Research Article

# Relationship between Age and Sex with Histopathological Differentiation of Colorectal Adenocarcinoma

**Sugiarto[1*], Alifia Nurfitriana[2], Mieke Marindawati[3]**

[1,3]Department of Pathology Anatomic, Medical Faculty, Universitas Muhammadiyah Jakarta, Indonesia
[2]Medical Faculty, Universitas Muhammadiyah Jakarta, Indonesia

*Corresponding author: sugi.icuk@gmail.com

## ABSTRACT

**Background:** Colorectal cancer is one of the most common cancers causing morbidity in both women and men. There is a tendency for women over 65 to show higher mortality and lower 5-year survival rate from colorectal cancer than their male counterparts of the same age. **Purposes:** To find out the relationship between age and sex with the degree of differentiation of colorectal adenocarcinoma in the Anatomical Pathology Laboratory of General Hospital of Cengkareng in 2015 – 2019. **Methods:** This study used a analytic study with a retrospective approach, with secondary data from the medical records of anatomic pathology examination results in colorectal adenocarcinoma patients in General Hospital of Cengkareng in 2019. **Result:** Based on the result of the chi-square statistical test, the relationship between age and the degree of differentiation of colorectal adenocarcinomas was found to be p-value 0.476 (a>0.05). Whereas the relationship between sex with the degree of colorectal adenocarcinoma was found to be p-value 0.049 (a<0.05). **Conclusion:** There is no relationship between age and the degree of differentiation of colorectal adenocarcinomas, but gender have correlation.

**Keywords:** age, colorectal adenocarcinoma, degree of differentiation, sex

## INTRODUCTION

Colorectal carcinoma is a malignant tumor originating from the epithelial cells of the gastrointestinal tract of the large intestine. The most common colon cancer according to WHO is adenocarcinoma. Cases of this cancer are most commonly found in North America, Western Europe, Australia and New Zealand (1).

Colorectal cancer is the most frequently found worldwide after lung cancer (11.6%) and breast cancer (11.6%) based on the 2018 GLOBOCAN report (10.2%) where the death rate from this cancer reaches 9.2% of all types of cancer worldwide. According to a report by the American Cancer Society, in 2019 in America it is estimated that there will be around 101,420 new cases of colon cancer, and 44,180 new cases of rectal cancer (2,3). The results of the 2018 International Agency and Research on Cancer epidemiological survey reported that in China there were 303,853 new cases of colorectal cancer (12.8% of all cancer incidents) in men, while in women there were 217 637 (11.3%) (4). The 2018 GLOBOCAN data report states that colorectal cancer in Indonesia is fourth, with 19 113 new cases (11.9%) in men and 10 904 cases (5.8%) in women (5).

In 2017, cancer's research by Ganapati at General Hospital of Cipto Mangunkusumo reported an incidence of colon cancer as much as 1.84% and rectal cancer as much as 2.71% (6). Another study by Indarti in 2015 for colorectal cancer at Cipto Mangunkusumo General Hospital reported a colorectal cancer incidence of 65.9% in men with a median age of 53 years, the majority occurring in the 50-59 year age group where the most histopathological type was adenocarcinoma (88.8%) and when diagnosed the most with stage IIIB (25.0%) (7). Colorectal cancer research by Winanda at RSU Dr. Soedarso Pontianak in 2013 stated that of a total of 64 colorectal cancer patients, the most common main symptom was bloody stools as many as 18 patients (28.12%), followed by symptoms of difficulty in defecating as many as 17 patients (26.12%). A total of 37 patients (57.81%) presented with Dukes stage C and 4 patients (6.25%) with Dukes stage D (8).

The known risk factors for colorectal cancer are a history of colon infection (ulcerative colitis or Crohn's disease), a family history of polyps or colon cancer, genetic, racial and ethnic factors, excessive consumption of red meat and processed meat, lack of physical activity, obesity, high alcohol consumption (9–12). Based on the data above, it can be concluded that the incidence of colorectal cancer in the world and in Indonesia is still very high, therefore researchers are interested in conducting research on colorectal adenocarcinoma cases at Cengkareng Hospital, West Jakarta. This research's aims to analize relationship between age and gender with the degree of differentiation of colorectal adeno-carcinoma based on histopatho-logical features.

## METHODS

This research use an analytic study with a retrospective approach, with secondary data from the medical records of anatomic pathology examination results in colorectal adenocarcinoma patients in General Hospital of Cengkareng in 2019. The sample for histopathological examination used is a colorectal mass biopsy or the result of colorectal tumor surgery. The sample was then stained with Hematoxylin-Eosin. Histopathological grades were categorized into low-grade (glandular formation $\geq$50%) and high-grade (glandular formation). Depth of invasion was classified according to pathological stage T into two categories, namely T1-T2 and T3-T4.

The place and time of this research was carried out at the Medical Record section of the Cengkareng Regional General Hospital starting from the period January 2015 – December 2019. After all the data that meet the inclusion criteria are collected, they will be recorded, grouped and then processed using a computer software program SPSS-21, and using univariate and bivariate analysis with *chi square* statistical tests.

