Earlier surveillance colonoscopy programme improves survival in patients with ulcerative colitis associated colorectal cancer: results of a 23-year surveillance programme in the Japanese population

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Patients with long-standing ulcerative colitis (UC) are known to have an increased risk for the development of colorectal cancer (CRC). The aim of this study was to clarify the cumulative risk for the development of dysplasia or invasive cancer and the effectiveness of surveillance colonoscopy in the Japanese population. A total of 217 patients received a total of 1027 surveillance colonoscopies between January 1979 and December 2001 at the University of Tokyo hospital. Patients with invasive cancer found in the surveillance group were compared to those referred to our hospital from the other hospitals without surveillance colonoscopy. Surveillance colonoscopy confirmed 15 patients with definite dysplasia. Of these, five were proved to have invasive cancer in the resected specimens. The cumulative risk for the development of invasive cancer at 10, 20, and 30 years was 0.5, 4.1, and 6.1%, respectively, while that for the development of definite dysplasia at 10, 20, and 30 years was 3.1, 10.0, and 15.6%, respectively. All the patients with invasive cancer in the surveillance group remained alive, while three out of four patients in the nonsurveillance group died. Our surveillance programme is useful for detecting UC-associated CRC, and survival may be improved by surveillance colonoscopy.

British Journal of Cancer (2003) 89, 1232–1236. doi:10.1038/sj.bjc.6601247 www.bjcancer.com

Keywords: colitic cancer; ulcerative colitis; surveillance colonoscopy; dysplasia; colorectal cancer

Patients with long-standing ulcerative colitis (UC) are known to have an increased risk for the development of colorectal cancer (CRC) (Ekbom et al, 1990). The recent meta-analysis study reported that the cumulative risk of developing CRC is estimated as 2% by 10 years, 8% by 20 years, and 18% by 30 years in patients with UC (Eaden et al, 2001). Ulcerative colitis-associated CRC is different from sporadic CRC in several ways. Patients with UC-associated CRC are younger than those with sporadic CRC, and even children are at risk for CRC in UC patients (Eaden et al, 2001). In addition, UC-associated CRC tends to be widespread and is difficult to detect by colonoscopy (Morson and Pang, 1967). Therefore, a specific surveillance programme should be established for patients with long-standing UC. The well-known risk factors for UC-associated CRC are the duration and extent of disease (Gyde et al, 1988; Ekbom et al, 1990; Leidenius et al, 1991). It is generally accepted that patients with total colitis for 8 years or longer and those with left-sided colitis for 12–15 years or longer should receive surveillance colonoscopy every 1 or 2 years in the Western countries (Winawer et al, 1997; Farrell and Peppercorn, 2002). However, the effectiveness of such programmes is still controversial (Lynch et al, 1993; Axon, 1994). In addition, the cumulative risk for the development of dysplasia or cancer has not been reported in the Asian populations. The aim of this study was to clarify the cumulative risk for the development of dysplasia or cancer and the effectiveness of surveillance colonoscopy for the detection of UC-associated CRC in the Japanese population. Our report outlines the results of a 23-year surveillance colonoscopy programme for detecting CRC in long-standing UC in the Japanese population, and as such, represents the first report of its kind in Japan.

MATERIAL AND METHODS

Patients’ selection

We performed a surveillance colonoscopy programme at the University of Tokyo hospital over a period of 23 years between January 1979 and December 2001. Surveillance colonoscopy was performed annually from 7 years after the onset of symptoms for patients suffering from total UC (proximal to the splenic flexure) and left-sided UC (distal to the splenic flexure). In several patients, surveillance colonoscopy scheduled for 7 years from the onset was performed several months earlier than 7 years. Such patients were included in this study. The extent of disease was defined with macroscopic findings at colonoscopy. Patients with proctitis were excluded from this study. Surveillance colonoscopy was also performed for those who had undergone subtotal colectomy and...
ileo-rectal anastomosis (IRA) to survey the retained rectum. Patients with known dysplasia or cancer at the time of referral were excluded. Those without evidence of dysplasia at the time of referral were entered into this programme.

