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INSIDE

Is Clot Burden on CT Angiogram Predictive of Mortality in Pulmonary Thromboembolism?

ABSTRACT & COMMENTARY

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Dr. Pierson reports no financial relationship relevant to this field of study.

This article originally appeared in the December 2008 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington. He reports no financial relationships relevant to this field of study.*

Synopsis: *A prospective study comparing angiographic clot burden score and ECG score in 105 patients with PE found no correlation between the two, and neither predictor correlated with 12-month mortality. In a second retrospective study of 33 consecutive patients with massive PE by conventional clinical criteria, there was also no correlation between findings on CT angiography and mortality.*

Sources: Subramaniam RM, et al. Pulmonary embolism outcome: A prospective evaluation of CT pulmonary angiographic clot burden score and ECG score. *AJR Am J Roentgenol*. 2008;190:1599-1604; Findik S, et al. Massive pulmonary emboli and CT pulmonary angiography. *Respiration* 2008;76:403-412.

WITH PULMONARY COMPUTED TOMOGRAPHIC (CT) ANGIOGRAPHY increasingly being used to diagnose acute pulmonary thromboembolism (PE), it has become commonplace to report not only the presence of clot when the study is positive, but also an estimate of the clot burden. In at least some institutions, the CT angiograms of patients with large quantities of visualized thrombus are read out as "massive PE." By examining the assumed relationship between the CT angiographic findings and clinical outcomes in patients with PE, two recent articles shed light on the clinical appropriateness of using such terminology.

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Subramaniam et al at Waikato Hospital in Hamilton, New Zealand, carried out a prospective study to examine the claimed predictive value of each of two published scoring schemes for patients with PE: the CT pulmonary angiographic burden score of Qanadli et al[1] and an electrocardiographic (ECG) score correlated to the extent of pulmonary perfusion impairment.[2] The CT score weighted different assessments of the site and degree of pulmonary arterial obstruction, the latter used to calculate the percentage of obstruction. The ECG score assigned varying weights to several measures related to right ventricular strain, such as right bundle branch block, precordial T wave inversion, and the S1Q3T3 pattern. Two CT angiographers independently determined the CT scores, and two clinicians independently determined the ECG score, for the 105 patients with positive CT angiograms of 523 consecutive patients who underwent evaluation. Correlations were sought between the two indices, and also with the patients' clinical outcomes, determined 12 months after diagnosis.

The mean (SD) clot burden score percentage was 23.7% (16.8%) and the mean (SD) ECG score was 2.4 (2.8) out of a possible 21. There was no significant correlation between the two indices at the time of diagnosis ($r = 0.09$; $p = 0.39$). At one year, 13 patients had died, and neither the CT clot burden score nor the ECG score correlated with whether they were alive or dead (all-cause mortality).

Findik et al at Ondokuz Mayis University, Samsun, Turkey, carried out a retrospective analysis of a different index of the extent of pulmonary arterial obstruction, along with clinical data and mortality, in 33 consecutive patients with massive PE. The latter was diagnosed by the presence of a systolic blood pressure < 90 mm Hg, syncope, and/or shock. All the patients had CT angiography and an assessment of right ventricular function. Hemodynamic severity was assessed by the extent of right ventricular dysfunction, the diameter of the main pulmonary artery, the shape of the interventricular septum, and the extent of obstruction to the pulmonary arterial circulation using a CT obstruction index.

All 33 patients had emboli in the central pulmonary arteries. All of them also had right ventricular dysfunction, which was judged to be severe in 94%. The shape of the interventricular septum was abnormal in all the patients, and the diameter of the main pulmonary artery was increased in 76% of them. The CT obstruction index was 50% or more in 85% of the patients. Twenty-eight (84%) of the patients survived, and Findik et al found no correlation between the CT angiographic findings and survival.

