Update in Hospital Medicine

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This Update in Hospital Medicine summarizes 11 of the most important papers from 2004 for physicians with active inpatient practices. The articles were identified through a MEDLINE search and through a detailed review of 15 major medical journals. We polled local and national experts to determine which issues should be given priority and selected articles on the basis of their ability to confirm or change the hospitalist's clinical practice. This sample represents a diversity of study types and topics from the major subspecialties in medicine as they apply to the practicing hospitalist.

Hospitalist Comanagement

Hospitalist–Orthopedic Comanagement Reduced Minor Complication Rates without Increasing Length of Stay or Cost

Huddleston JM, Long KH, Naessens JM, et al. Medical and surgical comanagement after elective hip and knee arthroplasty: a randomized, controlled trial. Ann Intern Med. 2004;141:28-38. [PMID: 15238368]

This randomized, controlled trial assessed the effect of hospitalist comanagement on postoperative complications and length of stay. Secondary outcomes were inpatient costs and patient, nurse, and physician satisfaction. The investigators enrolled 526 patients who were undergoing elective orthopedic surgery and who were at increased risk for postoperative medical complications. Patients were randomly assigned to receive comanaged care from a medical hospitalist–orthopedic team or standard postoperative care from orthopedic surgeons with medical consultation. Management protocols, including laboratory studies, β-blocker therapy, prophylaxis for deep venous thrombosis, nursing care, and physical therapy, were similar for all patients in both groups.

Under the team approach, hospitalists had primary responsibility for patient management. They examined the patient before anesthesia was administered, coordinated all perioperative medical care and subspecialty consultations, and managed all issues related to the patient's discharge from the hospital. In the standard postoperative care group, these aspects of care were managed by the anesthesiologist, surgeon, or primary care physician as appropriate.

Patients assigned to receive hospitalist comanagement had fewer minor complications (such as fever, electrolyte imbalances, and urinary tract infections) than patients in the standard postoperative care group (30.2% vs. 44.3%; difference, −14.1 percentage points [95% CI, −22.7 to −5.3 percentage points]). The frequency of intermediate complications (such as congestive heart failure, pulmonary embolism, ileus, and pneumonia) and major complications (such as myocardial infarction [MI], renal or respiratory failure, and death) was similar for both groups. There was no statistically significant difference in length of stay, total cost, and patient satisfaction. After adjustment for delayed patient discharges caused by difficulties in gaining admission to nursing homes, the mean length of stay for patients in the hospitalist model was shorter than the standard model (5.1 days vs. 5.6 days; difference, −0.5 day [CI, −0.8 to −0.1 day]). Surgeons and nurses preferred the hospitalist model.

In conclusion, hospitalist comanagement was associated with fewer minor medical complications and significantly higher satisfaction among surgeons and nurses. The study was limited by possible bias that may have been introduced because the care providers and the patients were aware of the intervention assignments. Another limitation was that both groups used the same strictly regimented postoperative protocol. In settings lacking such regimentation, the effects might be different and possibly enhanced.

Atrial Fibrillation

"Pill-in-the-Pocket" Treatment Is Feasible and Safe in Selected Patients with Recurrent Atrial Fibrillation

Alboni P, Botto GL, Baldi N, et al. Outpatient treatment of recent-onset atrial fibrillation with the "pill-in-the-pocket" approach. N Engl J Med. 2004;351:2384-91. [PMID: 15575054]

This "pill-in-the pocket" trial investigated the efficacy of self-administration of 1 dose of flecainide or propafenone to restore sinus rhythm in otherwise healthy patients with no structural heart disease who experienced intermittent episodes of lone atrial fibrillation. This nonrandomized study compared the effect of each drug with historical controls.

