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ORIGINAL ARTICLE

Low serum albumin at admission is a predictor of early colectomy in patients with moderate to severe ulcerative colitis

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Abstract

Background and Aim: Several studies have identified postinduction therapy predictors of long-term outcomes of ulcerative colitis (UC) in patients who experienced the first attack of the disease or relapsed after therapy. We aimed to identify the preinduction therapy predictors at admission that predicted early colectomy in patients with moderate to severe UC.

Methods: Ninety-five patients with moderate to severe UC who underwent induction therapy at the Kyoto Prefectural University of Medicine hospital between August 2008 and March 2020 were retrospectively included and categorized into two groups: the colectomy group (n = 27) and the noncolectomy group (n = 68). The clinical parameters (age, gender, disease extent, and disease activity on admission), induction therapies administered [including 5-aminosalicylic acid, steroids, immunomodulators, calcineurin inhibitor, and anti-Tumor Necrosis Factor (TNF)-α antibodies], and laboratory data (hemoglobin, albumin, C-reactive protein, and cytomegalovirus reactivation on admission) were evaluated and compared between the two groups. Multivariate logistic regression analyses were performed to identify significant predictors of early colectomy, and $P < 0.05$ was considered significant.

Results: All clinical parameters were not significant predictors of colectomy. Among laboratory parameters, the serum albumin level on admission was a significant independent predictor of colectomy (odds ratio: 6.097, 95% confidence interval: 1.8310–20.3047). Receiver operating characteristic curves were plotted for the serum albumin levels of the 95 patients at admission. The cut-off value of serum albumin was 2.45 g/dL.

Conclusions: When the serum albumin level of UC patients at admission is below 2.45 g/dL, we should consider presenting the option of surgical treatment to patients.

Introduction

Patients with ulcerative colitis (UC), a chronic inflammatory bowel disease (IBD), undergo repeated remission and relapses. Determining an unequivocal predictor of induction therapy outcomes would greatly benefit the management of these patients. Early identification of pretherapy predictors would be of great value from health and financial perspectives.

Previous studies have reported that the predictors of induction therapy failure include a high frequency of bowel movements after intensive induction therapy and a high C-reactive protein (CRP) level.[1–5] Furthermore, disease activity at diagnosis and lower serum levels of hemoglobin and albumin after the first induction therapy have also been reported as significant predictors of relapse and colectomy.[6] Recent reports have indicated that incomplete mucosal healing is an important predictor of relapse;[7] a meta-analysis revealed that mucosal healing is associated with long-term clinical remission, evasion of colectomy, and corticosteroid-free clinical remission.[8]

Furthermore, several studies in North America showed that the male gender, long disease duration, and hospitalization were the clinical predictors of colectomy.[9–11] Several prospective studies in Europe showed that a high serum CRP level was the predictor for colectomy.[4,12]

Background factors such as IBD-related genes, environment, and dietary habits vary depending upon the ethnicity.[13–15,16] The pathogenesis of UC is thought to be different between Asians and Caucasians. Hence, studies for determining the predictors of UC in Asian countries are important. A retrospective study on the prognosis of UC in Asian patients showed that the male gender and a disease duration of more than 5 years were the clinical predictors for colectomy.[17] However, this study evaluated the predictors based on clinical background. Few studies have considered laboratory data in determining the predictors for colectomy in Asian countries.[6] Shiga et al. reported predictors for the prognosis of UC patients based on the laboratory data obtained after induction therapy.[6] However, they did not consider the characteristics and laboratory data of patients before the induction therapy for investigating the predictors of colectomy.

Therefore, in the present study, using laboratory and clinical data, we retrospectively investigated pretherapy factors that could predict early colectomy in Asian patients with moderate to severe UC who required treatment on admission.

Methods

Ethics. This study was approved by the Ethics Committee of the Kyoto Prefectural University of Medicine (ERB-C-610-1) and was performed in accordance with the ethical principles of the Declaration of Helsinki.

Patients. Ninety-five patients with UC who were hospitalized for exacerbation and received induction therapy in the gastroenterology outpatient clinic of the Kyoto Prefectural University of Medicine between August 2008 and March 2020 were retrospectively enrolled in this study. The disease activity of all patients was classified from moderate to severe based on Truelove and Witts' criteria.[18] The average age was 43.1 years (SD 16.4). There were 61 men (64.2%) and 34 women (35.8%). The type of disease was total colitis in 81 patients (85.3%) and left colitis in 14 patients (14.7%). The average disease duration was 69.4 months (SD 88). The average disease activity (Lichtiger clinical activity index [CAI][19]) was 13.2 (SD 2.84). The patients were categorized into two groups. The noncolectomy group included 68 patients (71.6%) who achieved clinical remission by induction therapy and were discharged from the hospital, while the colectomy group included 27 patients (28.4%) who were resistant to induction therapy and underwent colectomy with continued hospitalization.

Methods. The clinical parameters (age, gender, disease extent, and disease activity [CAI]), induction therapies (with 5-aminosalicylic acid, steroids, immunomodulators, calcineurin inhibitor, and anti-Tumor Necrosis Factor-α (TNF-α) antibodies), and laboratory data (hemoglobin, albumin, and CRP levels and cytomegalovirus reactivation) on admission were evaluated and compared between the two groups. The induction therapies are detailed in Table 1.

