

ESOPHAGUS

PPIs reduce benign anastomotic strictures after esophagectomy

Benign anastomotic strictures after esophagectomy with gastric tube reconstruction occur frequently, even in the absence of risk factors, such as conduit ischemia or anastomotic leaks. “We knew from our previous studies that the tubulized stomach used for reconstruction produced considerable amounts of acid and that the acid gastric contents refluxed into the esophageal remnant,” explains Jan Johansson, lead author on the study. Johansson and colleagues hypothesized that anastomotic strictures may develop as a consequence of this exposure of acid gastric tube contents to the anastomotic site and decided to test whether or not prophylactic treatment with PPIs could protect against the development of benign anastomotic strictures.

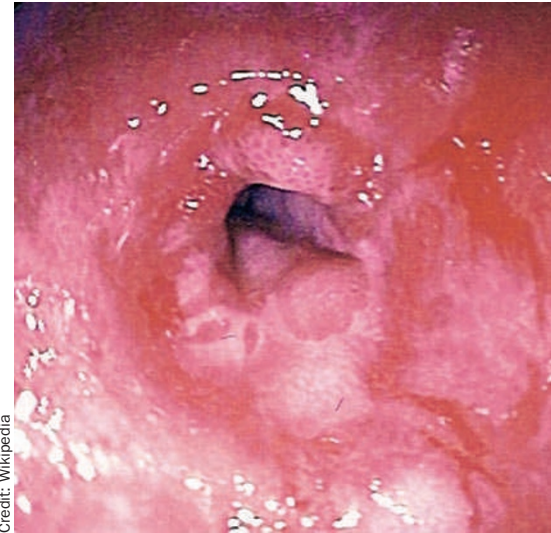
The researchers recruited 80 patients to the clinical trial who had undergone esophagectomy with gastric tube reconstruction at the study hospital in Lund, Sweden. All patients underwent this procedure to treat malignant tumors located in the distal esophagus or at the gastroesophageal junction, and patients had no signs of anastomotic leaks following surgery. Patients were randomly allocated to receive PPI therapy twice daily or no treatment for 1 year. The doses of PPIs given were those recommended for the treatment of patients with erosive esophagitis.

As the clinical and scientific views of what anastomotic strictures are differ, Johansson and colleagues agreed on a definition that covered both aspects; benign anastomotic strictures were defined as anastomotic narrowings that did not allow a standard diagnostic endoscope to pass without dilatation. Follow-up visits consisted of symptom evaluations and upper gastrointestinal endoscopies at 2, 4, 6, 9 and 12 months and a pH study that was performed

2 months after surgery. The 12-month follow-up visit was included to avoid misinterpretation of a malignant stricture that initially appeared benign. When a benign anastomotic stricture was found, as assessed by endoscopy, it was immediately dilated.

Of the 79 evaluable patients, 5 patients in the PPI group (5 of 39; 13%) and 18 patients in the control group (18 of 40; 45%) developed benign anastomotic strictures. In a Cox analysis, PPI treatment was an independent significant risk factor for the development of benign anastomotic strictures (relative risk [RR] 5.6, $P=0.001$). Patients in the control group had higher scores of erosive esophagitis ($P=0.002$) and more severe dysphagia ($P=0.032$). All but 2 of the 26 dilatations performed were associated with dysphagia. Patients in the PPI group had overall wider anastomoses than the patients in the control group at the 2, 4 and 6 month visits ($P=0.025$), but there was no difference in width of anastomoses at 9 or 12 months ($P=0.315$), probably because more benign anastomotic strictures developed in the control group during the first 6 months. The pH study showed significantly higher levels of acid exposure in the patients in the control group compared with the patients who received PPIs. This was true for the upright and supine positions, as well as postprandially.

The size of the circular staple cartridge used to construct the anastomosis was also an independent significant risk factor for the development of benign anastomotic strictures. The use of a 25 mm cartridge to create the anastomosis rather than a 28 mm or 31 mm cartridge significantly increased stricture formations (RR 2.9, $P=0.025$). The number of patients with anastomotic strictures who had a 25 mm cartridge for the construction of the anastomosis in the PPI group was 4 out



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of 5 patients compared with 9 out of 18 patients in the control group. The cause of more strictures and narrower anastomoses with the 25 mm cartridge compared with the larger cartridges is not fully understood, but may be an intrinsic effect associated with using a smaller device, or the effect of a natural healing process in a narrow esophagus.

Johansson *et al.* conclude that prophylactic use of PPIs reduces the formation of benign anastomotic strictures, as does the use of larger sized circular staple cartridges. “As a consequence of our findings, we now prescribe PPIs to patients with gastric tube reconstructions after esophagectomy for the first 6 months after surgery, which is the period when benign strictures are known to develop,” adds Johansson.

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Original article Johansson, J. *et al.* Impact of proton pump inhibitors on benign anastomotic stricture formations after esophagectomy and gastric tube reconstruction: results from a randomized clinical trial. *Ann. Surg.* **250**, 667–673 (2009)