Immunopathologia Persa

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Frequency of colorectal dysplasia and cancer among young patients with ulcerative colitis in a tertiary care hospital

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Received 9 May 2016
Accepted 28 Aug. 2016
Published online 5 Sep. 2016

Keywords: Ulcerative colitis, Colorectal dysplasia, Colorectal carcinoma, Inflammatory bowel disease

Abstract

Introduction: The rationale behind this study was to determine the burden of dysplasia and colorectal cancer in young patients with ulcerative colitis on histopathological examination. This facilitated early detection of dysplasia and colorectal cancer by regular endoscopic biopsies will guide the physicians on appropriate surveillance and management.
Objectives: To determine the frequency of colorectal dysplasia and colorectal cancer on histopathological examination in young (15-40 years) patients with ulcerative colitis.
Patients and Methods: 76 biopsies of already diagnosed cases of UC of young patients aged between 15-40 years of either gender were included. Specimens were fixed in 10% buffer formalin, paraffin embedded followed by cutting, slide preparation and staining with hematoxylin and eosin stain and examined under light microscope.
Results: There were 13 (17.2%) patients who were diagnosed for colorectal dysplasia, 03 (3.9%) with indefinite for dysplasia; 08 (10.5%) with low grade; and 02 (2.6%) with high-grade dysplasia. There were 03 (3.9%) patients who were diagnosed for colorectal carcinoma, 01 (1.3%) with grade 1; 01 (1.3%) with grade 2; and 01 (1.3 %) with grade three colorectal cancer.
Conclusion: Routine biopsies can identify dysplastic epithelium, an established marker for coexisting malignancy in patients with ulcerative colitis, and provide the rationale for surveillance of these patients.

Citation: Akhtar MH, Masud K, Nazar CMJ, Mumtaz MY, Bhatti TK. Frequency of colorectal dysplasia and cancer among young patients with ulcerative colitis in a tertiary care hospital. Immunopathol Persa. 2017;3(1):e04.

Introduction

Ulcerative colitis (UC) is a chronic disease that symptomatically has a relapsing and remitting course. Questions concerning the course that patient's individual disease may take, the prognosis and any associated complications are of paramount importance for the patients and the treating physicians. The answers to the above questions would not only help to guide treatment but would also assist the patient in planning their future. There are factors that increase the risk of colorectal cancer in UC. These include longer disease duration, greater proportion of colonic involvement, and younger age at diagnosis, coexistence of primary sclerosing cholangitis, family history of colorectal cancer and evidence of ongoing active colonic inflammation (1). The peak incidence of inflammatory bowel disease (IBD) occurs in individuals between the ages of 15 and 30 years, a second peak occurs between the ages of 50 and 80 years. Patients with IBD colitis are six times more likely to obtain colorectal cancer than the general population and have a higher frequency of multiple synchronous colorectal cancers. Because IBD incidences is highest among young people, the mean age for developing IBD-CRC is lower than for sporadic colorectal cancer (40–50 years of age vs. 60 years of age). The absolute risk of colorectal cancer 35 years after diagnosis

Key point

Routine colon biopsies can identify dysplastic epithelium, an established marker for coexisting malignancy in patients with ulcerative colitis, and provide the rationale for surveillance of these patients.

was 30% for young patients with pancolitis at diagnosis (2).

The risk for colorectal cancer in UC individuals is 2% at 10 years, 8% at 20 years and 18% at 35 years of disease duration (3). The first report of intestinal cancer occurrence in IBD was published over 80 years ago. Since then, numerous studies have addressed this issue, but the true risk of malignancy remains uncertain. Current screening endoscopy protocols are based on white light endoscopy (WLE) and random biopsies. Novel endoscopic techniques include chromoendoscopy (CE) and confocal laser endomicroscopy (CLE) (4). There is sufficient evidence in the literature that patients with long-term UC have an increased risk of colorectal cancer (5,6).

There is also evidence that cancers tend to be detected at an initial stage in individuals who are undergoing surveillance, and these patients have a correspondingly better prognosis. They found that 27% patients who underwent colectomy within 6 months of the initial detection of flat dysplasia-low grade dysplasia had a finding of cancer and high grade dysplasia (7,8). There is indirect evidence that surveillance is likely to be effective at reducing the risk of death from UC-associated colorectal cancer and indirect evidence that it may be acceptably cost-effective (9-11).

