

Hospital Medicine

Evidence-Based Information for Hospitalists
Intensivists, and Acute Care Physicians [ALERT]

ABSTRACT & COMMENTARY

Prescribers Are Continuing Opioids in Patients After Overdose

By *Deborah J. DeWaay, MD, FACP*

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

SYNOPSIS: Most opioid prescriptions are continued after a patient overdoses accidentally, and these patients are at higher risk for a recurrent overdose compared to those who have their prescriptions stopped.

SOURCE: Larochelle M, Leibschutz J, Zhang F, Ross-Degnan D, Wharam J. Opioid Prescribing After a Nonfatal Overdose and Association with Repeated Overdose. *Annals of Internal Medicine* 2016; 164:1-9.

Opioid use to treat non-cancer pain has been on the rise for several decades. In turn, there has been a significant rise in opioid addiction, overdoses and deaths. The number of emergency room visits because of nonmedical use of opioids was over 300,000 in 2008, double the amount in 2003. Patients with opioid overdose are more likely to have an opioid use disorder or to have a high opioid dose prescribed to them. Although opioid overdose and misuse is an indication to stop long-term opioid therapy, the effects of continuation of opioids after overdose had not been characterized. This study analyzes opioid use and subsequent overdoses after patients being treated for non-cancer pain present to an emergency department

(ED) or are admitted inpatient for an opioid overdose.

This retrospective study used the Optum database to select a cohort of patients that had a non-fatal opioid overdose while being treated with long-term opioids. This database included pharmacy, inpatient, and outpatient records of over 50 million patients from 50 states who have coverage through a major U.S. health insurance company. The cohort was sampled from records between May 2000 and December 2012. The patients had a median follow up of 15 months.

This study identified 14,725 patients, age 18-64, who had an opioid (index) overdose requiring an inpatient stay or an ED visit. Patients were excluded if they weren't enrolled 90 days prior to the initial

Financial Disclosure: *Hospital Medicine Alert's Physician Editor, Kenneth P. Steinberg, MD, Peer Reviewer Rachael Safyan, MD, Managing Editor Jill Drachenberg, and Associate Managing Editor Dana Spector have no relevant relationship related to the material presented in this issue.*

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Hospital Medicine Alert,
ISSN 1931-9037, is published monthly by
AHC Media, LLC
One Atlanta Plaza
950 East Paces Ferry NE, Suite 2850
Atlanta, GA 30326.
AHCMedia.com

GST Registration Number: R128870672.
Periodicals Postage Paid at Atlanta, GA 30304
and at additional mailing offices.

POSTMASTER: Send address changes to
Hospital Medicine Alert,
PO, Box 550669,
Atlanta, GA 30355.

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overdose so that continuous opioid use could be determined. The cohort was limited to 3379 patients who had consistent opioid use prior to the overdose as defined by: at least 3 opioid prescriptions filled at least 21 days apart, over 12 weeks duration of prescriptions and over 12 weeks supplied. Patients with cancer were excluded, unless they had non-melanoma skin cancer. In order to compare opioid use before and after the index overdose, authors calculated a morphine-equivalent dosage (MED) for each time an opioid was dispensed to a patient. The provider for each dispensing was noted. Patients were excluded if there was incomplete provider data. Benzodiazepine and buprenorphine use was also collected.

2848 patients, with an average age of 44 years and 60% female, were in the cohort and followed for a median of 10 months after the index overdose. 46% of patients had an average daily dose of 100mg MED or greater, 41% had a substance use disorder, 59% had a mental health diagnosis, and over 50% also had a benzodiazepine prescription. The average mean daily dose for the cohort increased from 152 - 164 MED 60 days prior to the index overdose to 184 MED one week prior to the overdose. Authors defined low, moderate and large dose opioids as <50, 50-100, and >100 MED respectively. After the overdose the average daily dose decreased to 118 MED on average for the cohort. Post-overdose, 70% of patients received a subsequent prescription within 90 days and 91% of patients received at least one opioid prescription during the follow up period. Over 30% of patients received prescriptions of > 100mg MED. 30% of patients switched to a new prescriber after the overdose.

