Evaluation of Effectiveness of Hemogram Parameters

In Colorectal Cancer Screening

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ABSTRACT

Colorectal cancer (CRC) frequency and cancer-related death rates can be reduced with screening methods. Due to the invasiveness of the colonoscopy procedure and the high rate of false positivity of stool-based tests, it was aimed to investigate whether hemogram parameters could be a potential alternative to assist screening methods.

Between January 2023 and December 2024 at Van YYU Faculty of Medicine Hospital, 605 patients who underwent colonoscopy for various indications were divided into groups and the age, gender, hemogram parameters taken before colonoscopy, such as RBC Count, Hb, Hct, WBC Count, Platelet Count, MPV, MCV, RDW, NLR, PLR, MLR, MPV/PLT ratio, Hb/PLT ratio, Lymphocyte/Monocyte ratio and the Hb/RDW ratio were investigated and then the usability of these hemogram parameters in colorectal cancer screening was studied.

Statistical differences were observed in WBC, Hemoglobin, hematocrit, MCV, RDW, lymphocyte, MPV/PLT, Hb/PLT, Lymphocyte/monocyte and Hb/RDW ratios with T Test between cancer patients and patients with normal colonoscopy findings. Additionally, in multiple group comparisons, a statistically significant difference was detected in age, WBC, RBC and MCV parameters.

This study is the most comprehensive study ever conducted with 18 hemogram parameters. As a result of binary and multivariate analysis, a statistically significant difference was detected in 10 parameters with T Test and in 4 parameters with multivariate analysis. It was concluded that hemogram parameters will be used alone or in addition to existing screening methods in colorectal cancer screening through prospective studies with the appropriate combination of these parameters.

Keywords: colorectal cancer, screening, hemogram parameters

Introduction

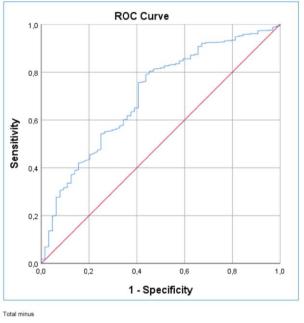
Colorectal cancers constitute the most common cancer group of the gastro intestinal tract and rank 2nd in the list of deaths from all cancers (1-3). Approximately 85% of colorectal cancers occur from polyps. Early detection and treatment of these polyps is important to reduce the risk of colorectal cancer (4). Screening methods are used for early detection of colorectal polyps and cancers. The gold standard in screening is colonoscopy (5). Since colonoscopy is an invasive procedure that requires colon preparation and general anesthesia and has complications, it is not suitable for every individual. (6). A fecal occult blood test(FOBT), which is a non-invasive test, is performed to narrow down the population to undergo colonoscopy(7). Although the FOBT test is useful in the early diagnosis of colorectal cancer, its use remains limited due to poor patient compliance (8). In Turkey, the situation is worse and the rate of FOBT is 13.2% (9). There is a need for a cheap, easily accessible and noninvasive test with good patient compliance that accurately narrows the indications for colonoscopy in the risk population for colorectal cancer screening. In this study, we wanted to investigate the usability of hemogram parameters.

Material and Methods

The study was conducted on patients aged between 18 and 80 who underwent colonoscopy in the endoscopy unit of Van Yüzüncü Yıl University Faculty of Medicine Hospital. Patients who underwent colonoscopy between January 2023 and December 2024 were included in the study. colonoscopy According to reports and histopathological results, the patients were divided into groups: colorectal cancer, polyp, 7 Inflammatory bowel disease, non-specific colitis or ileitis, normal findings, other benign findings, and the group with suspicion of malignancy on colonoscopy but histopathological data could not be obtained. Age, gender and the hemogram parameters that was taken before colonoscopy

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| Area | Std. Error | р | 95% Confidence Interval | | Cut off value | Sensitivity | Specificity |
|-------|------------|-------|-------------------------|-------------|---------------|-------------|-------------|
| | | | Lower Bound | Upper Bound | 93.0500 | 0.756 | 0.594 |
| 0.703 | 0.035 | 0.001 | 0.635 | 0.771 | 97.4500 | 0.651 | 0.609 |

