

Clinicopathological Profile of Colorectal Adenocarcinoma in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak

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ABSTRACT

Background: Colorectal adenocarcinoma is ranked third globally in the category of the most commonly diagnosed cancers, as reported by the Global Burden of Cancer (GLOBOCAN) survey in 2020. This condition ranks as the second leading cause of death from cancer with a mortality of 9.40%. Therefore, this study aimed to discover the clinicopathological profile of colorectal adenocarcinoma in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak in 2017–2020.

Methods: This descriptive study used secondary data from the histopathology reports of the Anatomical Pathology Laboratory obtained by total sampling, which were processed using Microsoft Excel.

Results: The total number of colorectal adenocarcinoma patients was 148, and the majority were in the category of 53–61 years, accounting for 30.41%, and 51.35% were female. The majority of the anatomical sites of tumors were in the "Rectum Not Otherwise Specified (NOS)", with a percentage of 35.14%. The most frequent histopathological subtype was adenocarcinoma NOS, accounting for 85.81%, while the majority of differentiation grade was well differentiated, with a percentage of 90.54%. The most TNM (Tumor, Node, Metastatic) staging system of the American Joint Committee on Cancer (AJCC) was IIA (33.78%). Based on the classification using the Dukes staging system, the most stage suffered by patients was C2 with a percentage of 39.86%.

Conclusions: In conclusion, the incidence of diagnosed colorectal adenocarcinoma cases increased yearly in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak. Further study of the clinical characteristics and analysis of risk factors in colorectal adenocarcinoma patients were important to support the development of effective preventive strategies.

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INTRODUCTION

Breast colorectal cancer is a malignancy in colon or rectum tissues and ranks third worldwide in the category of the most commonly diagnosed cancers, with 1,930,000 cases. It accounts for a 10.00% incidence rate, as reported by the Global Burden of Cancer (GLOBOCAN) survey in 2020. This condition is the second leading cause of death from cancer worldwide, with 930,600 cases and a mortality of 9.40% [1]. Riskesdas report in 2018 showed that there were already 1,017,290 people diagnosed with cancer in Indonesia [2]. Compared to

Riskesdas data in 2013 and 2018, an increase was recorded in the prevalence of Indonesia from 1.40% to 1.79%. Based on data from Dharmais Cancer Hospital in 2018, colorectal cancer was ranked fourth with a prevalence of 9.88% [2,3].

Cancer incidence is a significant challenge for every country in increasing the life expectancy of patients. The quality of health services provided and the characteristics of cancer suffered by patients can affect the prognosis [3]. Some factors affecting the prognosis include age, stage, location of the tumor, type of histopathology, and differentiation grade [4–8]. No study

publication has addressed the profile of colorectal adenocarcinoma in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak. Therefore, this study aims to discover the clinicopathological profile of colorectal adenocarcinoma, specifically the location of the tumor, histopathological subtype, differentiation grade, extension of the primary tumor (T), lymph node metastasis (N), distant metastasis (N), TNM (Tumor, Node, Metastatic) AJCC staging, and Dukes staging. This study is essential because the data is sufficiently needed to support other investigations related to colorectal adenocarcinoma. The results can also be a reference in the future in formulating better policies related to preventive measures, early detection, and management of colorectal cancer in Indonesia, specifically in the West Borneo region.

METHODS

This descriptive study described the clinicopathological profile of colorectal adenocarcinoma in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak from 2017 to 2020. It used secondary data collected from the histopathology reports of the laboratory. The origin, age, and gender of patients were grouped as the demographic characteristics of colorectal adenocarcinoma. Meanwhile, tumor location, histopathological subtype, differentiation grade, extension of the primary tumor (T), lymph node metastasis (N), distant metastasis (N), TNM AJCC, and Dukes staging were grouped as colorectal adenocarcinoma clinicopathological profile. The inclusion criteria for this study was colorectal adenocarcinoma patients who conducted a clinicopathological examination of the preparation of the operation results at the hospital from 2017 to 2020. Patients who had the results of examinations with types of histopathology other than adenocarcinoma were excluded. This study obtained permission from the Health Promotion Section Hospital through the approval of the Education and Research Section of Dr. Soedarso Hospital Pontianak with letter number 34/RSUD/KEPK/XII/2021.

