

Can initial inflammatory markers predict length of stay in uncomplicated diverticulitis?

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SUMMARY: Can initial inflammatory markers predict length of stay in uncomplicated diverticulitis?

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Aim. To investigate the ability of White Cell Count (WCC), Neutrophil count & C-Reactive Protein (CRP) levels at admission to predict length of stay (LOS) in patients with uncomplicated diverticulitis.

Method. This study was performed as a retrospective review of all patients admitted with CT proven uncomplicated diverticulitis over a one-year period. WCC, Neutrophils and CRP levels were recorded at admission. Uniform discharge criteria were used and length of stay measured. A correlation analysis was performed between the inflammatory markers and LOS.

Results. A total of 84 admissions with uncomplicated diverticulitis was included in this study. Average LOS 3.06 (range 1-7 days). On

admission average CRP was 55 (1-276), WCC 11.5 (4.5-35.6) and Neutrophils 8.37 (2.3-18.9). Peak inflammatory values were also measured with mean peak CRP 93.5 (3-325), WCC 11.6 (5.1-35.6) and neutrophils 8.47 (2.3-18.9). Inflammatory markers were correlated to LOS. Multivariate analysis and Fit Plots showed no correlation between any of the inflammatory markers and LOS. Using a modified Hinchey classification 8 patients were Hinchey 0, 60 Hinchey Ia and 16 Hinchey Ib. Hinchey classification was associated with longer LOS (Hinchey 0 mean LOS 2.63 days, Hinchey Ia 2.71 days, Hinchey Ib 4.4 days).

Conclusion. There was a high degree of variation in the inflammatory markers at admission, as well as the peak level of these inflammatory markers during the patients stay. The extent to which these markers were raised did not correlate with the patients' length of stay. As such, the use of inflammatory markers has limited prognostic value in patients with uncomplicated diverticulitis.

KEY WORDS: CRP - Diverticulitis - Inflammatory markers - Predictors - Severity.

Introduction

Diverticulitis is a common surgical condition. In Western countries the rate of diverticular disease increases to about 40% of patients over the age of 60. About 25% of patients with diverticula will at some point present to hospital with diverticulitis (1, 2).

The majority of patients, about 70-85%, who present with diverticulitis have a benign course and improve rapidly (3, 4). While a quick recovery is more common, it is important to identify which patients are more likely to have more serious complications or a prolonged hospital stay. This is especially important in today's age of limited hospital re-

sources where there is significant pressure on bed allocation and early discharge planning.

Objective investigations, which are easy to reproduce and already commonly performed, such as the White Cell Count (WCC), and CRP, could help with predicting the duration of hospital stay for patients with diverticulitis. Several studies have already looked at the use of these investigations to predict perforation or complicated diverticulitis with varying success (3, 5-8). There is a paucity of evidence looking at the role of biochemical markers in uncomplicated cases.

CT imaging is also increasingly used to investigate for complicated diverticulitis. CT findings correlating with the modified Hinchey classification have already demonstrated an association with length of stay in patients with complicated diverticulitis (6, 7, 9). Therefore the primary aim of the

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study is to investigate whether WCC, Neutrophils or CRP are useful in predicting the patients length of stay in hospital. A secondary aim of the study is to investigate the correlation between Hinchey classification and length of stay in patients with uncomplicated diverticulitis.

Patients and methods

We performed a retrospective review of all cases of diverticulitis over a 12-month period. Clinical coding yielded all cases of uncomplicated diverticulitis, with all case files reviewed over the 12-month period. Standard investigations performed consisted of WCC, CRP and a CT with Portal Venous phase IV contrast at admission to confirm the diagnosis. The CT scans were reviewed and classified according to the modified Hinchey classification (Table 1) (10). Complicated diverticulitis was defined as grade II - IV, with all other grades defined as uncomplicated. Exclusion criteria were based on the CT findings; as such 1 patient was removed as they had grade II (complicated) diverticulitis. All other patients were included in the study.

