ISSN: 2577 - 8005

Research Article

Medical & Clinical Research

Importance of Screening Colonoscopy for Colorectal Cancer among Inflammatory Bowel Disease Patients in Qatar

Nasrein Mohamed Elkomy[1*], Rafie Yakoob[1], Khalid Mohsin A Al-Ejji[1], Saad Rashid Mohamed Al-Kaabi[1], Khaleel Sultan[1], Prem Chandra[2] and Ahmed Elnajjar[1]

[1]HMC Gastroenterologist, Gastroenterology Department, 4th Floor ACC, Hamad medical corporation, Doha, Qatar

[2]MRC Bio-statistician, Medical research Center, hamad medical corporation, Doha, Qatar

[*]Corresponding author
Dr Nasrein Mohamed Elkomy, HMC Gastroenterologist, Gastroenterology Department, 4th Floor ACC, Hamad medical corporation, Doha, Qatar

Submitted: 08 May 2020; **Accepted**: 15 May 2020; **Published**: 21 May 2020

Abstract

Since 1920, inflammatory bowel disease (IBD) has been linked to increased incidence and mortality from colorectal adenocarcinoma (CRC). Several studies have found that screening colonoscopy reduced CRC mortality and improved survival in IBD patients. However, there are little or no data about the prevalence of CRC/Dysplasia in Qatar detected by screening colonoscopy and weather the Qatar gastroenterologists adhere to the international guidelines. Thus, the focus of the present study was to examine the rate of CRC and dysplasia in IBD patients who underwent a screening colonoscopy. The sample consisted of 153 patients who were diagnosed and treated for IBD. The results of the study showed high incidence rate of CRC/Dysplasia among IBD patients and it was also found that the gastroenterologists in Qatar did not strictly adhere to the international guidelines in relation to the time of first screening colonoscopy of IBD patients.

Key wards

Inflammatory Bowel Disease, Colonoscopy, Colorectal Cancer, Screening and Dysplasia

Introduction

Since 1920, inflammatory bowel disease (IBD) has been linked to increased incidence and mortality from colorectal adenocarcinoma (CRC). Although IBD-related CRC only accounts for 1–2% of all cases of CRC in the general population, the mortality rate in patients with a diagnosis of CRC in the setting of IBD is higher than of those afflicted with sporadic cases. CRC accounts for approximately 15% of all deaths in IBD patients [1]. Furthermore, in a population based cohort studies meta-analysis, reporting a CRC risk in Ulcerative colitis (UC) shows the risk for any patients with colitis to be 2% at 10 years, 8% at 20 years, and 18% after 30 years of disease and UC increases the risk of CRC 2.4-fold and standardized incidence ratios (SIRs) found to be ranged from 1.05 to 3.1, with a pooled SIR of 2.4 (95% CI, 2.1–2.7) [2]. Moreover, in one Danish study, the incidence rates of cancer among individuals with CD, UC, or in the general membership were 75.0, 76.0, and 47.1, respectively, per 100,000 person-years [3]. In another study, the overall incidence of CRC among IBD patients found to be 85 (95% CI: 82-109) cases per 100 000 person-years [4]. In addition, one Canadian study showed an increased Incidence ratio and ratio rate (IRR) of colon carcinoma for both Crohn disease patients (2.64; 95% confidence interval [95% CI], 1.69 – 4.12) and UC patients (2.75;95% CI, 1.91–3.97) [5]. Although, the prognosis for sporadic CRC and IBD-CRC is similar with a 5-year survival of approximately 50%, the average age of IBD-CRC diagnosis found to be 10 to 15 years younger than sporadic CRC in a Study conducted in in Eastern Europe [1]. The magnitude of that increased risk as well as how best to mitigate it remain a topic of ongoing investigation in the field [6]. Identifying patients at risk and implementing appropriate surveillance for these patients is central to managing the CRC risk in IBD. Many studies conducted in this field found that CRC risk in IBD increases with the increasing extent of colonic inflammation, longer duration of symptoms, and perhaps the severity of inflammation. Accordingly, the greatest risk is for patients whose entire colon has been affected pan colitis. In contrary, patients with proctitis alone are at a similar risk as the general population and those having only partial colonic involvements carry an intermediate risk. However, colon cancer does not distinguish between clinically active IBD and clinical remission. Patients whose disease has been clinically quiescent do not have a lower risk of neoplasia than those who have a more active disease course. There is some evidence that if the onset of UC is at a young age, the risk of malignant transformation is increased independent of either disease duration or anatomic extent, although this is disputed [6]. Several studies have suggested that if patients with UC also have primary sclerosing cholangitis (PSC) they may be at a higher risk of developing colorectal cancer [7]. Moreover, positive family history of colon cancer, smoking and folate depletion may affect the occurrence of colorectal cancer [8]. There is growing evidence that the chronic consumption of aminosalicylates, in particular sulphasalazine, may also provide some protection against colorectal cancer in patients with ulcerative colitis [9].

