American Journal of Emergency Medicine 37 (2019) 1912–1916

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Pentraxin-3: A strong novel biochemical marker for appendicitis in children

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ARTICLE INFO

Article history:
Received 18 November 2018
Received in revised form 8 January 2019
Accepted 11 January 2019

Keywords:
Pediatric
Appendicitis
Pentraxin-3
Biomarker
C-reactive protein

ABSTRACT

Introduction: Appendicitis is the most common surgical disease evaluated by pediatric surgeons in the emergency department. Despite the history, physical examination, laboratory tests and imaging methods, the misdiagnosis may be observed often in children. Pentraxin-3 (PTX-3) is an acute phase protein which is produced directly in the inflammatory tissue. Our aim was to investigate the diagnostic value of PTX-3 levels in appendicitis in pediatric patients and compare it with the other serum parameters.

Methods: Eighty-eight patients (aged <18 years) were included in this study [Group 1 (n = 28) healthy volunteers, Group 2 (n = 28) patients with non-specific abdominal pain, Group 3 (n = 34) patients underwent appendectomy]. Serum white blood cell (WBC), absolute neutrophil count (ANC), neutrophil/lymphocyte ratio (NLR), C-reactive protein (CRP) and PTX-3 values were measured.

Results: Median serum levels of WBC were higher in Group 2 and 3 than Group 1. ANS, NLR, CRP and PTX-3 were higher in Group 2 than Group 1 and were higher in Group 3 than the other groups. The highest sensitivity was found in NLR >3.5 [94.1 (95% CI = 80.3–99.3)] and PTX-3 > 5.6 ng/mL [91.8 (95% CI = 76.3–98.1)]. PTX-3 has the highest specificity among all of the parameters [90.7 (95% CI = 79.7–96.9)]. The area under the ROC curve showed that the diagnostic value of PTX-3 was greater than any other parameter [0.979 (95% CI = 0.92–0.99)].

Conclusion: In this study, we have shown that PTX-3 is very useful with high sensitivity and specificity in the diagnosis of appendicitis compared to WBC, ANS, NLR and CRP as a first in the literature.

1. Introduction

In pediatric patients, acute abdominal pain is a common complaint upon presentation to the emergency department and pediatric surgery department. In addition to completing a clinical history and physical examination, laboratory studies and imaging techniques are frequently used for the diagnosis, especially in children, because distinguishing between appendicitis and the nonsurgical causes of abdominal pain is still a challenge. To overcome this obstacle, researchers have been searching for new biomarkers that may help with such a diagnosis.

The pentraxins are a group of multimeric proteins that are responsible for the humoral innate immune response, and they are divided into long and short subgroups based on the length of the N-terminal region [1]. Short pentraxins include the C-reactive protein (CRP) and serum amyloid P component, which are primarily expressed in the liver as responses to inflammation, infection, and tissue damage. Pentraxin 3 (PTX-3) is the prototype of the long pentraxin group [2], and it is synthesized locally at the site of inflammation, by various cell types, including mesenchymal, myeloid, endothelial, and epithelial cells, in response to inflammatory cytokines and microbial components [3]. Both CRP and PTX-3 exhibit low plasma levels in healthy humans; however, their levels rise rapidly in inflammatory situations, with CRP reaching its maximum peak at 48 h and PTX-3 in 6 h [4]. The more rapid increase seen in PTX-3 is likely due to its local production by a number of cells, as well as the release of the PTX-3 stored in specific granules in the neutrophils [5]. Based on these features, PTX-3 is an effective inflammatory biomarker used in the diagnosis of many different diseases, such as coronary syndromes, respiratory system infections, sepsis, cancer, and pelvic inflammatory disease [3,6-8].

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https://doi.org/10.1016/j.ajem.2019.01.010
0735-6757/

In light of the abovementioned information, we planned to investigate the value of PTX-3 in the diagnosis of appendicitis in a pediatric population, and this is the first study to do so in the literature. Additionally, we aimed to determine whether this biomarker was superior to any other biomarkers currently being used in clinical practice, such as the complete blood count variables [white blood cell (WBC) count, absolute neutrophil count (ANC), and neutrophil/lymphocyte (N/L) ratio] and the CRP level.

