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Clinicopathological Characteristics of Colorectal Cancer in the Anatomical Pathology Laboratory of Dr. M. Djamil Padang 2017-2020

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Abstract. *Colorectal cancer is a malignant epithelial tumor originating from colorectal mucosa. Clinicopathology factors including age, gender, location, histopathological type, differentiation, depth of invasion, lymph node metastasis, and lymphovascular invasion are known affect the prognosis. This study aims to determine the clinicopathological characteristics of colorectal cancer at Anatomical Pathology Laboratory RSUP. Dr. M. Djamil Padang in 2017-2020 This study was descriptive observational with total sampling technique from medical records. Samples included all colorectal cancer patients in 2017-2020 who were fulfilled inclusion criteria, with total 251 samples. The results showed that the most patiens were female (52.2%), the age group were > 50 years (66.1%), mostly located in the rectosigmoid (71.7%). Most of the histopathological types were adenocarcinoma (79.7%), with low grade differentiation (88.8%). More than a half of tumor invasion was at T3 (58.2%). Mainly metastatic status to lymph nodes was Nx (54.2%) and lymphovascular invasion were positive in 60% samples that included the lymphovascular invasion examination. The conclusion of this study is most of colorectal cancer in Anatomical Pathology Laboratory RSUP. Dr. M. Djamil Padang in 2017-2020 are in advanced stage, Early detection needs to be done so that colorectal cancer can be diagnosed at an early stage.*

Keywords: *Colorectal Cancer, Clinical Features, Histopathology Features*

1. INTRODUCTION

Colorectal cancer is a malignancy originating from epithelial cells in the large intestine, namely the colon and rectum. Colorectal cancer is characterized by uncontrolled growth and spread of abnormal cells in the colorectal, if the spread of these cells is not controlled, it can result in death (Society AC, 2017). Based on the International Statistical Classification of Diseases and Related Health Problems (ICD)-11 Colon and rectal carcinomas include colon carcinoma (2B90), rectosigmoid carcinoma (2B91), and rectal carcinoma (2B93) (WHO ICD-11, 2021) Based on GLOBOCAN data in 2020, colorectal cancer is the third most common cancer in the world after breast cancer and lung cancer, with a higher incidence in men than women. Worldwide, 1,065,960 men and 865,630 women have colorectal cancer. With a total of 1,931,590 sufferers (10% of all cancer cases in the world) (Asia, 2020). Cases of death caused by colorectal cancer worldwide amounted to 935,173 people (9.4% of all cases of death caused by cancer), ranking second with the most deaths. Deaths from colorectal cancer by gender are men with a total of 515,637 people and women with a total of 419,536 people (Asia, 2020).

Indonesia is a country with a population of 273,523,621 people. New cases of cancer diagnosed in 2020 in Indonesia amounted to 396,914 people (World Health

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Organization, 2020). Colorectal cancer ranks fourth out of the total addition of new cases of cancer diagnosed in 2020, which amounted to 34,189 people. With 21,764 male sufferers and 12,425 female sufferers (World Health Organization, 2020). A study conducted by Hamdi (2013) in the period from January 2009 to December 2011 in the Anatomical Pathology Laboratory of the Faculty of Medicine, Andalas University, obtained data on colorectal cancer sufferers in Padang city totaling 260 cases out of 2703 cancer cases in the same year (Hamdi, 2015)

Cancer has various risk factors such as age and gender. The risk of colorectal cancer increases after the age of 40, and increases sharply in the age range of 50 to 55 years. The risk of developing colorectal cancer also doubles in each subsequent decade. Age is the most relevant factor influencing the occurrence of colorectal cancer (Anggunan, 2015). Men are the most common sufferers of colorectal cancer compared to women (Asia, 2020). In addition to the above, diet and lifestyle are also modifiable risk factors for colorectal cancer. Many factors can affect the prognosis and treatment of colorectal cancer, including histopathological characteristics in the form of histopathological images, degree of differentiation, depth of invasion, status of metastasis to lymph nodes, and lymphovascular invasion.

