INTRODUCTION

Colorectal cancer or colorectal cancer (CRC) is cancer that grows in the large intestine (colon) or at the very bottom of the large intestine connected to the anus (rectum). Colorectal cancer may be called colon or rectal cancer, depending on where the cancer grows.¹,²

Colorectal cancer is largely caused by the progressive accumulation of genetic and epigenetic changes that transform the normal colonic epithelium into an abnormal one. Some of the causes of CRC include Chromosomal instability, oncogenic mutations of the Rat Sarcoma (RAS) and B-Rapidly Accelerated Fibrosarcoma (BRAF) genes, mutations of polyposis coli adenomatous, family history, Inflammatory Bowel Disease (IBD), smoking, age and diet. Colorectal cancer usually develops in the lining of the colon or rectum.³,⁴

Colorectal cancer is the third most frequently diagnosed worldwide and one of the leading causes of cancer-related deaths. It is estimated that almost 150,000 new cases were diagnosed and 50,000 people died in 2008. In 2012 around 1.3 million new cases were reported diagnosed with CRC and nearly 700,000 patients died from CRC. Colorectal cancer occupies the fourth position with 694,000 deaths; 5.7% of people living with colorectal cancer of all types in Indonesia. Colorectal cancer in Indonesia ranks third in most cancers and has experienced a sharp increase in incidents, namely 12.8 per 100,000 adult population, with a mortality of 9.5% of all cancer cases.⁴,⁵

During the last two decades, many biomarkers have been studied extensively. One such marker is Carcinoembryonic Antigen (CEA). CEA is a tumor marker used in screening for several types of cancer, including colon, lung, stomach, thyroid, pancreatic, breast, bladder, and ovarian cancer. Molecular markers function for cancer detection, patient prognosis, and the right treatment to be given and can also be used to detect stage and therapy.⁵,⁶

Lymphocytes play a role in cytotoxic cell death, inhibition of proliferation and migration of tumor cells. Lymphopenia usually indicates the severity of the disease and can make cancer cells escape the Tumor-Infiltrating Lymphocyte (TIL) immunity. Tumor-infiltration Lymphocytes are formed by migrating lymphocytes and it has been shown that reduced TIL levels confer a poor prognosis, whereas monocytes may increase in tumor metastases. Cytokines secreted from monocytes are associated with poor prognosis in cancer patients.
such as tumor necrosis factor-alpha (TNF-α) and interleukin (IL)-1. In addition, macrophages originate from circulating monocytes and have a role in suppressing adaptive immunity and promoting angiogenesis, invasion, and migration.\textsuperscript{,5,7} Examination of Lymphocyte Monocyte Ratio (LMR), a laboratory biomarker that is easy to use to predict clinical outcomes in colon cancer patients, can also be done. LMR is a ratio calculated by dividing the absolute lymphocyte count by the monocyte count from a blood test.\textsuperscript{7}

A decrease in LMR can be associated with a poor prognosis in cancer patients, whereas an increase in LMR before treatment can give a good prognosis. LMR is a predictor for hematological malignancies as well as for cancer. Previous studies also demonstrated that LMR is a prognostic factor for CRC patients, but several studies suggest that CRC patients with low LMR have a poorer prognosis.\textsuperscript{,7,8}

Examining CEA and LMR levels in colorectal cancer patients is very easy to do, inexpensive, and can be used to predict clinical outcomes. Besides, CEA and LMR examinations in colorectal cancer patients have never been carried out in Indonesia, especially in Makassar, so we are interested in conducting this research.\textsuperscript{,9,10}

Based on the background description above, the researchers were interested in analyzing the relationship between CEA and LMR levels with the severity of colorectal cancer. In addition, this research is still rarely done. It is hoped that this research can provide scientific information about CRC patients.

METHODS

A retrospective observational cross-sectional study was conducted by collecting secondary data from the medical records of colorectal cancer patients at Dr. Wahidin Sudirohusodo General Hospital, Makassar. The research sample included all medical record data of colorectal cancer patients accompanied by CEA laboratory examination results and the number of Lymphocytes and Monocytes at Dr. Wahidin Sudirohusodo Hospital Makassar from January 2018 - August 2021. The study was conducted at the Medical Records Installation at Dr. Wahidin Sudirohusodo Hospital in August 2022.

The study population included medical record data of colorectal cancer patients at Dr. Wahidin Sudirohusodo General Hospital, Makassar. The research sample included all medical record data of colorectal cancer patients accompanied by CEA laboratory examination results and the number of Lymphocytes and Monocytes at Dr. Wahidin Sudirohusodo General Hospital Makassar from January 2018 - August 2021. The inclusion criteria were that the study sample was CRC patients diagnosed by a surgeon in the surgical department of Dr. Wahidin Sudirohusodo Makassar Hospital. There are data from CEA and CBC examination results. The exclusion criterion is that the required medical record data is incomplete.

Data analysis was performed using SPSS version 25.0 for Windows. The statistical analysis performed was descriptive statistical calculations and frequency distribution using the Kolmogorov-Smirnov statistical test to assess data normality, the ANOVA test, the Kruskal-Wallis test, and Spearman's Correlation test. The statistical test results are significant if the p-value <0.05.

