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ABSTRACT & COMMENTARY

Overdiagnosis of Chronic Kidney Disease in the Elderly

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SYNOPSIS: Older patients experience a physiological decline in estimated glomerular filtration rate. However, if the same levels are used to define chronic kidney disease for all adults, older patients not at a higher risk for kidney failure might still be classified with the disease.

SOURCE: Liu P, Quinn RR, Lam NN, et al. Accounting for age in the definition of chronic kidney disease. *JAMA Intern Med* 2021;181:1359-1366.

Investigators in Canada studied linked laboratory and administrative data that had accumulated from April 1, 2009, to March 31, 2017, for adults age 65 years and older with incident chronic kidney disease (CKD). Here, the authors defined CKD as an ongoing reduction in estimated glomerular filtration rate (eGFR) for more than three months below a fixed eGFR threshold or an age-adapted eGFR threshold. Non-CKD controls were age 65 years or older with a continuous eGFR of 60 mL/min/1.73 m^2 to 89 mL/min/1.73 m^2 for longer than three months and mild/normal albuminuria.

Compared to the age-adapted group, the fixed-threshold group was at a lower risk of kidney failure (1.7% vs. 3% at five years) and death (21.9% vs. 25.4%). In the fixed-threshold group, 75% of patients were age 65 years or older, with a baseline eGFR of 45 mL/min/1.73 m^2 to 59 mL/min/1.73 m^2 and mild/normal albuminuria. Compared to those in the non-CKD control group, the five-year risks of kidney failure and death among these older patients were similar. The risk of kidney failure was 0.12% or lower in both cohorts. The authors concluded current criteria for diagnosing adults with CKD may result in the overdiagnosis in seniors who are not at higher risk for kidney failure.

■ COMMENTARY

Controversy over the criteria for diagnosing CKD has been present in the nephrology literature over the past decade.[1-4] Some academic nephrologists have called

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for age-related criteria for diagnosing CKD to avoid overdiagnosis in seniors. There are normal age-related changes in kidney function that do not increase the risk of kidney failure.[5] Diagnosing any patient with a disease harms their sense of well-being, regardless of whether the disease is present.[6]

The eGFR measurement is a relatively new part of the routine chemistry panel. Serum creatinine remains a useful and reliable measure of kidney function. Some have called for an increase in the normal range for creatinine up to 1.5 mg/dL in seniors, especially those older than age 80 years.[6] Since most of my patients are older than age 80 years, I reassure them daily their kidneys are fine and will live and function as long as they do. In primary care, we could reduce the referrals to nephrologists and avoid the CKD diagnosis in many seniors. The eGFR rate and serum creatinine level are important measures for the appropriate dosing of some mediations, and that is good geriatric practice. ■

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ABSTRACT & COMMENTARY

Resistance Erodes Standard Treatment for Pneumonia

By Carol A. Kemper, MD, FACP

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

SOURCE: Haessler S, Lindenauer PK, Zilberberg MD, et al. Blood cultures versus respiratory cultures: 2 different views of pneumonia. *Clin Infect Dis* 2020;71:1604-1612.

To examine whether current guidelines for the treatment of pneumonia remain appropriate, researchers conducted a large multicenter study of adults with pneumonia admitted to 177 U.S. hospitals between 2010 and 2015. Patients admitted with a principal diagnosis of pneumonia, respiratory failure, acute respiratory distress syndrome, or sepsis with a secondary diagnosis of pneumonia, and who also had blood and/or respiratory cultures obtained on admission were included in the analysis. A total of 138,561 hospitalizations met criteria, of which 68% were considered community-acquired pneumonia (CAP) and 32% were deemed healthcare-associated pneumonia (HCAP).

Blood cultures were obtained on admission in 99% of hospitalizations, and respiratory cultures were obtained in 18%. Positive cultures were infrequent. Only 9.3% of all admissions tested positive, including 4.6% with a positive respiratory culture alone, 4.3% with a positive blood culture alone, and 0.3% with both positive respiratory and blood cultures. In those able to produce a sputum specimen, respiratory cultures were positive in 28%, and patients with HCAP were more likely than those with CAP to produce a positive sputum culture (33% vs. 25.4%; $P < 0.001$). Of all blood cultures obtained, only 4.7% were positive.

