



Relationship Between Eosinophil Levels and Histopathological Grading of Colorectal Carcinoma

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Abstract

Colorectal cancer (CRC) is a multifactorial disease and a leading cause of cancer-related mortality. CRC ranks as the second most common cancer globally and the third most frequently diagnosed malignancy worldwide. Several studies have suggested that elevated eosinophil levels in peripheral blood correlate with poor prognosis in colorectal cancer cases. This study aims to analyze the relationship between eosinophil levels and histopathological grading of colorectal carcinoma by evaluating peripheral blood eosinophil counts in correlation with CRC histopathology grading. This research employs a descriptive-correlational approach, utilizing univariate and bivariate analyses. The study findings indicate a significant correlation between eosinophil levels and histopathological grading of colorectal carcinoma at Wahidin Sudirohusodo General Hospital, Makassar.

Introduction

Eosinophil cells have been linked as a prognostic indicator for cancer. Eosinophils can stimulate angiogenesis and remodel tumor tissue. In routine pathology eosinophil infiltration is an easy parameter to assess. Elevated eosinophils are associated with patient survival and disease recurrence in Colorectal cancer patients (Prizment et al., 2016; Loktionov, 2019; Lopez-Perez et al., 2024; Ohkuma et al., 2021; Rimini et al., 2021; Harbaum et al., 2015; Saraiva & Carneiro, 2018; Ramadan et al., 2020).

Eosinophil levels are particularly elevated in tumor mucosal tissue and especially in the conditions surrounding CRC tumor tissue (Kasprzak, 2021; Handler et al., 2024; Reichman et al., 2019; Grisaru-Tal et al., 2020). This is attributed to the direct independent antitumorigenic activity of CD8⁺ lymphocytes. Although eosinophils are mainly found in tissues, in some diseases eosinophil levels in peripheral blood correlate with their presence in the affected tissue even to the severity of the disease (Ramirez et al., 2018; Wechsler et al., 2021; Diny et al., 2017; Rosenberg et al., 2013; Kovalszki & Weller, 2016; Simon et al., 2019).

In some studies it is said that high levels of eosinophils in peripheral blood have a correlation with poor prognosis in Colorectal cancer cases, therefore this study was conducted to see the relationship between eosinophil levels and Colorectal Carcinoma histopathology grading by evaluating eosinophil levels in peripheral blood associated with CRC histopathology grading. Based on the explanation above, the authors are interested in conducting research with the title "Relationship between Eusinophil Levels and Histopathology Grading of Colorectal Carcinoma at Wahidin Sudirohusodo General Hospital Makassar".

Methods

This study uses a descriptive correlational approach, because this method can determine the relationship / correlation between the independent and dependent variables well and widely in the research sample. The research design used is *Cross Sectional*. In this design can be done in the form of surveys, observations and collection of population data only once at a time. The research location at the Central General Hospital (RSUP) Dr. Wahidin Sudirohusodo Makassar Jalan Perintis Kemerdekaan No.Km.11, Tamalanrea Jaya, Kec. Tamalanrea, Makassar City, South Sulawesi, was conducted in December 2024 to January 2025

Research Variables

Dependent variables, consisting of: *Histopathology Grading of Colorectal Carcinoma* in *Colorectal* cancer patients at Dr. Wahidin Sudirohusodo Hospital Makassar. Assessment of tumor morphology is then classified based on the *differentiation* of cancer cells, into *well differentiated, poorly differentiated, and poorly differentiated*.

Independent variables, consisting of: Eosinophil levels in *Colorectal* cancer patients at Dr. Wahidin Sudirohusodo Hospital Makassar.

Population and Sample

The population was patients diagnosed with colon cancer at Dr. Wahidin Sudirohusodo Hospital Makassar, from January to December 2022. Samples were taken using the Total Sampling method with criteria: 1) Inclusion criteria are: Colorectal cancer patients at Dr. Wahidin Sudirohusodo Hospital Makassar; 2) Exclusion Criteria are: Colorectal cancer patients who have a history of allergies and atopy, Colorectal cancer patients with comorbid / parasitic infectious diseases and other infections, Colorectal cancer patients with a history of previous antibiotic use.

