Potential use of preoperative blood analysis to distinguish intestinal obstruction due to a foreign body or a neoplasm

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Master’s Thesis

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Potential use of preoperative blood analysis to distinguish if an intestinal obstruction is due to a foreign body or a neoplasm

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ABBREVIATIONS

AIC: Akaike Information Criterion

CI: Confidence Interval

CPK: Creatine Phosphokinase

FB: Foreign Body

GIN: Gastrointestinal Neoplasm

GIST: Gastrointestinal Stromal Tumor

I: Intussusception

MCHC: Mean Corpuscular Hemoglobin Concentration

N: Neoplasm

OR: Odds Ratio

R^2: Coefficient of determination

RDW: Red Blood Cell Distribution Width

wi: Akaike weight

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1. INTRODUCTION

Mechanical intestinal obstruction is a common problem found in dogs. The most common causes are foreign bodies (FB), intussusception and neoplasms or tumors. Dogs are curious animals and do not discriminate much about what they eat most of the time. Some dogs will ingest pieces of rubber, toys, clothes etc. According to MULLEN et al. (2020a), 80% of all mechanical obstructions are due to a foreign body.

Age is a good indicator of the possible cause of the obstruction. The younger the dogs are, the more they tend to swallow foreign bodies, whereas in older animals this may indicate a neoplasm. Intussusceptions are also more likely to occur in younger dogs. However, age alone is not enough to determine the cause of intestinal obstruction with certainty.

There is also a difference in the emergency of treating one cause or the other. The FB and intussusception are more urgent for surgery than a neoplasm. The latter usually develops slowly and could wait several hours, days or even weeks before intervening. For FB, MAWELL et al. (2020) have shown that delaying the procedure only increases the complexity of the surgery (higher number of enterotomies, longer anesthesia…). Both FB and intussusception carry a high risk of necrosis and perforation of the intestines. Other complications include septic peritonitis, additional intussusception, and megaesophagus in esophageal FB, melena or hematemesis, dehydration, acid-base disbalance, electrolyte disturbances, ileus… If the dog with intestinal obstruction is not treated, it can die within 3 to 4 days (HIGGS, 2024).

Until now, blood tests for intestinal obstruction have often been unspecific. According to NORDQUIST and CULP (2013), the most common findings are azotemia, hypochloremia, hyponatremia and hyperkalemia. It could be useful to find markers in the blood that give a more precise indication of the etiology of the bowel obstruction and thus of the further procedure and the urgency of the operation. Ideally, this should be a marker that can be easily tested in the clinic. A marker that is frequently checked during a blood test and by that is not overlooked. It should be cheap and easily accessible, yet accurate. It would be a great advantage if we could find a marker in the blood as it would be cheaper for the owner as we would not need an ultrasound.

2. OVERVIEW OF CURRENT KNOWLEDGE

2.1. Diagnosis and management of foreign body

According to CAIXETA et al. (2018), there is a predominance of male dogs with 62% of the population in their study and an average age of 4.5 years. In 98% of cases, they successfully detected a foreign body in dogs with radiographic and/or ultrasonographic examinations. There is also a majority of non-linear foreign bodies in dogs (HOBDAY et al., 2014) with 65%. In this study, the predilection place for foreign body is in the jejunum with 68% of the cases, which is similar to HAYES (2009) with 63%. HAYES (2009) also mentions some over-represented breeds such as Springer spaniels, Border collies, English bull terriers, Staffordshire bull terriers and Jack Russel terriers. The dogs ingested different types of FB: a piece of rubber, plastic, grass, twigs, hair, ball, stone, couch leather, cloth, walnut, plastic bag.

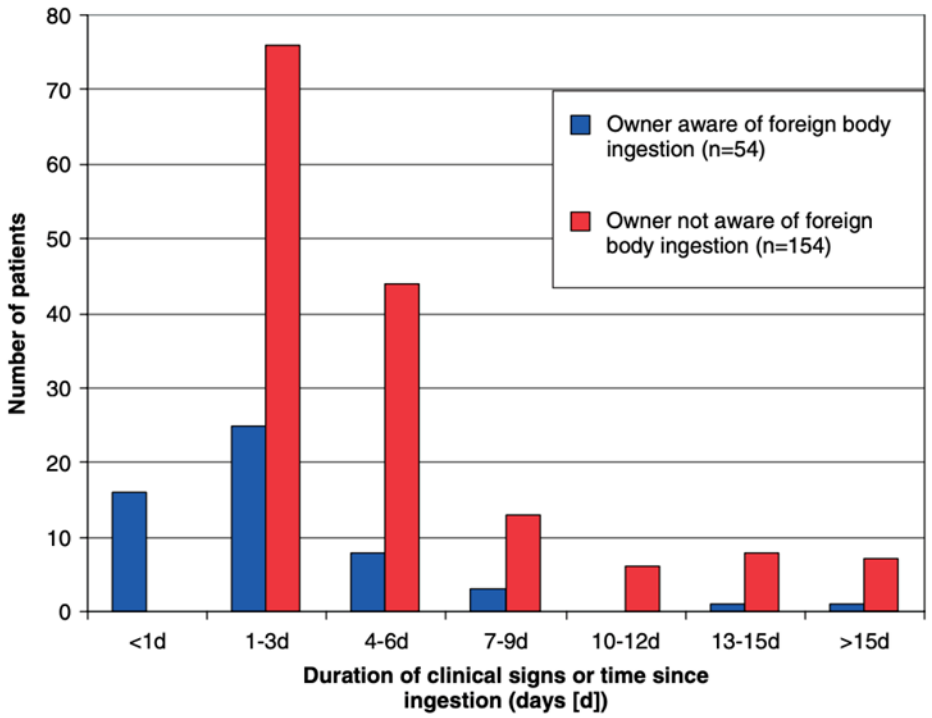

Fig. 1. Graph showing the duration of the clinical signs or the time since the animal ingested the FB before presentation for a definitive treatment (HAYES G., 2009).

When a dog ingests a FB, the clinical signs are mostly visible 1-3 days after ingestion, whether the owner witnessed it or not (Fig. 1). The clinical signs can be vomiting, diarrhea, abdominal pain, lower appetite, tenesmus or small amounts of feces, lethargic, or even biting or growling when picked up because of the abdominal tenderness. It depends on the type of

FB but also its location. About hematological findings, KOIKE et al. (1981) found an increase in hematocrit value and about biochemistry, the chloride level was below the normal range. TYRRELL and BECK (2006) compared the efficacy of using radiography versus ultrasound to diagnose gastrointestinal FB in small animals. It showed that 9/16 small animals were well diagnosed with X-ray whereas with ultrasound it was 100% rate. Therefore, ultrasound alone is enough to diagnose a FB. A FB elicits a dense acoustic shadowing and can create a hypoechoic area around it due to secondary tissue edema or hemorrhage. SHARMA et al. (2011) found that if there is an overall larger diameter of the jejunum with normal wall layering, one should check for FB in the intestines (Fig. 2).

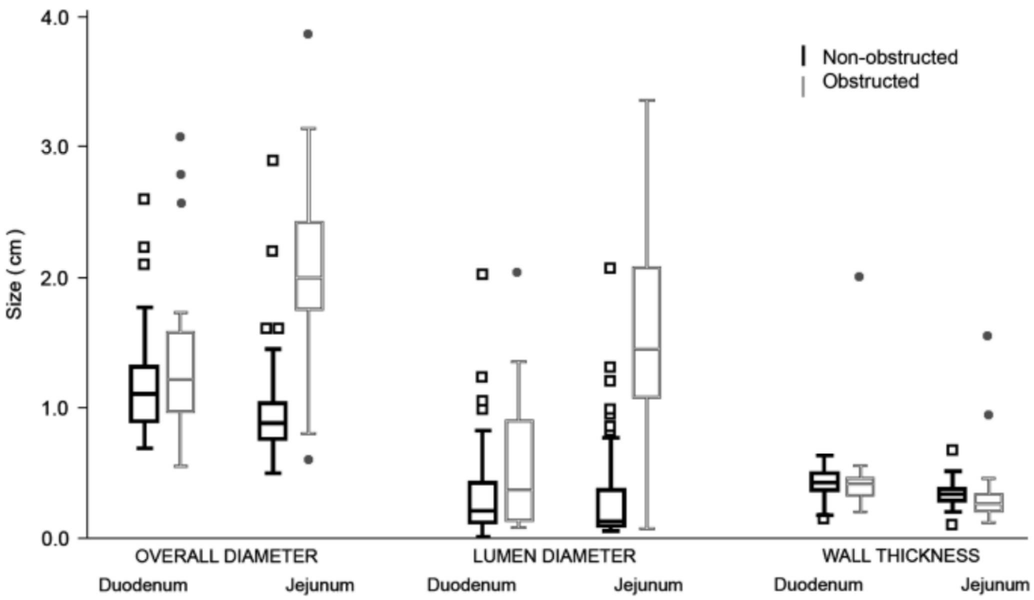

Fig. 2. Box and whiskers plots of canine small intestine size without small-intestinal mechanical obstruction (55 dogs) and with small-intestinal mechanical obstruction (27 dogs), obtained during ultrasonography. Overall diameter was measured from serosa-to-serosa; lumen diameter, mucosa-to-mucosa; wall thickness, serosa-to-mucosa (SHARMA et al., 2011).