## RESULTS

Based on data collected from the medical records of the Anatomical Pathology Laboratory of the Cengkareng Hospital from January 2015 to September 2019, the total number of colorectal malignancies was 85 patients. A total of 4 patients were excluded because there was no answer to the histopathological diagnosis and as many as 81 patients met the inclusion criteria.

**Table 1.** Distribution of Colorectal Adenocarcinoma Cases by Year

| Years | Histophatological Diagnosis | | Total |
| | Adenocarsinoma Colon | Adenocarsinoma Rectal | |
|---|---|---|---|
| 2015 | 6 | 5 | 11 |
| 2016 | 5 | 4 | 9 |
| 2017 | 11 | 10 | 21 |
| 2018 | 6 | 14 | 20 |
| 2019 | 11 | 9 | 20 |
| Total | 39 | 42 | 81 |

All 81 patients consisted of 39 patients diagnosed with colonic adenocarcinoma and 42 diagnosed with rectal adenocarcinoma. The highest number of colorectal adenocarcinoma patients was in 2017 (21 patients), while the least was in 2016 which was 9 patients.

**Table 2.** Patient characteristic based on age, sex and tumor location

| Characteristic | n(=81) | Percentage (%) |
|---|---|---|
| **Gender** | | |
| Male | 40 | 49.4 |
| Female | 41 | 50.6 |
| **Age (years)** | | |
| <40 | 10 | 12.3 |
| 40-49 | 13 | 16.0 |
| 50-59 | 31 | 38.3 |
| 60-69 | 16 | 19.8 |
| ≥70 | 11 | 13.6 |
| **Tumor Location** | | |
| Colon | 9 | 11.1 |
| Colon ascendens | 8 | 9.9 |
| Colon transversum | 8 | 9.9 |
| Colon descendens | 4 | 4.9 |
| Colon sigmoideum | 7 | 8.6 |
| Rectosigmoid | 11 | 13.6 |
| Rectum | 34 | 42.0 |

This study showed that the incidence of adenocarcinoma in female (50.6%) was only slightly higher than that in male (49.4%) based on the distribution of data in table 2. In addition, in this study, the mean age of patients was 54.8 years, with a median age of 54 years. The majority of patients were in the age range of 50-59 years (38.3%), the age of the youngest patient diagnosed with colorectal adenocarcinoma was 24 years while the oldest was 82 years. The most common tumor locations were in the rectum, which amounted to 34 patients (42.0%).

**Table 3.** Cases Distribution based on Differentiation, Metastatic and Stage

| Characteristic | n(=81) | Percentage % |
|---|---|---|
| **Differentiation Degree** | | |
| Well | 24 | 29.6 |
| Moderate | 53 | 65.4 |
| Poor | 4 | 4.9 |
| **Metastatic** | | |
| No Metastatic | 63 | 77.8 |
| Lymph gland | 16 | 19.8 |
| Other Organ | 2 | 2.5 |
| **Stadium** | | |
| Stadium A | 11 | 13.6 |
| Stadium B | 9 | 11.1 |
| Stadium C | 16 | 19.8 |
| Stadium D | 2 | 2.5 |
| No Stadium Data | 43 | 53.1 |

Table 3 showed that the most case were moderately differentiated adenocarcinoma (53 cases or 65.4%). The majority of these colorectal adenocarcinoma samples had lymph node metastases (16 cases or 19.8%), while 2 cases (2.5%) were found to have metastases to other organs. There were 43 medical records did not mention the data of colorectal cancer staging, hence we only carried out on 38 medical records. The most common stage was Dukes stage C, which was 16 cases (19.8%).

**Table 4.** Relationship between Age and Degree Differentiation

| Age (years) | n(=81) | Differentiation Degree | | | p-value |
|---|---|---|---|---|---|
| | | Well | Moderate | Poor | |
| <40 | 10 | 4 | 6 | 0 | 0.476 |
| ≥40 | 71 | 20 | 47 | 4 | |

Based on the data of this study, it was found that 81 colorectal adenocarcinoma patients were grouped into patients aged <40 years and 40 years, with degrees of differentiation including well, moderately and poorly differentiated adenocarcinomas. Patients with well-moderately degree of differentiation were included in the group of patients with moderately degree of differentiation. The results of statistical tests with chi square (Table 4) obtained p value = 0.476 which means that there is no relationship between age and the degree of differentiation of colorectal adeno-carcinoma based on histopathological features at the Anatomical Pathology Laboratory of Cengkareng Hospital.

Relationship between sex and degree of differentiation based on the research data (Table 5), showing the chi square statistical test results obtained p value = 0.049 which means that there is a relationship between sex and the degree of differentiation of colorectal adenocarcinoma based on histopathological descriptions at the Anatomical Pathology Laboratory of Cengkareng Hospital.