2. Methods

2.1. Patient variables

This prospective study was conducted in the pediatric surgery department of our university after receiving approval from the institution's Human Interventional Ethics Committee (approval number: 15022018/21). From February 2018 to July 2018, 88 patients <18 years old were consecutively included in this study. Group 1 consisted of otherwise healthy volunteers who were admitted to our clinic for outpatient surgery (n = 28). The patients with abdominal pain were divided into two groups. One group was made up of patients with nonspecific abdominal pain (NSAP) who were observed for 24–48 h and discharged (Group 2, n = 28). Those patients were contacted by phone 2 weeks after discharge in order to make sure that appendicitis did not develop during the follow-up period. The patients with obvious symptoms, like urinary tract infections, gastroenteritis, and respiratory system infections, were excluded from the study. Finally, the patients who underwent appendectomies were included in Group 3 (n = 34). The exclusion criteria for this group were as follows: pregnancy, prior surgery for abdominal conditions, pelvic inflammatory disease, concomitant ovarian pathologies, and chronic diseases.

2.2. Biochemical analyses

Upon admission to the clinic, 5 mL of blood was taken from each patient, and the WBC, ANC, PTX-3, and CRP values were obtained. The N/L ratio was calculated by dividing the absolute number of neutrophils by the absolute lymphocyte number. The blood samples were centrifuged for 5 min at 3000 rpm, and a volume of 2 cc of serum from each sample was separated into an Eppendorf tube and stored at −80 °C for the PTX-3 evaluation. After reaching a sufficient sample size, the PTX-3 levels of the serum samples were tested simultaneously in the microbiology laboratory of our university. This testing was conducted under double-blind conditions using a microenzyme-linked immunosorbent assay (micro-ELISA), consistent with the quantitative standards based on the Human PTX-3 ELISA Kit (Boster Biological Technology, Pleasanton, CA, USA) protocol. Finally, the samples were measured using an ELx808 Absorbance Microplate Reader (Bio Tek Instruments, Winooski, VT, USA) at a 450-nm wavelength.

2.3. Statistical analysis

The sample size was calculated using the G*Power 3.1 software program (Heinrich Heine University Düsseldorf, Düsseldorf, Germany). In a study of PTX-3 performed on adult patients, Aygun et al. found that the median PTX-3 levels are 3.28 ng/mL in patients with appendicitis and 0.97 ng/mL in patients without appendicitis [9]. Using these values, we calculated a sample size of minimum 16 individuals needed to be included in each group for 95% power and a 5% error level.

The data analysis was carried out using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA) and MedCalc statistical software (version 15.0; MedCalc Software bvba, Ostend, Belgium). The descriptive statistics were given as the number of units (n), percentile (%), mean ± standard deviation or median with interquartile range. The normal distribution of the numerical variables was determined by using the Shapiro-Wilk normality test. If the data complied with a normal distribution, the statistical differences between the groups were evaluated using the one-way analysis of variance and post hoc tests. If the data did not comply with a normal distribution, the Kruskal-Wallis and Mann-Whitney *U* tests were used. A p value of <0.05 was considered to be statistically significant.

The cut-off values were obtained using a receiver operating characteristic (ROC) analysis in order to differentiate between the non-appendicitis and appendicitis groups. The clinical performance parameters were defined with regard to the sensitivity, specificity, and likelihood ratio.

3. Results

This study included 60 patients who were admitted to the pediatric surgery department due to abdominal pain and 28 healthy volunteers. The demographic information and the WBC, ANC, N/L ratio, CRP, and PTX-3 values are shown in Table 1. The WBC serum level medians were higher in Groups 2 and 3 than in Group 1. The ANC, N/L ratio, CRP, and PTX-3 values were higher in Group 2 when compared to Group 1, and they were higher in Group 3 when compared to the other two groups. The distributions of all of the parameters between the groups are shown in Figs. 1 and 2.

The N/L ratio at >3.5 and PTX-3 level at 5.6 ng/mL exhibited the highest sensitivity, and the PTX-3 exhibited the highest specificity among all of the parameters (Table 2). The area under the ROC curve (AUC) showed that the diagnostic value of the PTX-3 was greater than any of the other biochemical parameters (AUC = 0.979) (Fig. 3).