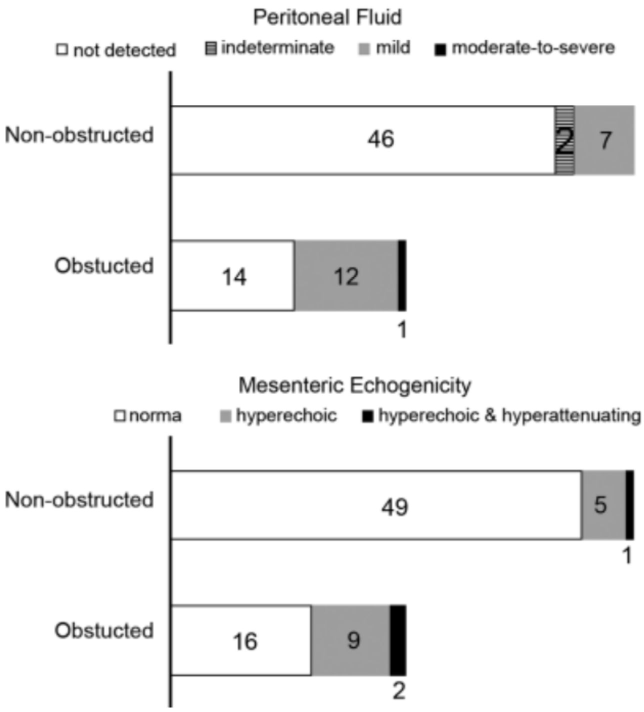

Fig. 3. Bar charts of mesenteric echogenicity and peritoneal fluid in dogs with and without small-intestinal mechanical obstruction, obtained during ultrasonography (SHARMA et al., 2011).

Additionally, they found that obstructed animals tend to have peritoneal fluid (around 50% of the cases) and hyperechoic mesenteric echogenicity (~30%) compared to non-obstructed animals (Fig. 3). Nevertheless, ~16% of non-obstructed animals had peritoneal fluid so it would be safer to consider it a non specific sign.

The gold standard to treat enteral FB is to do, through midline celiotomy, enterotomy aborally to the obstruction site. If there are complications such as perforation or necrosis, resection and anastomosis are required. Dogs undergoing enterotomies recover more easily than those having resection and anastomosis. According to LOPEZ et al. (2021), the odds of intestinal dehiscence for resection and anastomosis were approximately six times higher than the odds for enterotomy. It is a risk that needs to be warned to the owner. In our study, 70% had enterotomies, 22% resection and anastomosis and 8% were manually moved through the rectum. The prognosis is favorable with proper treatment and aftercare.

2.2. Diagnosis and management of intestinal intussusception

Occurring principally in young dogs, it is usually causing inappetence, vomiting, diarrhea, anorexia, difficult defecation, lethargy, abdominal tenderness. On abdominal palpation, it is possible to feel a firm tubular structure.

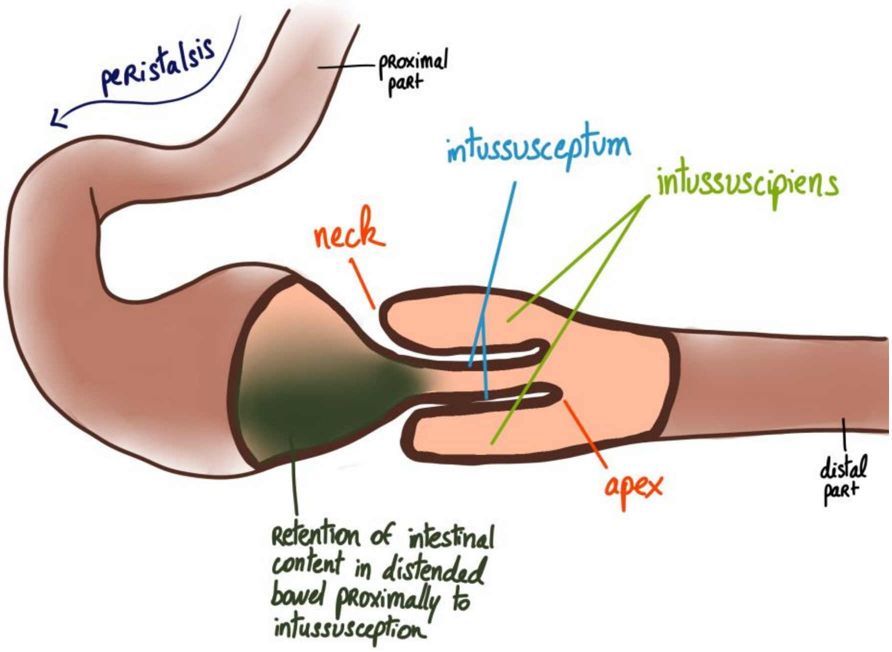

Fig. 4. Scheme of intussusception (E. Kohler).

Ultrasound is the best diagnostic imaging for intussusception. According to PATSIKAS et al. (2019), in cross-sectional view, the overlapping layers of the intussusceptum and intussuscipiens form more than five alternating hyperechoic and hypoechoic concentric rings, typically with a hyperechoic center. This is often referred to as “Onion rings” (Fig. 5).

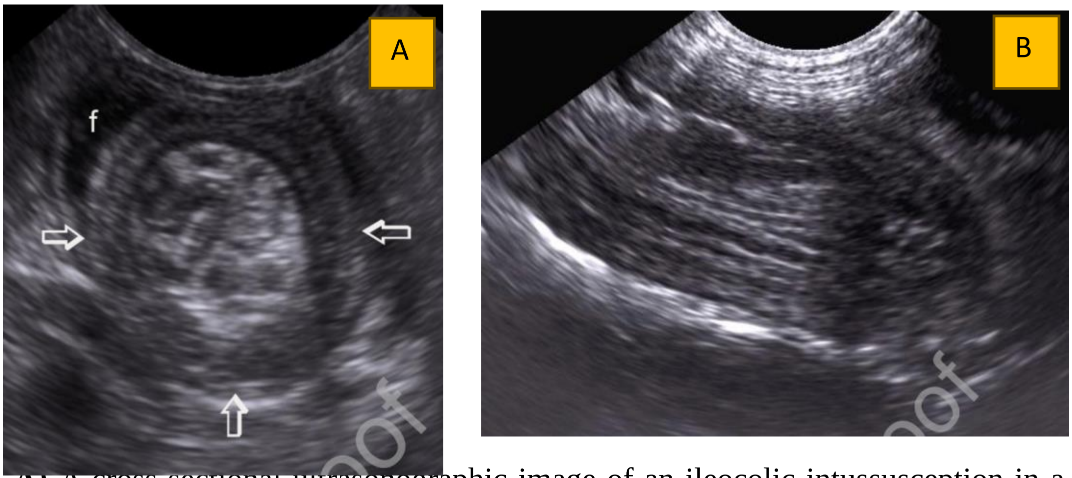

Fig. 5. A) A cross-sectional ultrasonographic image of an ileocolic intussusception in a dog reveals a mass with a target-like appearance. This mass is characterized by several concentric rings of alternating hyperechoic and hypoechoic layers surrounding a hyperechoic center. The diameter of the mass varies between 20.5 and 22.6 mm. Arrows mark the borders of the intussusception ("f" denoting peritoneal fluid). **B)** A longitudinal ultrasonographic image of a dog's intestinal intussusception showing multiple hyperechoic and hypoechoic parallel lines (PATSIKAS et al., 2019).