RESULTS

The result showed 148 cases of colorectal adenocarcinoma recorded in the Anatomical Pathology Laboratory. Furthermore, the incidence of diagnosed colorectal adenocarcinoma cases was found to increase yearly, with the most considerable frequency in 2020, accounting for 60 cases. The highest percentage increase occurred in 2018 with 100.00%, as shown in **Figure 1**.

The demographic characteristics of colorectal adenocarcinoma are shown in **Table 1**. The result of this study showed that the incidence of colorectal adenocarcinoma in the study area was dominated by patients from Pontianak, with 25 cases, accounting for 16.89%. Most cases occurred in patients aged 53 to 61 years, with a percentage of 30.41%, and a median age of 54 years was recorded in these cases. The youngest and oldest patients were 17 and 88 years old, respectively, and the proportion ratio between female patients was close to (1:1). Female patients comprised 76 cases and males consisted of 72 cases, with percentages of 51.35% and 48.65%, respectively.

Table 2 shows the clinicopathological profile of colorectal adenocarcinoma. Most of the anatomical locations were in the rectum NOS section, with 52 cases, accounting for 35.14%. The distal colon had a higher incidence of 31.08%, compared to the proximal percentage of 26.35%. Furthermore, the most colorectal adenocarcinoma histopathological subtypes were adenocarcinoma NOS, namely 127 patients, at 85.81%. The highest proportion for differentiation grade was well differentiated, with 134 patients, accounting for 90.54%.

Categorization according to the AJCC TNM showed that the majority were stage IIA, with 50 patients, accounting for 33.78%. Most primary tumor extension (T) categories were T3 and lymph node metastasis (N) were N0 with 117 and 72 cases, accounting for 79.05% and 48.65%, respectively. The most distant metastasis (M) was M0 found in 137 patients at 92.57%. Based on Dukes staging, the majority were C2, with 59 patients at 39.86%.

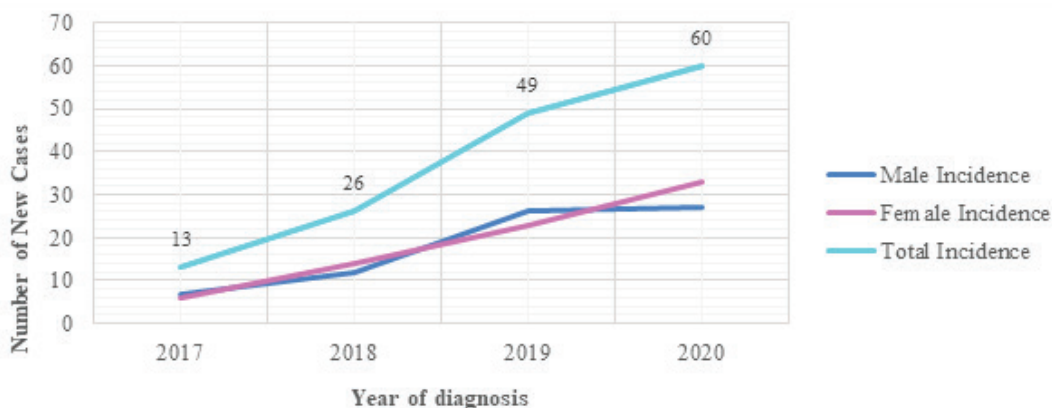


Figure 1. Graph of the incidence of colorectal adenocarcinoma in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak 2017–2020

Table 1. The demographic characteristics of colorectal adenocarcinoma patients in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak 2017–2020