58% of patients received at least one prescription for a benzodiazepine. The patients who had an active benzodiazepine prescription were more likely to also have an active opioid prescription. 7% of patients were put on buprenorphine post-overdose, and it was very uncommon for these patients to also have an active opioid prescription at the same time.

Repeated overdose occurred in 7% of the patients. Authors used Cox model analysis to calculate the adjusted hazard ratios of repeated overdose for large, moderate and low dose opioid prescriptions post overdose. They were as follows: 2.57

(CI, 1.72 to 3.85) for large dosages, 1.89 (CI 1.18-3.04) for moderate dosages, and 1.13 (CI, 0.69 to 1.85) for low dosages. The hazard ratio of repeated overdose was 1.74 (CI, 1.31 to 2.32) if there was a concomitant benzodiazepine prescription, whereas there was no association with repeated overdose and buprenorphine use.

This type of study can only demonstrate associations and cannot explain the reasons behind the post-overdose prescribing patterns. Authors hypothesize that prescribers may have not realized that the patient had overdosed. Other hypotheses are that the prescribers believed the overdose was a therapeutic error or they simply don't have the skills to treat opioid use disorder. This study shows that there is an association, not causality, between the opioid dosage post-overdose and recurrent overdose.

The authors offer several limitations to their study. First, this database is an insurance database, so it will not capture encounters for which the patients paid cash. Second, coding data was used so it is subject to miscoding error. Third, the patients in this study were all insured and therefore this data may not be generalizable.

■ COMMENTARY

Patients who overdose are commonly cared for on hospitalist services. There are several dilemmas that the hospitalist faces when discharging these patients. First, are they restarted on their opioids? Guidelines combined with this study make a compelling argument that they should not be, and if they are, the opioid dose should be much lower. There is a conundrum because these patients often have chronic pain, adjuvant therapy takes weeks to start working, and many patients are already on adjuvant therapy. This study gives some evidence to the guidelines and hopefully will help the physician explain to the patient why the prescription is not being restarted or is being modified. Second, communication with primary care providers is even more crucial with these patients so that they are aware of the overdose and understand why the prescription was not continued. Third, follow-up with mental health and addiction experts is crucial since the rate of concurrent psychiatric and substance use disorders is prevalent. ■

REFERENCES

1. Manchikanti L, et al, American Society of Interventional Pain Physicians. American Society of Interventional Pain Physicians (ASIPP) guidelines for responsible opioid prescribing in chronic non-cancer pain: Part 2—guidance. *Pain Physician* 2012; 15:S67-116.
2. Chou R, et al, American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain* 2009; 10:113-30.

ABSTRACT & COMMENTARY

Early Chest CT Can Improve Treatment for Community-acquired Pneumonia

By Samuel Nadler, MD, PhD

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

SYNOPSIS: In patients with suspected community-acquired pneumonia, early chest CT significantly changed management decisions.

SOURCE: Claessens YE, et al. Early chest computed tomography scan to assist diagnosis and guide treatment decision for suspected community-acquired pneumonia. *Am J Respir Crit Care Med* 2015; 192:974-982.

Community-acquired pneumonia (CAP) is a very common diagnostic consideration. Early diagnosis and administration of antibiotics can save lives. However, the clinical diagnosis is often uncertain and misdiagnosis is frequent. This leads to inappropriate treatment with unnecessary antibiotics and may obscure the real underlying diagnosis. Even chest radiographs (CXR) demonstrating abnormalities can be misleading, and the concordance of interpretations of these infiltrates is poor, regardless of practitioner experience.¹ Thus, reliance on clinical factors and CXRs may lead to misdiagnosis and mistreatment of many patients presenting with respiratory disease.