In dogs with intussusceptions that could be manually reduced during exploratory celiotomy (Fig. 6), the diameter of the target-like mass varied between 19 and 29 mm (PATSIKAS et al., 2019).

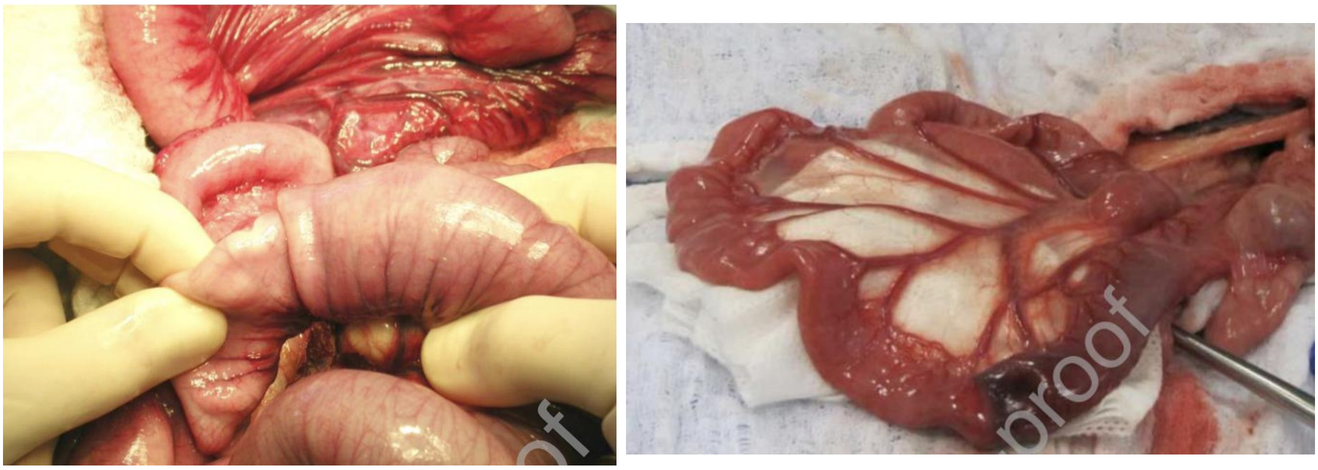

Fig. 6. Intraoperative view of an intussusception before and after manual reduction (PATSIKAS et al., 2019).

In humans, the presence of a thin external hypoechoic ring, less than 7.5 mm in thickness, around the target-like mass is often associated with reducible intussusceptions. On the other hand, the presence of fluid at the apex of the intussusception, enlarged lymph nodes within the intussuscepted bowel, and the absence of peristaltic activity are indicators of irreducible intussusceptions.

In general, through a midline celiotomy, manual reduction or intestinal resection and anastomosis correct intussusceptions, depending on if the affected segments are viable or not. It is recommended to repeat an ultrasound after anesthetic induction, as some intussusception can spontaneously reduce. Enteroplication is theoretically an option when there is recurrence of intussusceptions (up to 20% according to APPLEWHITE et al., 2001). The results indicate that enteroplication (Fig. 7) may be associated with life-threatening complications in dogs (intestinal strangulation, intestinal obstruction, second intussusception). However, the chances of needing a second surgery after intussusception correction were not different between dogs that had enteroplication during the initial procedure and those that did not.

Fig. 7. Enteroplication consists of adjoining small intestinal loops from duodenocolic ligament to the ileocolic junction that are gently placed side by side. The loops are sutured to each other with simple interrupted polydioxanone or polypropylene sutures (PATSIKAS et al., 2019).

With proper treatment and aftercare, the prognosis is good in case of idiopathic intussusception. Otherwise, it depends on the underlying condition.

2.3. Diagnosis and management of neoplasm obstructing the intestines

HAYDEN and NIELSEN (1973) state that rectal polyps, which cause tenesmus and bleeding, are the most common benign neoplasm. Among the malignant tumors, rectal carcinoma predominates. According to MATSUYAMA (2020), the most common small intestinal tumor is lymphoma and the most common colon tumor is adenocarcinoma. The following common neoplasms are gastrointestinal stromal tumors (GIST) and leiomyosarcoma. In this study, a sample was sent for histopathology to determine the type of tumor causing the obstruction. The dogs had lymphomas, leiomyomas or GIST (3 cases), lymphangiectasia, adenocarcinoma of the exocrine pancreas, intestinal adenocarcinoma, colon carcinoma, chronic inflammation, colon adenoma and two cases with unidentified masses near the rectum. It affects dogs between 6 and 9 years of age. The most common clinical signs of alimentary neoplasms are vomiting, anorexia, tenesmus, hematochezia, melena, inappetence, diarrhea, and lethargy. An abdominal mass may be palpable on clinical examination. Hematology and biochemistry are normal. However, hypoglycemia is often associated with leiomyomas and leiomyosarcomas. Some non-lymphomatous tumors have been associated with hypercholesterolemia and elevated alkaline phosphatase activity. Ultrasound is a fairly accurate tool to differentiate between enteritis and neoplasm. PENNINCK and al. (2005) confirm that the loss of intestinal wall layering represents around 51 times more chances to have a neoplasm than enteritis (Fig. 8).

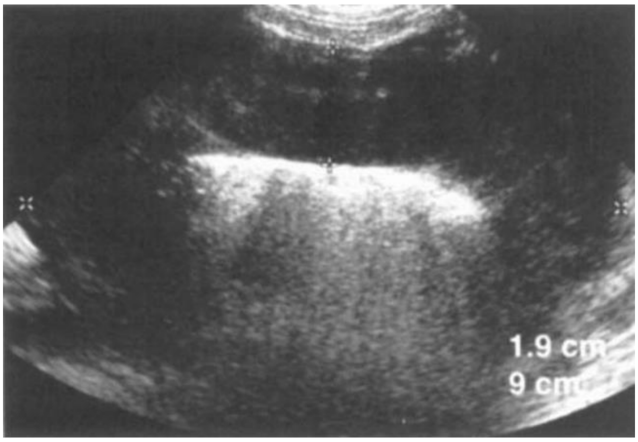

Fig. 8. Sonogram of an ileocecal segment in a dog with intestinal lymphoma. Highly thickened wall (1.9 cm) with complete loss of layering (PENNINCK et al., 2005).

The best way to treat and diagnose a non-lymphatic intestinal neoplasm is to resect (with margins greater than 4 cm, if possible) and anastomose the mass and send the full-thickness intestinal specimen to the laboratory. Additional chemotherapy and/or radiotherapy may be required. Metastasis is a negative prognostic factor. The prognosis of dogs with adenocarcinoma of the small intestine has a 1-year survival rate of up to 60%. In dogs with colorectal adenocarcinoma, the survival time can be up to 4 years. In dogs with GIST or leiomyosarcoma, the survival time is around 3 years. For lymphomas, it is usually less than 3 months, unless they are located in the colon. In this case, the median survival time can be up to 6 years (after chemotherapy, with or without surgery).

3. MATERIAL AND METHODS

To find the patients suitable for this study, the anesthesia protocols of the Clinic of Surgery, Orthopedics and Ophthalmology of the Faculty of Veterinary Medicine in Zagreb were reviewed for the period from November 2019 to February 2024. For this study, patients with FB, intussusception or a neoplasm causing mechanical intestinal obstruction were included. Blood values were collected before the animal was treated so as not to influence any parameters. Hematology and biochemistry are the most important as they are the most commonly used. The data was transferred to an Excel spreadsheet to generate all statistics. Inclusion criteria were data on the localization of the obstruction, the type of foreign body, the results of histopathological examination for neoplasm and the type of surgery they had undergone. Patients without hematologic or biochemical results or with unknown etiology of obstruction were excluded. The Ethical committee permission numbers are Class: 605-03/24-14/05 and Reg. No. 251-61-32-24-02.

