# CLINICAL STUDY

# Thrombocyte decrease and hemoglobin level as simple noninflammatory predictors of anastomotic leakage in rectalcancer surgery

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#### ABSTRACT

PURPOSE: The study aimed to determine a simple diagnostic test that could predict the risk of anastomotic leakage in early postoperative period.

METHODS: A single-center, retrospective study was conducted. The electronic medical records of patients who underwent resection for rectal tumor between January 1, 2016, and December 31, 2021, in University Hospital Olomouc, were reviewed. The data included risk factors for leakage and laboratory parameters commonly obtained.

RESULTS: The decrease in platelets was significant as for the possibility of being a marker of anastomotic leakage; OR = 0.980 (p = 0.036). A decrease of 34 or higher predicts leakage with a sensitivity of 45 % (95 % CI: 23.1–68.5 %) and specificity of 81.1 % (95 % CI: 75.2–86.1 %). Postoperative leukocyte blood level (OR = 1.134; p = 0.019) and leukocyte level on postoperative day 1 (OR = 1.184; p = 0.023) were significant predictors for leakage. WBC values  $\geq$  8.8 predict leakage with a sensitivity of 70.0 % (95 % CI: 45.7–88.1 %) and specificity of 55.3 % (95 % CI: 48.4–62.0 %). Hemoglobin blood level  $\leq$  79.5 predicts leakage with a sensitivity of 70.0 % (95 % CI: 45.7–88.1 %) and specificity of 62.2 % (95 % CI: 55.5–68.7 %). CONCLUSION: Despite the fact that the specificity and sensitivity of the followed parameters are low, they could serve as markers useful for early diagnosis or suspicion for leakage (*Tab. 5, Fig. 3, Ref. 14*). Text in PDF *www.elis.sk* 

KEY WORDS: anastomotic leakage, rectal tumor, thrombocytes, hemoglobin, white blood cells.

# Introduction

Anastomotic leakage (AL) remains the most challenging complication after colorectal surgery with rates varying between 1 and 19 % depending on the site of anastomosis, ileocolic (1–8 %), colocolic (2–3 %), ileorectal (3–7 %), colorectal or coloanal (5– 19 %) risk factors, and significantly also on AL definition. AL is associated with higher mortality and high short- and long-term morbidity rates, increased local recurrence, and impaired quality of life (1, 2).

Reoperation after AL has been associated with a high mortality rate accounting for up to 21.4 % of deaths and significantly worse recurrence-free and tumor-specific survival as compared to those treated conservatively (3).

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Considering the risks and complications associated with anastomotic leakage, the objective is to diagnose it as early and accurately as possible. According to available sources, the time from surgery to anastomotic leakage diagnosis varies between 4 to 12.7 days (4).

We have multiple options for more and less invasive diagnostic tools. The radiological standard is computed tomography (CT). CT scan alone gives a clear diagnosis of an anastomotic leak no sooner than in 8.5 days on average. We have to consider that in the early postoperative period, up to a quarter of CT scans in patients with conclusively confirmed leakage, are negative. Surgical revision alone, based on the clinical condition of the patient, shortens the time of establishing the diagnosis of a leak to 4.3 days (5). However, it is a very invasive way of diagnosis and involves very complicated rectal surgery. Here, we prefer endoscopic diagnosis for its accessibility and elegance while the subsequent treatment can vary from simple endoscopic drainage to surgical revision, depending on the extent of the lesion.

The reduction in time necessary for establishing the diagnosis is made possible by various laboratory and clinical scoring systems, which can be employed in the early postoperative period in a daily fashion. The most widely known is the DULK leakage score, which can shorten the diagnosis of a leak down to 4 days, while the other less well-known option is the DIACOLE score - which is quite complex and requires its own software for calculation. The prerequisite of both modalities for establishing the diagnosis early lies in employing the monitoring in a regular daily fashion.