4. Discussion

It is crucial to make the correct diagnosis of acute appendicitis in order to prevent further complications, like perforations, as well as to prevent unnecessary surgery. The diagnosis must be done also promptly, because the perforation risk is increased in a linear fashion with the duration of symptoms as stated in the study of Narsule et al. [10]. Surgeons rely on the clinical history and physical examination; however, especially in young or uncooperative children, the presumed diagnosis must be supported with additional laboratory tests or imaging modalities [11-13].

In this study, we investigated the role of PTX-3 in the diagnosis of acute appendicitis in children. We found that PTX-3 was very effective for distinguishing appendicitis with a high sensitivity and specificity. It was also evident that PTX-3 was superior to all

Table 1
Descriptive analysis and comparison of the laboratory parameters in the three groups.

Parameters	Group 1 (n = 28)	Group 2 (n = 26)	Group 3 (n = 34)
Age (years)	10.00 [8.00–12.75]	12.00 [9.75–14.00]	10.00 [7.00–13.00]
Sex, male/female (ratio)	24/7 (3.4:1)	12/14 (1:1.2)[c]	22/12 (1.8:1)
WBC (cells/μL)	7971 ± 1926	13,450 ± 6070[a]	16,100 ± 4332[a]
ANC (cells/μL)	3882 ± 1357	10,026 ± 6299[a]	13,088 ± 4304[b]
N/L ratio	1.47 ± 0.78	6.75 ± 8.50[a]	11.87 ± 10.41[b]
CRP (mg/L)	0.88 ± 0.68	17.41 ± 34.77[a]	42.09 ± 15.80[b]
PTX-3 (ng/mL)	1.09 ± 0.97	4.07 ± 1.55[a]	12.82 ± 4.96[b]

Values are expressed in mean ± SD or median [interquartile ranges].
[a] Different from Group 1 (p < 0.05).
[b] Different from Group 1 and Group 2 (p < 0.05).
[c] Different from Group 1 and Group 3 (p < 0.05).