Many studies showed screening colonoscopy reduces CRC mortality and improve survival in IBD patients. In one such study, Karlen et al, screening colonoscopy reduced CRC mortality

was by as much as 78%, although this did not reach statistical significance [10]. In another study, the 5-year CRC-related survival rate of patients in the surveillance group was 100% compared with 74% in the non-surveillance group (P=0.042) [11].

Historically, Europe and North America have been considered high incidence areas while Asia, Africa, and the Middle East have been considered low incidence areas, but as these countries have become industrialized, IBD has emerged and its incidence is rising dramatically. One study from Central Saudi Arabia on the epidemiology of juvenile onset IBD estimated an incidence of 0.5 per 100 000 per year and a prevalence of 5/100 000. In Qatar 1700, IBD cases reported over the last 20 years. Moreover, statistics released by the Ministry of Public Health's Qatar National Cancer Registry indicate that among all male cancers in Qatar in 2015, colorectal cancer was the second most common with 94 new cases reported [12]. Although IBD patients represent one of the highest risk groups for developing this dreaded complication, it is unknown whether the incidence and mortality of CRC is increased in IBD in Qatar populations. In this study, we aim to investigate the rate of CRC and dysplasia in an IBD diagnosed patient cohort in HMC, Qatar.

Methodology

A Retrospective cohort study of a sample of patients who were diagnosed and treated for IBD and follow up in HMC, Qatar, in the time between 01/01/1998 to 31/12/2018.

Inclusion criteria

IBD Patient diagnosed and treated in HMC
Patient age >18 year who may have IBD diagnosed at earlier age.
Fully active, able to carry on all pre-disease performance without restriction.
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., lighthouse work, office work, Ambulatory and capable of self-care but unable to carry out any work activities; up and about more than 50% of waking hours. Etc.

Exclusion criteria

Diagnosis and Treatment of IBD not done in HMC, Qatar.
Patients will be excluded from this study if they had been lost to follow-up or had colectomy for reasons other than colorectal dysplasia or cancer.

Study Population and StudySetting/Location

Patients with IBD in Gastroenterology unit at the Ambulatory care center as per clinical standards who were diagnosed using biopsy collected during colonoscopy and supporting blood tests will be included in the study who are given treatment based on diet and drugs for IBD. All IBD patients are followed up every 3 months as this being an auto – immune disease which keeps the patients under continuous care and follow-up. Patients diagnosed and treated between 1998 to December 2008 for IBD and followed up for 10 years after begin diagnosed.

Clinical and electronic records of patients diagnosed and treated for IBD retrospectively will be reviewed from CERNER in the gastroenterology unit. For all patients, the following variables will be recorded: Patients Demographic Data: Age, Sex, Nationality, Race, Dead or Alive, date of IBD diagnosis, Types of IBD, age group at diagnosis (<15, 15 to 29, 30 to 39, 40 to 49, 50 to 59, and ≥60 years of age, disease duration, extend of the disease (proctitis (E1), left-sided colitis(E2), or pancolitis (E3)), Inflammatory complications, PSC and Family history of CRC.

Time frame

Data from 01/01/1998 to 31/12/2018

Outcomes

The rate and incidence of CRC in IBD patients and the benefit of screening colonoscopy will be understood.

Data Analysis

Baseline demographic, clinical, laboratory and biochemical characteristics will be described with frequencies and percentage and mean±SD or median and range as appropriate. A two-sided P value of less than 0.05 will be considered to indicate statistical significance. Calculating person-years at risk for colorectal cancer and IBD related CRC incidence rate will be used as a measure of relative risk. Independent sample t-tests used to compare the means of different numerical variables between the two treatment groups with a significance threshold of 0.05.

