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Update in hospital medicine: Studies likely to affect inpatient practice in 2011

KEY POINTS

Dabigatran (Pradaxa) will likely start to replace warfarin (Coumadin) both to prevent stroke in patients with atrial fibrillation and to prevent recurrent venous thromboembolism.

Using a checklist during insertion of central venous catheters can decrease the rate of catheter-related bloodstream infections in the intensive care unit.

The overall survival rate of patients who undergo cardiopulmonary resuscitation in the intensive care unit is approximately 16%; the rate is lower in patients who are receiving pressor drugs and higher in those with ventricular tachycardia or ventricular fibrillation.

Patients lacking follow-up with a primary care physician within 30 days of discharge are at high risk of readmission and have a trend for longer length of hospital stay.

Preoperative stress testing for patients undergoing noncardiac surgery should be done selectively, ie, in patients at high risk.

A NUMBER OF STUDIES published in the last few years will likely affect the way we practice medicine in the hospital. Here, we will use a hypothetical case scenario to focus on the issues of anticoagulants, patient safety, quality improvement, critical care, transitions of care, and perioperative medicine.

AN ELDERLY MAN WITH NEW-ONSET ATRIAL FIBRILLATION

P.G. is an 80-year-old man with a history of hypertension and type 2 diabetes mellitus who is admitted with new-onset atrial fibrillation. In the hospital, his heart rate is brought under control with intravenous metoprolol (Lopressor). On discharge, he will be followed by his primary care physician (PCP). He does not have access to an anticoagulation clinic.

1 What are this patient's options for stroke prevention?

- ☐ Aspirin 81 mg daily and clopidogrel (Plavix) 75 mg daily
- ☐ Warfarin (Coumadin) with a target international normalized ratio (INR) of 2.0 to 3.0
- ☐ Aspirin mg daily by itself
- ☐ Dabigatran (Pradaxa) 150 mg daily

A new oral anticoagulant agent

In deciding what type of anticoagulation to give to a patient with atrial fibrillation, it is useful to look at the $CHADS_2$ score (1 point each for ***c***ongestive heart failure, ***h***ypertension, ***a***ge 75 or older, and ***d***iabetes mellitus; 2 points for prior ***s***troke or transient ischemic attack. This patient has a $CHADS_2$ score of 3, indicating that he should receive warfarin. An alternative is dabigatran, the first new anticoagulant agent in more than 50 years.

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In a multicenter, international trial, Connolly et al[1] randomized 18,113 patients (mean age 71, 64% men) to receive dabigatran 110 mg twice daily, dabigatran 150 mg twice daily, or warfarin with a target INR of 2.0 to 3.0. In this noninferiority trial, dabigatran was given in a blinded manner, but the use of warfarin was open-label. Patients were eligible if they had atrial fibrillation at screening or within the previous 6 months and were at risk of stroke—ie, if they had at least one of the following: a history of stroke or transient ischemic attack, a left ventricular ejection fraction of less than 40%, symptoms of congestive heart failure (New York Heart Association class II or higher), and an age of 75 or older or an age of 65 to 74 with diabetes mellitus, hypertension, or coronary artery disease.

At a mean follow-up of 2 years, the rate of stroke or systolic embolism was 1.69% per year in the warfarin group compared with 1.1% in the higher-dose dabigatran group (relative risk 0.66, 95% confidence interval [CI] 0.53–0.82, $P < .001$). The rates of major hemorrhage were similar between these two groups. Comparing lower-dose dabigatran and warfarin, the rates of stroke or systolic embolism were not significantly different, but the rate of major bleeding was significantly lower with lower-dose dabigatran.

In a trial in patients with acute venous thromboembolism, Schulman et al[2] found that dabigatran was not inferior to warfarin in preventing venous thromboembolism.

