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Profile of Colorectal Adenocarcinoma in Dr. Soetomo Hospital Surabaya Period 2018-2022

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ABSTRACT

Background: The incidence of colorectal cancer is increasing every year by about 8% with most patients in men. This cancer mostly occurs in old age above 50 years. Most colorectal cancers are of the adenocarcinoma type, which is most common on the left side of the colon. One of the determinant prognosis factors of colorectal adenocarcinoma is the depth of invasion, the deeper the correlate with invasion, the worse the prognose. ***Method:*** Descriptive research with a retrospective approach. The sample used data from histopathological examination results with a diagnosis of colorectal adenocarcinoma from surgery and biopsy material at the Anatomy Pathology Laboratory of Dr. Soetomo General Academic Hospital Surabaya for the period 2018-2022. ***Result:*** The total sample size was 143 cases with the most patients being male (60.84%) and the most age group being 51-60 (41.26%). The most common location was rectum (13.29%) with T stage (the most invasion depth was T3 (19.58%). The most common degree of differentiation was low degree (58.04%) with stage N (metastasis to lymph node) which was N0 (23.78%). ***Discussion:*** Age and lifestyle (drinking alcohol and smoking) are two of the many risk variables that affect the occurrence of colorectal cancer. The right-sided colon is the most typical site of adenocarcinoma, and it is linked to both KRAS and NRAS variables. The degree of differentiation can affect survival, although the depth of invasion and metastatic variables also affect prognosis. ***Conclusion:*** Colorectal adenocarcinoma is mostly found in men over 50 years of age with low differentiation and is most commonly located in the rectum.

Keywords: colorectal adenocarcinoma; invasion depth; prognostic factors

INTRODUCTION

Colorectal cancer is the most frequent malignancy of the gastrointestinal organs[1]. Data from Globocan 2022 shows that the incidence of colorectal cancer in Indonesia is ranked fourth at 8.7% with 35.676 new cases and is the fifth cause of death in the world, as much as 19.255 (7.9%) with 90% of colorectal cancer is adenocarcinoma type. Incidence of colorectal carcinoma in men ranks second with 21.903 (11.6%) cases and it ranks fourth in women with 13.773 (6.3%) cases. High risk of colorectal cancer at age 50 years and above[2].

According to WHO Classification Digestive Tumor 2019, colorectal adenocarcinoma is divided into several types based on histopathological features, including No Special Type (NOS) adenocarcinoma, mucinous carcinoma, signet ring cell carcinoma, medullary carcinoma, while for differentiation, colorectal adenocarcinoma is distinguished based on the glandular features obtained. If the glandular picture is >50% then it is classified as low grade differentiation and if the glandular picture is <50% then it is classified as high grade[1]. In terms of both shape and function, well-differentiated tumors are similar to normal tissue. They exhibit modest growth, low-grade malignancy, and high maturation. On the other hand, weakly differentiated tumors have a high-grade malignancy, fast progression, early metastasis, low maturation, and appearance that is similar to that of parent cells. Prognostic of an adenocarcinoma can be determined by the stage, one of which is seen from the depth of tumor invasion (pT). The deeper the tumor invasion, the worse the prognosis[34]. Profile colorectal adenocarcinoma is critical for improving diagnosis, personalizing treatment, understanding disease mechanisms, and advancing research. Data in Asia show that the incidence of colorectal adenocarcinoma is more prevalent at younger ages and with advanced stages, while in Padang colorectal adenocarcinoma is most prevalent in males aged 61-70 years and the most common location is in the rectum[29]. The profile of colorectal adenocarcinoma has not been done in Dr. Soetomo Hospital, so it is necessary to conduct such research for further research data.

The aim of this research is to analyze the character profile of colorectal adenocarcinoma based on age, gender, site, and histopathological diagnose, including histopathological features and grading differentiation at Dr. Soetomo General Academic Hospital Surabaya Indonesia during 2018-2022.

METHOD

This study was an observational descriptive study using medical record data. Data were obtained from all patients surgical and biopsy procedures with a histopathologic diagnosis of adenocarcinoma NOS examined in the anatomical pathology laboratory of Dr. Soetomo Hospital Surabaya in 2018-2022. The samples were then grouped based on sex (male and female), age (20–30, 31–40, 41–50, 51–60, 61–70, >71 years), location (sigmoid, rectum, ascending colon, transverse colon, descending colon), histopathological features (adenocarcinoma NOS, mucinous carcinoma), depth of invasion (T stage), and degree of differentiation, data tabulated and analyzed with statistical.

