RESEARCH COMMUNICATION

Clinical, Endoscopic and Pathogical Characteristics of Early-Onset Colorectal Cancer in Vietnamese

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Abstract

Background: The Asia Pacific consensus for colorectal cancer (CRC) recommends that screening programs should begin by the age of 50. However, there have been reports about increasing incidence of CRC at a younger age (i.e. early-onset CRC). Little is known about the features of early-onset CRC in the Vietnamese population. Aim: To describe the clinical, endoscopic and pathological characteristics of early-onset CRC in Vietnamese. Method: A prospective, cross-sectional study was conducted at the University Medical Center from March 2009 to March 2011. All patients with definite pathological diagnosis of CRC were recruited. The early-onset CRC group were analyzed in comparison with the late-onset (i.e. ≥ 50-year-old) CRC group. Results: The rate of early-onset CRC was 28% (112/400) with a male-to-female ratio of 1.3. Some 22.3% (25/112) of the patients only experienced abdominal pain and/or change in bowel habit without alarming symptoms, 42.9% (48/112) considering their symptoms intermittent. The rate of familial history of CRC in early-onset group was significantly higher that of the late-onset group (21.4% versus 7.6%, p<0.001). The distribution of CRC lesions in rectum, distal and proximal colon were 51.8% (58/112), 26.8% (30/112) and 21.4% (24/112), respectively; which was not different from that in the late-onset group ($\chi 2$, p = 0.29). The rates for poorly differentiated tumors were also not significantly different between the two groups: 12.4% (14/112) versus 8.3% (24/288) ($\chi 2$, p = 0.25). Conclusion: A high proportion of CRC in Viet Nam appear at an earlier age than that recommended for screening by the Asia Pacific consensus. Family history was a risk factor of early-onset CRC. Diagnosis of early-onset CRC needs more attention because of the lack of alarming symptoms and their intermittent patterns as described by the patients.

Keywords: Colorectal cancer - early-onset - familial history - Viet Nam

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Introduction

Colorectal cancer (CRC) is one of the most common cancers in Vietnam. The Asia Pacific consensus for colorectal cancer recommended that screening program should begin by the age of 50 (Sung et al., 2008). However, there have been reports about increasing incidence of CRC at a younger age (i.e. early-onset CRC) (Foroutan et al., 2008; Siegel et al., 2009). Therefore, investigation on the characteristics of patients with early-onset CRC is an urgent clinical demand in order to have a better screening strategy and early detection of CRC. Little has been known about the characteristics of early-onset CRC in Vietnamese population. The aim of this study was to describe the clinical, endoscopic and pathological characteristics of early-onset CRC in Vietnamese population.

Materials and Methods

Patients

Vietnamese patients who were less than 50 years of age, underwent colonoscopy at the Department of Endoscopy, University Medical Center in Hochiminh City from March 2009 to March 2011 and had the definite pathologic results of colorectal carcinoma were recruited. All patients were required to give their written informed consent before entering the study. The protocol was approved by the Ethics Committee of the Faculty of Medicine, University of Medicine and Pharmacy in Hochiminh City.

Method

This is a prospective, cross-sectional study. Clinical data including familial history of CRC and symptoms were collected according to a predetermined protocol. All of patients were performed colonoscopy using Olympus colonoscope Video Exera CF AI – 160. During endoscopic examination, the locations and the macroscopic features of CRC lesions were reported. The pathologically differentiation of colorectal carcinoma were graded using a three-tier scale: good, moderate or poor differentiation.

Statistical Analysis

Analyses were performed with SPSS for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA). Differences in proportion between the early-onset and the late-onset

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CRC subgroups were evaluated by chi-squared test or Fisher's exact test, as appropriate. Statistical significance was defined at the $P < 0.05$ level.

Results

Clinical characteristics

From March 2009 to March 2011, we recruited 400 CRC patients diagnosed at the Department of Endoscopy, University Medical Center in Hochiminh City. There were 112 (28%) patients with early-onset CRC, including 63 males (56.3%) và 49 female (43.8%). The male-to-female ratio is 1.3:1. 44 (11%) patients were under 40 and 68 (17%) were under than 50 years of age. The youngest patient in our case series was 17-year-old. There were 46 (11.5%) patients with familial history of CRC in first-degree relatives.

The proportion of patients with familial history of CRC in early-onset group was significantly higher than that in late-onset group (21.4% versus 7.6%, χ^2 test, $p < 0.001$). The number of first-degree relatives diagnosed with CRC in early-onset group was presented in Table 1. The association between patients'age and their youngest relatives'age at the time CRC diagnosis was established was presented in Table 2.