Fig. 1. Brief Results of ROC Analysis

procedure such as Red Blood Cell (RBC) Count and Hemoglobin (Hb), Hct, white Blood Cell (WBC) Count, platelet Count, Platelet volume (MPV), mean Erythrocyte Volume (MCV), erythrocyte Distribution Width (RDW), neutrophil-lymphocyte ratio (NLR), plateletlymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR), MPV/PLT ratio, Hb/PLT ratio, Lymphocyte/monocyte ratio and Hb/RDW ratio results were examined and the usability of hemogram parameters in colorectal cancer screening was investigated. Patients diagnosed with colorectal cancer, patients whose hemogram results could not be obtained, and patients whose colonoscopy could not be completed were excluded from the study.

Statistical Analysis: Descriptive statistics for among continuous variables the features emphasized; While it is expressed as Mean, Standard Deviation, Minimum and Maximum values, it is expressed as number and percentage for categorical variables. One-way analysis of variance was performed to compare group averages in terms of continuous variables. Following the analysis of variance, Duncan multiple comparison test was used to determine different groups, and T Test was used for pairwise group comparison. To determine the relationship between these variables, Pearson correlation coefficients were calculated separately in the groups. Chi-square test was used to determine the

relationship between groups and categorical variables. In the calculations, the statistical significance level was taken as 5% and the SPSS (ver: 21) statistical package program was used for the calculations.

Results

A total of 605 patients were included in the study. 291 of the patients were male, 314 were female and the average age was 49.02. The distribution of hemogram parameters according to gender is shown in table 1. Statistically significant differences were detected in the hemogram parameters of WBC, Hemoglobin, hematocrit, MCV, RDW, lymphocyte, MPV/PLT, Hb/PLT, Lymphocyte/monocyte and Hb/RDW ratios between cancer patients and patients with normal colonoscopy findings (tables 2). In multiple group comparisons, a statistically significant difference was detected between the cancer group and the other groups in Age, WBC, RBC and MCV parameters (Table 3).

Discussion

Colorectal cancer is an important health problem worldwide and in Turkey. According to the 2016 report of the American Cancer Society, colorectal cancer stands out as the third most common type of cancer in both men and women (2). Current statistical data in Turkey is similar to literature data. Colorectal cancer ranks third in cancer and second in cancer-related deaths for both genders (3). Despite being so common and lethal, the fact that most colorectal cancers develop from polyps enables screening programs to reduce both cancer frequency and cancer-related death rates by diagnosing this malignancy before it develops or at an early stage.

The primary goal of colorectal cancer screening is to reduce the incidence of cancer, facilitate early detection of malignancies, and reduce cancerrelated mortality rates. There are non-invasive and invasive methods in the field of colorectal screening. Fecal occult blood test (FOBT) and Fecal Immunochemical Test (FIT) are the most commonly used non-invasive methods. FIT is preferred due to its higher sensitivity and specificity compared to FOBT (10). Apart from modalities such sigmoidoscopy, these, as colonoscopy, double contrast barium enema and virtual colonoscopy are used. Colonoscopy is considered the gold standard for CRC screening, allowing detection and removal of precancerous

Table 1: Distribution of Parameters by Gender

| Variables | Female (n:314) | Male (n:291) | P value |
|----------------|---------------------|---------------------|---------|
| Age, years | 48.04 ± 16.30 | 50.08 ± 15.29 | 0.113 |
| WBC (10^3/L) | 6.97 ± 1.94 | 7.35 ± 2.35 | 0.033 |
| RBC (10^6/uL) | 4.37 ± 0.76 | 4.77 ± 0.73 | 0.001 |
| HMG (g/dL) | 13.29 ± 5.74 | 14.61 ± 6.38 | 0.008 |
| НСТ (%) | 40.07 ± 5.42 | 45.06 ± 25.13 | 0.001 |
| MCV (fL) | 85.29 ± 23.87 | 84.98 ± 10.34 | 0.838 |
| PLT (10^3/uL) | 320.56 ± 266.77 | 262.05 ± 79.75 | 0.001 |
| RDW (%) | 42.91 ± 13.34 | 41.20 ± 5.60 | 0.042 |
| MPV (fL) | 10.97 ± 7.82 | 9.98 ± 1.12 | 0.034 |
| NTF (10^3/uL) | 6.19 ± 33.82 | 4.61 ± 2.03 | 0.427 |
| MONO (10^3/uL) | 0.56 ± 0.52 | 0.64 ± 0.49 | 0.047 |
| LENF (10^3/uL) | 2.29 ± 0.79 | 2.22 ± 0.75 | 0.235 |
| NTF/LENF | 3.82 ± 26.30 | 2.78 ± 4.78 | 0.506 |
| PLT/LENF | 164.01 ± 204.41 | 141.32 ± 157.14 | 0.129 |
| MONO/LENF | 0.28 ± 0.33 | 0.35 ± 0.69 | 0.093 |

