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Colorectal cancer surveillance in inflammatory bowel diseases

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ABSTRACT

Colorectal cancer development is possibly the most important complication of inflammatory bowel diseases. Colorectal cancer generally develops in long-standing inflammatory bowel diseases. Although previously it was believed that there is higher risk in ulcerative colitis patients, nowadays, it has been shown that the risk for colorectal cancer is almost the same in both Crohn's disease and ulcerative colitis. Therefore, there are surveillance colonoscopy programs, which are being performed commonly to diagnose dysplasia and/or carcinoma at an early stage and to improve patients' outcome. The definitions of dysplasia and the approaches to this kind of patients are not still clear, also future studies are needed to clarify the cost-effectiveness of these programs. So far, only established advantage of surveillance in inflammatory bowel disease is to diagnose colorectal cancers at an earlier stage in patients involved in surveillance programs. [Turk J Cancer 2004;34(2):55-59]

KEY WORDS:

Colorectal cancer, surveillance, inflammatory bowel disease

Crohn's disease and ulcerative colitis are inflammatory diseases of gastrointestinal system of an unknown etiology. These diseases are acute and chronic with unpredictable relapses and remissions. The incidence of these diseases is much higher in Western Europe countries and Northern America when compared to central European and Asian countries (1-6). Rates in some of the underdeveloped countries are unknown and data from these countries are less reliable. The exact incidence of inflammatory bowel diseases (IBD) in Turkey is not known.

One of the most complex and frightening complications of IBD is the risk of malignancy. Crohn and Rosenberg (7) described the first case of IBD associated colorectal cancer in 1925. This case was described in a patient with ulcerative colitis. Carcinoma occurring in association with Crohn's disease was first described in 1948 (8). Since then, many studies tried to quantify the degree of increased cancer risk in such patients. Early studies in this field tended to overestimate this risk, calculating the cumulative cancer rate in ulcerative colitis patients rating from 16% to 43% (9-11). Later studies in contrast, have produced lesser cancer rates in ulcerative colitis, such as 1.4% at 18 years of disease duration and 5% at 20 years of disease duration (12,13). The discrepancy of these results is due to differences in study populations, follow up duration and treatment policies. In summary, most of the studies found the cancer risk in ulcerative colitis patients between 5 and 10% after

20 years and between 10 and 25% after 30 years of disease onset (14-16).

There is much controversy about colorectal carcinoma incidence in Crohn's disease. In 1965 and 1968, two reports from England indicated colorectal cancer incidence as 5% and 4% in Crohn's disease (17,18). A recent study compared the cancer risk between identically selected cohort patients with extensive ulcerative colitis and extensive Crohn's colitis. This study established a cumulative cancer frequency as 7% and 8% for Crohn's colitis and ulcerative colitis, respectively (19).

In 1967, Morson and Pang (20) first described flat dysplasia which occurred in ulcerative colitis. In 1981, Craft et al. (21) demonstrated dysplasia in colonic mucosa in two Crohn's disease patients. After subsequent studies have confirmed a link between flat dysplasia found in colorectal mucosa in IBD patients and colorectal carcinoma, physicians began performing periodic colonoscopic examinations with numerous biopsies in IBD patients. The identification of well-established risk factors for the development of colorectal cancer in IBD has led to the widely adopted practice of surveillance colonoscopy and biopsy in IBD patients with extensive colitis of greater than 8-10 years duration (22). The target of the surveillance programmes is to identify dysplasia in IBD patients before cancer develops, with the underlying assumption that the removal of dysplastic lesions will prevent subsequent cancer.

One prior study evaluating the extent of neoplastic changes in high risk IBD patients found that 33-34 biopsies from the colon and rectum must be examined if 90% likelihood of identifying dysplasia or cancer is present (23). In the same study, it was also found that 56-64 biopsies must be examined for the same purpose. Therefore, in the current practice two common ways of biopsy are followed; 4 quadrant biopsies from every 10 centimeter segment of colon and every 5 centimeter of rectum or 8 biopsies from each of 4 segments of colorectum (32 total biopsies). The current recommendation for the interval of surveillance colonoscopies in long-standing IBD patients is 1-2 years if no dysplasia or cancer was detected previously (24). Although there are well-defined recommendations mentioned above, daily practice varies. In a questionnaire-based study from United Kingdom it was reported that most of the British gastroenterologists (50%) took between 6 and 10 biopsies from the whole colon with 31% taking between 11 and 15. Besides, in the same study it was mentioned that most gastroenterologists (55%) repeated the examination in three years, 27% repeated after 1 year, 10% after 5 years and 8% of the gastroenterologists repeated the surveillance colonoscopy only if the patients developed new colonic symptoms (25). A recent study has demonstrated that the median number of colonic biopsies obtained during surveillance colonoscopy was 17 in New Zealand (26).

