which include dabigatran, a thrombin inhibitor, have been shown to be noninferior both in terms of safety and efficacy to warfarin, which was until recently, the only oral anticoagulant available. In some cases, these drugs have also been shown to be superior to warfarin. In addition, they do not require the intensive monitoring that is needed for warfarin, and they do not have the numerous interactions with other drugs and with diet. Use of these drugs has been limited, however, in part because of fears that they are not rapidly reversible in the event of a hemorrhage or a need for emergency surgery. Several different agents that may rapidly reverse one or more of the new oral anticoagulants are now under development.

In particular, Pollack and colleagues recently reported in the *New England Journal of Medicine* that idarucizumab, a humanized monoclonal antibody that binds specifically to dabigatran, reversed its anticoagulant effects within minutes. The study included 51 patients with serious acute bleeding (Group A), including 18 with intracranial hemorrhages, and 39 patients who needed emergency surgery (Group B). The ecarin clotting time (ECT), which is probably the best test for detecting the effects of dabigatran, was normalized in 89% of patients in group A and 88% of patients in group B when tests were done immediately after the first of the two doses of idarucizumab that patients received. The dilute thrombin time (TT), which is more widely available but less sensitive for detecting the effects of dabigatran was normalized in 98 and 93% of patients in groups A and B respectively. The ECT remained normal at 24 hours in 72% and 54% of patients respectively. For these analyses, the authors excluded the subsets of patients whose baseline ECT or TT was normal.

It is important to note that correction of laboratory abnormalities does not necessarily mean that there is clinical benefit. The paper presents limited data about clinical outcomes. There were 18 total deaths within the first month including 3 from intracranial hemorrhage within 96 hours. Deaths within 96 hours appeared to be related to the index event, while later deaths appeared related to coexisting conditions. These numbers do not seem surprising in view of the serious acute problems that all patients enrolled in the study had. Thrombotic complications (DVT, pulmonary emboli, left atrial clot, myocardial infarction, ischemic stroke) appeared in 5 patients from 2 to 26 days after treatment; anticoagulation had not been resumed in any of these patients, so again these results are not surprising.

■ COMMENTARY

Unfortunately, the authors report little about clinical outcomes. For patients in group B who underwent surgery, intraoperative hemostasis was described as normal in 92% of patients who underwent surgery emergently, so it is likely that there was at least subjective clinical benefit in Group B patients, though even for these patients, there was no control group.

For patients with intracranial hemorrhage, the authors state that modified Rankin scores were recorded at baseline and at 90 days, but they do not report data about the Rankin scores in this publication. We must hope that this information will be reported in a subsequent paper, but in the absence of a control population, this information will be difficult to interpret.

Despite the lack of data about clinical outcomes in this study, it is likely that the rapid reversal of anticoagulation achieved with idarucizumab will be beneficial. For intracranial hemorrhage patients in particular, there is a consensus in the field that rapid reversal of anticoagulation is critically important. Indeed, one of the performance metrics for comprehensive stroke centers is the percent of intracerebral hemorrhage patients with INR>1.4 who are treated with procoagulant agents. In this background, it is likely that a drug that immediately reverses the effects of dabigatran would have a clinical benefit for dabigatran-associated ICH.

In summary, idarucizumab rapidly reverses the effects of dabigatran and is likely to have important clinical benefits for patients with intracerebral hemorrhage and other disease processes in which reversal of anticoagulation is important. The recent paper by Pollack and colleagues, however, reported only limited results about clinical outcomes and lacked a control group that did not receive the study drug. Additional work will therefore be needed to determine if the drug actually improves clinical outcomes. ■

ABSTRACT & COMMENTARY

Community-acquired Pneumonia Requiring Hospitalization in Adults

By Dean L. Winslow, MD, FACP, FIDSA

Synopsis: An active population-based surveillance of community-acquired pneumonia (CAP) requiring hospitalization in adults 18 years of age and older was conducted in five hospitals in Chicago and Nashville. The incidence of CAP requiring hospitalization was highest in older adults. Despite extensive diagnostic testing, no pathogen was identified in most patients. Respiratory viruses were identified more frequently than bacteria.

Source: Jain S, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med 2015; 373: 415-27.

From January 2010 through June 2012 a total of 2488 (of 3634 eligible) adults were enrolled in an active population-based surveillance of community-acquired pneumonia requiring hospitalization in adult patients. Patients who had recently been hospitalized or who were severely immunosuppressed were excluded. Blood, urine, respiratory, and pleural specimens were systematically collected for testing by culture, serology, antigen detection and molecular diagnostic methods. In addition to routine bacteriological methods and urine antigen testing for S.pneumoniae and Legionella pneumophila, a variety of real-time PCR assays were systematically performed on respiratory samples and pleural fluid (when available).