To understand which combination of parameters were significant in this study, normality of data distribution was tested using the Shapiro-Wilk test. Pearson's or Spearman's coefficients were used to test association of variables 1, 2 and 3 (1 = FB, 2 = Intussusception, 3 = Neoplasm). The Akaike Information Criterion software tool (AICc) was used in the analysis and model selection was made using the following formula:

$$\boldsymbol{AICc = AIC + 2\,(k+2)(k+3)/T-k-3,}$$

in which T is the number of observations used for estimation and k is the number of predictors in the model (BURNHAM and ANDERSON, 2002). Model selection followed if $\Delta AIC<2$ units. Akaike's weight (*wi*) was also calculated, which represents the probability that the model is the best fitted among the other compared models. The basic premise of AIC analysis is that some phenomenon (dependent variable) should be described with as few independent variables (predictors) as possible. The most favorable model is the one with the lowest AIC value. In other words, AIC measures the information lost, meaning that the model with a lower AIC score indicates a better fit. After testing the normality of the distribution and the correlation of the predictor with the dependent variable, AIC analysis was performed for six out of 36 variables. As hematological predictors are the level of erythrocytes and hematocrit, hemoglobin and platelets, and from biochemical values are the level of bilirubin, potassium ions and sodium ions.

Testing the estimation value of the models extracted with the AIC tool was performed using multiple regression.

Based on the obtained multiple regression values, the outcome assessment equation according to model 7 would be as follows:

$$\textbf{Outcome} = \mathbf{3{,}513 - 0{,}010H - 0{,}292M - 0{,}023B}$$

Where:

H = hemoglobin levels

M = monocyte levels

B = bilirubin levels

Data were analyzed using Statistica 13.4.014 TIBCO Software Inc., 2018.

In the second part of the analysis, to determine whether a decrease or increase in the values of a parameter means that the presence of a disease (FB, intussusception or neoplasm) is more likely, the odds ratio was calculated using the free online software MedCalc. The confidence interval was set at 95% and the significance level at $p<0.05$.

4. RESULTS

On a sample of 76 dogs, of which 53 (70%) had a diagnosis of foreign body (FB), 10 (13%) of intussusception and 13 (17%) of neoplasm.

The analysis included the outcome values as dependent variables, while the values of hematologic (red blood cell count, hematocrit, hemoglobin, and platelets) and biochemical (bilirubin, potassium and sodium ions) characteristics were used as predictors. The distribution of most characteristics deviated significantly from normal. As these variables had no clear skewness (positive or negative), no data transformation was performed (Fig. 9, 10).

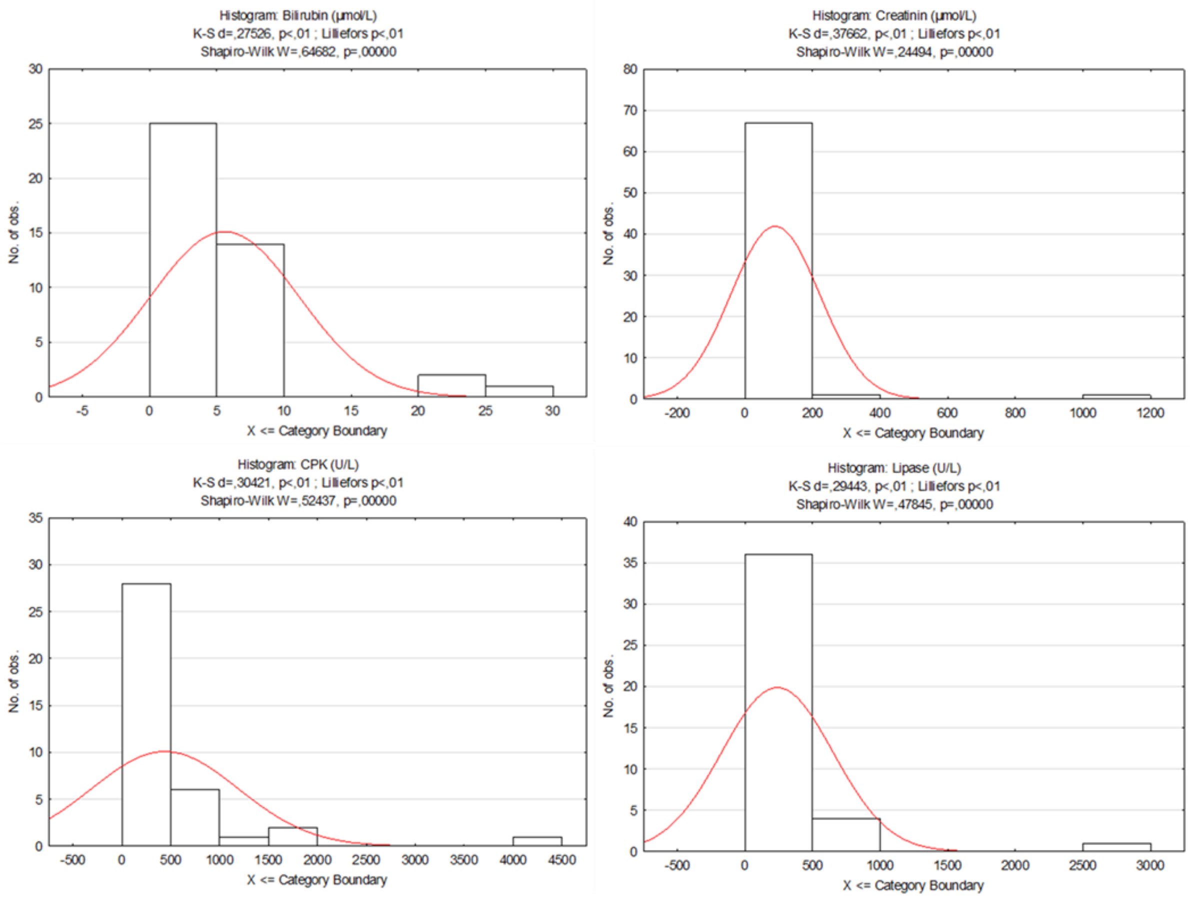

Fig. 9. Data distribution for Bilirubin, Creatinin, CPK and Lipase.

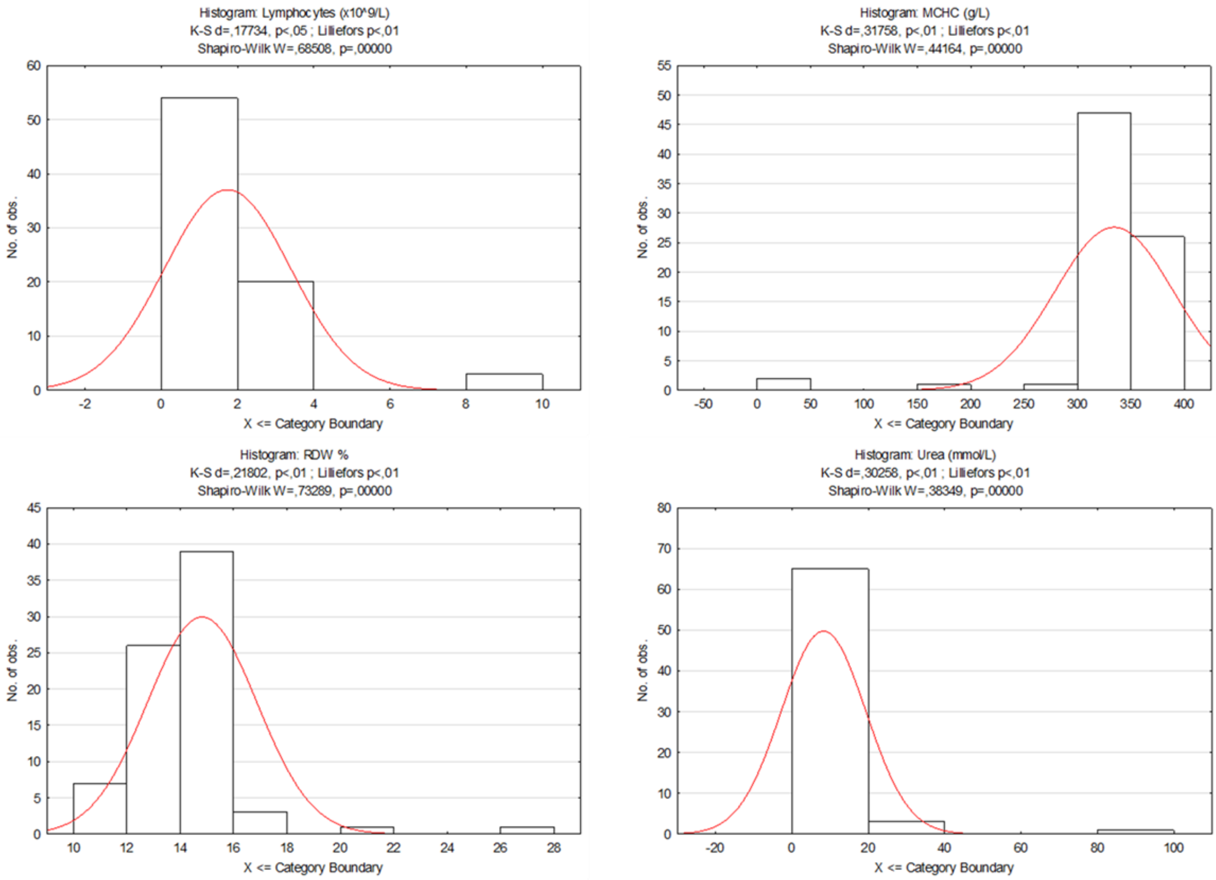

Fig. 10. Data distribution for Lymphocytes, MCHC, RDW and Urea.