Guidelines from the American College of Cardiology Foundation and the American Heart Association now endorse dabigatran as an alternative to warfarin for patients with atrial fibrillation.[3] However, the guidelines state that it should be reserved for those patients who:

- Do not have a prosthetic heart valve or hemodynamically significant valve disease
- Have good kidney function (dabigatran is cleared by the kidney; the creatinine clearance rate should be greater than 30 mL/min for patients to receive dabigatran 150 mg twice a day, and at least 15 mL/min to receive 75 mg twice a day)
- Do not have severe hepatic dysfunction (which would impair baseline clotting function).

They note that other factors to consider are whether the patient:

- Can comply with the twice-daily dosing required
- Can afford the drug
- Has access to an anticoagulation management program (which would argue in favor of using warfarin).

Dabigatran is not yet approved to prevent venous thromboembolism.

CASE CONTINUED: HE GETS AN INFECTION

P.G. is started on dabigatran 150 mg by mouth twice a day.

While in the hospital he develops shortness of breath and needs intravenous furosemide (Lasix). Because he has bad veins, a percutaneous intravenous central catheter (PICC) line is placed. However, 2 days later, his temperature is 101.5°F, and his systolic blood pressure is 70 mm Hg. He is transferred to the medical intensive care unit (ICU) for treatment of sepsis. The anticoagulant is held, the PICC line is removed, and a new central catheter is inserted.

2 Which of the following directions is incorrect?

- ☐ Wash your hands before inserting the catheter. The accompanying nurse is required to directly observe this procedure or, if this step is not observed, to confirm that the physician did it.
- ☐ Before inserting the catheter, clean the patient's skin with chlorhexidine antiseptic.
- ☐ Place sterile drapes over the entire patient.
- ☐ Wear any mask, hat, gown, and gloves available.
- ☐ Put a sterile dressing over the catheter.

Candidates for dabigatran should have good kidney function

A checklist can prevent infections when inserting central catheters

A checklist developed at Johns Hopkins Hospital consists of the five statements above, except for the second to last one—you should wear a *sterile* mask, hat, gown and gloves. This is important to ensure that sterility is not broken at any point during the procedure.

TABLE 1

Rates of survival to discharge after cardiopulmonary resuscitation in patients on or not on a pressor

SUBGROUP	ON PRESSOR	NOT ON PRESSOR
≥ 65 years old	9.4%	20.1%
< 65 years old	9.2%	22.7%
White	10.6%	23.0%
Nonwhite	5.7%	15.4%
Male	9.7%	21.6%
Female	8.7%	20.6%
≥ 3 causes of cardiopulmonary arrest	5.7%	16.2%
< 3 causes of cardiopulmonary arrest	10.2%	21.9%
Pulseless electrical activity or asystole	5.9%	15.2%
Ventricular tachycardia or fibrillation	22.6%	40.7%
Mechanical ventilation	7.6%	16.1%
No mechanical ventilation	12.4%	24.2%
Cardiopulmonary arrest at night or over the weekend	7.9%	19.3%
Cardiopulmonary arrest on a weekday	10.3%	23.1%
Total	9.3%	21.2%
On two or more pressors		6.4%
On one pressor		11.5%
Vasopressin		7.8%
Norepinephrine		8.0%
Phenylephrine		11.2%
Dopamine		11.3%
Dobutamine		23.0%
Epinephrine		19.8%

DATA FROM TIAN J, KAUFMAN DA, ZARICH S, ET AL; AMERICAN HEART ASSOCIATION NATIONAL REGISTRY FOR CARDIOPULMONARY RESUSCITATION INVESTIGATORS. OUTCOMES OF CRITICALLY ILL PATIENTS WHO RECEIVED CARDIOPULMONARY RESUSCITATION. AM J RESPIR CRIT CARE MED 2010; 182:501–506.

Pronovost et al[4] launched a multicenter initiative at 90 ICUs, predominantly in the state of Michigan, to implement interventions to improve staff culture and teamwork and to translate research into practice by increasing the extent to which these five evidence-based recommendations were applied. The mean rate of catheter-related blood stream infections at baseline was 7.7%; this dropped to 2.8% during the implementation period, 2.3% in the first 3 months after implementation, 1.3% in months 16 through 18, and 1.1% in months 34 through 36, demonstrating that the gains from this quality-improvement project were sustainable.