Of the 2488 enrolled patients, independent review of X-rays by a panel of study radiologists concurred with the radiographic diagnosis of pneumonia in 2320 (93%). Mean age of patients was 57 years. 78% of patients had some underlying medical condition (most commonly chronic lung disease, heart disease, immunosuppression or diabetes). 21%

of patients required ICU admission and 2% died. Incidence rates of CAP requiring hospitalization ranged from 6.7 cases/10,000 adults per year in patients ages 18-49 to 164.3 cases/10,000 adults per year in patients 80 years of age or older.

Of the 2259 patients who had radiographic evidence of pneumonia and specimens available for both bacterial and viral testing, a pathogen was detected in 38%, one or more viruses in 23%, bacteria in11%, bacterial + viral pathogen in 3%, and fungal or mycobacterial pathogen in 1%. Of the potential pathogens identified, the most common were rhinovirus in 9%, influenza virus in 6%, and Streptococcus pneumonia in 5%. Less common pathogens included human metapneumovirus (4%), RSV (3%), and parainfluenza virus (3%). Interestingly, Mycoplasma pneumoniae, Staph aureus, adenovirus, Legionella, and Enterobacteriaceae were each found in <2% of cases. A large peak of infection occurred during the winter of 2010-11 and was associated with a large number of Influenza cases and smaller peaks of S.pneumoniae and S.aureus cases.

■ COMMENTARY

This is an interesting surveillance study conducted by the CDC in two large U.S. cities over a 2-year period. The study highlights the burden of pneumonia requiring hospitalization, particularly in older adults. This study also emphasizes that, even when extremely sensitive molecular diagnostic tests are used, a pathogen can be identified in only a minority of cases of CAP and that viral pathogens are more common than bacterial ones. This study is a nice companion piece to the paper published by this same group at CDC earlier this year that focused on CAP requiring hospitalization in children (1). ■

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1. Jain S, et al. Community-acquired pneumonia requiring hospitalization among U.S. children. N Engl J Med 2015; 372: 835-845.

ABSTRACT & COMMENTARY

Serum Chloride Level Predicts Mortality in Acute Heart Failure

By Van Selby, MD

Assistant Professor of Medicine, UCSF Cardiology Division, Advanced Heart Failure Section, San Francisco

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

SOURCE: Grodin JL, et al. Prognostic role of serum chloride levels in acute decompensated heart failure. *J Am Coll Cardiol* 2015;66:659-666.

The association between serum sodium level and outcomes in acute decompensated heart failure (ADHF) is well-established. Serum chloride levels are also routinely obtained with basic chemistry panels, but the clinical significance of hypochloremia in ADHF has not been studied.

Grodin and colleagues reviewed data from 1318 patients hospitalized at the Cleveland Clinic with a discharge diagnosis of ADHF. They examined the association between the admission serum chloride level and all-cause mortality, and compared the prognostic significance of serum chloride and sodium levels. The relationship between serum chloride, sodium, and mortality was also evaluated in a validation cohort of 876 patients admitted to the Hospital of the University of Pennsylvania for heart failure (HF). Patients in both cohorts had predominantly systolic HF.

In univariate analyses, each unit increase in chloride was associated with a 6% decrease in mortality (hazard ratio [HR] per unit increase, 0.94; 95% confidence interval [CI], 0.92-0.95; $P < 0.001$). Admission serum sodium level was also associated with mortality (HR per unit increase, 0.95; 95% CI, 0.93-0.97; $P < 0.001$). In multivariate analyses adjusted for other clinical variables, the chloride level remained predictive of mortality (HR per unit increase, 0.93; $P < 0.001$), whereas serum sodium level was no longer independently associated with mortality (HR per unit increase, 1.03; $P = 0.18$). Of note, mortality risk was strongly associated with changes in serum chloride levels < 96 mEq/L, but did not vary significantly at values > 96.

The findings were similar in the cohort from Pennsylvania; serum chloride remained predictive in multivariate models adjusted for other clinical predictors (HR, 0.95; $P = 0.01$), while serum sodium was not (HR, 0.99; $P = 0.58$). The authors conclude that serum chloride levels measured during hospitalization for ADHF are

independently and inversely associated with long-term mortality, independent of serum sodium levels.

