Sep. 14th, 2021

Dear Editor-in-Chief

RE: The Role of Multidetector Computed Tomography in Patients with Acute Infectious Colitis

Thank you very much for giving us an opportunity to revise our manuscript. Three sets of comments by the reviewers have proved very useful in rewriting this paper. The revisions are based on the reviewers' comments and we respond to them point by point. We hope that these changes now make this paper acceptable for publication. The changes are shown as <mark>yellow color</mark> in the text, in the revised manuscript. Thank you in advance for your attention to our manuscript.

Sincerely,

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The article entitled "The role of multidetector computed tomography in patients with acute infectious colitis" has been reported that MDCT can be useful in suggesting an etiology of acute infectious colitis. The paper seems to be helpful for a specific diagnosis of infectious colitis and worth publishing. However, several points should be clarified for acceptance. The authors indicated that several MDCT parameters were significantly associated with bacterial colitis. In general, discrimination between bacterial and viral colitis may be usually done by more simple ways, for example, white blood cell and neutrophil counts or CRP. They should show superiority of MDCT by such as ROC analyses. In addition, they did not show weight of each parameter of MDCT. They should indicate which parameters are most important for discrimination of etiology or make a formula for prediction of bacterial colitis.

Answer) Thank you for your important comments. We agree with the reviewers that readers will be curious about the WBC and CRP findings. In order to concentrate on the analysis of CT findings, the statistics of serological tests were omitted, but according to the opinion of the reviewers, statistical analysis of serological tests was performed again. In statistical analysis, the mean values of WBC and CRP according to bacterial infection and viral infection were significantly different, but there was no meaningful value to differentiate the two. Contents about this have been added to introduction, method, result and discussion respectively.

Introduction

However, clinicians need blood and imaging tests to investigate the severity and extent, as well as to exclude other causes of abdominal pain. For blood tests, C-reactive protein and WBC, which can detect infection or inflammation, are mainly used. In particular, C-reactive protein may help differentiate pathogens

Method

C-reactive protein and WBC analysis: The mean values of C-reactive protein and WBC were calculated to compare the numerical differences between bacterial and viral colitis. In addition, by classifying the patient groups based on the number of presumed infection or inflammation, the difference between bacterial and viral colitis was analyzed. C-reactive protein was determined to

be 0.3 mg/dl or higher and WBC was 10000x10^9/L or higher to determine the presence of infection or inflammation. In addition, in order to find out whether there are differences in the clinical symptoms of colitis according to the etiology, the patient groups were classified and compared according to the three symptoms: fever, diarrhea, and abdominal pain.

Result

C-reactive protein and WBC analysis

Comparing the mean values of C-reactive protein, Bacterial colitis was higher than Viral colitis, which was statistically significant. However, there was no difference in the prevalence of bacterial and viral colitis classified according to the reference values of WBC and C-reactive protein and there was no statistical significance in differentiating the etiology by clinical symptoms.

Discussion

It was statistically significant that C-reactive protein was higher in bacterial colitis than in viral colitis, but it was not clear how high the threshold should be for suspicion. We took non-normal values as a reference point, but no statistical significance was found. However, in the case of Bacterial colitis, since the sensitivity of C-reactive protein was 93%, if it is elevated, it is necessary to consider Bacterial colitis as an exclusion diagnosis.

Table 1. Summary statistics of acute colitis prevalence for 6 lab and clinical factors by COI

	Value	Total	Viral	Bacterial	P-value*
Prevalence (%)			16	84	
Fever (%)	Yes	45	33	47	0.117
Diarrhea (%)	Yes	34	38	34	0.717
Abdominal pain (%)	Yes	36	43	35	0.473
Hematoma (%)	Yes	61	58	62	0.723
WBC (%)**	Yes	31	18	34	0.059
CRP (%)**	Yes	91	85	93	0.111

* Fisher's exact test

** Categorized from continuous variables

Table 2. Means of WBC and CRP by COI

	Total	Viral	Bacterial	P-value*
WBC	6818.00	5455.48	7086.38	0.12
CRP	8.86	3.54	9.90	0.00

* T-test

Table 3. Sensitivity and specificity of the 6 lab and clinical factors for predicting viral or bacterial acute colitis prevalence

CT outcome	Viral				Bacterial			
	Se	Sp	PPV	NPV	Se	Sp	PPV	NPV
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Fever (%)	32.50	52.71	11.93	79.85	47.29	67.50	88.07	20.15
Diarrhea (%)	37.50	66.01	17.86	84.28	33.99	62.50	82.14	15.72
Abdominal pain (%)	42.50	64.53	19.10	85.06	35.47	57.50	80.90	14.94
Hematoma (%)	57.50	38.42	15.54	82.11	61.58	42.50	84.46	17.89
WBC (%)*	17.95	65.66	9.33	80.25	34.34	82.05	90.67	19.75
CRP (%)*	85.00	6.90	15.25	70.00	93.10	15.00	84.75	30.00

* Categorized from continuous variables

Table 4. Odds ratios of viral or bacterial acute colitis prevalence for each of the 6 lab and clinical factors