The investigators enrolled 268 patients who presented to the emergency department or cardiology ward with atrial fibrillation that had begun within the past 48 hours. To be eligible for the study, patients were required to have normal systolic blood pressure, no symptoms of heart failure or syncope, and at least 1 but no more than 12 previ-

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ous episodes of atrial fibrillation. The patients received oral flecainide (200 to 300 mg) or propafenone (450 to 600 mg) to restore sinus rhythm; researchers at each site used the drug with which they were more familiar. A total of 58 patients (22%) withdrew from the study because of side effects or because they did not respond to the medication dose that was offered in the study center setting. The remaining 210 patients (mean age, 59 years [SD, 11]) were given a supply of the drug to which they initially responded and were instructed to take 1 pill at the onset of subsequent episodes of heart palpitations.

Patients served as their own historical controls and were followed for 15 months. The number of symptomatic episodes per month in the follow-up period (55 episodes per month) was similar to that in the year before enrollment (60 episodes per month). A total of 165 patients (79%) had 618 episodes of arrhythmia, and treatment with either drug successfully stopped palpitations in 534 of these episodes (94%). The mean time to resolution of symptoms was 113 minutes (SD, 84). Of 165 patients who had recurring symptoms, the drug was effective at stopping all arrhythmic episodes in 139 (84%). Of 12 patients (7%) who experienced adverse effects during 1 or more arrhythmic episodes, 1 had atrial flutter with a rapid ventricular rate and 11 had noncardiac side effects. Compared with the year before they enrolled in the study, patients had fewer monthly visits to the emergency department (5 vs. 46; $P < 0.001$) and fewer hospitalizations (2 vs. 15; $P < 0.001$).

In conclusion, the "pill-in-the-pocket" treatment approach seems to be a feasible and safe option for selected inpatients who have lone atrial fibrillation but are otherwise healthy enough to be discharged. It is associated with a high rate of adherence, a low rate of adverse events, and a marked reduction in emergency department visits and hospital readmissions.

Chronic Heart Failure

Rapid B-Type Natriuretic Peptide Measurement Improved Acute Dyspnea Evaluation and Treatment

Mueller C, Scholer A, Laule-Kilian K, et al. Use of B-type natriuretic peptide in the evaluation and management of acute dyspnea. N Engl J Med. 2004;350:647-54. [PMID: 14960741]

This investigation was a randomized, controlled study of 452 patients who presented to the emergency department with acute dyspnea. In 225 patients, physicians were given the results of rapid bedside measurements of serum B-type natriuretic peptide (BNP) levels to guide their management and triage decisions. Information regarding serum BNP levels was unavailable for decision making in the 227 patients in the control group. Primary end points were time to discharge and total cost of treatment.

The measurement of serum BNP levels reduced hospitalizations (75% vs. 85%; $P = 0.008$) and intensive care admissions (15% vs. 24%; $P = 0.010$). Median time to discharge was decreased in the group in which serum BNP levels had been measured (8 days vs. 11 days; $P = 0.001$), as was the mean total cost of treatment ($5410 vs. $7264; $P = 0.006$). There was no significant difference in 30-day mortality rates (10% in the group whose serum BNP levels were measured compared with 12% in the control group; $P = 0.45$).

One potential limitation of this study may be the statistically significant difference in the number of patients randomly assigned to each group who ultimately received diagnoses of chronic obstructive pulmonary disease (COPD). Specifically, 23% of the patients whose serum BNP levels were measured received COPD diagnoses compared with only 11% of those in the control group. One possible interpretation is that serum BNP levels helped physicians to more accurately diagnose COPD because this determination is especially useful for excluding heart failure as a cause of dyspnea. Another explanation could be that the study randomization failed and that more patients with COPD were assigned to undergo testing. Because patients with COPD typically have a shorter length of stay (and therefore lower hospitalization costs) than patients with heart failure, a disproportionate number of patients with COPD in the test group may have made serum BNP determination seem more useful than it would be if the test were studied in 2 groups with equal proportions of patients with COPD.

In conclusion, the addition of serum BNP determinations to standard methods of diagnosis and treatment may reduce the length of stay and hospitalization costs for patients with heart failure, but a larger study will be required to resolve the questions about randomization.

