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INSIDE

Growth of Intensive Care Unit Use and Costs

ABSTRACT & COMMENTARY

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

This article originally appeared in the January 2009 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor, Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, and Dr. Thompson is Staff Pulmonologist, VA Medical Center; Associate Professor of Medicine, University of Washington. Drs. Pierson and Thompson both report no financial relationships relevant to this field of study.*

Synopsis: *Through a retrospective analysis, this study examined ICU resource use and costs for 121,747,260 inpatient hospitalizations, and found a rapid rise in Medicare ICU use with stable adjusted daily critical care costs, but increasing costs for care outside the ICU.*

Source: Milbrandt EB, et al. Growth of intensive care unit resource use and its estimated cost of Medicare. *Crit Care Med* 2008;36:2504-2510.

Tracking the utilization of intensive care unit (ICU) resources is important in informing clinicians of patterns of use and costs of care, especially as the proportion of patients aged 65 and older increases and ICU resources remain limited. Milbrandt et al examined resource use and costs for the ICU and floor costs for inpatient Medicare prospective payment system hospitalizations during a 10-year period from 1994 to 2004. The findings of their retrospective review demonstrated that 33% of Medicare hospitalizations involved an ICU stay. Annual adjusted Medicare ICU costs increased 36% due to increased utilization. While adjusted ICU cost per day remained stable ($2,616 vs $2,575; 1994 vs 2004). adjusted floor cost per day rose due to decreased floor length of stay ($1,027 vs $1,488).

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COMMENTARY

Similar to other studies assessing ICU utilization,[1-3] the results of this study highlight that ICU use is on the rise, and leading to large increases in annual ICU costs for Medicare. While the daily cost of ICU care remained relatively stable, average-adjusted cost per floor day rose substantially due to reductions in floor length-of-stay, with the remaining days becoming more costly.

This study demonstrated that efforts to reduce length of stay do not seem to have an appreciable effect in the ICU. Milbrandt et al cite that interventions to decrease ICU length-of-stay, such as the use of sedation and analgesia protocols, ventilator weaning, and intensivist staffing, have the potential to reduce costs if widely applied in the ICU setting. ICU clinicians should be cognizant of the importance of targeted interventions aimed at improving care in the ICU with the goal of decreasing unnecessary ICU length of stay. Efforts to promote best care in the ICU, including the use of a daily goal sheet,[4] infection prevention measures, palliative care, and family care conferences[5] to discuss realistic treatment goals for critically ill patients, may help in decreasing ICU length of stay as well as ICU costs of care. ■

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Thrombophilia and Recurrent DVT

ABSTRACT & COMMENTARY

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

This article originally appeared in the January 2009 issue of Clinical Oncology Alert. *It was edited by William B. Ershler, MD, and peer reviewed by VR Veerapalli, MD. Dr. Ershler, of INOVA Fairfax Hospital Cancer Center, Fairfax, VA, is Director, Institute for Advanced Studies in Aging, Washington, DC, and Dr. Veerapalli is Staff Clinician, INOVA Fairfax Cancer Center. Dr. Ershler is on the speaker's bureau for Wyeth, and does research for Ortho Biotech, and Dr. Veerapalli reports no financial relationships relevant to this field of study.*

Synopsis: *The risk of recurrent venous thromboembolism (VTE) during extended anticoagulant therapy for thrombophilia remains poorly defined. Investigators analyzed 661 patients with idiopathic VTE who had been randomized to extended prophylaxis after three months of initial anticoagulation using either low-intensity (INR 1.5-1.9) or standard-intensity (INR 2.0-3.0) anticoagulation. Thrombophilic defects were identified in 42% of patients. The rate of recurrent VTE of only 0.9% per patient year was not influenced by thrombophilic abnormalities. Antiphospholipid antibodies trended toward increased recurrence (HR, 2.9; 95% CI: 0.9-10.5). The presence of thrombophilic defects did not increase the risk of recurrent VTE during extended anticoagulation relative to patients with idiopathic VTE without thrombophilic defects.*

Source: Kearon C, et al. Influence of thrombophilia on risk of recurrent venous thromboembolism while on warfarin: results from a randomized trial. *Blood*. 2008;112:4432-4436.