Table 1. Number of First-Degree Relatives Diagnosed with CRC in Early-Onset CRCs

Number of first-degree relatives with CRC	n	%
3 relatives	1	0.9
2 relatives	3	2.7
1 relative	20	21.4
Total	24	100

Table 2. The Association between Patients' Age who Had Familial History of CRC and their Youngest Relatives'age at the Time CRC Diagnosis was Established

Group	No	Sex	Age	Age of the youngest relative	Notes
A:	1	F	35	-	The youngest relative's age at the time CRC diagnosis was established was not known.
	2	M	37	-	
	3	F	42	-	
	4	F	46	-	
B:	5	M	36	23	The youngest relative was less than 60 years of age and patient was diagnosed with CRC at least 10 years later than his/her youngest relative.
	6	M	39	30	
	7	F	40	33	
	8	M	40	40	
	9	F	45	40	
	10	M	46	50	
	11	F	47	52	
	12	M	49	50	
C:	13	F	27	52	The youngest relative was less than 60 years of age and patient was 10 years older than his/her youngest relative.
	14	M	32	44	
	15	M	35	58	
	16	M	41	56	
	17	M	46	56	
D:	18	F	34	66	The youngest relative was diagnosed with CRC at 60 years of age or later.
	19	F	37	78	
	20	F	38	78	
	21	M	40	68	
	22	M	42	73	
	23	F	46	72	

All patients with early-onset CRC presented with symptoms (Table 3 and Table 4). However, 22.3% (25/112) of patients only experienced abdominal pain or change in bowel habit without alarming symptoms. 42.9% (48/112) of these patients considered their symptoms as intermittent pattern.

Endoscopic characteristics

In 69.6% (90/112) of patients, the cancer lesions had already made the bowel lumen so narrow that total colonoscopy could not be completed. The proportion of proximal CRC (i.e. lesion located from cecum to decending colon) in the early-onset group was not significantly different from that in the late-onset group (26.8% versus 21.5%, χ^2 test, $p = 0.29$). The location and the endoscopic growth forms of CRCs in the early-onset group is presented in Table 5.

Pathologic characteristics

The proportion of good, moderate and poor diffentiations of early-onset CRCs in our study were 6.3%, 81.2% and 12.5%, respectively. The rates of poor differentiated CRC in the early-onset and the late-onset groups were not significantly difference (12.5% versus 8.3%, χ^2 test $p = 0.25$).

Table 3. Symptoms of Patients with Early-Onset CRCs

Symptoms	n	%
Abdominal pain	71	63.4
Diarrhea	24	21.4
Constipation	27	24.1
Alternative diarrhea and constipation	11	9.8
Hematochezia	58	58.1
Weight loss	46	41.1
Anismus	38	33.9
Anemia	3	2.7

Table 4. Period of Time with Symptoms in Patients with Early-Onset CRCs

Period of time with symptoms	n	%	Cumulative %
< 1 month	12	10.7	10.7
1 - 3 months	53	47.3	58.0
> 3 - 6 months	20	17.9	75.9
6 - 12 months	19	17.0	92.9
> 12 months	8	7.1	100.0

Table 5. Early-Onset CRCs

	n	%	Cumulative %
Anatomic Distribution:			
Rectum	58	51.8	51.8
Sigmoid colon	24	21.4	73.2
Descending colon	6	5.4	78.6
Transverse colon	12	10.7	89.3
Ascending colon	12	10.7	100.0
Endoscopic Growth Forms:			
Sessile polypoid	85	75.9	75.9
Circular ulcerated	18	16.1	92.0
Pedunculated polypoid	3	2.6	94.6
Annular tumour with stenosis	1	0.9	95.5
Ulcerated	5	4.5	100.0

Discussion

The definition of "early-onset" is not consistent in previous studies on CRC. The age threshold of 40 or 50 was commonly used in different studies. In this study, we have chosen the age threshold of 50 as this is the cut-off age for CRC screening according to the recommendation of the Asia Pacific consensus (Sung et al., 2008). The proportion of early-onset CRC varies significantly according to the target populations. In our study, the proportion of patients who were less than 40 years-of-age was 11%. This proportion in a Turkish study was 13% (Savas et al., 2007). Recent studies in Indian population showed that even within a country, this proportion might highly vary from 12.6% to 39% (Nath et al., 2009; Peedikayil et al., 2009; Gupta et al., 2010).

Regarding the sex distribution, the male-to-female ratio in our study was 1.3:1. Similar studies in Jordan and Israel showed a predominant proportion of female in patients with early-onset CRC (Al-Jaberi et al., 2003; Neufeld et al., 2009). This could be explained partly by the racial and enviromental differences.