Pulmonary Embolism

Low-Molecular-Weight Heparin and Unfractionated Heparin Showed Similar Safety and Efficacy for Treating Pulmonary Embolism

Quinlan DJ, McQuillan A, Eikelboom JW. Low-molecular-weight heparin compared with intravenous unfractionated heparin for treatment of pulmonary embolism: a meta-analysis of randomized, controlled trials. Ann Intern Med. 2004;140:175-83. [PMID: 14757615]

The use of low-molecular-weight heparin has shifted the care of uncomplicated deep venous thrombosis to the outpatient setting. Although deep venous thrombosis and pulmonary embolism share common pathophysiologic characteristics, the role of low-molecular-weight heparin in

treating pulmonary embolism is less clear. Unfractionated heparin continues to be widely used for this condition.

This meta-analysis examined the utility of low-molecular-weight heparin versus unfractionated heparin for the treatment of pulmonary embolism. The investigators searched the literature that had been published up to 1 August 2003 and identified 12 randomized trials for inclusion in their analysis. These studies compared fixed-dose subcutaneous low-molecular-weight heparin with dose-adjusted intravenous unfractionated heparin for the treatment of nonmassive symptomatic or asymptomatic pulmonary embolism in the context of symptomatic deep venous thrombosis. The trials specifically included separate outcome data for patients with pulmonary embolism.

There was no statistically significant difference between low-molecular-weight heparin and unfractionated heparin in prevention of recurrent symptomatic venous thromboembolism at the end of treatment (1.4% vs. 2.4%; odds ratio, 0.63 [CI, 0.33 to 1.18]) or 3 months after treatment (3% vs. 4.4%; odds ratio, 0.68 [CI, 0.42 to 1.09]). The estimates were similar for patients who presented with symptoms of pulmonary embolism (1.7% vs. 2.3%; odds ratio, 0.72 [CI, 0.35 to 1.48]) and for those who were asymptomatic (1.2% vs. 3.2%; odds ratio, 0.53 [CI, 0.15 to 1.88]). Patients who received low-molecular-weight heparin experienced fewer major bleeding complications (1.3% vs. 2.1%; odds ratio, 0.67 [CI, 0.36 to 1.27]), but the difference was not statistically significant. The authors observed no difference in the safety and efficacy of the different preparations of low-molecular-weight heparin.

In conclusion, low-molecular-weight heparin seems to be similar to unfractionated heparin in safety and efficacy for treatment of either symptomatic or asymptomatic pulmonary embolism.

Catheter-Related Bloodstream Infections

The Differential Time to Positivity Test Was Highly Sensitive and Specific for Diagnosing Catheter-Related Bacteremia

Raad I, Hanna HA, Alakech B, et al. Differential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. Ann Intern Med. 2004;140:18-25. [PMID: 14706968]

This study assessed the utility of the differential time to positivity test in diagnosing catheter-related bacteremia as an alternative to the normal method of taking catheter cultures. Cultures require catheter removal, which limits their utility because they cannot guide physicians in determining which catheters need to be removed.

The differential time to positivity test measures the difference in time required for cultures of blood drawn from a catheter and blood drawn from a peripheral vein to become positive. Normally, the central line culture turns positive much sooner than the culture of the peripheral blood sample. The larger the differential in time to positivity, the more likely it is that the catheter is the source of the infection.

This study included 191 patients who had the same organism isolated from blood cultures drawn through a central venous catheter and a peripheral vein. The investigators compared the time to positivity for cultures of blood from the central venous catheter and from the peripheral vein. All catheters were removed and the semiquantitative roll-plate method was used as the gold standard in establishing which patients had a catheter-related infection.

Of the 191 patients, 108 had catheter-related bacteremia and 83 had non–catheter-related bacteremia. A differential time to positivity of 120 or more minutes (that is, catheter cultures turned positive ≥120 minutes before peripheral line cultures turned positive) had a positive likelihood ratio of 10.5 and a negative likelihood ratio of 0.21 for catheters in place for less than 30 days. For catheters in place for 30 days or more, the test had a positive likelihood ratio of 3.7 and a negative likelihood ratio of 0.09. The test had considerably less diagnostic utility if antibiotics had been administered through the catheter (positive likelihood ratio, 1.3; negative likelihood ratio, 0.32).