A Cox regression model was used to determine and assess the effect of various covariates and prognostic factors on survival time. A two-sided p value of less than 0.05 was considered statistically significant. All Statistical analyses will be done using statistical packages SPSS 22.0 (SPSS Inc. Chicago, IL).

Results

Patients Characteristic

By reviewing our hospital registry data base in the period between 1998 to 2018, 153 patients with an ulcerative colitis were included in our study, most of them are male, Non-Qatari and older than 50 years (61.4%, 69.3% and 53.6%). The majority of the patients had a Lt sided colitis without extra intestinal inflammatory complications (64.1 % and 95.4%) respectively. All the patient used 5 ASA and only 39.2 % and 20.9% of them used Azathioprine and Biological treatment respectively, see table 1.

Table 1: Patients Demographics Data

Characteristic	Number of the patients	Percentage
Age (years)		
>50	82	53.6%
<50	71	46.4%
Sex		
Male	94	61.4%
Female	59	38.6%
Nationality		
Qatari	47	30.7%
Non-Qatari	106	69.3%
Extend of the disease		
E3	50	32.7%
E2	98	64.1%
E1	5	3.3%
Treatment Received		
5ASA and steroids biological	32	20.9%

5 ASA and steroids AZA	60	39.2%
5 ASA	61	39.9%
Inflammatory Complications		
Yes	7	4.36%
No	146	95.4%
Screening colonoscopy outcome		
CRC and Dysplasia	7	4.6%
Pancolitis	24	15.7%
LT sided colitis	65	42.5%
Proctitis	15	9.8%
Pseudopolyps	10	6.5%
Normal	32	20.9%

Colorectal Cancer and Dysplasia

Among 153 patients with UC, 7 cases of CRC/dysplasia detected, 5 cases colorectal cancer and 2 cases adenomatous polyps. Calculated incidence rate of CRC/Dysplasia among UC cases found to be 7/153 = 4.58 (95% CI 2.23, 9.14). Calculated person-years at risk of CRC/Dysplasia among UC cases was 4.14 cases per person-years.

The mean of patients age and age at diagnosis for all groups (years) were 49.45 and 33.75 (SD+/-12.5 and 10.46) respectively. The mean of patients age and age of diagnosis for CRC/Dysplasia and Non-CRC/Dysplasia groups (years) were 53, 49.2 (SD+/- 10.2, 12.6) and 34.8, 33.7 (SD+/- 10, 10.5) respectively and the difference between the means weren't statistically significant (P = 0.49 and 0.16) respectively, see figure 1. The mean of the duration of ulcerative colitis (years) for all patients was 15.48 (SD+/-6.172), the mean duration of UC in CRC/Dysplasia and Non-CRC/Dysplasia groups (years) were 17 and 15.4 (SD+/- 4.9 and 6.2) respectively and the difference between the means was not statistically significant (P = 0.44). The mean time (years) of first screening was 11.125 (SD+/- 3.74) for all cases and were 11.167 (SD+/- 5.1153) and 11.123 (SD +/-3.7025) for CRC/Dysplasia and Non-CRC/Dysplasia groups respectively the difference between them wasn't statistically significant (P = 0.498), see figure 2. There is significant association between development of CRC/Dysplasia, gender and Extend of the UC, higher in male and Pancolitis (E3) (P = 0.032 and 0.030 respectively). There were no significant association between age, Nationality, treatment received, Ext intestinal inflammatory complications, PSC and duration of the disease (P = 0.334, 0.72, 0.458, 0.21, 0.149 and 0.506 respectively).