Note: WBC: White blood cell count, RBC: Red blood cell count, MCV: Mean corpuscular volume, RDW: Red cell distribution width, MPV: Mean platelet volume.

Statistical significance set at p<0.05.

lesions (5, 10). Screening is performed for individuals at intermediate to high risk, with high efficacy observed in those classified as high risk. Colonoscopy is recommended for individuals considered at high risk, but there are no standard recommendations for individuals identified as intermediate risk (5, 11).

Awareness and low participation rates in colorectal cancer screenings also pose a serious problem. The Netherlands has the highest participation rates 68.2%, while at the participation rates in the USA are around 63%. (12, 13). The awareness and participation in CRC screening is lower than expected in Turkey. Awareness and participation rates for FOBT and colonoscopy are 19.3% and 13.2% for FOBT and 31.7% and 10.0% for colonoscopy, respectively (14).

Although colonoscopy is the gold standard method for CRC screening, it is an invasive procedure. Colonoscopy-related complications hinder patient participation due to discomfort during the procedure, preparation requirements, and accessibility issues (5, 6, 10). Since stool-based tests have high false positive rates and low sensitivity, there is a clear need for new less invasive, more accurate and cost-effective CRC screening methods (15, 16). In this context, bloodbased tests are being investigated as a potential tool for CRC screening. Blood-based tests are preferred in the detection of colorectal cancer for reasons such as low risk, minimal pain and ease of sample collection; however, concerns about their accuracy warrant further research (17).

Prediagnostic WBC counts, including leukocytes and neutrophils, have been shown to increase as CRC diagnosis approaches. These prediagnostic values are also associated with worse survival outcomes, highlighting the potential of WBC counts as early indicators of CRC prognosis (18). In our study, the increased leucocyte levels were found to be significant in CRC cases (p = 0.001). It was determined that the WBC count is a prognostic indicator in colorectal cancer patients (19) and that the preoperative WBC count is an independent risk factor for survival in patients undergoing colorectal surgery (20).

Because hypohemoglobinemia is common in the population with CRC (21), colorectal cancer (CRC) screening in patients with hypohemoglobinemia is very important due to the iron deficiency anemia (IDA) can be an important