Patients were reviewed daily, with clinical examination as well as serial inflammatory marker testing to assess progress. All patients were admitted under the management of two general surgeons working at the hospital. Patients were managed with IV antibiotics, IV hydration and bowel rest. Oral dietary intake was gradually introduced as symptoms improved. Discharge criteria were comparable between the two surgeons. As such, patients were discharged once pain had settled and WCC and CRP were trending downwards. Upon discharge, retrospective data including

the patients demographics, patient comorbidities, length of stay, laboratory parameters, antibiotic use and Hinchey classification (CT) was collected.

The data was initially analyzed descriptively. Primary parameters assessed were the CRP, White Cell Count (WCC) and Neutrophils on admission. Secondary parameters assessed were the peak CRP, peak WCC and peak Neutrophil count during the patients admission. The mean and range for the patients CRP on admission, peak CRP, WCC on admission, peak WCC, Neutrophils on admission and peak neutrophil count were calculated. The laboratory parameters CRP, WCC and Neutrophils were further stratified into three groups based on magnitude, and the mean LOS for each group was calculated in order to broadly assess for trends.

In order to ascertain the relationship (if any) between these inflammatory markers and length of stay, a separate ANOVA (analysis of variance) linear regression analysis was performed on each data set to determine if any of the variables significantly influenced the length of stay, using the software package SAS. Some variables were further split at the median, to ascertain whether higher inflammatory marker values had a greater influence on LOS than lower values. Fit plots, with the dependent variable being LOS on the Y axis and the independent variable being the laboratory parameter on the X axis were drawn for initial CRP, WCC and Neutrophil count.

Results

After exclusion criteria, there were 84 admissions for uncomplicated diverticulitis over the 12-month period. Six patients had more than one admission

TABLE 1 - MODIFIED HINCHEY CLASSIFICATION BY WASVARY ET AL. (10).

0	Mild clinical diverticulitis
Ia	Confined pericolic inflammation or phlegmon
Ib	Pericolic or mesocolic abscess
II	Pelvic, distant intra-abdominal, or retroperitoneal abscess
III	Generalized purulent peritonitis
IV	Generalized fecal peritonitis

over the year. There were 39 male and 40 female patients. The average patient age at admission was 63 years, ranging from 30 to 88 years. The most common co-morbidities included hypertension, diabetes, AF and ischemic heart disease. 28 patients had a past history of previous admission for diverticulitis. All patients received intravenous antibiotic treatment with treatments being Amoxyl/Metronidazole/Gentamycin 45 patients, Cephazolin/ Metronidazole 20 patients, Timentin 4, Tazocin 4 and Ceftriaxone/Metronidazole 2. Antibiotics received are summarized in Table 2.

Inflammatory markers were further stratified into three groups by magnitude, and the average LOS for each group was calculated. Associated with each laboratory parameter is a P value, which looks at the association between the laboratory parameter and the length of stay. Data are recorded in Table 3.

On admission, the average CRP was 55, whilst the average peak CRP was 93.5. In terms of initial CRP, there was no apparent relationship between the subgroups and length of stay. In terms of peak CRP, it was perhaps evident that the length of stay

increased with increasing peak CRP, with a longer LOS in subgroup 2 and 3 (3.10 and 3.52 days respectively). Multivariate analysis, did not find a significant relationship between initial CRP and LOS ($P = 0.680$). The fit plot for initial CRP and LOS is exhibited in Figure 1 which shows that a reliable trend line cannot be discerned from the data.

The average initial WCC was 11.5 (10) with a range of 4.5 to 35.6 and the average peak WCC was 11.6 with a range of 5.1 to 35.6. The average length of stay appeared to increase within the subgroups, with subgroup 2 and 3 recording an average LOS of 3.07 and 3.21 days respectively. A similar trend was seen with peak WCC values; with subgroups of higher peak WCC values recording longer average LOS (3.14 days). Multivariate analysis however did not find a significant relationship between initial and peak WCC, and hospital LOS ($P = 0.737$ and 0.650 respectively).