Variables that show a statistically significant association with the dependent variable, using a significance threshold of 95% ($p<0.05$), were selected for the prediction model.

According to AIC ($\Delta AIC<2$ criterion), 17 models were selected, in which the number of predictors ranges from 1 to 4 (Table 1). Although the first model has the lowest ΔAIC value, according to the results of multiple regression, it is possible to estimate only 25.1% of the disease outcome ($R^2 = 0.251$).

Table 1. Akaike Information Criteria (AIC) selected models. *ΔAIC* represents relative difference between the best and each other model in the set, *wi* represents Akike weight, while R^2 represents a coefficient of determination.

RB	Model	*k*	*AIC*	*ΔAIC*	w_i	R^2
1.	Hemoglobin (g/L) + Monocytes ($x10^9$/L)	2	80.281	0.000	0.024	0.251
2.	Hemoglobin (g/L) + Thrombocytes (x10^9/L) + Monocytes ($x10^9$/L) + Sodium Na^+ (mmol/L)	4	80.434	0.153	0.022	0.223
3.	Hemoglobin (g/L) + Thrombocytes (x10^9/L) + Monocytes ($x10^9$/L)	3	80.575	0.294	0.021	0.310
4.	Hematocrit % + Thrombocytes (x10^9/L) + Monocytes ($x10^9$/L)+ Sodium Na^+ (mmol/L)	4	80.697	0.416	0.019	0.216
5.	Hemoglobin (g/L) + Potassium K^+ (mmol/L) + Monocytes ($x10^9$/L)	3	80.869	0.588	0.018	0.234
6.	Hemoglobin (g/L) + Monocytes ($x10^9$/L)+ Sodium Na^+ (mmol/L)	3	80.942	0.660	0.017	0.179
7.	Hemoglobin (g/L) + Monocytes ($x10^9$/L)+ Bilirubin (µmol/L)	3	81.137	0.856	0.016	0.365
8.	Hematocrit % + Monocytes ($x10^9$/L)	2	81.165	0.883	0.015	0.237
9.	Hematocrit % + Thrombocytes ($x10^9$/L)+ Monocytes ($x10^9$/L)	3	81.180	0.899	0.015	0.305
10.	Hematocrit % + Potassium K^+ (mmol/L) + Monocytes ($x10^9$/L)	3	81.226	0.945	0.015	0.229
11.	Hemoglobin (g/L) + Sodium Na^+ (mmol/L)	2	81.441	1.160	0.013	0.107
12.	Erythrocytes ($x10^{12}$/L) + Hemoglobin (g/L) + Monocytes ($x10^9$/L)	3	81.479	1.198	0.013	0.251
13.	Hematocrit % + Monocytes ($x10^9$/L) + Sodium Na^+ (mmol/L)	3	81.489	1.208	0.013	0.168
14.	Erythrocytes ($x10^{12}$/L) + Thrombocytes ($x10^9$/L)+ Monocytes ($x10^9$/L)) + Sodium Na^+ (mmol/L)	4	81.611	1.330	0.012	0.218
15.	Hemoglobin (g/L) + Thrombocytes ($x10^9$/L)+ Potassium K^+ (mmol/L) + Monocytes ($x10^9$/L)	4	81.627	1.346	0.012	0.253
16.	Hemoglobin (g/L)	1	81.677	1.396	0.012	0.208[1]
17.	Hematocrit % + Sodium Na^+ (mmol/L)	2	81.717	1.435	0.012	0.090

Since the distribution of hemoglobin values is significantly different from normal, the regression was made with a quadratic function.

According to the first model (hemoglobin + monocytes), FB (value 1) was correctly estimated in 65%, intussusception (value 2) in 70%, and neoplasm (value 3) in 15% of cases (Table 2). The values were incorrectly estimated by only one degree (Figure 11). In the case of intussusception and neoplasm, the assessment error represented an underestimation of the outcome, while in the case of FB, the assessment error appeared as an overestimation of the outcome. For value 1 and value 3 it is also logical.

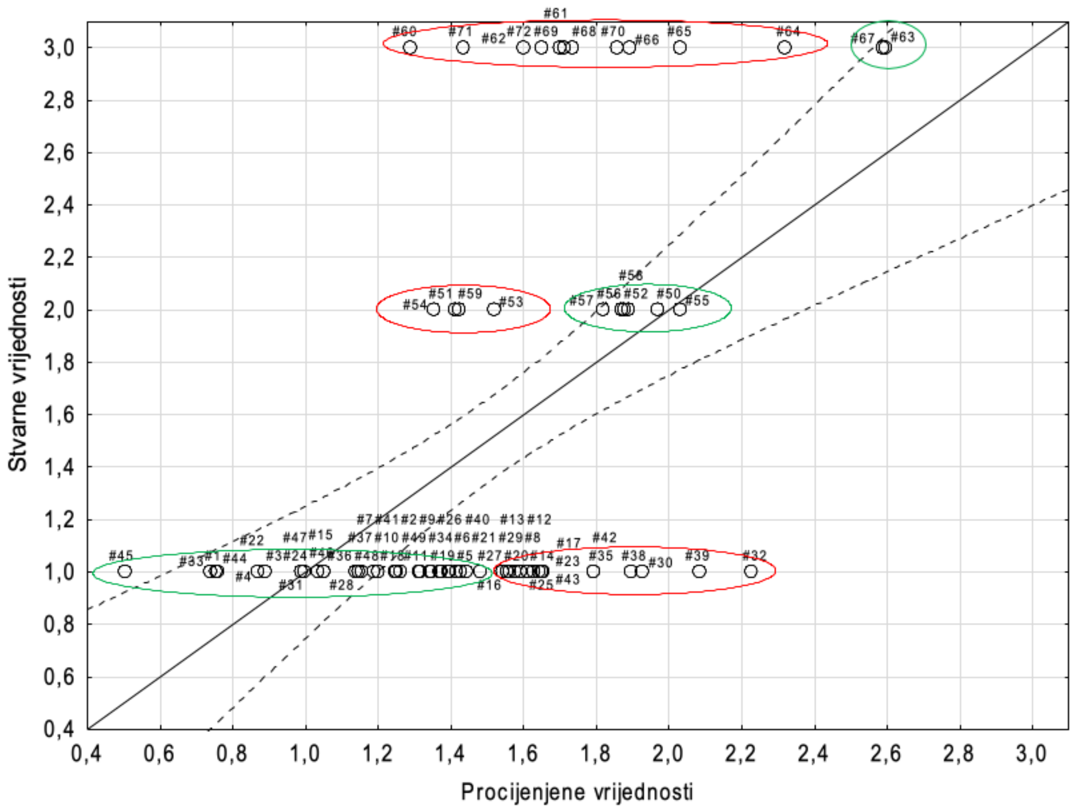

Fig. 11. Accuracy of outcome assessment according to the first model. X axis represents real values, while Y axis represents estimated values. Red-bordered ellipses represent the correct estimate, while green-bordered ellipses represent the wrong estimate.

Table 2. Comparison of the accuracy of the first and seventh outcome prediction models.