Data collection and analysis techniques

Data were collected from patient medical records showing the results of histopathology tests and routine blood laboratory tests, which were then processed using *Microsoft excel* for data analysis. Data analysis in this study used univariate and bivariate analysis. Univariate analysis was performed to analyze descriptively, explain and describe the characteristics of variables using frequency distribution or percentage in the form of tabulations or graphs of each research variable. Bivariate analysis to determine the correlation / relationship between dependent and independent variables with the *Chi Square* test with a significance degree of 5% so that if the *P values* ≤ 0.05 , it shows that there is a relationship between variables. Meanwhile, if $p > 0.05$, it indicates that there is no relationship between these variables.

Result and Discussion

Relationship between Eosinophil levels and *Colorectal Carcinoma* histopathology Grading

Table 1. Relationship of Variables (CRC predictive factors) to Histopathology group

Variable	Well Differentiated (n = 42) (Mean $\pm$ SD)	Poorly Differentiated (n = 58) (Mean $\pm$ SD)	P Value
Eosinophils (cells/mcL)	340.40 $\pm$ 340.55	492.66 $\pm$ 465.10	0.010

*Mann Whitney Test

Source: Secondary Data

In the study, the *Mann Whitney* non-parametric mean test was conducted with the results obtained that the eosinophil variable was significant to the histopathology type ($P < 0.05$).

Furthermore, eosinophils continued to the next analysis to determine the value of the intersection point.

The eosinophil cut-off point was determined using the *Receiver Operating Characteristics* (ROC) Curve Test to determine the optimal cut-off point of Eosinophil levels against the Histopathology group. with the assumption that the higher the blood eosinophil level, the more *poorly differentiated* the histopathology grading will be. The cut-off point for eosinophil levels was 296.4 cells with a sensitivity of 60.3% and a specificity of 59.5%.

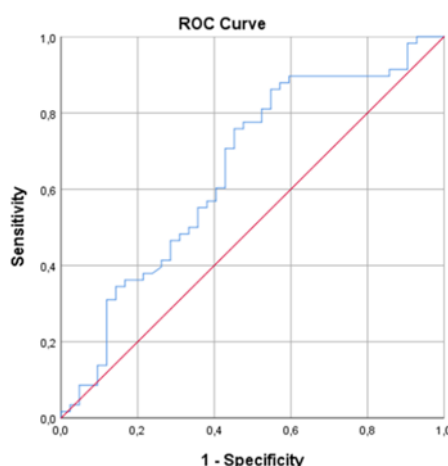


Figure 1. Determination of cut-off point for eosinophil levels (ROC curve)

By using the cut-off point obtained from the ROC, it was found that the majority of patients had high eosinophil levels, namely 53 patients (53%). While as many as 47 patients (47%) had low eosinophil levels.

So that the value of the relationship between eosinophil levels and histopathology grading is obtained from 47 patients who have low eosinophil levels, there are 25 patients (53.2%) who experience histopathology with the *well differentiated* category and 22 patients (46.8%) who experience histopathology with the *poorly differentiated* category. Whereas from 53 patients who had high eosinophil levels, there were 17 patients (32.1%) who had histopathology with the *well differentiated* category and 36 patients (67.9%) who had histopathology with the *poorly differentiated* category.

Table 2. Relationship between eosinophil levels and histopathology

			Histopathology		Total	P* value *Odds ratio (CI95%)
			Well Differentiated	Poorly Differentiated		
Eusinophil Group (cells/mcL)	<296,4	N	25	22	47	
		%	53,2%	46,8%	100,0%	
	>=296,4	N	17	36	53	0,033
		%	32,1%	67,9%	100,0%	2,40
Total		N	42	58	100	CI (1.06-5.42)
		%	42.0%	58.0%	100.0%	

*Chi-Square test, **Haenzel Coat test

Source: Secondary Data

From the table above, the *p-value* of the *chi-square* test is 0.033. This shows that there is a significant relationship between eosinophil levels and histopathology grading (*p-value* <0.05).