■ COMMENTARY

For decades, studies of the epidemiology and therapy of PE have used clinical criteria, not the estimated quantity of clot in the pulmonary arterial tree, to define "massive PE." The principal criteria are arterial hypotension and cardiogenic shock.[3] Arterial hypotension is defined as a systolic blood pressure < 90 mm Hg, or a drop in systolic arterial pressure of at least 40 mm Hg for at least 15 minutes. The definition of shock is less quantitative but includes evidence of tissue hypoperfusion and hypoxia, such as altered level of consciousness, oliguria, and/or cool, clammy extremities. Patients with massive PE defined in this way have an early mortality of at least 15%, with the degree and persistence of hemodynamic compromise generally the most powerful predictors of in-hospital death. Although PE is commonly encountered among hospitalized patients, in one multicenter study of 2454 patients admitted with this diagnosis, only 4.2% of them met criteria for massive PE.[4]

Although both the Subramaniam and Findik studies raise issues of patient selection and other design features (and the Findik study was grossly underpowered for differences in mortality), they both emphasize that massive PE is a clinical diagnosis and not determined by the angiographic extent of visualized thrombus. This is important because of the implications of this diagnosis for thrombolysis and other therapy. The new American College of Physicians Evidence-Based Clinical Practice Guidelines (8th edition) emphasize

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Questions & Comments

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the importance of clinical risk stratification, and recommend thrombolytic therapy in PE for patients with evidence of hemodynamic compromise.[5] The guidelines do not include the clot burden, as visualized by CT angiography, in either defining massive PE or in selecting appropriate therapy. ■

References

1. Qanadli SD, et al. New CT index to quantify arterial obstruction in pulmonary embolism: comparison with angiographic index and echocardiography. *AJR Am J Roentgenol*. 2001;176:1415-1420.
2. Iles S, et al. ECG score predicts those with the greatest percentage of perfusion defects due to acute pulmonary thromboembolic disease. *Chest*. 2004;125: 1651-1656.
3. Kucher N, Goldhaber SZ. Management of massive pulmonary embolism. *Circulation*. 2005;112:e28-e32.
4. Goldhaber SZ, et al. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet*. 1999;353:1386-1389.
5. Kearon C, et al. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133:454s-545s.

IV Valproic Acid vs Phenytoin: Old Standby or the New Challenger?

ABSTRACT & COMMENTARY

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

This article originally appeared in the December 2008 issue of Neurology Alert. *It was edited by Matthew Fink, MD, and peer reviewed by M. Flint Beal, MD. Dr. Fink is Vice Chairman, Professor of Neurology, Weill Cornell Medical College; Chief of Division of Stroke and Critical Care Neurology, NewYork-Presbyterian Hospital, and Dr. Beal is Professor and Chairman, Department of Neurology, Cornell University Medical College. Drs. Fink and Beal report no financial relationships relevant to this field of study.*

Synopsis: *Valproic acid and phenytoin were equally effective in the treatment of acute repetitive seizures and status epilepticus.*

Source: Gilad R, et al. Treatment of status epilepticus and acute repetitive seizures with i.v. valproic acid vs phenytoin. *Acta Neurol Scand*. 2008;118:296-300.

HISTORICALLY, BENZODIAZEPINES AND PHENYTOIN HAVE been used as first-line therapy in aborting status epilepticus (SE). The rationale for use of these two agents mainly rests on the 1998 results of the Veterans Affairs Cooperative Trial. The greatest response rate was seen in those patients who received benzodiazepines in addition to phenytoin (PHT), rather than PHT alone. Although the intravenous formulation of valproic acid (VPA) was officially approved by the FDA in 1996, the agent was not included in the Veterans Affairs Cooperative Trial and still has not received approval by the FDA for use in SE. Nevertheless, despite the lack of FDA approval, IV VPA continues to be used off-label by clinicians. Therefore, papers such as this one by Gilad et al are critical in defining the exact role of VPA in both acute repetitive seizures (ARS) and SE.

