

# Clinicopathological parameters analysis of post-resection colorectal carcinoma in Cut Meutia General Hospital, North Aceh

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## ABSTRACT

**Introduction:** Colorectal cancer is a malignancy that occurs in the colon and/or rectum and as the third most commonly diagnosed and second most fatal cancer globally.

**Objective :** This study aimed to determine the relationship between the clinicopathological parameters of colorectal cancer.

**Methods:** The research was retrospective cross-sectional study design. Data were collected from medical records of post-resection colorectal cancer patients during 2018-2021 at the Anatomical Pathology Laboratory Cut Meutia Hospital North Aceh based on the inclusion and exclusion criteria. A total sample size of 30 samples. The relationship between clinicopathological parameters was analyzed by Chi-square test.

**Results:** Age was significantly associated with tumor size ( $p=0.01$ ), grading ( $p=0.05$ ) and depth of invasion ( $p=0.02$ ). In addition, histological type was significantly associated with tumor location ( $p=0.05$ ) and tumor size had a significant relationship with depth of invasion ( $p=0.05$ ).

**Conclusion:** The study indicates that clinicopathological parameters might underlie tumor progression and prognosis in colorectal carcinoma.

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## INTRODUCTION

Colorectal cancer is a malignancy that originates from the large intestine and rectum tissues (Kemenkes RI, 2018). Colorectal cancer as the third most common malignancy and the second most deadly cancer worldwide, accounting for approximately 1.4 million new cases per year (Arnold et al., 2017). Epidemiology studies show that the risk of developing colorectal cancer is about 1 in 20 people. Men have a higher risk of developing colorectal cancer than women. Global Burden of Cancer Study reported that there are estimated 1.93 million new colorectal cancer cases diagnosed, and 0.94 million colorectal cancer caused deaths in 2020 worldwide. Southeast Asia has a total of 106.995 cases with a ratio of 60.505 cases in men and 46.490 cases in women. According to WHO 2018 data, the incidence of colorectal cancer in Indonesia was 12,1% of adult people and mortality rates is predicted to reach 6,9% of all cancer diagnoses. The colorectal cancer is more common in men than women, in males is 7,7% and in females is 4,4% (Hossain et al., 2022).

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Although the colorectal cancer screening have reduced the incidence and mortality, the further prevention strategies are still needed to reduce the incidence and mortality of colorectal cancer. Cancer prevention is achieved through primary, secondary, and tertiary methods. Primary cancer prevention is achieved through the promotion of health and wellness and reduction of risks known to contribute to cancer development. Secondary prevention refers to early detection of lesions, including a balanced diet and physical activity. tertiary prevention aims to reduce the risk of death and to prevent the patients from being disabled and early detection of secondary malignancies (Molska & Reguła, 2019).

In order to improve the chances of successful treatment and longer survival for colorectal cancer patients, it is crucial to enhance prevention and promptly identify the disease at its earliest stages (Salibasic et al., 2019). Clinical aspects include elevated levels of Carcinoembryonic Antigen (CEA), perforated or obstructed primary tumors, and metastatic tumors associated with the poorer prognosis. Pathological aspects such as the stage of the tumor (lymph node involvement, penetration of serosa, peritoneal carcinomatosis, and distant spread), characteristics of the primary tumor (the depth of penetration into the bowel wall, histological subtype, grade and differentiation, invasive of tumor budding, invasion of veins and lymphatic vessels, perineural invasion, and lymphocytic infiltration), and the condition of surgical resection margins (clear or affected). In addition, preoperative radiochemotherapy may lead to the reduction of tumor size, aid in surgical removal, and potentially impact long term prognosis. The prognosis is commonly more favorable for tumors that have a complete response. Adjuvant chemotherapy following surgery also has an impact on the prognosis (Marzouk & Schofield, 2011).