Globally, the World Health Organization (WHO) states that the histological classification of colorectal cancer is divided into adenocarcinoma, mucinous adenocarcinoma, signet ring cell carcinoma, adenosquamous carcinoma, medullary carcinoma, and undifferentiated carcinoma (WHO, 2006). According to Hamdi's research (2013), the most common histological classification was adenocarcinoma with 217 cases or 83.46% of the total percentage of cases, followed by mucinous adenocarcinoma with 31 cases or 11.92% of the total percentage of cases (Hamdi, 2015). Tumor grading is also something that affects the prognosis of colorectal cancer. Tumor grading it self is the appearance of the tumor based on how abnormal the tumor cells and tumor tissue look under a microscope. In general, colorectal cancer grading is divided into Well differentiated, Moderately differentiated, Poorly differentiated, and Undifferentiated (National Cancer Institute, 2021).

Based on research conducted at Dr. H. Abdul Moeloek Lampung Hospital in 2014, it was found that the grading of colorectal cancer from 52 samples was 40 samples with good differentiation (77%), 10 samples with moderate differentiation (19%), and 2 samples with poor differentiation (4%) (Anggunan, 2015). The depth of tumor invasion in colorectal cancer is divided into Tx to T4b which is used as a guideline in determining

the stage of the tumor (Sasputra IN, 2015). Lymphovascular invasion is the presence of blood vessel cancer cells and is considered the initial step in the spread of cancer. The lymphatic system is the main route of cancer spread. Based on research conducted by Wenzhou Medical University published on August 13, 2019, the results of the study were obtained in the form of stage III colorectal carcinoma with positive lymphovascular invasion (+) having an increased risk of death of 95%. The findings of this study indicate that the presence of lymphovascular invasion (LVI) is a significant prognostic indicator in patients with stage III colorectal cancer (Zhong J-W, 2019).

Metastasis to lymph nodes regional lymph nodes by tumor cancer cells are often associated with decreased survival of colorectal cancer patients. This is supported by the theory that fatal distant metastases are often based on cancer cell metastasis to regional lymph nodes (Naxerova K, 2017).

Based on the background above and because there has been no recent research related to the histopathological picture of colorectal cancer, researchers are interested in conducting a study entitled Clinicopathological Characteristics of Colorectal Cancer in the Anatomical Pathology Laboratory of Dr. M. Djamil Padang Hospital in 2017-2020.

2. RESEARCH METHOD(S)

This type of research is descriptive with a cross-sectional research design to determine the clinical and histopathological characteristics of colorectal cancer patients at Dr. M. Djamil Padang General Hospital. This study uses secondary data in the form of medical records of Colorectal Cancer patients registered at the Pathology Laboratory of Dr. M. Djamil Padang General Hospital in 2017-2020.

The population in this study were all colorectal cancer patients in the anatomical pathology laboratory of Dr. M. Djamil Padang General Hospital in 2017-2020. The sample in this study was the entire population that met the inclusion criteria. Inclusion Criteria: All patients who underwent colorectal cancer resection in the Anatomical Pathology Laboratory of Dr. M. Djamil Padang General Hospital recorded in the medical record in the period 2017-2020.

The sampling technique in this study was Total Sampling, namely all subjects who met the inclusion criteria were selected as samples. In this study, 251 samples were obtained that met the inclusion criteria. All samples were included as sources of research data.

Secondary data in the form of medical records were taken from the Medical Records Section at the Anatomical Pathology Laboratory of Dr. M. Djamil Padang General Hospital. From the medical records, the data needed for this study were taken, such as age, gender,

location, histopathological features, degree of differentiation, depth of invasion, status of metastasis to the lymph nodes, and lymphvascular invasion. The data that has been obtained will be analyzed using univariate analysis which will be presented descriptively in the form of a frequency distribution table. This study has passed ethical review with letter number: LB.02.02/5.7/503/201.

FINDINGS

This study was conducted on 251 colorectal cancer patients in the anatomical pathology laboratory of Dr. M. Djamil Padang Hospital in 2017-2020.