Seventy-four adult patients with either ARS or SE, older than age 18, were included in this open-label study. Patients with baseline abnormal liver function tests or previous toxic serum levels of VPA were excluded from the study. For this study, SE was defined as greater than 30 minutes of continuous seizure activity or two or more sequential seizures without clinical recovery. ARS was defined as two or more repetitive seizures with clinical recovery between seizures during a 5- to 6-hour period. The primary endpoint was cessation of clinical seizure activity within 20 minutes of either VPA or PHT infusion, without rescue medication intervention. The secondary endpoint was assessment of infusion tolerability over the subsequent 24 hours.

The IV VPA patient group received 30 mg/kg given over 20 minutes. The PHT patient group received an infusion of 18 mg/kg, also given over 20 minutes. Patients were treated randomly in the emergency room in a 2:1 ratio of either VPA or PHT infusion. If seizure control was not achieved by infusion of the first study drug, then patients were treated with the other study drug. Patients who failed both study drug infusions were then treated with IV midazolam at a dosage of 0.2 mg/kg and were subsequently transferred to the intensive care unit. Electroencephalography was performed in select cases of clinically suspected non-convulsive status where patients did not regain consciousness.

Forty-nine patients were treated with IV VPA and 25 patients were treated with PHT. Nearly two-thirds of patients in the study experienced breakthrough seizures secondary to subtherapeutic anti-epileptic drug levels or

non-compliance. Post-stroke epilepsy made up approximately 25% of patients. Twelve percent of both the IV VPA and IV PHT groups required rescue medication. No significant side effects were found in the VPA group. One patient in the PHT group (no prior cardiac history) experienced ventricular premature beats during the infusion, one experienced vertigo, and one was noted to develop hyponatremia.

■ **COMMENTARY**

In this study, IV VPA treatment was as efficacious as IV PHT treatment as first-line treatment for ARS and SE. Other studies also have documented the efficacy of IV VPA; however, lack of uniformity in loading doses of IV VPA and rate of infusion make any definite conclusions about VPA in acute treatment of seizures difficult. Although this particular study was prospective, the open-label nature of the study introduces potential bias. Also, more than two-thirds of the patients were acute repetitive patients, rather than patients in SE, potentially influencing an overall better outcome for either PHT or VPA infusion.

Despite the above design flaws, Gilad et al present some compelling evidence for the use of VPA. This study and others have shown good tolerability of IV VPA. In our center, IV VPA has been used as a second-line (in cases of phenytoin allergy) or third-line agent in the treatment of SE, before the use of phenobarbital, particularly in patients in whom intubation is not being considered. Multiple studies have shown good tolerability of IV VPA at a rate of 6 mg/kg/min.[1-6] Theoretically, with an infusion rate of 6 mg/kg/min and dosage of 25-30 mg/kg, in an average 70 kg individual, IV VPA can be administered in approximately 5 minutes. There are also particular instances where VPA would be the agent of choice in aborting status, such as absence of status epilepticus.

As awareness of SE grows, more prompt treatment of this neurologic emergency hopefully will result in less need to proceed to anesthetic agents. Valproic acid, with its relatively rapid onset of action and minimal side effects, may evolve into an attractive choice in the treatment of SE and ARS. ■

References

1. Ramsay RE, et al. Safety and tolerance of rapidly infused Depacon. A randomized trial in subjects with epilepsy. *Epilepsy Res*. 2003;52:189-201.
2. Sinha S, Naritoku DK. Intravenous valproate is well tolerated in unstable patients with status epilepticus. *Neurology*. 2000;55:722-724.
3. Venkataraman V, Wheless JW. Safety of rapid intravenous infusion of valproate loading in epilepsy patients. *Epilepsy Res*. 1999;35:147-153.
4. Wheless J, Venkataraman V. Safety of high intravenous valproate loading doses in epilepsy patients. *J Epilepsy*. 1998;11:319-324.
5. Naritoku DK, Mueed S. Intravenous loading of valproate for epilepsy. *Clin Neuropharmacol*. 1999;22: 102-106.
6. Wheless JW, et al. Rapid infusion with valproate sodium is well tolerated in patients with epilepsy. *Neurology*. 2004;63:1507-1508.

