

Dabigatran reduces risk of stroke and embolism in patients with AF

Clinical question Is dabigatran safer and more effective than warfarin for the prevention of complications of atrial fibrillation (AF)?

Bottom line Dabigatran was slightly more effective than warfarin at preventing stroke and embolism, especially the dosage of 150 mg given twice a day, and may reduce all-cause mortality (number needed to treat [NNT] = 200 over 2 years). It will be important to balance efficacy with the higher cost but greater convenience of dabigatran when comparing it with standard warfarin therapy. (Level of evidence = 1b)

Synopsis Dabigatran etexilate is an oral alternative to warfarin that directly inhibits thrombin. In this study, patients were randomized to receive dabigatran, 110 mg twice a day; dabigatran, 150 mg twice a day; or warfarin targeted to an INR (International Normalization Ratio) between 2.0 and 3.0. Although patients and physicians were masked to the dose of dabigatran, they were not masked to the choice of dabigatran or warfarin. However, outcome assessors were masked to both, which is more important. The researchers enrolled 18,113 patients, with a mean age of 71 years. Groups were balanced at the start of the study, analysis was by intention to treat, and patients were followed up for a median of 2 years. Only 20 patients were lost to follow-up. In general, clinical outcomes were similar between the 110-mg dose of dabigatran and the warfarin. When compared with warfarin, the 150-mg dose of dabigatran was associated with a lower risk of stroke and death from vascular causes, but a slightly higher risk of MI. Major bleeding was less common with the 110-mg dose than with warfarin (but not with the 150-mg dose). On balance, the net benefit was similar between the two doses of dabigatran; the lower risk of ischemia with the higher dose was balanced by a lower risk of bleeding

with the higher dose. All-cause mortality was 3.75% in the 110-mg-dose group, 3.64% in the 150-mg-dose group, and 4.13% in the warfarin group. The comparison between dabigatran 150 mg and warfarin was of borderline statistical significance ($P = .051$, NNT = 200 for 2 years). Using the CHADS score as a measure of risk of stroke, only patients with a score of 3 or higher benefited from the lower dose, while all patients benefited from the higher dose.

Connolly SJ, Ezekowitz MD, Yusuf S, et al; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med*. 2009;361(12):1139-1151.

Ultrasonography may be best first test for detecting renal stones in children

Clinical question Which radiologic test should be ordered first for the evaluation of suspected urolithiasis in children?

Bottom line Although not as accurate as CT, ultrasonography (US) identified almost all clinically important renal stones in children presenting with suspected urolithiasis. The benefits of US include no ionizing radiation and lower costs. Stronger evidence from a randomized trial comparing outcomes from similar children initially undergoing either US or CT scanning is needed before setting a standard of practice. (Level of evidence = 1b)

Synopsis Although US has a lower sensitivity and specificity than CT for detecting renal stones in adults, US may be more accurate in children because of their lower body mass index. The benefits of US include no ionizing radiation and lower costs. These investigators prospectively enrolled 50 consecutive patients younger than 18 years presenting with acute signs or symptoms of urolithiasis. Each child underwent US and a CT scan, within 50 to 80 minutes of each other. The radiologist on call read each study, and two additional radiologists masked to clinical information also

independently reviewed each scan. Eight pediatric urologists independently reviewed clinical data and the official reading of the US first, then the CT, for all patients with discordant findings. Renal stones were identified in 68% of patients on CT and in 52% of patients on US. The average stone size missed by US was 2.3 mm. The overall sensitivity and specificity of US for detecting nephrolithiasis was 76% and 100%, respectively. This compares with the sensitivity and specificity of the noncontrast CT at 99% and 98%, respectively. A total of 16 discrepancies were identified between US and CT: In seven of these cases, the consensus agreement from the reviewing pediatric urologist was that the missed stones would not alter clinical management because of their size and location and the high likelihood of spontaneous passage. In the remaining cases, the clinicians estimated that additional studies (ie, CT scans) or observation would be recommended.

Passerotti C, Chow JS, Silva A, et al. Ultrasound versus computerized tomography for evaluating urolithiasis. *J Urol*. 2009;182 (suppl 4):1829-1834.