In conclusion, the differential time to positivity test may help determine if a catheter is the source of a patient's infection without the unnecessary removal of uninfected catheters. This test is particularly reliable for catheters through which antibiotics have not been administered.

Nephropathy

Sodium Bicarbonate Hydration before Contrast Exposure Was Better than Sodium Chloride Hydration for Preventing Nephropathy

Merten GJ, Burgess WP, Gray LV, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. JAMA. 2004;291:2328-34. [PMID: 15150204]

Contrast-induced nephropathy is a common complication of radiographic procedures. This prospective trial randomly assigned 119 patients with stable serum creatinine levels of 97.2 μmol/L or greater (≥1.1 mg/dL) to receive sodium chloride ($n = 59$) or sodium bicarbonate ($n = 60$) before and after iopamidol administration (370 mg of iodine/mL). The patients received an infusion of either sodium chloride or sodium bicarbonate (154 mmol/L) as a bolus of 3 mL/kg of body weight per hour for 1 hour before iopamidol contrast administration, followed by an infusion of 1 mL/kg per hour for 6 hours after the procedure. The investigators measured serum creatinine levels at

baseline and at 1 and 2 days after contrast exposure. The primary outcome was contrast-induced nephropathy, which was defined as an increase in serum creatinine level of 25% or more within 2 days of contrast administration.

Contrast-induced nephropathy occurred in 8 patients (14%) who received sodium chloride and in 1 patient (2%) who received sodium bicarbonate (mean difference, 12 percentage points [CI, 2.6 to 21.2 percentage points]; $P = 0.020$). Among the 9 patients who had contrast-induced nephropathy, the mean baseline level of serum creatinine was 146.7 μmol/L (1.66 mg/dL). None of the patients who received the sodium bicarbonate infusion experienced heart failure, respiratory alkalosis, or other side effects.

In conclusion, sodium bicarbonate hydration before contrast exposure was more effective than sodium chloride hydration for prophylaxis of contrast-induced renal failure. This effect was similar to that observed with *N*-acetylcysteine administration in previous studies (1). The use of sodium bicarbonate has a practical advantage, however, because it can be delivered 1 hour before the procedure or test whereas *N*-acetylcysteine prophylaxis must be started 12 hours before exposure to contrast. Furthermore, the efficacy of *N*-acetylcysteine in preventing contrast-induced renal failure in all patients remains controversial.

Fluid Resuscitation

Fluid Resuscitation with Albumin or Normal Saline Resulted in Similar Outcomes among Patients in Intensive Care Units

Finfer S, Bellomo R, Boyce N, et al. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med. 2004;350:2247-56. [PMID: 15163774]

This study compared the effect of fluid resuscitation with either albumin or saline on mortality rates in critically ill patients with similar baseline characteristics. The multicenter, randomized, double-blind trial involved a total of 6997 patients receiving care in intensive care units; 3497 were assigned to receive 4% albumin for intravascular fluid resuscitation, and 3500 were assigned to receive saline. The primary outcome was death from any cause during the 28-day period after randomization.

There were 726 deaths in the albumin group compared with 729 deaths in the saline group (relative risk for death, 0.99 [CI, 0.91 to 1.09]; $P = 0.87$). There was no difference in organ failure ($P = 0.85$), days in the intensive care unit (6.5 [SD, 6.6] in the albumin group vs. 6.2 [SD, 6.2] in the saline group; $P = 0.44$), days of hospitalization (15.3 [SD, 9.6] vs. 15.6 [SD, 9.6]; $P = 0.30$), days of mechanical ventilation (4.5 [SD, 6.1] vs. 4.3 [SD, 5.7]; $P = 0.74$), and days of renal replacement therapy (0.5 [SD, 2.3] vs. 0.4 [SD, 2.0]; $P = 0.41$).