Outcome	Model 1		Model 7	
	Correct (%)	Incorrect (%)	Correct (%)	Incorrect (%)
FB	65	35	72	28
intussusception	70	30	80	20
neoplasm	15	85	38	63

With the seventh model (hemoglobin + monocytes + bilirubin), the accuracy of the assessment according to the outcome rapidly improves (Table 2). In this outcome, variable 1 (FB) had 72% of outcomes correctly estimated, which is a 7% increase in estimation accuracy compared to the previous model. For variable 2, the accuracy of assessment increased by 10%, and in variable 3 by more than twice (from 15 to 38%). The increase in the accuracy of the assessment can be seen more clearly if the graphic representations of the accuracy assessment are compared (Figure 11 and 12). According to Figure 12, the separation of correct and incorrect outcome assessments is very pronounced in cases 2 and 3, while in case 1 the zone of separation between correct and incorrect is relatively small.

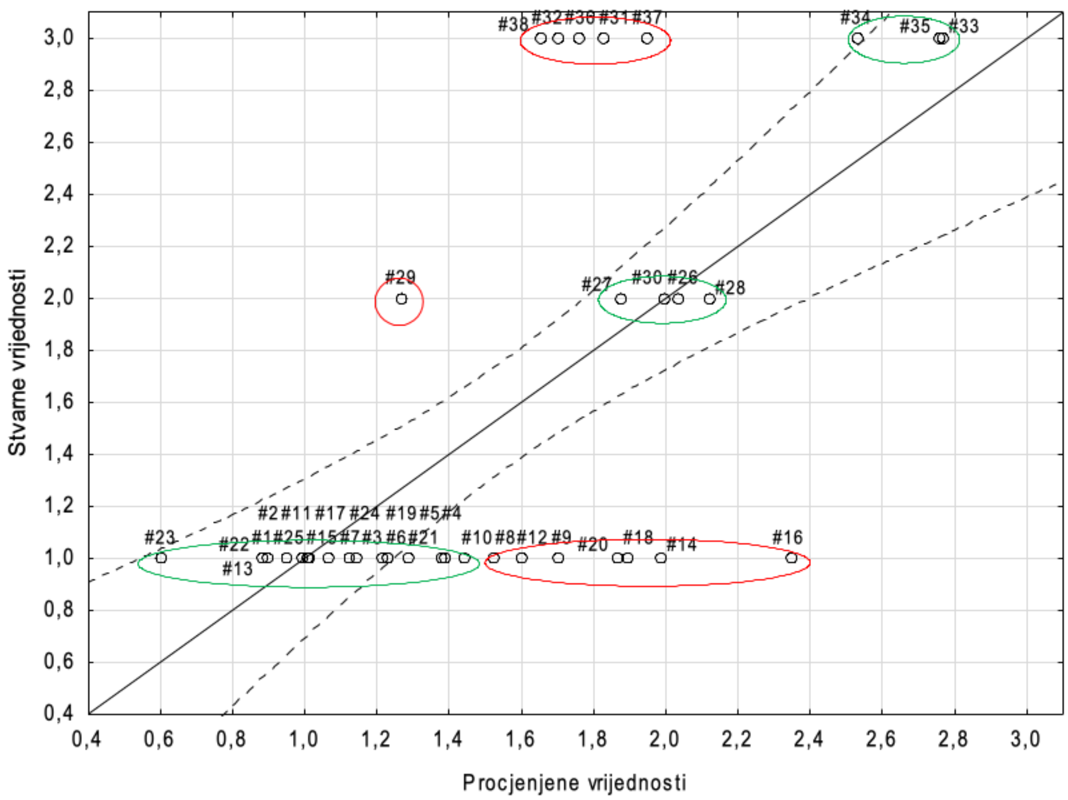

Fig. 12. Accuracy of outcome assessment according to the seventh model. X-axis represents real values, while Y-axis represents estimated values. Red-bordered ellipses represent the correct estimate, while green-bordered ellipses represent the wrong estimate.

Table 3. Results of the multiple regression of the assessment of the findings according to model 7 (numbers marked in red indicate significant differences).

	β	*Std.Err. of „β“*	*b*	*Std.Err. of „b“*	*t*(34)	*p*
Intercept	-	-	3,513	0,449	7,827	0,000
Hemoglobin (g/L)	-0,460	0,139	-0,010	0,003	-3,301	0,002
Monocytes (x10^9/L)	-0,300	0,135	-0,292	0,131	-2,225	0,033
Bilirubin (μmol/L)	-0,163	0,137	-0,023	0,020	-1,192	0,242

According to the results of the multiple regression of model 7 (Table 3), hemoglobin level (β = -0.460) and monocyte level (β = -0.300) had a more significant impact in prediction than bilirubin level (β = -0.163). All three characteristics have a negative sign, which means that as their values increase, the value of the result decreases. For example, a decrease in hemoglobin is more significant than a decrease in bilirubin and shows that something is happening in the gut. In addition, the p-value of bilirubin is above 0.5, which means that it is not statistically significant. A decrease in these three parameters does not mean that it is below the reference range, but the trend.

Now it is interesting to see if a decrease/increase in one parameter can specifically distinguish between FB, intussusception or neoplasm.

Data were sorted according to the reference values as normal (0), above the range (+) and below (-) the range. The reference values were:

- Erythrocytes: (5,5-8,5) x10^{12}/L
- Hematocrit: 37-55 %
- Hemoglobin: 120-180 g/L
- Monocytes: 3-10% or (0,15-1,35) x10^{9}/L
- Bilirubin: up to 8,6 µmol/L
- Potassium: 3,6-5,8 mmol/L
- Sodium: 140-155 mmol/L

The levels of blood parameters within reference values, above and below them are presented in Fig. 13.

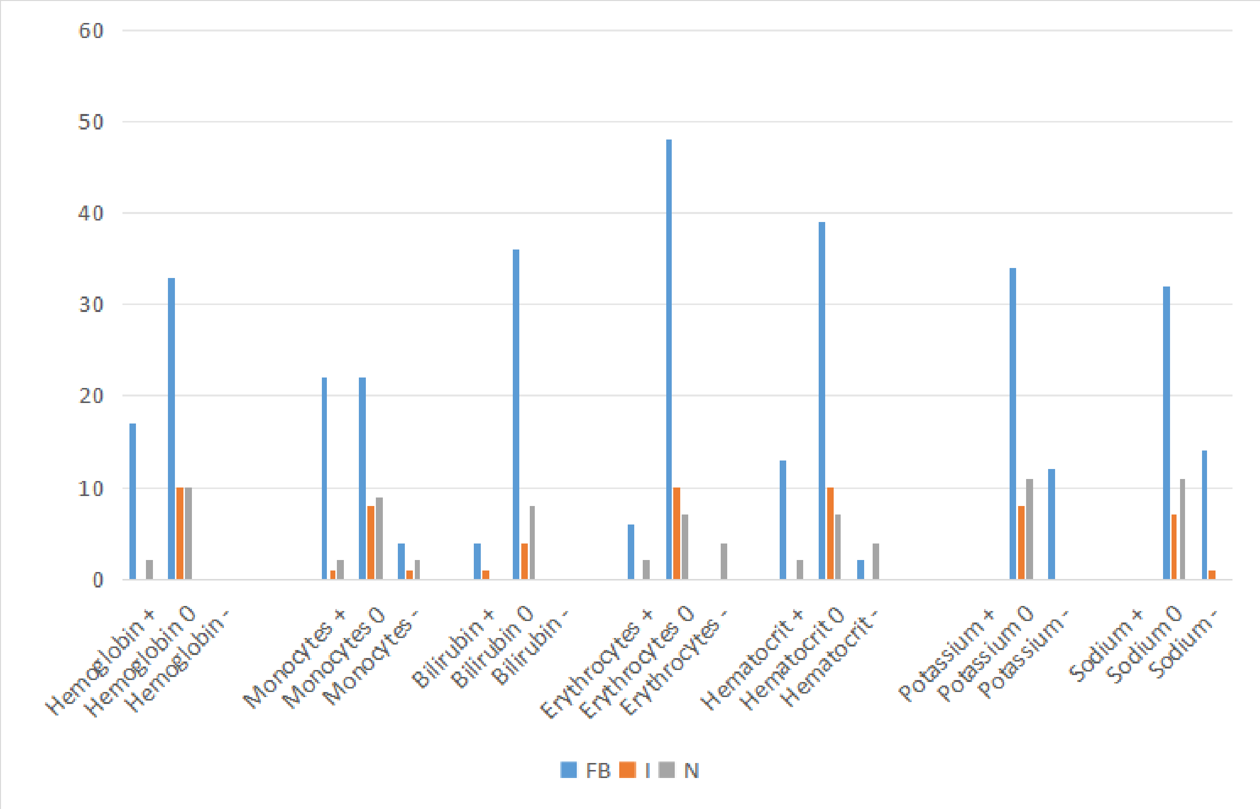

Fig. 13. Number of patients with detected levels of analyzed blood parameters within reference values (0), above (+) and below (-) reference values. Missing data were excluded from calculation. FB indicates foreign body, I intussusception and N neoplastic disease.