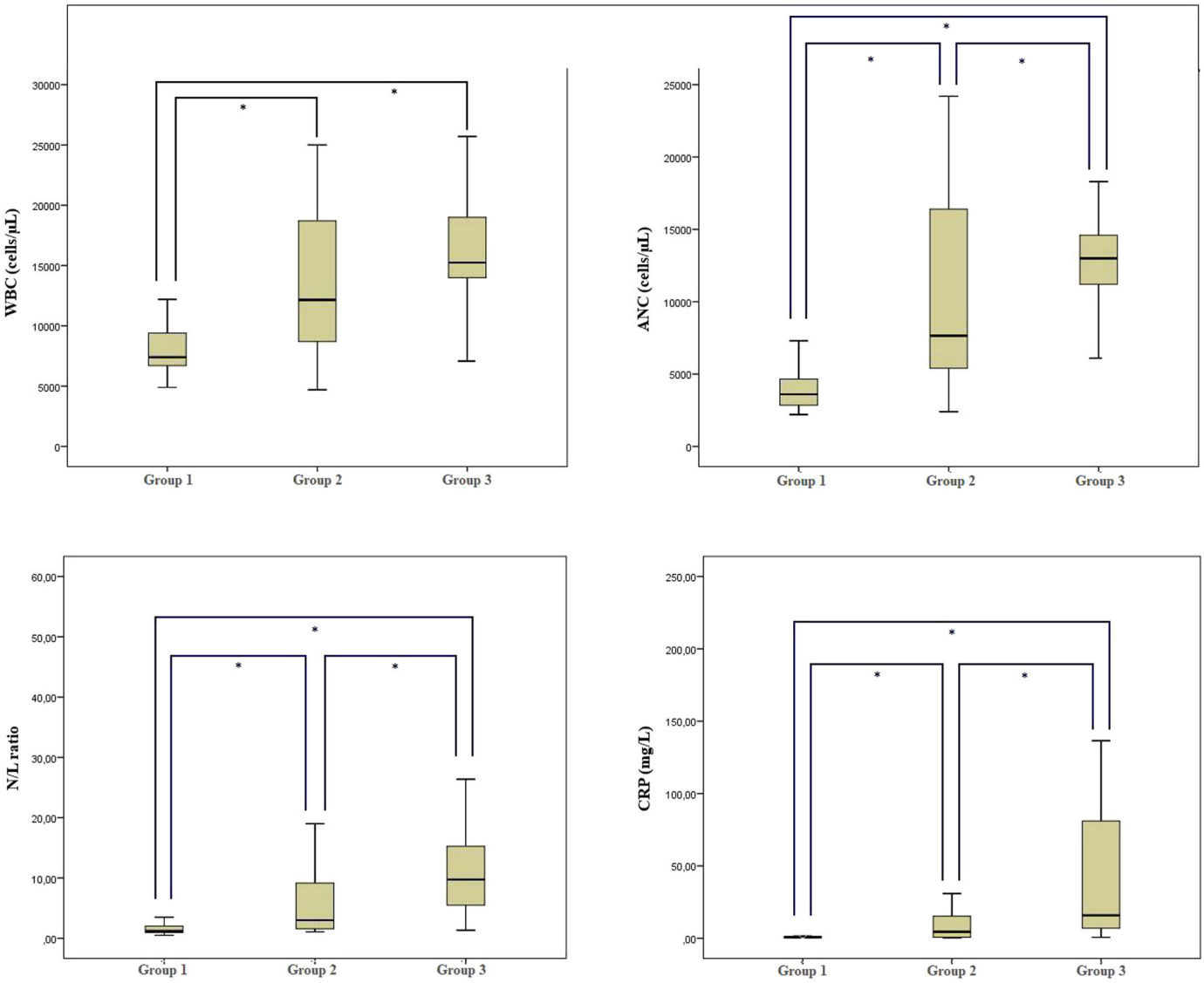

Fig. 1. Comparison of the serum WBC, ANC, N/L ratio, CRP levels between healthy controls (Group 1), non-specific abdominal pain (Group 2) and appendicitis patients (Group 3). * = $p < 0.05$.

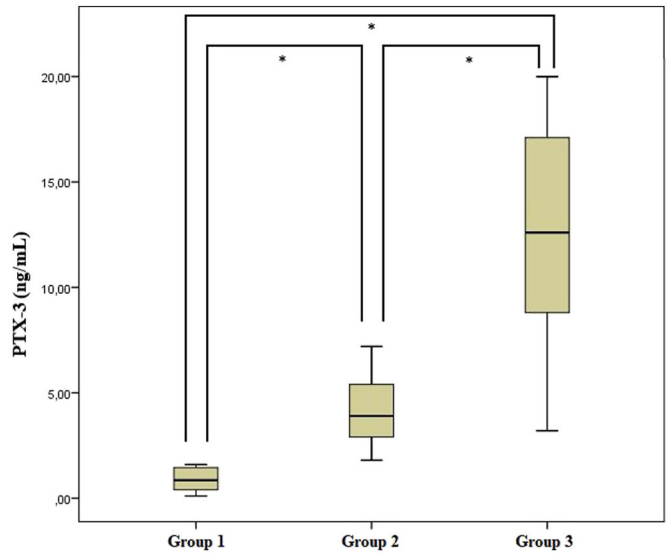

Fig. 2. Comparison of the serum PTX-3 levels between three groups. * = $p < 0.05$.

of the other markers used in clinical practice (i.e., WBC, ANC, N/L ratio, and CRP values), with a high accuracy (AUC = 0.979).

The complete blood count is the most commonly ordered laboratory test for children suspected of having appendicitis. The most commonly used diagnostic scoring systems (the Alvarado score and Pediatric Appendicitis Score) include an elevated WBC count and left shift (neutrophil predominance, absolute neutrophil count >75%) [14,15]. However, the WBC results are usually nonspecific, because elevations may be seen in numerous infectious diseases [16]. In our study, the WBC values of the healthy controls (Group 1) were lower than those in the other two groups, but there was no difference between the group with nonspecific abdominal pain and the appendicitis group. Kessler et al. reported a 69% elevation in the WBC count of appendicitis patients and a 56% elevation in non-appendicitis patients, with a sensitivity of 77% and a specificity of 63% at a level above 10,000 cells/μL [17]. In their study, Allister et al. reported that the appendicitis patients had elevated WBC values that were greater than those of the control subjects (14,200 cells/μL vs. 10,600 cells/μL) [18]. Therefore, we believe that the WBC count has a limited diagnostic utility for discriminating appendicitis in patients with right lower quadrant pain.