In conclusion, 4% albumin offered no meaningful benefit over the use of normal saline for intravenous fluid replacement. The authors noted that the cost of 4% albumin is $232 per dose compared with $2.32 per dose of saline. There may be other indications for albumin, but preload augmentation for critical care patients is not one of them.

Antiplatelet Therapy

Clinical Trial Data Favor Aspirin or Clopidogrel as First-Line Agents for Most Patients with Vascular Disease

Tran H, Anand SS. Oral antiplatelet therapy in cerebrovascular disease, coronary artery disease, and peripheral arterial disease. JAMA. 2004;292:1867-74. [PMID: 15494585]

Physicians often use different antiplatelet drugs for patients with cerebrovascular, coronary artery, and peripheral arterial disease despite similar pathophysiologic characteristics. This article reviewed the evidence supporting the use of different antiplatelet therapies for these diseases. The authors' systematic review of the literature from January 1960 to August 2004 included data from 111 studies, all of which had a treatment period that lasted 10 days or more. Of 111 studies, 22 focused on cerebrovascular disease and involved more than 30 000 patients. Forty-seven studies focused on coronary disease and involved approximately 60 000 patients. The remaining 42 studies focused on peripheral arterial disease and involved more than 9000 patients.

Aspirin reduced the risk for recurrent stroke by 22% (CI, 15.2% to 27.5%) compared with placebo ($P < 0.001$). Clopidogrel reduced the relative risk for recurrent stroke, MI, and vascular death by 8.7% (CI, 0.3% to 16.5%) compared with aspirin ($P = 0.040$); however, clopidogrel provided no additional benefit when added to aspirin therapy, and there was a higher risk for major and life-threatening bleeding with this combination. Ticlopidine reduced the risk for recurrent stroke, MI, and vascular death by 23% compared with placebo ($P = 0.020$); the risk for nonfatal stroke or death was reduced by 12% compared with aspirin. However, ticlopidine's adverse effects preclude its use on a widespread clinical basis; 25% of patients experienced diarrhea or rash, and a smaller percentage experienced neutropenia or thrombocytopenic thrombotic purpura. Dipyridamole alone or in combination with aspirin had the same effect as aspirin alone.

Compared with placebo, aspirin reduced the risk for death after ST-segment elevation MI by 23% and the risk for recurrent MI by 49%. The lasting benefits of aspirin extended for at least 10 years. Aspirin also offered a benefit to patients receiving thrombolytic therapy with streptokinase or other agents, reducing the odds of stroke, MI, or vascular death by 30% in patients with ST-segment eleva-

tion MI. In patients with a history of non–ST-segment elevation MI, aspirin reduced the risk for stroke, recurrent MI, or vascular death by 46%.

In patients with peripheral vascular disease, aspirin reduced the risk for serious vascular events by 23% compared with placebo. In these patients, ticlopidine reduced the risk for coronary and cerebrovascular events by 34% (relative risk reduction, 0.66 [CI, 0.40 to 0.96]), but side effects limited its use. Clopidogrel reduced the risk for major vascular events by 24% (CI, 8.9% to 36.2%) compared with aspirin ($P = 0.003$). A subgroup analysis revealed that clopidogrel offered a significantly greater benefit to patients with peripheral arterial disease when used to prevent subsequent MI and cerebrovascular events.

In conclusion, current evidence supports the use of aspirin or clopidogrel, but not both, as first-line agents for cerebrovascular disease. Extended-release dipyridamole may play a significant role, and its use is currently under study. Current evidence supports the use of aspirin monotherapy for patients with stable angina and for those who have had ST-segment elevation MI. Combination therapy with clopidogrel and aspirin is recommended for unstable angina and after non–ST-segment elevation MI or percutaneous coronary interventions. Current evidence supports the use of aspirin or clopidogrel, either alone or in combination, as first-line therapy for patients with peripheral arterial disease.

