Colorectal Cancer in Young Patient:
A Distinguished Disease Entity?

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ABSTRACT

Background: Some studies suggested that colorectal cancer at young age had a distinct biological characteristic: more advanced stage at time of diagnosis, poorer differentiated, and consisted of large proportion of mucin producing tumors.

Aim of the study: To analyze clinical and histopathological differences between young aged colorectal cancer patients (< 40 years old) and the older patients

Methods: A cross-sectional retrospective study was conducted among our colorectal cancer patients in a general hospital between 1999-2004, using C.18, C.19, C20 ICD X code in medical record searching. It was requested that the patients had surgical treatment in Dr. Sardjito General Hospital. An inconclusive clinical staging and/or histological data were among the exclusion criteria. Chi-square, Fisher's exact test, T-test, and Mann Whitney U-test was performed to analyze the difference between patients < 40 years old and ≥ 40 years old, in respect to diagnostic staging, histological type, histological grade (differentiation), CEA level, hemoglobin, albumin, tumor location, and chief complain. With p < 0.05 was considered as significant.

Results: Sixteen young aged (< 40 years old) and 72 older patients had been identified. No differences in gender proportion and mean of symptoms to diagnosis period between two groups. No statistical differences between young aged and the older patients in diagnostic staging, histological grade and type, CEA level, and hemoglobin. Young aged patients had higher albumin value at presentation (p = 0.014), all had left sided tumors (p = 0.035), more complain of anal pain (p < 0.001), and less change of bowel habits complain (p = 0.009)

Conclusion: The study results had failed to confirm the difference in respect to diagnostic staging, histological type and grade, CEA level, and hemoglobin. Most of our young aged patients had left sided tumors with chief complain of anal pain, and less complain of change of bowel habits

Keywords: Young aged colorectal cancer patients, cross sectional analysis, clinical and histological difference

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INTRODUCTION

Colorectal cancer has been the 2nd leading cause of death due to malignancy after lung cancer in the United States. Approximately 130,200 new cases were found in year of 2,000 with mortality rate of 56,300.[1] There is still no data concerning the incidence of the disease in Indonesia.

Foreign references have been consistently mentioned colorectal cancer as the disease mostly occurs in 4th - 5th decades of life.[1,2] Age had been reported as major risk factor of sporadic incidence of colorectal cancer. Other risk factor such as hereditary is much less frequent and characterized by occurrence of disease in younger patients who had positive family history. However, in general, colorectal cancer is rarely found in people whose age is under 40 years old. In accordance with increased aging population, the incidence of colorectal cancer has also been increased.[2] Study on 291 patients with colorectal cancer in Bandung showed that incidence was already increased in much younger age, 30 years old with the peak incidence in sixth decade.[3]

Age was reported as contributing factor in carcinogenic process both positively or negatively. Researchers had reported that cancer in young patients had different characteristics from those which occurred in the older ones. Younger age is associated with more advanced stage of disease at time of diagnosis, had worse mucinous production and differentiation profiles.[4,5] Moreover, colorectal cancer in young patient was reported to be more aggressive and had poor prognosis.[6,7] The issue that sporadic colorectal cancer which occurs in young patients is a different disease entity from those which occurs in older ones and hereditary in nature had already been addressed. Involvement of tumor suppressor gene or disappearance of heterozygocity or mutation was considered to have role in tumor development pathogenesis.[8] On the other side, some experts had not found differences of clinical features or prognosis between colorectal cancer in different age groups of young and older ones.[9,10] To investigate the characteristics of colorectal cancer in young age group in our population and their difference from the older ones, we had conducted retrospective analysis in colorectal cancer patients in our hospital.

METHODS

This study aims to investigate the differences in clinical features and histologic description of colorectal cancer in young age (less than 40 years old) compare to the older ones. Design of study is cross sectional from retrospective data. Thus, we have collected data retrospectively obtained from medical record between 1999 and 2004. ICD code X: C.18 (colon cancer), C.19 (rectosigmoid cancer), and C.20 (rectal cancer) were used in medical record searching.

Inclusion criteria of this study were all medical records with ICD X code for colorectal cancer after laparotomy surgical procedure in our hospital and copy of histopathologic examinations. Exclusion criteria were incomplete data of medical records which made us could not determine staging of cancer at time of diagnosis, no conclusion of differentiation grade and histologic type of the tumor.

Data collecting consists of demographic aspects (age at time of diagnosis, gender), clinical aspects (chief complain, duration of symptom until diagnosis was established, family history of cancer, previous history of neoplastic disease), tumor location/site (based on primary tumor finding on surgery/caecal biopsy, ascending colon, hepatic flexure, transversum colon, splenic flexure, descending colon, rectosigmoid, rectum), staging at time of diagnosis (stage I to V according to American Join Committee Classification), differentiation grade (high grade include poor differentiated, undifferentiated; low grade include moderate and mild differentiation), histologic type (adenocarcinoma, mucinous carcinoma, or signet ring cell carcinoma), laboratory data (hemoglobin, albumin, BUN, creatinin, AST, ALT, CEA, and random blood glucose at time of diagnosis).

