REVIEW

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Update in Outpatient General Internal Medicine: Practice-Changing Evidence Published in 2017

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ABSTRACT

Clinicians are challenged to identify new practice-changing articles in the medical literature. To identify the practice-changing articles published in 2017 most relevant to outpatient general internal medicine, 5 internists reviewed the following sources: 1) titles and abstracts from internal medicine journals with the 7 highest impact factors, including *New England Journal of Medicine*, *Lancet*, *Journal of the American Medical Association*, *British Medical Journal*, *Public Library of Science Medicine*, *Annals of Internal Medicine*, and *JAMA Internal Medicine*; 2) synopses and syntheses of individual studies, including collections in the American College of Physicians Journal Club, Journal Watch, and Evidence-Based Medicine; 3) databases of synthesis, including Evidence Updates and the Cochrane Library. Inclusion criteria were perceived clinical relevance to outpatient general medicine, potential for practice change, and strength of evidence. This process yielded 140 articles. Clusters of important articles around one topic were considered as a single-candidate series. A modified Delphi method was utilized by the 5 authors to reach consensus on 7 topics to highlight and appraise from the 2017 literature

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PATENT FORAMEN OVALE CLOSURE IN PATIENTS WITH CRYPTOGENIC STROKE REDUCES RECURRENT STROKE RISK, BUT PATIENT SELECTION IS IMPORTANT[1-3]

Existing practice guidelines state that clinicians should not routinely refer patients with cryptogenic ischemic stroke for patent foramen ovale closure.[4] Two new randomized controlled trials and an exploratory analysis of long-term results from a previous trial provide evidence for the use of percutaneous patent foramen ovale closure devices in these settings.

Results

In the Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence (CLOSE) trial, 663 patients with patent foramen ovale and large interatrial shunts or atrial septal aneurysm were randomized to patent foramen ovale device closure or medical therapy, and followed for a mean of 5.3 years. There were significantly fewer strokes in the patent foramen ovale closure group (0 vs 14 [6%]; hazard ratio 0.03; 95% confidence interval [CI], 0-0.26).[1] In the Septal Occluder and Antiplatelet Medical Management for Reduction of Recurrent Stroke or Imaging-Confirmed TIA [transient ischemic attack] in Patients with patent foramen ovale (REDUCE) trial, 664 patients with patent foramen ovale, of whom 81% had moderate-large interatrial shunts, were randomized to patent foramen ovale closure plus antiplatelet therapy or antiplatelet therapy alone and followed for a mean of 3.2 years. There were significantly fewer clinical ischemic strokes in the patent foramen ovale closure group (6 [1.4%] vs 12 [5.4%]; hazard ratio 0.23; 95% CI, 0.09-0.62).[3] In the Randomized Evaluation of Recurrent Stroke Comparing patent foramen ovale Closure to Established Current Standard of Care Treatment (RESPECT) trial, 980

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patients with patent foramen ovale, of whom 49% had a substantial interatrial shunt and 36% had an atrial septal aneurysm, were randomized to patent foramen ovale device closure or medical therapy.[2] The previously published primary analysis at a median of 2.1 years of follow-up showed no significant benefit to patent foramen ovale closure.[5] The exploratory analysis that followed these patients for a median of 5.9 years showed significantly fewer strokes in the patent foramen ovale closure group (18 [3.6%] vs 28 [5.8%], hazard ratio, 0.55; 95% CI, 0.31-0.999).[2]

In all 3 studies, patients were excluded if they were 60 years or older. Adverse events related to device implantation ranged from 1.4% to 5.9%, and 2 of the studies reported a significantly higher incidence of atrial fibrillation in the patent foramen ovale closure groups.

Limitations

The REDUCE and RESPECT trials were industry funded. The RESPECT trial data published in the 2017 exploratory analysis do not represent the primary analysis. Overall, event rates were relatively low in all studies.

Implications for Practice

Clinicians should refer patients ages 16-59 years with cryptogenic ischemic stroke and patent foramen ovale associated with moderate-large interatrial shunt or atrial septal aneurysm for consideration of percutaneous patent foramen ovale closure. Periprocedural complication rates and a higher risk of atrial fibrillation with patent foramen ovale closure should inform decision-making.

CLINICAL SIGNIFICANCE

- Consider patent foramen ovale closure in cryptogenic stroke.
- For stable angina symptoms, optimizing medications is as effective as stenting.
- Administer new shingles vaccine to adults ≥50 years, including those previously vaccinated.
- Asymptomatic microscopic hematuria is most cost-effectively evaluated by cystoscopy plus ultrasound.
- Hypertension guidelines set treatment goal <130/80 mm Hg.
- Consider proton pump inhibitor coprescription with aspirin to reduce gastrointestinal bleeding in the elderly.
- All nonsteroidal anti-inflammatory drugs are associated with myocardial infarction.

NO DIFFERENCE IN EXERCISE TIME, ANGINA, OR QUALITY OF LIFE BETWEEN PERCUTANEOUS CORONARY INTERVENTION AND OPTIMAL MEDICAL TREATMENT IN PATIENTS WITH STABLE ANGINA[6]

The unblinded, non-placebo-controlled, 2007 Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial demonstrated no difference in mortality or cardiac events in patients treated with percutaneous coronary intervention plus optimal medical therapy vs optimal medical therapy alone; percutaneous coronary intervention reduced angina at years 1 and 2 but not at year 5.[7] Despite these findings, there has been minimal adoption of optimal medical therapy in patients with stable angina prior to percutaneous coronary intervention, while procedures for this indication continue to rise.[8] In this context, the authors of the Objective Randomised Blinded Investigation with optimal medical Therapy of Angioplasty in stable angina (ORBITA) trial conducted the most rigorous study to date to help determine the role of percutaneous coronary intervention vs optimal medical therapy on symptoms of stable angina.[6]

Results

Patients with stable angina and severe, single-vessel disease (n = 230) were enrolled. Prerandomization data were collected after 6 weeks of optimizing antianginal medications targeting heart rate ≤60 beats per minute, ≥2 antianginal drugs, high-dose statin therapy, and aspirin. Two hundred patients underwent randomization to percutaneous coronary intervention with drug-eluting stent or sham procedure. The incremental difference in exercise time between groups was not statistically significant. Secondary outcomes including incremental angina, quality of life, and physical limitation between groups also showed no significant difference. The only outcome favoring percutaneous coronary intervention was the dobutamine stress echocardiography peak stress wall motion score index.

Limitations

Three-fourths of patients in ORBITA were men, and ethnicity was not reported, which limits generalizability. Patients with multivessel disease were excluded. ORBITA was not designed to assess cardiac events and mortality. Optimizing medication was resource intensive and may be more challenging in real-world practice.

Implications for Practice

ORBITA results suggest that the short-term improvement in angina symptoms seen in the COURAGE trial may have been related to the placebo effect of percutaneous coronary intervention and lack of blinding. With no change in meaningful clinical outcomes, it further challenges the common use of percutaneous coronary intervention over optimal medical therapy in stable angina. Including ORBITA trial results in shared-decision-making conversations with patients will be important, although caution is advised in overgeneralizing these findings to patients dissimilar to those included in the study.