This study hypothesized that the use of early computed tomography (CT) of the chest would improve the diagnosis and subsequent management of CAP. This was a prospective, interventional study in four tertiary teaching hospitals between November 2011 and January 2013. Enrolled in this study were 319 adults > 18 years of age who presented to the emergency department (ED) with suspicion of CAP. The criteria for CAP included: new onset of systemic symptoms (sweats, chills, aches, temperature > 38°C or < 36°C) and symptoms of lower respiratory tract infection (cough, sputum, dyspnea, chest pain, or altered breath sounds). Exclusions included: pregnancy, hospice patients, inability to complete the study, CURB-65 score of 3 or higher, or the need for ICU admission. A local radiologist performed CXRs and reported findings in a standardized fashion. Multi-detector chest CT using a low-dose protocol was performed as soon as possible afterward and was similarly interpreted. At this point, the ED physician completed a clinical report assigning a pneumonia probability and treatment plan. Three independent

evaluators who were experts in pulmonary medicine, infectious disease, or radiology subsequently adjudicated each assessment and defined the likelihood of CAP based on clinical and radiographic data and assigned a probability of CAP (definite, probable, possible, or excluded). Each case was then re-evaluated using data from the time of clinical discharge up to day 28 and assigned a final probability category.

After the initial clinical assessment and chest radiograph, the percentages of patients assigned to the CAP probability categories of definite, probable, possible, or excluded were 44.9%, 36.9%, 16.9%, and 1.2%, respectively. After chest CT, these categories shifted to 50.9%, 10.9%, 9.4%, and 28.8%, respectively. Adjudicating committee assignments were 47%, 8.7%, 11.3%, and 32.9%, respectively. At the 28-day final adjudication, the distribution was 47%, 4.1%, 10.7%, and 38.2%, respectively. Interestingly, of the 120 patients without parenchymal infiltrates on CXR, 40 had infiltrates on CT that conventional CXR missed. Conversely, of the 188 patients with parenchymal infiltrates on CXR, CT scans excluded CAP in 56 patients. Based on these CT findings, the ED physician modified the probability of CAP diagnosis in 187 of the patients (58.6%; 95% confidence interval, 53.2-64.0%). Of these patients, 59 were upgraded and 128 downgraded based on CT, including 11 of 36 patients previously considered as definite CAP by CXR.

■ COMMENTARY

This was an intriguing study that clearly showed the limitations of clinical factors and CXRs to diagnose CAP. More than half (58.6%) of the pre-CT probabilities of CAP were altered after chest CT. Prior to chest CT, 64.7% of patients were intended

to start antibiotic therapy and after chest CT, researchers ended the administration of antibiotics in 29 patients. Furthermore, 51 patients who did not receive antibiotics after CXRs were then administered therapy after receiving a CT scan. Three pulmonary emboli were discovered, and cardiac failure was diagnosed in 11 patients. Furthermore, 45 patients had a change in level of care, including 22 outpatients being admitted and 23 admissions changed to discharges. Overall, modifications of antibiotics or site of care occurred in 60.8% of patients.

It appears that most of the changes in diagnostic probability were in marginal cases. The percentage of “probable” CAP cases decreased with progressive assessments from 36.9% with CXR and clinical suspicion alone, to 10.9% after CT, to 8.7% after committee adjudication, and to 4.1% at 28 days. The number of “possible” cases decreased from 16.9% to 9.4% with chest CT. In a univariate secondary analysis, among 188 out of 308 patients with an infiltrate on CXR, CT excluded CAP in 56 patients. These patients, compared to the 132 with infiltrates confirmed on CT, tended to be older (71.1 vs 63.2 years of age; $P = 0.0131$), have lower white blood cell (WBC) counts (10.2 vs $12.6 \times 10^3/\text{mm}^3$; $P = 0.283$) and lower C-reactive protein (CRP) levels (78 vs 163.3 mg/L; $P = 0.0074$). Conversely, among 120 patients without infiltrates on CXR who also

had a CT, 40 patients had CT infiltrates compatible with CAP. Compared to the 80 patients without CT infiltrates, those 40 patients with CT infiltrates were more likely to have crackles on exam (48.7% vs 26.6%; $P = 0.0169$), higher WBC counts (12.3 vs $10.2 \times 10^3/\text{mm}^3$; $P = 0.0387$), and higher CRP levels (138.1 vs 59.9 mg/L; $P = 0.0037$). Thus, clinical factors such as lung auscultation and CRP still seem to have a good predictive value for CAP.