The incidence and mortality of colorectal carcinoma are still relatively high in Indonesia. Appropriate and structured early detection has been reported to reduce the morbidity and mortality of colorectal carcinoma cases in western countries. Histopathological examination of colorectal carcinoma from postresection specimens is valuable for predicting patient prognosis. Research related to the examination of clinicopathological parameters is expected to be able to assess risk factors and prognosis and become a consideration for patient management. This research aims to determine the relationship between the clinicopathological parameters of post resection colorectal carcinoma in Cut Meutia General Hospital, North Aceh.

## **METHODS & MATERIALS**

The study design was a retrospective analysis using a cross-sectional research approach. Data were collected from medical records of post-resection colorectal cancer patients during 2018-2021 at the Anatomical Pathology Laboratory Cut Meutia Hospital North Aceh. The sampling method based on the purposive sampling. The clinicopathological parameters consisted of age, sex, tumor location, and tumor size, histopathological parameters (histological type, grading and depth of invasion). Data were analyzed using Chi Square test. This study was approved by the Research Ethics Committee Universitas Muhammadiyah Sumatra Utara Faculty of Medicine (No.815/KEPK/FKUMSU/2022).

## **RESULT**

The research was conducted at the Anatomical Pathology Cut Meutia Hospital North Aceh. Data were collected from medical records of post-resection colorectal cancer patients during 2018-2021. A total of 30 patients were selected for the study. Of the total, 16 (53.3%) were male patients, with the mean age of the entire patients being  $48.7 \pm 14.1$  years. Tumors were localized at the

colon in 11 cases (36.7%), caecum in 1 case (3.3%), sigmoid colon in 4 cases (13.3%), rectum in 3 cases (10%), and at the rectosigmoid in 11 cases (36.7 %). The tumor diameter was <5.1 cm in 19 (63.3%) cases. The histological type showed that most of the patients was classic adenocarcinoma in 29 (96.7%) cases. The histologic grade was well in 20 (66.7%) cases, moderate in 8 (26.7%), and poorly in 2 (6.6%). The depth of tumor invasion was detected in 13 (43.3%) cases had penetrated the muscularis propria to subserosa and visceral peritoneal invasion in 11 (36.7%) cases (Table 1).

**Table 1.** Clinicopathological parameters of post-resection colorectal carcinoma patients

| Clinicopathological Profile | Frequency<br>(n = 30) | Percentage<br>(%) |
|-----------------------------|-----------------------|-------------------|
| <b>Sex</b>                  |                       |                   |
| Male                        | 16                    | 53,3              |
| Female                      | 14                    | 46,7              |
| <b>Age</b>                  |                       |                   |
| ≤49 Years                   | 12                    | 40                |
| >49 Years                   | 18                    | 60                |
| <b>Histological type</b>    |                       |                   |
| Adenocarcinoma              | 29                    | 96,7              |
| Mucinous adenoca            | 1                     | 3,3               |
| <b>Tumor location</b>       |                       |                   |
| Colon                       | 11                    | 36,7              |
| Cecum                       | 1                     | 3,3               |
| Sigmoid                     | 4                     | 13,3              |
| Rectum                      | 3                     | 10,0              |
| Rectosigmoid                | 11                    | 36,7              |
| <b>Tumor Size</b>           |                       |                   |
| < 5cm                       | 19                    | 63,3              |
| ≥ 5 cm                      | 11                    | 36,7              |
| <b>Grading</b>              |                       |                   |
| Well                        | 20                    | 66,7              |
| Moderate                    | 8                     | 26,7              |
| Poorly                      | 2                     | 6,6               |
| <b>Depth of invasion</b>    |                       |                   |
| T2                          | 6                     | 20                |
| T3                          | 13                    | 43,3              |
| T4                          | 11                    | 36,7              |

