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- 119 Risk of colorectal cancer in patients with diverticular disease
Meyer J, Buchs NC, Ris F

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Risk of colorectal cancer in patients with diverticular disease

Jeremy Meyer, Nicolas Christian Buchs, Frédéric Ris

Jeremy Meyer, Nicolas Christian Buchs, Frédéric Ris, Division of Digestive Surgery, University Hospitals of Geneva, Genève 1211, Switzerland

ORCID number: Jeremy Meyer (0000-0003-3381-9146); Nicolas Christian Buchs (0000-0001-9255-3929); Frédéric Ris (0000-0001-7421-6101).

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Correspondence to: Jeremy Meyer, MD, PhD, Doctor, Division of Digestive Surgery, University Hospitals of Geneva, Rue Gabrielle-Perret-Gentil 4, Genève 1211, Switzerland. jeremy.meyer@hcuge.ch
Telephone: +41-79-5533182
Fax: +41-22-3727707

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Abstract

Colorectal cancer constitutes an important burden on the healthcare system. Screening at-risk populations to reduce colorectal cancer-related morbidity and mortality has become part of good clinical practice. However, recommendations regarding subgroups of patients with diverticular disease are subject to controversy.

Herein, we review the most recent literature regarding the prevalence of colorectal cancer in patients with diverticular disease, diverticulitis and uncomplicated diverticulitis.

The recent literature does not identify diverticular disease as a long-term risk factor for colorectal cancer. However, the risk of colorectal cancer is increased in the short-term period after hospitalization related to diverticular disease. According to a recent systematic review and meta-analysis, the prevalence of colorectal cancer is 1.6% in patients with acute diverticulitis who underwent colonoscopy. The risk of having colorectal cancer after an episode of acute diverticulitis is 44-fold higher than that of an age- and gender-adjusted reference population. Despite lower among patients with uncomplicated episode, the risk of colorectal cancer remains 40-fold higher in that subpopulation than that in the reference population.

To conclude, the recent literature describes an increased risk of colorectal cancer among patients with acute diverticulitis compared to the reference population. Colonoscopy is therefore recommended in patients with diverticulitis to exclude colorectal cancer.

Key words: Diverticulosis; Diverticulitis; Colonoscopy; Screening; Tumor; Risk factor

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Core tip: The present manuscript reviews the current literature reporting on the prevalence of colorectal cancer

in patients with diverticular disease. The prevalence of colorectal cancer among subgroups of patients with diverticulitis and uncomplicated diverticulitis is discussed, with the objective of providing recommendations for colorectal cancer screening.

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INTRODUCTION

In 2018, colorectal cancer (CRC) will represent 8.1% of estimated cancer cases and will account for 15.6% of estimated cancer deaths in the United States^[1]. At-risk populations are screened to reduce CRC-related morbidity and mortality and to reduce healthcare costs.

CRC IN DIVERTICULAR DISEASE

Some authors consider diverticular disease a risk factor for CRC. For instance, Stefansson *et al.*^[2] reported a standardized incidence ratio (SIR) of 5.8 (95%CI: 4.6-7.3) over a 2-year period for CRC in patients with diverticular disease compared to controls without diverticular disease. That risk persisted for 10 years for patients with left-sided disease. Later, Granlund *et al.*^[3] performed a case-control population-based study including 41037 CRC patients matched with 82074 controls. They identified that hospitalization for diverticular disease in the previous 6 mo was a risk factor for CRC with an odd ratio (OR) ranging between 22.75 (95%CI: 14.06-36.82) and 31.49 (95%CI: 19.00-52.21). Thereafter, that risk was not significantly different from that of the population without diverticular disease^[3]. More recently, Huang *et al.*^[4] followed 41359 Asian patients with diverticular disease and 165436 age- and gender-matched patients without diverticular disease. They found annual incidences of CRC of 0.62% and 0.15%, respectively, in these populations. Among patients with diverticular disease, the hazard ratio (HR) for CRC was 5.08 (95%CI: 4.19-4.91). After excluding the first year of follow-up, the adjusted HR dropped to 0.98 (95%CI: 0.85-1.13)^[4]. Therefore, both of these large-scale population-based studies, which included 2 geographically distinct populations, were distinct from the findings of Stefansson *et al.*^[2] by revealing an increased risk of CRC only during the short period of follow-up after hospitalization/diagnosis for diverticular disease. Although the identification of uncomplicated diverticular disease as a risk factor for CRC remains a subject of controversy^[5-8], we note that the usual reasons for diverticular disease-related hospitalization are diverticular bleeding and diverticulitis.

