Original Research Article

DOI: http://dx.doi.org/10.18203/2349-2902.isj20174488

Diagnostic value of C-reactive protein and neutrophil-limphocyte ratio in perforated appendicitis at Hasan Sadikin Hospital Bandung

Reno Rudiman*, Tommy Ruchimat, Yohanes Ferdinand

Department of Surgery, Division of Digestive Surgery, Hasan Sadikin Hospital, Faculty of Medicine, Padjadjaran University, Bandung, West Java, Indonesia

Received: 18 July 2017 Accepted: 18 August 2017

*Correspondence: Dr. Reno Rudiman.

E-mail: rudiman@unpad.ac.id

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The diagnosis of appendicitis depends on the subjective criteria of clinical examination. However, distinguishing acute perforated appendicitis (local peritonitis) and non-perforated is often difficult especially in the elderly population that usually not clinically specific unless it has developed into generalized peritonitis. Between the non-perforated acute appendicitis and perforate should be distinguished because of different surgical approaches. Creactive protein (CRP) and neutrophil-lymphocyte ratios are known to be associated with various conditions such as malignancy, heart disease, and inflammation, including acute perforated appendicitis. This examination not only is cheaper, but also feasible and available in peripheral hospitals compared to other supports such as ultrasound or CT scan, but this examination has not been routinely used so the purpose of this study is to examine the diagnostic accuracy of both laboratory parameters so as to assist a surgeon to determine whether the case of appendicitis has been perforated or not and can provide information to patients and the families about the diseases and surgical techniques to be performed.

Methods: This study used cross sectional analytic in two groups, appendicitis with and without perforation group to know the value of sensitivity, specificity, positive predictor value, negative predictor value, from CRP and RNL in both groups.

Results: Of the 46 patients who met the inclusion criteria, the mean age of patients with perforated appendicitis was 33.73±17.101, male sex counted 26 patients (56.5%) and women 20 patients (43.5%). Based on ROC curve analysis, CRP = 76,65 and RNL = 8,825 were obtained, and sensitivity, specificity, positive guess, negative prediction and accuracy value for CRP were 88.0%, 71.4%, 78 %, 5%, 83.3% and 80.4%; While for RNL of 64.0%, 80.9%, 80.0%, NDN, and 71.7%.

Conclusions: CRP and RNL have a strong diagnostic value and is moderately strong in cases of perforated appendicitis.

Keywords: C-reactive protein, Neutrophil-lymphocyte ratio, Non-perforated appendicitis, Perforated appendicitis

INTRODUCTION

Perforated appendicitis is generally associated with an abscess or phlegmon, having an incidence rate of approximately 2 per 10000, with a proportion of 25% of all cases of appendicitis. It is more common in elderly patients due to unspecific clinical manifestations and

comorbidity. The high risk of perforation also increases with increasing duration of symptoms (6% risk after the first 36 hours). 1,3-5 The diagnosis of acute appendicitis depends on subjective criteria such as onset of symptoms, type of pain, and physical examination. Distinguishing acute appendicitis with perforation (local peritonitis) based on clinical findings is often difficult especially in elderly patients unless it has developed into generalized

peritonitis. If a case of appendicitis is suspected of perforation, the median laparotomy incision should be considered so it is important to distinguish whether perforation has occurred. Investigations such as ultrasound or CT scan can help establish a diagnosis of perforated appendicitis and assist a surgeon to determine the approach of surgical technique. However, these are not always available in health institutions or emergency units in developing country hospitals, especially in remote areas and the costs are also relatively expensive, so we can rely solely on clinical and routine laboratory examinations such as white blood count.^{1,2,6}

There has been a growing interest in laboratory studies used to support the diagnosis of conditions such as malignancy, heart disease and inflammation process like appendicitis, including c-reactive protein (CRP) and neutrophil-lymphocyte ratios. This examination is feasible especially in peripheral areas where radiologist support is not always available and the cost relatively cheaper. In the previous study it has been mentioned how the CRP and RNL parameters are related to inflammatory cases as in the case of appendicitis, but none of the single parameters, whether the number of leukocytes, neutrophils, or CRPs can be used to a simple and perforated acute appendicitis. 8-10

The examination of CRP and RNL has not been a routine examination in diagnosing perforated appendicitis. In view of the above description, the researcher wishes to try to do research on diagnostic test of CRP and RNL examination in diagnosing perforated appendicitis, so that it can help a surgeon in determining surgical technique approach while providing information to patient and family about the disease and surgical technique approach that will be performed.