AN ACQUIRED, OR HEREDITARY, THROMBOPHILIC ABnormality will be identified in around 30%-60% of unprovoked (aka, idiopathic) venous thromboembolism

(VTE) cases. A variety of thrombophilic defects have been described, such as factor V Leiden, the prothrombin gene mutation, anticardiolipin antibodies, elevated factor VIII and homocysteine, as well as deficiencies of antithrombin, protein C, and protein S. Although VTE recurrence is considerable after stopping anticoagulation, thrombophilic defects do not appear to increase the risk of VTE recurrence relative to patients without such a thrombophilia.[1] Limited data have been published on whether thrombophilia influences the risk of recurrent VTE while on anticoagulation therapy.

Kearon et al evaluated extended-duration anticoagulation following three months of anticoagulation for unprovoked VTE, comparing low-intensity warfarin (INR 1.5-1.9) to standard-intensity (INR 2.0-3.0) in the ELATE trial.[2] The data demonstrated that low-intensity extended prophylaxis was less effective in preventing recurrent VTE relative to standard-intensity treatment. The author examined this dataset for the impact of thrombophilic defects on VTE recurrence risk while on anticoagulation. Thrombophilic risk factors assessed included factor V Leiden, prothrombin gene variant 20210 G > A, anti-thrombin deficiency, lupus anticoagulant, anticardiolipin antibody, elevated homocysteine, elevated factor VIII above the 90th percentile, or elevated factor XI above the 90th percentile. In the ELATE trial, 739 patients were enrolled. Only 661 were included in the present retrospective analysis. Some patients had known anticardiolipin antibodies before screening and were excluded (2.1% of total), and some refused to participate. Thrombophilic defects included factor V Leiden in 26.5%, the prothrombin gene mutation in 9.3%, an antiphospholipid antibody in 8.2%, and antithrombin deficiency in 3.6%. Ten percent of patients had elevated factor VIII, factor XI, and homocysteine. Proteins C and S were not assessed, as patients were on warfarin. In summary, 42% had no abnormality, 41% had one abnormality, 14% had two abnormalities, and 2% had three abnormalities. The mean follow-up was 2.3 years, with a mean rate of 0.9% per year risk of recurrent DVT on warfarin. The recurrence risk was considerably higher at 1.5% in the low-intensity arm relative to 0.4% in the standard-intensity arm.

Comparing patients with one of the seven identified thrombophilic defects to those without, showed no increased risk of recurrence (HR, 0.7; 95% CI, 0.3-2.0). Individual defects did not confer an increased risk, although among 54 patients with anti-phospholipid antibody, three events occurred that translated into a 2.3% annual recurrence risk (HR of 2.9, 95% CI: 0.8 to 10.5).

■ COMMENTARY

The duration of anticoagulation is one of the major management challenges of venous thromboembolism (VTE). In unprovoked VTE, the authors previously confirmed that extended prophylaxis, after three months of anticoagulation using low-intensity anticoagulation (INR 1.5-1.9), increases the risk of VTE recurrence relative to standard-intensity anticoagulation (INR 2.0-3.0). For unprovoked VTE, a search for thrombophilic defects will uncover an acquired or inherited defect in a considerable portion. VTE recurrence risk, after discontinuation of anticoagulation, appears similar to those with an identified thrombophilic defect compared to those without.

In this report, Kearon et al, using the ELATE clinical trial database, found that among patients with thrombophilic defects of factor V Leiden, prothrombin gene mutation, elevated homocysteine, factor VIII and XI, or antithrombin deficiency, VTE recurrence appeared similarly low relative to those without such an identified defect. Further, harboring two or more defects did not increase VTE risk. Although the numbers were quite small (ie, three events), patients with antiphospholipid antibody showed a non-significant trend toward increased recurrence on extended prophylaxis. Of note, patients with known antibodies prior to screening for the study were excluded.

