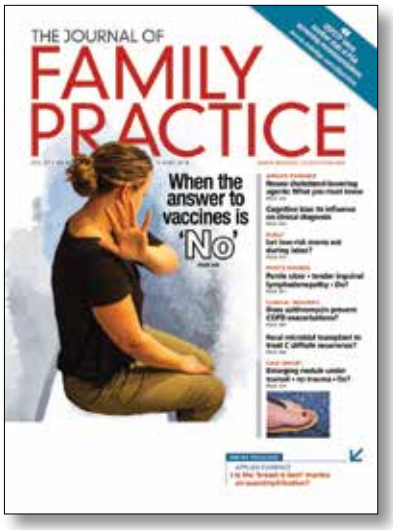
A closer look at an ezetimibe discussion



Although I look forward to receiving *JFP* each month, I was initially disappointed in Dr. Jonathon M. Firnhaber's article, "Newer cholesterol-lowering agents: What you must know" (*J Fam Pract*. 2018;67:339-341,344,345), because of what appeared to be a superficial discussion of the medication ezetimibe. The potential role of PCSK9 inhibitors in extremely high-risk individuals was well discussed, but my first read left me with the impression that ezetimibe should be used more widely.

It seemed that in the section for ezetimibe, the author was suggesting using it for primary prevention. The line, "Consider adding ezetimibe to maximally tolerated statin therapy for patients not meeting LDL-C goals with a statin alone" left me a bit confused, as the most widely used guideline (that by the American College of Cardiology/American Heart Association Task Force on Practice Guidelines) states that there is no goal low-density lipoprotein cholesterol (LDL-C) level for primary prevention in patients without known cardiovascular disease (CVD) because studies have not been done to support this concept.[1]

But upon rereading the article, I realized the statement was placed at the end of a section that discussed secondary prevention based on the IMPROVE-IT study.[2] This trial included only patients with previous acute coronary syndrome, one of the populations at highest risk.

I write just to reinforce the importance of considering what evidence we have for primary prevention. Although there is a value to rechecking LDL-C levels to assess compliance, there really is no convincing evidence that we should treat to a goal LDL-C level in someone who does not already have CVD. So the addition of ezetimibe to a statin in these patients is not recommended. Thus, the often-quoted strategy: "Start them on the right statin, and don't look back."

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References

1. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(suppl 2):S1-S45.
2. Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372:2387-2397.

Author's response

Thank you, Dr. Crump, for your feedback. I suspect that most clinicians would welcome more robust outcomes data on ezetimibe, but to date none have been published.

The IMPROVE-IT trial[1] offers the best supportive evidence for the use of ezetimibe, but still finds only a 2% absolute risk reduction (ARR) in a composite endpoint (cardiovascular death, nonfatal myocardial infarction, unstable angina requiring rehospitalization, coronary revascularization ≥30 days after randomization, or nonfatal stroke), equating to a number needed to treat (NNT) of 50.

The largest meta-analysis of ezetimibe trials—published prior to IMPROVE-IT—combined 31,048 patients to find an ARR for myocardial infarction of 1.1% (NNT=91) and an ARR for stroke of 0.6% (NNT=167), with no difference in cardiovascular death.[2]

Because of its limited outcomes data, ezetimibe is best reserved for patients unable to tolerate statin therapy, for those in whom statin therapy is contraindicated, or for those not meeting LDL-C reduction goals with a statin alone. This position is also supported by the United Kingdom's National Institute for Health and Care Excellence (NICE).[3]

Finally, you are correct that the 2013 American College of Cardiology/American Heart Association Guideline on the Assessment of Cardiovascular Risk does not advocate a number-driven LDL-C goal, but rather recommends a risk-based moderate

Most clinicians would welcome more robust outcomes data on ezetimibe, but to date none have been published.

(30%-50%) or high-intensity (>50%) LDL-C reduction goal.[4]

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References

1. Cannon C, Blazing M, Giugliano R, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med*. 2015;372:2387-2397.
2. Savarese G, Ferrari G, Rosano G, et al. Safety and efficacy of ezetimibe: a meta-analysis. *Int J Cardiol*. 2015;201:247-252.
3. National Institute for Health and Care Excellence. Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia. Technology appraisal guidance [TA385]. February 24, 2016. www.nice.org.uk/guidance/ta385. Accessed September 12, 2018.
4. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63:2935-2959.

Disagreement over a Case Report Dx

Based on the magnetic resonance imaging (MRI) scans presented in the Case Report, "Bilateral wrist pain • limited range of motion • tenderness to palpation • Dx?" (*J Fam Pract*. 2018;67:160-162), I disagree with the diagnosis.

Contrary to the assertion by Drs. Shehata and Hizon that the patient had "fractures extending through the scaphoid waist," this young girl actually had bilateral osseous contusions (ie, microtrabecular fractures) of the radial aspect of the scaphoid and did not have complete scaphoid waist fractures. Also, the MRI scans demonstrate intact ulnar cortices bilaterally, indicating that there is no complete scaphoid waist fracture.

These are typical "FOOSH" (fall on outstretched hand) injuries and would be expected to have an exceedingly good prognosis with immobilization. As to whether or not this affects medical management, such as how long the cast remains on the arm, I would have to defer to an orthopedic surgeon's judgment.

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Author's response

Thank you for your comments. You are correct that the MRI scans shown do not demonstrate a complete fracture through the scaphoid, but rather a microtrabecular fracture. We did not intend to make the distinction between the 2 entities because management for both is similar. The teaching point of this case was to impress upon clinicians that these types of fractures may be subtle even on MRI, and that if they are not treated appropriately, they can progress to complete fracture or result in non-union and long-term pain and disability.

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