The Ochsner Journal 12:185–187, 2012

Advancing Evidence-Based Practice

A Quarterly Compilation of Research Updates Most Likely to Change Clinical Practice

Indranill Basu Ray, MD

Department of Hospital Medicine, Ochsner Clinic Foundation, New Orleans, LA
Section Editor, The Ochsner Journal

CARDIOLOGY

CYP2C19 Genotype May Not Increase Risk of Cardiovascular Events in Patients Taking Clopidogrel

Clopidogrel (Plavix) comes with a warning that recommends genetic testing for the CYP2C19 genotype prior to use. The American Heart Association and the American College of Cardiology maintain that insufficient evidence exists to recommend routine screening [J Am Coll Cardiol. 2010 Jul 20;56(4):321]. A new review of 32 studies (data from 42,016 patients with acute coronary syndrome or stable coronary heart disease) appears to support the dissenting view. An analysis limited to studies with at least 200 events (10,570 patients) showed no significant difference in cardiac event rates between CYP2C19 carriers and noncarriers. In a metaanalysis of 11,012 patients with the genotype, clopidogrel was associated with reduced risk of cardiovascular events compared to placebo (risk ratio 0.8, 95% confidence interval [CI] 0.72-0.89). This reduction was similar to that found in the overall analysis disregarding genotype (risk ratio 0.84, 95% CI 0.79-0.89) (level 2 [mid-level] evidence) [JAMA 2011 Dec 28;306(24):2704].

EMERGENCY MEDICINE

Use of CT Angiography in Low-Risk Patients With Suspected ACS Appears to Safely Increase Discharge From Emergency Department to Home

Patients with suspected acute coronary syndrome (ACS) are often admitted to the hospital from the emergency department (ED), but their symptoms often have noncardiac causes. Multidetector computed tomography angiography (MDCTA) can rule out significant coronary artery disease and may be able to rule out ACS. In a recent trial, 1,392 low-risk patients with suspected ACS were randomized to MDCTA or standard care. Of 929 patients randomized to MDCTA, 767 underwent the scan, and 83% of those had a negative result. The rate of discharge from ED to home was 49.6% for MDCTA vs 22.7% for standard care ($P<.05$, number needed to treat [NNT] 4). MDCTA was associated with a significantly shorter median hospital stay (18 hours vs 24.8 hours, $P<.001$). At 30-day follow-up, no patients in either group had died, and there were no significant differences in rates of acute myocardial infarction, revascularization, or invasive angiography (level 2 [mid-level] evidence) [N Engl J Med 2012 Apr 12;366(15):1393].

ENDOCRINOLOGY

Combination of Metformin Plus Insulin May Not Reduce Mortality Compared to Insulin Alone in Patients With Type 2 Diabetes

The American Diabetes Association and the European Association for the Study of Diabetes recommend the combined use of metformin and insulin for patients with type 2 diabetes mellitus who are inadequately treated with lifestyle modifications and oral antidiabetic agents [Diabetologia 2009 Jan;52(1):17]. A new review of 26 randomized trials compared the effects of combination therapy vs insulin alone in 2,286 patients. Metaanalyses showed no significant differences in all-cause mortality (risk ratio 1.3, 95% CI 0.57-2.99) or cardiovascular mortality (risk ratio 1.7, 95% CI 0.35-8.3) (level 2 [mid-level] evidence). No deaths occurred in 11 of 16 trials that reported mortality as an outcome, but follow-up was too short in most trials to draw reliable conclusions about mortality [BMJ 2012 Apr 19;344:e1771]. While a mortality or cardiovascular benefit from continuing metformin cannot be ruled out based on these data, the analysis shows that the benefit remains unproven.

HEMATOLOGY/ONCOLOGY

Ruxolitinib May Improve Survival in Patients With Myelofibrosis

Ruxolitinib, a selective inhibitor of Janus kinase 1 and 2, has been associated with clinical benefit in a previous case series of patients with myelofibrosis [N Engl J Med 2010 Sep 16;363(12):1117]. In a new trial,

309 patients with intermediate- to high-risk myelofibrosis were randomized to ruxolitinib vs placebo orally twice daily. At median follow-up of 51 weeks, mortality was 8.4% for ruxolitinib vs 15.6% for placebo (P=.05, NNT 14) (level 2 [mid-level] evidence). At 24 weeks, ruxolitinib was associated with significantly greater rates of patients with ≥50% reduction in total myelofibrosis-related symptoms (45.9% vs 5.3%, P<.001, NNT 3) and patients with ≥35% reduction in spleen volume (41.9% vs 0.7%, P<.001, NNT 3) [N Engl J Med 2012 Mar 1;366(9):799].