This analysis has important limitations. First, not all thrombophilic defects were assayed, such as deficiencies of proteins C and S. Second, some of the defects are relatively mild thrombophilic risk factors, such as factors XIII and XI. Most importantly, the number of recurrent VTE events was relatively small. While the relative risks appeared similar in patients receiving standard- and low-intensity anticoagulation, most events occurred in the low-intensity prophylaxis cohort. As Kearon et al point out, the recurrence risk was only 0.4% per patient year using standard-intensity anticoagulation. Thus, we must be cautious about inferences regarding recurrence risk, as standard-intensity prophylaxis is the norm in clinical practice. Similarly, there are inadequate numbers of patients having two defects for factor V Leiden (homozygosity) to draw conclusions.

These results must also be interpreted in the context of the study. Thrombophilic defects did not increase recurrence risk compared to patients with unprovoked DVT. One can assume most patients with unprovoked VTE have a thrombophilic defect, whether identified or occult.

The findings of this study provide confidence of a low

DVT recurrence risk using extended standard-intensity warfarin prophylaxis, even among subjects with a thrombophilic defect. The results are consistent with prior data showing a low recurrence rate using anticoagulation for secondary prophylaxis among patients harboring a factor V Leiden mutation[3] or uncommon thrombophilic defects.[4] The presence of an antiphospholipid antibody could heighten recurrence risk of VTE, but the data are inadequate to recommend a different prophylactic strategy (eg, INR of 2.5-3.5). ■

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Is It Time to Jump off the Intensive Insulin Therapy Bandwagon?

ABSTRACT & COMMENTARY

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

This article appeared in the January 2009 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD.*

Synopsis: *This single-center, randomized controlled trial demonstrated that intensive insulin therapy targeting blood glucose values of 80-110 mg/dL does not improve mortality, but does increase the incidence of hypoglycemia in a group of critically ill medical and surgical patients.*

Source: Arabi YM, et al. Intensive versus conventional insulin therapy: A randomized controlled trial in medical and surgical critically ill patients. *Crit Care Med*. 2008;36:3190-3197.

ALTHOUGH THE ORIGINAL STUDY BY VAN DEN Berghe et al sparked interest in the use of intensive insulin therapy in the ICU,[1] subsequent studies have cast doubt on the efficacy and safety of this practice.[2] Arabi et al sought to further clarify these issues by comparing the use of intensive (IIT) and conventional (CIT) insulin protocols in a combined medical-surgical intensive care unit (ICU) patient population.

The authors conducted a randomized, controlled trial in a combined medical-surgical-trauma ICU at a single institution. They included all ICU patients > 18 years of age with a serum glucose > 110 mg/dL within the first 24 hours of admission, and excluded all patients with Type I diabetes mellitus, diabetic ketoacidosis, documented hypoglycemia on the current admission, or a variety of other criteria. All included patients were started on an insulin drip (250 units Humulin® R insulin in 250 mL of 0.9% normal saline) and were then randomized to have blood glucose values maintained between either 80-110 mg/dL or 180-200 mg/dL. There was no blinding of the treatment assignment. Blood glucose values were initially monitored every hour, with adjustments in the frequency of monitoring based upon whether the patient had low or stable glucose values. The primary outcome variable was ICU mortality and secondary endpoints included hospital mortality, ICU and hospital length of stay, duration of mechanical ventilation, number of hypoglycemic events, the need for renal replacement therapy, and the incidence of ICU-acquired infections. These outcome variables were compared using t-tests, chi-square tests, and proportional tests and the analysis was based on the intention-to-treat principle.

