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Age and Sex Difference Between Low-grade and High-grade Colorectal Adenocarcinoma

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Abstract

Colorectal cancer is currently the second leading cause of death in the world. Sex, age, and histological grading have interesting prognostic values for colorectal cancer to be studied further. The purpose of this study was to examine the differences in age and sex to the histological grading of low-grade and high-grade colorectal adenocarcinoma. This analytical descriptive study used 65 samples of formalin-fixed paraffin-embedded (FFPE) from patients diagnosed with colorectal adenocarcinoma based on histopathological examination with Hematoxylin-Eosin staining, period 2014 to 2016. Data obtained for age, age group < 45 years 12 samples (18.5%), 36 samples in the 45-65 age group (55.4%), and 17 samples in the 65-year age group (26.2%). For sex, 36 samples (55.4%) and 29 samples (44.6%) were female. For the histological grade of low-grade colorectal adenocarcinoma, 43 samples (66.2%) and high-grade 22 samples (33.8%). The data were then analyzed using the Chi-square test, age against the degree of histology obtained p-value of 0.383 (p>0.05), for sex to the degree of histology obtained p-value of 0.338 (p>0.05). The conclusion there are no statistically significant differences between age and sex to histological grades of low-grade and high-grade colorectal adenocarcinoma.

Keywords: age; sex; low-grade and high-grade colorectal adenocarcinoma.

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1. Introduction

The incidence of colorectal cancer varies widely throughout the world and is currently the second leading cause of death in the world. Based on data from the Global Cancer Observatory in 2020, it was found that the incidence of colorectal cancer in men was higher (23.4 per 100,000/year) compared to women (16.2 per 100,000/year) and men aged > 45 years (85.3 per 100,000/year). diagnosed as colorectal cancer compared to women aged > 45 years (57.8 per 100,000/year) [1,2]. In line with these data, several previous studies stated that sex had a significant relationship with the development of colorectal cancer [3,4]. In addition to sex, young age (<40 years) also has a poor prognostic value against colorectal cancer [5,6].

Histological grading of colorectal cancer refers to the degree of tumor differentiation. The degree of differentiation in colorectal cancer is determined by the glandular structure field [7]. Histological grading of colorectal cancer also has a poor prognostic value on the survival ability of colorectal cancer patients [8,9]. Further studies are needed regarding sex and age against histological degrees to add information about the factors that influence the development of colorectal cancer.

2. Materials and Method

This research is an analytic observational study with a cross-sectional design. We collected a sample of 65 cases diagnosed as low-grade or high-grade colorectal adenocarcinoma based on histopathological examination from 2014 to 2016. The samples came from the Wahidin Sudirohusodo anatomic pathology laboratory and Hasanuddin University Hospital in Makassar. Sampling was done by simple random sampling. using an archive of Hematoxylin-Eosin (HE) preparations and a paraffin block/formalin-fixed paraffin-embedded (FFPE).

Evaluation of the histological grade of colorectal cancer on hematoxylin-eosin preparations was based on the percentage of the glandular structure of the tumor mass, where ≥ 50% of the glandular formations belonged to the low-grade histological grade group, whereas <50% of glandular formations were included in the high-grade histological grade group and for age, categorization divided into 3 groups; < 45 years (adults), 45-65 years (elderly) and > 65 years (seniors). The data were analyzed using SPSS 23 software windows to determine the difference in age and sex between the histological degrees of low-grade and high-grade adenocarcinomas. This research has obtained an ethical clearance statement from the ethics committee of the Faculty of Medicine, Hasanuddin University.

3. Result

Based on table 1 shows the distribution of colorectal cancer by age, sex, and histological grading of colorectal adenocarcinoma. For age, the youngest patient diagnosed with colorectal adenocarcinoma was 27 years old and the oldest 79 years old, where the mean age of the sample was 56.49 years. For sex, more males (55.4%) than females (44.6%). For the histological grade of colorectal adenocarcinoma, the low-grade (66.2%) was higher than the high-grade (33.8%).

Table 1: Distribution and characterization of colorectal adenocarcinoma based on age, sex, and histological grading

Characteristics	N (%)
Age	
Minimum	27
Maximum	79
mean	56.49
median	57
Sex	
Man	36 (55.4%)
Woman	29 (44.6%)
Histological grading	
Low-grade	43 (66.2%)
High-grade	22 (33.8%)

Table 2 shows the highest age in the low-grade colorectal adenocarcinoma group in the 45-65-year age range (40%) as well as the high-grade group, the highest in the 45-65-year age range (15.4%). From these data, a chi-square test was performed, the p-value = 0.383 ($p > 0.05$) which means that there is no significant difference in age between low-grade and high-grade adenocarcinomas.

Table 2 also shows data that in low-grade adenocarcinoma, the number of samples of men (33.8%) and women (32.3%) did not have a significant difference while in the high-grade group, men (55.4%) were more than women. (12.3%). Chi-square test analysis was performed with these data and obtained p-value = 0.338 ($p > 0.05$) which means that there was no significant difference between the histological degrees of low-grade colorectal adenocarcinoma and high-grade colorectal adenocarcinoma.