During the surveillance colonoscopy, in addition to flat mucosa, if an elevated mass like lesion is seen particular attention should be paid. The biopsies obtained from this elevated lesion can reveal dysplastic changes, if so, they are called dysplasia-associated lesion or mass (DALM). Blackstone et al. (27) first described these kind of elevated lesions in 1981. Since then, it has been considered that the identification of DALMs in colorectal mucosa in these patients is an indication for colectomy (27,28). To differentiate DALMs from adenomatous polyps is simple; if polyp formation is in non-colitic mucosa it is called as adenomatous polyp, if it is in colitic mucosa it is called as DALM. Like DALMs, adenomatous polpys are also dysplastic and potentially pre-malignant. However, it is widely accepted that adenomatous polyps can be removed by colonoscopic intervention (28,29). The approach to the patients with DALMs has begun to change. In 1999, back to back two reports have indicated that DALMs observed in colorectal mucosa of IBD patients without any flat dysplasia in colonic mucosa can be treated by colonoscopic resection just as like as sporadic adenomas (30,31). Rubin et al. (31) followed 48 patients with ulcerative colitis and Crohn's disease and determined 60 polyps (10 in non-colitic mucosa and 50 in colitis mucosa) in these patients' colon. All polyps were resected by colonoscopic polypectomy. The mean follow-up duration of these patients was 4.1 years (range, 0.8 year – 9.6 years). Follow-up colonoscopies after initial polypectomy revealed that 52% of the patients had no further polyp development while in 13 patients (27%) further polyps were detected in the same vicinity and in 10 patients (21%) further polyps were detected in different location. Dysplasia and/or carcinoma in flat dysplasia were not reported in any patients. The other study performed by Engelsgjerd et al. (30), which investigated ulcerative colitis patients with DALMs also revealed similar results. Mean follow-up

duration was 42.4 months after the initial polypectomy in that study. In no patient, colorectal adenocarcinoma was developed during the study period.

The approach to a patient with long-standing IBD and with dysplasia diagnosed in flat mucosa is much clearer. It has been shown that, the predictive rate for carcinoma of high-grade dysplasia was 40% (32). There is another study indicating that if high-grade dysplasia confirmed by two different gastrointestinal pathologists is present there is approximately a 42% chance of cancer already being present and colectomy is indicated (33).

The predictive value of low-grade dysplasia somehow varies. Woolrich et al. (34) demonstrated that, low-grade dysplasia in flat mucosa served as an indicator of future adenocarcinoma in 18% of the patients. In general, many clinicians may not refer patients with low-grade or indefinite grade dysplasia in flat mucosa for colectomy but rather prefer repeating colonoscopy and taking biopsies 3-6 months after the initial colonoscopy. Gorfine et al. (35) demonstrated that 77 patients out of 590 patients with long-standing ulcerative colitis have at least one focus of dysplasia. Thirty-three of these 77 patients also were found to have invasive carcinoma (42.8%). In that study, authors indicated that, even in patients with low-grade dysplasia (11 patients), seven patients had subsequent invasive carcinoma (2 of them had stage III colorectal carcinoma). In a study from Mayo Clinic, 18 patients with long-standing ulcerative colitis were evaluated (36). The patients enrolled into this study were diagnosed as low-grade dysplasia at their initial colonoscopy and were followed up in the same center for a median 32 months of follow-up. Cumulative incidences of neoplastic progression after the diagnosis of low-grade dysplasia were reported as 13% at one year, 26% at two years and 33% at five years. Only one patient developed colorectal cancer (Duke's C) 74 months after the initial finding of low-grade dysplasia.

The benefit of colonoscopic surveillance in chronic IBD is not proven and debate surrounds the efficacy and cost effectiveness of such programs (36,37). So far, the best evidence that supports the benefit of colonoscopic surveillance is that cancers detected in IBD patients in a surveillance program appear to be at an earlier stage than those that are detected in individuals not undergoing surveillance (38,39). Choi et al. (38) evaluated a total of 41 patients with long standing ulcerative colitis and colorectal carcinoma. Nineteen patients were under surveillance program, and colon cancer stage was found to be earlier in patients under surveillance than in patients those were not. The 5-year survival rate was 77.2% for the surveillance group and 36.3% for the no-surveillance group.

IBD is a risk factor for colorectal cancer. These patients should undergo well-designed surveillance programs. If high-grade dysplasia in flat mucosa and/or DALM is identified, they must be referred to colectomy. In cases with low-grade dysplasia in flat mucosa, approach is in favor of referring to colectomy. More studies are needed to evaluate cost-effectiveness of this kind of surveillance programs.

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