Statistical analysis. All statistical analyses were performed using JMP 10 (SAS Institute, Cary, NC, USA) and GraphPad Prism (Version 6.0) (GraphPad Software, Inc., San Diego, CA, USA). All tables were created by JMP 10, and all figures were drawn by GraphPad Prism.

Table 1 The induction therapies between the noncolectomy and colectomy groups

	Noncolectomy (n = 68)	Colectomy (n = 27)
5-Aminosalicylic acid	66 (97.1%)	26 (96.3%)
Steroid	47 (69.1%)	25 (92.6%)
Immunomodulator	20 (29.4%)	16 (59.3%)
Calcineurin inhibitor	10 (14.7%)	7 (25.9%)
Anti-TNF-α antibodies	11 (16.2%)	11 (40.7%)

All parameters were considered single variables. The parameters with $P < 0.05$ on univariate analysis were used to perform a multivariate logistic regression analysis to determine their influence on early colectomy. The results of the logistic regression analysis were expressed using odds ratio (OR) and 95% confidence intervals (CIs) with the P values. Variables excluded from the multivariate analysis were represented as 'n.e.' (not entered). The level of significance was set at 5%.

Results

Table 1 shows the differences in the induction therapies (such as steroid, immunomodulator, and anti-TNF-α antibody usage) between the colectomy and noncolectomy groups. Table 2 provides data on the age and gender distribution between the two groups and shows the intergroup differences in the number of patients with pancolitis and high CAI. Furthermore, Table 2 shows the intergroup differences in the laboratory parameters, including the serum CRP level, hemoglobin level, serum albumin level, and CMP reactivation.

As shown in Table 3, univariate analysis revealed that, among clinical characteristics, patients with pancolitis (OR: 2.053, P = 0.0478) and patients who received steroids (OR: 1.965, P = 0.0170), immunomodulators (OR: 1.295, P = 0.0098), and anti-TNF-α therapy (OR: 1.781, P = 0.0154) had a statistically higher risk of colectomy. Furthermore, univariate analysis also revealed that, among laboratory characteristics, patients with a high serum CRP level (OR: 0.888, P = 0.0049), low serum hemoglobin (OR: 0.178, $P < 0.0001$), and low serum albumin level (OR: 7.692, $P < 0.0001$) had a statistically higher risk of colectomy.

Multivariate analyses revealed that serum albumin level on admission was an independent predictor of early colectomy (OR: 6.097, 95% CI: 1.8310–20.3047; Table 3). To evaluate the predictors, receiver operating characteristic curves were plotted for the serum albumin level at admission for all 95 patients. The area under the curve, sensitivity, and specificity were 82.1, 81.5, and 76.5%, respectively. The cut-off value for serum albumin was 2.45 g/dL (Fig. 1); around 22 of the 38 patients (57.9%) with levels below the cut-off at admission underwent an early colectomy, while only 5 of the 57 (8.8%) patients with levels above the cut-off underwent an early colectomy (Fig. 2).

Table 2 Comparison of clinical parameters and laboratory data between the noncolectomy and colectomy groups

	Noncolectomy (n = 68)	Colectomy (n = 27)
Age (years)	42.5 (17–76)	44.6 (16–73)
Gender		
Male	43 (70.3%)	18 (66.7%)
Female	25 (29.7%)	9 (33.3%)
Disease extent left sided	13 (19.1%)	1 (3.7%)
Pancolitis	55 (80.9%)	26 (96.3%)
Disease duration (months)	74.6 (1–392)	56.2 (1–219)
Clinical activity index	12.6 (8–18)	14.9 (9–21)
C-reactive protein (mg/dL)	3.98 (0.02–25.3)	7.48 (0.06–18.65)
Hb (g/dL)	10.5 (5.9–17)	8.4 (5.9–13.1)
Alb (g/dL)	3.05 (1.5–4.7)	2.20 (1.6–3.9)
Cytomegalovirus positive (%)	48.5	48.1

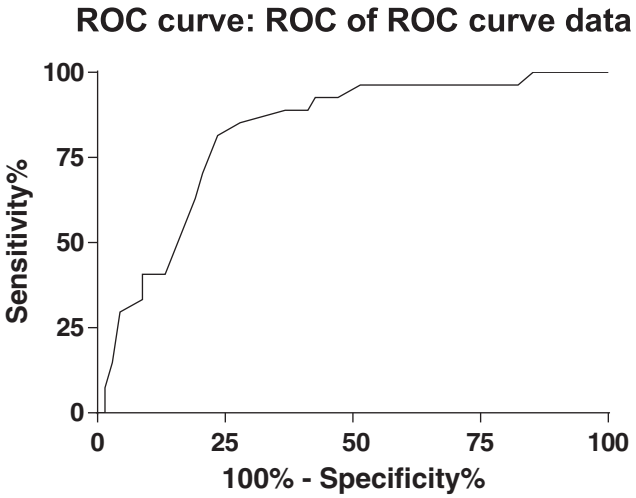

Figure 1 Receiver operating characteristic curves for colectomy based on the serum albumin levels at admission.