METHODS

The study was conducted at the Emergency ward, Digestive Surgery Division, Department of Surgery, Clinical Pathology Laboratory and Anatomical Pathology of Dr. Hasan Sadikin Hospital, Bandung, West Java from January 1st to May 15th, 2017. This study has obtained approval and recommendation from Health Research Ethics Committee of Faculty of Medicine, Padjadjaran University/Dr. Hasan Sadikin Hospital. Samples were taken from subjects who met the inclusion and exclusion criteria.

Inclusion criteria

- Patients aged 14 years or older who were diagnosed as appendicitis with a Tzanakis score of 8 or more
- Willing to be operated.

Exclusion Criteria

Patient with chief complaint diffuse abdominal tenderness

- Patients with other acute infectious diseases
- Patients with previous liver diseases
- Patients with comorbidity (heart disease, malignancy, diabetes mellitus, tuberculosis, AIDS and autoimmune diseases)
- Patients with severe sepsis or septic shock
- Patients who performed appendectomy but with histopathologic result not appendicitis.

The determination of the sample size was based on statistical calculation by establishing 95% confidence level, and adjusted to the research objectives and the data type in the study. Based on the statistical formula, a total of 46 samples is required for this study.

The design of the study was cross sectional analytic in two groups, namely group of non-perforated and perforated acute appendicitis.

All patients who met the inclusion criteria were taken blood sampling for blood count type, and CRP prior to the surgery. Patients then performed surgery and the intraoperative findings are noted with histopathologic confirmation later on as the gold standard. Grouping and data analysis using SPSS 24.0 statistical program to obtain the value of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy.

RESULTS

Table 1 shows the characteristics of the patients. The mean age is 33.73 ± 17.101 , with 26 male patients (56.5%) and 20 females (43.5%). Mean CRP value is 159.10 ± 134.907 . Mean value RNL is 8.83 ± 5.849 .

Table 1: Characteristics of patients.

Variable	N=46
Age	
Mean±Std	33.73±17.101
Median	28
Range (min-max)	14-77
Gender	
Male	26 (56.5%)
Female	20 (43.5%)
CRP	
Mean±Std	159.10±134.907
Median	135.050
Range (min-max)	0.80-505.90
RNL	
Mean±Std	8.83±5.849
Median	8.250
Range (min-max)	0-31

Table 2 describes the comparison between age and sex in the perforated and simple acute appendicitis group. For the age group of appendicitis patients accompanied by perforation had an average of 33.36±16.582 whereas in

the appendicitis patient group without perforation had an average of 34.19±18.101. There were 17 males (68%) and 8 females (32%). Patients in perforated appendicitis

group, while in simple acute appendicitis group there were 9 males (42.9%) and 12 female patients (57.1%) (p > 0.05).

Table 2: Comparison between age and sex in the perforated and simple acute appendicitis group.

	Perforation	Perforation		
Variable	Positive (+)	Negative (-)	P-value	
	N=25	N=21		
Age			0.903	
Mean±Std	33.36±16.582	34.19±18.101		
Median	28	28.000		
Range (min-max)	14-67	15-77		
Sex			0.087	
Male	17 (68.0%)	9 (42.9%)		
Female	8 (32.0%)	12 (57.1%)		

Table 3: Comparison between CRP and NLR in the perforated and simple acute appendicitis group.

	Perforation	Perforation		
Variable	Positive (+)	Negative (-)	P-value	
	N=25	N=21		
CRP			<0.01	
Mean±Std	210.09±114.651	98.39±134.370		
Median	241.500	32.600		
Range (min-max)	1.30-505.90	0.80-388.80		
RNL			<0.01	
Mean±Std	11.40±5.693	5.77±4.466		
Median	11.600	4.290		
Range (min-max)	4.29-31.00	0-14.60		

Table 3 describes the comparison between CRP and in the perforated and simple acute appendicitis group. The mean value for CRP in the perforated appendicitis group is 210.09 ± 114.651 , while in the group without perforation is 98.39 ± 134.370 . The mean value for RNL in the perforated appendicitis group is 11.40 ± 5.693 while in the group without perforation is 5.77 ± 4.466 (p < 0.01).