Several studies have investigated the relationship between blood eosinophil levels and histopathological characteristics of *Colorectal Carcinoma* (CRC). While the specific

correlation between peripheral blood eosinophil counts and histopathological grading of CRC is still rarely explored. Research by Pretlow et al. in 1983 observed that the number of tissue-infiltrating eosinophils decreased with tumor progression in colorectal neoplasms. This finding suggests that a decrease in tissue eosinophilia may reflect the potential malignancy of neoplastic lesions. Whereas in another study conducted by Rosman et al. in 2022 which evaluated trends in peripheral blood eosinophil counts over time and their association with future diagnosis of colorectal cancer. Found that patients with a positive linear increase in peripheral eosinophils over time had a higher risk for colorectal cancer, which suggests that changes in blood eosinophil levels may be an indirect clue to the role of eosinophils in the pathogenesis of colorectal cancer. This supports and is in line with the results obtained in this study.

The worse the differentiation of a CRC tumor, the more difficult it is to be recognized by eosinophils so that eosinophils that should be in tumor tissue as a chemokine response from the body will instead circulate in the blood in greater numbers. However, this study did not show a picture of eosinophil levels in histopathology tissue.

Conclusion

Based on the results of research and discussion, the researcher concluded that there is a correlation between eosinophil levels and *Histopathology grading of Colorectal Carcinoma* patients at Wahidin Sudirohusodo General Hospital in 2022. Where the higher the level of eosinophils in the blood shows the worse the histopathology grading (*poorly differentiated*).

This study is still a cross-sectional study to see the correlation of eosinophil levels with *Colorectal Carcinoma histopathology grading*. For future research, further observations should be made to explain the direct correlation between the number of eosinophils in the blood and the histopathological grading of colorectal carcinoma because currently the research is still limited.

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References

- Diny, N. L., Rose, N. R., & Čiháková, D. (2017). Eosinophils in autoimmune diseases. *Frontiers in immunology*, 8, 484. <https://doi.org/10.3389/fimmu.2017.00484>
- Grisaru-Tal, S., Itan, M., Klion, A. D., & Munitz, A. (2020). A new dawn for eosinophils in the tumour microenvironment. *Nature Reviews Cancer*, 20(10), 594-607. <https://doi.org/10.1038/s41568-020-0283-9>
- Handler, K., Raju, D., Gurtner, A., Dalessi, T., Brügger, M. D., Crepaz, D., ... & Arnold, I. C. (2024). Eosinophils restrict CRC metastasis by inhibiting pro-tumorigenic SPP1+ macrophage differentiation. *bioRxiv*, 2024-12. <https://doi.org/10.1101/2024.12.13.628333>
- Harbaum, L., Pollheimer, M. J., Kornprat, P., Lindtner, R. A., Bokemeyer, C., & Langner, C. (2015). Peritumoral eosinophils predict recurrence in colorectal cancer. *Modern Pathology*, 28(3), 403-413. <https://doi.org/10.1038/modpathol.2014.104>
- Kasprzak, A. (2021). The role of tumor microenvironment cells in colorectal cancer (CRC) cachexia. *International journal of molecular sciences*, 22(4), 1565.