Table 2
The sensitivity and specificity percent of the parameters in diagnosing acute appendicitis.

Parameters	Sensitivity (95% CI)	Specificity (95% CI)	+LR (95% CI)	−LR (95% CI)	AUC (95% CI)
WBC > 12,700	85.3 (68.9–95.0)	79.6 (66.5–89.4)	4.19 (2.4–7.2)	0.18 (0.08–0.4)	0.806 (0.71–0.88)
ANC > 11,100	76.4 (58.8–89.3)	81.4 (68.6–90.7)	4.13 (2.3–7.4)	0.29 (0.2–0.5)	0.828 (0.73–0.90)
N/L ratio > 3.5	94.1 (80.3–99.3)	77.8 (64.4–88.0)	4.24 (2.6–7.0)	0.08 (0.02–0.3)	0.863 (0.77–0.93)
CRP > 5.0	82.4 (65.5–93.2)	81.5 (68.6–90.7)	4.45 (2.5–7.9)	0.22 (0.1–0.5)	0.853 (0.76–0.92)
PTX-3 > 5.6	91.8 (76.3–98.1)	90.7 (79.7–96.9)	9.85 (4.2–22.8)	0.10 (0.03–0.3)	0.979 (0.92–0.99)*

Abbreviations: +LR: Positive likelihood ratio, −LR: Negative likelihood ratio, CI: Confidence interval, AUC: Area under curve [*: different from other parameters, $p < 0.001$].

In the ANC values, there was a difference between the nonspecific abdominal pain group (Group 2) and the appendicitis group (Group 3), which was also reported in the studies by Khan et al. and Benito et al. [19,20]. In a study conducted by Fergusson et al., a neutrophil count of >11,000 cells/mm^3 revealed a 59% sensitivity and 88% specificity, while Kharbanda et al. found similar results with 69% sensitivity and 75% specificity [21,22]. Our study revealed similar percentages with regard to a moderate power of discrimination between the appendicitis patients and those with NSAP.

The diagnostic value of the N/L ratio has been investigated by many researchers. Our study revealed a significant difference between the three groups with regard to the N/L ratio, which is in accordance with the results seen in the literature. In a former study, we found a 90% sensitivity and an 88% specificity at a level of >3.5 for the N/L ratio, which suggests that an N/L ratio of 3.5 may be used as a diagnostic cut-off value for children with appendicitis [23]. When investigating the N/L ratio, Nazik et al. found significantly higher values in the appendicitis patients (mean = 6.06 ± 4.1) than in the control patients (mean = 1.24 ± 0.8) [24].

The CRP is the most characteristic and widely used acute phase reactant in humans [25]. We found an increasingly high sensitivity and specificity, reaching up to a mean of 15.80 mg/L in the appendicitis group. Previously, sensitivities of 0.58–0.85 and specificities of 0.33–0.82 were reported [26-29]. Mikaelsson et al. found that children with a CRP level of 25 mg/L or higher were more likely to have appendicitis, while Rodrigez-Sanjuan et al. found that children with a CRP level >17 mg/L were more likely to have appendicitis [28,30]. We found a CRP level of >15.80 mg/L in the appendicitis group, which was consistent with these two articles.