Statistical analysis of significant difference of 2 proportions using *chi-square* analysis or *Fischer exact test*. Comparison of mean between 2 groups using *t-test* or if distribution of data were not normal we used *Mann-Whitney* test. Hypothetic testing was two-tailed with $p < 0.005$ was considered significant.

RESULT

Three hundred and twenty eight medical records were obtained with code C.18, C.19 and C.20. Finally, we had 88 medical records included in this study. Sixteen patients were under 40 years old (young patients), and 72 patients were above 40 years old (older patient).

Mean age of young patient group was 31.6 years (SD ± 7.2 years) with median age of 33.5 years. Age was ranging from 14 to 39 years. Mean age of older patient group was 55.9 years old (SD ± 10.4 years) with median age of 55.5 years old. Age in older group was ranging from 40 to 78 years old. Number of male patients in young group was 8 (50%), while in older group were 40 (55.5%). There is no significant difference of male proportion between these two group ($p = 0.686$).

Table 1. Differences between Young and Older Age Group Based on Age, Sex, and Tumor Location

	< 40 years N=16	≥ 40 years N = 74	p
Age (years old)			
mean ± SD	31.6 ± 7.2	55.9 ± 10.4	
median	33.5	55.5	
Male proportion (%)	8 (50)	40 (55.5)	0.686
Tumor location in colon and rectum (%)			
- caecum	0	5 (6.9)	(left vs. right side)
- ascenden	0	7 (9.7)	0.035
- hepatic flexure	0	2 (2.8)	
- transversum	0	2 (2.8)	
- splenic flexure	0	2 (2.8)	
- descenden	0	4 (5.5)	
- rectosigmoid	1 (6)	10 (13.9)	
- rectum	15 (94)	40 (55.5)	

Table 2. Comparison of Patient's Chief Complaints

	< 40 years	≥ 40 years	p
Altered defecation pattern (%)	28.6	44.9	0.009
Hematoschezia (%)	42.8	33.0	0.866
Pain/tenderness in abdomen/anus (%)	28.6	16.9	< 0.001
Abdominal mass (%)	0	5.1	0.337

The tumor in younger group located mostly in the rectum (94%) and the rest were in rectosigmoid (6%).There was no tumor found in other location in this group. In older group, tumor locations were varied but mostly were in the rectum (55.5%), followed by rectosigmoid (13.9%), ascending colon (9.7%), caecum (6.9%),descending colon (5.5%), and hepatic flexure, splenic flexure, and transversum colon were all accounted 2.8%. If we compare the incidence of right sided cancer (starting from caecum to splenic flexure) and the left side (starting from descending colon to distal), there was significant difference of incidence bet to the older one. Young group had mostly left sided cancer. Table 1 showed proportion of age, gender and tumor location between young and older group.

Clinical symptom characteristics in young group were hematoschezia (42% of all complaints), followed by altered defecation pattern, and pain or tenderness in abdomen or anus (28%). In the older group, altered defecation pattern were the most reported complaint (44.9%), followed by hematoschezia (33%), pain or tenderness in abdomen (16.9%) and abdominal mass (5.1%). If we compare the two groups, the older group frequently complained of altered defecation pattern (p = 0.009) while the young group mostly complained for pain in abdomen/anus (p < 0.001). Table 2 showed the pattern of these clinical symptoms in the 2 groups.

Mean period of clinical symptom occurred until diagnosis was confirmed for young group was 8.66 ± 8.6 months with median of 6 months. Older group has mean period of 7.8 ± 9.6 months with median of 6 months. There was no significant difference of mean period between these two groups (p = 0.709; 95% CI: - 4.1 to 5.9). If we classified in period of less than 1 month, 1-6 months, more than 6 months and more than 12 months; most of patients of young group had period of 1-6 months (50%). The same was also observed in the older group (47.8%) (table 3). There were 3 patients in older group who had not been determined the period and they were excluded of percentage calculation.

Tabel 3. Comparison of Period Between First Symptom and Diagnosis Making

	< 40 years	≥ 40 years	p
Mean period of symptom-diagnosis making (month ± SD)	8.66 ± 8.6	7.8 ± 9.6	0.320
Median symptom-diagnosis making (month)	6	6	
Mean period of symptom-diagnosis making (%)			
▪ < 1 month	6.25	14.50	
▪ 1 - 6 months	50.00	47.80	
▪ ≥ 6 - 12 months	31.25	27.50	
▪ > 12 months	12.50	10.10	

Comparison of hemoglobin (Hb) level at admission between young and older group was not significantly different (p = 0.080). Mean Hb in young age was 12.4 ± 3.2 gr% with median 12.9 g%. In the older group mean Hb level was 11.2 ± 2.2 g% with median Hb of 11.0 g%.

Albumin level at admission was significantly different between the two groups (p = 0.014). Young age group had higher mean albumin level of 3.8 ± 0.9 g/dL with median of 4.1 g/dL; while the older group had mean albumin level of 3.1 ± 0.9 g/dL and median 3.1 g/dL. In this analysis, there were 2 patients from young age group and 8 patients from older group who had no data on albumin level.

