CRAB score for prediction of colectomy within 2 years following admission for acute severe ulcerative colitis

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Abstract

Background: The Oxford and Swedish indexes were developed to predict in-hospital colectomy in acute severe ulcerative colitis (ASUC), but not long-term prediction, and all these indexes were based on Western data. Our study aimed to analyze the predictors of colectomy within 3 years of ASUC in an Indian cohort and derive a simple predictive score.

Methods: A prospective observational study was conducted in a tertiary health care center in South India over a period of 5 years. All patients admitted with ASUC were followed up for a period of 24 months after the index admission, to look for progression to colectomy.

Results: A total of 81 (47 male) patients were included in the derivation cohort. Fifteen (18.5%) patients required colectomy during a follow-up period of 24 months. On regression analysis, C-reactive protein (CRP) and serum albumin were independent predictors of 24-month colectomy. The CRAB (*CRP* + *Alb*umin) score was obtained by multiplying coefficient of beta to albumin and CRP (CRAB score = CRP x 0.2 – Albumin x 0.26). The CRAB score demonstrated an AUROC of 0.923 and a score of >0.4 with a sensitivity of 82% and specificity of 92% for the prediction of 2-year colectomy following ASUC. The score was validated in a validation cohort of 31 patients, and at >0.4, the score had a sensitivity of 83% and a specificity of 96% in predicting colectomy.

Conclusion: CRAB score is a simple prognostic score that can predict 2-year colectomy in ASUC patients with high sensitivity and specificity.

Keywords: Colectomy, inflammatory bowel disease, ulcerative colitis

INTRODUCTION

Acute severe ulcerative colitis (ASUC) is a life-threatening condition affecting around 15–25% of patients with ulcerative colitis (UC).[1,2] Corticosteroids are the cornerstone for the management of ASUC. For patients not responding to intravenous (IV) corticosteroids, anti-tumor necrosis factor (TNF) agents and cyclosporine are second-line options.[1] Patients failing to respond to the above therapy ultimately require colectomy, as

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the absence of response carries a high mortality risk. Identification of predictors of colectomy is required since morbidity, mortality, and costs increase with the length of hospitalization prior to surgery.

The Oxford and Swedish indexes were developed to predict in-hospital colectomy in ASUC, and not long-term colectomy risk. Moreover, these indexes were based on data from the Western population. In-hospital colectomy rates have rapidly decreased during the last two decades with the advent of rescue therapy, like infliximab and cyclosporine, but the colectomy rate within 1 or 2 years of ASUC has not significantly reduced. Cesarini *et al.* reported that the Oxford index no longer predicts in-hospital colectomy rates, in addition to its shortcoming in predicting long-term colectomy rates.[2] A medium to long-term correlation has been found between C-reactive protein (CRP)/albumin ratio and colectomy in two recent studies.[3,4] Another recent review concludes that new scoring systems are required to predict response to treatment and colectomy.[5] Even though there are many scoring systems for in-hospital colectomy, there are only a very few scoring systems for long-term colectomy following ASUC. All these data point toward the need for a new score for the prediction of colectomy in ASUC. Hence, our study aimed to analyze the predictors of in-hospital and long-term colectomy in an Indian cohort of ASUC patients.

PATIENTS AND METHODS

This was a prospective observational study conducted in the department of gastroenterology, at a tertiary healthcare center in South India, over a period of 5 years (July 2015–2020). All those patients presenting with ASUC, defined by Truelove Witts criteria, and willing to give consent were taken up for the study and followed up for a period of 24 months to look for progression to colectomy. In case of recurrence of ASUC during follow-up, only the first episode was considered. A derivation cohort included patients who were recruited from July 2015 to 2017, and those recruited from July 2017 to 2018 were used as validation cohorts.

Therapeutic management

Patients hospitalized for ASUC were treated according to the standard guidelines.[6] Patients not responding to IV corticosteroids after 3–5 days of therapy were considered for salvage medical therapy like cyclosporine or anti-TNFs. *Cytomegalovirus* infection was confirmed by the presence of inclusion bodies in the histopathological examination, and testing for *Clostridium difficile* infection (CDI) was done with a toxin and glutamate dehydrogenase (GDH) assay. Patients were followed up for a period of 24 months from the time of hospital admission to look for in-hospital and long-term colectomy.

Study outcomes

The primary outcome of the study was the occurrence of colectomy within 2 years after the index hospital admission for ASUC. Secondary outcomes included corticosteroid responsiveness, the need for rescue therapy, and in-hospital colectomy.