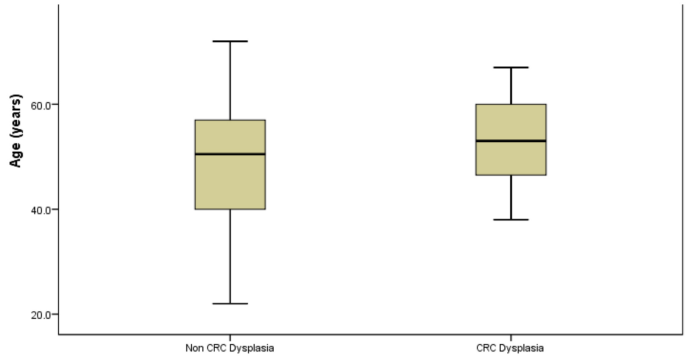

Figure 1: Comparison between the means of patients age (years) for CRC/Dysplasia and Non CRC/Dysplasia groups

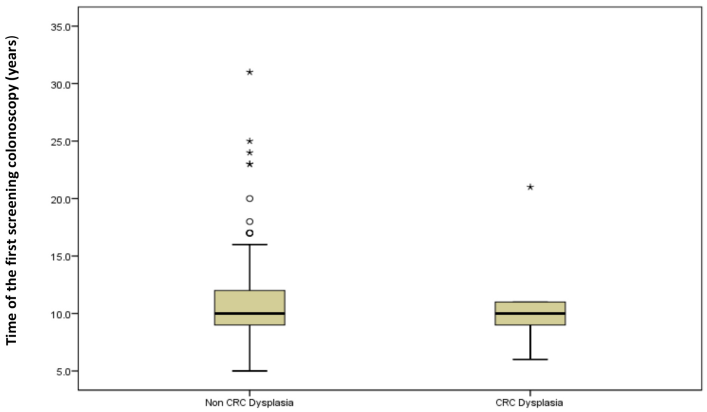

Figure 2: Comparison between the means of the time of first screening colonoscopy (years) of CRC/Dysplasia and Non CRC/Dysplasia groups

Discussion

Our study confirms the existence of an increased risk of CRC/Dysplasia in UC patients with our study recorded higher incidence rate of CRC/dysplasia (4.5%) compared to 3.7% prevalence of CRC in 54478 patients with UC estimated by meta-analysis, this may be attributed to smaller sample size and inclusion of cases with adenomatous polyps in our study [13]. Moreover, this study showed that pancolitis to be a risk factor for developing CRC/Dysplasia in our patients as being shown by Ekbom study, RR for developing CRC in IBD patients found to be 1.7, 2.8 and 14.8 in proctitis, Lt sided colitis and pancolitis respectively [14]. Unlike previous studies by Marchesa and meta-analysis by Soetikno et al which showed that the RR and OR of developing CRC among patients of UC with PSC was 9-18 and 4.09 (95% CI, 2.89-5.76) respectively compared to UC patients without UC, our study showed that PSC is not a risk factor for CRC/Dysplasia despite the percentage of PSC was 4% and 14% among Non-CRC/Dysplasia and CRC/Dysplasia our UC patients groups respectively [15, 16]. Furthermore, our study found that the risk of CRC and dysplasia was high among male population, as being showed also Söderlund et al study (RR of CRC among UC male and female patients were 2.6 (95% CI: 2.2-3.1) and 1.9 (95% CI: 1.5-2.4) respectively) [17]. In contrary to Nieminen et al study, which showed that the disease duration was associated with an increase in annual risk of dysplasia by 4.5%, in this study disease duration wasn't a risk factor for developing CRC in our UC patients [18]. Older patients with IBD are at higher risk for developing CRC, as being shown by many studies, e.g in Baars, J et al study HR for 10 years older age 2.25; 95 % CI 1.92–2.63 was related to early CRC [19]. However, we couldn't confirm that older age is a risk factor for CRC/Dysplasia development.

Limitations

It is Un doubtfully that there are limitations of our retrospective study design, but on other hand conducting a prospective study design won't be feasible because of relatively low incidence of CRC in IBD patients and considerable time-interval for CRC development in IBD patients. We have a relatively small sample size and our study may have been underpowered to identify the small absolute risk.

Conclusion

Our study showed relatively high incidence rate of CRC/Dysplasia among our IBD patients compared to international figures and our gastroenterologist physicians are not firmly adherent to the time of first screening colonoscopy in IBD patients.

Acknowledgment

I would like to express my deep and sincere gratitude to all my supervisors for providing invaluable guidance through research. Dr Nasrein Elkomy is the main author responsible of submitting the study, collecting and analyzing the data and writing the manuscript. Dr RY, KE, SK and KS planned the study. PC did data analysis. AN helped me in data collection.