A total of 523 patients were enrolled in the study, 266 in the IIT group and 257 in the CT group. The groups were well-matched, except the IIT group was younger and had less diabetes and lower inclusion blood glucose values. The average daily insulin dose was 71.2 ± 50.2 units in the IIT group and 31.4 ± 42.4 units in the CIT group. The average glucose level was 115 ± 18 mg/dL in the IIT group and 171 ± 34.2 mg/dL in the CIT group. There were no differences in mortality between the IIT and CIT groups (13.5% vs 17.1%; $p = 0.30$), but IIT was associated with a higher incidence of hypoglycemia (defined as blood

glucose < 40 mg/dL), with 28.6% of the IIT patients experiencing at least one episode of hypoglycemia compared to only 3.1% in the CIT group. Patients who had hypoglycemia had higher ICU mortality than those who did not (23.8% vs 13.7%); in sub-group analysis, IIT was associated with decreased mortality in patients with BMI < 26.2 kg/m^2 or APACHE II < 22 and increased ICU mortality in patients with GCS < 9. There were no differences between IIT and CIT in any of the other secondary endpoints.

■ COMMENTARY

Even though it was a single-center trial involving only surgical patients, the study by van den Berghe et al provoked a sea change in ICU practice, marked by the widespread adoption of intensive insulin therapy protocols in both medical and surgical ICU patients.[1] This bandwagon effect was similar to that seen after single trials showed possible benefits from recombinant activated protein C and corticosteroid therapy in patients with septic shock. The data from Arabi et al, along with a growing literature on the topic, suggest it may be time to jump off the IIT bandwagon and reevaluate our current practices. Granted, the current study was a non-blinded trial at a single institution with only 21 ICU beds, but the results are in line with those of other recent trials demonstrating that intensive insulin therapy with tight glucose targets is associated with an increased incidence of hypoglycemia and/or no clear mortality benefit.[2,3] Whether these protocols should be abandoned altogether is not clear from these studies, but the increased incidence of hypoglycemia, which is being increasingly documented in these and other trials, suggests that we should at a minimum move away from protocols with strict glucose targets of 80-110 mg/dL and instead accept more modest goals of glucose values in the mid-100 mg/dL range and focus on avoiding severe hyperglycemia. ■

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Pulmonary Vein Isolation vs AV Node Ablation Plus Pacing

ABSTRACT & COMMENTARY

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Dr. DiMarco is a consultant for Novartis, and does research for Medtronic and Guidant.

This article originally appeared in the January 2009 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Rakesh Mishra, MD. Dr. Crawford is Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco, and Dr. Mishra is Assistant Professor of Medicine, Weill Medical College, Cornell University. Dr. Crawford serves on the speaker's bureau for Pfizer, and Dr. Mishra reports no financial relationships relevant to this field of study.*

Source: Khan MN, et al. Pulmonary-vein isolation for atrial fibrillation in patients with heart failure. *N Engl J Med*. 2008;359:1778-1785.

KHAN ET AL REPORT A MULTICENTER TRIAL COMPARing pulmonary vein isolation vs AV junctional ablation with biventricular pacing in patients with atrial fibrillation and heart failure. Patients were eligible for the study if they had an ejection fraction of less than 40%, were on appropriate medical therapy, could complete a six-minute walk test, and had class II or III New York Heart Association congestive heart failure. Patients were randomized to either a rhythm control strategy involving pulmonary vein isolation with additional antiarrhythmic therapy, if required, vs AV junctional ablation and biventricular pacing. Pulmonary vein isolation was performed using standard techniques. Additional ablation lesions in the left and right atrium were permitted at Khan et al's discretion. Repeat procedures were permitted if there were recurrent arrhythmias. The primary endpoint of the study was a composite of changes in the ejection fraction, the distance on a six-minute walk test, and the Minnesota Living with Heart Failure score at six months.

Over a 36-month period, 177 patients were screened in 11 centers. Eighty-one patients eventually were randomized. Forty-one were assigned to the pulmonary vein isolation group and 40 were assigned to the AV node ablation with biventricular pacing group. Most patients in both groups had previously received amiodarone in an effort to control

their atrial fibrillation. The mean age was 60 ± 8 years, and more than 90% of the entire group was male. Approximately half of the patients had paroxysmal atrial fibrillation; the other half had either persistent or long-standing atrial fibrillation. The heart rate at rest was 81 bpm and the baseline QRS duration was 91 m/sec.