The diagnosis of leakage by means of the abdominal secretion analysis is still an experimental method requiring complex procedures, which have not yet reached routine clinical practice. Promising results were shown by ELISA diagnosis of monocyte chemoattractant protein 2 (CCL8/MCP-2), leukemia-inhibiting factor (LIF), and epithelial-derived neutrophil-activating protein (CXCL5/ENA-78) which were significantly elevated in peritoneal fluid but not in serum samples from patients subsequently developing anastomotic leakage after colorectal surgery (6). However, the best prediction was achieved on the 3rd postoperative day.

We aimed to determine whether there is a simple screening parameter that could indicate the risk of anastomotic leakage in the early postoperative period.

# Method

# Study design

The aim was to determine whether there was a possibility of a simple diagnostic test that would be based on commonly obtained laboratory parameters and at the same time indicative of patients at risk of anastomotic leakage development in a very early postoperative period after curative resection for rectal tumor.

The study is in accordance with the Declaration of Helsinki and was conducted in compliance with the Strengthening the Reporting of Observational Studies (STROBE) guidelines (7). All 237 subjects included in this study signed an informed consent form for the use of personal data and were provided with written information about the study.

The primary endpoint was to diagnose anastomotic leakage, which we defined and graded by the International Study Group of Rectal Cancer (ISREC) in 2010 (8). Leakage was diagnosed by clinical status, laboratory results and confirmed by computed

Tab. 1. General characteristics of the cohort, and its relationship to anastomotic leak for-
mation; the only parameter with statistical significance, of all the observed, is male gender;
p-values were evaluated by Chi-square test or Fisher's exact test.

		Whole Cohort		No leal	k (n=217)	Leaks	Leaks (n=20)		
	-	No	%	No	%	No	%	- р	
	f	86	36.3 %	84	38.7 %	2	10.0 %	0.011	
Gender	m	151	63.7 %	133	61.3 %	18	90.0 %	0.011	
	Ι	22	9.3 %	20	9.2 %	2	10.0 %		
ASA score	II	181	76.4 %	165	76.0 %	16	80.0 %	1 000	
ASA Store	III	33	13.9 %	31	14.3 %	2	10.0 %	1.000	
	IV	1	0.4 %	1	0.5 %	0	0.0 %		
Smoking	No	192	81.0 %	177	81.6 %	15	75.0 %	0.550	
history	Yes	45	19.0 %	40	18.4 %	5	25.0 %		
Alcohol	No	100	42.2 %	91	41.9 %	9	45.0 %	0.791	
consumption	Yes	13/	57.8%	126	58.1 %	11	55.0 %		
Previous	No	130	54.9 %	118	54.4 %	12	60.0 %	0.629	
operation	Yes	107	45.1 %	99	45.6 %	8	40.0 %		
Major	No	197	83.1 %	179	82.5 %	18	90.0 %	0.541	
operation	Yes	40	16.9 %	38	1/.5 %	2	10.0 %		
Relationship to	N0 Var	208	8/.8%	188	86.6 %	20	100.0 %	0.145	
	N	121	12.2 70	29	13.4 %	15	0.0 %		
Radiotherapy	N0 Vac	131	55.5 % 44.5 %	116	55.1% 16.2.0/	15	/5.0 %	0.067	
A 4 -	res	105	44.5 %	200	40.3 %	3	25.0 %		
Autoimmune	N0 Vac	10	95.8 % 4 2 %	208	95.9 % 4 1 %	19	95.0 % 5.0 %	0.593	
	N	210	4.2 70	200	4.1 70	10	3.0 %		
Other cancer	N0 Vac	218	92.0 %	200	92.2 % 7 8 %	18	90.0 %	0.667	
uisease	N	19	0.0 /0	17	/.0 /0	2	10.0 /0		
Hypertension	N0 Vac	101	42.6 % 57.4 %	93	42.9 % 57 1 %	8 12	40.0 %	0.805	
Thursid	No	215	00.7.0/	124	20.0.0/	20			
disease	N0 Vec	213	90.7 %	195	89.9 % 10 1 %	20	0.0%	0.230	
Heart	No	100	80.2.%	175	80.6 %	15	75.0%		
disease	Ves	190 47	19.8 %	42	19.4 %	5	25.0 %	0.560	
Eat metabolism	No	145	61.2 %	132	60.8 %	13	65.0 %		
disorder	Yes	92	38.8 %	85	39.2 %	7	35.0 %	0.714	
Diabetes	No	200	84.4 %	185	85.3.%	15	75.0%		
mellitus	Yes	37	15.6 %	32	147%	5	25.0 %	0.212	
	No	219	92.4 %	202	93.1 %	17	85.0 %		
Lung disease	Yes	18	7.6 %	15	6.9 %	3	15.0 %	0.184	
	No	230	97.0 %	211	97.2 %	19	95.0 %		
Renal disease	Yes	7	3.0 %	6	2.8 %	1	5.0 %	0.465	
Hematologic	No	231	97.5 %	211	97.2 %	20	100.0 %	1 000	
disorders	Yes	6	2.5 %	6	2.8 %	0	0.0 %	1.000	
	1	212	89.5 %	193	88.9 %	19	95.0 %		
Number of	2	22	9.3 %	21	9.7 %	1	5.0 %	0.772	
	3	3	1.3 %	3	1.4 %	0	0.0 %		
	25	10	4.2 %	10	4.6 %	0	0.0 %		
	28	77	32.5 %	73	33.6 %	4	20.0 %		
Size of stapler	29	102	43.0 %	91	41.9 %	11	55.0 %	0.274	
	31	45	19.0 %	41	18.9 %	4	20.0 %		
	33	3	1.3 %	2	0.9 %	1	5.0 %		
	0	19	8.1%	17	7.9%	2	10.0 %		
	I II	/8	33.1 % 0.8 %	2	33.3 % 0.0 %	6	30.0 %	0.726	
	11 Ha	2 49	20.8 %	46	21.3 %	3	15.0 %		
Tumour stage	IIb	2	0.8 %	2	0.9 %	0	0.0 %		
	IIIa	15	6.4 %	14	6.5 %	1	5.0 %		
	IIIb	42	17.8 %	39	18.1 %	3	15.0 %		
	IIIc	9	3.8 %	8	3.7 %	1	5.0 %		
	IV	20	8.5 %	16	7.4 %	4	20.0 %		