Demographic characteristics	Cases (n=148)	Percentage (%)
Origin		
Bengkayang Regency	6	4.05
Kapuas Hulu Regency	4	2.70
Kayong Utara Regency	1	0.68
Ketapang Regency	4	2.70
Kubu Raya Regency	12	8.11
Landak Regency	10	6.76
Melawi Regency	4	2.70
Mempawah Regency	10	6.76
Sambas Regency	19	12.84
Sanggau Regency	14	9.46
Sekadau Regency	4	2.70
Sintang Regency	6	4.05
Pontianak City	25	16.89
Singkawang City	24	16.22
No Data	5	3.38
Age		
17–25 year	5	3.38
26–34 year	12	8.11
35–43 year	12	8.11
44–52 year	36	24.32
53–61 year	45	30.41
62–70 year	24	16.22
71–79 year	9	6.08
80–88 year	5	3.38
Gender		
Male	72	48.65
Female	76	51.35

Table 2. Colorectal adenocarcinoma clinicopathological profile in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak 2017–2020

Clinicopathology profile	Cases (n=148)	Percentage (%)
Location of the Tumor		
Colon Proximal	39	26.35
Caecum	10	6.76
Ascending colon	15	10.14
Hepatic flexure of the colon	2	1.35
Transverse colon	12	8.11
Colon Distal	46	31.08
Splenic flexure of the colon	1	0.68
Descending colon	9	6.08
Sigmoid colon	29	19.59
Rectosigmoid Junction	7	4.73
Overlapping lesion of the Colon	4	2.70
Colon NOS	7	4.73
Rectum NOS	52	35.14

Clinicopathology profile	Cases (n=148)	Percentage (%)
Histopathological subtype		
Adenocarcinoma NOS	127	85.81
Mucinous adenocarcinoma	14	9.46
Signet-ring cell carcinoma	7	4.73
Differentiation Grade		
Well-differentiated	134	90.54
Moderately differentiated	7	4.73
Poorly differentiated	3	2.03
Without explanation	4	2.70
Extension of the primary tumor (T)		
Tx	0	0.00
T0	0	0.00
Tis	0	0.00
T1	14	9.46
T2	9	6.08
T3	117	79.05
T4a	3	2.03
T4b	5	3.38
Lymph node metastasis (N)		
Nx	0	0.00
N0	72	48.65
N1a	22	14.86
N1b	23	15.54
N1c	0	0.00
N2a	11	7.43
N2b	20	13.51
Distant metastasis (M)		
M0	137	92.57
M1	11	7.43
TNM AJCC Staging		
0	0	0.00
I	17	11.49
IIA	50	33.78
IIB	2	1.35
IIC	0	0.00
IIIA	2	1.35
IIIB	45	30.41
IIIC	21	14.19
IVA	7	4.73
IVB	1	0.68
IVC	1	0.68
IV without full description	2	1.35
Duke's Staging		
A	10	6.76
B1	6	4.05
B2	53	35.81
B3	0	0.00
C1	5	3.38
C2	59	39.86
C3	4	2.70
D	11	7.43

AJCC: American Joint Committee on Cancer; NOS: not otherwise specified

DISCUSSION

Pontianak City is the capital of West Borneo and also the designated location for the establishment of Dr. Soedarso Hospital [9]. The number of colorectal adenocarcinoma diagnoses in the Anatomical Pathology Laboratory from 2017 to 2020 was higher than in other cities in West Borneo, with a percentage of 16.89%. The city center generally has higher diagnoses because these areas have closer and easier access to health facilities for managing colorectal adenocarcinoma [10,11].

The incidence of colorectal adenocarcinoma increases progressively from the age of 40 years and experiences a sharp sharply at 50 years [12]. This study showed that 30.41% of colorectal adenocarcinoma cases occur between the ages of 53 and 61 years. The study conducted by Devianti & Agus [13] at Dr. Achmad Mochtar Bukittinggi Hospital from 2015 to 2017 also showed results that were not significantly different. In this case, the average age of patients was over 50 years, with most patients found in the age group of 51-60 years, accounting for 26.90%. Age is a known risk factor for cancer because of the duration of carcinogenesis, the sensitivity of aging tissues to environmental carcinogens, and other physical changes that favor cancer initiation and growth [4].

