RESEARCH ARTICLE

Colorectal Cancer and Precancerous Lesions Associated with Ulcerative Colitis in Thailand

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Abstract

Background: Ulcerative colitis(UC) is important risk factor of colorectal cancer. Many evidences from western countries confirmed this relationship but limited studies were reported in ASEAN. This study was aimed to investigate prevalence, clinical presentations, endoscopic findings, histopathology, disease progression and risk for colorectal cancer(CRC) of UC patients in Thailand. Methods: We conducted a retrospective cohort study using computer data base from Thammasat University Hospital, Pathumthani, Thailand between September 2011 and December 2015, follow-up through May 2016. Diagnosis of UC was confirmed by histopathology and whole clinical course. **Results:** We identified 6,082 patients who diagnosed with colitis during the study period. Of whom, only 22 patients(<1%) was confirmed of UC. Male to female ratio was 13:9 (mean age of 47.2 years). Clinical presentations were bloody diarrhea in 86.4%, watery diarrhea in 31.8% and abdominal pain in 59.1%. According to Montreal classification, disease extensions were ulcerative proctitis in 22.7%, distal UC in 50%, and pancolitis in 27.3%. Disease grading was mild in 31.8%, moderate in 9.1%, and severe in 59.1%. The prevalence of precancerous lesions were 2/22 patients(9.1%). There was no definite invasive colorectal cancer patient during study period. However, history of malnutrition was significantly higher in patients with dysplasia than those without dysplastic lesions(50%vs.0%, P-value=0.045). There was no difference in duration and disease extension between 2 groups. Interestingly, subgroup analysis demonstrated that pancolitis was significantly more common in female than male (55.6%vs.7.7%,P-value=0.02,OR=15.0, 95%CI=1.3-169.9). Furthermore, patients' age> 35 years had significantly more severe colitis than younger group (81.25%vs.0%, P-value=0.0006) **Conclusions:** Although UC is rare disease in ASEAN, precancerous lesions for CRC were not uncommon. UC with pancolitis was common in female whereas severe colitis was common in elderly patients. Proper screening program and careful surveillance for precancerous lesions in patients at risk might be appropriate approach for early detection and improvement the treatment outcome.

Keywords: Colorectal cancer- ulcerative colitis- Thailand

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Introduction

Colorectal cancer (CRC) is one of the important cancers worldwide. CRC is the third most commonly diagnosed cancer in males and the second in females, with more than one million new cases and more than 600,000 deaths per year (Park et al., 2008; Pandurangan, 2013; Torre et al., 2015). Patients with ulcerative colitis (UC) have increased risk of developing CRC(Mokarram et al., 2015). The overall prevalence of CRC in UC patients in western countries, based on meta-analysis of 116 studies, was approximately 3.7%. The probability of developing CRC was 2%, 8%, and 18% by 10, 20, and 30 years after diagnosis. CRC incidence rates also varied geographically, with higher risk among patients in USA and UK than other countries (Eaden et al., 2001). Risk of developing CRC in UC patients also varied between 0.9 to 8.8-fold depending on the studies and countries (Ekbom et al., 1990; Langholz et al., 1992; Bernstein et al., 2001; Eaden et al., 2001; Winther et al., 2004; Lakatos and Lakatos, 2008; Triantafillidis et al., 2009). In Asian countries, the prevalence of CRC in UC seems to be lower than in western countries and lack of reports from ASEAN. Previous studies demonstrated that prevalence of CRC was 0.37%, 0.87%, 0.94%, and 1.5% in South Korea, China, India, and Taiwan, respectively (Venkataraman et al., 2005; Kim et al., 2009; Yun et al., 2009; Wei et al., 2012; Zhang et al., 2015). The incidences of CRC in patients with UC in western countries have been decreasing which might be from improved medical therapy and dysplasia screening program (Jess et al., 2012).