In terms of Neutrophil count, the average initial Neutrophil count was 8.37 with a range of 2.3-18.9. The average peak Neutrophil count was similar; 8.47 with a range of 2.3-18.9. There was no apparent

TABLE 2 - PATIENT CHARACTERISTICS.

Patient data		Number (%)
Gender	Male	39 (47%)
	Female	45 (53%)
Mean age		63 (34-88)
Previous diverticulitis		28 (36%)
CT Findings 0		8
CT Findings 1a		60
CT Findings 1b		16
Antibiotics received	Triple AB	51 (60%)
	Cephazolin & Metronidazole	24 (27%)
	Ceftriaxone & Metronidazole	4 (5%)
	Tazocin	4 (5%)
	Timentin	2 (3%)

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TABLE 3 - LABORATORY PARAMETERS VS LOS.

Parameter	Average (range)	Subgroup	LOS	P Value
Initial CRP	55.3 (1-276)	1 - 27	2.82	0.680
		27 - 65	3.41	
		66 - 276	2.81	
Peak CRP	93.5 (3-325)	3 - 59	3.00	0.-
		60 - 105	3.10	
		107 - 325	3.52	
Initial WCC (10 ⁵)	11.5 (4.5-35.6)	4.5 - 9.9	2.79	0.738
		10 - 12.6	3.07	
		12.7 - 35.6	3.21	
Peak WCC	11.6 (5.1-35.6)	5.1 - 9.9	2.79	0.650
		10 - 12.8	3.14	
		12.8 - 35.6	3.14	
Initial Neutrophils	8.37 (2.3-18.9)	2.3 - 6.8	2.82	0.291
		6.9 - 9.3	3.21	
		9.4 - 18.9	3.04	
Peak Neutrophils	8.47 (2.3-18.9)	2.3 - 7	2.82	0.221
		7.1 - 9.6	3	
		9.7 - 18.9	3.25	

TABLE 4 - CT CLASSIFICATION VS MEAN LOS.

CT classification	Number	Mean Age	Mean LOS
Hinchey 0	8	62.5	2.63
Hinchey 1a	60	62	2.71
Hinchey 1b	16	65	4.40

trend of increasing LOS with increasing initial Neutrophil count within the subgroups, with the average LOS increasing to 3.21 days and decreasing to 3.04 days for groups 2 and 3 respectively. In terms of peak Neutrophil count, the LOS appeared to trend up-

wards between groups 2 and 3. Consistent with CRP and WCC, multivariate analysis yielded no significant trend between initial and peak neutrophil count and patient LOS (P = 0.291 and 0.221 respectively).

Discussion and conclusion

Diverticulitis is a common presentation but a challenging condition to predict clinically (11). While usually a rapidly resolving condition amenable to conservative management there are some patients who will have a prolonged duration of symptoms. Even with modern imaging techniques challenges remain to identify which patients are likely to