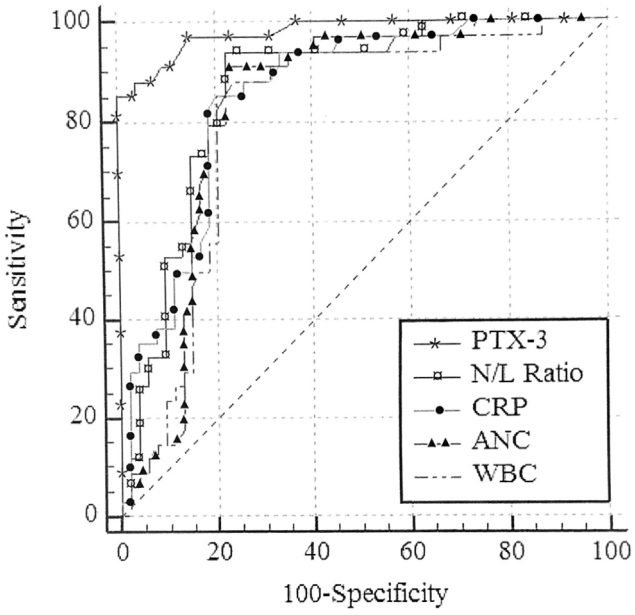

Fig. 3. ROC curves for WBC, ANC, N/L ratio, CRP and PTX-3 to discriminate appendicitis from non-appendicitis.

PTX-3 was the first long pentraxin identified, and it is different from the CRP in terms of producing cells and inducing signals. It is made locally in response to inflammation, at the inflammation site. Based on this feature, PTX-3 may be used as a novel diagnostic tool, because it may directly reflect the tissue involvement of an inflammatory process better than the CRP [7]. An increase in the PTX-3 level has been well-described in many infectious diseases (e.g., pneumococcal infections, sepsis, pelvic inflammatory disease, cholecystitis, and urinary tract infections) as well as inflammatory diseases, like acute myocardial infections and preeclampsia [6,8,31-35].

In our study, we found a significant difference between the three groups, with higher PTX-3 levels in the appendicitis patients. There is one study in the literature by Aygun et al. that investigated the diagnostic value of PTX-3 in acute appendicitis in adults [9]. They found significant differences between the appendicitis group (median = 3.28 ng/mL) and both the NSAP group (median = 1.31 ng/mL) and control group (median = 0.97 ng/mL). Our results were similar to those, but the PTX-3 value in the appendicitis group was higher (median = 12.60 ng/mL) in our study. Muller et al. found that the serum PTX-3 levels were correlated with the severity of the infection in critically ill patients [7]. Based on this data, we can speculate that the usual delay associated with children being admitted to the hospital was the reason for the higher PTX-3 values in our study.

In order to evaluate the clinically discriminative capacities of these biochemical parameters, we performed a ROC curve analysis. We found that the AUC of the ROC analysis of the PTX-3 values was higher when compared to the other parameters ($p < 0.001$). The positive likelihood ratio was also high, which shows the power of the true discrimination of appendicitis by the PTX-3 level. Hamed et al. showed that the AUC of the PTX-3 values [IQR = 0.92 (0.87–0.97)] was higher than those of the CRP values [0.82 (IQR = 0.72–0.91)] and WBC values [0.59 (IQR = 0.46–0.72)] on the first day of hospitalization in sepsis patients [36]. In their study, Aygun et al. found a lower AUC for the PTX-3 values (AUC = 0.739) when compared to the results of our study [9]. This finding may indicate that the PTX-3 level is more sensitive in the pediatric population than in adults with appendicitis.

Limitations of this study include the following: (a) This study is a single-center study conducted in a tertiary hospital and has a relatively small sample size, therefore it may not reflect the entire population of patients with suspected appendicitis. (b) One group consists of patients with "non-specific abdominal pain" instead of patients with "abdominal pain". However, we do not believe that this situation affects the performance of this test because our most important problem is to differentiate NSAP from appendicitis in the current practice. NSAP is a diagnosis of exclusion made by the clinician, who cannot diagnose an organic pathology. If specific pathologies like gastroenteritis, urinary tract infection or respiratory infection are diagnosed already, there will be no need for complementary tests. (c) Period of time from the beginning of

the complaints to blood draw is not investigated (disease progression bias). In the study of Wu et al., they showed that inflammatory markers (WBC and CRP) may provide a favorable diagnostic value at different time points in the diagnosis of appendicitis [37]. Also, Benito et al. stated that the diagnostic performance of the tests (WBC, CRP, ANC, procalcitonin, calprotectin, APPY1) was superior in children in whom the onset of pain was >24 h [19]. As we showed that PTX-3 increases in patients with appendicitis, the correlation of elevation of PTX-3 with time may be investigated also.