CRC associated with inflammatory bowel disease believed to begin from no dysplasia then progress to indefinite dysplasia, low-grade dysplasia, high-grade dysplasia and finally turn to be invasive adenocarcinoma, although some CRC could be raised without proceeding from dysplasia (Triantafillidis et al., 2009; Pandurangan and Esa, 2014). The risk of CRC in UC depend upon

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duration and extention of disease. Patients with IBD and long-standing extensive colitis, defined as colitis for >10 years and involving ≥50 percent of the colon, were at risk for CRC. Patients without long-term extensive colitis have a risk for CRC similar to general population (Beaugerie et al., 2013). Patients with ulcerative proctitis and proctosigmoiditis might be not increased risk for CRC (Levin, 1992). Patients with primary sclerosing cholangitis (PSC) was also increased risk for CRC compared to those without PSC (Jess et al., 2012). Furthermore, histories of postinflammatory pseudopolyps appear to be a predictive factor for cancer. Other factors that had shown to contribute to CRC development included family history of CRC, smoking, and backwash ileitis (Nuako et al., 1998; Heuschen et al., 2001; Xie and Itzkowitz, 2008). Surveillance colonoscopy and use of anti-inflammatory medications may reduce the risk of colorectal cancer (Velayos et al., 2006).

Many evidences from western countries have confirmed the relationship between UC and risk for CRC. However, there are limited studies in ASEAN countries. This study was aimed to investigate the prevalence, clinical presentations, endoscopic findings, histopathology and monitoring disease progression of UC patients in a tertiary care center in Thailand. This study also tried to identify risk factors for colorectal cancer in this specific group of patients.

Materials and Methods

A retrospective cohort study of UC patients was conducted in Thammasat University Hospital, Pathumthani, Thailand between September 2011 and December 2015, follow-up through May 2016. The diagnosis of UC was confirmed by histopathology and whole clinical course. All the clinical information, endoscopic finding, and histologic finding of patients were reviewed, and relevant data were recorded into a clinical collecting form. Each variable was compared between UC patients with or without precancerous lesions. The study was conducted according to the good clinical practice guideline and was approved by ethics committee of Thammasat university hospital, Thailand.

Statistical analysis

All statistical analyses were performed by using SPSS Statistics version 19.0 (IBM Corp., Armonk, NY). The information was expressed as frequency, mean ± standard deviation (SD). Continuous variables were compared by the Student's t-test, and categorical variables were compared by Chi-square or Fisher's exact test where appropriate. The P-values < 0.05 was considered as statistical significant.

Results

We identified 6,082 patients who diagnosed with colitis. Of whom only 22 patients (<1%) was confirmed of ulcerative colitis. Male to female ratio was 13:9 with mean age of 47.2 years. Clinical presentations were bloody diarrhea in 86.4 %, watery diarrhea in 31.8 %, abdominal pain in 59.1 %, Tenesmus in 18.2%, fever in 13.64%, weight loss in 36.4 %, anemia in 27.3%, constipation in 4.6%, and extra-intestinal manifestations in 22.7 %. Anemia was the most common physical finding presented in 63.6%, follow by abdominal tenderness (36.4%), blood per rectal examination (36.4%), abdominal distension (13.6%), mass per rectal examination(13.6%), chachexia (9.1%), palpable mass (9.1%), history of malnutrition (4.6%), and fever (4.6%). For extra-intestinal manifestations, there were ocular involvement in 13.64%(9.1% episcleritis, and 4.6% uveitis), arthritis in 18.2% and dermatologic involvement in 9.1% (4.6% pyoderma gangrenosum, and 4.6% apthous ulcer). According to Montreal classification, the disease extensions were ulcerative proctitis in 22.7 %, distal ulcerative colitis in 50 %, and pancolitis in 27.3 %. The disease grading was mild in 31.8 %, moderate in 9.1 %, and severe in 59.1 %. For endoscopic finding, erythematous mucosa and friability were found in all patients. There were erosion, ulceration, and spontaneous bleeding in 45.5%, 36.4%, and 36.4%, respectively. Pseudopolyp was found in 45.5%. 77.3% of patients had evidence of chronic colitis in histology from mucosal biopsy.

The prevalence of precancerous lesions were 2/22 patients (9.1 %) (1 patient with low-graded dysplasia and another with carcinoma in situ). Mean duration from onset to dysplasia was 1,840 days. There was no definite invasive colorectal cancer in this study. There was no difference with age between patients with or without dysplasia (67.5 years vs. 45.2 years, P-value= 0.12). However, history of malnutrition was significantly higher in patients with dysplasia and those without dysplastic lesions (50% vs. 0%, P-value= 0.045). Age> 60 years, weight loss, cachexia and palpable mass at presentation tended to be more common in patients with dysplasia than without these lesions (100% vs. 30%, P-value= 0.06, 100% vs. 30%, P-value= 0.06, 50% vs. 5%, P-value= 0.09, 50% vs. 5%, P-value= 0.09, respectively). There was no difference in duration and extension of disease between