Among the 41 patients in the pulmonary vein isolation group, eight patients required repeat ablation procedures for either recurrent atrial fibrillation or atrial flutter. At six months, 71% of these patients were free from atrial fibrillation and off antiarrhythmic medications. An additional 17% were free of atrial fibrillation while taking an antiarrhythmic drug. Atrial fibrillation continued in the AV junctional ablation and biventricular pacing group, and 30% of the patients converted from a paroxysmal pattern to a persistent pattern. In contrast, recurrent atrial fibrillation in the pulmonary vein isolation group was always paroxysmal in nature. At six months, the ejection fraction had improved from 27 ± 8% to 35 ± 9% in the pulmonary vein isolation group. In the AV junctional ablation group, the ejection fraction was 29 ± 7% at baseline and 28 ± 6% after six months. The pulmonary vein isolation group showed a small change in left atrial diameter (from 4.9 ± 0.5 cm to 4.5 ± 0.4 cm), whereas there was a slight increase in left atrial diameter in the biventricular pacing group. The six-minute walk test distance improved from 269 ± 54 m at baseline to 340 ± 49 m at six months in the pulmonary vein isolation group. A smaller increase was noted in the AV junctional ablation group (281 ± 44 m to 297 ± 36 m). Quality of life also improved more in the pulmonary vein isolation group.

Occasional procedural complications were noted in both groups. In the pulmonary vein isolation group, three patients had groin bleeding, one had a pericardial effusion, and another developed pulmonary edema. Asymptomatic pulmonary vein stenosis was noted in two patients. In the AV junctional ablation with biventricular pacing group, two patients had left ventricular lead dislodgements, two had high left ventricular pacing thresholds, two had pocket hematomas, and one had a pneumothorax.

Khan et al conclude that in patients with atrial fibrillation and congestive heart failure, a strategy involving pulmonary vein isolation is superior to AV junctional ablation and pacing. Patients undergoing pulmonary vein isolation had greater improvements in left ventricular function, functional status, and quality of life.

■ COMMENTARY

This paper shows that an intervention that can successfully restore and maintain sinus rhythm in a high proportion of patients can benefit patients with atrial fibrillation and congestive heart failure. However, before we start recommending this approach in all patients with heart failure, we should recognize some limitations to the study.

This was a multicenter study in which patients were recruited at 11 centers with great experience in atrial fibrillation ablation. Despite this, only 81 patients could be recruited over a 3.5-year period. This may have been because patients were reluctant to undergo an irreversible procedure like AV junctional ablation and biventricular pacing; certainly the patients in the trial represent a very select group of patients. The endpoints in the study were changes in ejection fraction, functional status, and quality-of-life score. There were no deaths in either group. Other relevant endpoints, including hospitalization, are not reported. In fact, it might be anticipated that the need for hospitalization would have been higher in the pulmonary vein isolation group because of recurrent atrial fibrillation recurrences in some of the patients. Further studies will be necessary to see if hospitalizations and economic cost would be decreased by more widespread use of ablation procedures. From the data, it is also hard to know whether the patients had effective rate control while in atrial fibrillation. We are only provided data on the resting heart rate, and the data apparently combine values for both patients in sinus rhythm and those in atrial fibrillation. If a patient has controlled resting and exercise ventricular rates during persistent atrial fibrillation and has a normal QRS duration at baseline, why should we expect them to improve with AV junctional ablation and biventricular pacing? The theoretical benefits produced by regularization of the ventricular rate might well be overcome by substituting pacing, even biventricular pacing, for normal ventricular activation. Finally, the group was relatively young, with a mean age of only 60, and almost all the patients were male. Whether the pulmonary vein isolation approach would be as successful in older patients and women remains to be established. ■

Improving Palliative Care in the ICU

ABSTRACT & COMMENTARY

By Ruth Kleinpell, PhD, RN

This article appeared in the January 2009 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD.*

Synopsis: *A quality improvement intervention aimed at improving palliative care in the ICU resulted in improvements of nurse-assessed quality of dying and a reduction in ICU length of stay, but no changes in family perceptions of quality of dying or satisfaction with care.*

Source: Curtis JR, et al. Integrating palliative and critical care: Evaluation of a quality-improvement intervention. *Am J Respir Crit Care Med* 2008;178:269-275.

