Colorectal Cancer Metastasis and the Risk Factors

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ABSTRACT

Background: Colorectal cancer (CRC) is the fourth most prevalent cancer in the world and is positioned the second most common cancer in the United States. Patients with CRC in Indonesia showed a greater proportion. In Jakarta, 47.85% of CRC cases occur under the age of 45 years. The purpose of this study was to determine metastasis and the factors that influence CRC patients.

Method: This study was conducted retrospectively from January 2003-December 2007 in Cipto Mangunkusumo hospital. Patients are eligible if they underwent colonoscopy, tumor biopsy, anatomical pathology, abdominal CT scan, abdominal ultrasonography, and radiology procedures.

Results: Of all 1,615 patients who underwent colonoscopy procedure, 377 patients were diagnosed with colorectal cancer. Subject that met the criteria consisted of 86 patients, where 56 (65.1%) male. The most aged was 51-60 years old (26.7%), mean age 47.90 ± 14.53 years old. The tumor is most commonly located in the rectum and sigmoid 40 (46.5%), in which 18 (45%) among them had metastasized. Compared with male patients, female patients experienced more metastases, but not statistically significant. Among the patients with metastasized CRC, 42.3% of them < 40 years old, 37.2% patients were 41-60 years old, and 29.4% patients > 60 years old. Well-differentiated CRC produced larger number of metastatic cases than poorly-differentiated CRC. Poorly-differentiated CRC tended to produce adjacent metastasis, and also happened in relatively young age in compared with well-differentiated cancer.

Conclusion: There was significant correlation between younger age group with a poor degree of histopathologic differentiation. Patients with CRC consist of more male patients than female ones. Factors sex, age group, histopathologic subtypes, and tumor location was not associated with metastasis.

Keywords: colorectal cancer, metastasis, well-differentiated, poorly-differentiated

INTRODUCTION

Colorectal cancer (CRC) is the fourth most prevalent cancer in the world and occupies the second most prevalent in the United States.[1] The mean age of CRC patients in the United States is 67 years.[2] The incidence of CRC is highly varied between one country and another. The number of CRC incidence in industrial countries such as USA, Canada, England, Western Europe, and Australia is higher than that in regions such as Asia, Africa, and South America.[3] The incidence of CRC in Asian countries seem to have rapidly increased in the last decades.[4] According to Western literature, the prevalence of CRC at the age below 50 years was 2.8%.[5] Almost 147,000 new cases and ± 57,000 deaths due to CRC occurred in USA during the year in 2004. Almost 10% of all cancer incidences in the world are CRC, with similar prevalence between males and females.[6] Patients with CRC in Indonesia showed a different proportion. In Jakarta, for instance at age below 45 years are 47.85% of cases.[7]

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METHOD

This study was conducted retrospectively for 5 years from January 2003 to December 2007 in Cipto Mangunkusumo hospital, Jakarta, by collecting medical records of patients who underwent colonoscopy, biopsy, and anatomical pathology procedures. Patients are eligible if they underwent colonoscopy, tumor biopsy, anatomical pathology, abdominal CT scan, abdominal ultrasound, and radiology examinations. Adjacent metastasis is those found in periaorta/abdominal lymph nodes. Distant metastasis are those found in the liver, lungs, bones, and pelvic organs. Patients are excluded if the medical data were not complete.

Statistical analysis using univariate method to determine the distribution of CRC incidence, bivariate method using Chi-square, and $p < 0.05$ indicates significant result.

RESULTS

Patients who underwent colonoscopy procedure are 1,615 subjects, consisting of 377 patients with CRC and 1,238 patients without CRC. Of the 377 patients with CRC, 86 patients met the inclusion criteria. Based on the sex, consisted of 56 (65.1%) male and 30 (34.9%) female. Most age above 51 years old were 40 (46.5%) patients, and the mean age of 47.90 ± 14.53 years.
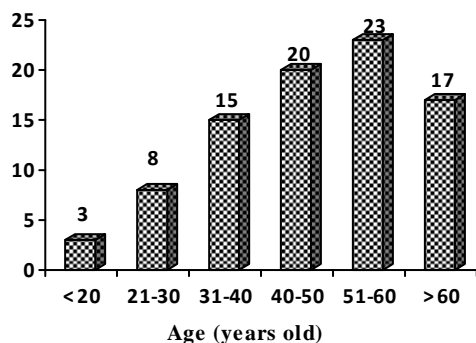

Figure 1. Age distribution of CRC patients

Based on the location the tumor was highly found in rectum and sigmoid 40 (46.5%) cases, and these were the ones most frequently progressed to metastasis which occurred in 18 (45.0%) cases (table 1).

Table 1. Metastasis and tumor location

Tumor location	No metastasis n (%)	Metastasis n (%)	n	p
Ascending colon	14 (73.7)	5 (26.3)	19	0.493
Transversal colon	9 (64.3)	5 (35.7)	14	
Descending colon	9 (69.2)	4 (30.8)	13	
Rectum and sigmoid	22 (55.0)	18 (45.0)	40	

The male patients show higher number of cases without metastasis, while the females show relatively higher number of adjacent metastasis and distant metastasis. This result was not statistically significant (figure 2).

