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Disease severity does not affect the interval between IBD diagnosis and the development of CRC: Results from two large, Dutch case series ☆

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Abstract

Background: The increased risk of colorectal cancer (CRC) in patients with inflammatory bowel disease (IBD) is well established. The incidence of IBD-related CRC however, differs markedly between cohorts from referral centers and population-based studies. In the present study we aimed to identify characteristics potentially explaining these differences in two cohorts of patients with IBD-related CRC.
Methods: PALGA, a nationwide pathology network and registry in The Netherlands, was used to search for patients with IBD-associated CRC between 1990 and 2006. Patients from 7 referral hospitals and 78 general hospitals were included. Demographic and disease specific parameters were collected retrospectively using patient charts.
Results: A total of 281 patients with IBD-associated CRC were identified. Patients from referral hospitals had a lower median age at IBD diagnosis (26 years vs. 28 years (p=0.02)), while having more IBD-relapses before CRC diagnosis than patients from general hospitals (3.8 vs. 1.5

Abbreviations: RH, Referral hospital; GH, General hospital.

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($p<0.01$)). In patients from referral hospitals, CRC was diagnosed at a younger age (47 years vs. 51 years ($p=0.01$)). However, the median interval between IBD diagnosis and diagnosis of CRC was similar in both cohorts (19 years in referral hospitals vs. 17 years in general hospitals ($p=0.13$)).
Conclusions: IBD patients diagnosed with CRC treated in referral hospitals in The Netherlands are younger at both the diagnosis of IBD and CRC than IBD patients with CRC treated in general hospitals. Although patients from referral centers appeared to have a more severe course of IBD, the interval between IBD and CRC diagnosis was similar.

1. Introduction

Longstanding inflammatory bowel disease (IBD) increases the risk of colorectal carcinoma (CRC), although the risk may be lower than previously perceived. A frequently cited meta-analysis reported cumulative incidence rates for patients with ulcerative colitis (UC) up to 18% after 30 years of disease.[1] Patients with Crohns' colitis (CD) seem to carry a slightly lower risk of CRC than UC patients.[2,3] Although these data are widely acknowledged and have been used to design surveillance guidelines for patients with longstanding IBD,[4,5] there is an ongoing debate about the magnitude of the risk of CRC in patients with colitis. Remarkably, the CRC risks derived from population-based studies are consistently lower than those from referral center-based studies.[6–9] This discrepancy has been attributed to differences in disease severity. The more severe IBD-phenotype in patients cared for in referral hospitals is thought to result in a higher CRC risk in the long run.[10] Whether differences in treatment or demographic parameters play a role is presently unknown.

The aim of the present study was to compare two large cohorts of IBD patients with CRC with regard to demographic and disease specific characteristics. We compared a cohort from referral hospitals (RHs) with a cohort from general hospitals (GHs) and hypothesized that IBD patients from RHs had more extensive and severe disease, resulting in an accelerated inflammation-dysplasia-carcinoma sequence with subsequently early development of IBD-related CRC as compared to IBD patients from GHs.

2. Patients and methods

2.1. Patients

PALGA, a nationwide histopathology database in the Netherlands, was used to identify patients with IBD and a subsequent diagnosis of CRC.[11] We identified all IBD patients diagnosed with CRC in 78 general hospitals and 7 referral hospitals in the period from 1990 until 2006. To minimize interference with sporadic CRC, all patients with CRC diagnosed above the age of 65 were excluded. Patients were recruited from referral hospitals (RHs) and general hospitals (GHs). Both cohorts have been described before.[12,13] Patients diagnosed with CRC before or within 12 months after the diagnosis of IBD were excluded.

2.2. Data collection

Data were collected by two researchers using identical data collection forms and employing the same definitions. Variables and definitions have been reported in detail in previous reports.[12,13] In brief, the maximum histological and endoscopic extent and severity of inflammation (scored as mild, moderate or severe) were obtained from all endoscopy and histopathology reports prior to CRC diagnosis. In UC and indeterminate colitis disease extent was considered left-sided if the most proximal point of inflammation was distal to the splenic flexure. Inflammation extending proximally to the splenic flexure was considered extensive disease. In CD, extensive disease was defined as involvement of more than 50% of the colonic mucosa. The number of exacerbations was defined as all documented endoscopic flares or occurrence of IBD-related symptoms requiring a change in medication, surgery or hospitalization.

2.3. Statistical analysis

Categorical variables were analyzed using the Chi-square test. Continuous variables were analyzed with Student's *t*-test or Mann–Whitney *U*-test depending on data distribution. Kaplan–Meier survival analysis was used to calculate CRC-related mortality and the log rank test was used to compare CRC-related mortality between GH patients and RH patients. A two sided p-value <0.05 was considered significant. SPSS version 15 for Windows was used to perform all statistical analyses.

2.4. Ethical considerations

This study was carried out with the approval of and in accordance with the privacy and ethical guidelines of the privacy committee of PALGA and in accordance with the ethical guidelines of the research committee of both institutions.

3. Results

3.1. Patients

After the PALGA search and review of the patient files, a diagnosis of CRC after a diagnosis of IBD was confirmed in 346 patients. A total of 65 patients were excluded. Reasons for exclusion were the simultaneous diagnosis of CRC and IBD (31 patients), a CRC diagnosis within 12 months after IBD diagnosis (13 patients), CRC diagnosis at an age of 65 years or older (18 patients) and unknown date of IBD diagnosis (3 patients). In total, 281 patients were included for further analysis. One-hundred and twenty-one (43%) patients were treated in RHs and 160 (57%) patients were treated in GHs (from 78 of 93 GHs present in The Netherlands). Men were