Among those with positive blood cultures alone, *Streptococcus pneumonia* (33%) and *Staphylococcus aureus* (22%) were the most common organisms isolated, followed by *Escherichia coli* (11.8%), *Klebsiella* spp. (4.6%), *Pseudomonas aeruginosa* (3.5%),

group B strep (2.7%), *Haemophilus influenzae* (2%), and *Proteus mirabilis* (1.6%). More than one-third of *S. aureus* bacteremias were methicillin-resistant (36%). In contrast, in those with only positive respiratory cultures, *S. aureus* (33.6%) and *Pseudomonas aeruginosa* (17%) were the most common isolates. In those with both positive blood and respiratory cultures, *S. aureus* was more common (44.5%; 41% were methicillin-resistant), followed by *S. pneumoniae* (32%) and *Pseudomonas aeruginosa* (7.7%).

The prevalence of resistance to recommended first-line CAP antibiotics (i.e., ceftriaxone plus azithromycin or a respiratory quinolone) was assessed by organism and by culture site. A total of 209 patients were excluded because their organisms lacked clear Clinical & Laboratory Standards Institute (CLSI) breakpoints. Overall, 42% of admissions with a positive culture grew an organism resistant to first-line therapy for CAP, including 27% of those with positive blood cultures. Gram-negative organisms isolated in either blood or respiratory cultures were more likely to be resistant to CAP therapy than gram-positives (51.8% vs. 35.4%). Patients with only positive respiratory cultures were twice as likely to yield organisms resistant to CAP therapy, but their outcomes were better, suggesting some organisms represented colonizers rather than true pathogens.

Although two-thirds of patients in this study were considered to have CAP and one-third HCAP, empirical antibiotic therapy administered at the time of admission did not necessarily reflect these designations. For those with only positive respiratory, only positive blood, or both positive respiratory and blood cultures, anti-methicillin-resistant *S. aureus* (MRSA) antibiotics were administered to 42%, 48%, and 66%, respectively ($P < 0.001$). Similarly, HCAP-guideline antibiotics were administered in 11.8%, 15.7%, and 27%, respectively, and four or more antibiotics were administered in 17.5%, 21%, and 33%, respectively. This suggests providers were cognizant of the severity of disease at presentation and the risk of MRSA and multidrug-resistant organisms (MDRO) in some patients.

Despite these efforts, patients with both positive blood and sputum cultures generally exhibited more acute and chronic illness, with significantly higher case fatality rates (25%) than those patients with only positive blood (12%) or respiratory cultures (11%). Also, they recorded significantly longer lengths of stay.

■ COMMENTARY

Predicting the bacterial etiology of pneumonia on presentation to the hospital, when empirical antibiotic therapy must be chosen, is challenging. The choice depends on many factors, including acuity of the presentation, chronicity of underlying disease, recent residence in long-term care, and the anticipated flora. Not mentioned in this article is the benefit of "flagging" those patients with recognized MDROs from prior cultures in an electronic system, as well as the use of nares MRSA polymerase chain reaction to identify those patients at risk for MRSA pneumonia. These data suggest CAP therapy may no longer be relevant for many patients with CAP, and the required use of the current CAP bundle with limited antibacterial therapy choices should be re-assessed. ■

ABSTRACT & COMMENTARY

Slow, Steady, and Synchronized Wins the Race

By Joshua Moss, MD

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SYNOPSIS: In patients with atrial fibrillation and heart failure, definitive rate control via atrioventricular junction ablation and biventricular pacing resulted in a significant reduction in all-cause mortality vs. pharmacologic rate control.

SOURCE: Brignole M, Pentimalli F, Palmisano P, et al. AV junction ablation and cardiac resynchronization for patients with permanent atrial fibrillation and narrow QRS: The APAF-CRT mortality trial. *Eur Heart J* 2021;Aug 28:ehab569. doi: 10.1093/eurheartj/ehab569. [Online ahead of print].

Ideal management of atrial fibrillation (AF) in patients with heart failure remains a challenge. Rhythm control via left atrial catheter ablation in this population has been associated with a lower mortality rate compared with medical therapy. However, restoration and maintenance of sinus rhythm in patients with longstanding persistent AF can be much more difficult.

Brignole et al studied the effect of atrioventricular (AV) junction ablation plus biventricular pacing

(cardiac resynchronization therapy [+CRT]) for rate control of "permanent AF" compared with pharmacologic rate control.

After exclusions, 133 heart failure patients (mean age, 73 years; 53% male) from 11 European centers were randomized 1:1 to AV junction ablation +CRT or drug therapy. Patients had to have experienced symptomatic AF for more than six months that was considered unsuitable for AF ablation or for which AF ablation had failed and QRS duration ≤ 110 msec. Randomization was stratified by ejection fraction (EF; ≤ 35% and > 35%). The mean EF was 41%. An implantable cardioverter-defibrillator (ICD) was implanted in both groups if clinically indicated.