5. Conclusions

In this study, we showed that the PTX-3 levels were significantly higher in the pediatric appendicitis patients than in the abdominal pain and healthy patients, with a high accuracy. These findings imply that a high PTX-3 level is a strong indicator of appendicitis and may help distinguish children with appendicitis from children with non-specific abdominal pain.

Further studies should be planned to investigate the timely increase in the PTX-3 level with regard to its quick response to inflammation in order to diagnose these patients faster, and to monitor the clinical progression of suspected appendicitis patients. Additionally, the differences between perforated and nonperforated appendicitis cases should also be investigated, with larger patient numbers in each of the groups.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding source

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] Vilahur G, Badimon L. Biological actions of pentraxins. Vascul Pharmacol 2015;73:38–44.
[2] Cieślik P, Hrycek A. Long pentraxin 3 (PTX3) in the light of its structure, mechanism of action and clinical implications. Autoimmunity 2012;45:119–28.
[3] Giacomini A, Ghedini GC, Presta M, Ronca R. Long pentraxin 3: a novel multifaceted player in cancer. Biochim Biophys Acta, Rev Cancer 2018;1869:53–63.
[4] Peri G, Introna M, Corradi D, Iacuitti G, Signorini S, Avanzini F, et al. PTX3, a prototypical long pentraxin, is an early indicator of acute myocardial infarction in humans. Circulation 2000;102:636–41.
[5] Jaillon S, Peri G, Delneste Y, Fremaux I, Doni A, Moalli F, et al. The humoral pattern recognition receptor PTX3 is stored in neutrophil granules and localizes in extracellular traps. J Exp Med 2007;204:793–804.
[6] Koh SH, Shin SG, Andrade MJ, Go RH, Park S, Woo CH, et al. Long pentraxin PTX3 mediates acute inflammatory responses against pneumococcal infection. Biochem Biophys Res Commun 2017;493:671–6.
[7] Muller B, Peri G, Doni A, Torri V, Landmann R, Bottazzi B, et al. Circulating levels of the long pentraxin PTX3 correlate with severity of infection in critically ill patients. Crit Care Med 2001;29:1404–7.
[8] Yang SF, Wu TF, Tsai HT, Lin LY, Wang PH. New markers in pelvic inflammatory disease. Clin Chim Acta 2014;431:118–24.
[9] Aygun A, Katipoglu B, Ĭmamoglu M, Demir S, Yadigaroglu M, Tatli O, et al. Diagnostic value of plasma pentraxin-3 in acute appendicitis. J Invest Surg 2017:1–6.
[10] Narsule CK, Kahle EJ, Kim DS, Anderson AC, Luks FI. Effect of delay in presentation on rate of perforation in children with appendicitis. Am J Emerg Med 2011;29:890–3.
[11] Kulik DM, Uleryk EM, Maguire JL. Does this child have appendicitis? A systematic review of clinical prediction rules for children with acute abdominal pain. J Clin Epidemiol 2013;66:95–104.
[12] Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: Nationwide analysis. Arch Surg 2002;137:799–804.
[13] Groselj-Grenc M, Repse S, Vidmar D, Derganc M. Clinical and laboratory methods in diagnosis of acute appendicitis in children. Croat Med J 2007;48:353–61.
[14] Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986;15:557–64.
[15] Samuel M. Pediatric appendicitis score. J Pediatr Surg 2002;37:877–81.
[16] Kwan KY, Nager AL. Diagnosing pediatric appendicitis: usefulness of laboratory markers. Am J Emerg Med 2010;28:1009–15.
[17] Kessler N, Cyteval C, Gallix B, Lesnik A, Blayac PM, Pujol J, et al. Appendicitis: evaluation of sensitivity, specificity, and predictive values of US, Doppler US, and laboratory findings. Radiology 2004;230:472–8.
[18] Allister L, Bachur R, Glickman J, Horwitz B. Serum markers in acute appendicitis. J Surg Res 2011;168:70–5.