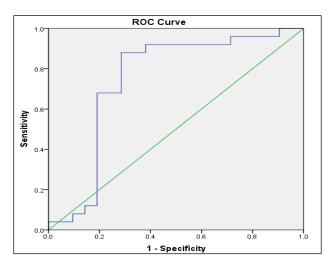


Figure 1: CRP ROC curve.

Based on ROC curve (Figure 1 and 2), the cut-off points for CRP and NLR were obtained at 76.65 and 8.825 consecutively. The value of the under the curve (AUC) area for CRP was 74.7% (p <0.01) while for NLR 80.4% (p <0.01) (Table 4 and 5).

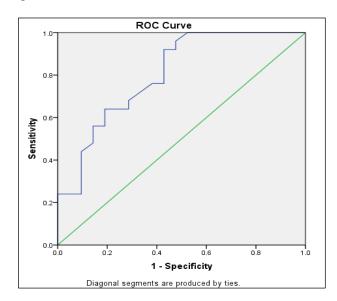


Figure 2: NLR ROC curve.

Table 4: Area under the curve (AUC) value for CRP.

Area	SD	Asymptotic significant ^b	Asympto confident interval Lower limit	
0.747	0.083	< 0.01	0.585	0.909

^aasumption below nonparametric; ^bnul hypothesis: real area = 0.5

Table 5: Area under the curve (AUC) value for NLR.

Area	SD	Asymptotic significant ^b	Asympto confider interval Lower Limit	otic 95% ace Upper Limit
0.804	0.065	< 0.01	0.676	0.932

^aasumption below nonparametric; ^bnul hypothesis: real area = 0.5

There were 22 patients (88.0%) with CRP >76.65 in perforated group, and 6 patients (28.6%) without perforation; while there were 3 patients (12.0%) with CRP <76.65 in perforated group, and 15 patients (71.4%) without perforation (p <0.01) (Table 6). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy are 88.0%, 71.4%, 78.5%, 83.3%, and 80.4% consecutively.

Table 6: Comparison between CRP categoric in the perforated and simple acute appendicitis group.

Variable	Perforation Positive (+)	Negative (-)	P-value
	N=25	N=21	
CRP categ	oric		< 0.01
>76.65	22 (88.0%)	6 (28.6%)	
<76.65	3 (12.0%)	15 (71.4%)	

Table 7: Comparison between NLR categoric in the perforated and simple acute appendicitis group.

	Perforation		_
Variable	Positive (+)	Negative (-)	P-value
	N=25	N=21	
NLR Categoric			< 0.01
>8.825	16 (64.0%)	4 (19.0%)	
< 8.825	9 (36.0%)	17 (81.0%)	

There were 16 patients (64.0%) with NLR >8.825 in perforated group, and 4 patients (19.0%) without perforation; while there were 9 patients (36.0%) with NLR <8.825 in perforated group, and 17 patients (81.0%) without perforation (p < 0.01) (Table 7). The sensitivity, specificity, positive predictive value, negative predictive value and accuracy are 64.0%, 80.9%, 80.0%, 65.3%, and 71.7% consecutively.

DISCUSSION

The result of this study is consistent with the literature which suggests that there is a slight difference in predominance in male over female (1.2-1.3: 1) and is most prevalent in 2nd to 4th decades.¹

The cut-off points for CRP and NLR in perforated group were obtained at 76.65 and 8.825 consecutively. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy for CRP and NLR are 88.0%, 71.4%, 78.5%, 83.3%, 80.4% and 64.0%, 80.9%, 80.0%, 65.3%, and 71.7% consecutively. This result is similar with previous several studies. 11,13,20

It can be concluded that in this study, the cut-off point for NLR was no better than the other studies because the sensitivity and specificity numbers were still lower. As for the cut-off point for CRP is still superior to the study conducted by Moon H in terms of sensitivity.²⁰

The limitation of this research is the histopathologic interpretation as the gold standard was performed by a resident (although it is approved by the consultant), and the small number of samples in this study.