■ COMMENTARY

The authors should be commended for challenging the long-held assumption that sodium is the key electrolyte in the pathophysiology of heart failure. Furthermore, in an era where the search for novel biomarkers often leads to increasingly complex and costly laboratory techniques, they chose to study a parameter that has been measured as part of standard care for decades. The pathophysiological role of chloride in heart failure is not well understood, mainly because it has not been studied in detail. Many of the same maladaptive responses that reduce serum sodium in HF also impact chloride levels. These include elevated levels of both arginine vasopressin and angiotensin II. Yet, these similarities alone cannot explain why chloride would be an even stronger prognostic marker than sodium. The authors suggest chloride plays a broader homeostatic role, serving as a buffer for cations and helping the kidney eliminate salt and water. This argument is further supported by the important role of chloride in a wide variety of other bodily functions, including maintenance of osmotic balance and muscle function. Regardless of the mechanism, the strong statistical association between chloride levels and mortality suggests further investigation may yield new insights that help shape our understanding of HF.

This study does have several limitations. The cohorts studied were obtained from two large, tertiary academic centers, and not necessarily representative of the broader ADHF population. The multivariate models did not include many well-known prognostic markers in HF, such as systolic blood pressure and natriuretic peptide levels. Furthermore, it must be emphasized that adding chloride levels to the multivariate predictive model had a very modest effect on the overall predictive ability. The C-statistic, a marker of discriminative ability, only increased from 0.68 to 0.69 with the addition of chloride level. The cohorts studied in this analysis were comprised of patients with primarily systolic HF, so we cannot conclude that chloride levels maintain their prognostic utility in those with preserved ejection fraction (unlike sodium, whose association with mortality has been proven in both preserved and reduced ejection fraction).

There is still a lot of work to be done on this topic. Future studies will need to validate the prognostic role of chloride in broader HF cohorts and elucidate the pathophysiological role of chloride in HF. Eventually, interventions that specifically target hypochloremia may improve the care of patients with ADHF, a condition for which we have yet to identify a therapy that meaningfully improves outcomes. Despite the limitations and further work needed, for now we have a new prognostic marker that is widely available and possibly more useful than serum sodium level for estimating prognosis in ADHF. ■

Oral Nutritional Supplementation for Hospitalized COPD Patients Pays Off

SOURCE: Snider JT, et al. Effect of hospital use of oral nutritional supplementation on length of stay, hospital cost, and 30-day readmissions among Medicare patients with COPD. *Chest* 2015;147:1477-1484.

In contrast to many of the other top 10 causes of death in the United States, chronic obstructive pulmonary disease (COPD) deaths are increasing, such that COPD is now the third most common cause of death. Although a variety of pharmacologic interventions are available to improve symptoms and decrease exacerbations, none has been shown to reduce mortality.

COPD is associated with increased risk for malnutrition, which may lead to further respiratory function compromise and immune dysfunction. Might nutritional supplementation of patients admitted for COPD improve outcomes?

Snider et al utilized the Premier Research Database, which contains hospitalization information from 460 U.S. hospitals and 46 million hospitalizations. The authors compared outcomes in persons > 65 years of age admitted for COPD (n = 378,419) who received oral nutritional supplementation (n = 10,322) vs those who did not. Outcomes of interest were length of hospital stay, hospitalization costs, and readmission rates.

Oral nutritional supplementation was announced with numerous favorable results: Length of stay was reduced by 21.5%, readmission rate was reduced by 7%, and even the cost of hospitalization was reduced by 12.5%. Overall, the results suggested that for every dollar spent on oral nutritional supplementation, the hospital saved $18.

It is clear oral nutritional supplementation has been employed in a small minority of COPD admissions (10,322 out of 378,419 admissions). These favorable results should prompt reconsideration of the value — health wise and economic — of oral nutritional supplementation in patients admitted for COPD. ■

CME INSTRUCTIONS

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CME QUESTIONS

1. In the study reported by Pollack et al., idarucizumab was shown to:

a. Improve survival in patients who needed surgery while on dabigatran

b. Improve survival in patients with serious acute bleeding while on dabigatran

c. Reverse the anticoagulant effect of dabigatran

d. Reverse the anticoagulant effect of rivaroxiban

e. All of the above

2. The PADIS-PE study by Couturaud and colleagues compared 6 months of anticoagulation to 24 months after an unprovoked pulmonary embolism. In that study, prolonged anticoagulation led to which of the following outcomes:

a. A statistically significant reduction in recurrent venous thromboembolism

b. A statistically significant increase in bleeding

c. A statistically significant reduction in mortality

d. A statistically significant reduction in strokes

e. All of the above

3. Which of the following cause for intracerebral hemorrhage and typical location of the ICH are correct?

a. Arteriolosclerosis – cortical/subcortical regions

b. Cerebral amyloid angiopathy - deep structures of the brain, such as the basal ganglia, thalami or brainstem

c. Cerebral amyloid angiopathy – cortical/subcortical regions

d. Arteriolosclerosis - deep structures of the brain, such as the basal ganglia, thalami or brainstem

e. C and D

CME OBJECTIVES

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

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and;
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems.

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