Table 4. Comparison of Hemoglobin and Albumin Levels at Admission

	< 40 years	≥ 40 years	p
Hb level (g% ± SD)	12.4 ± 3.2	11.2 ± 2.2	0.203
Albumin level (g/dL ± SD)	3.8 ± 0.9	3.1 ± 0.9	0.023

From carcino-embryonic antigen (CEA) examination during hospitalization we only obtained data from 10 patients in young age group and 36 patients in older group. The comparison of data with CEA level 5 as cut-off value had not showed significant difference (p = 0.7) (table 5).

Table 5. Comparison of CEA Levels

	< 40 years	≥ 40 years	p
CEA level < 5(%)	2 (20)	11 (30.5)	0.7
CEA level ≥ 5(%)	8 (80)	25 (69.5)	

Comparison of tumor histologic type showed adenocarcinoma dominant in the two groups (68.75% in young group and 80.5% in older group). There were no significant difference in incidence of adenocarcinoma, mucinous carcinoma or signet ring cell carcinoma between young age group and older group (p = 0.323; 0.478 and 0.457, subsequently).

Table 6. Comparison of Tumor Histologic Type

	< 40 years n = 16	≥ 40 years n = 72	p
Adenocarcinoma (%)	11 (68.7)	58 (80.5)	0.323
Mucoid carcinoma (%)	4 (25)	12 (16.7)	0.478
Signet ring cell (%)	1 (6.3)	2 (2.8)	0.457

If we analyzed more deeply, histologic grade comparison in adenocarcinoma group had shown no significant difference between low grade and high grade between young group and older group (p = 0.587). Table 5 showed the comparison.

Tabel 7. Comparison of Tumor Histologic Grade in Adenocarcinoma Type

	< 40 years n = 11	≥ 40 years n = 58	p
High grade (%)	0	7 (12.1)	0.587
Low grade (%)	11 (100)	51 (87.9)	

Comparisons of staging at time of diagnosis in most of patients in the two groups were in stage III (37.5% in young group and 38.9% in older group). There is no significant difference of percentage between young group and older one for each staging level. Table 6 showed the comparison of both groups.

Table 8. Comparison of Staging at Time of Diagnosis

	< 40 years n= 16	≥ 40 years n = 72	p
▪ Stage I (%)	3 (18.7)	3 (4.2)	0.071
▪ Stage II (%)	4 (25.0)	26 (36.1)	0.396
▪ Stage III (%)	6 (37.5)	28 (38.9)	0.918
▪ Stage IV (%)	3 (18.7)	15 (20.8)	1.000

DISCUSSION

Previous studies had showed some controversies on the difference in clinical characteristics, histopathologic type or prognosis of colorectal cancer in the young and older patients. Rodriguez-Bigas et al in case series of 68 patients with colorectal cancer whose age less than 30 years had found 82% were in stage III/IV at time diagnosis, 79.4% were died in median follow up of 21.5 months and 64.7% who had undergo curative surgery were found to had recurrent disease in median of 12 months. Recently, Al Jaberi et al, in comparative study of two groups (under 40 and more than 40 years old) had found that young age had more advanced staging at time of diagnosis, and greater proportion of mucinous carcinoma and signet ring cell carcinoma. Taylor et al, found that actuarial survival rate of colorectal cancer patients aged less than 40 years old was lower than older ones. This result was contradictory with study of Bosola et al, who found no significant difference in stage at time of diagnosis between patients whose age under 40 years and the older ones. Isbitsner et al, in national research of New Zealand found no significant difference on 10 years survival rate of colorectal cancer patients whose age under 40 years old and the older ones. Lastly, Alici et al, had evaluated 84 colorectal cancer patients whose age were under 40 years old vs. 382 patients older found no significant differences in staging at time of diagnosis or 5 year survival rate.

This study aims to analyze clinical characteristics and histopathologic type of patients with colorectal cancer whose age less than 40 years old in our hospital between 1999 to 2004. Several clinical aspects and histopatologic feature considered to have prognostic value that have been evaluated were tumor location, CEA level, staging at time of diagnosis, histologic type, and histologic grade. In addition, main chief complain, Hb level and albumin level were also analyzed. There is no significant difference in patients less than 40 years old compare to those in older age in CEA level, Hb level, staging at time diagnosis, histologic type, and histologic grade. Tumor location in young patient were generally in the left side (left sided cancer) consist of rectal and rectosigmoid cancer with chief complain of hematoschezia and pain in abdomen and anus. Albumin level was higher in young patients but there were no clinical data on nutritional status to analyze the cause of the difference was due to malnutrition that frequently found in elderly or other causes.

Limitation of the study is small sample and many subjects must be excluded due to incomplete data.

CONCLUSION

This study did not confirm the difference of colorectal cancer which occurred in patients less than 40 years old compared to older ones observed from CEA level, stage at time of diagnosis, histologic type, and histologic grade.

Tumor location of colorectal cancer in group of young population in this study had been found mostly left sided, and consisted of rectal and rectosigmoid cancer with main chief complain anal pain and less patients were found to have altered defecation pattern.

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