Three Biomarkers Tied to Esophageal Ca Risk

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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. ■

Continued from previous page

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. ■