In the ablation +CRT arm, the procedures were performed within 30 days of randomization. In the drug therapy arm, significantly more patients were on digoxin after a planned 30-day optimization period (60% vs. 32%), with therapy optimized to achieve a resting heart rate < 110 bpm. More than 80% of patients in both arms remained on beta-blocker therapy. Six patients in the ablation +CRT arm either did not undergo ablation or failed cardiac resynchronization therapy implant, and 18 patients in the drug arm crossed over to ablation +CRT. Investigators ended the trial prematurely after interim analysis met prespecified criteria for stopping. The primary outcome measured was all-cause mortality, which occurred in 11% of patients in the ablation +CRT arm and 29% of patients in the drug arm (HR, 0.26; 95% CI, 0.10-0.65; $P = 0.004$) using an intention-to-treat analysis.

In a prespecified subgroup analysis, the overall mortality benefit was similar in patients with EF > 35% (HR, 0.27; 95% CI, 0.08-0.84; $P = 0.024$) and EF ≤ 35% (HR, 0.34; 95% CI, 0.06-1.92; $P = 0.22$). Appropriate ICD shocks for ventricular tachyarrhythmias occurred in four patients in the ablation +CRT arm and one patient in the drug arm. Five patients experienced inappropriate ICD shocks for AF with rapid ventricular rates, all in the drug arm. Three patients required lead repositioning, and one patient required repeat AV junction ablation. A sensitivity analysis to assess the potential interaction of differential digoxin usage was consistent with the primary analysis. The authors concluded AV junction ablation +CRT was superior to pharmacologic therapy alone for preventing mortality in patients with heart failure and AF.

■ COMMENTARY

Several trials have demonstrated improved outcomes with catheter ablation of AF via pulmonary vein isolation (PVI) in patients with heart failure, generally attributed to superior rhythm control and less exposure to potentially toxic antiarrhythmic drugs. For example, the AATAC trial showed a 56% reduction in all-cause mortality with ablation vs. amiodarone.[1] The CASTLE-AF trial showed a 47% reduction in all-cause mortality with catheter ablation vs. any medical therapy (whether rate or rhythm control).[2] However, duration of AF before enrollment in those trials was relatively short overall (mean duration = 8.5 months in AATAC; 71% less than one year in CASTLE-AF).

By contrast, the APAF-CRT trial authors studied patients with "permanent" AF, with a median arrhythmia duration of 19 months in the CRT group and 18 months in the drug group. Patients were, on average, nine years older than CASTLE-AF participants and 12 years older than AATAC participants. They also likely were more ill, with 68% presenting with New York Heart Association class III or worse heart failure symptoms (vs. 29% in CASTLE-AF). In fact, mortality in the drug therapy arm of APAF-CRT was 29% through a median follow-up of 29 months vs. 25% in the medical therapy arm of CASTLE-AF through a median follow-up of 38 months. Thus, the previously demonstrated benefits of more extensive left atrial catheter ablation likely would not have been expected in the APAF-CRT population.

Long-term rhythm control via PVI generally is poor in permanent AF (particularly with only one procedure), and procedural complications likely are more frequent in older patients with less clinically stable heart failure. Ablation of the AV junction plus pacemaker implant typically is simpler and safer, with far less need for repeat procedures. Using a CRT device, even in patients with EF > 35%, alleviates the long-term risks associated with RV-only pacing. Hypothetically, conduction system pacing would produce similar or better results, but longer-term risks and benefits require further study in this population.

The APAF-CRT population was small, and medical rate control was not achieved or assessed in a standardized way. However, median resting heart rate in the drug therapy arm was 82 bpm after only 30 days of optimization, suggesting a reasonable degree of control was achieved (with digoxin in many, and amiodarone or sotalol in about 10%). The difference in outcomes was profound despite a relatively high percentage of crossovers.

Overall, the APAF-CRT trial confirms an additional tool for lowering the mortality rate in certain patients with heart failure and AF, and a powerful tool at that. For patients without longstanding arrhythmia who are reasonable candidates for PVI, catheter ablation of AF should be strongly considered based on multiple prior studies. For patients with EF ≤ 35% and left bundle branch block, CRT likely is indicated anyway, and AV node ablation clearly can improve biventricular pacing burden. However, for symptomatic heart failure patients in whom the AF is deemed more permanent, even with

narrow QRS or EF > 35%, AV junction ablation and CRT implantation may win the race. ■

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ABSTRACT & COMMENTARY

Homelessness and COVID-19

By Carol A. Kemper, MD, FACP

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

SOURCE: Cha S, Henry A, Montgomery MP, et al. Morbidity and mortality among adults experiencing homelessness hospitalized with COVID-19. *J Infect Dis* 2021;224:425-429.