It should be aware that nearly half of Vietnamese patients with early-onset CRC may considered their symptoms as intermittent pattern. In addition, about 22.3% of these patients did not have alarming symptoms. These clinical characteristics may make it difficult to differentiate CRC from benign or functional bowel disorders and lead to a late diagnosis. In our case series, 69.6% of CRC lesions had been so endoscopically advanced that the colonoscope could not pass through the lesions to complete the colon examination while 75.9% of patients had symptom onset within 6 months. There is good evidence to show that most CRCs develop from colorectal adenomas and they are usually asymptomatic in early stage (Stryker et al., 1987). In addition, colorectal polypectomy has been proved to reduce the CRC incidence (Winawer et al., 1993; Kahi et al., 2009). In Vietnam, there is no national screening p rogram for CRC (Rex et al., 2009). Therefore, identification the characteristics of patients who have high risk of CRC is very urgent.

In our study, the proportion of patients who had familial history of CRC in the early-onset CRC group was significantly higher than that in the late onset group (21.4% vs 7.6%, $p < 0.001$). Our result also mirrors those of studies on other populations (Karsten et al., 2008; Makela et al., 2010). Data from Table 2 showed some defects of the health care system in Vietnam which should be improve so that not to miss the chance to detect early CRC in high-risk individuals. According to the recent guidelines of the American College of Gastroenterology, patients at increased risk (a first-degree relative with CRC at age < 60 years or two first-degree relatives diagnosed at any age) should be advised to have screening colonoscopy starting at age 40 years, or 10 years younger than the earliest diagnosis in their family, which ever comes first (Rex et al., 2009). 50% (12/24) patients who had familial history of CRC (i.e. group A and group B) in our study would have diagnosed early if this screening strategy was followed. As a consequence, a good management of CRC should not be restricted to the treatment of patients themselves but also a good consultation to their relatives regarding their risk levels, the symptoms of CRC and the appropriate age to start surveillance program. 25% (6/24) of patients who had familial history of CRC in our study had the earliest diagnosis in their family younger than 50 years, which is one of the characteristics recommended to surveillance for Lynch syndrome according to the revised Bethesda guidelines (Umar et al., 2004). However, the methods for testing microsatellite instability is not available in Vietnam at the moment. Even Amsterdam criteria is also difficult to apply because of the lack of national registry of pathological results and the insufficient awareness of the disease in Vietnamese population. Our study showed an urgent need to develop these facilities in Vietnam. At the moment, the our surveillance strategy will be mainly based on the family history of CRC in order to identify high risk individuals. Regarding the cut-off age for screening program for patients at average risk, both of the Asian-Pacific consensus and the American College of Gastroenterology recommend to start at age 50 years. Our study showed that 24.9% of CRC in Vietnamese populatin was early-onset. Previous studies in India also reported a significant proportion of early-onset CRC (Nath et al., 2009; Gupta et al., 2010). As a consequence, the cut-off age of 50 for starting surveillance may be not appropriate in some Asian populations including Vietnamese.

The most common endoscopic CRC growth forms in our study were sesile polypoid and circular ulcerated. 73.2% of the lesions located in the rectosigmoid segment. Previous studies in other Asian populations also reported the same results (Fazeli et al., 2007; Yantiss et al., 2009; Gupta et al., 2010). Regarding the pathologic differentiation of CRCs, there was no significant difference in proportion of poor-differentiated CRC between the early-onset and the late-onset subgroups. However, several studies in other populations reported that poor-differentiated CRC tended to cluster in the early-onset group (Al-Jaberi et al., 2003; Fazeli et al., 2007; Karsten et al., 2008; Nath et al., 2009; Gupta et al., 2010). The heterogeneous results of these studies may be because our pathologic results were based on endoscopic-based specimens, which might have some errors compared to surgical-based specimens, or because there were differences in oncogenic factors and racial factors among these populations. Future studies to compare the accuracy in defining CRC differentiation between endoscopic-based and surgical-based specimens are required.

In conclusion, the proportion of early-onset CRC in Vietnamese population was 28%. 73.2% of the lesions clustered in the rectosigmoid segment. There was no significant difference in location and pathologic differentiation of CRC in early-onset and late-onset group. The diagnosis of early-onset CRC often required a high suspiction as a large number of patients reported intermittent pattern of symptom and might not have alarming symptoms. Familial history of CRC is a risk factor of early-onset CRC which should be addressed in all patient presenting with bowel disorders. A good management of CRC should include a good consultation for first-degree relatives of the patients about their risk levels and the role of surveillance.

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