The extent of disease was classified at the first surveillance colonoscopy. If the observed extent was less than the extent that had been observed previously, the greatest extent of disease was classified at the extent of the disease. If the observed extent had increased, it was defined as disease progression. A total of 217 patients were retrospectively reviewed in this study (surveillance group). In all, 123 patients with total UC (one patient underwent IRA during surveillance because of intractable disease), 68 with left-sided UC (in 14 of whom the disease had progressed to total colitis) and 27 with post-IRA were retrospectively reviewed. A total of 1027 colonoscopies were performed for the purpose of surveillance. During the same period, four patients, who had not received surveillance colonoscopy and who had been diagnosed at other hospitals as having symptomatic invasive cancer, were referred to us for surgical treatment (nonsurveillance group).

Surveillance colonoscopy

We offered patients annual total colonoscopy, preferentially during the remission state. Biopsy specimens were taken from flat mucosa at least every 10 cm of the whole colorectum, and additional biopsy specimens were taken from lesions with any remarkable endoscopic abnormalities such as those that were elevated and those with colour changes.

Histopathology

Biopsy specimens were fixed with formalin and stained with Haematoxylin and Eosin, and graded as high-grade dysplasia (HGD), low-grade dysplasia (LGD), indefinite for dysplasia (IND), or negative for dysplasia according to the criteria of the Inflammatory Bowel Disease/Dysplasia morphology study group (Riddell et al., 1983).

Follow-up

Total proctocolectomy was performed when patients were found to have HGD. We performed follow-up colonoscopy within 3 months for patients with LGD or IND. Surgery was performed for patients with persistent LGD or LGD with dysplasia-associated lesion or mass. A well-defined elevated lesion resembling a sporadic adenomatous polyp without dysplastic change of the surrounding mucosa was treated as coincidental adenoma and polypectomy was performed. Such lesions were not included in the category of dysplasia in this study. Otherwise, annual colonoscopy was performed.

Evaluation

The cumulative risk for dysplasia and invasive cancer in the surveillance group was evaluated. Patients with invasive cancer in both surveillance and nonsurveillance groups were reviewed in terms of the age of onset, gender, duration of disease, Dukes’ classification, and survival.

Statistics

StatView software (SAS Institute Inc, Cary, NC, USA) was used for statistical analyses. The cumulative dysplasia-free and cancer-free rates were calculated by the Kaplan–Meier method.

RESULTS

Results of surveillance colonoscopy

High-grade dysplasia or LGD were detected in 15 patients through our surveillance programme. Of these, twelve patients suffered from total colitis. Two patients were status post-IRA, both of whom had had total colitis preoperatively. Only one patient had left-sided colitis. A summary of the results of the surveillance colonoscopy is shown in Figures 1 and 2.

Six patients were found to have HGD at surveillance colonoscopy, all of whom underwent colectomy. Four of them had invasive cancer and two had HGD in the resected specimens. Nine patients were found to have LGD at surveillance colonoscopy. Of the three patients who underwent colectomy, one had invasive cancer and one had HGD. The other patient was found to have flat LGD at surveillance colonoscopy, and negative for dysplasia at the two following colonoscopies. However, she preferred to undergo colectomy to close follow-up colonoscopy, and no dysplasia was found in the resected specimens. Two patients continued to receive surveillance colonoscopy and no dysplasia was found after LGD was detected. Four patients were lost to follow-up. Two of them had undergone operation in other hospitals, and pathological reports were not available for review.
Dysplasia-free survival
The cumulative dysplasia (HGD or LGD)-free survival curve and cumulative cancer-free survival curve in patients with long-standing UC in the surveillance group are shown in Figure 3. The cumulative risk for the development of invasive cancer at 10, 20, and 30 years (95% confidence interval) was 0.5% (0–1.5), 4.1% (0–8.3), and 6.1% (0.2–12.0), respectively, while that for the development of definite dysplasia at 10, 20, and 30 years (95% confidence interval) was 3.1% (0.6–5.6), 10.0% (4.3–15.7), and 15.6% (6.4–24.8), respectively.

