Published in final edited form as:
World J Surg. 2013 May ; 37(5): 982–983. doi:10.1007/s00268-013-1952-6.

Short- and Long-Term Mortality After Appendectomy in Sweden 1987–2006: Influence of Appendectomy Diagnosis, Sex, Age, Co-morbidity, Surgical Method, Hospital Volume, and Time Period—A National Population Based Cohort Study

Frederick Thurston Drake and **David R. Flum**
Department of Surgery, University of Washington Medical Center, Seattle, WA, USA

This article is Roland Andersson's most recent addition to his important body of work focused on appendicitis and appendectomy [1]. Using a large Swedish database, Andersson has reaffirmed what previous studies in the Unites States [2] and the United Kingdom [3] have also demonstrated: negative exploration for suspected appendicitis and subsequent so-called negative appendectomy (NA), often considered by surgeons to be a harmless procedure, may not be benign and may be a marker of something worse. There are several important outcomes in appendectomy patients. Although we disagree with Andersson that "avoiding *mortality* is the ultimate goal in the management of patients with suspected appendicitis" (emphasis added), the data presented in this paper suggest that both long-term and short-term mortality may be adversely affected when patients who are incorrectly diagnosed with appendicitis undergo appendectomy.

Compared to patients with nonperforated appendicitis, the risk of death after NA was increased in the short term [hazard ratio (HR) 3.32, 95 % CI 2.21–4.94] and in the long term (HR 1.76, 95 % CI 1.54–2.00). Indeed, these HRs were larger than those for perforated appendicitis (compared to nonperforated appendicitis). Interestingly, at 5 years, the standardized mortality ratio (SMR) showed that mortality for patients who underwent appendectomy for nonperforated and perforated appendicitis fell below societal baseline (SMRs of 0.71 and 0.92, respectively). By contrast, for NA the SMR remained elevated at 5 years, at 1.27.

Readers will certainly be interested in how it is that appendectomy for appendicitis is associated with a reduction in 5-year mortality compared to that for the general Swedish population. In our judgment, it likely arises from two sources. As Andersson discusses in his article, there is likely a "healthy patient bias," by which individuals judged healthy enough to undergo an operation were preferentially selected for surgical treatment of their suspected appendicitis (instead of applying antibiotics or observation). Another potential contributor arises from the fact that long-term mortality was calculated from 90 days to 5 years—excluding those patients who died within 89 days of surgery. Sicker patients who were less able to withstand surgery may have died early, which would have left healthier patients in

daveflum@u.washington.edu. ftdrake@u.washington.edu.

the remaining cohort measured out to 5 years. In terms of the increased 5-year mortality observed among NA patients, the data presented here establish a clear association between NA and an increasing number of co-morbid conditions, which can affect survival. Additionally, if we recognize NA as a marker of *missed* diagnoses, in which appendicitis was suspected but instead there was an occult but potentially serious intraabdominal process, the finding of increased long-term mortality may represent the sequelae of these unrecognized processes. Andersson's analysis accounted for the presence of additional diagnoses identified at the time of operation by categorizing those separately from the "entirely negative appendectomy," but ongoing processes missed by the surgeon at the time of laparotomy or laparoscopy (e.g., ulcerative colitis, Crohns disease, other colitides) may contribute to the long-term reduction in mortality seen in NA patients. In summary, although these data cannot be used to prove that NA, in and of itself, is harmful, there is certainly no evidence to suggest that it is harmless.

There are other important findings. Most notably, Andersson found no association between hospital volume and postoperative mortality at 30 days or at 5 years. Additionally, he found that short-term mortality of laparoscopic appendectomy was not different than that of open appendectomy. However, at 5 years, the HR of laparoscopic versus open procedures was lower, at 0.83 (95 % CI 0.73–0.94). Andersson suggests that the reduction in mortality compared to open procedures likely arises from selection bias (healthier patients are more often chosen for laparoscopic than for open surgery), not, as other investigators have suggested, that long-term benefits accrue to patients because the laparoscopic approach causes less systemic stress response than open surgery. Given that patients were nonrandomly allocated to laparoscopic or open procedures, it is difficult to choose one interpretation over the other. It bears mentioning as well that data collection began in 1987. Early laparoscopic surgery outcomes were perhaps not as good as later outcomes from surgeons more experienced with laparoscopy. Conversely, patients from the earlier era, which we are told had higher baseline mortality, are more likely to be included in the open category, which would tend to bias the results toward laparoscopy.

The central message of this article is that, as Andersson writes, diagnostic accuracy is critical. Just because appendectomy is relatively well-tolerated by patients and not prone to serious complication does not mean that it should be undertaken without careful consideration. One cannot determine from these data whether NA itself is harmful or if it is a marker of underlying poor health or other conditions that ultimately lead to worse outcomes. As a marker of something else, we would not expect these outcomes to change with a better diagnostic workup focused specifically on appendicitis—unless the improved workup leads to a correct alternative diagnosis for patients who can then be started on appropriate therapy. A prospective trial of ultrasonography in patients with suspected appendicitis showed that alternative diagnoses can be frequently detected by experienced, highly-qualified sonographers [4]. For these reasons, and although we recognize that this strategy may not be appropriate in all of the many diverse health care settings around the world, our group has advocated the routine use of advanced diagnostic imaging (ultrasonography, computed tomography, magnetic resonance imaging) as a means of safely reducing NAs in patients suspected of having appendicitis. This is especially critical in reproductive-age women, but analysis of a large cohort of patients in Washington state

demonstrated that the use of preoperative imaging in men is also associated with a significant reduction in NAs [5].

At the same time, as Andersson pointed out in a recent letter to the *British Medical Journal* [6], there are almost certainly some cases of appendicitis that are self-resolving. As we achieve greater sensitivity in diagnosing appendicitis, we will likely increase the number of patients treated whose disease might otherwise resolve spontaneously. These competing interests—improving diagnostic accuracy to reduce the number of unnecessary (and potentially harmful) operations and, simultaneously, not over-treating patients with appendicitis that may be self-limiting—represent the newest challenges in the management of this disease. As is true in much of medicine, when we learn more, we find that we actually know less. This is certainly the case with appendicitis, a beguiling condition with many questions still to be answered.

References

1. Andersson R. Short- and long-term mortality after appendectomy in Sweden 1987 to 2006: influence of appendectomy diagnosis, sex, age, co-morbidity, surgical method, hospital volume, and time period—a national population-based cohort study. World J Surg. 2012 doi:10.1007/s00268-012-1856-x.
2. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg. 2002; 137:799–804. [PubMed: 12093335]
3. Faiz O, Clark J, Brown T, et al. Traditional and laparoscopic appendectomy in adults: outcomes in English NHS hospitals between 1996 and 2006. Ann Surg. 2008; 248:800–806. [PubMed: 18948807]
4. Drake FT, Florence MG, Johnson MG, et al. Progress in the diagnosis of appendicitis: a report from Washington state's surgical care and outcomes assessment program. Ann Surg. 2012; 256:586–594. [PubMed: 22964731]
5. Rettenbacker T, Hollerweger A, Gritzmann N, et al. Appendicitis: should diagnostic imaging be performed if the clinical presentation is highly suggestive of the disease? Gastroenterology. 2002; 123:992–998. [PubMed: 12360459]
6. Andersson, RE. RE: Safety and efficacy of antibiotics compared with appendectomy for treatment of uncomplicated acute appendicitis: meta-analysis of randomised controlled trials [rapid response letter]. 2012. http://www.bmj.com/content/344/bmj.e21 56/rr/578331/. Accessed 30 Sept 2012