Data collection and statistical analysis

The laboratory, endoscopic, and radiological parameters were recorded. Univariate analysis to find out the predictors of 24-month colectomy was done with Chi-square and t-tests, and those significant variables were put into logistic regression to identify the independent predictors of colectomy. Then the beta coefficient of significant variables was multiplied to the corresponding variable and the sum of the products of the beta coefficient and significant variables was done to propose a new score. This score was plotted on AUROC, and the cutoff was identified to predict colectomy in 24 months. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 23.0; SPSS Inc., Chicago, IL, USA).

RESULTS

Baseline characteristics

A total of 81 patients were included in the derivation cohort, and 31 patients were included in the validation cohort. There was no statistically significant difference in study variables between the derivation and validation cohort [Table 1].

Out of 81 patients, 10 presented with the first exacerbation of UC, and none of them progressed to colectomy in 24 months. In the derivation cohort, 16 (19.7%) patients had a poor response to steroids, and of them, 7 patients responded to rescue therapy (6 on cyclosporine and 1 on infliximab). The rest 9 (11.1%) patients (all on cyclosporine) underwent in-hospital colectomy after a median duration of 15 (range 7–21) days, and there was no in-hospital mortality. Among the remaining 72 patients, 6 patients underwent colectomy during the 24-month follow-up. Figure 1 shows the treatment and outcome of patients in the derivation cohort.

Predictors of colectomy

In the derivation cohort, a total of 15/81 (18.5%) patients underwent colectomy over a follow-up period of 24 months. Hemoglobin, CRP, and albumin, which were statistically significant by univariate analysis, were put into multivariate analysis [Table 2].

Table 1: Comparison of baseline parameters between the derivation and validation cohort

Parameters	Derivation cohort (*n*=81)	Validation cohort (*n*=31)	*P*
Age, in years	52.9 years	53.42 years	0.89
Hemoglobin in gm%	10.84±1.85	10.68±2.01	0.69
Total leucocyte count ×10³/mm³	10.83±2.98	10.64±2.69	0.76
Platelet count ×10⁵/mm³	5.00±0.48	5.03±0.51	0.82
ESR	33.38±15.914	31.29±12.75	0.51
CRP in mg/dL	27.41±15.42	28.63±18.12	0.72
Sr. albumin in mg/dL	34.53±6.88	34.00±7.26	0.72
INR	1.08±0.09	1.10±0.09	0.21
Sr. creatinine, in mg/dL	0.85±0.16	0.88±0.17	0.44
Colectomy	15 (18.5%)	6 (19.4%)	0.91

Table 2: Comparison of patients requiring and not requiring colectomy within 2 years in the derivation cohort

Parameters	Colectomy (*n*=66)	No colectomy (*n*=15)	*P*
Males	40	7	0.24
Age, in years	53.53±16.96	50.07±13.37	0.207
Extensive colitis, E3	14	15	0.000
Hemoglobin, in gm%	9.91±0.53	11.05±1.98	0.031
Total leucocyte count ×10³/mm³	10750±3283	11191±2101	0.609
Platelet count ×10⁵/mm³	4.95±1.2	5.21±0.8	0.061
ESR	32.79±17.56	36±15	0.484
CRP, in mg/dL	22.19±8.97	50.4±17.11	0.000
Albumin, in mg/dL	36.3±6.32	26.73±2.15	0.000
INR	1.08±0.09	1.05±0.47	0.168
Creatinine, in mg/dL	0.86±0.17	0.84±0.1	0.716
Sodium, in mEq/L	133.6±3.21	132.8±3.77	0.150

In the multivariate analysis, serum albumin and CRP were independent predictors of colectomy at 24 months. The beta coefficient of significant variables was multiplied by the corresponding variables, and their sum was calculated to propose a new score [Table 3].

The beta coefficient of albumin was -0.26, and CRP was 0.2. So, the new CRAB score (CRP + Albumin) was as follows: CRAB score = CRP x 0.2 − Albumin x 0.26. The CRAB score was plotted in AUROC, and the AUROC of a new score in predicting colectomy in ASUC within 24 months was 0.923 (95%CI: 0.913–0.975) [Figure 2a]. At a cutoff value of >0.4, the CRAB score had a sensitivity of 82% and a specificity of 92% in predicting colectomy within 24 months.

Validation of the score
The new score was validated in a cohort of 31 patients, among whom 4 patients underwent colectomy during the

same hospital admission and 2 during the follow-up period of 24 months. In the validation cohort, the CRAB score had an AUROC of 0.953 (95%CI: 0.861–1.000) [Figure 2b]. At a cutoff of >0.4, the new score had a sensitivity of 83% and a specificity of 96% in predicting 24-month colectomy. Those patients who underwent colectomy were having pancolitis in the derivation and validation cohort, and thus, the absence of pancolitis can rule out the possibility of colectomy.