Objectives

To determine the frequency of colorectal dysplasia and colorectal cancer on histopathological examination in young (15-40 years) patients with UC.

Materials and Methods

Ulcerative colitis

UC is primarily a mucosal and submucosal disease characterized by surface ulceration, dense lymphoplasmacytic and neutrophilic infiltrate in the lamina propria, cryptitis, crypt abscesses (collection of neutrophils in the glandular lumen) leading to progressive distortion and destruction of glands which show marked decrease in cytoplasmic mucin, goblet cells depletion and irregular shapes.

Dysplasia and colorectal carcinoma

Dysplasia

The earliest histologic appearance of this progression plays a significant role in cancer prevention by providing the first clinical systematized that this sequence is underway and helping as an endpoint in colonoscopic surveillance of patients at high risk for colorectal cancer. Both conditions are diagnosed on biopsy (histopathology).

Grades of dysplasia on standardized classification (7).

1. Negative for dysplasia; inflamed or regenerating mucosa with normal maturation of glandular epithelium. Mitotic figures and histological features of regeneration are confined to the lower half of the glands.

2. Indefinite for dysplasia; when epithelium has features suggestive of dysplasia but changes are insufficient to be unequivocally diagnostic.

3. Positive for dysplasia-low grade dysplasia (LGD); glands lined by cells having hyperchromatic, enlarge nuclei with preserved polarity, mucinous differentiation is decreased, dystrophic goblet cells. Atypia may focally reach the surface.

4. Positive for dysplasia-high grade dysplasia (HGD); glands lined by atypical cells having prominent nuclear pleomorphism with hyperchromatic often rounded nuclei that are stratified throughout the cells. Glands showing branching architecture. Atypia extends to the surface.

Colorectal cancer

The most lethal long-term complication of chronic IBD, is the conclusion of a complicated structure of molecular and histologic derangements of the intestinal epithelium characterized by glands of variable differentiation lined by anaplastic cells having large, hyperchromatic nuclei and prominent nucleoli with prominent mitotic activity often with atypical forms.

Grades of colorectal cancer

Grade I; composed predominantly of well-formed glands lined by anaplastic cells, in a desmoplastic stroma.

Grade II; less well-formed glands with focal cribriform architecture.

Grade III; tumor grows in solid sheets with no distinct gland formation.

Study design

A prospective cross-sectional study.

Settings

Study was carried out in Histopathology Unit, Department of Pathology, Pakistan Institute of Medical Sciences (PIMS) Islamabad. Duration of study was six months from the approval of synopsis. Sample size was 76 (calculated by using WHO sample size calculator taking level of significance = 95%, anticipated population proportion = 27%, absolute precision required = 10%

Inclusion criteria; biopsies of already diagnosed cases of UC of young patients (15-40 years). All patients from both genders were involved.

Exclusion criteria; previously diagnosed case of colorectal malignancy, patients on chemotherapy, any contraindication to biopsy, patients unwilling to undergo biopsy and patients above 40 years of age.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. After the informed consent, patients were included in study based on clinical signs and symptoms of UC. The research was approved by the ethical committee of Pakistan Institute of Medical Sciences Islamabad.

Data collection

Patients' demographic data along with registration number, presenting complaints, and clinical profile was entered on the Performa. After the informed consent, patients were included in study based on clinical signs and symptoms of UC. All the biopsy specimens were immediately

fixed in 10% buffer formalin. Following gross examination, the tissue was paraffin embedded, followed by cutting, slide preparation and staining with hematoxylin and eosin stain. Macroscopic and microscopic findings were commented upon. Slides for histopathology were examined under light microscopy by consultant pathologist and postgraduate medical student and diagnosis was recorded.

Dara analysis procedure

All data entered and analyzed using SSPS version 10.0. Frequency and percentage was calculated for qualitative variables like gender, colorectal cancer and dysplasia. Mean ± standard deviation (SD) was calculated for quantitative variables like age of the patients.