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tomography scanning. Treatment was indicated according to the CT findings. Surgical revision was performed in case of grade C lesion and further diagnosis by endoscopy was proceeded in case of more favorable findings. No therapeutic intervention was done in patients with grade-A lesion while those with grade B were treated endoscopically during the diagnostic procedure.

The secondary endpoint was to identify the statistical significance of standard, routinely collected laboratory parameters in patients with a proven anastomotic leak in the early postoperative period and thus to identify patients at risk for leak development. We focused on the evaluation of white blood cells, platelets, and red blood cells levels, their trends, and correlations from patient samples collected immediately after surgery and on the following day.

#### Settings

The study was conducted at a Faculty Hospital Olomouc, a complex oncology center. Study included data of patients after rectal resection who met the inclusion criteria. Data were obtained from the institutional database covering the period from January 1, 2016, to December 31, 2021.

## Participants

Enrolled were 237 patients with rectal cancer requiring surgical treatment at the Department of Surgery, Faculty Hospital Olomouc, Czech Republic. Inclusion criteria were as follows: non-emergent surgery, primary anastomosis, age over 18 years, and patients with a pathologically confirmed rectal tumor (localized not further than 15 cm from anal verge). Exclusion criteria were as follows: acute surgery, construction of primary oostomy, resections for benign lesions, ulcerative colitis or rectal form of Crohn disease, when the surgery was considered as a reoperation, reversal of a stoma, and ileo pouch-anal anastomosis All operations were performed

Tab. 2. General characteristics of the cohort, and its relationship to anastomotic leak formation; the only parameter with statistical significance, of all the observed, is lower age; p values were evaluated by Mann-Whitney U test.