Ultimately, the decision to use CT scanning for the diagnosis of CAP will require a thorough analysis of the cost of care and the outcomes data. It may very well be that the improved diagnostic accuracy of CT scanning will reduce the cost of care enough to offset the cost of additional CT scans. Furthermore, earlier administration of antibiotics with CT-confirmed CAP and prevention of unnecessary antibiotics in those without CAP might also improve health outcomes. Both these factors should be prospectively examined before entertaining the widespread adoption of routine CT for the diagnosis of CAP. ■

REFERENCE

1. Hopstaken RM, et al. Inter-observer variation in the interpretation of chest radiographs for pneumonia in community-acquired lower respiratory tract infections. *Clin Radiol* 2004;59:743-752.

ABSTRACT & COMMENTARY

Blood Transfusion in Cardiac Disease Patients

By Michael Crawford, MD, Editor

SYNOPSIS: An observational study confirms the hypothesis that ischemic heart disease patients may do better with higher hemoglobin levels as compared to ICU patients without heart disease.

SOURCES: Ding YY, et al. Hemoglobin level and hospital mortality among ICU patients with cardiac disease who received transfusions. *J Am Coll Cardiol* 2015;66:2510-2518.

Rao SV, Vora AN. Transfusion in ischemic heart disease: Correlation, confounding, and confusion. *J Am Coll Cardiol* 2015;66:2519-2521.

The threshold hemoglobin (Hgb) level for red blood cell transfusion in hospitalized patients with cardiac disease is controversial. Thus, investigators from Boston University studied the Veterans Affairs (VA) electronic database to determine the Hgb level at which blood transfusion was associated with lower hospital mortality in medical ICU patients with cardiac disease. ICU admissions who had at least one transfusion in the first 30 days were the transfusion group; all others were the no transfusion group. The Hgb nadir was the lowest level before transfusion, or if not transfused the lowest level in the first 30 days in the ICU. Other variables included ICU admission diagnoses, comorbid conditions, and demographic characteristics. Researchers used adjusted linear regression analyses to analyze

more than 5 years of ICU admissions data. Among the 258,826 ICU admissions, hospital death occurred in 12% and transfusions were noted in 12% during the first 30 days in the ICU. In addition to being older and sicker, those who died were twice as likely to have received a transfusion. In patients without cardiac disease, transfusion was associated with reduced adjusted hospital mortality when Hgb was < 7.7 g/dL. Above this level, transfusion was associated with higher mortality. In patients with cardiac disease, the corresponding level was 8.7 g/dL and 10 g/dL when the ICU admission diagnosis was acute myocardial infarction (MI). Sensitivity analyses in a smaller subset with more complete data showed that the Hgb levels below which mortality was reduced by transfusion

could be about 1 g/dL lower than that for the total population. The authors concluded that in patients admitted to the ICU with comorbid cardiac disease, the Hgb level below which transfusion was associated with lower hospital mortality was < 8-9 g/dL and < 9-10 g/dL if the admitting diagnosis was acute MI.

■ COMMENTARY

Since the 1999 publication of the Transfusion Requirements in Critical Care (TRICC) randomized trial, critical care physicians and hospitals have pushed to restrict blood transfusions to those with a Hgb < 7 g/dL because this group showed lower mortality vs the comparison < 10 g/dL group. Cardiologists were concerned when this advice was applied to patients with acute ischemic heart disease (IHD) because the myocardium extracts nearly all the oxygen to it from the blood. The only way to deliver more oxygen to the myocardium is to deliver more oxygen, and a low Hgb would limit this. Some small observational studies supported this belief that higher Hgb thresholds for transfusion in IHD patients lowered mortality, but not all. Randomized, controlled trials (RCT) in acute coronary syndrome patients were called for. Two small pilot RCTs with a total of 155 patients showed conflicting results. It now seems unlikely that a large RCT will ever be conducted on this topic.