Table 1

| Case | Age of Onset (years) | Age at operation (years) | Duration (years) | Histologya | Depth | Dukes | Locationb | Extentc | Survival |
|------|----------------------|--------------------------|------------------|------------|-------|-------|-----------|----------|----------|
| 4    | 16                   | 37                       | 21               | mod,pors > well | sm   | A     | R         | L        | Alive 7y5m |
| 5    | 56                   | 65                       | 9                | well to mod    | sm   | A     | S         | T        | Alive 5y10m |
| 6    | 28                   | 41                       | 13               | well          | sm   | A     | T(IRA)    | L        | Alive 16y10m |
| 7    | 36                   | 49                       | 13               | well          | mp   | A     | C         | T        | Alive 12y10m |
| 8    | 21                   | 41                       | 20               | well > mod > por | ss   | B     | R         | T        | Alive 9y8m  |

Non surveillance group

| Case | Age of Onset (years) | Age at operation (years) | Duration (years) | Histology | Depth | Dukes | Locationb | Extentc | Survival |
|------|----------------------|--------------------------|------------------|-----------|-------|-------|-----------|----------|----------|
| 21   | 44                   | 29                       | 21               | well      | ss    | B     | D         | T        | Alive 1y10m |
| 29   | 42                   | 29                       | 13               | sig       | se    | C     | S         | T        | Dead 1y    |
| 20   | 40                   | 29                       | 20               | muc > mod > por | se   | C     | D         | T        | Dead 2y5m  |
| 29   | 47                   | 29                       | 18               | sig       | se    | C     | D         | T        | Dead 1m    |

DISCUSSION
We performed a surveillance programme to detect UC-associated CRC for 23 years, which we believe to be the first surveillance programme reported in the Asian population. Our data suggest that our surveillance programme was useful for detecting UC-associated CRC, although the study was not performed in a randomised manner and lead-time bias together with selection bias could not be avoided. Some authors doubt whether surveillance colonoscopy can detect UC-associated CRC earlier and thereby improve the prognosis (Axon, 1994). However, it is generally accepted that surveillance colonoscopy is important and is the only way for detecting UC-associated CRC at this time (Winawer et al, 1995). Therefore, this kind of study could not be performed in a randomised manner.

Our programme successfully identified UC-associated CRC at an earlier stage than other surveillance studies. Dukes’ stages in the surveillance group were A in four and B in one, whereas those in the nonsurveillance group were C in three patients and B in one patient. It had been reported that patients with UC-associated CRC at Dukes’ A and B showed a good survival rate, but those at Dukes’ C showed an extremely poor prognosis (Heimann et al, 1992). Our data are compatible with that report. Patients with UC-associated CRC in the surveillance group showed better prognoses than those in the nonsurveillance group. All the patients in the surveillance group remained alive, whereas three out of four patients died. The mean postoperative follow-up period was 126 months (70–202), and 41 months (1–133) for the surveillance and nonsurveillance group, respectively.

The cumulative dysplasia-free and cancer-free survival rates in patients with long-standing ulcerative colitis in the Japanese population.

Figure 3

Prognosis, surveillance group vs nonsurveillance group
The patients with invasive cancer in the surveillance group had a better prognosis than those in the nonsurveillance group. The clinicopathological features in both groups are listed in Table 1. Five patients in the surveillance group were found to have invasive cancer. Dukes’ stages in the surveillance group were A in four and B in one, whereas those in the nonsurveillance group were C in three, and B in one. All the patients with invasive cancer in the surveillance group remained alive, whereas three out of four patients died. The mean postoperative follow-up period was 126 months (70–202), and 41 months (1–133) for the surveillance and nonsurveillance group, respectively.
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