Table 1. Distribution of Characteristics of Colorectal Cancer Patients by Gender, Age, and Tumor Location

Karakteristik Pasien	Frekuensi (n=251)	Persentase (%)
Jenis Kelamin		
Laki-Laki	120	47,8
Perempuan	131	52,2
Usia		
≤50th	85	33,9
>50th	166	66,1
Lokasi		
Ascending	37	14,7
Descending	19	7,6
Transversum	15	6,0
Rectosigmoid	180	71,7

Table 2. Distribution of Histopathological Characteristics of Colorectal Cancer

Derajat Differensiasi		
Low Grade	223	88,8
High Grade	28	11,2
Kedalaman Invasi		
Tx	3	1,2
Tis	1	0,4
T1	1	0,4
T2	55	21,9
T3	146	58,2
T4	45	17,9
Metastasis Ke KGB		
KGB yang diperiksa ≥ 12		
No	22	8,8

Karakteristik Histopatologi	Frekuensi (n=251)	Persentase (%)
Tipe Histopatologi		
Adenocarcinoma	200	79,7
Mucinous adenocarcinoma	44	17,5
Signet ring cell carcinoma	6	6
Adenosquamous Carcinoma	0	0
Medullary Carcinoma	1	4
Undifferentiated Carcinoma	0	0

N1	17	6,8
N2	21	8,4
KGB yang diperiksa < 12		
0	8	3,2
1-5	41	16,3
6-11	6	2,4
KGB tidak dapat ditentukan		
Nx	136	54,2
Invasi Limfovaskular		
Positif	24	9,6
Negatif	16	6,4
Tidak Dicantumkan	211	84,1

Based on table 1, it can be concluded that in this study, most colorectal cancer patients in the Anatomical Pathology Department of RSUP. Dr. M. Djamil Padang in 2017-2020 were female (52.2%). Based on age, colorectal cancer is more common in the age group >50 years (66.1%). The majority of colorectal cancer patients are located in the rectosigmoid section (71.7%).

Based on table 2, it can be concluded that in this study, most of the histopathological characteristics of colorectal cancer in the Anatomical Pathology Department of RSUP. Dr. M. Djamil Padang in 2017-2020 were of the adenocarcinoma histopathological type (79.7%), with the majority of low-grade differentiation (88.8%). The depth of tumor invasion was highest at T3 (58.2%), with the status of metastasis to the lymph nodes being the most undetermined, which was 54.2% and more than half of the samples that included positive lymphovascular invasion examination results (60%).

3. DISCUSSION

Based on the research results, the largest age group in colorectal cancer cases at Dr. M. Djamil Padang General Hospital in 2017-2020 was the age group >50 years, which was 166 samples (66.1%). This result is in line with the literature which states that the average age of colorectal cancer sufferers is over 50 years old. A study conducted at the Faculty of Medicine, Andalas University from May 2013 to March 2014 also obtained the same results, namely the age group >50 years (57.56%) (Kurniawan T, 2017). Research at Sanglah Hospital, Bali for the period 2013-2017 also found that the age of the most colorectal cancer patients was 50-60 years (39.7%) (Gunasekaran V, 2019).

The results of this study illustrate the theory that the risk of colorectal cancer increases after the age of 40 years, and increases sharply in the age range of 50 to 55 years. The risk of developing colorectal cancer also doubles in each subsequent decade.

Age is the most relevant factor influencing the occurrence of colorectal cancer (Anggunan, 2015).

The most common gender in this study was female, which was 131 samples (52.2%). This result is in line with a study conducted at the Faculty of Medicine, Andalas University in the period January 2009 to December 2011 which found that the most colorectal cancer sufferers were female, as many as 141 patients (54.23%) (Hamdi, 2015). In a study conducted at Dr. M. Djamil Padang Hospital in 2015-2017, it was also found that the most colorectal cancer sufferers were female, which was 50.6% (Desvi NSD, 2018). This result is in contrast to a study conducted at the Faculty of Medicine, Andalas University in May 2013 to March 2014 which found that the male gender was 105 patients (51.22%) (Kurniawan T, 2017). A study conducted at RSUD DR. H. Abdul Moeloek Lampung Province in 2014 found the most male gender with a total of 28 patients (54%) (anggunan, 2015). According to theory, the highest incidence of colorectal cancer is in men. However, this is not related to the risk factors of the type gender, but rather due to lifestyle risk factors such as a diet high in red meat, smoking, and alcohol consumption. The differences in research results indicate that gender is not a risk factor for colorectal cancer. The low cases of colorectal cancer in women are closely related to estrogen hormone levels which are protective factors to prevent colorectal cancer. In this study, the majority of patients were >50 years old, this age has entered menopause in women, so estrogen levels as a protective factor are also low. Researchers suspect that this is one of the causes in this study that women suffer more from colorectal cancer (Society AC, 2017).

