Annals of Gastroenterology (2012) **25,** 79-80

Barrett's esophagus: an exaggerated risk?

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Title: Incidence of adenocarcinoma among patients with Barrett's esophagus.
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Journal: *N Engl J Med* 2011;365:1375-1383

Summary

Over the last decade, the therapy of early Barrett's neoplasia has significantly changed by the introduction of endoluminal therapy. Nowadays, endoscopic resection of mucosal cancer in combination with radiofrequency ablation of the remaining Barrett's epithelium, has replaced surgery as a first choice treatment for this condition. In view of this changed treatment paradigm, it has become even more important to detect neoplastic changes at an early stage, because it will dramatically alter the patients' quality of life and prognosis [1].

In a recent epidemiological study, Hvid-Jensen et al [2] present a large population-based cohort study involving virtually all Danish patients identified with Barrett's esophagus between 1992 and 2009. They collected data on 11,028 patients with Barrett's esophagus with a follow-up period of 5.2 years on average. Within one year of the index endoscopy, 131 patients were newly diagnosed with adenocarcinoma. These were regarded as missed cases and not incorporated in the incidence calculation. During the following years, an additional 66 new cases of adenocarcinoma were registered, yielding an incidence rate of 0.12% or 1.2 cases per 1000 patient-years. This is much lower than the assumed risk of 0.5% that is used to substantiate surveillance guidelines. Nevertheless, with a relative risk of 11.3 for patients with Barrett's esophagus, the risk of developing adenocarcinoma is still significantly elevated in comparison to the general population. The authors wonder if surveillance of Barrett's patients is still warranted in view of their findings.

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Conflict of Interest: None

Received 28 December 2011; accepted 29 December 2011

Opinion

For sure, these data will not immediately change our daily clinical practice of Barrett's surveillance. Some methodological issues need to be addressed. First, although the Danish registry is claimed to be almost complete (98%), this study still remains a retrospective analysis of prospectively collected data and it is not sure how this compares to other prospectively collected data. For instance Sharma et al [3] reported a combined risk of 5.6% for adenocarcinoma and high grade dysplasia in a cohort of 618 patients with endoscopically and histologically confirmed Barrett's esophagus (intestinal metaplasia) during a 4.1-year follow up. However, the major confounder in the present study is the lack of endoscopic data. Data collection is solely based on pathology registration of intestinal metaplasia and adenocarcinoma. As such we do not know if all these patients had endoscopic evidence of a Barrett's esophagus (was there for instance intestinal metaplasia at the cardia), or about the disease extent. Additionally, other risk factors are not identified, such as BMI, smoking and alcohol consumption. Thirdly, it is probably not right to extrapolate the Danish data to the world population. It is therefore conceivable that, besides a possible selection bias in previous studies, a higher risk population in other countries may account for the higher reported incidence of neoplasia. Recent data from the US show that the overall esophageal adenocarcinoma incidence increased from 3.6 per million in 1973 to 25.6 per million in 2006 [4]. Clearly, this is not reflected in this Danish cohort study. Therefore, one cannot conclude to just abandon Barrett's surveillance as a whole, based on this single nation cohort study. This debate is more socio-economic and ethical in nature than scientific. The study does confirm the increased risk of neoplasia in Barrett's patients but also confronts us once again with the limitation of our daily clinical practice. Indeed, adenocarcinoma is often diagnosed without a previous history of Barrett's esophagus [2,3], and indeed as endoscopists we do feel that we take a redundant amount of biopsies to diagnose few new cases of cancer. Rather than reopening the debate on whether to survey these patients or not, the current study merely substantiates the need for a proper risk stratification and diagnostic tool to detect more patients with Barrett's disease before they develop cancer and also to select those that

benefit from surveillance or even early preventive treatment. New diagnostic developments such as the Cytosponge test [5] look very promising, in particular if they could be combined with the identification and testing of molecular markers [6,7]. Further development and identification of patient related and molecular risk factors will hopefully allow making Barrett's surveillance more cost-effective.

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