		Whole cohort	No Leak	Leaks	р
	Average	65.8	66.4	59.7	
Age	SD	11.2	11.3	9.0	
(years)	Median	67.0	68.0	60.5	0.004
	Minimum	29.0	29.0	44.0	
	Maximum	93.0	93.0	75.0	
	Average	26.9	26.9	26.9	
BMI	SD	4.8	4.8	4.7	
$(kg/m^2)$	Median	26.8	26.7	27.4	0.953
	Minimum	0.0	0.0	18.1	
	Maximum	42.4	42.4	37.5	
Tumour	Median	10.0	10.0	9.5	
distance	Minimum	3	4	3	0.517
(cm)	Maximum	15	15	15	
Thickness	Median	9.0	9.0	10.0	
of donut	Minimum	2	2	5	0.318
(mm)	Maximum	19	19	15	
Tumour distance	Median	17.5	18.0	15.0	
- distal edge of	Minimum	2	2	3	0.186
specimen (mm)	Maximum	65	65	41	

by surgeons experienced in coloproctology (over ten years of experience in colorectal tumor surgery).

In addition to standard postoperative care, the follow-up included active search for complications according to the DULK leakage score. The follow-up was brought to a finish with the diagnosis of leakage or approximately 3–6 months after the surgical procedure when the patient was re-evaluated, and the insertion of loop ileostomy was performed according to the findings.

#### Variables

We collected information on age, sex, tumor distance, body mass index (BMI), American Society of Anesthesiologists (ASA) score, history of abdominal surgery, tumor and autoimmune disease, hypertension, cardiac, thyroid gland, pulmonary, kidney and hematological disease, history of smoking and alcohol consumption. We took blood and recorded blood count immediately after the surgery and in the morning of the next day. We monitored the change in serum hemoglobin, leukocytes, thrombocytes, and actively searched for the signs of leakage.

#### Diagnosis of AL

AL was diagnosed through clinical and radiologic findings by (a) presence of air or abscess near the site of anastomosis detected on computed tomography (CT); (b) purulent or enteric discharge through the drainage tube; and/or (c) clinical signs of peritonitis and/or presence of fecal or purulent discharge during re-operation.

Tab. 3. Evaluation of the predictor of leak for the difference group of the observed parameters. Platelet decrease is shown to be a statistically significant prediction parameter; p value was evaluated by Mann-Whitney U test.

		No leak	Leaks	р	
	Median	11	14		
Hb difference	Minimum	-15	-8	0.335	
	Maximum	85	37		
	Median	-2.15	-2.60		
WBC difference	Minimum	-12.92	-12.14	0.608	
	Maximum	5.89	4.83		
	Median	-14	-28		
Thrombocyte difference	Minimum	-102	-69	0.023	
	Maximum	88	4		
	Median	-1.49	-0.40		
Ratio Hb/WBC difference	Minimum	-30.31	-20.60	0.567	
	Maximum	54.58	5.47		
	Median	-2.90	-1.28		
Ratio Th/WBC difference	Minimum	-33.91	-36.72	0.275	
	Maximum	32.97	14.75		

Tab. 4. Results of logistic regression analysis – estimation of OR parameters for leak prediction.

	Sig	OP	95 % C.I. for OR		
	Sig.	ÜK	Lower	Upper	
Hb difference	0.522	1.014	0.972	1.058	
WBC difference	0.466	0.948	0.822	1.094	
Thrombocyte difference	0.036	0.980	0.962	0.999	
Ratio Hb/WBC difference	0.684	0.984	0.908	1.065	
Ratio Th/WBC difference	0.798	1.008	0.951	1.067	

# Biases

The source of possible bias can be attributed to a small set of patients and low number of leaks, which downplays the general validity of the results. There is also the possibility of unintended selection bias based on geographical location and university hospital's catchment area.

# Statistical methods

IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA) was used for data analysis. The quantitative parameters of patients were compared using the Mann-Whitney U test. The Chisquare test and Fisher's exact test were used to compare qualitative parameters. Significant factors were determined using Cox regression analysis. Logistic regression analysis was used to calculate the odds ratio (OR) of each parameter. Optimal cut-off values were derived from receiver operating characteristic curves. Normally distributed data were tested using the Shapiro-Wilk test. All tests were performed at the significance level of 0.05.

# Results

## Participants

A total of 656 patients with rectal tumor received surgery during the study period, 239 patients (151 men and 86 women) met the inclusion criteria.

