

Canadian Association of General Surgeons, the American College of Surgeons, the Canadian Society of Colorectal Surgeons, and the American Society of Colorectal Surgeons: Evidence Based Reviews in Surgery – Colorectal Surgery

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The term “evidence-based medicine” was first coined by Sackett and colleagues as “the conscientious, explicit and judicious use of the current best evidence in making decisions about the care of individual patients.”¹ The key to practicing evidence-based medicine is applying the best current knowledge to decisions in individual patients. Medical knowledge is continually and rapidly expanding and reading all of the medical literature is impossible for an individual clinician. For clinicians to practice evidence-based medicine, they must have the skills to read and interpret the medical literature so they can determine the validity, reliability, credibility, and utility of individual articles, ie, critical appraisal skills. In general, critical appraisal requires that the clinician have some knowledge of biostatistics, clinical epidemiology, decision analysis, and economics as well as clinical knowledge.

The Canadian Association of General Surgeons and the American College of Surgeons jointly sponsor a program entitled “Evidence Based Reviews in Surgery (EBRS),” supported by an educational grant from Ethicon Inc and Ethicon Endo Surgery Inc and Ethicon Endo Surgery. The primary objective of this initiative is to help practicing surgeons improve their critical appraisal skills. Beginning in 2007, EBRS also included a module covering topics in colorectal surgery. Each academic year, 6 clinical articles are chosen for review and discussion. The articles are selected not only for their clinical relevance to colorectal surgery, but also to cover

a spectrum of methodological issues important to surgeons; for example, causation or risk factors for disease, natural history or prognosis of disease, quantifying disease (measurement issues), diagnostic tests and the diagnosis of disease, and the effectiveness of treatment. Both methodological and clinical reviews of the article are performed by experts in the relevant areas and posted on the EBRS-CRS website. As well, a listserv discussion is held where participants can discuss the monthly article. Members of the Canadian Association of General Surgeons (CAGS), and the American College of Surgeons (ACS), can access Evidence Based Reviews in Surgery–Colorectal through the Canadian Association of General Surgeons website (www.cags-accg), the American College of Surgeons website (www.facs.org/education/ebars.html), the Canadian Society of Colon and Rectal Surgeons (CSCRS) website (www.cscrs.ca), and the American Society of Colon and Rectal Surgeons (ASCRS) website (www.fascrs.org). All journal articles and reviews are available electronically through the website. Surgeons who participate in the current (modules) packages can receive CME and/or Maintenance of Certification credits by completing an evaluation and a series of multiple choice questions. For further information about EBRS-CRS, readers are directed to the CAGS, ACS, CSCRS, and ASCRS websites or should email the administrator, Marg McKenzie at mmckenzie@mtsina.on.ca.

In addition to making the reviews available through the CAGS and the ACS websites, a condensed version of the reviews will be published in the *Diseases of the Colon & Rectum*. We hope readers will find EBRS useful in improving their critical appraisal skills and also in keeping abreast of new developments in general surgery. Comments about EBRS may be directed to mmckenzie@mtsina.on.ca.

SELECTED ARTICLES

Salem TA, Molloy RG, O'Dwyer PJ. Prospective five-year follow-up study of patients with symptomatic uncomplicated diverticular disease. *Dis Colon Rectum*. 2007;50:1460–1464.

Chautems RC, Ambrosetti P, Ludwig A, Mermillod B, Morel P, Soravia C. Long-term follow-up after first acute episode of sigmoid diverticulitis: is surgery mandatory. A prospective study of 118 patients. *Dis Colon Rectum*. 2002;45:962–966.

In this article we will be reviewing the above clinical articles. Some similarities exist in both articles, but they address very different issues related to diverticular disease.

COMMENTARY: Prognosis is the term used to describe the likely outcome of an illness. Knowing the prognosis of a disease is important so clinicians can decide whether treatment is indicated and they can counsel patients on what the likely outcome of the disease will be. Often, outcome varies depending on whether certain patient or disease characteristics are present and these are known as prognostic factors. In some diseases, the prognosis is well known. For instance, the prognosis of most cancers is known. Furthermore, there are well accepted staging systems that adjust the predicted outcome based on validated prognostic factors. To the contrary, much less is known about the prognosis of other diseases, one of those being diverticular disease. Despite that diverticula are common findings, especially in the elderly population of Western countries, and that diverticulitis is frequently encountered in surgical practice, the prognosis of diverticular disease still is uncertain. The areas of uncertainty include when to operate in patients who have had episodes of acute diverticulitis (after 1 or 2 or even after several episodes of successful nonoperative treatment of diverticulitis?), and should recommendations be altered for younger patients with diverticulitis and those with complicated diverticular disease (eg, abscess). Much of the uncertainty is due to the evidence being of relatively poor quality, either because the data are incomplete or inadequate and/or the follow-up is short.