MIND-BODY MEDICINE/NEUROLOGY

Tai Chi Reduces Falls Compared to Resistance Training in Patients With Parkinson Disease

A recent trial evaluated the effects of tai chi to reduce falls in 195 patients with Parkinson disease. Patients with mild to moderate Parkinson disease were randomized to tai chi vs resistance training vs stretching for 60-minute sessions twice weekly for 24 weeks. At the end of treatment, the rate of falls was significantly lower in the tai chi group (62 total falls, corresponding to a rate of 0.22 falls per patient-month) than in either the resistance training group (133 falls, 0.51 falls per patient month, P=.05, vs tai chi), or the stretching group (186 falls, 0.62 falls per patient-month, P=.005, vs tai chi) (level 1 [likely reliable] evidence). Tai chi was also associated with significantly greater improvement in balance compared to both groups and significantly greater improvement in gait, strength, and motor scores compared to stretching [N Engl J Med 2012 Feb 9;366(6):511].

OBSTETRICS AND GYNECOLOGY

Ulipristal Acetate Controls Uterine Bleeding and Reduces Discomfort in Women With Symptomatic Fibroids

Two recent trials evaluated the efficacy of ulipristal acetate, a selective progesterone receptor modulator, in women planning to have surgery for symptomatic fibroids. In the PGL4001 Efficacy Assessment in Reduction of Symptoms Due to Uterine Leiomyomata (PEARL) I trial, 242 women with excessive uterine bleeding were randomized to oral ulipristal acetate (5 mg vs 10 mg daily) vs placebo. At 13 weeks, uterine bleeding was controlled in 91% of women taking ulipristal 5 mg, in 92% taking ulipristal 10 mg, and in 19% taking placebo (P<.001, NNT 2 for each ulipristal dose vs placebo) (level 1 [likely reliable] evidence). Amenorrhea rates were 73% for ulipristal 5 mg, 82% for ulipristal 10 mg, and 6% for placebo (P<.001, NNT 2 for each ulipristal dose vs placebo). Both ulipristal doses were associated with reduced discomfort (P≤.001), and no significant differences in surgical rates or adverse events were found [N Engl J Med 2012 Feb 2;366(5):409].

PEARL II compared the same 2 daily doses of ulipristal for 13 weeks vs 3 monthly intramuscular injections of leuprolide acetate 3.75 mg in 301 women. Rates of uterine bleeding were not significantly higher for ulipristal: 90% for ulipristal 5 mg, 94% for ulipristal 10 mg, and 86% for leuprolide (level 1 [likely reliable] evidence). The 10 mg ulipristal dose was associated with significantly greater bleeding control vs leuprolide in a per-protocol analysis (P=.03, NNT 12). The incidence of hot flashes was significantly lower in both ulipristal groups (11% for ulipristal 5 mg, 10% for ulipristal 10 mg, 40% for leuprolide, P<.001, NNT 4 for each ulipristal dose vs leuprolide), and no significant differences in pain reduction, surgical rates, or severe adverse events were found [N Engl J Med 2012 Feb 2;366(5):421].

ORTHOPEDIC SURGERY

Targeted Shoulder Exercises Improve Function and Reduce Surgery for Subacromial Impingement Syndrome

A recent trial evaluated the efficacy of a targeted exercise program to reduce the need for surgery in 102 patients with persistent subacromial impingement syndrome. Patients with symptoms for >6 months were randomized to 1 of 2 supervised exercise programs for 12 weeks. The targeted exercise program included eccentric strengthening exercises for the rotator cuff, concentric and eccentric strengthening exercises for the scapula stabilizers, and manual mobilization. The control program included

Level 1 [likely reliable] Evidence: research results addressing clinical outcomes and meeting an extensive set of quality criteria that minimize bias.

Level 2 [mid-level] Evidence: research results addressing clinical outcomes and using some method of scientific investigation, but not meeting the quality criteria to achieve level 1 evidence labeling.

Level 3 [lacking direct] Evidence: reports that are not based on scientific analysis of clinical outcomes. Examples include case series, case reports, expert opinion, and conclusions extrapolated indirectly from scientific studies.

general movement exercises for the neck and shoulder. The targeted exercise group had a significantly higher rate of patients reporting either recovery or large improvement in symptoms (69% vs 24%, $P<.001$, NNT 3) (level 1 [likely reliable] evidence). Surgery was performed on 20% of the targeted exercise group vs 63% of controls ($P<.001$, NNT 3) [BMJ 2012 Feb 20;344:e787].

Acknowledgment

The source of these research summaries is the DynaMed Weekly Update (http://dynamed.ebscohost.com/about/weekly-update), a compilation of articles selected from the top peer-reviewed medical journals as those most likely to change clinical practice. The editor gratefully acknowledges DynaMed's permission to present this material.