Based on the research results, the location where colorectal cancer occurs most is in the rectosigmoid, which is 180 samples (71.7%). These results are in line with the literature stating that the location of 55% of colorectal cancer is in the rectosigmoid (Robbins, 2007). These results are in line with research conducted at the Faculty of Medicine, Andalas University in the period January 2009 to December 2011 which found that the most common location of colorectal cancer was in the rectum with 131 patients (50.39%) (Hamdi, 2015). In a study conducted at Dr. M Haulussy Ambon Hospital in the period January 2012–June 2013, the most common location of colorectal cancer was in the rectum with 20 patients (69%) (Ariska M, 2013). In a study conducted at Dr. M Haulussy Ambon Hospital in the period January 2012–June 2013, the most common location of colorectal cancer was in the rectum with 20 patients (69%). M. Djamil Padang in 2015-2017 the location of the most colorectal cancer was the rectum, which was 74.1%

(Desvi NSD, 2018). The location of colorectal cancer can be divided into 2 parts, namely the right side (caecum, ascending colon, and transverse colon) and the left side (descending colon, sigmoid colon, and rectum) which are limited by the splenic flexure (Misdraji J, 2019). One of the 3 main molecular pathways for colorectal cancer is chromosomal instability which is a mutation of the APC protein which is a tumor suppressor gene. The difference between the occurrence of right and left side colorectal cancer cases is the gene that causes the cancer itself. Right-sided colorectal cancer is mostly caused by KRAS gene mutations but on the left side it is mostly caused by APC gene mutations. APC gene mutations are found in 80% of all cases colorectal cancer. That is what causes colorectal cancer to occur in the rectosigmoid (left side) (Stintzing S, 2017).

In this study, Adenocarcinoma was the most common histopathological type, with 192 samples (79.7%). This result is in line with a study conducted at the Faculty of Medicine, Andalas University from May 2013 to March 2014 which found that the most common histopathological type of colorectal cancer was adenocarcinoma, with 168 patients (81.95%).35 A study conducted at Sanglah Hospital, Bali from 2013-2017 also found the same results, with 118 patients (97.5%) having adenocarcinoma (Gunasekaran V, 2019). These results are in line with the theory that 90% of colorectal cancer cases are adenocarcinoma. Colorectal adenocarcinoma has a dominant glandular appearance with little stroma. Tumor cells are tall columnar and change to cuboidal in worse differentiation (Teng XD, 2005). The highest degree of colorectal cancer differentiation in this study was low-grade, which was 223 samples (88.8%). This result is in line with a study conducted in the anatomical pathology laboratory of Dr. Kariadi Hospital, Semarang from August 2020 to November 2020, which found that the highest degree of colorectal cancer differentiation was low-grade, which was 32 samples (80%) (Lesmana VA, 2020). In a study conducted in the anatomical pathology laboratory of Dr. Achmad Mochtar Hospital, Bukittinggi from April to May 2018, the highest degree of differentiation was low-grade, which was 116 patients (80%) (Devianti L, 2019). A study conducted in 4 anatomical pathology laboratories in West Sumatra also found that the highest degree of differentiation was low-grade, which was 28 patients (71.8%) (Liana N, 2022). The degree of differentiation is one of many factors used to help predict how likely colorectal cancer is to grow and spread. The American Cancer Society divides the differentiation grade of colorectal cancer into Low-Grade (Well-Moderately) and High-Grade (Poorly). High-grade differentiated colorectal cancer tends to grow and spread

more quickly than low-grade differentiated colorectal cancer. However, other factors are also important in determine a patient's prognosis, such as how far the cancer has spread (Cancer, 2014).