Results

Demography of population

Seventy-six biopsies of diagnosed cases of UC of young patients (15-40 years) of either gender were included in the study. Patient's demographic data along with registration number, presenting complaints, and clinical profile was entered on the Performa. Previously diagnosed cases of colorectal malignancy, patients on chemotherapy, who had any contraindication to biopsy or who were unwilling to undergo biopsy and patients above 40 years of age were excluded. All the biopsy specimens were immediately fixed in 10% buffer formalin. Following gross examination, the tissue was paraffin embedded, followed by cutting, slide preparation and staining with hematoxylin and eosin (H&E) stain. Macroscopic and microscopic findings were commented upon. Slides for histopathology was examined under light microscopy by consultant pathologist and postgraduate medical student and diagnosis was recorded. Fifty patients (65.8%) were males with the mean age of 28.88 years ± 7.22 SD and 26 (34.2%) were females with mean age of 26.38 years ± 7.26 SD. Cumulative mean age was 28.03 years ± 7.33 SD. Demographic results are shown in Table 1.

Frequency of dysplasia and CRC in study population

Out of total 76 patients selected for the study, 60 (78.9%) patients were negative for any dysplasia or colorectal carcinoma as per our operational definition. There were 13 (17.2%) patients who were diagnosed for dysplasia as per our operational definition. These were 3 (3.9%) with indefinite for dysplasia, 8 (10.5%) with low grade dysplasia, 2 (2.6%) with high grade dysplasia. There were 3 (3.9%) patients who were diagnosed for colorectal carcinoma as per our operational definition 1 (1.3%) with grade one colorectal cancer, 1 (1.3%) with grade two colorectal cancer and 1 (1.3%) with grade three of colorectal cancer. Results are shown in Table 2.

Table 1. Demographic profile of the study population

	No. (%)	Mean age ± SD (years)
Male	50 (65.8)	28.88 ± 7.22
Females	26 (34.2)	26.38 ± 7.26
Total	76 (100)	28.03 ± 7.33

Table 2. Frequency of dysplasia and CRC

Diagnosis	No.	%	Cumulative percentage
Negative	60	78.9	78.9
Indefinite for dysplasia	03	3.9	82.9
Low grade dysplasia	08	10.5	93.4
High grade dysplasia	02	2.6	96.1
CRC grade 1	01	1.3	97.4
CRC grade 2	01	1.3	98.7
CRC grade 2	01	1.3	100
Total	76	100 .	

Discussion

UC is a chronic inflammatory disorder considered by relapsing and remitting episodes of inflammation limited to the mucosal layer of the colon (13). UC has been sub-classified based on its clinical presentation and extent of involvement. This has provided a uniform framework for studies evaluating the genetic, serologic, and clinical factors that predict the evolution of the disease (13). The age of onset of most cases of UC and Crohn disease is between 15 and 40 years. Many studies suggest a bimodal age distribution for both disorders with a second peak between 50 and 80 years. It is not clear whether this second peak relates to greater susceptibility to disease with increased age, the late expression of an earlier environmental exposure, or misdiagnosis of ischemic colitis as IBD. There appear to be small differences in IBD incidence by gender. Several observational studies have suggested an association between acute gastroenteritis and the development of UC (14,15). As an example, a case-control study included over 3000 patients with incident IBD and over 11 600 controls (14). Patients may have systemic symptoms including fever, fatigue, and weight loss. Patients may also have dyspnea, and palpitations due to anemia secondary to iron deficiency from blood loss, autoimmune hemolytic anemia or anemia of chronic disease. The Mayo scoring system can also be used to assess disease severity and monitor patients during therapy (14). Scores range from 0 to 12 with higher scores indicating more severe disease. Evaluation of a patient with suspected UC leads to exclude other causes of colitis, to determine the diagnosis of UC, and to establish the extent and severity of the illness. The diagnosis of UC is based on the presence of chronic diarrhea for more than four weeks and evidence of chronic colitis on endoscopy and biopsy. Endoscopic findings in patients with UC are nonspecific. Biopsies of the colon taken on endoscopy are necessary to establish the chronicity of inflammation and to exclude other causes of colitis. The biopsy aspects suggestive of UC consist crypt abscesses, crypt atrophy crypt branching, shortening and disarray. Epithelial cell abnormalities consisting mucin depletion and Paneth cell metaplasia may be detected. Inflammatory aspects of UC contain increased lamina propria cellularity, basal lymphoid aggregates, and lamina and basal plasmacytosis (13,14). Basal plasmacytosis may also be a predictor of relapse in individuals with seemingly well-controlled UC with complete mucosal healing. Sub-