#### Descriptive data

From the basic demographic data, we confirmed the statistical significance of male sex on the development of leakage (p = 0.011) and lower age as a statistically significant parameter for the development of leakage in rectal tumor (median 60.5 vs 67.0 p = 0.004).

Tab. 5. Estimation of the unadjusted value of OR statistic in predicting leak formation for parameters measured on the day of surgery and those measured on POD 1. Leukocyte levels immediately after surgery and on POD 1 are significant predictors of leak formation.

Operation day					Postoperative day 1 (POD1)			
		95% CI for OR				OD	95% CI for OR	
р	0K	Lower	Upper	ł	р	OK	Lower	Upper
0.019	1.143	1.023	1.277	0.0	23	1.184	1.024	1.369
0.061	1.028	0.999	1.058	0.0	89	1.029	0.996	1.064
0.060	1.007	1.000	1.015	0.3	25	1.004	0.996	1.013
0.155	0.903	0.785	1.039	0.2	72	0.939	0.840	1.050
0.350	0.967	0.902	1.037	0.3	01	0.969	0.912	1.029
	p 0.019 0.061 0.060 0.155 0.350	Operation   p OR   0.061 1.028   0.060 1.007   0.155 0.903   0.350 0.967	Operation day   p OR 95% CI Lower   0.019 1.143 1.023   0.061 1.028 0.999   0.060 1.007 1.000   0.155 0.903 0.785   0.350 0.967 0.902	Operation day   95% CI for OR   p OR 25% CI for OR   Lower Upper   0.019 1.143 1.023 1.277   0.061 1.028 0.999 1.058   0.060 1.007 1.000 1.015   0.155 0.903 0.785 1.039   0.350 0.967 0.902 1.037	Operation day   95% CI for OR   Lower Upper   0.019 1.143 1.023 1.277 0.0   0.061 1.028 0.999 1.058 0.0 0.0   0.060 1.007 1.000 1.015 0.3 0.2 0.350 0.967 0.902 1.037 0.3	Operation day Pos   p OR 95% CI for OR Lower p p   0.019 1.143 1.023 1.277 0.023   0.061 1.028 0.999 1.058 0.089   0.060 1.007 1.000 1.015 0.325   0.155 0.903 0.785 1.039 0.272   0.350 0.967 0.902 1.037 0.301	Operation day Postoperative   p OR 95% CI for OR Lower p P OR   0.019 1.143 1.023 1.277 0.023 1.184   0.061 1.028 0.999 1.058 0.089 1.029   0.060 1.007 1.000 1.015 0.325 1.004   0.155 0.903 0.785 1.039 0.272 0.939   0.350 0.967 0.902 1.037 0.301 0.969	Operation day Postoperative day 1 (P   p 0R 95% CI for OR Lower p 0R 95% CI Lower   0.019 1.143 1.023 1.277 0.023 1.184 1.024   0.061 1.028 0.999 1.058 0.089 1.029 0.996   0.060 1.007 1.000 1.015 0.325 1.004 0.996   0.155 0.903 0.785 1.039 0.272 0.939 0.840   0.350 0.967 0.902 1.037 0.301 0.969 0.912

Tab. 6. Estimation of AUC statistic of parameters measured immediately after surgery; highest AUC value is that for hemoglobin and for parameters measured on POD 1, the highest AUC value is that for the leukocyte blood level.

	Operation day				Postoperative day 1 (POD1)			
		AUC	95% CI for AUC			ALIC	95% CI for AUC	
	р	AUC	Lower	Upper	р	AUC	Lower	Upper
Leukocyte (WBC)	0.076	0.620	0.506	0.734	0.035	0.642	0.520	0.765
Hemoglobin (Hb)	0.035	0.643	0.516	0.770	0.123	0.604	0.455	0.754
Thrombocyte (TC)	0.101	0.611	0.462	0.759	0.419	0.555	0.401	0.708
ratio Hb/WBC	0.288	0.572	0.455	0.688	0.178	0.591	0.646	0.718
ratio TC/WBC	0.349	0.563	0.419	0.708	0.075	0.621	0.485	0.756



Fig. 1. ROC curve for platelet difference parameter relative to leak incidence.