**Table 2.** The Relationship between clinicopathological parameters

|                   | Sex  | Histological Type | TumoSize | Grading | Depth of invasion | Location |
|-------------------|------|-------------------|----------|---------|-------------------|----------|
| Age               | 1.00 | 1.00              | 0.01*    | 0.05*   | 0.02*             | 0.63     |
| Sex               |      | 0.46              | 0.63     | 0.35    | 0.72              | 0.71     |
| Histological Type |      |                   | 1.00     | 0.77    | 0.41              | 0.05*    |
| Tumor Size        |      |                   |          | 0.14    | 0.05*             | 0.59     |
| Grading           |      |                   |          |         | 0.21              | 0.68     |
| Depth of invasion |      |                   |          |         |                   | 0.59     |

\*Chi Square test

Analysis of the relationship between clinical and pathological parameters was carried out using the Chi-square test. There were significant relationships between age with the tumor size (p=0.01), grading (p=0.02) and depth of invasion (p=0.02). In addition, histological type was

significantly related to tumor location ( $p=0.05$ ) and tumor size also had a significant relationship with the depth of invasion ( $p=0.05$ ). No other significant relationships were found with other variables among study subjects (Table 2).

## DISCUSSION

The data revealed that the age of colorectal carcinoma patients was 17-72 year ( $48.7 \pm 14.1$ ). The common cases were more than 49 years. A study conducted in Sanglah hospital, Bali reported the most cases of colorectal carcinoma in 50-60 years (Gunasekaran et al., 2019). After 50 years of age, the incidence of colorectal cancer increases significantly, it related to accumulation of somatic mutations that role in the progression of cancer and decrease of immune response (Robbins SL, Ramzi S. C, 2018). There were 2 cases in younger patient (17 years) from this study. Carcinoma Colorectal under 40 years, generally associated with several risk factors, especially familial adenomatous polyposis (Brunicadi et al., 2017). Data from the American Cancer Society (2020) reported a shift in incidence of Colorectal carcinoma towards younger population caused interaction of hereditary factors and changes of lifestyle such as an unhealthy diet (ACS., 2020). In this study, colorectal carcinoma cases was common among male patients. Numerous studies have reported the percentage patients of male : female = 53,7% : 46,3% and 55,9% : 44,1% (Halder et al., 2013;Novitasari & Mulyadi, 2016).

The tumor location post resection was common found at the colon and rectosigmoid were 36,7%, respectively. A previous study reported that colorectal carcinoma localized at the ascending colon (31,7%), descending colon (43,2%), and rectum (25,1%) (Novitasari & Mulyadi, 2016). World Health Organization reported that most of colorectal carcinoma found at the sigmoid colon and rectum, with a tendency at descending colon rather than ascending colon. Halder et al., reported that increasing of the carcinomas proportion at proximal colon associated with increasing of age (Hamilton et al.,2010).

The histological type showed that most of the patients was classic adenocarcinoma in 29 (96.7%) cases. This result agrees with Kurniawan (2017) who reported that most histological type of colorectal carcinoma was adenocarcinoma in 168 cases (81,95%) (Kurniawan et al., 2017). WHO reported that more than 90% of carcinoma colorectal was adenocarcinoma (Hamilton et al.,2010). Chron's disease is common referred to as the initial lesion turn into an adenocarcinoma. The overall incidence of adenocarcinoma arising in Chron's disease is approximately 20% (Brunicadi et al.,2017). Another histological type is mucinous adenocarcinoma (3,3%). Mucinous adenocarcinoma (MAC) is a particular type of adenocarcinoma (AC) where more than half of the tumor consists of extracellular mucin pools. It is found in approximately 6-21% of all cases in colorectal cancer (CRCs). The prognosis of MAC is a topic of ongoing discussion. Most research suggests that MAC is harder to treat and has a less positive outcome compared to AC. The cases of mucinous adenocarcinoma are commonly encountered in patients diagnosed with Hereditary Non Polyposis Colorectal Cancer (HNPCC) or Lynch syndrome and this represent high-grade Microsatellite Instability – High (MSI-H) tumors (Bong et al., 2022).