CRC IN DIVERTICULITIS

Diverticulitis accounts for more than 200000 hospital admissions per year in the United States^[9]. The prevalence of CRC in patients suffering from diverticulitis has remained poorly documented for decades, but has recently come under the spotlight. In 2013, Sharma *et al.*^[10] performed a systematic review and meta-analysis of colonoscopy results from 1970 patients with diverticulitis treated with nonsurgical management. They described a prevalence of CRC of 1.6% in that population^[10]. This prevalence was, however, not compared to the prevalence of a reference population. Moreover, selection bias for colonoscopy could not be excluded. To this end, our group compared the incidence of CRC in 506 patients with computed tomography-proven diverticulitis to that of an age- and gender-matched reference population. We found a one-year incidence of CRC of 1.9% in patients with diverticulitis, an incidence that was 44-fold higher (95%CI: 18.58-75.96) than that in the reference population^[11]. One year later, Grahnat *et al.*^[12] confirmed these results by describing a SIR of 20 (95%CI: 10.2-35.7) for sigmoid cancer in 890 patients with CRC compared to their reference population. We also note that Sharma *et al.*^[10] did not include recent population-based large-scale studies in their systematic review and meta-analysis. The population-based study of Huang *et al.*^[4] reported an annual incidence of CRC of 0.49% in the subgroup of 31216 Asian patients with diverticulitis, whereas Mortensen *et al.*^[13] reported that 977 of the 40496 patients hospitalized for diverticulitis were diagnosed with CRC within a year, for an annual incidence of 2.41%. In the latest study, diverticulitis constituted a risk factor for CRC, with an OR of 2.20 (95%CI: 2.08-2.32)^[13]. That increased risk was not identified in the Asian study [HR of 1.08 (95%CI: 0.91-1.28) for CRC among the subgroup of patients with diverticulitis]^[4].

Nevertheless, it seems reasonable to consider that the risk of CRC is increased in the first year after diagnosis of diverticulitis, especially in Western societies. Fifty-seven percent of CRC cases in the study by Mortensen *et al.*^[13] were diagnosed during that period. The risk of CRC might be increased due to difficulties in distinguishing CRC from diverticulitis based on computed tomography, resulting in an initial misdiagnosis, despite the contribution of information bias that cannot be excluded. Indeed, Mortensen *et al.*^[13] reported an increased rate of colonoscopy in the diverticulitis population (57%) when compared to the reference population (10%). Taken together, this evidence led professional societies to recommend performing colonoscopy after an episode of diverticulitis^[14,15].

Furthermore, we note that some authors reported a low prevalence of CRC among patients with uncomplicated diverticulitis and suggested exempting them from colonoscopy^[16-19]. According to the systematic review and meta-analysis by Sharma *et al.*^[10], the pre-

valence of CRC in these patients was 0.7%. However, in our study, we described the prevalence of CRC in patients with uncomplicated diverticulitis to be 40-fold higher than that in the reference population^[11]. Unfortunately, large-scale population-based studies have not distinguished uncomplicated diverticulitis from complicated diverticulitis. Therefore, evidence is lacking to provide recommendations for this subgroup of patients.

Some studies did not identify cases of CRC among young Asian or Hispanic patients with diverticulitis^[20,21]. Further, in their large-scale study, Huang *et al.*^[4] described a higher HR for CRC among old patients than among young patients. Moreover, in our study^[11] and the study by Grahnat *et al.*^[12], all CRC patients were older than 70 years. Additionally, the increased risk documented by our study was age-adjusted, confirming that the increased risk observed among diverticulitis patients was not only due to a global increase in CRC prevalence among older patients. Therefore, the prevalence of CRC seems to be lower among young patients than among old patients, but this remains to be confirmed by large-scale studies.

CONCLUSION

To conclude, the recent literature describes an increased risk of CRC among patients with acute diverticulitis compared to the reference age-matched population. Colonoscopy is therefore recommended in patients with diverticulitis to exclude CRC. However, the evidence is not convincing enough to determine whether subgroups of patients - those with an uncomplicated episode of diverticulitis and/or young patients - might be exempted from colonoscopy. Future studies are needed to determine the prevalence of CRC in patients with uncomplicated diverticulitis, looking more specifically at age groups and providing large-scale population-based comparisons with reference populations. A new systematic review and meta-analysis aggregating the most recent studies, including the latest population-based studies, is necessary. In addition, to our knowledge, no study provides recommendations for patients with a recent colonoscopy to exclude interval colorectal cancer. These questions are of critical importance to better identify at-risk patients in order to provide the best benefit/risk ratio for CRC screening in patients with diverticulitis.

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