Other parameters reflecting the general condition that we expected to affect leak formation, namely American Society of Anesthesiologists (ASA) score (p = 1.0), history of smoking (p = 0.550), or alcohol consumption (p = 0.791) did not reach statistical significance. Associated diseases from personal history that were associated with worse blood oxygen distribution or overall blood distribution also did not reach statistical significance, namely

heart disease (p = 0.560), hypertension (p = 0.805), fat metabolism disorder (p = 0.714), pulmonary disease (p = 0.184) or hematological disease (p = 1.0). As for surgery alone, neither major previous surgery (p = 0.541) nor surgery with rectum involvement (p = 0.145) had an effect on the development of anastomotic leak, as was the case in the number of charges (p = 0.772), stapler size (p = 0.274), distance of tumor from sphincter (p = 0.517) or distal resection line (p = 0.186), donut thickness (p = 0.318), or previous radiotherapy (p = 0.067). The final disease stage was also without statistical significance (p=0.726) (Tabs 1 and 2).

# Outcome data

The incidence of leaks was 6.27 % (15 patients, 8 with protective loop ileostomy and 7 without). The incidence of leaks was 6 times in the upper rectum (11-15 cm above the anal verge; 2.5 %), and 9 in the middle and lower rectum (3–10 cm, 3.77 %). As for clinically significant leaks only, the in-

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cidence would be 5.4 % (13 patients). The distribution of stages of the disease relative to the incidence of leaks was spread quite evenly with the maximum incidence in stage III where there were 5 leaks (IIIa 1x, IIIb 3x, IIIc 1x,) followed by stages 0, I, II, and IV, with 2, 3, and 3 leaks, respectively. Surprisingly, the effect of radiotherapy on leak formation was minimal (in 2 patients only).

## Results

Statistical comparison of basic laboratory values of hemoglobin, leukocyte, thrombocytes and their ratios, and trends in the early postoperative period were divided into the assessment of the prediction of leak based on the difference in the change in each parameter and for each parameter separately.

In the difference group, the decrease in platelets was a significant candidate for being a marker of anastomotic leak (OR = 0.980; p = 0.036). The cut-off value is 34. A postoperative platelet decrease of 34 or higher predicts leakage with a sensitivity of 45 % (95% CI: 23.1–68.5 %) and specificity of 81.1 % (95% CI: 75.2–86.1 %). The OR statistic is 3.512 (95% CI: 1.366–9.029); p = 0.009 (Tabs 3 and 4, Fig. 1).

As for statistics for each parameter, separately, the postoperative leukocyte blood level (OR = 1.134; p = 0.019) and leukocyte level on postoperative day 1 (POD 1) (OR = 1.184; p = 0.023) were significant predictors of leak development (Tab. 5).

Estimation of the AUC statistics: Of the parameters measured immediately after surgery, the highest AUC value was that for hemoglobin (AUC = 0.643; p = 0.035) with cut-off value of 79.5. Hemoglobin blood level  $\geq$  79.5 predicts leakage with a sensitivity of 70.0 % (95% CI: 45.7–88.1 %) and specificity of 62.2 % (95 % CI: 55.5–68.7 %). Among the parameters measured by POD 1, the high-

est AUC value was that for the leukocytes (AUC = 0.642; p = 0.035) with cut-off value of 8.8. Leukocyte blood level values  $\geq$  8.8 predict leakage with a sensitivity of 70.0 % (95% CI: 45.7–88.1 %) and specificity of 55.3 % (95 % CI: 48.4–62.0 %) (Tab. 6, Figs 2 and 3).

### Discussion

To prevent the worst outcomes in patients with AL, early diagnosis is crucial. If the patient's ability to naturally heal is compromised, AL can occur, even if the surgery is flawless. Therefore, the gaining of ability to predict which patients are at high risk for AL would facilitate more careful monitoring and faster diagnosis for AL. In general, male sex (OR = 2.40, p = 0.004), Charlson comorbidity index > 5 (OR = 1.72, p = 0.025), and T3/T4 stage tumors (OR = 2.25, p = 0.017) were risk factors for AL after rectal resection (9). From our study, male gender (p = 0.011) and higher age (age of 60 years; p = 0.004) were statistically confirmed.