jects with UC generally present with episodes of bloody diarrhea that last for weeks to months. With treatment, the course of UC typically contains of intermittent exacerbations interchanging with long periods of complete symptomatic remission (14,15). Overall, patients who present initially with proctitis have a more benign disease course and frequently respond to topical therapy, whereas those who present with more extensive disease require systemic therapy and have a higher risk of colectomy. Approximately sixty-seven percent of subjects have at least one relapse ten years following the diagnosis (15). The risk of relapse depends on the age at initial diagnosis (15). Approximately 20% to 30% of patients with (15,16) UC are at boosted risk for colorectal cancer. The risk of colorectal cancer seems to be highest in individuals with pancolitis, while individuals with proctitis and proctosigmoiditis are possibly not an augmented risk of colorectal cancer, regardless of the duration of illness. The colorectal cancer risk begins to increase 8 to 10 years following the beginning of symptoms in individuals with pancolitis (17,18). Other factors that are associated with an augmented risk of colorectal cancer comprise endoscopic and histological intensity of inflammation, positive family history of sporadic colorectal malignancy (two-fold increased risk), and post-inflammatory pseudo-polyps (two-fold increased) (17,18). It is generally accepted that colorectal cancer in IBD is preceded by dysplasia. Hence, dysplastic epithelium may be an indicator for coexisting malignancy and provides the rationale for surveillance. A uniform terminology for dysplasia in IBD has been proposed (18). The predictive value of dysplasia has been best studied in UC. There is general agreement that the finding of high-grade dysplasia necessitates prompt colectomy due to high rate of synchronous colorectal cancer (e.g. 42% [10 of 24] in one study) (18). The relatively young age at which colorectal cancer develops in patients with IBD has led to efforts to stratify patients at greatest risk. The goal of most surveillance programs has been the finding of dysplasia, which is accompanying with a high risk of colorectal cancer (17,18). There is also evidence that malignancies tend to be detected at an earlier stage in subjects who are undergoing surveillance, and these individuals have a respectively better prognosis. There is indirect findings that surveillance is likely to be effective at lowering the risk of death from UC-associated colorectal cancer and indirect evidence that it may be acceptably cost-effective (17-19). This facilitated early detection of colorectal cancer by regular endoscopic biopsies which guided the physicians on appropriate management, thus improved patients' outcome. Therefore, present study was planned to determine the frequency of colorectal dysplasia and colorectal cancer on histopathological examination in young patients with UC. Our findings are in agreement with the previously published investigations on the subject research aimed to assess the outcome of a newly initiated pilot screening program for screening colorectal neoplasia among UC patients in India. In their prospective study from an academic hospital setting, individuals with UC at high risk of colorectal neoplasia were offered screening by magnifying chromocolonoscopy and the incidence of neoplastic lesions was considered (17). They enrolled 29 (70.7%) of 41 eligible patients [a median age of 46 (interquartile range 36-54.5) years; 17 (58.6%) men] for surveillance; 41 colonoscopies were undertaken over 42 months. The median illness duration was 10 (interquartile range 7.5-14.5) years. Sixteen (55.1%) had extensive colitis. They found that on initial screening, low-grade dysplasia was seen in 5 (17.2%) and high-grade dysplasia in 3 (10.3%). Of these three, one accepted proctocolectomy immediately, one underwent surgery for adenocarcinoma and one refused surgery. Twelve follow-up colonoscopies in nine subjects exposed three new low-grade dysplasia. They concluded that high-grade dysplasia and subsequent adenocarcinoma can be detected with careful follow-up in Indian patients with long-standing UC but acceptance of surveillance and subsequent therapy are suboptimal. We found evidence that screening and surveillance programs are useful for detecting neoplasias in UC, and need to be customized for this region (18,19).