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ON THE WEB

More of this month's POEMs are available at www.jaapa.com:

- Corticosteroids are beneficial for Bell's palsy, but antiviral agents are uncertain
- Low-volume sulfate-based colonoscopy preparation is effective and well tolerated
- LUNA does not alleviate chronic pelvic pain
- Surgery and nonsurgical treatments for carpal tunnel have similar outcomes

Corticosteroids are beneficial for Bell's palsy, but antiviral agents are uncertain

Clinical question Are both corticosteroids and antiviral agents beneficial for the treatment of Bell's palsy?

Bottom line Corticosteroids alone are beneficial in the treatment of Bell's palsy, but antiviral agents alone are not. The value of combined treatment with corticosteroids and antiviral agents compared with corticosteroids alone remains uncertain. Total corticosteroid treatment doses greater than an equivalent dose of 450 mg of prednisone are superior to lower doses. (Level of evidence = 1a)

Synopsis The value of both corticosteroids and antiviral agents in the treatment of Bell's palsy remains uncertain. These investigators thoroughly searched multiple databases including Medline, Embase, Web of Science, conference proceedings and abstracts, bibliographies of relevant articles, clinical trial registries, and noted experts for randomized controlled trials evaluating either corticosteroids or antiviral agents in the management of Bell's palsy. No language restrictions were applied. Two people independently critiqued all studies for inclusion criteria and methodologic quality using standard criteria. Differences were resolved by consensus agreement. A total of 18 studies (N = 2,786 patients)—eight evaluating corticosteroids, seven evaluating antiviral agents, and three evaluating both corticosteroids and antiviral agents—met all criteria. Follow-up occurred for a median of 6 months. Evidence quality was graded as moderate to high for the individual studies. Corticosteroids alone significantly reduced the risk of unsatisfactory facial recovery (number needed to treat [NNT] = 11; 95% CI, 8-25) and synkinesis and autonomic dysfunction (NNT = 7; 6-10). Higher doses (greater than the equivalent of 450 mg prednisone) produced a significantly greater benefit than lower doses. Antiviral agents alone were not significantly beneficial, but antiviral agents combined with

corticosteroids were borderline significantly superior to corticosteroids alone (relative risk = 0.75; 0.56-1.00). The authors found no evidence for publication bias or significant heterogeneity in the results.

de Almeida JR, Al Khabori M, Guyatt GH, et al. Combined corticosteroid and antiviral treatment for Bell palsy. A systematic review and meta-analysis. *JAMA*. 2009;302(9):985-993.

Low-volume sulfate-based colonoscopy preparation is effective and well tolerated

Clinical question Is a low-volume, sulfate-based formula safe and effective as a colon-cleansing preparation?

Bottom line A 960-mL oral sulfate solution given as a split dose—half the evening before and half the morning of the procedure—is a well tolerated and effective bowel preparation. (Level of evidence = 1b)

Synopsis Polyethylene glycol (PEG) is poorly tolerated because of the high volume that must be ingested, and sodium phosphate can, in rare cases, cause renal failure. These authors studied an alternative, a 960-mL oral sulfate solution, comparing it with two liters of PEG in two similarly designed clinical trials. In the first study, 387 patients took the entire preparation the day before their colonoscopy; in the second study, 364 patients took half of the preparation the day before the procedure and half the morning of the procedure. Analysis was by intention to treat, and patients were excluded if they had significant pre-existing bowel disease. Allocation was concealed, but patients were not masked to the preparation. The colonoscopists, however, were masked to the preparation, and they were assessing the outcomes. The mean age of participants was 56 years. Although elderly patients were not specifically excluded, the age range of participants is not reported. In study 1 (entire preparation given the day before), the preparation was described as adequate by the colonoscopist 94% of the time for sulfate and 95% for PEG ($P = NS$). In study 2

(preparation split between two days), the preparation was described as adequate 99% of the time for both groups. Split dosing resulted in more excellent preparations. Patients receiving sulfate had slightly higher vomiting scores, but the difference was probably not clinically meaningful (0.16 on a 5-point scale). Adverse events were rare, did not differ between groups, and most were unlikely to be related to the preparation. There were no clinically significant changes in electrolyte levels or renal function.