Given this background, this mega-observational analysis of more than 250,000 ICU admissions in the VA health system is of interest. It confirmed the TRICC study by showing that in ICU patients with no cardiac disease, the beneficial threshold was 7-8 g/

dL, but in patients with cardiac comorbidities it was 8-9 g/dL and with acute MI it was 9-10 g/dL. Interestingly, both the American Association of Blood Banks and the American College of Cardiology/American Heart Association guidelines recommend a threshold of < 8 g/dL for patients with IHD. Thus, the weight of evidence and opinion seems to support higher Hgb thresholds for transfusion in IHD patients. The authors wisely suggested that there is probably a continuum of risk in ICU patients different from those with isolated medical disease, those with cardiac comorbidities, and those admitted with acute coronary syndrome. Also, some acute coronary syndrome patients may have severe medical illnesses, such as septic shock and pneumonia. Thus, considerable clinical judgment is required, and Hgb threshold levels are just guidelines.

There are significant limitations to this study. The accompanying editorial points out that the statistical techniques used are somewhat novel for an observational study and not fully vetted. Of course, the larger the study, the less likely all the details one would desire are present. For example, we do not know the do-not-resuscitate status of the patients. Also, only 3% of the study population is women, but that represents about 7000 individuals. In addition, the data analyzed is from 2001-2005. Newer concepts and therapies may have altered ICU care in the last 10 years. Finally, this study does not shed any light on heart failure patients, which is an even more complex situation. For now, the transfusion Hgb threshold for IHD patients should increase at least 1 g/dL to < 8 and perhaps higher, especially for acute MI patients. ■

BRIEF REPORT

Fecal Microbiota Transplantation: Patients Need No Convincing

By Carol A. Kemper, MD, FACP

Clinical Associate Professor of Medicine, Stanford University, and Division of Infectious Diseases, Santa Clara Valley Medical Center

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

SOURCES: Drekonja D, et al. Fecal microbiota transplantation for *Clostridium difficile* infection. A systemic review. *Ann Intern Med* 2015;12:630-638.

Surawicz CM. Fecal microbiota transplantation: What we know and what we need to know. *Ann Intern Med* 2015;162:662-663.

Relapsing and refractory *Clostridium difficile* infection (CDI) has become a real challenge for clinicians and affected patients alike. Some patients wind up in a seemingly never-ending cycle of illness, gradual improvement, followed by a prolonged vancomycin taper, and eventual relapse. Relapse occurs in 15-30% of patients following an

initial (successfully treated) episode, and further relapse occurs in > 50% of those with second or subsequent episodes. Reports of successful resolution of this nasty infection using fecal microbiota transplantation (FMT) has generated enthusiasm. But available studies vary in their approach, their timing, the frequency of treatment (single dose

vs multiple doses over several days), and several guidelines now have been proposed for screening of potential donors. Some recommend FMT for those with two or more episodes, whereas the American College of Gastroenterology suggests FMT can be considered in those with three or more episodes.

Researchers performed a systematic review of the available literature related to FMT. Two randomized, controlled trials, 28 case series, and five case reports were identified for a total of 561 FMT subjects. Combining the results of the two randomized clinical trials, 27 of 36 patients treated with FMT had resolution of symptoms (75%). One of these studies administered material via nasogastric (NG) tubes, with successful resolution of symptoms in 81% at 3 months. In contrast, < 30% of patients in the two comparator arms receiving vancomycin treatment or vancomycin lavage had sustained resolution of symptoms at 3 months. In the first study, FMT was administered following 4-5 days of orally administered vancomycin (500 mg four times daily). Interestingly, 8 of the 43 patients included in this study were enrolled after their first episode of CDI. In the second randomized, controlled study, FMT was administered via NG vs colonoscopy in 20 patients, with resolution of symptoms in 60% vs 80% ($P = 0.63$). FMT was administered 3 days following completion of anti-CDI treatment.