RESULT

During 2018 until 2022, the data collection of adenocarcinoma population is 143 cases with dominant in men. The incidence occurred mostly in the age range of 51-60 years with the most tumor location in the rectum (Table 1).

TABLE 1: The distribution characteristic of colorectal adenocarcinoma.

Characteristic	Total N (%)
Population	143
Sex	
Male	87 (60.84)
Female	56 (39.16)
Age	
20-30	4 (2.78)
31-40	17 (11.89)
41-50	31 (21.68)
51-60	59 (41.26)
61-70	24 (16.78)
>71	8 (5.59)
Site	
Colon ascending	16 (11.19)
Colon transversum	10 (7.93)
Colon descending	9 (6.29)
Sigmoid	14 (9.8)
Rectum	19 (13.29)
Procedure	
Biopsy	77 (53.85)
Surgery	66 (46.15)

Data for colorectal adenocarcinoma type and grade were taken from biopsy and surgery samples. Based on histopathological features, colorectal adenocarcinoma is divided into several types. The types of adenocarcinoma found in the population were NOS adenocarcinoma and mucinous carcinoma. Data for stage T and stage N were taken from the surgery sample. (Table 2).

TABLE 2: Histopathological feature of colorectal adenocarcinoma.

Histopathology	Total N (%)
T Stage	
pT1	1 (0.67)
pT2	22 (15.38)
pT3	28 (19.58)
pT4	15 (10.49)
N/A	77 (53.85)
Type	
Adenocarcinoma NOS	120 (83.92)
Mucinous carcinoma	23 (16.08)
Differentiation	
Low grade	83 (58.04)
High grade	60 (41.96)
N stage	
N0	35 (25.47)
N1a	10 (6.99)
N1b	6 (4.2)
N2a	8 (5.59)
N2b	7 (4.86)
N/A	77 (53.85)

DISCUSSION

The most common type of cancer in the gastrointestinal system is colorectal cancer. The increasing incidence of colorectal cancer may be caused by KRAS and NRAS mutations due to diet and lifestyle[4]. In addition, gut microbiota may also play a role in colorectal cancer pathogenesis and progression by modulating anti-cancer immune responses. Several genetic mutations can also cause colorectal adenocarcinoma, including: APC (*Adenomatous Polyposis Coli gene*) mutations that function as tumor suppressors can cause genetic instability resulting in the accumulation of β-catenin protein in the nucleus which affects tumor differentiation and growth[5], p53 mutations and MCC (*mutated in colon cancer*)[6].

The results obtained the highest incidence rate in men 87 (60.84%) compared to women 56 (39.16%). This is in accordance with the American Cancer Society where men have a 30% higher risk than women and men diagnosed with colorectal cancer have a worse prognosis and 40% higher mortality[7]. Colorectal cancer incidence rate in the United States is mostly in males about 66.9%[11,16]. The incidence rate in Indonesia is more men about 11.6%[39], while the data at Dr. Soetomo hospital in 2013-2015 obtained the number of male patients as many as 100 patients[35]. This can be related to exposure to risk factors (smoking, lifestyle and hormones)[8]. Frequent consumption of red meat and processed meat can increase the risk of obesity, insulin resistance and increased bile secretion resulting in colorectal cancer growth[9]. Alcohol content in the form of acetaldehyde is a carcinogen that increases the risk of colorectal cancer but depends on alcohol polymorphism enzyme metabolism[10]. Active smokers have a 2-3-fold higher risk for colorectal carcinoma because the carcinogenic content in cigarettes causes mutations in DNA[8].