Quality Improvement Interventions and Surgical Antimicrobial Prophylaxis

ABSTRACT AND COMMENTARY

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This article originally appeared in the December 2008 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, and peer reviewed by Connie Price, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University; Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center, and Dr. Price is Assistant Professor, University of Colorado School of Medicine. Dr. Deresinski serves on the speaker's bureau for Merck, Pharmacia, GlaxoSmithKline, Pfizer, Bayer, and Wyeth, and does research for Merck, and Dr. Price reports no financial relationships relevant to this field of study.*

Synopsis: *Forty-four acute care hospitals participated in a prospective study over four years to determine the effect of quality improvement (QI) interventions on appropriate prescribing of surgical antimicrobial prophylaxis. Hospitals were randomly assigned to either feedback on the results of the ongoing audit vs feedback plus an intensive collaborative intervention group. Both groups showed improvement in most quality indicators, but there appeared to be no benefit of the intensive QI collaborative intervention over performance feedback.*

Source: Kritchevsky SB, et al. The effect of a quality improvement collaborative to improve antimicrobial prophylaxis in surgical patients: a randomized trial. *Ann Intern Med*. 2008;149:472-480, W89-W93.

In this study, 44 acute care hospitals each randomly sampled 100 surgical cases (cardiac, hip, or knee replacement, hysterectomy) at both baseline and during the remeasurement phase of the study. All hospitals received a comparative feedback report. Twenty-two hospitals were randomly assigned to the intervention group where each hospital held two in-person meetings led by experts, monthly teleconferences, and supplemental, educational materials were distributed. The quality parameter used as the primary outcome measure was the receipt of one dose of antibiotics within 60 minutes of surgery (120 minutes for vancomycin), with secondary outcomes of change in proportion of patients receiving any antibiotics, administration of antibiotics for 24 hours or less, administration of an appropriate antibiotic, and receipt of a single, preoperative dose plus any of the other five measures.

In the intervention group, 76.3% of patients received appropriately timed preoperative antibiotics at baseline, and 83.2% at remeasure. In the feedback-only group, the numbers were 74.8% at baseline and 85.3% at follow- up. Of those in the intervention group, the baseline and follow-up values for receipt of prophylaxis were 97.4% and 98.9%, respectively, with nearly identical values for the feedback-only group. Appropriate duration of antibiotics increased from 51.3% to 69.5% in the intervention group, with similar change seen in the feedback-only group. Appropriate antibiotic selection was high at baseline (93.8%) and did not change significantly in either the intervention or feedback groups. Interestingly, the proportion of patients who received a single, preoperative dose decreased slightly from 85.1% to 80.2% in the intervention group but did not change in the feedback-only group.

■ COMMENTARY

Antimicrobial prophylaxis in the setting of surgery represents a significant proportion of the use of antibiotics in the United States and contributes to the cost of care. Inappropriate administration of antimicrobial prophylaxis has been shown to result in reduced prophylactic efficacy, as well as excessive costs and potential selection of antibiotic-resistant organisms when prophylaxis is given for an excessive duration. While this study did not show any incremental benefit of intensive collaborative QI interventions, the good news is that it demonstrated that appropriately communicated feedback to prescribing providers did result in improvement of antimicrobial-prescribing practices in the surgical prophylaxis setting. It is likely that similarly conducted audits with communicated feedback also could be effective in improving antimicrobial prescribing for a variety of infections in both the inpatient and outpatient settings, where guidelines exist. ■

Bridging Anticoagulant Therapy for Mechanical Valve Patients

ABSTRACT & COMMENTARY

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Dr. Crawford is on the speaker's bureau for Pfizer.