In general, cohort studies are the preferred design for studying the prognosis of a disease. They may be performed retrospectively or prospectively. Patients or individuals with the condition should be assembled in a well defined period of time to ensure all individuals are included in the cohort. In retrospective cohort studies, the cohort is previously assembled and the follow-up is available at the start of the study. In prospective cohort studies, the cohort is assembled and it is followed prospectively. The criteria for including patients into the study should be well defined, explicitly stated, and accepted by clinicians as defining the disease in question. Similarly, the outcomes of interest should be well defined and patients should be followed up for an adequate period of time to ensure that if an

event is going to occur, it probably will be observed in the time frame of the study. Ensuring that all patients or individuals with the condition are entered into the study and that all are accounted for at the end of the study is important to minimize bias.

In this review, we look at 2 articles that address the issue of the natural history or prognosis of diverticular disease. The conclusions differ, probably because of differences in various aspects of the studies. Salem and colleagues state that the objective of their study was to determine the long-term natural history of symptomatic diverticular disease, whereas Chautems and colleagues aim was to determine what the long-term outcome of patients treated nonoperatively after a first acute episode of sigmoid diverticulitis is.

Salem et al performed a retrospective cohort study that included patients who were found to have diverticula while being assessed for abdominal pain. Patients were recruited over a 21-month period (ending in April 2001) to a pragmatic randomized controlled trial that included all patients referred by general practitioners in a geographic region of Scotland for investigation of large-bowel symptoms (with the exception of those with a mass on rectal examination or a previous history of adenoma or a family history of colorectal cancer or iron deficiency anemia). A total of 1131 patients were included in the original trial; 166 of these patients had endoscopic findings of diverticula. One of these patients required colectomy for a symptomatic stricture and another 27 were excluded because of symptoms attributable to other diseases, leaving a cohort of 138 patients. The authors used a combination of telephone-based questionnaire of the patient/family physician and evaluation of hospital records to confirm whether patients had been admitted with a complication related to diverticular disease (based on ICD10 codes) to follow patients. The questionnaire was administered in September 2005 so there was a median follow-up of 5.5 years with a range of 4.2 to 6.7 years. Of the 138 patients with diverticular disease eligible for follow-up, 119 patients could be located and agreed to participate in the study (86% of eligible and 72% of the 166 patients identified in the original study with diverticular disease). Of these, 3 patients (2.5%, 95% CI 0.9–7.1%) developed or required surgery for symptomatic diverticular disease. This was defined as either an episode of acute diverticulitis (based on symptoms plus an elevation in inflammatory markers) or complicated diverticular disease (defined as development of associated stricture, fistula, abscess, mass, significant bleeding, or perforation). There was no adjustment for prognostic factors because of the small number of outcomes. The authors concluded that “symptomatic uncomplicated diverticular disease seems to run a long-term benign course with a very low incidence of subsequent complications.”

Chautems et al included all patients admitted over a 5-year period (October 1986 to December 1991) to a single

institution (a university hospital providing primary and tertiary care for patients in the region) with a history and clinical findings of sigmoid diverticulitis plus either a CT scan of the abdomen or water-soluble contrast enema consistent with the diagnosis. Patients were excluded if they had a prior episode of acute diverticulitis or required surgery on that admission. A total of 144 patients meeting these criteria were admitted to the hospital during this period, although 6 were excluded because an initial CT was not “contributive.” The severity of the clinical presentation is not clear, although 30 patients were reported to have severe findings (abscess, extraluminal air, or contrast) on CT at presentation. Also, it is uncertain whether the cohort was assembled retrospectively or prospectively with the former being more likely. Outcomes were ascertained by sending a follow-up questionnaire to patients and/or family doctors and searching records of the University Hospital of Geneva to see whether patients had been readmitted for diverticular disease.