RESULTS

A total of 53 patients were included in this study, who had complete data on LMR, CEA and Grade PA. Table 1 describes the characteristics of the research data. The number of patients with male sex was 38 people (71.7%) and 15 women (28.3%). The age group of the patients ranged from 32 to 84 years, with a mean of 58.1 ± 11.3 years. The most severe degree of CRC was moderate, 29 people (73.6%), followed by mild degree, 8 people (15.1%), and severe degree, 6 people (11.3%). Subjects’ LMR values varied between 0.92 - 200.00 ng/ml, with a mean of 2.29 ± 1.48. Based on the normality test, the distribution of LMR data is normally distributed. CEA levels of the samples varied between 0.56 - 200.00 ng/ml, with a mean of 53.5 ± 78.70 ng/ml (Table 1). Based on the normality test, the distribution of CEA data is not normally distributed.

The next analysis describes a statistical test to determine the relationship between LMR and CEA with CRC grade. In Table 2, a comparison of the LMR values (median and mean) according to the PA grade with the ANOVA test was found to be the highest in the moderate grades (3.38 and 3.49) and the lowest in the heavy grades (2.04 and 2.22), but not statistically significant (p>0.05) (Table 2).

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The subsequent analysis uses Spearman's Correlation test to find a correlation between LMR and CEA with Grade PA. From Table 4, there was no significant correlation between LMR and CRC grade ($p>0.05$). In the correlation of LMR values with CEA levels (Table 5), there is a significant negative correlation between LMR and CEA, where the higher the LMR value, the lower the CEA level, or conversely, the lower the LMR value, the higher the CEA level ($p<0.01$).

### DISCUSSION

In the results of this study, the incidence of colorectal cancer in males was higher than in females. The number of patients with male sex was 38 people (71.7%) and 15 women (28.3%). Based on the Surveillance, Epidemiology and End Results Program results from the National Cancer Institute, incidents in the United States increased in males compared to females. Many countries in Asia report a significant association between male sex and a higher incidence of CRC. In data in Korea, the incidence of males ($40.2/100,000$) experiencing CRC was more elevated than females ($22.2/100,000$) in 2015. Other countries reported the same thing, such as Japan ($64.8/100,000$ for males; $36.7/100,000$ for females, 2013), China ($20.7/100,000$ for males; $14.4/100,000$ for female, 2014), and Hong Kong ($44.6/100,000$ for male; $27.6/100,000$ for female, 2016). This could be due to the influence of the protective effect of estrogen and progesterin on women against CRC, which may also be caused by diet and lifestyle.$^{11,12}$

The age group of the patients ranged from 32 to 84 years, with a mean of $58.1 \pm 11.3$ years. This is also in accordance with the risk factors for CRC, which increase dramatically after the age of 50 years. Approximately 90% of cases are found in those over 50 years of age, and most are aged 35-64 years. Several studies have also stated that the higher the life expectancy, the higher the incidence of CRC mortality in that region.$^{11}$

The most severe degree of CRC was moderate, 29 people (73.6%), followed...
reported that CEA and CA 19-9 had no relationship with CRC grade, stating that CEA has no prognostic value, only the evaluation value of the stage.\(^16,17\)

The subsequent analysis is to find a correlation between LMR and CEA with Grade PA using Spearman’s Correlation test. From Table 4, there was no significant correlation between CEA and CRC grade (\(p>0.05\)) and no significant correlation was found between LMR and CRC grade (\(p>0.05\)). With the Spearman test, no relationship was found between CEA and LMR with CRC grade, the same previous studies, et al have done before.\(^16-18\)

Although these two markers are often used, CEA and LMR are better used before therapy, after therapy, their value becomes insignificant.\(^16-18\)

In the correlation of LMR values with CEA levels (Table 5), there is a significant negative correlation between LMR and CEA, where the higher the LMR value, the lower the CEA level, or conversely, the lower the LMR value, the higher the CEA level (\(p<0.01\)). Research by Li et al showed that CEA and LMR could be combined for diagnostic efficacy in detecting colon cancer as early as possible.\(^9\)

Colon cancer patients have lower LMR values compared to CEA, the opposite occurs in benign tumors in the colon. This shows the good diagnostic ability of LMR and CEA for early diagnosis. This is consistent with various previous studies.\(^19-22\)

**CONCLUSION**

The results showed that the higher the LMR value, the lower the CEA level, or vice versa (\(p<0.01\)). A decrease in LMR can be associated with a poor prognosis in cancer patients, whereas an increase in LMR before treatment can give a good prognosis. Various studies have shown that CEA and LMR can be combined for diagnostic efficacy in detecting colorectal cancer as early as possible. ColoRectal cancer patients have lower LMR values compared to CEA, the opposite occurs in benign tumors in the colon. This shows the good diagnostic ability of LMR and CEA for early diagnosis.

**CONFLICT OF INTEREST**

There is no competing interest regarding the manuscript.
ETHICS CONSIDERATION

The research permit was approved by the Health Research Ethics Commission, Faculty of Medicine, Universitas Hasanuddin, Universitas Hasanuddin General Hospital and Dr. Wahidin Sudirohusodo Makassar with number: 439/UN4.6.4.5.31/PP36/2022.

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AUTHOR CONTRIBUTION

All authors equally contribute to the study from the conceptual framework, data acquisition, and data analysis, until reporting the study results through publication.

REFERENCES