In the various case series, researchers performed FMT in 480 patients with a history of 3-12 relapses over a 3-27 month period. Although none of these studies included a comparator arm, 85% reportedly remained disease-free following administration of FMT. In addition to these, there were seven smaller non-comparator studies for patients with refractory CDI, all using various methods, with an overall resolution rate of 55%. Symptomatic improvement was observed in 0-100%.

A third randomized, controlled trial, not published in time to be included in this analysis, demonstrated

successful resolution of symptoms in 90% of patients treated with FMT vs 26% in a vancomycin treatment group; researchers ended the study prematurely because of this substantial difference in favor of FMT.

In conclusion, FMT appears effective in approximately 55-90% of patients with relapsing and refractory CDI, and will prove a blessing to those who have been in a miserable cycle of recurrent disease. Observed side effects were minimal and included complaints of cramping, bloating, nausea, transient fever, and dizziness. One patient receiving FMT through a misplaced NG tube developed pneumoperitoneum and polymicrobial bacteremia.

Many questions remain, including who, what, and how. Various protocols are used to screen donors, and methods for administration of FMT differ. For those without access to stool, one company is marketing frozen stool from pre-screened healthy donors. I've had several enterprising patients who have tried various approaches, including small home tap water enemas mixed with stool (strained to remove the peas and carrots), to capsules stuffed with a spouse's stool, kept refrigerated, and swallowed the day following completion of orally administered vancomycin. A couple of patients have tried 10 capsules twice a day for 1-2 days, one of whom relapsed a week later, and tried it again with success. While expressing initial reluctance, patients were quick to embrace this approach following yet another relapse. One of the randomized, controlled trials above indicated that patients were initially squeamish, but when contacted 3 months later, 97% said they would do it again.

It's amazing that such a simple procedure — administration of a small amount of fecal material — can effect such an important change in your bowel flora. But that is how we develop our flora, with ingestion of fecal material from the world around us, bit by bit. As one of my favorite instructors is fond of saying, "Think of the world as covered by a thin layer of feces." ■

ABSTRACT & COMMENTARY

Is Sodium Restriction Detrimental in Chronic Heart Failure?

By *Van Selby, MD*

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

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

SYNOPSIS: In an observational study of outpatients with NYHA class II or III heart failure, dietary sodium restriction (< 2500 mg/day) was associated with increased risk of death or heart failure hospitalization.

SOURCE: Doukky R, et al. Impact of dietary sodium restriction on heart failure outcomes. *JACC Heart Fail* 2016;4:24-35.

Dietary sodium restriction is perhaps the most common self-care recommendation patients with

chronic heart failure (HF) receive. However, data evaluating the effectiveness of sodium restriction are

sparse, and the few studies that do exist have shown conflicting results.

To evaluate the relationship between dietary sodium restriction and clinical outcomes in chronic HF, Doukky et al analyzed data from the HF Adherence and Retention Trial (HART), a multicenter study of 902 patients with New York Heart Association (NYHA) functional class II or III systolic or diastolic HF. Patients were followed for a median of 36 months, and sodium intake was assessed using a food frequency questionnaire. Patients were classified as either sodium restricted (< 2500 mg/d) or unrestricted (\geq 2500 mg/d), and propensity score matching was used to address possible confounders. The primary outcome was the composite of death or HF hospitalization.

Sodium restriction was associated with a significantly higher risk of death or HF hospitalization (42.3% vs 26.2%; hazard ratio [HR], 1.85; $P = 0.004$). The difference was primarily due to higher rates of HF hospitalization (HR, 1.82; $P = 0.015$), though there was also a nonsignificant increase in the rate of death ($P = 0.074$). Subgroup analyses found the increased risk associated with sodium restriction was particularly high in patients not taking angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers (HR, 5.78; $P = 0.002$) and patients with milder NYHA class II symptoms (HR, 2.36; $P = 0.003$). Sodium restriction was not associated with any significant effect on quality of life, 6-minute walk distance, or symptom severity. The authors concluded that dietary sodium restriction may have a detrimental effect on outcome in patients with symptomatic chronic HF. They stress that a randomized clinical trial is warranted to resolve the issue.