Adverse Events following Hospital Discharge

Adverse Events, Half of Which Were Preventable or Ameliorable, Occurred after Hospital Discharge in One Fourth of Patients

Forster AJ, Clark HD, Menard A, et al. Adverse events among medical patients after discharge from hospital. CMAJ. 2004;170:345-9. [PMID: 14757670]

The view that a patient's discharge from the hospital is a single event as opposed to an ongoing process is an important flaw in the health care system. This prospective trial included 328 general internal medicine patients who were discharged from 2 campuses of a Canadian teaching hospital during a 14-week period. Data were assimilated from patient interviews and medical record reviews at 30 days. Reviewers independently recorded adverse patient outcomes following discharge from the hospital. Adverse events were characterized according to their relationship to medical management (for example, medication errors and inappropriate treatments), severity, remediability, and preventability. The inter-rater reliability was 86% for adverse event determination, 73% for preventability, and 90% for remediability.

An adverse outcome following discharge was observed in 204 (62%) of the 328 patients enrolled in the study. Of the 204 adverse outcomes, 76 (incidence, 23% [CI, 19% to 28%]) were directly related to medical management and could therefore be classified as adverse events. Of these 76 adverse events, 21 were determined to be preventable errors and 17 were ameliorable. The adverse events included medication errors (72%), therapeutic errors (16%), and nosocomial infections (11%). Although most adverse events were transitory, 25% of these patients had a temporary disability that limited their functional status and 3% had permanent disability. Another 3% died as a result of the adverse event.

This study suggests that there is a need for system-based quality improvement in patient transitions out of the hospital. Discharge should not be viewed as a single point in time but as an important process of ensuring a safe transition. The authors speculate that the discharge process could be improved by establishing early telephone contact with patients after they return home and by integrating home care services more fully. Elderly patients are also at higher risk for adverse events because they have difficulty returning for follow-up evaluations; therefore, discharge planning for these patients should address this eventuality.

Dementia

Nursing Home Residents with Advanced Dementia Typically Do Not Receive Optimal Palliative Care

Mitchell SL, Kiely DK, Hamel MB. Dying with advanced dementia in the nursing home. Arch Intern Med. 2004;164:321-6. [PMID: 14769629]

This study compared the quality and characteristics of end-of-life care for nursing home patients who have advanced dementia with that given to patients with cancer. The Minimum Data Set (Health Care Financing Administration, Washington, DC) is a federally mandated, standardized data collection tool for tracking all patients in licensed nursing homes in the United States. The investigators used the Minimum Data Set to identify persons 65 years of age or older with advanced dementia ($n = 1609$) and terminal cancer ($n = 883$) who died within 1 year of admission to a nursing home. The 2 groups were compared for frequency of advance care planning, incidence of burdensome interventions, presence of pain and physical symptoms, and incidence of psychiatric conditions.

At the time of nursing home admission, only 1.1% of residents with advanced dementia were perceived to have a life expectancy of less than 6 months. However, 71% of these patients died within 6 months of admission. The mean time to death was 121 days in patients with advanced dementia compared with 62 days in patients with cancer. Before death, 55% of patients with dementia had a

do-not-resuscitate order compared with 86% of patients with cancer.

Patients with dementia were more likely than those with cancer to receive burdensome interventions at the end of life. Compared with patients with cancer, patients with severe dementia were more likely to experience tube feeding (5.2% vs. 25%; $P < 0.001$), laboratory tests (32.3% vs. 49%; $P < 0.001$), restraints (6.3% vs. 11.2%; $P < 0.001$), and intravenous therapy (7.1% vs. 10.1%; $P = 0.010$).

In conclusion, this study revealed that most physicians do not think of severe dementia as a terminal condition. Consequently, most patients with severe dementia do not receive optimal palliative care. Providers need to be educated about when and how to initiate end-of-life care for this patient population. The time of hospitalization is an ideal setting for identifying patients with severe dementia, initiating discussions with the patient and the patient's family regarding palliative care and advance care planning, and setting the stage for ongoing nursing home care.

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