Cha et al examined risk factors and outcomes for homeless adults admitted to an acute care hospital with COVID-19. Using the COVID-NET population-based surveillance system for acute care hospitalizations in 10 different states, plus the Influenza Hospital Surveillance Project for four additional states, data on laboratory-confirmed COVID-19 hospitalizations were collected. Among nearly 29,000 hospitalizations, only 8,728 cases had sufficient documentation regarding housing at the time of admission. Of these, 199 were homeless adults. The median age was 53 years, and 84% were Black, Latino, or other non-Hispanic other race/ethnicity. Most patients (83%) had at least one significant health condition, 32% had diabetes, and 24% were considered obese; tobacco use (46%) and alcohol abuse (34%) were common; and 8% had mental health issues. A majority (54%) of these homeless patients were hospitalized for > 4 days, 17% were admitted to the ICU, and 11% required mechanical ventilation. Six patients died, five of whom were age 50 years or older. As has been observed previously, disease severity was associated with increasing age.

■ COMMENTARY

Despite the anticipated poor outcomes, I was surprised this homeless cohort performed this well. Mortality for COVID-19 cases admitted to the hospital early during the pandemic was reportedly as high as 12% to 18%. A 2020 study of 11,210 COVID-19 admissions to 92 acute care hospitals across 12 states (many of which were included in this homeless study) revealed an all-cause mortality of 20.3%, and 31.8% required mechanical ventilation.[1] More recent data suggest hospital mortality from COVID-19 may have improved. In a 2021 study of 192,550 adult hospitalizations with COVID-19 at 555 acute care hospitals in the United States, 13.6% of adults died during the index hospitalization and another 3% were transitioned to hospice care.[2] Since February 2020, our community hospital in Mountain View, CA, has provided care for 1,000 COVID-19 patients, with an overall mortality of 9.3%. One-fourth of admissions required ICU care and one-fourth of those died. That the homeless cohort in this study experienced much better outcomes than any of these data suggests they may have been admitted for other complicating health reasons or perhaps for psychosocial concerns.

The COVID-19 pandemic has heightened the need for better care and planning for homeless persons. Those who are homeless, especially people who reside in camps or shelters, are at higher risk for COVID-19 infection; their hygiene, dentition, and general health suffer as the result of their homelessness, and their poor health belies their years, putting them at risk for more severe COVID-19. It also makes COVID-19 discharge planning a challenge; thankfully, our public health department has invested in several "COVID hotels" with private rooms, hot showers, and meals as needed.

The first step would be screening for homeless status on admission to any acute care hospital. Only 30% of admissions identified in this study had adequate documentation of housing. In January 2019, California Senate Bill 1152 was created, requiring acute care hospitals to screen for homelessness on admission and to offer appropriate vaccinations, such as hepatitis A and influenza, as well as screening for appropriate infectious diseases, such as HIV, hepatitis B, and tuberculosis. Originally intended to halt an outbreak of hepatitis A in the homeless populations in several California counties, this extra screening in care for homeless persons is helping solve many problems, including the administration of COVID-19 vaccination to this vulnerable population. ■

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ABSTRACT & COMMENTARY

Surgical Approaches to Decompression in Degenerative Lumbar Spondylolisthesis

By Joshua Weaver, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

SYNOPSIS: For patients with symptomatic lumbar stenosis and single-level spondylolisthesis who were refractory to conservative treatment, there was no significant difference between outcomes in those who underwent decompression surgery with instrumented fusion vs. decompression surgery without fusion.

SOURCE: Austevoll IM, Hermansen E, Fagerland MW, et al. Decompression with or without fusion in degenerative lumbar spondylolisthesis. *N Engl J Med* 2021;385:526-538.