The number of patients with the corresponding values of the individual blood parameters analyzed is shown in Figure 3. Statistically significant values were found when comparing hematocrit values below the normal range in patients diagnosed with neoplasm and foreign body (OR=11.149, CI95 % 1.7030 to 72.9103, p=0.0119). These results suggest that when hematocrit values are below the reference values, there is an 11.149-fold probability that the underlying cause is neoplastic disease. Similarly, erythrocyte levels below reference values indicate the possibility that the underlying cause is neoplastic disease rather than a foreign body (OR=58.2, CI 95% 2.8365 to 1194.1558, p=0.0084). Other comparisons were not significant. The following values that came closest to statistical significance were obtained by comparing the monocyte values (higher than the reference values) between foreign body and intussusception as the underlying cause (OR=8.00, CI 95% 0.921 to 69.45, p=0.0593) and foreign body and neoplastic disease (OR=4.50, CI 95% 0.871 to 23.249, p=0.072).

Regarding the operations the patients underwent, 70% of the patients only required an enterotomy for the foreign body, 22% had to undergo resection and anastomosis and 8% were able to remove it with manual massage. For the neoplasms, 8 out of 13 (the others did not mention the type of surgery) underwent resection and anastomosis, which is logical given the diagnosis.

5. DISCUSSION

Gastrointestinal symptoms such as loss of appetite, diarrhea, constipation and anorexia are common findings in the case of enteropathy in dogs (JERGENS and SIMPSON, 2012). As previously mentioned, canine obstructive intestines disease (one of the most common causes of enteropathy in dogs) can have a variety of causes related to the severity and emergency of the condition. Mechanical obstruction can have various causes and is usually divided into partial and complete obstruction. The underlying pathology is either extrinsic (i.e. adhesions, hernias, intra-abdominal masses, etc.) or intrinsic (i.e. neoplasms, inflammatory diseases, malformations, bowel obstruction, foreign bodies, etc.) (CAPPELL and BATKE, 2008; GRIFFITHS and GLANCY, 2020). In this study, the mechanical obstruction was analyzed separately according to whether it was caused by a foreign body, an intussusception or a neoplasm of the intestine.

In small animal practice, intestinal obstructions caused by FB are a common finding (ARONSON et al., 2000; PAPAZOGLOU et al., 2003). According to MULLEN et al. (2020b), FB obstructions are involved in about 80% of all mechanical intestinal obstructions in dogs. Similarly, in this study of 76 dogs with obstruction, 70% of the animals (N=53) were diagnosed with FB. Regarding the location of the obstruction, 68% of obstructions in this study were in the jejunum, which is consistent with HAYES (2009) who reported a 63% prevalence of jejunal obstruction in FB. The following 22% of obstructions in this study were found in the ileum. Another fairly common cause of intestinal obstruction is intussusception. Intestinal intussusception has often been reported as a consequence of other conditions, including inflammation, parasitic infections, but also foreign bodies and intestinal neoplasms (LEVITT and BAUER, 1992). The prevalence of intussusception in dogs can vary greatly in different studies. IBRAHIM et al. (2022) reported a prevalence of 42.5% in German Shepherds and 25% in Labrador Retrievers. LAROSE et al. (2020) reported a lower prevalence of 14.4% in Labrador Retrievers and 9.2% in German Shepherds. In this study, 13% of dogs (N=10) had intestinal intussusception, which is closer to the results published by LAROSE et al. (2020). The category of neoplasia is also a large variable, as different tumor types can lead to a wide range of changes in the blood.

According to the “WHO Histological Classification of Tumors of the Digestive System of Domestic Animals",” malignant epithelial tumors of the intestine include adenocarcinoma (tubular, papillary and mucinous), signet ring cell carcinoma, undifferentiated and adenosquamous carcinoma (HEAD et al., 2003). Patients in this study were diagnosed with lymphomas, leiomyomas or gastrointestinal stromal tumors, fibrosarcomas, adenocarcinomas of the exocrine pancreas, intestinal adenocarcinomas, colon carcinomas and colon adenomas, among others. In this study, 17% (N=13) of the dogs with obstructions had neoplasms. A possible breed-related predisposition for certain tumor types is still debated, with some authors claiming that there is a breed-related predisposition, while others claim the opposite (PATNAIK et al., 1997; SULLIVAN et al. 1987; SAITO et al., 2020). However, the data indicate that purebredness and increasing age are risk factors for the development of gastrointestinal neoplasms (GIN). Despite the fact that GIN are rather rare in dogs, they are usually malignant (SWAN and HOLT, 2002). Lymphoma is the most common gastrointestinal neoplasm in dogs, and the different types together account for up to 14% of all neoplasms in dogs. According to SLAVIERO et al (2020), other or non-lymphoid GIN represented only 0.4% of the total sample biopsies (N=24711) or 0.6% of the identified neoplasms.

As said previously there are differences in the emergency of treating mechanical obstruction of intestines, regarding the underlying cause. In other words, FB and intussusception are more urgent for surgery than a neoplasm, as they can result in severe complications that will develop rapidly, but also every delay can result in a need for more complicated procedures (MAXWELL et al., 2020). If intestinal blockage caused by FB or intussusception is not treated as soon as possible, animal can die within 3 to 4 days (HIGGS, 2024). Therefore, adequate and reliable diagnosis is needed during patient triage. Further, since there are possibility for misdiagnosis, supplemental analysis could aid proper diagnosis and increase accuracy of applied diagnostic method or test. In available literature, x-ray analysis is deemed rather accurate in diagnosis of intestinal obstruction caused by FB (HOBDAY et al., 2014). Radiolucent FB may present some problems, but radiographs may detect segmental dilation of intestines, which is not pathognomonic sign, but can point to mechanical obstruction (GRAHAM et al., 1998; MCNEEL and RIEDESEL, 1998; TYRELL and BECK, 2006; SHARMA et al. 2011; CIASCA et al., 2013). In such cases, x-ray analysis can be supplemented by contrast imaging, repeated analysis or ultrasound examination. Intussusceptions and neoplasms are mainly diagnosed using the ultrasound examination (PENNICK et al., 2015; PATSIKAS et al., 2019).

Analysis of blood parameters is a less used method to diagnose intestinal obstruction. BOAG et al. (2005) reported hypochloremia, metabolic alkalosis, hypokalemia and hyponatremia in dogs with FB caused intestinal obstruction. In that, nature of FB (linear or non-linear) can cause differences in levels of sodium, potassium, chloride or blood urea nitrogen (BOAG et al., 2005; HOBDAY et al., 2014). Further problem is that despite the fact that these findings are even statistically significantly different between dogs with linear and non-linear FB, they can hardly be used for diagnostic purposes since despite being different; these values are still within reference values. KOIKE et al. (1981) found that four out of five dogs with FB obstruction of intestines had increased hematocrit values. SOGAME et al. (2018) found that 30% of dogs (N=21) with intestinal lymphoma had high neutrophil counts, and of them 14% (N=3) had immature neutrophils. Out of 71 examined dogs (28%, N=20) had anemia, and 55% (out of 69) had hypoalbuminemia. However, results of hematology are highly dependent on the type of the tumor, and potential metastases. Usually, the hematology and biochemistry are non-specific. In this study, a comparison of variations of blood parameters within and outside of reference values, with respect to the underlying cause of obstruction, was performed. Out of 17 models, based on AIC selection criteria and R^2 values, with respect whether two or more variables were included in the model, models 1 and 7 were selected as the most appropriate. According to the first model (hemoglobin + monocytes), FB obstruction was correctly predicted in 65%, intussusception in 70%, and neoplasm in only 15% of cases. If three variables were analyzed (7^{th} model, hemoglobin + monocytes + bilirubin), the accuracy of the prediction increased for FB obstruction to 72%, for intussusception to 80% and for neoplasm as the underlying cause of obstruction to 38%. Also, the model showed that separation zone between correct and incorrect predictions is relatively narrow in the case of FB obstruction. The multiple regression analysis of model 7, showed that hemoglobin levels (β = -0.460) and the monocyte levels (β = -0.300) had more significant impact in prediction than the bilirubin levels (β = -0.163). Due to the negative harbinger, it is possible to conclude that lower values of these parameters are associated with positive findings. This is even more emphasized in the case of hemoglobin and monocytes. In other words, decreased values of hemoglobin, monocytes and bilirubin will indicate that most likely the underlying cause of obstruction is intussusception or foreign body. If possible, these findings should be accompanied by the results of x-ray or ultrasound analysis. If later methods are not available, model 7 can indicate with more than 70% of accuracy whether immediate surgery is needed. One should also bear in mind that this model includes higher and lower values, which are not necessarily outside of the reference limits. If blood parameters were analysed with respect to the reference limits it is visible that if the hematocrit values are below normal it can be highly suspected (OR=11.149 compared to FB) that the underlying cause is neoplastic disease. This is in accordance with the findings of KOIKE et al. (1981) who found increased hematocrit values in dogs with FB obstruction.

