Study shows in vivo endomicroscopy improves detection of Barrett's esophagus-related neoplasia

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New research shows that the addition of confocal laser endomicroscopy to high-definition white-light endoscopy enables improved real-time endoscopic diagnosis of Barrett's esophagus dysplasia (neoplastic tissue) by using targeted biopsies of abnormal mucosa to reduce unnecessary mucosal biopsies and potentially reduce costs. It may also positively influence patient care by changing the plan for immediate endoscopic management. The study appears in the February issue of *GIE: Gastrointestinal Endoscopy*, the monthly peer-reviewed scientific journal of the American Society for Gastrointestinal Endoscopy (ASGE).

Barrett's esophagus (BE) is a precancerous change in the epithelial lining of the esophagus that is associated with the development of esophageal cancer. The current best, though imperfect, marker of neoplastic progression is dysplasia (abnormality in cells which have undergone early changes on a path toward possible malignancy) detected in mucosal biopsy specimens of the lining of the esophagus obtained at the time of endoscopy. High-grade dysplasia is associated with a high rate of progression to invasive esophageal cancer. Detection and pathologic confirmation of early BE neoplasia (high-grade dysplasia or early esophageal cancer) is important because endoscopic therapy at this point is highly successful. Unfortunately, neoplasia in BE may not be evident even with only endoscopic inspection, so the current standard of care is endoscopic surveillance with high-quality white-light endoscopy using systematic 4-quadrant biopsies every 1 to 2 cm of BE length and targeted

biopsies of any mucosal irregularities. A large number of biopsies may be required using this random biopsy method, resulting in high cost and increased time. This method has a low (1 percent to 10 percent) diagnostic yield for neoplasia and may result in lower adherence to practice guidelines.

Confocal laser endomicroscopy (CLE) is a relatively new endoscopic imaging technique that combines endoscopy and microscopic imaging of the gastrointestinal (GI) mucosa (the superficial lining of the GI tract). A previous single-center, randomized, crossover study, demonstrated a greater diagnostic yield for the detection of BE neoplasia with an in vivo fluorescein-aided endoscope-based CLE system (eCLE).

"Our study compared the diagnostic yield and accuracy of high definition white-light endoscopy (HDWLE) and random biopsy with that of HDWLE plus real-time eCLE imaging and targeted tissue sampling of BE, and determined the impact of in vivo eCLE on real-time clinical decision making in patients with BE," said study lead author Marcia Irene Canto, MD, MHS, FASGE, Johns Hopkins University, Baltimore, Maryland. "We found that real-time eCLE and targeted biopsy after HDWLE can improve the diagnostic yield and accuracy for neoplasia and significantly impact in vivo decision making by altering the diagnosis and guiding therapy."

Methods

This was a multicenter, randomized, controlled trial of 192 adult patients with BE undergoing routine surveillance or referred for early neoplasia from February 2010 to December 2012 at academic medical centers. The researchers' objective was to compare high-definition white-light endoscopy (HDWLE) alone with random biopsy (RB) and HDWLE plus eCLE and targeted biopsy (TB) for diagnosis of BE neoplasia. Patients were randomized to HDWLE plus RB (group 1) or HDWLE with eCLE

and TB (group 2). Real-time diagnoses and management plans were recorded after HDWLE in both groups and after eCLE in group 2. Blinded expert pathology diagnosis was the reference standard. The main outcomes were diagnostic yield, performance characteristics, and clinical impact.

Results

HDWLE plus eCLE and TB (group 2) led to a lower number of mucosal biopsies and higher diagnostic yield for neoplasia (34 percent vs 7 percent), compared with HDWLE and RB (group 1) but with comparable accuracy. HDWLE plus eCLE and TB tripled the diagnostic yield for neoplasia (22 percent vs 6 percent) and would have obviated the need for any biopsy in 65 percent of patients. The addition of eCLE to HDWLE increased the sensitivity for neoplasia detection to 96 percent from 40 percent without significant reduction in specificity. In vivo CLE changed the treatment plan in 36 percent of patients. An eCLE was performed successfully and safely in all patients. There were no adverse reactions to fluorescein administration.

The researchers noted several limitations including that the study was only at academic centers with highly experienced endoscopists. The results may not be generalizable to community-based physicians, less-experienced practitioners and nonacademic practices. Second, they used the eCLE system, and their findings may not be generalizable to other pCLE systems. Also, the endoscopists were not blinded to prior endoscopy and pathology results because these were necessary for standard medical care and in vivo decision making regarding biopsy or EMR.

The researchers concluded that the addition of in vivo imaging with eCLE to HDWLE is associated with improved targeting of neoplasia, a decrease in unnecessary mucosal biopsies and a significant change in

diagnosis and management plans in patients with BE. The approach of real-time CLE diagnosis and imaging-guided therapy represents a potential paradigm shift in BE surveillance. Research studies are needed to address training in CLE, comparative effectiveness studies of advanced endoscopic imaging techniques, the role of imaging-guided therapy and advances in CLE devices and contrast agents.

In an accompanying editorial, Manuel Berzosa, MD and Michael B. Wallace, MD, MPH, Mayo Clinic, Jacksonville, Florida, stated, "This is an important study for Barrett's esophagus surveillance because it demonstrates that a targeted biopsy strategy using endoscope based confocal laser endomicroscopy can be a superior alternative to random biopsy protocols."

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