Table 1. Demographic Data of All Patients

Clinical factors	n (%)
Male	13 (59.1 %)
Mean age	47.2 years
Symptoms	
Watery diarrhea	7 (31.8%)
Bloody diarrhea	19 (86.4%)
Colicky pain	13 (59.1%)
Fever	3 (13.6%)
Extension of diseases	
Proctitis	5 (22.7%)
Distal UC	11 (50%)
Pancolitis	6 (27.3%)
Severity	
Mild	7 (31.8%)
Moderate	2 (9.1%)
Severe	13 (59.1%)

Table 2. Clinical Factors Associated Development of Colonic Dysplasia

	n (%)	p-value
Male (%)	1 (50%)	0.41
Mean age	67.5	0.12
Age ≥ 60, n (%)	2 (100%)	0.06
Mean duration to diagnosis (Days)	592.5	0.53
Symptoms, n (%)		
Bloody diarrhea	2 (100%)	0.37
Colicky pain	1 (50%)	0.41
Fever	0 (0%)	0.37
Weight loss	2 (100%)	0.06
Anemia	1 (50%)	0.27
Malnutrition	1 (50%)	0.04
Extension, n (%)		0.63
Proctitis	0 (0%)	0.29
Distal UC	1 (50%)	0.5
Pancolitis	1 (50%)	0.27
Severity, n (%)		0.47
Mild	0 (0%)	0.23
Moderate	0 (0%)	0.41
Severe	2 (100%)	0.17
Relapse, n (%)	1 (50%)	0.32

these 2 groups in our study.

Subgroup analysis demonstrated that pancolitis was significantly more common in female than male (55.6% vs. 7.7%, P-value= 0.02, OR= 15 95%CI= 1.3-169.9). Furthermore, patients age> 35 years had significantly more severe colitis than younger group (81.25% vs. 0%, P-value= 0.0006).

Discussion

Colorectal cancer (CRC) has been increasing in significance in developing countries like ASEAN including Thailand (Sermsri et al., 2014). Patients with UC have an increased risk of developing CRC. The overall prevalence of CRC in UC patients in western countries was estimated to be 3.7% (Eaden et al., 2001). Data from Asian countries were limited, potentially due to the lower UC incidence. The incidence of dysplasia in UC is difficult to determine and varies among different studies. A previous study demonstrated that cumulative probability of developing precancerous lesions or carcinoma was 4% at 15 years, 7% at 20 years, and 13% at 25 years (Lennard-Jones et al., 1990). In meta-analysis of 20 surveillance studies, the cancer incidence was 14 of 1,000 person years duration (pyd) and the incidence of any advanced lesion was 30 of 1,000 pyd (Thomas et al., 2007). The prevalence of precancerous lesions in our study was 9.1 % without definite invasive colorectal cancer. These might be explained by lower number of UC patients in Thailand and inadequate surveillance in our country.

The duration and extension of disease were considered to be risk factors for developing CRC in UC patients (Beaugerie et al., 2013). However, there was no difference in duration and extension of disease between patients with or without dysplasia in our study. The ethnic and environmental difference along with short-term follow-up may contribute to these findings. Mean duration from onset to dysplasia in our study was approximately 5 years. Longer follow-up period may lead to early detection of colorectal cancer. Dysplasia in UC patients remained impact on patient's prognosis. When Low-grade dysplasia (LGD) is detected, there is a 9-fold risk of developing cancer and 12-fold risk of developing advanced lesion (Thomas et al., 2007). Concurrent CRC or high-grade dysplasia (HGD) was found in 19% of patients with LGD (Ullman et al., 2003; Odze et al., 2004; Triantafillidis et al., 2009). HGD carries a 43% risk of synchronous malignancy (Kornfeld et al., 1997). Our study suggested that history of malnutrition might be an important risk to develop precancerous lesion of CRC whereas age> 60 years, weight loss, cachexia and palpable mass tended to be more common in patients with dysplastic patients. These findings might be important for clinicians raising concern and consider screening program in patients at risks.

In conclusion, although UC is rare disease in ASEAN, precancerous lesions for colorectal cancer in these patients were not uncommon. Proper screening program and careful surveillance for precancerous lesions in patients at risk might be appropriate approach for early detection and improvement the treatment outcome.

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