Similarly, erythrocyte levels lower than the reference limits indicate to a possibility that neoplastic disease is present in the intestines.

This study has several limitations, which are mainly related to the fact that this was a retrospective analysis, which is highly dependent on the quality of the collected data. One of potential cause of variations is in the place of obstruction. Some 68% (34 out of 50) FB and 54% of neoplasms were blocked in the jejunum. 3 out of 13 neoplasms were in the rectum. For intussusception, the blockage is mainly near the ileum and ileocecal valve with 60% of the patients and 40% for jejunum. Sometimes both were intussuscepted into each other. Those numbers are an estimation as not all the patients' record specified the location of the blockage. Second, in some cases, a FB (especially linear ones) can lead to intussusception, thus overlapping both conditions. In this study, it was considered primarily as FB but then the blood results remain a mix of both. Third one is in the duration of the illness. If an owner witnessed the dog ingesting a toy, they will directly go to the emergency care and blood levels will not be changed significantly.

Finally, potential weakness of this study lies in the fact that certain data and procedures related to the animals included in this study could not be completely checked and validated. Taking blood results before any treatment was given to the patient cannot be certified as the owners may have taken the dog to another clinic, the anamnesis was not always complete, or it was a condition that lasted quite a long time and it was not possible to be certain that it was the first blood results. This may modify a lot the study by changing some critical values. If for example a blood transfusion was given before, the erythrocytes level, hemoglobin and hematocrit are modified. Another potential source of bias is related to the fact that not each animal had the data in each parameter.

6. CONCLUSION

- Appropriate prediction models can include two variables (hemoglobin and monocytes) and three variables (hemoglobin, monocytes and bilirubin).

- A decrease in hemoglobin and monocyte levels can correctly predict FB obstruction in 65% of cases, invagination in 70% and neoplasm in 15%.

- A decrease in hemoglobin, monocytes and bilirubin can predict with 72% accuracy that the dog has a foreign body, with 80% an intussusception and with 38% a neoplasm.

- If more accurate methods, such as X-ray or ultrasound, are not available, models 1 and 7 can indicate which patients should be prioritized for surgery.

- If the hematocrit value is below the normal range, the probability that the cause of the disease is a neoplasm and not an FB is 11 times higher.

- If the erythrocyte value is below the normal range, the probability that the cause is a neoplasm is 58 times higher than in the case of an FB.

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8. SUMMARY

Potential use of preoperative blood analysis to distinguish intestinal obstruction due to a foreign body or a neoplasm

Elisa Kohler

Mechanical intestinal obstruction in dogs is quite common and is usually a life-threatening condition. In an emergency situation, the basic protocol is to analyze the hematology and biochemistry. Therefore, finding a blood marker that could guide the veterinarian to a specific etiology (foreign body, intussusception or neoplasm) would be helpful for the upcoming surgery and prognosis. The majority of mechanical intestinal obstruction are due to foreign body. This study analyzed a sample of 76 dogs, of which 50 had a diagnosis of foreign body, 10 had intussusception, and 13 had neoplasm. A decrease of hemoglobin, monocytes and bilirubin could imply a non-neoplastic obstruction (in 72% a foreign body and in 80% an intussusception), whereas this decrease is only 38% chances for a neoplasm. A decrease below the reference value of the hematocrit and/or the erythrocytes level suggest more a neoplasm than a foreign body. Results of this study indicate that pre-operative blood analysis can point with certain accuracy to the underlying cause of obstruction and assist other methods to make more confident decision about the emergency of the condition. The most common surgeries for foreign body cases are enterotomies whereas for neoplasm and intussusception, it is mainly resection and anastomosis, depending on the viability of the intestines.

Key words: dogs, intestinal obstruction, prediction, blood parameters

9. SAŽETAK

Mogućnost primjene prijeoperacijske analize krvi za razlikovanje crijevne opstrukcije uzrokovane stranim tijelom ili novotvorevinom

Elisa Kohler

Mehanički začep crijeva pasa vrlo je česta i po život opasna pojava. U hitnim slučajevima osnovni protokol je provedba prijeoperacijske hematološke i biokemijske analize. Stoga bi pronalaženje krvnog pokazatelja koji bi mogao usmjeriti veterinara prema specifičnoj etiologiji (strano tijelo, invaginacija ili novotvorevina) bilo od pomoći za predstojeću operaciju i prognozu. Većina mehaničkih crijevnih opstrukcija uzrokovana je stranim tijelom. Ovo istraživanje analiziralo je uzorak od 76 pasa, od kojih je 50 imalo dijagnozu stranog tijela, 10 invaginaciju, a 13 novotvorevinu. Sniženje razine hemoglobina, monocita i bilirubina moglo bi značiti ne-neoplastičnu opstrukciju (u 72% slučajeva ukazuje na strano tijelo, a u 80% na invaginaciju), dok ovo smanjenje predstavlja samo 38% mogućnosti za novotvorevinu. Pad ispod referentne vrijednosti hematokrita i/ili razine eritrocita više ukazuje na novotvorevinu nego na strano tijelo. Rezultati ove studije pokazuju da analiza krvi prije operacije može s određenom točnošću ukazati na temeljni uzrok opstrukcije i pomoći drugim metodama u donošenju pouzdanije odluke o hitnosti stanja. Najčešći kirurški zahvati za slučajeve stranog tijela su enterotomije, dok su za novotvorevine i invaginaciju uglavnom resekcija i anastomoza, ovisno o vitalnosti crijeva.

Ključne riječi: psi, opstrukcija crijeva, predviđanje, krvni pokazatelji

10. CURRICULUM VITAE

I was born the 27th of May 1998 in Orléans, France. From 2013 to 2016, I went to Lycée Voltaire high school in Orléans where I got the baccalaureate in Science. After that, I did two years of prépa BCPST (Biology, Chemistry, Physics and Geology). In 2018, I applied to the Faculty of Veterinary Medicine of the University of Zagreb, Croatia, in which I was accepted and fulfilled my six years cursus in English.

In 2019, I was part of the Plavi Project at the faculty and with a team of three people we produced a poster with a QR code for coastal tourist agencies to promote 'dolphin friendly behavior' and make them help the scientists to monitor the dolphins' population through pictures.

In 2021, I volunteered for a month in a wildlife hospital (association Goupil), south of France. I learnt how to bandage birds' wings, general husbandry about birds of prey, other birds, foxes, hedgehogs and other little mammals, how to force-feed birds and how to reinsert them in nature.

In 2022, I volunteered as a veterinarian intern at RAREC (Rainforest Awareness Rescue and Education) in Peru for a month. There, I gave therapies, monitored anesthesia, did nightshifts for nocturnal patients, learnt how to handle primates, their general husbandry, how the conservation and reintroduction of monkeys work, the implementation of emergency measures for an epidemy and I did a health checkup of a dolphin.

In July 2023, I worked as a veterinary nurse in Clinique du Gabereau in France.

In May 2024, I did an Erasmus internship of two months at Blanchardstown Veterinary Hospital in Dublin. I monitored anesthesia, administered therapies and anesthetics, prepared the animals for surgery, assisted in surgery, did castrations of dogs and cats by myself and helping the clinicians when needed.