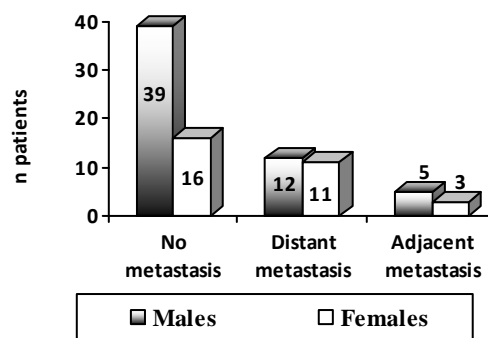Figure 2. Metastasis based on sex

In this study, patients with metastasized CRC based on age group were 11 patients < 40 years old, 16 patients between 41-60 years old, 5 patients > 60 years old. However, this difference was not statistically significant (figure 3).
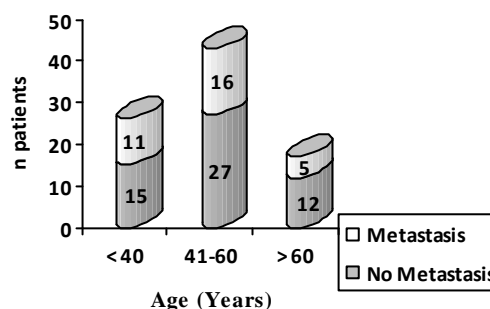

Figure 3. Metastasis based on age group

Based on histopathological differentiation was found that the well-differentiated cancer showed slightly higher number of cases of distant metastasis than the poorly-differentiated. Meanwhile, cases with no metastasis and adjacent metastasis were slightly higher in poorly-differentiated cancer (table 2).

Table 2. The distribution of metastasis based on anatomical pathology

	Well-differentiated n (%)	Poorly-differentiated n (%)	n
No metastasis	23 (62.2)	32 (65.3)	55
Distant metastasis	11 (29.7)	12 (24.48)	23
Adjacent metastasis	3 (8.1)	5 (10.2)	8
Total	37	49	86

In this study also found that group of poorly-differentiated cancer is more frequent in relatively young age group compared with well-differentiated. This correlation was statistically significant ($p < 0.05$) table 3).

Table 3. Anatomical pathology based on mean of age

	n	Mean of age	SD	p
Well-differentiated	37	52.30	14.44	0.014*
Poorly-differentiated	49	44.57	13.82	

* significant

DISCUSSION

In this study, it was found that the CRC patients consist of 56 (65%) male and of 30 (34%) females with a ratio of 1.9 : 1. According to Chandler, CRC incidence does not highly differ between males and females (1.2:1).[8] The incidence of CRC in this study is 23.3%. Study by Chong et al, reported the incidence of CRC as 7.4%.[9] Moreover, study by Tamura et al from Japan reported that it was 42.5 males and 25.6 females per 100,000 population.[10] According to the location of the tumors found mostly in the rectum and sigmoid (46.5%). This result is similar to reports by Tamura et al from Japan.[10]

In this study, the mean age of patients with CRC was 51-60 years old, which consisted of 23 (26.7%) patients. In Italy, Bertoglio et al reported their study from February 1999 to January 2003 found 26 cases of CRC was identified, which consists of 14 males and 12 females with age range 48-76 years.[11]

Based on sex, male patients with no metastasis were more prevalent than female patients. Meanwhile, patients with distant and adjacent metastasis consisted of slightly more females than males. CRC patients who experienced metastasis consist of relatively higher number of patients in the age group < 40 years old than the age group of 41-60 years old and > 60 years old. For comparison, Minardi et al reported that the young CRC patients was found in higher number between cases of advanced stage (Dukes C and D) with low 5-year survival rate.[12]

Based on the degree of histopathological differentiation, well-differentiated cases which experienced distant metastasis were found slightly higher compared to poorly-differentiated ones. Meanwhile, no metastasis and adjacent metastasis were found slightly higher in poorly-differentiated cases compared to well-differentiated ones.

In this study, factors of sex, age group, and the degree of histopathological differentiation were correlated to metastasis, but the effect was not statistically significant. The important factor which determines long-term result of CRC if there is a metastasis in local lymph nodes (adjacent metastasis). Lymph nodes are involved in stage II CRC.[13]

Liver is the second most frequent organ to be involved in CRC metastasis after the lymph nodes. In Europe and US, lesions in the liver most frequently describe metastasis rather than primary malignancy.[14] According to Donald et al, when first identified, less than a quarter of CRC patients had occurred in the liver metastases (distant metastasis), and the presence or absence of liver metastasis was the starting point which determines survival.[15]

This study also measured the correlation between the degree of histopathologic differentiation and the mean of age. It was discovered that the poorly-differentiated degree was found more in the relatively young age (44.5 ± 13.82 years) compared to the well-differentiated ones (52.30 ± 14.44 years). This correlation was statistically significant ($p < 0.05$).

In this studied identified 37 (43%) patients with well-differentiated cases and 49 (57%) patients with poorly differentiated cases. Study in the UK, Chandler et al reported on 7 cases of CRC, 35% was identified as well-differentiated, and 48% was identified as poorly-differentiated.[8]

Similarly, a study of 19 CRC cases, which consisted of 14% of well-differentiated, 42% of moderate, and 44% of poorly-differentiated. Study by Kaneko et al reported that CRC patients in which metastasis had spread to the lymph node around perirectal area, inferior mesenterics, and periaortal area, were approximately 55%.[16]

CONCLUSION

From the result of this study, a significant correlation was found between the rate of younger age and the poor degree of histopathologic differentiation. Patients with CRC consisted of males more than females. Factors sex, age group, histopathological subtypes, and tumor location were not associated with metastasis.

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