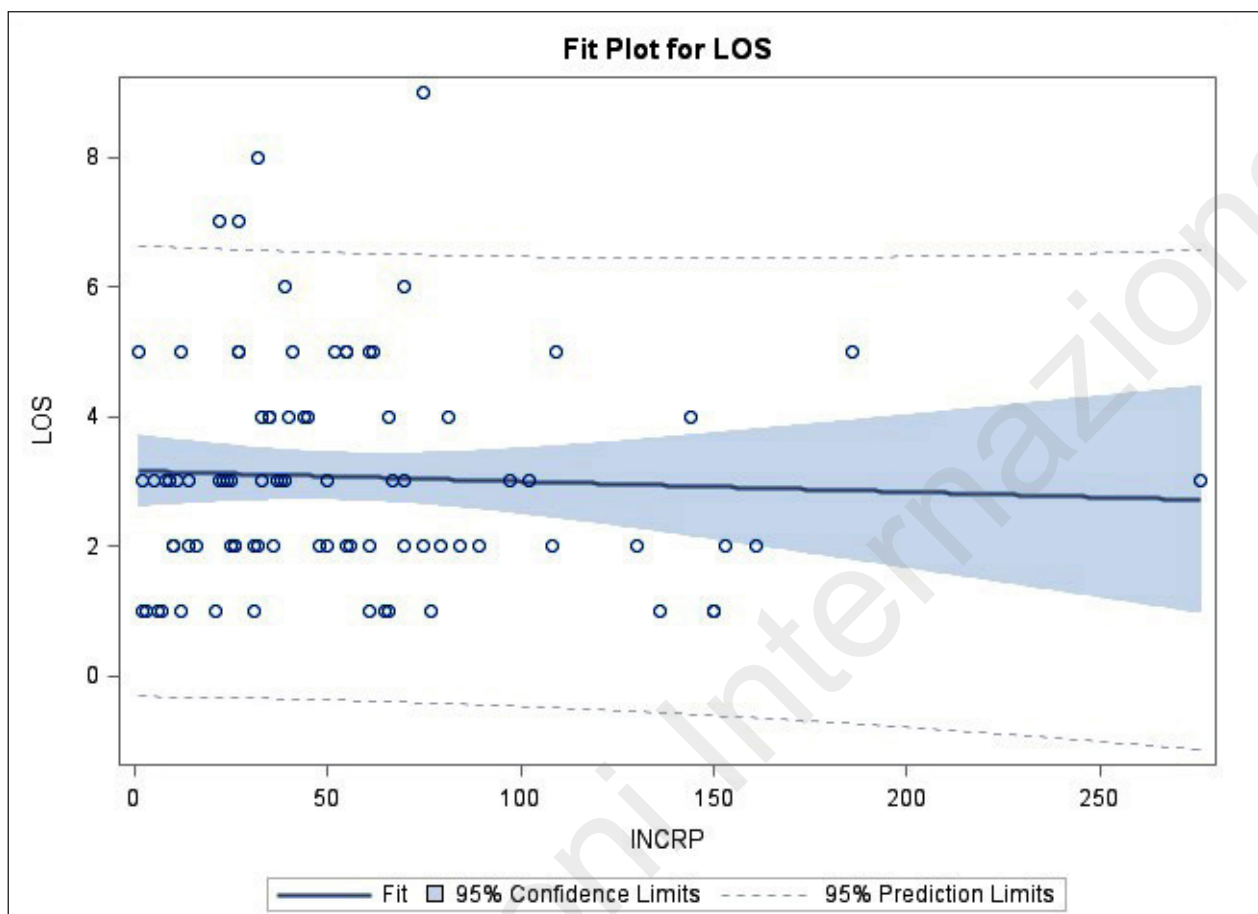


Figure 1 - Fit Plot for LOS compared to Initial CRP.

recovery quickly. The aim of this study was to investigate if inflammatory markers taken at the time of admission can be used to differentiate patients who respond quickly *versus* more slowly.

Previously a 48-hour rule was suggested. If the patient showed significant subjective improvement or objective improvement in the first 48 hours, this would predict LOS or the need for surgery (3). In our hospital population 45% of patients were discharged in 2 days or less, rendering a 48-hour rule ineffective.

A 2014 study into the role of CRP to predict clinical severity looked at 182 patients, 158 uncomplicated diverticulitis and 24 complicated (6). They reported that a CRP of >170 was associated with longer LOS 3.45 days *vs* 15.7 days. However, these patients all had complicated diverticulitis and required laparotomy or drainage. If these are excluded the study did not compare the effect of inflammatory markers in just the uncomplicated diverticulitis patients. This study also looked at the Hinchey classifi-

cation as an independent predictor for LOS and likewise noted that higher Hinchey classification was associated with longer LOS. However, the study did not subdivide the Hinchey classification into Ia and Ib based on CT findings but used the older, operative findings based, original Hinchey classification.