DISCUSSION

Acute, severe UC poses a risk of colonic perforation, which is a medical emergency. Patients at high risk for colectomy need to be identified in order to facilitate aggressive management strategies and optimize care. Even those
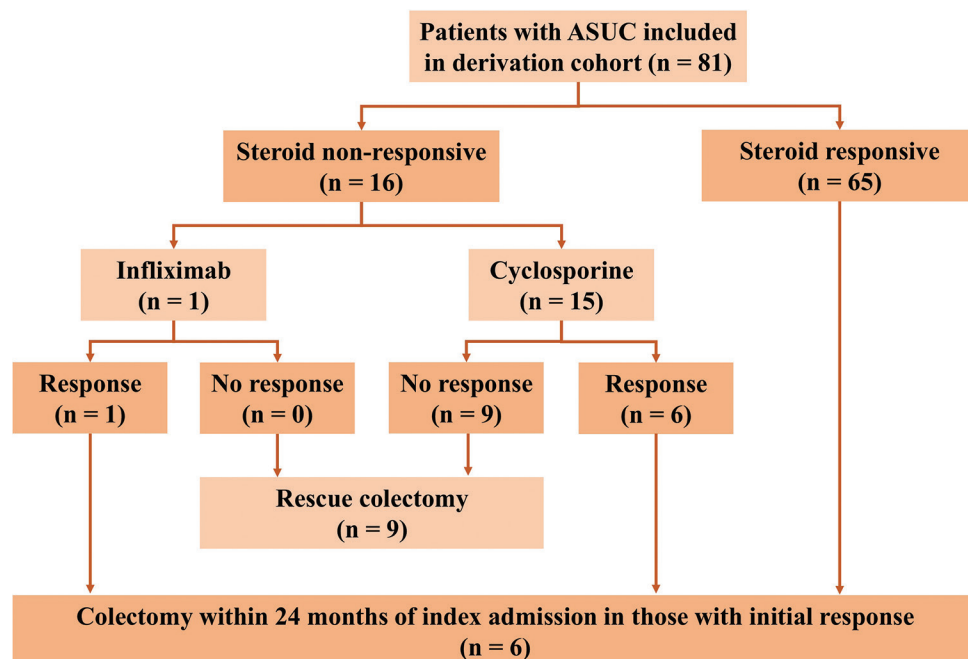
Figure 1: Flowchart showing the treatment and outcome of patients with acute severe ulcerative colitis (ASUC) in the derivation cohort
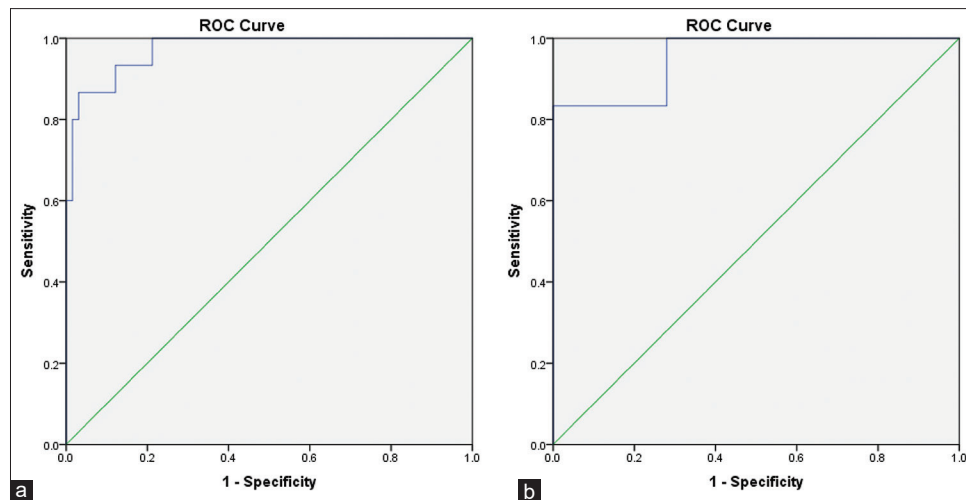
Figure 2: Receiver operating characteristic curve for CRAB score in (a) derivation cohort and (b) validation cohort

patients who respond to initial medical therapy remain at risk of colectomy in future. In the present study also, 21/112 (18.7%) patients required colectomy over a period of 2 years after ASUC. Consequently, prognostic factors for colectomy have attracted a great deal of attention in patients with ASUC.