If this intervention and collaborative model were implemented in all ICUs across the United States and if similar success rates were achieved, substantial and sustained reductions could be made in the 82,000 infections, 28,000 deaths, and $2.3 billion in costs attributed to these infections annually.

CASE CONTINUED: HE IS RESUSCITATED

P.G. is started on a 1-L fluid bolus but he remains hypotensive, necessitating a norepinephrine drip. He does well for about 6 hours, but in the middle of the night he develops ventricular tachycardia and ventricular fibrillation, and a code is called. He is successfully resuscitated, but the family is looking for prognostic information.

3 What are P.G.'s chances of surviving and leaving the hospital?

- ☐ 5%
- ☐ 8%
- ☐ 15%
- ☐ 23%

A registry of cardiopulmonary resuscitation

Tian et al[5] evaluated outcomes in the largest registry of cardiopulmonary resuscitation to date. In this analysis, 49,656 adult patients with a first cardiopulmonary arrest occurring in an ICU between January 1, 2000, and August 26, 2008, were evaluated for their outcomes on pressors vs those not on pressors.

The overall rate of survival until discharge was 15.9%. However, the rate was lower by more than half in those who were receiving pressor agents than in those not on pressors (9.3% vs 21.2%; $P < .0001$). The rate was lower still—6.4%—in those receiving two or more pressors (compared with 11.5% in those receiving one pressor). In patients on a single pressor, the rates varied by agent: 7.8% with vasopressin, 8.0% with norepinephrine,

11.2% with phenylephrine, 11.3% with dopamine, 23.0% with dobutamine, and 19.8% with epinephrine (TABLE 1).

Other independent predictors of a lower survival rate were nonwhite race, mechanical ventilation, having three or more immediate causes of cardiopulmonary arrest, age 65 years or older, and cardiopulmonary arrest occurring at night or over the weekend.

Fortunately, for our patient, survival rates were higher for patients with ventricular tachycardia or fibrillation than with other causes of cardiopulmonary arrest: 22.6% for those on pressors (like our patient) and 40.7% for those on no pressors.

CASE CONTINUED: HE RECOVERS AND GOES HOME

P.G. makes a remarkable recovery and is now ready to go home. It is the weekend, and you are unable to schedule a follow-up appointment before his discharge, so you ask him to make an appointment with his PCP.

4 What is the likelihood that P.G. will be readmitted within 1 month?

- ☐ 5%
- ☐ 12%
- ☐ 20%
- ☐ 25%
- ☐ 30%

The importance of follow-up with a primary care physician

Misky et al,[6] in a small study, attempted to identify the characteristics and outcomes of discharged patients who lack timely follow-up with a PCP. They prospectively enrolled 65 patients admitted to University of Colorado Hospital, an urban 425-bed tertiary care center, collecting information about patient demographics, diagnosis, payer source, and PCPs. After discharge, they called the patients to determine their PCP follow-up and readmission status. Thirty-day readmission rates and hospital length of stay were compared in patients with and without timely PCP follow-up (ie, within 4 weeks).

Patients lacking timely PCP follow-up were 10 times more likely to be readmitted (odds ratio [OR] = 9.9, P = .04): the rate was 21% in patients lacking timely PCP follow-up vs 3% in patients with timely PCP follow-up, P = .03. Lack of insurance was associated with lower rates of timely PCP follow-up: 29% vs 56% (P = .06), but did not independently increase the readmission rate or length of stay (OR = 1.0, P = .96). Index hospital length of stay was longer in patients lacking timely PCP follow-up: 4.4 days vs 6.3 days, P = 0.11.

Comment. Nearly half of the patients in this study, who were discharged from a large urban academic center, lacked timely follow-up with a PCP, resulting in higher rates of readmission and a nonsignificant trend toward longer length of stay. Timely follow-up is necessary for vulnerable patients.