Di Palma JA, Rodriguez R, McGowan J, Cleveland MB. A randomized clinical study evaluating the safety and efficacy of a new, reduced-volume, oral sulfate colon-cleansing preparation for colonoscopy. *Am J Gastroenterol*. 2009;104(9):2275-2284.

LUNA does not alleviate chronic pelvic pain

Clinical question Is laparoscopic uterosacral nerve ablation (LUNA) effective for the treatment of women with chronic pelvic pain?

Bottom line LUNA is no more effective than sham surgery in alleviating chronic pelvic pain of uncertain etiology in adult women. (Level of evidence = 1b-)

Synopsis LUNA is a therapeutic procedure performed after a diagnostic laparoscopy in women with chronic pelvic pain of uncertain etiology. These investigators identified 487 women with chronic pelvic pain lasting longer than 6 months referred for diagnostic laparoscopy. After inspection of the pelvis, eligible patients found to have no other significant pathology (eg, endometriosis, adhesions, or serious pelvic lesions) randomly received (concealed allocation assignment) operative interruption of nerve trunks in the uterosacral ligaments or sham skin incisions corresponding to additional port sites used for the LUNA procedure. Individual patients masked to their treatment group assignment self-reported outcomes using a 10-cm visual analog pain scale (VAS). Complete follow-up occurred for 80% of patients at 12 months and for 72% at 5 years. Using intention-to-treat analysis, there were

no significant differences reported between the LUNA group and the no-LUNA group for noncyclical pain, dysmenorrhea, dyspareunia, or health-related quality of life. The study was 80% powered to detect a predetermined clinically significant 1.2-cm difference on the VAS.

Daniels J, Gray R, Hills RK, et al; LUNA Trial Collaboration. Laproscopic uterosacral nerve ablation for alleviating chronic pelvic pain: a randomized controlled trial. *JAMA*. 2009;302(9):955-961.

Surgery and nonsurgical treatments for carpal tunnel have similar outcomes

Clinical question In patients with mild to moderate carpal tunnel syndrome, does surgery provide superior pain relief than multimodal nonsurgical treatment?

Bottom line In this study, the surgical treatment of patients with mild to moderately severe carpal tunnel syndrome produced clinically insignificantly greater improvement in symptoms and function than treatment with a multimodal nonsurgical approach

that included subtherapeutic doses of ibuprofen. (Level of evidence = 2b-)

Synopsis These researchers randomly assigned 116 patients with a clinical diagnosis (not all patients had electrodiagnostic testing) of mild to moderately severe carpal tunnel syndrome of at least 2 weeks' duration to surgery (open or endoscopic approach based on the whim of the surgeon) or multimodal nonsurgical treatment. Nonsurgical treatment consisted of ibuprofen 200 mg three times a day, six visits with a hand therapist, and therapeutic ultrasound for patients without improvement at 6 weeks. At the end of 12 months, 10% of the patients were lost to follow-up and excluded from the analysis. In general, doing this has a tendency to bias the results in favor of the intervention. The researchers used symptom and function scales that were each graded from 1 to 5. Generally, a 15% change in a scale is thought to be clinically meaningful. At the end of 12 months, using intention-to-treat analysis, the

symptom and function scores improved in both groups. Although the magnitude of change on the symptom and function scales were statistically greater for patients treated surgically, the differences are not clinically important. At the end of 1 year, almost 40% of the patients assigned to nonsurgical treatment wound up with surgery and only 20% of patients had at least three visits with the hand therapist. One can argue whether the dose of ibuprofen used in this study has any therapeutic value. Given all these problems, a more rigorous trial with more robust outcome assessments, therapeutic doses of an NSAID, and greater control over intervening events is needed.

Jarvik JG, Comstock BA, Kliot M, et al. Surgery versus non-surgical therapy for carpal tunnel syndrome: a randomised parallel-group trial. *Lancet*. 2009;374(9695):1074-1081.

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