There is no doubt that inflammation plays a role in AL, but so far, it remains unclear as to which cellular and molecular aspects of inflammation are related to AL. It is a complex process, and according to the available evidence, the gut microbiome plays a key role in its regulation. Several anti-inflammatory interventions and their role in the prevention of AL have been investigated but the studies led to contrasting results. It seems that the elimination of inflammation does not necessarily play a major role since anti-inflammatory drugs failed to prevent AL. Consequently, it is difficult to define the dominant mechanism yielding a beneficial or detrimental effect (10).

From the available literature, we know that there are several dozen papers dealing with the idea of diagnosing leakage using inflammatory markers. The results in their conclusions usually reach statistical significance on postoperative days 3 and 4.



Fig. 2. ROC curve for hemoglobin blood level measured immediately after surgery relative to leakage prediction.



Fig. 3. ROC curve for white blood cells level measured on postoperative day 1, for the leak.

Mik in his report (Colorectal Cancer Open Surgery) on 724 patients evaluated CRP and neutrophil-to-lymphocyte ratio (NLR).; NLR on POD4 was higher in the AL group:  $9.03 \pm 4.13$  vs.  $4.45 \pm 2.25$ ; p = 0.0012; sensitivity 69 %, specificity 78 %, PPV 49 %, NPV 88 % at cut-off point of 6.5 (11).

In a study conducted on 134 patients, Munoz evaluated CRP, procalcitonin, and white blood cell levels using ROC analysis; the best AUC of CRP and PCT levels was on POD 3 (0.837 and 0.947, respectively). A CRP cut-off level at 163 mg/l yielded 85 % sensitivity, 80 % specificity, and 99 % negative predictive value (NPV). A PCT cut-off level at 2.5 ng/ml achieved 85 % sensitivity, 95 % specificity, 44 % positive predictive value, and 99 % NPV (12). The leukocyte level did not reach statistical significance, but the number of patients in the cohort was small.

Pedersen investigated 129 patients who underwent laparoscopic colorectal surgery in a fast-track regimen. WBC measurements showed the best cut-off value on POD 2, where WBC >  $12 \times 10^9$ had a sensitivity of 90 % and specificity of 62 % (13).

There are considerably few papers dealing with early diagnosis of leakage and reaching statistical significance. The idea of early diagnosis of leakage, even preoperatively, was discussed by Morimoto in his paper on preoperative measurement of leukocyte blood levels in patients with left-sided colorectal cancer. This study analyzed preoperative predictors of AL in 208 patients who underwent resections for left-sided CRC. The cut-off value for WBC (6,200/ $\mu$ L) had the highest sensitivity of 81.8 % and negative predictive value of 98.4 %, as well as the lowest likelihood ratio of 0.289; (AUC = 0.773) but the study was focused on left-sided tumors (14).

Our study is based only on a cohort of patients with radically removed rectal tumor and it also shows statistically significant non-inflammatory predictors of anastomotic leakage. The platelet count dropping to the value of 34 predicts leakage with a sensitivity of 45 % and a specificity of 81.1 %, while hemoglobin level  $\leq$ 79.5 just after surgery predicts leakage with a sensitivity of 70.0 % and specificity of 62.2 %, and WBC level  $\geq$  8.8 POD1 predicts leakage with a sensitivity of 70.0 % and specificity of 55.3 %.

The objective of the work is to find an easily and quickly detectable parameter that does not require special testing procedures and at the same time yields good sensitivity and specificity in meeting this condition already in the early postoperative period.

To summarize, this study revealed that values such as platelet decline, hemoglobin, and leukocyte blood levels may help predict postoperative AL risk in rectal tumor surgery. These markers can identify the risk of AL at a very early point in the postoperative period, which facilitates early and effective employment of preventive methods.

# Conclusion

None of the available studies have described a non-inflammatory marker that would in the early postoperative period predict the development of rectal anastomosis leakage as shown in our report. These are platelet decline and hemoglobin level. Although these parameters have low specificity and sensitivity, they could be a useful marker leading to the diagnosis or suspicion for anastomotic leakage.

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