The commonest depth of invasion of our study had invaded the muscularis propria to subserosa (T3) in 13 (43.3%) cases and visceral peritoneal invasion ( T4) in 11 (36.7%) cases. Whereas the least cases were tumors invaded the muscularis propria (T2) as much as 20%. This result agrees with Sander et al (2013) who reported that the most colorectal carcinoma cases had invaded the tunica serosa (T3) in 20,2% cases. This cases were higher than tumor had invaded the tunica muscularis (19%) and the submucosa invasion (0,8%) (Dwijayanthi et al., 2020).

In our study, the commonest grading at presentation was well-moderate differentiation (93.4%). This finding simulates well with those reported by Maker et al (2021) of 74 cases (90.0%) in Sanglah hospital. According to the study by Ozer et al (2019) reported that low-grade colorectal carcinoma consisting of 30 (16.2%) well differentiated cases and 124 (67.0%) moderately differentiated cases, while 31 (16.8%) cases is high grade poorly differentiated (Maker & Sriwidayani, 2021; Ozer et al., 2019).

The result of this research has showed that there were a significant relationships between age with the tumor size, grading and depth of invasion. The tumor size > 5 cm, poorly differentiated and tumor had invaded the muscularis propria to subserosa occur in the older age group as recorded in this study. This result agrees with Sutrisna (2018) who reported that colorectal carcinoma predominately with poorly differentiated in 44 (50%) cases (Sutrisna, 2018).

Precancerous polyps can take 10 to 15 years to become cancerous. Colorectal cancer screening can detect these tumors at an early stage and prevent their growth in the first location by detecting and eliminating precancerous polyps during colonoscopy (ACS, 2021). Mechanism of a carcinogenesis advanced adenoma to carcinoma increases with age. Metastasis is a multistage process as the tumor separates from the primary tumor and forms a secondary focus at a distant site. Benign tumors generally take for 17 years advanced to stage cancer progressively and less than 2 years for colorectal cancer to have the ability to metastasize. Therefore, a late stage tends to be found in older age patients due to increased tumor progression to metastasize to other organs (Novitasari & Mulyadi, 2016; Hossain et al., 2022).

In our study, we found histological type was significantly related to tumor location. Adenocarcinoma was common found at the colon and rectosigmoid. The incidence of adenocarcinoma is more common in the left colon or rectum, but tends to decrease with screening by colonoscopy. The occult blood test screening is more sensitive for left colon tumors. Molecular aspects, therapeutic strategies, and surgical complications also different between the left and right colon (Kurniawan et al., 2017). According to the study by Ozer et al (2019) reported that colorectal carcinoma was commonly localized in the left colon (31,9% ascending, 5,9% transverse colon) while the right colon consisted of descending colon 14,6%, sigmoid 25,4% and rectum 22,2% (Ozer et al., 2019).

Tumor size was significantly related to depth of invasion. In this study, most tumor sizes > 5cm cases had invaded the muscularis propria to subserosa. In general, clinical Symptoms are not felt or not specific in colorectal carcinoma patients, so that many patients who are diagnosed have a large tumor mass. Patients diagnosed with early-stage are generally found incidentally through physical examinations. The Clinical symptoms such as constipation, melena, and pain in the abdomen are the most common symptoms that patients complain. The depth of tumor invasion is an important factor in determining the patient's prognosis. Tumor had invaded the submucosa cause infiltration into blood vessels and lymph vessels, which is thought to be the first step of the metastatic process to lymph nodes and surrounding organs. Determination of the depth of invasion and the boundaries of the postoperative incision is very important in risk prevention (Kouyama et al., 2016; Hegde et al., 2017).

## CONCLUSION

This research concluded that there was a significant relationships between age with the tumor size, grading and depth of invasion. histological type was significantly related to tumor location. Tumor size was significantly related to depth of invasion.

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