- Kovalszki, A., & Weller, P. F. (2016). Eosinophilia. *Primary care*, 43(4), 607. <https://doi.org/10.1016/j.pop.2016.07.010>
- Loktionov, A. (2019). Eosinophils in the gastrointestinal tract and their role in the pathogenesis of major colorectal disorders. *World journal of gastroenterology*, 25(27), 3503. <https://doi.org/10.3748/wjg.v25.i27.3503>
- Lopez-Perez, D., Prados-Lopez, B., Galvez, J., Leon, J., & Carazo, A. (2024). Eosinophils in colorectal cancer: emerging insights into anti-tumoral mechanisms and clinical implications. *International Journal of Molecular Sciences*, 25(11), 6098. <https://doi.org/10.3390/ijms25116098>
- Ohkuma, R., Kubota, Y., Horiike, A., Ishiguro, T., Hirasawa, Y., Ariizumi, H., ... & Wada, S. (2021). The prognostic impact of eosinophils and the eosinophil-to-lymphocyte ratio on survival outcomes in stage II resectable pancreatic cancer. *Pancreas*, 50(2), 167-175. <https://doi.org/10.1097/mpa.0000000000001731>
- Pretlow, T. P., Keith, E. F., Cryar, A. K., Bartolucci, A. A., Pitts, A. M., Pretlow, T. G., ... & Boohaker, E. A. (1983). Eosinophil infiltration of human colonic carcinomas as a prognostic indicator. *Cancer research*, 43(6), 2997-3000.
- Prizment, A. E., Vierkant, R. A., Smyrk, T. C., Tillmans, L. S., Lee, J. J., Sriramaraio, P., ... & Limburg, P. J. (2016). Tumor eosinophil infiltration and improved survival of colorectal cancer patients: Iowa Women's Health Study. *Modern pathology*, 29(5), 516-527. <https://doi.org/10.1038/modpathol.2016.42>
- Ramadan, S., Saka, B., Yarikaya, E., Bilici, A., & Oncel, M. (2020). The potential prognostic role of peritumoral eosinophils within whole tumor-associated inflammatory cells and stromal histological characteristics in colorectal cancer. *Polish Journal of Pathology*, 71(3), 207-220. <https://doi.org/10.5114/pjp.2020.99787>
- Ramirez, G. A., Yacoub, M. R., Ripa, M., Mannina, D., Cariddi, A., Saporiti, N., ... & Dagna, L. (2018). Eosinophils from physiology to disease: a comprehensive review. *BioMed research international*, 2018(1), 9095275.
- Reichman, H., Itan, M., Rozenberg, P., Yarmolovski, T., Brazowski, E., Varol, C., ... & Munitz, A. (2019). Activated eosinophils exert antitumorigenic activities in colorectal cancer. *Cancer immunology research*, 7(3), 388-400. <https://doi.org/10.1158/2326-6066.cir-18-0494>
- Rimini, M., Franco, P., De Bari, B., Zampino, M. G., Vagge, S., Frassinetti, G. L., ... & Casadei-Gardini, A. (2021). The prognostic value of the new combined Hemo-Eosinophil Inflammation Index (HEI Index): A multicenter analysis of anal cancer patients treated with concurrent chemo-radiation. *Cancers*, 13(4), 671. <https://doi.org/10.3390/cancers13040671>
- Rosenberg, H. F., Dyer, K. D., & Foster, P. S. (2013). Eosinophils: changing perspectives in health and disease. *Nature Reviews Immunology*, 13(1), 9-22. <https://doi.org/10.1038/nri3341>
- Rosman, Y., Hornik-Lurie, T., Meir-Shafir, K., Lachover-Roth, I., Cohen-Engler, A., Munitz, A., & Confino-Cohen, R. (2022). Changes in peripheral blood eosinophils may predict colorectal cancer—A retrospective study. *World Allergy Organization Journal*, 15(10), 100696. <https://doi.org/10.1016/j.waojou.2022.100696>
- Saraiva, A. L., & Carneiro, F. (2018). New insights into the role of tissue eosinophils in the progression of colorectal cancer: a literature review. *Acta medica portuguesa*, 31(6),

329-337. <https://doi.org/10.20344/amp.10112>

Simon, S. C., Utikal, J., & Umansky, V. (2019). Opposing roles of eosinophils in cancer. *Cancer Immunology, Immunotherapy*, 68, 823-833. <https://doi.org/10.1007/s00262-018-2255-4>

Wechsler, M. E., Munitz, A., Ackerman, S. J., Drake, M. G., Jackson, D. J., Wardlaw, A. J., ... & Merkel, P. A. (2021, October). Eosinophils in health and disease: a state-of-the-art review. In *Mayo clinic proceedings* (Vol. 96, No. 10, pp. 2694-2707). Elsevier. <https://doi.org/10.1016/j.mayocp.2021.04.025>