The youngest patient in the study was a male person and 17 years old. The patient had a poorly differentiated grade of colorectal adenocarcinoma, with a TNM stage of T1N0M0. Dukes Staging was A, and the anatomical location was on the left side, with the histopathology sub-type being adenocarcinoma NOS. Although still at an early stage, cancer in these patients has a poor differentiation grade and is more aggressive. This result is consistent with the reports of other studies that the incidence of colorectal adenocarcinoma in young people presents a worse appearance, due to rapid disease progression in young patients [14].

This study also showed that the number of events in female and male patients was close to the ratio (1:1). Generally, most investigations found that colorectal adenocarcinoma was more common in men. The study conducted by the American Cancer Society between 2012 and 2016 found that the incidence of colorectal adenocarcinoma was 30.00% higher in males than in females [15]. The high incidence in female patients may be related to the use of sex hormones, such as estrogen to protect against cancer. Estrogen hormone levels decline with age, and the presence of receptor- β (ER β) in females protects against colorectal adenocarcinoma. Estrogen prevents colorectal adenocarcinoma by inhibiting the inflammatory factor IL-6. Most women have entered menopause, where estrogen levels and ER β begin to decrease, thereby triggering the development of cancer cells [16,17]. Menopause is the end of the menstrual cycle, which usually occurs between the ages of 45 and 55, but can occur earlier

[18]. This study showed that of the 76 female patients, 65, constituting 85.52%, were above the age of 45, exceeding the count below 45 years old.

In this study, the most tumor anatomical site in colorectal adenocarcinoma patients was in the rectum NOS section, with 52 cases, accounting for 35.14%. NOS stands for "Not Otherwise Specified," which is part of the WHO ICD classification code for an unspecified or unqualified event [19]. Tumors in rectum NOS show a lack of specificity regarding the precise location. Rectum becomes the most common location and has a greater tendency for colorectal adenocarcinomas because it is related to the defecation process and easier to detect based on the anatomical location and general morphology. Low-fiber diets also led to stool concentrates and increased stool transit. Consequently, the contact between the carcinogens and the mucous membranes of the colon and rectum is quite long [20]. One of the carcinogenic substances in food is amin-heterocyclic. Individuals who frequently consume red meat cooked for a long time at high temperatures have a high risk of colorectal adenocarcinoma due to the relatively high amin-heterocyclic content [21,22].

The percentages of incidence in the proximal, distal colon, and rectum were 26.35%, 31.08%, and 35.14%, respectively. These percentages were consistent with the report of WHO that the higher incidence of colorectal adenocarcinoma was in the distal colon or rectum [23]. Colon cancer may have a different growth pattern than the rectal. Flat lesions (depressed type) occurred more often in the colon than in the rectum and post increased difficulty in detection compared to early lesions. Meanwhile, polypoid non-depressed types (more visible), containing villous components were more common in rectum [24,25]. A link between inflammatory diseases of the gastrointestinal tract that persist for a long time and the process of carcinogenesis are other causes of the left side colon being the location of colorectal adenocarcinoma [23]. According to a previous study, inflammation is one of the hallmarks of cancer [26]. Tumorigenesis associated with inflammatory bowel disease (IBD) is a product of a persistent inflammatory microenvironment. At the molecular level, the induction of host-to-inflammatory damage occurs through the direct or indirect action of cytokines, such as IL-1p, IL-6, and TNF-a. This interaction includes oncogenic transcription factors, including NF-kB, leading to the induction of inflammatory response. The factors include matrix proteases, pro-angiogenic, and anti-apoptotic. Furthermore, the frequent multifocality of IBD-associated dysplasia of the colorectum and cancer reflects a field effect where extensive mucosa regions are populated by epithelial clones. These clones harbor aneuploidy or deleterious mutations and can expand and progress. The inflammatory environment promotes cell damage due to oxidative stress through increased production and accumulation

of reactive oxygen species. These cells are included in the initiation and progression of neoplasia by producing mutagenic DNA adducts and enhancing immune responses that further increase tissue damage [23].