Conflict of Interest

I declare that neither me nor coauthors of this manuscript have significant competing financial, professional or personal interests that might have influenced the performance or presentation of the work described in this manuscript.

References

1. Dyson JK, Rutter MD (2012) Colorectal cancer in inflammatory bowel disease: What is the real magnitude of the risk? World J Gastroenterol 18: 3839-3848.
2. Jess T, Rungoe C, Peyrin-Biroulet L (2012) Risk of Colorectal Cancer in Patients with Ulcerative Colitis: A Meta-analysis of Population-Based Cohort Studies. Clinical Gastroenterology and Hepatology 10: 639-645.
3. Herrinton LJ, Liu L, Levin TR, Allison JE, Lewis JD, et al. (2012) Incidence and Mortality of Colorectal Adenocarcinoma in Persons With Inflammatory Bowel Disease From 1998 to 2010. Clinical—Alimentary Tract August 143: 382-389.
4. Söderlund S, Brandt L, Lapidus A, Karlén P, Broström O, et al. (2009) Decreasing time-trends of colorectal cancer in a large cohort of patients with inflammatory bowel disease. Gastroenterology. 136: 1561-1567.
5. Bernstein CN, Blanchard JF, Kliewer E, Wajda A (2001) Cancer Risk in Patients with Inflammatory Bowel Disease A Population-Based Study. Cancer 91: 854-862.
6. Rutter MD, Saunders BP, Wilkinson KH, Rumbles S, Schofield G, et al. (2006) Forbes A Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 130: 1030-1038.
7. Rosy Wang, Rupert W (2014) Leong Primary sclerosing cholangitis as an independent risk factor for colorectal cancer in the context of inflammatory bowel disease: A review of the literature. World J Gastroenterol 20: 8783-8789.
8. Lakatos PL, Lakatos L (2008) Risk for colorectal cancer in ulcerative colitis: Changes, causes and management strategies. World J Gastroenterol 14: 3937-3947.
9. Ham M, Moss AC (2012) Mesalamine in the treatment and maintenance of remission of ulcerative colitis. Expert Rev Clin Pharmacol 5: 113-123.
10. Karlén P, Kornfeld D, Broström O, Löfberg R, Persson PG, et al. (1998) Is colonoscopic surveillance reducing colorectal cancer mortality in ulcerative colitis? A population based case control study Gut 42: 711-714.
11. M W M D Lutgens, B Oldenburg, P D Siersema, A A van Bodegraven, G Dijkstra, et al. (2009) Colonoscopic surveillance improves survival after colorectal cancer diagnosis in inflammatory bowel disease Br J Cancer 101: 1671-1675.
12. Rasul KI, Awidi AS, Mubarak AA, Al-Homsi UM (2001) Study of colorectal cancer in Qatar. Saudi Med J 22: 705-707.
13. Eaden JA, Abrams KR, Mayberry JF (2001) The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48: 526-535.
14. Ekbom A, Helmick C, Zack M, Adami HO (1990) Ulcerative colitis and colorectal cancer. N Eng J Med 323: 1228-1233.
15. Marchesa P, Lashner BA, Lavery IC, Milsom J, Hull TL, et al. (1997) The risk of cancer and dysplasia among ulcerative colitis patients with primary sclerosing cholangitis. Am J Gastroenterol 92: 1285-1288.
16. Soetikno RM, Lin OS, Heidenreich PA, Young HS, Blackstone MO (2002) Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. Gastrointest Endosc 56: 48-54.
17. Söderlund S, Brandt L, Lapidus A, Karlén P, Broström O, et al. (2009) Decreasing time-trends of colorectal cancer in a large cohort of patients with inflammatory bowel disease. Gastroenterology 136: 1561-1567.
18. Nieminen U, Jussila A, Nordling S, Mustonen H, Färkkilä MA (2014) Inflammation and disease duration have a cumulative effect on the risk of dysplasia and carcinoma in IBD: A case–control observational study based on registry data. Int J Cancer 134: 189-196.
19. Baars JE, Kuipers EJ, van Haastert M, Nicolaï JJ, Poen AC, et al. (2012) Age at diagnosis of inflammatory bowel disease influences early development of colorectal cancer in inflammatory bowel disease patients: a nationwide, long-term survey. J Gastroenterol 47: 1308-1322.