CT outcome	Viral				Bacterial			
	OR	95% CI		P-value	OR	95% CI		P-value
Fever (%)	0.58	0.27	1.24	0.16	1.73	0.81	3.68	0.58
Diarrhea (%)	1.28	0.59	2.76	0.53	0.78	0.36	1.69	1.28
Abdominal pain (%)	1.42	0.68	2.99	0.35	0.70	0.33	1.48	1.42

Hematochezia (%)	0.74	0.35	1.58	0.43	1.35	0.63	2.88	0.74
WBC (%)*	0.34	0.13	0.85	0.02	2.98	1.18	7.53	0.34
CRP (%)*	0.37	0.12	1.12	0.08	2.72	0.89	8.32	0.37

Adjusted for age, season, sex, diabetes, cardiovascular diseases, and cancer history

* Categorized from continuous variables

ROC curve
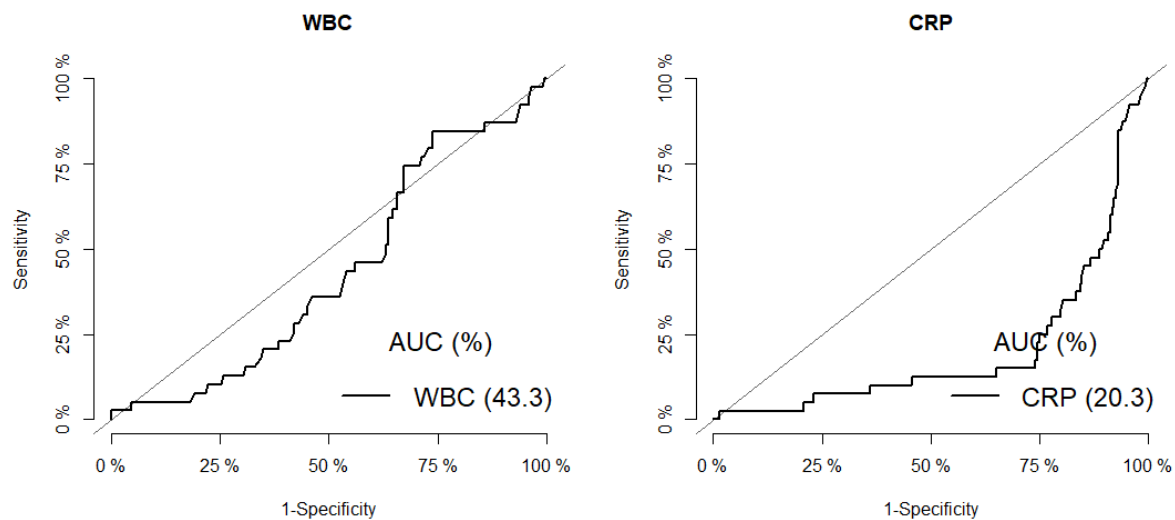
The parameters of bacterial colitis, except for small bowel involvement and comb sign had a significantly higher odds ratio than parameters of viral colitis. Among the parameters, the highest odds ratio was obtained in mucosal thickening. Based on this, we consulted with a statistician to obtain a formula that can increase the discrimination point, but it was difficult to obtain a certain formula. However, only in summer, if there is at least one of the 4 parameter(submucosal edema, mucosal enhancement, continuous distribution, mucosal thickening), the specificity is high, so the early start of antibiotic administration was recommended under suspicion of bacterial infection. In addition, we received additional English proofreading. Your comment was really helpful in reviewing this paper. We appreciate your efforts.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The study aims to examine the usefulness of multidetector computed tomography in distinguishing the etiology of acute infectious colitis. The topic is interesting and could be useful in every day practice. As authors explain, the study has several limitations: this study was performed in a retrospective, observational, and single center manner, there was no control group of patients without colitis, and also, there were more patients in the bacterial colitis group (84%) compared to too few patients in the viral colitis group (16%). The present study only dealt with infectious colitis. Thus, a large prospective and well-designed study, including protocols—such as MDCT, serology/bacteriology, and endoscopy result—is necessary. English language need to be improved. Regards

Answer) We thank your accurate comments. We are also aware of the limitations, and we will do our best to conduct well-designed research that compensates for the limitations later. and We received additional English proofreading as recommended. Thank you again.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: In the retrospective study of Yu et al. the authors aimed to investigate if CT is valuable in discriminating bacterial colitis from viral colitis. They found that multidetector CT parameters of wall thickening, submucosal edema, mucosal enhancement, serosal involvement, empty colon sign, continuous distribution, accordion sign, mucosal thickening, and lymph node enlargement may all be suggestive of bacterial colitis. They also determined that in summertime at least one positive finding in four CT parameters (namely submucosal edema, mucosal enhancement, continuous distribution, mucosal thickening) is suggestive of a bacterial infection. The study is very interesting and very useful for the quick differentiation between bacterial and viral colitides. Though the inclusion of a higher number of cases, and more disease types (including IBD, microscopic colitides etc.) would help to significance of the study, the current results are also impressive and can be the preliminary basis for a further extended investigation. The study is well designed and well presented, the images are all help the understanding of the text. The discussion is clear and logical. The used reference list are all adequate. I suggest to accept the manuscript for publication.

Answer) We really appreciate the reviewer's positive comments.