The results of this study show that the most significant proportion of colorectal adenocarcinoma histopathology subtypes from 2017 to 2020 was adenocarcinoma NOS, accounting for 85.81%. According to the International Agency for Research on Cancer (IARC), adenocarcinoma NOS is a conventional sub-type of adenocarcinoma without any special additional features when distinguished from others [27]. The main pathological difference among adenocarcinoma NOS, mucinous adenocarcinoma, and signet ring cell carcinoma is the number of mucins produced. The sub-types that produce more mucin generally have a worse prognosis and lower survival. WHO defines mucinous adenocarcinoma as an adenocarcinoma comprising more than 50.00% extracellular mucin with malignant epithelial. Meanwhile, signet ring cell carcinoma is filled with more than 50.00% of signet ring cells with many intracytoplasmic mucin vacuoles [23,28].

The study by Teka et al. [5] showed that the risk of mortality in colorectal adenocarcinoma patients was five times higher in those with the signet-ring cell carcinoma histology sub-type compared to adenocarcinoma NOS. The five-year survival rate of adenocarcinoma NOS was better than others. Mucinous adenocarcinoma and signet ring cell carcinoma mainly occur in more severe stages of cancer, namely III and IV. Such worse prognoses could be related to the differentiation grade and the growth of tumors, which exhibited aggressive invasiveness, leading to higher rates of invasion of lymphovascular [23,28,29].

The grading of colorectal adenocarcinoma is based on gland formation and the least differentiated components, such as low and high-grade tumors [23]. The results showed that the largest category was "well-differentiated" with a total of 134 cases at 90.54%. However, the study conducted by Minhajat et al. [8] at Dr. Wahidin Sudirohusodo Hospital from January 2008 to April 2012 showed that the majority was "moderately differentiated", accounting for 45.30%. Differentiation grade may affect the prognosis of colorectal adenocarcinoma. According to Ueno et al. [30], 5-year relapse-free survival was well, moderately, and poorly differentiated, with percentages of 91.10%, 82.90%, and 74.70%, respectively. A relationship was found between the differentiation grade and the metastasis of colorectal adenocarcinoma. In this case, patients with worse differentiation showed a more profound invasion of the intestinal wall and more lymph node metastasis. Furthermore, a relationship was found between the differentiation grade and the incidence of metastasis. Distant metastasis was found to be most common in poorly differentiated adenocarcinomas with 62.00%. The correlation between differentiation and metastasis in

colorectal adenocarcinoma was due to increased mitosis and malignant cell hyperproliferation in poorly differentiated adenocarcinoma compared to the excellent or moderate [8]. A previous study showed that more than 50.00% of poorly differentiated adenocarcinoma cases had lymph node metastasis [14]. The differences between this study with Minhajat et al. [8] were due to a distinct factor. In this study, a significant number of patients fell in the N0 category in lymph node metastasis (N), while M showed the absence of metastasis. As a result, the majority of differentiation showed good conditions, implying "well-differentiated".

Cancer staging classification is used to determine its extent and the prognostic value of patients [31]. The two commonly used classification systems in contemporary times are TNM and Dukes staging. TNM was created by the American Joint Committee on Cancer (AJCC). This method classifies cancer stages based on primary tumor extension (T), regional lymph nodes (N), and distant metastases (M). The newest classification is the 8th edition of TNM and was put into use on 5 June 2018 [22,32]. The results of this study showed that the majority of TNM AJCC were stage III, with a total of 68 patients at 45.95%. When reviewed based on TNM AJCC 8th edition, which provided additional alphabetical details, the most stage was IIA, accounting for 50 patients at 33.78%. Stage IIA signified that the tumor invaded the muscularis propria up to the pericolorectal layer (T3). Furthermore, there is no evidence of metastasis to the regional lymphatic node (N0), and it has not undergone distant metastasis (M0).