Our population is similar to other studies, notably in terms of the clinical and biological characteristics.[7-9] There was no statistically significant difference in colectomy between males and females in both the test and validation cohorts. Among the quantitative variables analyzed for predicting colectomy in a 24-month colectomy, hemoglobin, albumin, and CRP were statistically significant. Low levels of albumin were also mentioned in previous studies as a predictor of colectomy.[3,10] CRP was also significant in previous studies in predicting colectomy.[11,12]

A steroid response was seen in 65 patients and a non-response in 16 patients. Those patients with steroid non-response underwent rescue therapy with infliximab or cyclosporine. Fifteen out of 16 patients who did not have a response to steroids preferred to go for cyclosporine, and one wanted to start infliximab. The large proportion of cyclosporine compared to infliximab was purely because of patient preference, as the patients were given the opportunity to select between the treatment options after explaining them the pros and cons of both options.

A recent French study analyzed patients' risk of colectomy within 1 year of hospital admission for ASUC.[13] Among the clinical, biomarker, and endoscopic parameters, previous treatment with TNF antagonists or thiopurines, CDI, serum CRP, and albumin were independent predictors of colectomy. They developed a scoring system based on these factors, assigning 1 point for each item. A score of 3–4 was considered high risk and associated with a 51.2% (score 3) to 100% (score 4) risk of colectomy within 1 year and was externally validated. In our patients, none of them had prior exposure to anti-TNF agents, and CDI was seen in only 2 cases. However, as seen in our study, CRP and albumin remain important predictors.

De Cristofaro *et al.*[14] followed up on ASUC patients who achieved response following treatment with IV steroids or infliximab and analyzed the long-term risk and predictors of colectomy. Over a median period of 46 months, 29/116 (25%) patients underwent colectomy, of whom 65% required surgery within the first year after index admission. A serum albumin level <3 g/dL (OR: 6.9, 95%CI: 2.08–22.8) and colonic dilation >5.5 cm at admission (OR 8.5, 95%CI: 1.23–58.3) were found to be independent predictors of colectomy. This is similar to our finding of serum albumin being an independent predictor of colectomy. However, we could not assess the effect of colonic dilatation as the same data were not available.

A previous study from North India studied the long-term outcomes of patients after a first episode of ASUC and their predictors.[15] Around 11% of the patients required colectomy at index admission and 26% over a median follow-up of 56 months. A model based on four clinical variables – response to IV steroids within 7 days of hospitalization, prior steroid use during the first year of

Table 3: Multivariate analysis of significant variables

	B	S.E	Wald	df	Sig.	Exp (B)	95.0% Confidence Interval for B	
Hemoglobin	-0.075	0.338	0.049	1	0.825	0.928	0.970	1.903
CRP	0.203	0.069	8.636	1	0.003	1.225	-0.053	0.014
Albumin	-0.257	0.134	3.663	1	0.056	0.773	0.011	0.019
Constant	0.134	3.568	0.001	1	0.970	1.144	-0.023	-0.003

diagnosis, longer interval from diagnosis to ASUC, and a number of extra-intestinal manifestations – predicted colectomy with an accuracy of 77%. Another study from the same group reported that left-sided colitis and extensive colitis did not differ in the rate of colectomy at index admission for ASUC (12% versus 15%, $P = 0.4$) and colectomy in follow-up (31% versus 23%, $P = 0.17$).[16] They concluded that there was no correlation between the extent of disease at the ASUC index and the probability of a subsequent colectomy. However, in the present study, all patients who underwent colectomy had pancolitis, and the absence of pancolitis can rule out the possibility of colectomy, which was validated in the validation cohort.

A score combining these predictors is highly predictive of the occurrence and risk magnitude of colectomy within 2 years after admission, and a replicative cohort confirmed these results. The present score is easy and includes only two parameters, which improves usability. A prospective study design with validation adds to the strength of the study. However, there are a few limitations to the present study that need discussion. We could not analyze the utility of the radiological and endoscopic parameters for colectomy prediction. However, considering that it is assessed on the first day of hospitalization, it can assist physicians in planning therapeutic management even before endoscopic evaluation. In a previous study from India, an Ulcerative Colitis Endoscopic Index of Severity score >6 at admission and a day 3 fecal calprotectin (FC) level >1000 μg/g were independent predictors of steroid failure requiring rescue therapy or colectomy.[17] We did not routinely measure FC in ASUC and, hence, could not analyze its predictive role.

To conclude, around one-fifth of the patients presenting with ASUC require a colectomy over 24 months. The CRAB score is a simple prognostic score that can predict 24-month colectomy risk in ASUC patients at admission with high sensitivity and specificity. In the absence of pancolitis, progression to colectomy is rare. Further prospective studies are required to validate the findings of the study.

Conflicts of interest
There are no conflicts of interest.

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