Low back pain radiating to the legs often is caused by degenerative lumbar stenosis from disc bulges and overgrowth of the facet joints and ligaments causing compression of the nerve roots. Spondylolisthesis, or misalignment of the spine in which one vertebra has slipped forward from the vertebra below it, also commonly can contribute to stenosis and pain. If this pain does not improve with medication and physical therapy, surgical decompression may be performed to relieve symptoms. Surgical techniques vary widely, with some techniques involving instrumented fusion of the vertebral bodies (e.g., with screws, rods, or cages), and other techniques that are less invasive and do not require fusion. In 2016, the authors of two studies compared decompression with or without fusion in lumbar stenosis, finding slightly different results. Subsequent analyses of these studies led to ambiguous conclusions and persistent questions regarding the superiority of one technique over the other.[1,2]

In this trial, 267 people with low back pain radiating to the legs that was refractory to conservative treatment for three months who had lumbar spinal stenosis and at least 3 mm of spondylolisthesis at the stenotic level were randomized into two groups: decompression-alone and decompression with fusion. The decompression alone group underwent a posterior decompression that was bilateral, ipsilateral, or ipsilateral with crossover to the contralateral side. The fusion group underwent posterior decompression with implantation of various hardware at the discretion of the surgeon.

Demographic characteristics were similar among the two groups. Outcomes were measured at three months, one year, and two years. The primary outcome was a reduction in a disability score (Oswestry Disability Index [ODI]) by 30% or more from baseline by two years. Secondary outcomes included mean change in the ODI score, a claudication scale, functional impairment scale, satisfaction with treatment score, numeric rating scale for leg and back pain, and a quality-of-life scale.

For the primary outcome, 71.4% in the decompression-alone group and 72.9% in the fusion group showed a reduction of at least 30% in the ODI score, showing noninferiority of decompression alone compared to decompression with fusion. Similarly, no significant difference was found in the secondary outcomes of improvement in claudication, functional impairment, leg and back pain, satisfaction, or quality of life. Duration of surgery, length of hospitalization, and blood loss during surgery were significantly less in the decompression-alone group. There was a trend toward the patients in the decompression-alone group needing re-operation by two years compared to the fusion group, although this was not statistically significant.

■ COMMENTARY

Although studies from 2016 have suggested similar outcomes in different surgical techniques for lumbar stenosis (decompression with fusion vs. decompression without fusion), there has remained a debate over which type of surgery is superior. This recent study adds to the body of evidence indicating surgical decompression without fusion is not inferior to surgical decompression with fusion. This is important, since minimally invasive surgery without fusion is less complicated, less invasive, cheaper, and possibly safer than surgery involving fusion.

There were important limitations to this study. It is difficult to generalize this study to all patients with lumbar stenosis since it was limited to those with spondylolisthesis at one level. Some experience this degenerative condition at multiple levels, and some live with lumbar stenosis without any spondylolisthesis. Patients with severe neural foraminal stenosis were excluded in this study, although it is not uncommon

for patients to experience this condition along with spondylolisthesis. Patients with prior fusion surgeries were excluded. Twenty percent of patients included exhibited dynamic instability of the spondylolisthesis on flexion/extension imaging, but these patients were lumped with the total group, and subgroup analysis on surgery type (fusion vs. decompression without fusion) in this subgroup could not be conducted since this study was not powered adequately to do so.

Regardless, this is a valuable study that highlights the fact that in cases of single-level spondylolisthesis and lumbar stenosis, a less invasive surgical approach produces similar outcomes to more invasive fusion surgery. In general, less invasive approaches are favored because of reduced risk of complications and faster recovery. This is an important discussion clinicians can have both with their patients and their colleagues regarding treatment options. However, surgical treatment options often are quite nuanced and involve many factors, including number of levels of spondylolisthesis, presence of scoliosis, presence of significant neural foraminal stenosis, presence of dynamic instability with various movements of the spine, history of osteoporosis, baseline activity levels, and history of prior surgical fusion, among others.

Many of these conditions may lead a surgeon to choose fusion as an empirically superior alternative to decompression without fusion. Future studies should include these subgroups for further characterization. Comparison of specific minimally invasive decompression surgical techniques and hardware types for fusion surgeries need to be studied in more detail, too. ■

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PHARMACOLOGY UPDATE

Celecoxib and Tramadol Hydrochloride Tablets (Seglentis) C-IV

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

The FDA has approved an analgesic combination of celecoxib, a selective cyclooxygenase-2 inhibitor, and tramadol, an opioid analgesic. The formulation is a co-crystal containing 1:1 molecular ratio of tramadol and celecoxib (CTC). It is distributed as Seglentis.

INDICATIONS

CTC can be prescribed to adults to help them manage acute pain that is severe enough to require an opioid analgesic.[1] It should be reserved for patients for whom non-opioid analgesics have not or are not expected to provide adequate analgesia, or for patients who have not tolerated or are not expected to tolerate alternative non-opioid treatments.[1] Prescribers should consider prescribing naloxone based on the patient's risk for overdose.