CONCLUSION

At the end of the study, is can be concluded that C-reactive protein and lymphocyte neutrophil ratio has a strong and moderate diagnostic value in diagnosing the perforated appendicitis.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

institutional ethics committee

REFERENCES

- Jaffe BM, Berger DH. The Appendix. In: Brunicardi FC, editor. Schwartz's Principle of Surgery. 9th edition. New York: McGraw-Hill; 2010:1073-1089.
- Tanrıkulu Y, Yılmaz G, Tanrıkulu SC, Temi V, Köktürk F, Çağsar M, et al. A prospective clinical study of the effects of the physical features of the appendix on perforation. Ulus Travma Acil Cerrahi Derg. 2015;21(6):440-5.
- 3. Barreto SG, Travers E, Thomas T, Mackillop C, Tiong L, Lorimer M, et al. Acute perforated appendicitis: An analysis of risk factors to guide surgical decision making. Indian J Med Sci. 2010;64:58-65.
- 4. Bickell NA, Aufses AH, Rojas M, Bodian C. How time affects the risk of rupture in appendicitis. J Am Coll Surg. 2006;202:401-6.
- 5. Ditillo MF, Dziura JD, Rabinovici R. Is it safe to delay appendectomy in adults with acute appendicitis? Ann Surg. 2006;244:656-60.

- Andersson RE, Hugander AP, Ghazi SH, Ravn H, Offenbartl SK, Nystrom PO, et al. Diagnostic value of disease history, clinical presentation, and inflamatory parameters of appendicitis. World J Surg. 1999;23:133-40.
- 7. Goodman DA, Goodman CB, Monk JS. Use of neutrophil: Lymphocyte ratio in the diagnosis of appendicitis. Am Surg. 1995;61(3):257-9.
- 8. Vaughan-Shaw PG, Rees JR, Bell E, Hamdan M, Platt T. Normal inflammatory markers in appenicitis: evidence from two independent cohort studies. J R Soc Med Sh Rep. 2011;2(43):1-7.
- Al-gaithy ZK. Clinical value of total white blood cells and neutrophil counts in patients with suspected appendicitis: Retrospective study. World J of Emerg Surg. 2012;7:32.
- Panagiotopoulou IG, Parashar D, Lin R, Antonowicz S, Wells AD, Bajwa FM, et al. The diagnostic value of white cell count, C-reactive protein and bilirubin in acute appendicitis and its complications. Ann R Coll Surg Engl. 2013;95:215-21.
- 11. Ishizuka M, Takayuki S, Kubota K. Neutrophil to lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. Int Surg. 2012;97:299-304.
- 12. AJI SP. The correlation of Neutrophil-Lymphocyte ratio with complicated appendicitis at Hasan Sadikin Hospital Bandung. Bandung. 2015.
- 13. Muhamad HB, Saeed KA, Fatah BK. Histopathological study of acute appendicitis, the role of neutrophil to lymphocyte ratio in its diagnosis. Basrah J Surg. 2010;16(9):84-9.
- 14. Yazici M, Ozkisacik S, Oztan MO, Gürsoy H. Neutrophil/lymphocyte ratio in the diagnosis of

- childhood appendicitis. Turk J Pediatr. 2010;52(4):400-3.
- 15. Turner JR. Acute appendicitis. In: Kumar V, Abbas AK, Fausto N, Robbins SL, Cotran RS (ed) Robbins and Cotran pathologic basis of disease 7th edition. Elsevier Inc; 2005;17:870-871.
- 16. McGowan DR, Sims HM, Zia K, Uheba M, Shaikh IA. The value of biochemical markers in predicting a perforation in acute appendicitis. Anz J Surg. 2013;83:79-83.
- 17. Colley CM, Fleck A, Goode AW, Muller BR, Myers MA. Early time course of the acute phase protein response in man. J Clin Pathol. 1983;36:203-7.
- 18. Gibson PH, Croal BL, Cuthbertson BH, Small GR, Ifezulike AI, Gibson G, et al. Preoperative neutrophil-lymphocyte ratio and outcome from coronary artery bypass grafting. Am Heart J. 2007;154:995-1002.
- Moon HM, Park BS, Moon DJ. Diagnostic value of C-reactive protein in complicated appendicitis. J Korean Soc Coloproctol. 2011;27:1226.
- 20. Malla BR, Batajoo H. Comparison of Tzanakis score versus Alvarado score in the effective diagnosis of acute appendicitis. Kathmandu Univ Med J (KUMJ). 2014;12(45):48-50.

Cite this article as: Rudiman R, Ruchimat T, Ferdinand Y. Diagnostic value of C-reactive protein and neutrophil-limphocyte ratio in perforated appendicitis at Hasan Sadikin Hospital Bandung. Int Surg J 2017;4:3196-3200.