■ COMMENTARY

Excessive sodium intake is associated with fluid retention, and many episodes of acute decompensated HF are often attributed to “sodium binges” in patients with stable chronic HF. For decades, sodium restriction has been a cornerstone of appropriate HF management, and the benefits of sodium restriction were so obvious that a trial evaluating its effectiveness seemed unnecessary. Current U.S. guidelines recommend patients with symptomatic HF restrict sodium intake to between 2000-3000 mg/day.

More recently, investigators are evaluating the effectiveness of sodium restriction more rigorously, and the results have been mixed. Several small studies have shown a clear benefit, with decreased signs and symptoms of HF as well as improved event-free survival. However, other studies have shown no clear benefit associated with sodium restriction, especially in patients

with milder (class I-II) HF. The Doukky study is important for two reasons. First, the patients were recruited from a large, multicenter clinical trial. Second, the study evaluated an objective clinical outcome and found increased adverse outcomes among sodium-restricted patients.

Why would sodium restriction be harmful? Small studies have shown that sodium restriction increases neurohormonal activation by worsening intravascular volume depletion. Sodium restriction may also worsen hemodynamics, with a decrease in cardiac index and increase in systemic vascular resistance. In the Doukky study, patients not receiving angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers showed an especially high risk of adverse events with sodium restriction, suggesting the effect is mediated through neurohormonal pathways. Interestingly, sodium restriction was associated with a greater increase in adverse outcomes among patients with milder, class II symptoms. This is similar to what has been reported in other studies. It is possible that more symptomatic (class III) patients are particularly prone to hypervolemia, and, therefore, sodium restriction is beneficial for preventing worsening fluid overload. Class II patients, on the other hand, experience the detrimental neurohormonal activation from sodium restriction without seeing the benefits related to hypervolemia.

Limitations include the retrospective design, small sample size, and use of a food frequency questionnaire to measure dietary sodium intake. The authors used propensity matching to eliminate confounders, but it is still possible the sodium-restricted patients comprised a sicker group overall. This study offers no information regarding the utility of sodium restriction during hospitalization for acute HF.

Despite these limitations, the Doukky study adds to a growing body of research suggesting dietary sodium restriction may not be beneficial, perhaps even harmful in chronic HF. In response to this increasing evidence, the most recent European guidelines have removed any formal recommendation regarding sodium restriction, and the 2013 American Heart Association/American College of Cardiology guidelines downgraded the strength of their long-standing recommendation regarding dietary sodium restriction from class I (recommended) to class IIa (reasonable). Given the prevalence of chronic HF and the widespread use of recommendations regarding dietary sodium intake, many in the field echo the authors' call for a randomized trial to rigorously evaluate the effectiveness of these recommendations. Until then, there is no clear evidence to support aggressive sodium restriction in chronic HF, especially in patients with mild disease. ■

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CME QUESTIONS

1. Which of the following are reasons per guidelines to discontinue long-term opioid use?

- A. Misuse of opioids by the patient
- B. The patient doesn't have clinical signs of pain such as elevated blood pressure or heart rate.
- C. Adverse event, such as overdose
- D. The patient has developed tolerance
- E. A and C

2. Based on the study by Claessens et al., the use of CT scanning in patients presenting with a suspicion of community-acquired pneumonia (CAP) demonstrated:

- A. The cost-effectiveness of using a chest CT scan in the evaluation of CAP
- B. No clinical benefit
- C. More accurate diagnosis but not change in the use of antibiotics
- D. An increase in the proportion of patients in whom CAP was excluded
- E. All of the above

3. Though not yet confirmed by a prospective randomized trial, according to the large observational study by Ding and colleagues, what is the best hemoglobin transfusion threshold for ICU patient with comorbid cardiac disease?

- A. < 7 mg/dL
- B. < 8 mg/dL
- C. < 9 mg/dL
- D. < 10 mg/dL

CME OBJECTIVES

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

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

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