This article originally appeared in the December 2008 issue of Clinical Cardiology Alert. *It was peer reviewed by Rakesh Mishra, MD. Dr. Mishra is Assistant Professor of Medicine; Weill Medical College, Cornell University; Assistant Attending Physician, NewYork-Presbyterian Hospital. Dr. Mishra reports no financial relationships relevant to this field of study.*

Source: Spyropoulos AC, et al. Perioperative bridging therapy with unfractionated heparin or low-molecular-weight heparin in patients with mechanical prosthetic heart valves on long-term oral anticoagulants (from the REGIMEN Registry). *Am J Cardiol*. 2008;102:883-889.

Unfractionated heparin (UFH) is the standard bridging therapy for patients with mechanical heart valves who need to temporarily stop oral anticoagulants. Small case series have suggested that low molecular weight heparin (LMWH) may be useful for this purpose. Accordingly, a multicentered registry of patients undergoing bridging therapy was interrogated to assess outcomes in those with mechanical valves put on UFH vs LMWH. Patients were involved in the trial if they needed bridging for elective surgical procedures. Adverse outcomes over 30 days after the procedure were noted. This was an observational study, and no set protocol for bridging was followed.

Results: Of the 1,077 patients requiring bridging, 245 were on oral anticoagulants for mechanical heart valves; UFH was used in 73 and LMWH in 172. The groups were fairly comparable, although there were more men and more bileaflet valves in the LMWH group. About one-quarter of both groups were also on antiplatelet drugs. About 40% of both groups had major surgery. Duration of bridging therapy was similar in both groups, but the LMWH patients were discharged earlier on average. There were no significant differences in adverse events between treatment groups, but the rate of major

bleeding was higher in the UFH group (8.8 vs 4.2%). Spyropoulos et al concluded that in patients with mechanical valves, bridging therapy with LMWH is feasible and safe and allows for earlier discharge.

■ COMMENTARY

Mechanical prosthetic valve patients are high-risk patients for anticoagulation cessation, as valve thrombosis may occur after 48 hours of subtherapeutic INR values. Therefore, they often undergo bridging therapy with heparin for surgical procedures. In this registry study of bridging therapy, 25% had mechanical valves. There has been interest in using LMWH because it can be given as an outpatient therapy and does not require blood test monitoring of anticoagulation levels. However, up until 2002, there was a black box warning in the package inserts of LMWHs not to use them with mechanical valves because of a lack of data suggesting their effectiveness in this situation. Several small studies have shown equivalent efficacy to UFH, so this warning has been modified, but lack of strong data has dampened enthusiasm for the use of LMWH for this purpose.

This registry study is the largest experience reported with LMWH for prosthetic valves. The study group was a high-risk one: 50% had mechanical mitral valves; two-thirds had hypertension; half had atrial fibrillation; and one-quarter had heart failure. Also, 40% had major surgery and one-quarter were also on antiplatelet drugs. The composite endpoint of major adverse events, including death, thromboembolism, and major bleeding favored LMWH (5.5 vs 10.3%), but the difference was not statistically significant. The thromboembolism risk on LMWH was < 1%. Importantly, about 70% of the patients treated with LMWH were either outpatient or were in the hospital < 24 hrs. Most of the patients received enoxaparin at full therapeutic doses twice a day.

One reason for the lower bleeding rates for LMWH was that patients undergoing surgery with a high risk of bleeding, such as cardiothoracic surgery, were more often put on UFH because it can be reversed more easily. Other limitations include the observational nature of the study without a randomized treatment protocol. Also, the power to detect some endpoints was limited because of a lack of events. For example, only one patient in each group experienced a thromboembolic event. However, this study confirms the results of smaller studies and supports the conclusion that LMWH for bridging patients on oral anticoagulants with mechanical valves who need surgery is safe and efficacious and may reduce costs by permitting earlier discharge from the hospital. ■

It's Time to Have the Talk

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

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Dr. Wilke reports no financial relationship to this field of study.