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|-----------------------------|---------------------|---------------------|---------|
| Parameter | Cancer (n=64) | Normal (n=234) | P-Value |
| WBC $(10^{3}/\mu L)$ | 8.07 ± 2.56 | 6.75 ± 1.93 | 0.001 |
| Hemoglobin (g/dL) | 12.43 ± 2.39 | 13.82 ± 2.06 | 0.001 |
| Hematocrit (%) | 39.03 ± 6.79 | 42.34 ± 5.61 | 0.001 |
| RDW (%) | 43.13 ± 5.79 | 41.12 ± 6.13 | 0.020 |
| MCV (fL) | 80.64 ± 7.11 | 84.44 ± 9.26 | 0.003 |
| Lymphocytes $(10^3/\mu L)$ | 2.07 ± 0.87 | 2.31 ± 0.72 | 0.026 |
| MPV/PLT Ratio | 0.0325 ± 0.0100 | 0.0449 ± 0.0415 | 0.018 |
| Hemoglobin/PLT Ratio | 0.0411 ± 0.0140 | 0.0579 ± 0.0521 | 0.015 |
| Lymphocyte/Monocyte Ratio | 3.55 ± 1.86 | 4.73 ± 1.95 | 0.001 |
| Hemoglobin/RDW Ratio | 0.2958 ± 0.0763 | 0.3507 ± 0.1289 | 0.001 |
| Platelet $(10^3/\mu L)$ | 331.63 ± 91.89 | 297.60 ± 301.90 | 0.374 |
| MPV (fL) | 9.82 ± 0.89 | 10.56 ± 6.19 | 0.343 |
| Neutrophils $(10^3/\mu L)$ | 5.52 ± 2.38 | 6.60 ± 39.12 | 0.826 |
| RBC $(10^{6}/\mu L)$ | 4.41 ± 0.77 | 4.58 ± 0.67 | 0.074 |
| Monocytes $(10^3/\mu L)$ | 0.64 ± 0.23 | 0.61 ± 0.76 | 0.702 |
| Neutrophil/Lymphocyte Ratio | 3.69 ± 2.94 | 4.08 ± 30.46 | 0.848 |
| Platelet/Lymphocyte Ratio | 185.93 ± 92.75 | 150.73 ± 229.49 | 0.231 |
| Monocyte/Lymphocyte Ratio | 0.36 ± 0.19 | 0.29 ± 0.47 | 0.292 |
| | | | |

Table 2: Distribution of Blood Parameters According to Colonoscopy Findings (Cancer vs Normal)

Note: Statistical significance p<0.05

indicator of underlying malignancies, especially right-sided CRC in individuals over 40 years of age (22). A study by Almilaji et al shows that iron deficiency anemia is an important determinant of right-sided colorectal cancer (CRC) and that individuals screening for CRC in with hypohemoglobinemia may improve early diagnosis and potentially increase prognosis (23). In our study, hemoglobin values were lower than in normal individuals, and this was statistically significant (p = 0.001).

Mean corpuscular volume (MCV) has emerged as a potential indicator in colorectal cancer (CRC) screening, particularly to detect advanced colorectal cancer (ACRC). MCV offers a noninvasive, cost-effective alternative that may increase early diagnosis, especially in older particularly populations. This approach is important given the challenges and limitations associated with current CRC screening methods, such as low participation rates and the need for accurate and accessible more techniques. Integration of MCV into CRC screening protocols could potentially improve detection rates and

patient outcomes. A study by A Leischker shows that reduced mean corpuscular volume (MCV) serves as an independent predictor for the detection of advanced colorectal cancer (ACRC) in patients even in the absence of symptoms. This suggests that MCV may be a valuable clinical determine the indicator to necessity of colonoscopy in elderly patients and highlights its role in colorectal cancer screening, and these findings highlight the importance of considering MCV levels alongside traditional screening methods to improve early diagnosis of ACRC (24). In our series, MCV was found to be lower in individuals with CRC, and this was significant in both T test and multivariate analysis (p = 0.03).

Red cell distribution width (RDW) has emerged as a potential biomarker in colorectal cancer (CRC) screening and provides insights into tumor characteristics and patient prognosis. RDW, a measure of variation in red blood cell size, is routinely included in complete blood count tests and has been associated with systemic inflammation and cancer progression. Its role in CRC screening is multifaceted, covering