Several studies have identified that dysplasia and colorectal cancer in UC develop via pathways distinct from sporadic colorectal cancer and may occur in flat mucosa indistinct from surrounding tissue (19-22). They also found that surveillance guidelines have emphasized the approach of periodic endoscopic evaluation and systematic random biopsies of involved mucosa. Given the imperfect nature of this random approach, they have focused on improved surveillance techniques and recommends that neoplasia is endoscopically visible in many individuals. In their retrospective review that used the University of Chicago Inflammatory Bowel Disease Registry and the clinical administrative database, all cases of dysplasia or colorectal cancer in UC between November 1994 and October 2004 were identified (23,24). Visible dysplasia was defined as a lesion reported by the endoscopist that resulted to directed biopsy and that was established by pathology. Invisible dysplasia was defined as dysplasia diagnosed on pathology but not described on endoscopy. They also determined per-lesion and per-patient sensitivities. They detected that there were 1339 surveillance tests in 622 individuals with UC. Forty-six individuals were detected having dysplasia or colorectal carcinoma at a median age of 48 years and with median duration of illness of 20 years. Of these patients, 77% had pancolitis, 21% had left-sided colitis, and 2% had proctitis. These patients had 128 surveillance examinations (median 3 per patient; range, 1-9 per patient), and, in 51 examinations, 75 separate dysplastic or cancerous lesions were identified (mean, 1.6 lesions per patient; standard deviation, 1.3). Thirty-eight of 65 patients with dysplastic lesions (58.5%) and 8 of 10 malignancies (80.0%) were visible to the endoscopist as 23 polyps and masses, one stricture, and 22 irregular mucosa. The per-patient sensitivities for dysplasia and for malignancy were 71.8% and 100%, respectively. They concluded that dysplasia and cancer in UC are endoscopically visible in majority of patients and may be reliably recognized during scheduled examinations (25,26). Research aimed to determine whether

dysplasia is noticeable during unchanging surveillance colonoscopy by assessing only patients who had dysplasia without overt carcinoma. They systematically reviewed the medical records, endoscopy pathology databases amongst 1997 and 2004 at the University of Pennsylvania Health System (27-31). Individuals with IBD and dysplasia were recognized and their medical charts reviewed. They found that of the 113 patients with colonic dysplasia established by pathology at our center, 102 (90%) had UC. Forty-nine of the 102 (48%) individuals with UC conducted colonoscopic assessment prior to dysplasia recognition. This group was nominated as our investigation cohort. Overall, 72 macroscopic abnormalities were found at 49 colonoscopies, containing 55 polypoid lesions, 12 areas of ulceration, three areas of nodularity, one irregular hemicircumferential lesion and one area of stricture. Overall, 58 dysplastic sites were identified; 51 were macroscopically visible (87.9%) and seven were macroscopically invisible (12.1%). They assumed that most of the dysplasia in UC is endoscopically visible. However, additional prospective evaluation of a large number of patients is required to validate the current findings. Our findings have the potential to modify current suggestions for surveillance biopsies in UC if validated by prospective studies (32,33).

Another investigation revealed whether gastroenterologists at Hamilton Health Sciences (Hamilton, Ontario) adhered to recommendations for UC surveillance issued by the Canadian Association of Gastroenterology and to retrospectively exam in the incidence and type of dysplasia detected and the subsequent outcome of individuals with dysplasia (i.e. colorectal cancer colectomy, dysplasia recurrence). They carried out a retrospective chart review of all subjects with UC undergoing colonoscopy screening at Hamilton Health Sciences from January 1980 to January 2005. Individuals were categorized by the extent of colonic disease. Limited left-sided colitis (LSC), pancolitis and any disease progress with concurrent primary sclerosing cholangitis (33,34). They detected a total of 141 individuals fulfilled eligibility criteria. Around 921 endoscopies were conducted for patients, comprising 453 for surveillance, which were conducted by 20 endoscopists. In general, screening was conducted on 90% of patients, and shadowing at the appropriate time in 74%. There was a statistically meaningful rise in the mean proportion of biopsies per colonoscopy after the modalities were published ($P < 0.01$ for all categories). Colonic dysplasia was observed in 24 of 141 patients (17.0%), with 17 of 24 (70.8%) detected at surveillance. Two individuals (8.3%) had colorectal cancer successfully treated. The mean age of individuals with dysplasia was 56.1 years, with a mean disorder duration of 10.9 years in left-sided colitis versus 11.8 years in pancolitis (P was not significant). Colectomy was not recommended for any individuals with flat dysplasia. No individuals increased to high-grade dysplasia or colorectal cancer. Individuals with pancolitis had a higher incidence of neoplasia (21% [18 of 86]) than individuals with left-sided colitis (12% [6 of 49]; $P = 0.24$). Forty-one individuals (29.5%) had at least one hyperplastic or inflammatory polyp. they supposed that for the preponderance of patients who underwent surveillance colonoscopies, their procedures were realized within the recommended time intervals, and biopsy obedience has improved. Dysplasia tended to develop after approximately 10 years of syndrome duration and in middle age, with flat dysplasia being rare. Interventions ensued to, no dysplasia progressing to colorectal cancer, implying effective prevention.

