Endoscopic Mucosal Resection Useful for Barrett's

BY ALICIA AULT
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WASHINGTON — Endoscopic mucosal resection seems to be safe and effective for Barrett's esophagus with high-grade dysplasia or intramucosal adenocarcinoma, and may help patients avoid an esophagectomy, according to a small study presented at a symposium sponsored by the Society of Surgical Oncology.

The procedure has been used to remove focal dysplastic lesions arising in Barrett's endothelium. Although that is successful initially, over time the rates of recurrence increase significantly, said Dr. Andrew Ross of the University of Chicago. This is not surprising, because most Barrett's dysplasias are microscopic and multifocal, so removing just a single focus probably is not very effective, he said.

Clinicians in Europe have shifted to using esophageal mucosal resection (EMR) to completely remove entire segments of Barrett's esophagus, resulting in high remission rates out to 18 months, Dr. Ross said.

Aiming to replicate the European results, he and his colleagues reviewed a prospectively collected database on all patients undergoing EMR for high-grade dysplasia (HGD) or intramucosal adenocarcinoma (IA) at the University of Chicago over a 5-year period.

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There were 46 procedures in 26 patients (21 men and 5 women), with a median age of 65.5 years. Of these patients, 15 had HGD, 8 had IA, and 3 had a combination of the two. Half of the patients had short-segment and half had long-segment Barrett's. The median length in the long-segment Barrett's was 5.1 cm.

All patients underwent endoscopic ultrasound to rule out adenopathy and submucosal invasion. The EMRs were performed with a single-channel upper endoscope, but the surgical techniques evolved over time. Argon plasma coagulation was applied to resection margins. Surveillance endoscopy with a 4-quadrant biopsy every 1-2 cm was performed at 6-month intervals. All patients were maintained on twice-daily proton pump inhibitors.

Of the 26 patients, 16 have completed the protocol so far; 8 are awaiting the first follow-up endoscopy. There has been complete eradication—defined as normal-appearing squamous epithelium in surveillance endoscopy—in 11 patients who have been followed for a mean of 16 months. Two patients had residual HGD or IA, two had residual Barrett's with low-grade dysplasia, and one had residual Barrett's alone.

One patient was removed from the study because a submucosal invasion was discovered after the first EMR, and another died of unrelated causes. Most of the patients went home right after the EMR session.

The primary complication thus far has been esophageal stricture, affecting 7 (30%) of the 26 patients. Most saw a resolution of any dysphasia after one or two sessions of balloon dilation, but two patients had to have 10 dilations, Dr. Ross

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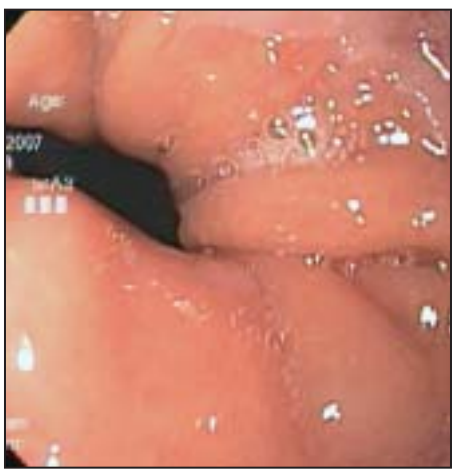
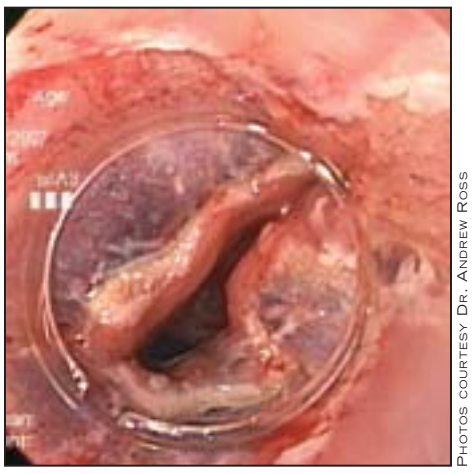


Barrett's esophagus with high-grade dysplasia is shown before the procedure.