| Paramete rs | Cancer (n:64) | Polyp (n:84) | IBD (n:41) | Non- spesif | Normal (n:233) | Other findin | Patology missing | P value |
|----------------|------------------|-------------------|------------------|-----------------------|-------------------|-----------------------|---------------------|---------|
| | | | | ic colit (n:59) | | gs (n:107) | (n:15) | |
| Age, | 56.5±12.96 | 58.14±11.99 | 41.97±15.5 | 39.32 | 45.72±15.99cd | / | | 0.001 |
| years | ab | a | 9d | ±14.2 0e | | 51.34± 15.77b c | 58.26±15.14 a | |
| WBC | 8.07±2.56a | 7.30±2.09ab | 8.06±2.77a | 7.03± 2.34b | 6.75±1.93b | 7.02±1 .87b | 7.53±1.30ab | 0.001 |
| RBC | 4.40±0.77a | 4.51±0.66a | 4.55±1.50a | 4.68± | | | | 0.037 |
| | | | | 0.68a | 4.58±0.66a | 4.68±0 .68a | 4.06±0.59b | |
| HMG | 12.42±2.38 | 14.82±11.25 | 13.63±5.82 | 15.60 ±12.0 9 | 13.81±2.05 | 13.84± 2.09 | 11.69±2.06 | 0.053 |
| НСТ | 39.03±6.78 | 41.54±5.74 | 41.14±8.32 | 43.38 ±5.08 | 42.34±5.61 | 46.33± 40.44 | 36.46±5.73 | 0.143 |
| MCV | 80.64±7.10 b | 85.53±15.81 b | 93.82±58.8 9a | 85.16 ±6.36 b | 84.44±9.26b | 86.07± 13.16b | 82.40±8.74b | 0.033 |
| PLT | 331.6±9.8 | 293.3±95.17 | 297.3±124. 3 | 165.9 ±73.8 | 295.3±301 | 265.1± 83.2 | 325.8±118 | 0.426 |
| RDW | 43.12±5.79 ab | 44.96±23.16 ab | 43.05±8.22 ab | 40.88 ±6.53 b | 41.12±6.13b | 41.01± 4.21b | 46.46±9.39a | 0.028 |
| MPW | 9.82±0.88 | 10.65±3.87 | 9.88±0.87 | 10.33 ±1.01 | 10.56±6.19 | 10.97± 9.31 | 10.22±1.42 | 0.890 |
| NTF | 5.52±2.37 | 4.48±1.87 | 5.24±1.99 | 4.38± 1.90 | 6.59±39.12 | 4.27±1 .54 | 4.96±1.46 | 0.985 |
| MONO | 0.64±0.23 | 0.58±0.19 | 0.64±0.31 | 0.55± 0.18 | 0.60 ± 0.76 | 0.56±0 .22 | 0.59±0.15 | 0.934 |
| LENF | 2.07±0.86 | 2.37±0.83 | 2.16±0.69 | 2.19± 0.72 | 2.31±0.72 | 2.27±0 .80 | 1.84±0.60 | 0.058 |
| NTF/LE NF | 3.68±2.93 | 2.20±1.54 | 2.93±2.78 | 2.40± 2.07 | 4.07±30.46 | 2.72±7 .10 | 5.20±3.66 | 0.983 |
| PLT/LN F | 185.9±92.7 | 140.7±75.6 | 150.8±92.3 | 129.3 ±46.5 | 157.2±229 | 156.6± 243 | 193.9±83.7 | 0.645 |
| MONO/ LNF | 0.35±0.19 | 0.27±0.14 | 0.30±0.12 | 0.27± 0.11 | 0.29±0.46 | 0.36±1 .04 | 0.38±0.25 | 0.840 |

Table 3: Multiple Group Comparisons Using Duncan Multiple Comparison

a,b,c \rightarrow : Different lower cases in the same row represent statistically significant differences among the groups. No lettering was made for the features for which no difference was found to be significant. Department of General Surgery, Van Yuzuncu Yil University Faculty of Medicine

diagnostic, prognostic and predictive aspects. One study found 80% sensitivity and 60% specificity for RDW in predicting colon cancer. This suggests that RDW may serve as a useful marker in the early detection of colorectal cancer, complementing current screening methods (25). Another study suggests that red blood cell distribution width (RDW) may serve as an additional marker for differential diagnosis in colorectal cancer (CRC), particularly in identifying right-sided CRC. It showed a sensitivity of 76.3% and a specificity of 64.2%, highlighting the importance of RDW in clinical assessments regarding CRC localization (26). In our series, a significant difference was found between CRC cases and normal individuals (p = 0.02).

Lymphocyte count plays an important role in colorectal cancer (CRC) screening, serving as a prognostic marker and helping stratify patients for treatment decisions. It was found that high lymphocyte count was associated with a higher 5-year overall survival (OS) rate compared to low lymphocyte count (27). In our series, lymphocyte values showed a significant decrease compared to normal individuals (p = 0.026).