**Tabel 5.** Relationship between Sex and Differentiation Degree

| Gender | N (=81) | Differentiation Degree | | | p-value |
|---|---|---|---|---|---|
| | | Well | Moderate | Poor | |
| Male | 40 | 16 | 21 | 3 | 0.049 |
| Female | 41 | 8 | 32 | 1 | |

## DISCUSSION

The distribution of colorectal adenocarcinoma cases by sex did not show a significant difference between male and female patients, namely, the ratio of men (49.4%) and women (50.6%). This is not in accordance with the research by Annisa Febi Indarti at Cipto Mangunkusumo General Hospital in 2009-2014, which stated that male patients were more dominant (65.9%) than female (34.1%) (7). GLOBOCAN 2018 data states that the incidence of colorectal cancer is more in men than women (2). Research with a larger number of samples is very much needed for further research at Cengkareng Hospital that relates these differences in characteristics based on sex.

In this study, the majority of colorectal cancer patients were aged 50-59 years (38.3%). The same result was also reported by Annisa Febi Indarti who reported that the majority of colorectal adenocarcinoma patients were at the age of 50-59 years (30.6%). Abdul Hamas Izzaty's research at Moewardi Hospital Surakarta in 2010-2013, found that colorectal carcinoma patients were more in the 50-79 years age range (63.5%). Data from the American Cancer Society, for the period 2009-2013, the average incidence decreased by 4.6% per year in individuals aged ≥65 years and 1.4% per year in the age range 50-64 years, but increased by 1.6% at age < 50 years. Therefore the similarities in the characteristics of adenocarcinoma patients based on age turned out to be the most at the age of 50 years, but according to the American Cancer Society the tendency for this cancer to increase every year at a young age.

Research data also showed that the most common location of colorectal cancer was in the rectum (42.0%) and the lowest location was in the descending colon (4.9%). A similar research report was obtained by Dian Ratnasari at Dr. RSUP. Kariadi Semarang (period 2008-2011) that the most common location for colorectal cancer was found in the rectum (54.6%) which was supported by a research report by Novia Nasution at H. Adam Malik Hospital Medan (2015-2017), with 29 cases (35.8%) and the least is the descending colon as many as 2 cases (2.5%) (13). This study also shows that the highest degree of differentiation is moderately (65.4%) and the least is poorly differentiation. Dian Ratnasari at RSUP Dr. Kariadi Semarang reported that most colorectal adenocarcinomas were well differentiated (68.1%), while the least were found with poorly differentiation degrees (8.4%). as well as reports from RSUD Dr. H. Abdul Moeloek in 2014 for well-differentiated adenocarcinoma (77%), while only 4% of poorly differentiated adenocarcinomas.

The description of metastatic adenocarcinoma in this study mostly did not find metastases (77.85%), but there were 2 cases of metastases to other organs (2.5%). This result is not in accordance with the research at Dr. RSUP. Kariadi Semarang reported metastases in the majority of cases which amounted to 43 (71.7%) (14). Bivariate analysis of the data of this study was carried out starting with grouping the data by age with the degree of differentiation of each patient. After the chi square statistical test, the p value = 0.476 (p value = >α = 0.05) which means that there is no relationship between age and the degree of differentiation of colorectal adenocarcinoma. This is in accordance with research by Anggunan at RSUD Dr. H. Abdul Moeloek Lampung Province (2014), with p value = 0.356 (α> 0.05) (15). Research by Kurahmawati (2012) cited by Teddy Kurniawan, et al. shows that age is a risk factor influencing the incidence of colorectal carcinoma (16). The pathomechanism of age that can cause colorectal malignancies is thought to be due to the accumulation of DNA mutations in the cells that make up the colonic wall with increasing age and also due to a decrease in immune function, as well as the increased intake of carcinogenic agents) (17). Several studies have shown that epigenetic modification plays an important role. in cancer cell development. The accumulation of gene mutations and epigenetic changes can initiate a benign adenoma to become a malignant adenocarcinoma (17,18).

The results of the chi square statistical test that reviewed the relationship between sex and the degree of differentiation of each patient, obtained p value = 0.049 (α < 0.05) indicating a significant relationship between gender and the degree of differentiation based on histopathological descriptions. Anggunan (2014), stated that sex-related mechanisms could be part of the risk factors for colon carcinoma, suggesting that there are differences in the reception of androgen, estrogen and progesterone receptors in colon carcinoma cells and normal cells. [16-18] One of the protective factors against colonic carcinoma is the estrogen hormone receptor ERβ, this was proven in experiments on mice which showed that ERβ increased proliferation and suppressed the differentiation and apoptosis of colonic mucosal cells (19,20).

## CONCLUSION

Well-moderately differentiation is the grading of adenocarcinoma. There is no significant relationship between age and the degree of differentiation. On the contrary, sex has a significant correlation. This study shows the incidence of adenocarcinoma that is female greater than in males, and the age range was 50-59 years old. Most tumors were located in the rectum.

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## CONFLICT OF INTEREST

The author(s) declare that they do not have a conflict of interest and that they do not have affiliations or relationships with any organization or entity that could raise biased questions or statements in the discussion and conclusion sections of the paper.

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