The results of this study found that the incidence of colorectal adenocarcinoma was around 24-75 years old with the highest incidence of 51-60 years old[4]. Incident trend in Australia continent and American continent increase at ages over 50[12,13], may be due to a diet rich in animal protein and fat and low in fiber, calcium, vitamin D and folic acid[12,33], while the incidence rates on the Asian continent (the Republic of Korea and China) increased in the 40-59 age group for both men and women[14]. People aged 65 years and above have a higher risk of colorectal cancer compared to those aged 50-64 years and about 30 times greater risk compared to those aged 50-64 years[9], can be caused by decreased consumption of vegetables and fruits and an increase in consumption of red meat and processed meat[33]. The colorectal cancer incidence rate in Iraq shows more at the age of >50 years about 66.6%[15]. This increased risk is related to dietary intake and increased visceral fat levels which activate hormonal components of total body fat that promote the development of colorectal adenocarcinoma, through the secretion of proinflammatory cytokines, which cause inflammation in the colon and rectum, insulin resistance, and modulation of metabolic enzymes such as adiponectin or lectin [10].

Based on WHO classification of digestive tumor 2019 colorectal adenocarcinoma is divided into several types, namely NOS adenocarcinoma, mucinous adenocarcinoma, signet ring cell carcinoma, medullary carcinoma, adenosquamous carcinoma and others[18]. in this study only 2 types of adenocarcinoma were obtained, namely NOS adenocarcinoma and mucinous adenocarcinoma. The most common location of colorectal cancer in the right-sided colon compared to the left side. Right-side colorectal cancer is more likely has cells containing mucinous, signet ring cells, undifferentiated[31]. This makes colorectal cancer on the right side have mucinous type and signet ring cells type. Different immunological processes in the right and left side colon may be one of the causes, where inflammation in epithelial cells by secreting interleukin-6 will increase the permeability of these cells[32]. Colorectal cancer on the right side has more microsatellites tumors with high microsatellite instability (MSI) causing mutations or inactivation of DNA mismatch repair systems. Tumors with high microsatellite instability are characterized by mutation or inactivation of DNA mismatch repair system, and consequently, single nucleotide mutations and repeated microsatellite sequence length changes in the genome are observed in these tumors[25]. In addition, such tumors have distinct molecular carcinogenic characters including KRAS, BRAF mutations. KRAS is a proto-oncogene that can induces tumorigenesis in several types of cancer[26]. About 35–40% of colorectal carcinoma cases have mutations in the KRAS gene. This mutation affects codons 12, 13, and 61 and is a single nucleotide point mutation. This mutation appears while colorectal carcinoma carcinogenesis is developing[36].

The depth of invasion is one of the prognoses in colorectal adenocarcinoma. The regulation of invasion includes the following processes: angiogenesis, basement membrane disintegration, disruption of tight junctions, and epithelial-to-mesenchymal transition (EMT)[37]. Furthermore, the extracellular matrix of the basement membrane, which typically serves as a mechanical barrier to tumor cell migration and invasion, can be broken down by the formation of matrix metalloproteinase (MMP), which can initiate the invasion process[38]. This study only obtained 66 specimens that could be evaluated for invasion depth. This is because 77 biopsy tissues could not be evaluated for depth of invasion because the material examined was only small tissue[30]. Depth of invasion (T stage) has been shown to affect survival, with high T stage associated with poor survival and increased metastasis[34], in addition to the depth of invasion that affects staging is metastasis to lymph nodes (N) which is calculated from the number of glands that have tumor infiltration in them. The more metastases obtained, the worse the prognosis. Colorectal cancer located on the right side of the colon tends to metastasize to the peritoneum and has a worse prognosis, while those located on the left side have more metastases to the lungs[34].

Tumor differentiation in colorectal adenocarcinoma is based on the gland images obtained, where the more glands obtained (>50%) the lower the differentiation[27]. The results of this study found that colorectal adenocarcinoma with low-grade differentiation had the most 83 (58.04%) cases compared to grade high differentiation as many as 40 (61.96%) cases. This is similar to previous studies which stated that low-grade differentiation colorectal adenocarcinoma was most common compared to high-grade differentiation. The degree of differentiation has a major impact on survival rates and is an important prognostic indicator. Patients 5-year survival rate is higher when they have low-grade differentiation[28]. More than 50% of cases of high-grade differentiation are associated with lymph node metastases, but low-grade differentiation is less likely[17].

CONCLUSION

The results of this study indicate that the incidence of colorectal adenocarcinoma in Dr. Soetomo Surabaya Hospital in 2018-2022 is mostly male with the most age between 51-60 years, with the most locations in the rectum (left-sided colon). Most of the histopathology results obtained were colorectal adenocarcinoma with low-grade differentiation. And the majority of samples were collected from biopsy material.