Red blood cell count (RBC) contributes significantly to prognostic assessment in colorectal cancer (CRC) screening by demonstrating overall survival outcomes. The study found that patients with higher RBC levels ($\geq 3.9 \times 10^{-12}/L$) experienced significantly improved overall survival compared to those with lower levels (28). In our series, lower RBC numbers were detected in individuals with CRC than in normal individuals (p = 0.037).

The lymphocyte-to-monocyte ratio (LMR) is a valuable screening tool, with low levels indicating more advanced stages of CRC. The lymphocyteto-monocyte ratio (LMR) serves as an indicator of inflammation and shown has significant differences between colorectal cancer (CRC) patients and healthy individuals (29). In our study, LMR rates were found to be lower in individuals with cancer (p=0.001). Studies have also shown that a high LMR is associated with improved overall survival (OS) and recurrence-free survival (RFS) in CRC patients (30, 31). One study found that MPV/PC was lower in colorectal cancer patients compared to those with adenomatous polyps and healthy controls (32). Mean Platelet Volume (MPV) is a measure of the average platelet size in the blood and is considered a marker of platelet activation. It reflects the functional status of platelets, which can be affected by various physiological and pathological conditions, including cancer (33, 34). The ratio of MPV to platelet count (PC), known as MPV/PC, has been highlighted as a potentially more informative marker for cancer diagnosis than MPV or PC alone. This ratio provides a better diagnostic and predictive value by integrating both

the size and quantity of platelets (35, 36). Studies show that the MPV/PLT ratio is significantly lower in CRC patients compared to those with adenomatous polyps and healthy controls. This suggests that a lower MPV/PLT ratio may be indicative of the presence of CRC (37). In our study, MPV/PC was found to be lower in individuals with CRC. (p=0.018). Although the Hb/RDW ratio alone is not sufficient for the diagnosis of CRC, its combination with other markers increases diagnostic accuracy. Combined use of RDW with CEA and CA19-9 specificity increases sensitivity and in distinguishing CRC patients from healthy controls (38). In our study, the Hb/RDW ratio was found to be lower in individuals with CRC than in normal individuals (p=0.001). A low Hb/RDW ratio is similarly associated with advanced disease stages and poorer prognosis in CRC patients (39). Additionally, we could not find any studies in the literature on the Hb/Plt ratio, which we found to be statistically significantly lower in individuals with CRC compared to normal individuals in our series (p=0.005).

Although the combined use of neutrophillymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and monocyte-lymphocyte ratio (MLR) were found to be useful parameters in predicting the surveillance analysis of endometrial cancer, they were not found to be effective in predicting the diagnosis of colorectal cancer in our study (40, 41).

ROC analysis was performed to determine a cut off value that can be used to identify patients who need colonoscopy and those who do not need colonoscopy by using the value formed by the sum of haemogram values. As a result of the ROC analysis, the area under the curve was found to be 0.703 square units and statistically significant (p<0.001). Accordingly, Sensitivity was found to be 75.6% and Specificity was found to be 59.4% for 93.05 cut off value, while Sensitivity was found to be 65.1% and Specificity was found to be 60.9% for 97.45 cut off value.

Accordingly, if patients with a value lower than 93.05 are sent to colonoscopy, it is predicted that 75.6% of these patients will actually require colonoscopy, similarly, if patients with a value above this value (93.05) are not sent to colonoscopy, it is predicted that 60.9% of them will not require colonoscopy.

In conclusion, the incidence of CRC and cancerrelated mortality rates can be reduced with screening methods. Due to the invasive nature of colonoscopy and the high rate of false positivity in stool-based tests, we demonstrated in this study that hemogram parameters are a potential alternative. The limitation of this study is that it is retrospective. The presented study is the most comprehensive study ever conducted with hemogram parameters and was conducted with 18 hemogram parameters, and as a result of binary and multivariate analyses, statistically significant differences were detected in 10 parameters with T test and in 3 parameters with multivariate analysis. As a result of this study, we believe that prospective studies with the appropriate combination of these parameters will be used in CRC screening by hemogram parameters alone or in addition to existing screening methods.

Conflicts of Interest: The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Patient Permission/Consent Declaration: Verbal consent was obtained from the cases included in the study by calling the contact numbers registered in the system.

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