Table 2: Histological grading of colorectal adenocarcinoma based on age and sex

	Colorectal Adenocarcinoma		**Amount**	
Characteristics	*Low-grade* *N= 43*	*High-grade* *N= 22*	Total = 65	**P *Value***
Age				
< 45 years	8 (12.3%)	4(6.2%)	12(18.5%)	
45-65 years	26 (40%)	10(15.4%)	36(55.4%)	
> 65 years	9 (13.8%)	8(12.3%)	17(26.2%)	0.383
Total	43 (66.1%)	22 (33.9%)	65 (100%)	
Sex				
Man	22 (33.8%)	14 (33.8%)	36(55.4%)	
Woman	21 (32.3%)	8(12.3%)	29(44.6%)	0.338
Total	43 (66.1%)	22 (33.9%)	65 (100%)	

4. Discussion

Currently, colorectal cancer is still cancer with the second-highest mortality rate in the world. The data

found that the incidence of colorectal cancer began to increase significantly at the age of > 45 years, this is to data from the global cancer observatory in 2020 where the age of patients diagnosed with colorectal cancer is 3 times more at the age of 45 years compared to age < 45 years [2]. Although the number of recorded cases of colorectal cancer is high for those aged 45 years, in some countries with a high Human Development Index (HDI) it was found that most colorectal cancers are diagnosed earlier, this is associated with increased colonoscopy screening and early treatment of lesions. precursor. The American Cancer Society 2018 has lowered the recommended age for initiation of screening for individuals at risk from 50 years to 45 years [1].

This study analyzed the histological degrees of low-grade and high-grade colorectal cancer based on sex and age which were divided into 3 groups, < 45 years (adults), 46-65 years (elderly), and > 65 years (seniors). The transformation of normal colonic mucosa into invasive cancer develops through a stage of accumulation of genetic, and epigenetic changes and is supported by environmental factors. This transformation is based on specific factors and pathogenic mechanisms that are complex and heterogeneous in which genetic chromosomal instability (CIN) factors, microsatellite instability (MSI) pathways and exacerbated by epigenetic instability factors CpG island methylator phenotype (CIMP) are the main etiologic factors in this process [10–12]. This genetic pathway difference will give a different histological morphological picture including tubular formation. Histology of colorectal cancer based on tubular appearance is generally considered a stage-independent prognostic variable, and high-grade histology is associated with poor patient survival [7,12,13].

Our results showed that the histological grades of low-grade and high-grade colorectal cancer by sex and 3 age groups were not found to be significantly different although there was an increasing trend in the data where the number of male patients was more than female, both at low-grade histology as well as high-grade. Likewise, the histological degrees of low-grade and high-grade colorectal cancer by age group shows a tendency for data on patients diagnosed with colorectal cancer to increase with age, especially in the 46-65-year age group. This study also showed data that the number of patients aged < 45 years and 65 years did not have a significant difference. These data support several reports from previous studies, where the increasing number of young patients (< 45 years) who tend to present with advanced disease (high-grade histology) indicates a poor prognosis [5,6]. The increasing number of high-grade colorectal cancer patients at a young age can be caused by genetic and epigenetic factors, lifestyle, speed in establishing a diagnosis related to the implementation of screening, selection of therapy, and access to health facilities that support therapy. Increased screening activities for patients with complaints related to colorectal organs are an effective way to detect early precursor lesions that can develop into cancer so that they can be found and treated more quickly and appropriately for a better prognosis [5].

In addition to age, sex is also a topic that is widely studied in colorectal cancer patients. In this study, there was no significant difference in the degree of low-grade and high-grade histology concerning sex. Several previous studies have shown that sex differences that lead to sex hormones have implications for the initiation and development of colorectal cancer [3,4]. Pre-menopausal patients have a 5-year better survival rate than male patients of the same age, and younger women (< 45 years) show lower mortality than older women (> 50 years) [4]. In addition to hormonal factors, certain genetic and epigenetic differences between the sexes can determine the risk of colorectal cancer [14,15]. High CpG island methylator phenotype, tumor location, sex, and tumor

differentiation are prognostic factors for colorectal cancer. The high CpG island methylation phenotype associated with tumor location indicates a high number of female patients with tumors in the right colon. The high CpG island methylator phenotype is also frequently associated with older age, poor differentiation, and BRAF mutation [10].

The lack of sample size and the variation of the variables studied were limitations in this study, so the data obtained were not significant between the histological grades of low-grade and high-grade colorectal adenocarcinoma to age and sex, although the data showed a tendency that this was in line with previous studies.

5. Conclusion

Through statistical tests, there was no significant difference between the histological grading of low-grade and high-grade colorectal adenocarcinoma concerning age and sex.

6. Suggestion

For further research, it is possible to use more samples with more diverse variables

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