This article originally appeared in the November 29, 2008 issue of Internal Medicine Alert. *It was edited by Stephen Brunton, MD, and peer reviewed by Gerald Roberts, MD. Dr. Brunton is Clinical Professor, University of California, Irvine, and Dr. Roberts is Clinical Professor of Medicine, Albert Einstein College of Medicine. Dr. Brunton is a consultant for Sanofi-Aventis, Ortho-McNeil, McNeil, Abbott, Novo Nordisk, Eli Lilly, Endo, EXACT Sciences, and AstraZeneca, and serves on the speaker's bureau for McNeil, Sanofi-Aventis, and Ortho McNeil, and Dr. Roberts reports no financial relationships relevant to this field of study.*

Synopsis: *Terminally ill cancer patients who had end-of-life discussions with their physician had better quality of life during their last week, and their caregivers had an easier bereavement.*

Source: Wright AA, et al. Associations between end-of-life discussions, patient mental health, medical care near death, and caregiver bereavement adjustment. *JAMA*. 2008;300: 1665-1673.

ALTHOUGH THERE ARE MULTIPLE BENEFITS TO ADmission to hospice for a terminally ill patient and the patient's family, frequently, referral never happens or occurs too late. There are many real and perceived roadblocks to admission, including a paucity of hospice services, patients' overly optimistic self-prognoses, physicians' inadequate skills at prognostication and end-of-life (EOL) communications, and a concern that the necessary conversations leading to hospice referral might precipitate a major depressive episode.

This prospective, longitudinal, cohort study, conducted at seven outpatient cancer centers in five cities (four in New England and one in Texas), was designed to examine what really happens when physicians have EOL discussions with end-stage cancer patients. Subjects were recruited from September 2002 until February 2008. To be eligible, patients had to have distant metastases or cancer refractory to first-line chemotherapy, be at least 20 years old, and have an informal caregiver (ie, family or friend). Six hundred thirty-eight patient-caregiver dyads were

enrolled. Only the 332 patients who died were included in this study. Patients were, on average, 58-years-old at the time of enrollment. Most were married (60%), white (64%), male (55%), and had health insurance (57%). Breast, colorectal, pancreatic, and lung cancers comprised 58% of the diagnoses. Caregivers were, on average, 51-years-old and predominantly female (77%). Most were spouses (51%) or adult children (24%).

Psychosocial factors and functional status were determined. The use of aggressive treatment (eg, admission to an intensive care unit [ICU], ventilation, resuscitation, chemotherapy, feeding tubes) was documented by chart review. Patients and caregivers were interviewed. Patients were asked, "Have you and your doctor discussed any particular wishes you have about the care you want to receive if you are dying?" Shortly after death, caregivers were asked, "In your opinion, how would you rate the overall quality of the patient's death/last week of life?" A median of 6.5 months after death, the caregivers were interviewed about their psychological adjustment.

Patients died a median of 4.4 months after enrollment. Most (63%) could not remember having an EOL discussion with their physician. There was a wide disparity between sites of care in this regard, ranging from 62% to 16%. There were no associations between EOL discussions and patients' demographic characteristics, whether they had insurance, what kind of cancer they had, how close they felt to their physician, whether they were religious, or whether they had social support. Positive associations were found for lower performance status, higher symptom burden, and shorter survival times. There was no association of EOL discussions with a patient feeling depressed or developing any DMS4 diagnosis. Patients who had an EOL discussion with their physician were more likely to accept that their illness was terminal, prefer palliative over curative care, and have completed "Do Not Resuscitate" declarations. They received less aggressive treatment and were more likely to have been in hospice for more than a week. Caregivers rated the quality of life (QOL) of their loved ones' last week of life as significantly worse if they received aggressive care. They reported feeling less prepared for the patient's death, and were more likely to develop a major depressive disorder, to feel regret over their loved one's death, and have worse QOL and self-reported health following their loved one's death.

