# Colonoscopy after acute diverticulitis: from clinical epidemiology to clinical management. Are we there yet?

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Acute diverticulitis (AD) is a significant clinical and economic burden, with over 200,000 inpatient admissions and costs exceeding 2 billion dollars annually.[1] Current guidelines recommend colonoscopy after AD resolution "in an effort to exclude misdiagnosis of colorectal cancer (CRC) in patients who have not undergone recent high-quality colonoscopy."[2] However, this is a conditional recommendation based on low-quality evidence. Some studies suggest that this recommendation may be too broad. Understanding the risk of CRC in persons with AD is a necessary starting point for identifying when colonoscopic evaluation should be considered or may be required. However, the population risk requires placement into the appropriate clinical context by considering factors such as age, family history, symptoms, and signs that preceded the episode of AD, along with the timing and findings of a previous colonoscopy.

In our experience, current practice is driven by the guidelines, but usually without consideration of these other factors. Assuming no symptoms, signs, previous colonoscopy, or high-risk family history, knowing the risk of CRC after AD would help us understand the expected yield of colonoscopy so that benefits and risks could be more explicitly considered. Recent data suggest that colonoscopy may be best applied selectively to AD patients. A meta-analysis of 31

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observational studies (of which only 2 were performed in the United States) that included 50,445 patients found a pooled prevalence of CRC in AD of 1.9% (95% CI, 1.5%-2.3%). The prevalence of CRC in complicated disease was 7.9%, compared with 1.3% for uncomplicated disease.[3]

This difference suggests that patients with complicated disease may require colonoscopy. In addition to the aforementioned factors, specific radiographic findings may further distill the AD population. CT is not an acceptable diagnostic test for CRC, and there is a risk for false negative results in the setting of AD.[4] However, a small retrospective study showed "nontargeted" CT to have a sensitivity of 72.4% for CRC.[5] In a 2016 study of 110 patients with CT evidence of AD who underwent colonoscopy, CRC was present in none of 102 patients with definitive radiographic diverticulitis alone, compared with 4 of 8 patients in whom there was a concern for CRC.[6] These data suggest that historical, clinical, and diagnostic data can be used to identify AD patients in need of further evaluation.

Consideration of colonoscopy after AD raises 2 related but distinct questions. The clinical epidemiologic question is this: "What is the risk (ie, prevalence) of CRC and advanced adenoma (AA) in a representative AD population?" The clinical management question is this: "Who should undergo colonoscopy after an AD episode?" The study by Tehranian et al[7] in this issue is relevant to the first question. It was a retrospective study of 474 patients who had clinical and radiographic evidence of AD and who underwent colonoscopy a median of 4 months after (but as long as 6.6 years after) the episode. With the time interval between AD and colonoscopy, the study was not strictly a cross-sectional study (to measure pure prevalence) but rather a short-term

follow-up study that measured mostly CRC and AA prevalence but might have included some incident lesions. The authors compared the occurrence of CRC and AA in this group with that in 2 historical control groups of individuals who underwent screening colonoscopy: a meta-analysis of more than 68,000 persons[8] and a local cohort of more than 28,000 patients. Based on the finding of a higher frequency of CRC among AD patients than among screened control individuals (2.7% vs 0.8% and 0.3%, respectively), with no difference between complicated and uncomplicated disease, the authors conclude that colonoscopy after AD is "advisable."

We commend the authors for adding a large-scale U.S. study to those from other countries, mostly from Europe. Study strengths include the rigorous process for case identification, manual review (by a single reviewer!) of more than 5000 CT scan reports, the large case sample size, and the comparison with 2 large control groups. The study findings beg the question of who requires colonoscopy after AD. How should these findings be translated—ie, how do we go from a clinical epidemiologic study to a clinical practice recommendation? Let's first examine the study for the validity of its risk estimates.

Despite several strengths, the study limitations may affect how we interpret the numerical results. One limitation, acknowledged by the authors, is selection bias; just over half of the patients identified as having AD on CT did not have a subsequent colonoscopy identified in the electronic medical record (although they may have had it elsewhere). The majority of these unevaluated patients had uncomplicated disease; their inclusion would have likely lowered the prevalence of CRC. Additionally, 32 (6.8%) of the 474 patients had CT findings suggestive of CRC; however, the number of CRCs within this small but very important subgroup is not

provided. It is possible that this factor alone accounted for many or nearly all of the 13 patients with CRC. How could these 2 features—one a methodologic limitation, the other a study design decision—have affected the prevalence estimate for CRC? Could adjustment for these factors reduce the observed prevalence into the average-risk screening range of 0.9% to 1.1%?[9,10]

If we assume that 7 of 13 CRCs were present among the 32 patients in whom CRC was suspected radiographically, the prevalence of CRC in the remaining larger subgroup would be 6 of 442 (1.36%; 95% CI, 0.50% to 2.93%). If we further assume that there were no CRCs among the 504 patients for whom no record of a subsequent colonoscopy was found, then the prevalence of CRC becomes 6 of 946 (0.63%; 95% CI, 0.23% to 1.38%), which is consistent with the prevalence of CRC in studies of average-risk screening colonoscopy. Even a few cancers among the 504 unevaluated patients would not have a clinically significant effect on this prevalence estimate. And these calculations include the patients with complicated disease: a subgroup that we expect would elevate the prevalence of CRC.

We acknowledge that some might consider our assumptions to be too extreme, but their effect on the prevalence of CRC illustrates why these clinical epidemiologic data alone cannot be used to make a clinical recommendation for colonoscopic evaluation. On the basis of the literature and our experience, patients with complicated disease and those with radiographic suspicion of CRC have the greatest need for colonoscopy. For the remaining patients, the decision needs to be made on a case-by-case basis. In the absence of complicated disease and radiographic suspicion of CRC, the expected prevalence of CRC would seem to be no higher than in the screening setting.

The new and welcomed findings from Tehranian et al[7] provide a "ballpark" estimate of the prevalence of CRC—one that requires clinical integration with the aforementioned patient-specific factors, practical considerations ("screening" someone who has yet to be screened and may otherwise be nonadherent), and patient preferences. Epidemiologic data are helpful for framing clinical questions, but the path from clinical epidemiology to clinical management is a winding one. This scenario is a good reminder that it is incumbent on us to integrate the best available research evidence with clinical expertise and patient values and preferences as signposts to navigate challenging clinical decisions.

**Disclosure**

*All authors disclosed no financial relationships.*

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