[19] Benito J, Acedo Y, Medrano L, Barcena E, Garay RP, Arri EA. Usefulness of new and traditional serum biomarkers in children with suspected appendicitis. Am J Emerg Med 2016;34:871–6.
[20] Khan AN, Sawan A, Likourezos A, Schnellinger M, Garcia E. The usefulness of procalcitonin in the diagnosis of appendicitis in children: a pilot study. Emerg Med Int 2012;2012:317504.
[21] Fergusson JA, Hitos K, Simpson E. Utility of white cell count and ultrasound in the diagnosis of acute appendicitis. ANZ J Surg 2002;72:781–5.
[22] Kharbanda AB, Cosme Y, Liu K, Spitalnik SL, Dayan PS. Discriminative accuracy of novel and traditional biomarkers in children with suspected appendicitis adjusted for duration of abdominal pain. Acad Emerg Med 2011;18:567–74.
[23] Yazici M, Ozkisacik S, Oztan MO, Gürsoy H. Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. Turk J Pediatr 2010;52:400–3.
[24] Nazik S, Avci V, Küskü Kiraz Z. Ischemia-modified albumin and other inflammatory markers in the diagnosis of appendicitis in children. Ulus Travma Acil Cerrahi Derg 2017;23:317–21.
[25] Agrawal A, Singh PP, Bottazzi B, Garlanda C, Mantovani A. Pattern recognition by pentraxins. Adv Exp Med Biol 2009;653:98–116.
[26] Wu HP, Chang CF, Lin CY. Predictive inflammatory parameters in the diagnosis of acute appendicitis in children. Acta Paediatr Taiwan 2003;44:227–31.
[27] Peltola H, Ahlqvist J, Rapola J, Räsänen J, Louhimo I, Saarinen M, et al. C-reactive protein compared with white blood cell count and erythrocyte sedimentation rate in the diagnosis of acute appendicitis in children. Acta Chir Scand 1986;152:55–8.
[28] Rodríguez-Sanjuán JC, Martin-Parra JI, Seco I, Garcia-Castrillo L, Naranjo A. C-reactive protein and leukocyte count in the diagnosis of acute appendicitis in children. Dis Colon Rectum 1999;42:1325–9.
[29] Paajanen H, Mansikka A, Laato M, Kettunen J, Kostiainen S. Are serum inflammatory markers age dependent in acute appendicitis? J Am Coll Surg 1997;184:303–8.
[30] Mikaelsson C, Arnbjornsson E. The value of C-reactive protein (CRP) determinations in patients with suspected acute appendicitis. Ann Chir Gynaecol 1984;73:281–4.
[31] Ketter P, Yu JJ, Cap AP, Forsthuber T, Arulanandam B. Pentraxin 3: an immune modulator of infection and useful marker for disease severity assessment in sepsis. Expert Rev Clin Immunol 2016;12:501–7.
[32] Aksungur N, Ozogul B, Ozturk N, Arslan S, Karadeniz E, Korkut E, et al. Prognostic importance of pentraxin 3 levels in acute cholesistitis. Ulus Travma Acil Cerrahi Derg 2015;21:380–4.
[33] Jaillon S, Moalli F, Ragnarsdottir B, Bonavita E, Puthia M, Riva F, et al. The humoral pattern recognition molecule PTX3 is a key component of innate immunity against urinary tract infection. Immunity 2014;40:621–32.
[34] Latini R, Maggioni AP, Peri G, Gonzini L, Lucci D, Mocarelli P, et al. Lipid Assessment Trial Italian Network (LATIN) investigators. Prognostic significance of the long pentraxin PTX3 in acute myocardial infarction. Circulation 2004;110:2349–54.
[35] Akhter T, Wikström AK, Larsson M, Larsson A, Wikström G, Naessen T. Serum Pentraxin 3 is associated with signs of arterial alteration in women with preeclampsia. Int J Cardiol 2017;241:417–22.
[36] Hamed S, Behnes M, Pauly D, Lepiorz D, Barre M, Becher T, et al. Diagnostic value of Pentraxin-3 in patients with sepsis and septic shock in accordance with latest sepsis-3 definitions. BMC Infect Dis 2017;17:554.
[37] Wu HP, Chen CY, Kuo IT, Wu YK, Fu YC. Diagnostic values of a single serum biomarker at different time points compared with Alvarado score and imaging examinations in pediatric appendicitis. J Surg Res 2012;174:272–7.