■ COMMENTARY

This was not a randomized study, so no causal relationships can be inferred. On the other hand, the size of the study lends weight to its conclusions. Although the patients were recruited from cancer centers, there is no reason to believe that they differ from your patients who have advanced cancer. How similar are you to their doctors? Intuitively, oncologists should be more skilled at EOL discussions simply by dint of practice, but primary care physicians may have an edge by virtue of long association. We can only hope that these patients suffered dementia or were overly medicated to explain the dismal rate of EOL conversations.

Physicians are programmed to "do something" when presented with a patient in need. What can we do to help our terminally ill patients? We can employ a wider range of palliative options. Kutner et al showed that for advanced cancer patients, massage therapy can have an immediate beneficial effect on pain and mood.[1] We can be better stewards of limited resources. In the current study, admission to an ICU was one of the factors associated with no EOL discussion. Rady and Johnson looked at this in 2004 from the perspective of informed consent.[2] In this study, none of the patients transferred to the ICU, all of whom died there, had an EOL or palliative care discussion. Not only was this a violation of patient autonomy, it was outrageously expensive ($33,252 for those who were transferred vs $8,549 for those who weren't). We can learn to be better communicators. Even when presented with opportunities to connect with terminally ill patients, we don't take advantage of them.[3] We can help the caregivers. Caregivers who report greater religiousness have lower rates of depression at follow-up,[4] suggesting collaboration with religious support groups. We can begin our discussions about hospice much earlier, even as we attempt treatment. On average, patients in the current study died after four months. Admission to hospice when the patient is near death (ie, death within three days) is associated with major depressive disorders in caregivers.[5] We can do more; our patients deserve it. ■

References

1. Kutner JS, et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. *Ann Intern Med*. 2008;149:369-379.
2. Rady MY, Johnson DJ. Admission to intensive care unit at the end-of-life: is it an informed decision? *Palliat Med*. 2004;18:705-711.
3. Morse DS, et al. Missed opportunities for interval empathy in lung cancer communication. *Arch Intern Med*. 2008;168:1853-1858.
4. Fenix JB, et al. Religiousness and major depression among bereaved family caregivers: a 13-month follow-up study. *J Palliat Care*. 2006;22:286-292.

5. Bradley EH, et al. Depression among surviving caregivers: does length of hospice enrollment matter? *Am J Psychiatry*. 2004;161:2257-2262.

CME Questions

1. **Based on the two recent studies of CT angiographic clot burden and outcomes from pulmonary embolism, the amount of clot burden correlated with which of the following?**
   a. All-cause mortality.
   b. ECG abnormalities.
   c. Both all-cause mortality and ECG findings.
   d. Neither all-cause mortality nor ECG findings.

2. **The study by Spyropoulos et al, comparing the use of low-molecular weight heparin (LMWH) to unfractionated heparin (UFH) as perioperative bridging therapy for patients with mechanical valves on oral anticoagulants, revealed that:**
   a. LMWH was associated with significantly more episodes of bleeding.
   b. LMWH and UFH were not statistically different in preventing major adverse events.
   c. UFH was superior to LMWH in preventing perioperative thromboembolism.
   d. patients receiving bridging therapy with UFH had shorter hospital lengths of stay.

3. **In the report by Wright et al, end-of-life care discussions in terminally ill patients were associated with:**
   a. a greater number of depressive episodes in the caregivers.
   b. prolonged ICU lengths of stay.
   c. a greater likelihood that the patient accepted that their illness was terminal.
   d. a greater likelihood of the patient subsequently feeling depressed or abandoned.

Answers: 29. (d); 30. (b); 31. (c)

CME Objectives

The objectives of *Hospital Medicine Alert* are to:

• review pertinent safety, infection control, and quality improvement practices;

• discuss diagnosis and treatment of acute illness in the hospital setting; and

• review current data on diagnostic and therapeutic modalities for common inpatient problems. ■