REFERENCES

[1] Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, Washington KM, Carneiro F, Cree IA. The 2019 WHO classification of tumours of the digestive system. Histopathology. 2020 Jan;76(2):182.

[2] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, Jemal A. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2024 May;74(3):229-63.

[3] International Agency for Research on Cancer, editor. WHO classification of tumours of the digestive system. International Agency for Research on Cancer; 2019.

[4] Weledji EP. The Etiology and Pathogenesis of Colorectal Cancer. Clin Oncol. 2024;9:2046.

[5] Rathva B, Desai SV. Colorectal cancer: Etiology, pathogenesis, and current treatment. Journal of Innovations in Pharmaceutical and Biological Sciences (JIPBS). 2020;7(4):20-4.

[6] Kasi A, Handa S, Bhatti S, Umar S, Bansal A, Sun W. Molecular pathogenesis and classification of colorectal carcinoma. Current colorectal cancer reports. 2020 Oct;16:97-106.

[7] American Cancer Society. Colorectal Cancer Facts & Figures 2017–2019; American Cancer Society: Atlanta, GA, USA, 2017.

[8] Sawicki T, Ruszkowska M, Danielewicz A, Niedźwiedzka E, Arłukowicz T, Przybyłowicz KE. A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms and diagnosis. Cancers. 2021 Apr 22;13(9):2025

[9] Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Gastroenterology Review/Przegląd Gastroenterologiczny. 2019 Jan 6;14(2):89-103.

[10] Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. International journal of molecular sciences. 2017 Jan 19;18(1):197.

[11] Gu M, Thapa S. Colorectal cancer in the United States and a review of its heterogeneity among Asian American subgroups. Asia-Pacific Journal of Clinical Oncology. 2020 Aug;16(4):193-200.

[12] Feletto E, Yu XQ, Lew JB, St John DJ, Jenkins MA, Macrae FA, Mahady SE, Canfell K. Trends in colon and rectal cancer incidence in Australia from 1982 to 2014: analysis of data on over 375,000 cases. Cancer Epidemiology, Biomarkers & Prevention. 2019 Jan 1;28(1):83-90.

[13] Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nature reviews Gastroenterology & hepatology. 2019 Dec;16(12):713-32.

[14] Zhou J, Zheng R, Zhang S, Zeng H, Wang S, Chen R, Sun K, Li M, Gu J, Zhuang G, Wei W. Colorectal cancer burden and trends: comparison between China and major burden countries in the world. Chinese journal of cancer research. 2021 Feb 2;33(1):1.

[15] Ibrahem S, Ahmed H, Zangana S. Trends in colorectal cancer in Iraq over two decades: incidence, mortality, topography and morphology. Annals of Saudi medicine. 2022 Jul;42(4):252-61.

[16] White A, Ironmonger L, Steele RJ, Ormiston-Smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK. BMC cancer. 2018 Dec;18:1-1.

[17] Minhajat R, Benyamin AF, Miskad UA. The relationship between histopathological grading and metastasis in colorectal carcinoma patients. Nusantara Medical Science Journal. 2020:51-60.

[18] WHO, 2019. WHO *classification of tumors digestive system tumor*, 5th,edn,vol 1, International Agency for Research on Cancer, France

[19] Lesko J, Rastović P, Azinović A, Đurasović S, Bogut A, Zovko J, Pavlović M, Zovko Z. Association of colorectal carcinoma and metabolic syndrome. Medicinski Glasnik. 2020 Feb 1;17(1).

[20] White A, Ironmonger L, Steele RJ, Ormiston-Smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK. BMC cancer. 2018 Dec;18:1-1.

[21] Tong GJ, Zhang GY, Liu J, Zheng ZZ, Chen Y, Niu PP, Xu XT. Comparison of the eighth version of the American Joint Committee on Cancer manual to the seventh version for colorectal cancer: A retrospective review of our data. World journal of clinical oncology. 2018 Nov 11;9(7):148.

[22] Johncilla M, Yantiss RK. Histology of colorectal carcinoma: proven and purported prognostic factors. Surgical pathology clinics. 2020 Sep 1;13(3):503-20.