Since the lack of timely PCP follow-up results in higher readmission rates and possibly a longer length of stay, a PCP appointment at discharge should perhaps be considered a core quality measure. This would be problematic in our American health care system, in which many patients lack health insurance and do not *have* a PCP.

A MAN UNDERGOING GASTRIC BYPASS SURGERY

A 55-year-old morbidly obese man (body mass index 45 kg/m^2) with a history of type 2 diabetes mellitus, chronic renal insufficiency (serum creatinine level 2.1 mg/dL), hypercholesterolemia, and previous stroke is scheduled for gastric bypass surgery. His functional capacity is low, but he is able to do his activities of daily living. He reports having dyspnea on exertion and intermittently at rest, but no chest pain. His medications include insulin, atorvastatin (Lipitor), aspirin, and atenolol (Tenormin). He is afebrile; his blood pressure is 130/80 mm Hg, pulse 75, and oxygen saturation 97% on room air. His baseline electrocardiogram shows no Q waves.

Catheter-related bloodstream infections cause 28,000 deaths and cost $2.3 billion each year

5 Which of the following is an appropriate next step before proceeding to surgery?

- ☐ Echocardiography
- ☐ Cardiac catheterization
- ☐ Dobutamine stress echocardiography or adenosine thallium scanning
- ☐ No cardiac testing is necessary before surgery

Is cardiac testing necessary before noncardiac surgery?

Wijeysundera et al[7] performed a retrospective cohort study of patients who underwent elective surgery at acute care hospitals in Ontario, Canada, in the years 1994 through 2004. The aim was to determine the association of noninvasive cardiac stress testing before surgery with survival rates and length of hospital stay. Included were 271,082 patients, of whom 23,991 (8.9%) underwent stress testing less than 6 months before surgery. These patients were matched with 46,120 who did not undergo testing.

One year after surgery, fewer patients who underwent stress testing had died: 1,622 (7.0%) vs 1,738 (7.5%); hazard ratio 0.92, 95% CI 0.86–0.99, P = .03. The number needed to treat (ie, to be tested) to prevent one death was 221. The tested patients also had a shorter mean hospital stay: 8.72 vs 8.96 days, a difference of 0.24 days (95% CI –0.07 to –0.43; $P < .001$).

However, the elderly patients (ie, older than 66 years) who underwent testing were more likely to be on beta-blockers and statins than those who did not undergo testing, which may be a confounding factor.

Furthermore, the benefit was all in the patients at intermediate or high risk. The authors performed a subgroup analysis, dividing the patients on the basis of their Revised Cardiac Risk Index (RCRI; 1 point each for ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes, renal insufficiency, and high-risk surgery).[8] Patients with an RCRI of 0 points (indicating low risk) actually had a higher risk of death with testing than without testing: hazard ratio 1.35 (95% CI 1.03–1.74), number needed to harm 179—ie, for every 179 low-risk patients tested, one excess death occurred. Those with an RCRI of 1 or 2 points (indicating intermediate risk) had a hazard ratio of 0.92 with testing (95% CI 085–0.99), and those with an RCRI of 3 to 6 points (indicating high risk) had a hazard ratio of 0.80 with testing (95% CI 0.67- 0.97; number needed to treat = 38).

Comment. These findings indicate that cardiac stress testing should be done selectively before noncardiac surgery, and primarily for patients at high risk (with an RCRI of 3 or higher) and in some patients at intermediate risk, but not in patients at low risk, in whom it may be harmful. Stress testing may change patient management because a positive stress test allows one to start a beta-blocker or a statin, use more aggressive intraoperative and postoperative care, and identify patients who have indications for revascularization. ■

Survival after cardiac arrest depends on use of pressors, age, race, cause of arrest, mechanical ventilation, and when the arrest occurred

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CME ANSWERS

Answers to the credit tests on page 487 of this issue

Hypothermia after cardiac arrest **1C 2D** Vancomycin **1C 2A** Bronchial thermoplasty for asthma **1A 2D**