DOSAGE

Each CTC tablet contains 56 mg of celecoxib as well as 44 mg of tramadol. The recommended initial dose is two tablets every 12 hours as needed for pain relief.[1] CTC should be used for the shortest duration possible and prescribers should consider the patient's pain severity; response; prior analgesic treatment experience; and risk factors for addiction, abuse, and misuse.[1] Patients should be monitored for respiratory depression for the first 24-72 hours of treatment.

POTENTIAL ADVANTAGES

This is a first-in-class active pharmaceutical ingredient of co-crystal of tramadol and celecoxib.[2] Pharmacologists took compounds with differing physiochemical properties and modified the intrinsic dissolution rate (IDR) profiles of each to provide a coordinated, more synchronized release vs. independent administration of each (separately or in a fixed dose combination). This could produce better pharmacodynamics and, ultimately, bimodal clinical benefit.

POTENTIAL DISADVANTAGES

The co-crystals carry the same warning for tramadol and other opioid analgesics (i.e., addiction, abuse, and misuse). Tramadol can lead to drug-drug interactions involving CYP3A4 and CYP2D6 and could produce serotonin syndrome and seizures. The warning label for celecoxib includes cardiovascular and gastrointestinal risk. The most frequently reported adverse reactions with CTC were nausea (30.1%), vomiting (15.8%), dizziness (16.9%), and headache (11.5%).[1] Both individual components are available in generic form

at similar dosages. CTC is classified as a Schedule IV controlled substance and requires a Risk Evaluation and Mitigation Strategy.

COMMENTS

The safety and efficacy of CTC was evaluated in a randomized, double-blind, double-dummy, parallel study in subjects with acute postoperative pain following unilateral first metatarsal osteotomy with internal fixation.[1] Subjects (n = 637) were randomized at a ratio of 2:2:2:1 to CTC two tablets every 12 hours, tramadol 50 mg every six hours, celecoxib 100 mg every 12 hours, or placebo. Subjects reported a mean baseline pain intensity of 6.7 on a 11-point (0-10) Numeric Pain Rating Scale. The primary efficacy endpoint was the timed weighted summed pain intensity difference over 48 hours (SPID48). The CTC group recorded statistically better mean SPID48 scores than any other groups after bunionectomy.[1]

CLINICAL IMPLICATIONS

CTC is a novel co-crystal product that synchronizes a bimodal approach of an NSAID and an opioid analgesic. A multimodal approach to pain management generally is recommended, with a goal of reducing opioid use.[3] Fixed-dose combinations limit the ability to use the lowest effective opioid dose, with ongoing reassessment of risks and benefits. Tramadol carries risks of addiction, abuse, and misuse. Furthermore, in a matched cohort study (n = 88,902), tramadol was associated with a higher rate of all-cause mortality within one year of initiation among individuals ≥ age 50 years with osteoarthritis vs. celecoxib, diclofenac, naproxen, and a rate similar to codeine (hazard ratios ranged from 1.70 to 1.88 vs. other NSAIDs).[4] Although CTC is novel in its bimodal approach for pain that requires an opioid analgesic, wide use in practice may be limited. Launch is planned for early 2022, and pricing is unavailable. ■

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CME QUESTIONS

1. What is the risk for an otherwise healthy patient age 65 years and older for kidney failure if their estimated glomerular filtration rate (eGFR) is 45 mL/min/1.73 m² to 59 mL/min/1.73 m²?
a. Twice the risk of kidney failure over the next 10 years vs. an eGFR of 60 mL/min/1.73 m² and higher
b. Twice the risk of requiring dialysis over the next 15 years vs. normal kidney function
c. Twice the risk of death over the next 10 years of kidney failure-related problems
d. No increased risk of kidney failure or death

2. Decompressive surgery for lumbar stenosis without fusion was noninferior to decompressive surgery with fusion within which group?
a. Scoliosis
b. Multilevel spondylolisthesis
c. Single-level spondylolisthesis
d. Neural foraminal stenosis

3. Which characterization of patients with heart failure and atrial fibrillation is most likely to record lower mortality rates with atrioventricular junction ablation plus cardiac resynchronization therapy vs. patients on drug therapy alone?
a. Paroxysmal atrial fibrillation
b. Persistent atrial fibrillation
c. Permanent atrial fibrillation
d. Asymptomatic atrial fibrillation