Another investigation involving retrospective cohort investigation compared the rate of progression to advanced neoplasia among proximal and distal dysplasia in individuals with UC (34). They detected that among 121 patients with low-grade dysplasia, all 7 who progressed to colorectal cancer and six of 8 who developed to high grade dysplasia had distal low-grade dysplasia initially. Subjects with distal low grade dysplasia had a significantly shorter time to progression than those with proximal low grade dysplasia ($P = 0.019$); 5-year AN-free survivals for distal and proximal low-grade dysplasia were 75 ± 7% and 95 ± 3%, respectively (hazard ratio [HR] 5.0; 95% CI, 1.1-22.0). Moreover, flat low-grade dysplasia was meaningfully more likely to progress than raised low-grade dysplasia on univariate testing (HR 3.6; 95% CI, 1.3-10.1). Neither morphology nor sidedness remained meaningful in multivariable testing, although there was little change in the HRs (HR 2.4; 95% CI, 0.8-7.1 for morphology; HR 3.5; 95% CI, 0.7-16.8 for sidedness) in proportional hazards modeling. They concluded that in patients with long-standing, extensive UC, distal low-grade dysplasia is more common and develops more rapidly to advanced neoplasia than proximal low-grade dysplasia. Another study aimed to study the risk of progression of low-grade dysplasia to advanced neoplasia, named as high-grade dysplasia or colorectal cancer for UC subjects undergoing surveillance based on location and morphology of high-grade dysplasia (35). They studied 997 UC subjects who underwent 3152 surveillance colonoscopies from 1998 to 2011 and calculated Kaplan-Meier estimates and frequency rates. They detected that of the 102 subjects with high-grade dysplasia (65 raised and 37 flat), 5 (4.9%) individuals developed to advanced neoplasia (3 high-grade dysplasia and two colorectal cancer) after a median follow-up of 36 months (interquartile range 18-71 months). Original location of dysplasia was in the proximal colon in forty-seven, distal colon in 55 subjects. Four of the 5 (80%) patients with advanced neoplasia had initial dysplasia in the distal colon. Distal colonic high-grade dysplasia had an incidence rate for advanced neoplasia of 2.1 cases per hundred subject/years at risk, while proximal high-grade dysplasia had an incidence of 0.5 cases per hundred subject/years. Flat high-grade dysplasia in the distal colon was more likely to progress to advanced neoplasia (hazard ratio = 3.6; 95% CI [1.3-10.6]). Twenty of the 102 patients (15 flat and 5 raised) underwent colectomy; 2 (10%) had evidence of advanced neoplasia in colectomy (one high-grade dysplasia and one colorectal cancer), 9 had high-grade dysplasia and remaining 9 did not have dysplasia. They concluded that the frequency of progression of high-grade dysplasia

to advanced neoplasia is low. Flat dysplasia located in the distal colon is associated with a greater risk of progression to advanced neoplasia.