THIS STUDY REPORTS ON THE RESULTS OF A SINGLE-hospital study of a quality improvement intervention to improve palliative care in the ICU. An interdisciplinary intervention designed to improve the ability of ICU clinicians to provide palliative care focused on providing clinician education through the use of a teaching video, poster boards, and pamphlets; training of ICU champions on palliative care concepts in a half- or full-day training session; and the use of family satisfaction data to provide feedback to the ICU team. The intervention occurred over a 10-month period. Family members of patients who died in the ICU after a minimum stay of six hours before death or within 24 hours of transfer to another hospital location from the ICU were surveyed 4-6 weeks after the patient's death. ICU nurses who cared for the patients were surveyed within 48 hours of the patient's death. Responses from 275 family members revealed no significant improvement in family-assessed quality of dying or satisfaction with care, but responses from 523 nurses demonstrated significant improvements in nurse-assessed quality of dying and a reduction in ICU length of stay through the integration of palliative care in the ICU.

■ COMMENTARY

Palliative care focuses on symptom management, promoting treatment based on patient and family preferences, and facilitating care for patients with life-threatening illness and their families with a focus on comfort and quality of life.[1] Palliative care is increasingly being integrated into the care of patients in the ICU. There is growing recognition that integrating palliative care in the ICU is beneficial for patients with complex symptom management issues or with end-of-life care, as well as for their family members.

A number of national initiatives have focused on improving palliative care in the ICU, including the Center to Advance Palliative Care (www.capc.org/palliative-care-across-the-continuum/intensive-care-unit), the Robert Wood Johnson Foundation program for promoting palliative care excellence in the ICU (www.promotingexcellence.org), and the American College of Critical Care Medicine,[2] among others.

Interventions and strategies for improving palliative care in the ICU have specifically focused on improving communication, promoting family involvement, utilizing interdisciplinary team rounds, creating a supportive ICU culture for end-of-life care, and integrating palliative care consultations in the ICU.[2-4]

The results of this study show that focused efforts to integrate palliative care through the use of an interdisciplinary intervention designed to improve ICU clinicians' ability to provide palliative and end-of-life care in the ICU were beneficial in decreasing length of stay and in quality of dying ratings by nurses. This study contributes to the body of literature on integrating palliative care in the ICU and indicates that additional focus on providing direct interventions to family members may be needed to improve family perceptions of quality of care. The study did not demonstrate improvements in family perceptions of the quality of dying or in family satisfaction ratings, and it is evident that additional research is indicated to further explore the impact of interventions addressing palliative care on family members. ■

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CME Questions

32. Annual adjusted Medicare ICU costs were found to increase due to which of the following factors?

a. Increased utilization
b. Increased ICU length of stay
c. Increased ICU costs of care
d. Increased use of invasive ICU treatments
e. Increased ICU resource use

33. Thrombophilic defects, such as factor V Leiden, showed what impact on venous thromboembolism (VTE) recurrence while on extended warfarin prophylaxis for unprovoked VTE?

a. VTE recurrence was dramatically increased for patients with a thrombophilic defect compared to those without.
b. The risk of bleeding using extended duration anticoagulation was prohibitive and thus should not be used.
c. VTE recurrence for patients with a thrombophilic defect was not increased compared to those without.
d. Antiphospholipid antibodies interfered with monitoring the INR on warfarin.

34. In the study by Arabi et al on intensive insulin therapy (IIT) in the a combined medical-surgical ICU, what percentage of patients in the IIT group experienced an episode of hypoglycemia (blood glucose < 40 mg/dL)?

a. 3%
b. 10%
c. 28%
d. 45%

35. In patients with systolic heart failure and atrial fibrillation, which strategy appears superior?

a. AV node ablation and bi-ventricular pacing
b. Antiarrhythmic drugs
c. Pulmonary vein isolation and antiarrhythmic drugs as necessary
d. None of the above

Answers: 32. (a); 33. (c); 34. (c); 35. (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. ■