Of the original 138 patients meeting the entry criteria, 20 patients were lost to follow-up before 1 year and 6 were lost to follow-up between 1 and 10 years of follow-up, so 112 (81%) had complete follow-up. Thirty-eight patients had a poor outcome. Overall, 71% (95% CI 62%–79%) patients were alive without a poor outcome at 5 years. A total of 37 patients underwent an operation: 31 of 38 patients who had a poor outcome and 6 patients who had a good outcome. On the other hand, 7 of the 38 patients with a poor outcome did not have surgery, 5 because they were considered to be unfit for surgery, and 2 because they refused. The majority (26 of 38) of the patients who developed a poor outcome did so within the first 2 years. Age and severity of the initial attack were predictive of poor outcome. Patients presenting with “severe” diverticulitis had a 49% risk of “poor outcome” at 5 years, compared with 22% in those with “mild” diverticulitis. Patients under the age of 50 had an increased risk of poor outcome on univariate analysis only (44% vs 24%). An important outcome of this study, which was not stressed, is that no emergency operations were required in the follow-up period. Nevertheless, these authors concluded that “young patients with severe diverticulitis on CT should undergo elective surgery after a first acute episode, because the likelihood of poor outcome is high.”

So, the question is: do either of these studies elucidate the natural history of diverticula and diverticular disease? Sadly, the information from these studies adds little to the body of evidence that is previously available and thus, neither study will likely change management of patients with diverticular disease. Of the 2 studies, the results of the Chautems study may be more relevant to surgeons. The study by Salem may be more generalizable to patients with diverticulosis who have minimal to no symptoms. Although the symptoms that patients reported were attributed to diverticular disease in the Salem et al study, most

experts would be skeptical that they really were. The authors in fact acknowledge that it is “difficult to exclude irritable bowel syndrome, rather than diverticular disease, as the cause for some patient’s symptoms.” Thus, the results of this study may be more generalizable to patients who have asymptomatic diverticula. Another limitation of this study is that there was a median follow-up of only 5.5 years, which is not adequate for evaluating the natural history of the disease. Last, the sample size is small so it does not allow one to determine which individuals are at higher or lower risk for developing symptomatic or complicated diverticular disease.

The study by Chautems et al fails to address one of the most controversial questions in the management of diverticulitis. Because surgery was recommended to patients who had a second episode of diverticulitis, the natural history of this disease (ie, what happens after a second episode) is unknown. Whereas previous guidelines recommended surgery in most individuals after 2 attacks of diverticulitis, a more conservative approach in treating patients, at least those with relatively uncomplicated diverticulitis episodes, is now followed, but there are few data to know whether this is appropriate. Their primary outcome event was “poor outcome” but it was poorly defined and the exact indication for operation (recurrence, abscess, stenosis, and fistula) was not presented. Thus, we still are left not knowing when and in whom we should recommend elective resection for patients with a past history of diverticulitis. Indeed, whereas the study by Chautems et al recommends that surgery be performed after 2 attacks, one could also conclude that 50% of patients who had a severe attack could avoid an unnecessary operation. Even if one were to look only at the younger patients with severe diverticulitis, a similar conclusion could be made, noting that over one third of patients could avoid an unnecessary operation. The devil is in the details, of course, and knowledge of the severity of the second attack, which often is less severe than the first attack, and the exact indication (fistula or abscess) would likely be more important considerations than the occurrence of an episode of simple recurrent diverticulitis especially since emergency surgery was not required in any of the patients.

The generalizability of these results is further limited because patients who did not require admission to the hospital were excluded from the cohort. Another concern is that “Ambrosetti’s criteria” were used to grade the severity of the diverticulitis rather than the Hinchey classification. The Ambrosetti staging system classifies patients as mild or severe based on the presence or absence of abscess, extraluminal air, or extraluminal contrast on CT scan, whereas the Hinchey classification subclassifies the “severe” episodes into those with pericolic abscess, pelvic abscess, and free perforation. This is particularly important when discussing abscesses, because previous studies

have shown that patients who have had diverticulitis complicated by pelvic abscesses have a higher likelihood of recurrence.

Thus, there is clearly a need for a better understanding of the natural history of diverticular disease. Hopefully these studies and others like them will stimulate investigators to undertake long-term, large-scale, multicenter studies to determine the true natural history of diverticular disease. However, we are not there yet!

ACKNOWLEDGMENT

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1. Evidence-Based Medicine Working Group. Evidence-based medicine: a new approach to teaching the practice of medicine. *JAMA*. 1992;268:2420–2425.