In a comparison based on the primary tumor extension (T) grouping, it was found that most cases were patients who had the T3 category, namely 117 patients, accounting for 79.05%. T3 means a condition when the tumor invades the muscularis propria to the pericolorectal/fatty/serous layer [32]. An examination based on the most profound tumor invasion showed that there were five patients in stage T4b, with a percentage of 3.38%. T4b is a condition where a tumor directly invades or becomes attached to an organ. In this study, the condition of T4b included two cases with infiltration into the ovaries, one in the uterus, one in vesica urinaria, and one attachment to the liver, with percentages of 40.00%, 20.00%, 20.00%, and 20.00%, respectively. Cases of attachment in several peritoneal organs are caused by the anatomical factors adjacent to the organ of tumor growth origin [33]. A total of five patients with T4b had metastasis in the lymph nodes (100.00%), and one suffered distant metastasis in the liver (20.00%). The advanced stage of the primary tumor (T) is associated with a reduction in the long-term outcome of cancer patients [29,34].

The grouping of lymph node metastasis (N) showed that most cases were patients who had N0 category, namely 72 cases, accounting for 48.65%. N0 category

represents a condition with no metastasis to the regional lymphatic node [32]. Consistent with the analysis by Liu et al. [35], it was observed that the majority of (N) metastatic categories were NO, accounting for 66.89%. The presence of lymph node metastasis (N) was associated with diminished survival and a worsening prognosis, particularly with an increased number of metastases in the gland [29,34]. Hu et al. [36] showed that the 5-year survival rate of colorectal adenocarcinoma patients in the presence of lymph node metastasis was 31.00%. Lymph node metastasis in colorectal adenocarcinoma is an important indicator for postoperative chemotherapy adjuvant, and an accurate classification is required to predict the prognosis of patients [37].

The grouping of distant metastasis (M) showed that the majority had M0 category, namely 137 patients, accounting for 92.57%, and the least was M1, with 11 patients at 7.43%. Consistent with Wang et al. [38], M0 category was also obtained as the largest category, with a percentage of 70.00%. The results of this study showed that the most distant metastasis (M1) occurred in the liver organs, accounting for 63.63%. Furthermore, the most frequent distant metastasis in colorectal adenocarcinoma is in the liver organ, followed by the lungs. This condition was related to the spread through the circulatory system to the liver. Blood from the colon and rectum follows the portal system to the liver before continuing to the lungs through the heart. However, in some conditions, there was metastasis to the lungs without including the liver. This different pattern can be caused by lymphatic circulation, as reported by previous studies [8,33]. Tumors with distant metastasis (M) generally exhibit a worse prognosis [29,34].

The result showed the highest proportion of Dukes staging of colorectal adenocarcinoma in the Anatomical Pathology Laboratory was at C2, with 59 patients, accounting for 39.86%. The C2 category shows that the tumor has invaded the muscularis propria to the pericolorectal layer and lymph node metastases are present [22,31]. Consistent with the study by Magaji et al. [39] at the University Malaya Medical Center on colorectal adenocarcinoma patients from January 1, 2001, to December 31, 2010, the highest proportion was in category C with 30.20% of cases. However, the study by Minhajat et al. [8] at Dr. Wahidin Sudirohusodo Makassar showed that C2 was the second most common category after D, with percentages of 24.60% and 26.80%, respectively. This condition occurs due to the prevalence of distant metastases in the cases encountered in Minhajat et al. [8].

CONCLUSIONS

The incidence of diagnosed colorectal adenocarcinoma cases increased yearly in the Anatomical Pathology Laboratory of Dr. Soedarso Hospital Pontianak. The majority

of patients in the age range of 53-61 years old showed the most prevalent histopathological sub-type, which was well-differentiated adenocarcinoma NOS. In addition, the most frequent TNM AJCC staging was IIA, and the most Dukes staging suffered was C2. Further studies of the clinical characteristics and analysis of risk factors in colorectal adenocarcinoma patients were required to support the development of preventive strategies.

DECLARATIONS

Competing interest

The authors declare no competing interest in this study.

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