There have been multiple other studies to investigate the use of inflammatory markers to predict complicated diverticulitis or the need for surgery. A 2012 study (5) looked at WCC, CRP and body temperature to differentiate uncomplicated *vs* complicated diverticulitis. On reviewing 426 patients they found that WCC and temperature were of no use and CRP can only give an indication of complicated diverticulitis. However, they point out that while patients with perforation tend to have a higher CRP, 39% of patients with perforation had a low CRP. Their conclusion was that CRP was not robust enough to safely predict complicated diverticulitis. Another study in 2014 (7) investigated 295 patients

looking at uncomplicated *vs* complicated diverticulitis found that CRP was significantly higher in the complicated group. Their conclusions were that a CRP < 50 at admission correlates to uncomplicated diverticulitis and that these patients may not require a CT on admission. This view was shared by a review conducted in 2013 (11). However, in both papers CRP was not investigated for LOS. Another 2010 study (8) of 247 patients found that a CRP of <50 suggests perforation is unlikely, while a CRP >200 is suggestive of perforation. However, the Authors are forced to concede that even in their small study, if a threshold of CRP <50 was used 12 cases of perforation would have been missed.

Therefore, a significant body of evidence explores the diagnosis, management, surgical intervention and predictors of LOS in patients with complicated diverticulitis. The scope for this study is established from the lack of evidence exploring patients with uncomplicated diverticulitis. Though easier to manage as patients respond well to antibiotics, it is imperative to explore this group as they make up the vast majority of inpatient admissions (1-3, 5-7, 11-13). In an ageing population with increasing incidence of diverticulitis, the objective identification of patients who are likely to require a longer LOS yields great importance.

Commonly tested laboratory parameters are CRP, WCC and Neutrophil count, with larger values often implicated with more severe disease. Some subgroups displayed increasing patient LOS with higher laboratory parameters. These were peak CRP, initial WCC, peak WCC and peak Neutrophil count. Our ANOVA model however unequivocally indicated that there is no significant relationship between any of the three laboratory parameters and LOS. This is further exhibited in the fit plots comparing CRP, WCC and Neutrophil count on admission *versus* LOS, whereby there was no discernable trend. A review of our CT findings however, did find significantly longer LOS in patients with increasingly severe diverticulitis on CT (Hinchey 1a, Hinchey 1b) (Table 4). This is in keeping with other publications.

Therefore, it can be asserted that the magnitude of these laboratory markers yields no significant impact on patient LOS. Therefore the use of these markers is more suited towards diagnosis, rather than prognosis. Scope for further research includes

studying different biomarkers. A recent study investigated the role of faecal calprotectin in diagnosing uncomplicated diverticulitis and in monitoring therapeutic response in UD (14). An interesting possibility may be to investigate the role of nutrition status and LOS in diverticular patients. A 1992 article (15) looked at Albumin <30 and Haemoglobin <120 and found these were associated with longer hospital stays in patients with diverticular disease. These simple markers may have a role to play in predicting the recovery in diverticulitis patients.

Given that other studies have suggested that inflammatory markers correlate with severity of diverticulitis we investigated whether our patient population was in some way significantly different to that of other study populations. However, a review of our patient demographics, recurrent presentation rates, average inflammatory markers, and average LOS was consistent with other recent studies (6-9, 11). Our age distribution, gender inequality with a majority female population and rate of recurrent presentations was also in line with other publications. The average WCC 11 and CRP 56 was likewise comparable to the uncomplicated diverticulitis patients in other studies. We did however have a higher rate of DM 14% compared to 9% (6) and 5% (8). Our average LOS was actually shorter, 3.06 days, than the uncomplicated groups of other studies, 3.45 days (6) or 5.6 days (7).

In conclusion, there is no relationship between biochemical markers CRP, WCC and Neutrophil count and patient LOS in cases of uncomplicated diverticulitis. The study population compares well with recent literature. There was a significant relationship between the severity of disease on CT and the LOS, based on the Hinchey Classification. This is also consistent with other studies of uncomplicated diverticulitis. Though CRP and WCC and Neutrophil count was not reliable for predicting patient LOS, other biochemical markers may hold the answer therefore giving scope for further research. Ultimately being able to objectively identify which patients will have an increased LOS is of great importance.

Conflict of interest

Authors declare no conflict of interest.

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