In summary, the UC individuals surveyed have a much lesser risk of dying from colorectal carcinoma than do non-surveyed individuals, although randomized investigations are lacking. The inter- and intra-observer variability of dysplasia among pathologists is a major pitfall in the surveillance of these individuals, and also the impact of active inflammation, making dysplasia valuation difficult (36). Sjöqvist et al (37) in his study addressed this practical issue based on the proposals from the Swedish Gastroenterological Association by evaluating complete colonoscopies with multiple biopsies from the entire colon and rectum at regular intervals, surveillance programs for high-risk UC patients aim at identifying mucosal dysplasia in order to choice CRC-prone individuals for prophylactic colectomy. He found that screening colonoscopy should be performed approximately 8-10 after onset of disease. After negative results for screening or surveillance colonoscopy, the intervals between colonoscopies should not surpass two years. Biannual investigations of between eight and twenty years period have been adopted in the Swedish investigations, with annual colonoscopies from that point. Findings of colorectal cancer, a dysplasia-associated lesion or mass (DALM) with high-grade dysplasia or low-grade dysplasia or high grade dysplasia in flat mucosa, are measured as suggestions for proctocolectomy, as well as repeated, confirmed findings of multifocal low grade dysplasia. The managing of unifocal low-grade dysplasia in flat mucosa is controversial. He concluded that the safest way of handling UC patients at high risk of emerging colorectal cancer is by accomplishment regular colonoscopic surveillance. Dysplasia is a useful prognostic marker for ensuing malignancy development but has its boundaries. A combination of enhanced colonoscopic surveillance using markers those are more sensitive than dysplasia might be an appropriate modality to manage the increased CRC risk in these individuals. Patients with UC have 10 fold-increased risk for developing colorectal carcinoma. Regardless of typical locations of colorectal carcinoma in the sigmoid colon and rectum, other locations were also frequently detected (e.g. right hemicolon or multifocal distribution). Histologically colorectal malignancies are frequently present as mucinous adenocarcinoma (signet-ring cell carcinoma). The risk for malignancy relates to expansion, intensity, duration and therapeutic responsiveness of chronic colonic inflammation. It appears pathogenetically to be similar in UC and Crohn disease. Colorectal malignancy in IBD arises from epithelial dysplasia. While, there are no reliable biological indices available to date, surveillance-programs continue to rely on the detection of dysplasia (unequivocal intraepithelial neoplasia). The interval for surveillance colonoscopy depends upon the duration and extent of illness and the existence of further risk factors (e.g. family history of colon cancer or primary sclerosing cholangitis). Investigation should be implemented every five years for individuals at lower risk (developed colitis with no active endoscopic or histologic inflammation or Crohn's colitis involving less than 50% of the colon). Investigation should be performed every year for individuals at higher risk (extensive colitis with moderately active endoscopic or histologic inflammation, a stricture in the preceding five years, dysplasia in the aforementioned five years that was not improved surgically, primary sclerosing cholangitis or a family history of colorectal malignancy in a first-degree relative younger than fifty years of age). Detection of dysplasia by colonoscopy brings 70%-85% sensitivity. Endoscopic surveillance should start after 8 years of disease›s duration in pancolitis, after ten to twelve years in left- sided colitis and after twelve years in Crohn›s disease of the colon, with regular intervals every 1-2 years. 3-5 biopsies should be conducted every 10 cm from mucosa free of inflammation. Furthermore, every fine or discrete alteration of the mucosal surface should be recorded. Multiple biopsies should also be taken from this minimal lesions and also from more macroscopically suspicious areas like plaques, nodular lesions or stenosis. The clinical consequence of a positive screening for dysplasia is colectomy due to an assumed risk of cancer of about 40%-70%. Dysplasia in macroscopically suspect regions manifest the highest risk of cancer (non-adenoma like dysplasia), followed by multiple high-grade lesions without a macroscopic lesion, and multiple low-grade dysplasia. Detection of single dysplastic lesions in flat mucosa should be supported by a control endoscopy after 2-6 months, and if dysplasia is seen again, colectomy is recommended (36,38).

Conclusion

Routine endoscopic biopsies can identify dysplastic epithelium, an established marker for coexisting malignancy in patients with UC, and provide the rationale for surveillance of these patients. Colorectal carcinoma can also be detected at an early stage, which may result in better management of these patients.

Limitations of the study

Small sample size was the mail limitation of our study.

Conflicts of interest

None to be declared

Authors' contribution

MHA, KM and CMJN helps in data gathering, data interpretation, and manuscript preparation (Thesis work). MYM and TKB; study design, interpretation of data and patients support

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

No source of funding

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