The same lesion is shown immediately after endoscopic mucosal resection.

PHOTOS COURTESY DR. ANDREW ROSS

Three Biomarkers Tied to Esophageal Ca Risk

BY ROBERT FINN
San Francisco Bureau

LOS ANGELES — A combination of three biomarkers may reliably predict which patients with Barrett's esophagus will progress to esophageal adenocarcinoma, Dr. Patricia L. Blount reported at the annual meeting of the American Association for Cancer Research.

In a study involving 243 patients with Barrett's esophagus, 79.1% of patients who had all three genetic abnormalities on baseline endoscopic biopsy progressed to esophageal adenocarcinoma within 6 years. Conversely, among patients who had none of the abnormalities, there was not a single progression to cancer in almost 8 years. Progression rates for patients with one and two abnormalities were 5.7% and 28.4%, respectively, at 6 years.

Compared with patients with no abnormalities, patients with any two of the abnormalities were 9 times more likely to progress to esophageal adenocarcinoma, and those with all three of the abnormalities were 39 times more likely to progress during an average follow-up of 71 months; these differences were statistically significant. Patients with one abnormality were 1.8 times more likely to progress than those with no abnormalities, but this was not a significant difference.

In general, only about 10% of patients with Barrett's esophagus progress to esophageal adenocarcinoma, noted Dr. Blount, of the Fred Hutchinson Cancer Research Center, Seattle. Even frequent endoscopic surveillance can miss the small, focal lesions signaling progression to cancer. Thus, a reliable method of predicting progression could have far-reaching clinical effects. The investigators are working to translate this research into a practical test that does not require the facilities of a research laboratory, he said.

The investigators focused on DNA aneuploidy and tetraploidy and on alterations in the genes for the tumor-suppressor proteins TP53 and CDKN2A accompanied by a loss of heterozygosity (LOH) for those genes. Patients who had either aneuploidy or tetraploidy, 17p LOH (loss of heterozygosity on the short arm of chromosome 17), or 9p LOH (similarly, on chromosome 9) were more likely to progress to cancer.

As in other studies, the results of this study suggested that the use of NSAIDs may be protective against progression to esophageal adenocarcinoma.

The study was funded by the National Institutes of Health. Dr. Blount said that she had no conflicts of interest to disclose. ■

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said. The strictures are probably occurring because the endoscopists found it more effective to do the total resection in one session—thus eliminating the scar tissue that resulted from doing the procedure in two sessions. Resection results are better, but strictures have increased.

Dr. Ross and his colleagues were also able to compare pre-EMR and post-EMR histopathology. The EMR removes large tissue specimens. There was histopathologic concordance in 70% of cases, but two patients were upstaged and six were downstaged according to the post-EMR histopathology, he said.

"It's a little bit concerning in that we rely heavily as endoscopists on the pinch biopsy specimens in the management, treatment, work-up, etc., of patients with Barrett's," Dr. Ross said.

Post-EMR histopathology revealed that HGD and IA were buried under normal-appearing squamous epithelium in nine patients, he said. "If you're doing surveillance endoscopy and you biopsied normal-appearing tissue, you may have missed cancerous lesions beneath the muscosa."

Compared with the standard biopsy protocol, EMR appears to provide more accurate histopathologic diagnosis and tumor staging, and it is a safe and effective alternative for eradicating HGD and IA in Barrett's, Dr. Ross said.

Stricture formation is a risk, especially with longer segments, he said.

"These preliminary data are encouraging," he said, adding that larger studies with longer follow-up are needed before widespread adoption of the technique.

He also noted the need for technological advances. "This is a difficult procedure to perform because our instruments are rudimentary and difficult to utilize."

Dr. Ross has no conflict of interests to disclose. ■