[23] Ammendola S, Turri G, Marconi I, Burato G, Pecori S, Tomezzoli A, Conti C, Pedrazzani C, Barresi V. The presence of poorly differentiated clusters predicts survival in stage II colorectal cancer. Virchows Archiv. 2021 Feb;478:241-8.

[24] Maurya S, Patel S, Srikantegowda H. A Study of Significance of Poorly Differentiated Clusters in Colorectal Carcinomas: Association with Histopathological Prognostic Factors. Journal of Clinical & Diagnostic Research. 2020 Nov 1;14(11).

[25] Baran B, Ozupek NM, Tetik NY, Acar E, Bekcioglu O, Baskin Y. Difference between left-sided and right-sided colorectal cancer: a focused review of literature. Gastroenterology research. 2018 Aug;11(4):264.

[26] Xie MZ, Li JL, Cai ZM, Li KZ, Hu BL. Impact of primary colorectal Cancer location on the KRAS status and its prognostic value. BMC gastroenterology. 2019 Dec;19:1-9.

[27] Chen K, Collins G, Wang H, Toh JW. Pathological features and prognostication in colorectal cancer. Current Oncology. 2021 Dec 13;28(6):5356-83.

[28] Rimbert J, Tachon G, Junca A, Villalva C, Karayan-Tapon L, Tougeron D. Association between clinicopathological characteristics and RAS mutation in colorectal cancer. Modern Pathology. 2018 Mar 1;31(3):517-26.

[29] Liana N, Helmizar R, Ruhsyahadati R, Jelmila SN, Triyana R, Lismawati L. The Profile of Colorectal Adenocarcinoma at Dr. M. Djamil General Hospital Padang, Indonesia. Nusantara Hasana Journal. 2024 Jun 10;4(1):65-70.

[30] Menon G, Recio-Boiles A, Lotfollahzadeh S, et al. Colon Cancer. [Updated 2024 Apr 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470380/

[31] Lee MS, Menter DG, Kopetz S. Right versus left colon cancer biology: integrating the consensus molecular subtypes. Journal of the National Comprehensive Cancer Network. 2017 Mar 1;15(3):411-9.

[32] Ulanja MB, Rishi M, Beutler BD, Sharma M, Patterson DR, Gullapalli N, Ambika S. Colon cancer sidedness, presentation, and survival at different stages. Journal of oncology. 2019;2019(1):4315032.

[33] Gu MJ, Huang QC, Bao CZ, Li YJ, Li XQ, Ye D, Ye ZH, Chen K, Wang JB. Attributable causes of colorectal cancer in China. BMC cancer. 2018 Dec;18:1-9.

[34] Chen K, Collins G, Wang H, Toh JW. Pathological features and prognostication in colorectal cancer. Current Oncology. 2021 Dec 13;28(6):5356-83.

[35] Thamrin H, Ilmiah K, Tirthaningsih NW. Profile of Colorectal Tumor in Gastroentero-Hepatology Center, Departement Of Internal Medicine, Dr Soetomo Hospital, Surabaya. Folia Medica Indonesiana. 2020 Mar 1;56(1):15-8.

[36] Mastutik G, Rahniayu A, Rahaju AS, Kurniasari N, I'tishom R. The Mutation Status Of Kras Gene Codon 12 And 13 In Colorectal Adenocarcinoma (Status Mutasi Gen Kras Kodon 12 dan 13 di Adenocarcinoma Kolorektal). Indonesian Journal of Clinical Pathology and Medical Laboratory. 2016;23(1):12-7.

[37] Rahniayu A, Oey RC, Mastutik G. Differences in the Expression of CD44 and EMMPRIN in Various Spectra of Mucinous Ovarian Tumors.

[38] Hambalie LA, Rahaju AS, Mastutik G. The correlation of EMMPRIN and EGFR overexpression toward muscle invasiveness in urothelial carcinoma of bladder. Indian Journal of forensic medicine & toxicology. 2021;15(2):2709-15.

[39] Globocan (2022). Estimated cancer incidence, mortality and prevalence worldwide in 2022. Available at https://globocan.irc.fr/pages/fact_sheets_cancer.aspx? cancer=colorectal. Accessed at September, 09 2024