

A Major Study Examines Endoscopies That Fail to Detect Esophageal Cancer

Led by experts at University of Colorado Cancer Center, the endoscopy research includes data from over 15,000 patients.

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An endoscopy — using a fiber-optic tube to peer inside the body and collect biopsy samples — can be an invaluable way to detect [cancer of the esophagus](#). But sometimes, an endoscopy can miss esophageal cancer, which doesn't get detected until weeks or months later.

A study led by [University of Colorado Cancer Center](#) member [Sachin Wani](#), MD, sought to better understand the problem, drawing on data from more than 15,000 individuals with newly diagnosed Barrett's esophagus, the only precancerous condition for esophageal adenocarcinoma.

Esophageal adenocarcinoma is the most common type of esophageal cancer in the United States and also is more commonly diagnosed among men. It's a deadly cancer with poor five-year survival rates, and most patients with this cancer present at an advanced stage.

Researchers found a big gap between hospitals in how good they were at detecting cancer and dysplasia — pre-cancerous abnormal conditions — on an initial endoscopy in patients with Barrett's esophagus.

Wani is a professor in the [CU Anschutz Department of Medicine's Division of Gastroenterology and Hepatology](#). He holds the Katy O. and Paul M. Rady Endowed Chair in Esophageal Cancer Research and is executive director of the CU Cancer Center's [Rady Esophageal and Gastric Center of Excellence](#).

[A manuscript](#) on the study has been accepted by the journal Clinical Gastroenterology and Hepatology but is not yet published.

→ [How Endoscopic Therapy Cured Vic Padilla's Precancerous Barrett's Esophagus](#)

Barrett's a key risk factor

Esophageal cancer starts when cells mutate and multiply within the lining of the esophagus, the

tube carrying food from the mouth to the stomach. [The American Cancer Society projects](#) about 22,070 new esophageal cancer diagnoses in the United States this year and about 16,250 deaths.

Esophageal adenocarcinoma starts in gland cells in the lower esophagus. Rates of the disease have been rising over the last several decades.

“Esophageal adenocarcinoma is lethal, and despite all the efforts we’ve made in screening and surveillance, we’ve really not been able to make a dent on the epidemiology of this cancer. It has a dismal five-year survival rate,” Wani says.

Barrett’s esophagus — a precancerous condition involving damage to the lining of the esophagus, linked to chronic stomach acid reflux — is a key risk factor for esophageal adenocarcinoma. Endoscopies for Barrett’s esophagus are considered the best way to find warning signs of cancer, such as lesions in glandular cells lining the esophagus.

But Wani’s study notes there is “growing literature” on cases of esophageal adenocarcinoma and high-grade dysplasia that were missed in Barrett’s esophagus patients undergoing screening and surveillance endoscopies, “undermining the effectiveness of these practices.”

“This really drills down to one major issue,” Wani says. “The fact is that patients, even after they undergo an endoscopic screening exam that is negative for any cancer or high-grade dysplasia can still wind up getting a cancer diagnosis a relatively short time after that so-called negative endoscopy. And this undermines our whole effort to detect early cancer.”

→ [Sachin Wani, MD, Oversees Clinical Trials of New Esophageal Cancer Screening Device](#)

Key takeaways

The study compared rates of cancer and neoplasia detected through endoscopies to instances of post-endoscopy esophageal cancer (PEEC) and post-endoscopy esophageal neoplasia (PEEN) that were not found until 30 days to a year after an endoscopy that didn’t detect them. It’s believed to be the first large population-based study to make these comparisons.

The most important takeaways from this study, Wani says, are that “nearly a quarter of esophageal cancers are diagnosed 30 to 365 days after an endoscopic exam that was negative for esophageal cancer” — PEEC — “and there is significant variability among hospitals in the rates of detection of esophageal cancer or dysplastic changes among patients with Barrett’s esophagus.”

The study points to what “appears to be an inverse relationship between our ability to detect cancer or dysplastic changes during the first endoscopy and detection of PEEC,” he adds. “A similar relationship has been described in the colorectal cancer space, where it is well established that an endoscopist’s adenoma detection rate” — the ability to detect precancerous colon polyps — “has an inverse relationship with post-colonoscopy colorectal cancer.”

Wani says that “the future lies in further establishing quality metrics for upper endoscopic examinations like we have for colonoscopy.”

→ [Mark Koebrich's Journey: From Television to Triumph Over Esophageal Cancer](#)

Drawing on national data sets

Wani's population-based analysis drew on data on all 15,178 people in Finland and Sweden who were diagnosed with Barrett's esophagus from 2006 to 2020 through an “index” (initial) endoscopy. The data for the study came from national health-data registries maintained by several Nordic nations — data sets that Wani has used in prior research.

“These data [have] been so fruitful in addressing so many important knowledge gaps, because all patients are followed within the same health care system and their follow-up data are well captured,” Wani says. “This is incredibly difficult to do in the United States.”

Out of the 15,178 Barrett's esophagus patients whose records were analyzed, 198 people developed esophageal cancer. Of that group:

- 18% of the cancer cases were found within 30 days of their first endoscopy.
- 22% were “missed” cancers (PEEC) found 30 days to a year after an exam detected no cancer.
- 60% of the cancer cases were detected more than a year after the index endoscopy, suggesting that even the best initial screening may not have detected them.

The study showed major differences between hospitals in initial cancer and neoplasia detection rates, Wani says. Overall, hospitals with higher detection rates tended to have fewer cases of missed cancer later on.

→ [Compassionate Care Fuels Family's Desire to Change Esophageal Cancer Paradigm](#)

More research needed

The study cites several factors that may lead to missed cancer, including a lack of compliance with the standardized “Seattle protocol” for performing endoscopic biopsies in Barrett's esophagus cases, inadequate time inspecting the “Barrett's segment” – the portion of the esophagus affected by Barrett's – during endoscopy, and inability to recognize certain lesions that could harbor abnormal tissue growth that could lead to or harbor cancer. In other cases, a rapidly progressing

cancer might not be detected by even the highest quality initial endoscopy.

Measuring how well doctors and health centers do at detecting cancer during endoscopies could be an important quality measure, and that better detection might mean fewer missed cancers, the study suggests.

Wani says that more research is needed to establish an “ideal” detection rate, to standardize and improve detection methods, to develop training programs to help doctors improve, and to verify whether improving detection rates would actually reduce the rates of PEEC and PEEN.

High-quality examinations

“Our findings highlight the importance of a high-quality endoscopic examination for patients when they get diagnosed with Barrett’s esophagus, including using the best endoscope available, spending adequate time inspected the Barrett’s segment, and ensuring that we take samples using a structured biopsy protocol,” Wani says.

He adds that those methods are used at the CU Cancer Center for Barrett’s patients. “We take a lot of pride in performing high-quality examinations for our patients,” he says, adding that the Rady Center is “addressing several knowledge gaps as it relates to improving screening strategies.”

Several investigators from Finland and Sweden collaborated in the research, including senior author Jesper Lagergren, MD, PhD, of the Karolinska Institutet and Karolinska University Hospital in Stockholm.

“I want to acknowledge the incredible sense of collaboration that Lagergren has, and our friends across the Atlantic have been so generous in sharing their database,” Wani says.

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