Based on the results of the study, the depth of invasion of colorectal cancer was greatest to the depth of T3, which was 146 samples (58.2%). This result is in line with a study conducted at the Faculty of Medicine, Andalas University from May 2013 to March 2014, the depth of invasion was greatest to the subserosa layer (T3), which was 73 patients (47.4%) (Kurniawan T, 2017). This result is also in line with a study conducted at Hasan Sadikin General Hospital, Bandung, which found that the depth of invasion of colorectal cancer was greatest to the subserosa layer (T3), which was 20.2%.48 In a study conducted at Sendai Kousei Hospital, Miyagi, Japan in 2016, the depth of invasion was greatest at T1, which was 52 patients (Hashimoto R, 2016).

The depth of invasion of colorectal cancer is divided from T1 to T4, T3 is the invasion of cancer cells to the serosa layer of the large intestine. A study found that the deeper the invasion of cancer cells into the intestinal lining, the higher the recurrence rate (Nomura, 2019). The difference in the results of the depth of invasion is closely related to the early detection of colorectal cancer itself, in Indonesia early detection of colorectal cancer has not been as good as in other countries, resulting in delayed diagnosis in colorectal cancer patients in Indonesia. Most colorectal cancer patients have come with a deep depth of invasion.

Based on the results of the study, the status of metastasis to the lymph nodes was the most Nx, which was 136 samples (54.2%). This result is not in line with the study conducted in the anatomical pathology laboratory of Dr. Kariadi Hospital, Semarang, from August 2020 to November 2020, which found the status of metastasis to the lymph nodes was the most at N0, which was 16 samples (40%) (Lesmana VA, 2020). The status of metastasis to the lymph nodes in colorectal cancer is useful for predicting the type of adjuvant therapy that will be given. Many studies have found a relationship between the status of metastasis to the lymph nodes and the survival of colorectal cancer patients. Adequate lymph node evaluation is very important for accurate cancer staging. The theory states that the minimum acceptable number of lymph nodes is 12 nodes, but the number of nodes taken from colorectal cancer patient specimens varies widely and often does not meet this recommendation. Factors such as tumor location, surgical technique, and handling of the specimen by the pathologist can affect the results of lymph node examination (Maguire A, 2014). Most of the lymph node metastasis status in colorectal

cancer patients in the Anatomical Pathology Laboratory of Dr. M. Djamil Padang Hospital in 2017-2020 could not be determined because no lymph nodes were found in the anatomical pathology examination or no lymph nodes were found macroscopically or microscopically. 40 samples that included the results of lymphovascular invasion examination, 24 samples were positive (60%) and 16 samples were negative (40%). In a study conducted in 4 anatomical pathology laboratories in West Sumatra, the most lymphovascular invasion was positive, namely 31 samples (79.5%). In a study conducted at RSCM in 2017-2018, the status of lymphovascular invasion was mostly negative, which was 12 samples (52.2%) (Hilbertina N, 2020).

In this study, the majority of lymphovascular invasion assessment indicators have not been included because lymphovascular invasion examinations were only carried out in 2019. Lymphovascular invasion indicates that cancer is already in the blood vessels and/or lymph vessels in the large intestine, which results in a high probability that cancer cells can metastasize to surrounding organs. However, this does not mean that the cancer cells cannot be cured. The results of this lymphovascular invasion examination can be a reference in determining the right adjuvant therapy after the cancer cells are removed (cancer, 2014). The writing of the conclusions of the results of the anatomical pathology examination is not yet uniform, because the Lymphvascular invasion examination was only carried out in 2019, causing researchers to have to read in detail the microscopic description of the anatomical pathology examination.

4. CONCLUSION AND SUGGESTION

The most common age of colorectal cancer patients is in the age group over 50 years, with the most common gender being female, and the most common location being rectosigmoid. The most common histopathological type of colorectal cancer is adenocarcinoma. The most common degree of differentiation of colorectal cancer patients is low-grade. The majority of colorectal cancer patients have a depth of invasion to the serosal layer (T3). Most of the metastasis status to the lymph nodes cannot be determined (Nx). Positive Lymphovascular Invasion can be found in more than half of the samples that list the lymphovascular invasion status.

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