

COMMENTED SUMMARIES FROM CURRENT MEDICAL LITERATURE

DOES A SURGICAL ANTIREFLUX PROCEDURE DECREASE THE INCIDENCE OF ESOPHAGEAL ADENOCARCINOMA IN BARRETT'S ESOPHAGUS? A META-ANALYSIS

SUMMARY: The risk of adenocarcinoma of the esophagus is increased among those with Barrett's esophagus (BE). Whether the risk of cancer in the setting of BE can be decreased by a surgical antireflux procedure (SARP) is unclear. This study compared the reported incidence of esophageal adenocarcinoma in subjects with BE who underwent SARP with those with BE who had medical management. We used MEDLINE to perform a meta-analysis of the English language literature published from 1966 through October 2001. We reviewed abstracts found with the search term "Barrett's esophagus" and the following: "adenocarcinoma," "esophageal neoplasm," "proton pump inhibitor," "fundoplication," or "antireflux procedure." Study entry criteria included 1) trial or cohort study with a report of cancer risk expressible in cancers per patient-year, 2) histologic confirmation of BE and any adenocarcinomas, and 3) adequate description of intervention (medical vs SARP). Data were abstracted by two reviewers using standardized forms. Subgroup comparisons were made using only medical management studies published in the last 5 yr. Multivariable regression controlling for subject age, country of origin, and BE length was performed. We reviewed 1,247 abstracts, and 34 met the inclusion criteria. There were a cumulative 4,678 patient-years of follow-up in the SARP group and 4,906 patient-years in the medical group. The cancer incidence rate in the SARP group was 3.8 cancers/1000 patient-years, compared with 5.3 in the medical group ($p = 0.29$). Similarly, there was no significant difference between cancer rates when comparing SARP with medical series reported in the last 5 yr (3.8/1000 patient-years vs 4.2/1000 patient-years, $p = 0.33$). Multivariate analysis controlling for subject age, country of origin, and BE length did not alter these findings. The reported risk of adenocarcinoma in subjects with BE is low and not significantly decreased by a surgical antireflux procedure. Antireflux surgery in the setting of BE should not be recommended as an antineoplastic measure.

COMMENT: Barrett's esophagus (specialized columnar metaplasia of the lower esophagus) is considered to be a complication of chronic gastroesophageal reflux disease (GERD) predisposing the affected individual to adenocarcinoma of the esophagus.¹ GERD itself is also considered a chronic disease needing maintenance medical therapy or surgical intervention in most instances.² Recent data indicate that the longer the duration and severity of GERD, the higher the chance of malignant transformation of the metaplastic Barrett's mucosa.³ Surgical anti-reflux procedures, whether open or laparoscopic, are effective in controlling the patients' symptoms well at least in short and mid-term. Whether anti-reflux surgery can reverse or halt the process of malignant transformation of the metaplastic Barrett's mucosa is a matter of dispute.⁴

In the November issue of the American Journal of Gastroenterology Corey et al have published a careful meta-analysis to see whether anti-reflux surgery affects the incidence of development of adenocarcinoma of the lower esophagus.⁵ They have reviewed 1,247 abstracts extracted from the MEDLINE and selected 49 to go through in detail, of which 16 met their inclusion criteria for the meta-analysis. Reviewing the bibliographies of these 49 articles they identified 18 more articles meeting their inclusion criteria, so overall 34 articles (either randomized controlled trials (RCT) or cohort) touching their objectives were included in the meta-analysis. They found that there was no difference between the surgically and medically managed patients⁶ regarding the later incidence of adenocarcinoma of the lower esophagus. In an accompanying editorial Philip Katz appreciates Corey's work and comments that the role of anti-reflux surgery in the management of chronic GERD may still be unclear and it should certainly not be proposed to anybody on the sole basis of preventing a potential adenocarcinoma in the context of Barrett's esophagus. Interestingly Katz has been one of the first people who reported that anti-reflux surgery decreases the chance of development of

later adenocarcinoma of the lower esophagus.⁷ His scientific way of thinking makes him see newer evidence carefully and free from any prejudice therefore admitting that the earlier evidence (partly produced by his own team) is not valid anymore. This is an important lesson to keep in mind: “science is based on current good quality evidence, no matter how inconsistent with our beliefs or work, and as scientists we should be ready to surrender to better and stronger evidence”.

High quality meta-analyses are among the best sources of evidence as they compile individual research works into a well-structured, meaningful summary. Despite this great potential, meta-analyses are subject to some flaws themselves. Therefore, the quality of a meta-analysis should be taken into account when quoting them.⁸ Corey et al’s meta-analysis, although carefully conducted and fluently narrated, suffers from some shortcomings, which should be noted:

- 1) It is not clear how many of the studies enrolled were RCTs and how many cohorts.
- 2) The quality of the RCTs included has not been assessed, or at least the results are not shown (i.e., homogeneity, randomization process, and allocation concealment). This will affect the quality of the meta-analysis substantially.
- 3) It is not clear how many of the cohorts were retrospective and how many prospective. This also affects the quality of the meta-analysis.
- 4) How many of the studies included had reported “all” the variables of interest of the authors.
- 5) The medically followed patients by Katz et al⁷ are not included in the table. In addition, Katz and colleagues have reported on 15 patients undergoing surgical anti-reflux procedures, while Correy et al have mentioned it to be 16.
- 6) In the report by Klinkenberg-Knol published in 2000, the focus has been on the potential gastric complications of long-term omeprazole treatment.⁹ They have not looked systematically at Barrett’s esophagus, neither have they stated any systematic biopsies of the lower esophagus or any Barrett’s mucosa. They state “However, reporting of Barrett’s esophagus throughout this long study was not always consistent from one visit to another or from one endoscopist to another in any given patient. Endoscopy techniques and equipment have also improved over recent years, making identification of Barrett’s esophagus more reliable. Also, areas of severe esophagitis can make the diagnosis of the underlying Barrett’s epithelium difficult or heal, not infrequently, with columnar metaplasia. We therefore believe that interpretation of these data must be cautious.” In addition, some of their patients had had anti-reflux surgery prior to enrollment to the study. It is not clear how many of the BE patients had the operation, while all of them have been included in the medical therapy group. Considering this, their data regarding Barrett’s esophagus may not be reliable enough to be included in such a meta-analysis.
- 7) The same points mentioned in item 6 apply to the other article by Klinkenberg-Knol published in 1994 and included by Corey et al.¹⁰
- 8) Corey et al have only looked at the literature indexed in the MEDLINE, while other important databases such as the EMBASE, which has only a 40% overlap with MEDLINE, have not been searched. Therefore, some important data may have been omitted which could have affected the outcome of this meta-analysis.

Although the concept conveyed by Corey et al is shared by many working in the field including the author, but considering these shortcomings, it should be stated that the quality of this meta-analysis is not as high as it could have been. Therefore, it should be looked at with care and waiting for higher quality studies to address the issue.

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