Discussion

We found several predictors for colectomy in patients with moderate to severe UC. These included treatment with steroids, immunomodulators, and anti-TNF-α antibodies; pancolitis; and low serum hemoglobin and albumin levels at admission. Multivariate analyses revealed that, of these, a low serum albumin level was the strongest predictor of colectomy. This is the first study to demonstrate that a low serum albumin level on admission is a predictor of early colectomy for patients with moderate to severe UC.

Most studies have reported that treatment with intravenous steroids (as a remission induction therapy) and salvage therapy were the predictors of colectomy in acute severe UC.[20,21] However, most studies were performed before the clinical application of TNF-α antibodies in the treatment of patients with UC. Recently, it was reported that the total incidence of colectomy decreased with an increased use of TNF-α antibodies.[22] However, this report included results of a long-term observation; therefore, they were not comparable to our findings. Considering short-term studies, Gibson et al. reported that an accelerated infliximab-induction regimen reduced the need for early colectomy.[23] Therefore, it is important to analyze the therapeutic background of the patients, including the use of anti-TNF-α antibodies.

It has been reported that the extent of disease in UC patients may be a predictor of colectomy.[24–26] However, while a univariate analysis in our study revealed that UC patients with pancolitis had a higher rate of colectomy than patients with left-sided colitis (P = 0.0478), it was not the most significant clinical predictor. Contrastingly, previous studies have reported that the extent of disease is the most important predictor of colectomy in UC patients; however, these studies did not consider serum markers in multivariate analyses for evaluating the predictors for

Table 3 Risk of colectomy shown by univariant analysis and multivariant analysis

	Univariant analyses			Multivariant analyses		
	Odds ratio (OR)	95% confidence interval (CI)	P value	OR	95% CI	P value
Male (*vs* female)	0.857	0.261–2.815	0.7522	—		
Age (per 1 year)	0.992	0.965–1.019	0.5597	—		
Relapse (*vs* first attack)	3.094	0.683–14.019	0.9892	—		
Pancolitis (*vs* Left sided)	2.053	0.683–14.019	0.0478	n.e.		
5-Aminosalicylic acid	2.863	0.756–10.841	1.000	—		
Steroid	1.965	0.698–5.531	0.0170	n.e.		
Immunomodulator	1.295	0.494–3.398	0.0098	n.e.		
Calcineurin inhibitor	1.376	0.557–3.402	0.2386	—		
Anti-TNF-α antibodies	1.781	0.640–4.958	0.0154	n.e.		
Clinical activity index	0.738	0.0018–0.2003	0.0004	n.e.		
C-reactive protein (mg/dL)	0.888	0.8149–0.9686	0.0049	n.e.		
Hb (g/dL)	0.178	0.068–0.4687	<0.0001	n.e.		
Alb (g/dL)	7.692	2.827–20.93	<0.0001	6.097	1.8310–20.3047	0.0072
Cytomegalovirus positive (*vs* negative)	1.025	0.294–3.570	0.8561	—		

n.e., not entered.

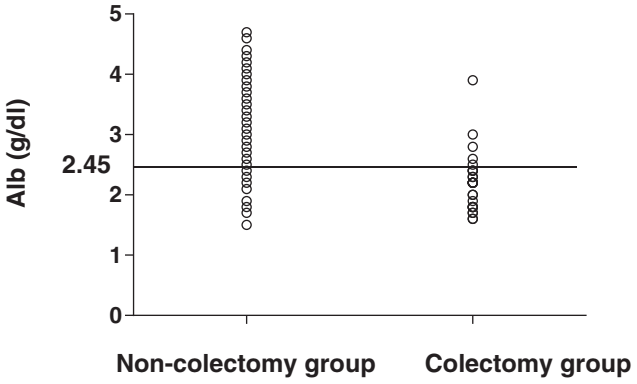

Figure 2 Comparison of the serum albumin levels between the non-colectomy and colectomy groups.

colectomy, and the duration of the disease and the condition of the patients were different from those in our study. Travis et al.[4] demonstrated that a high serum CRP level (>45 mg/L) and frequent stools (>8/day) were the predictors of colectomy. Lindgren et al.[5] also demonstrated that continued CRP elevation on day 3 of an intravenous steroid treatment strongly predicted colectomy and clinical steroid resistance in acute attacks of UC. It also predicted that a more aggressive medical treatment should be considered at an early stage. These reports indicate that serum CRP level is an important predictor of colectomy. In our study, 21 of the 68 cases in the noncolectomy group and 19 of the 27 cases in the colectomy group presented with CRP levels above 45 mg/L. Because no patients in the previous studies were treated with anti-TNF-α antibodies, and all patients were not treated with steroids in the induction therapy, it is hard to compare these reports and our study directly. Actually, in the present study, CRP level was not a candidate for the predictors of colectomy.

Kumar et al. reported that lower levels of serum hemoglobin in UC patients could be a predictor of colectomy.[27] A univariate analysis in their study revealed that low hemoglobin and low serum albumin levels were associated with treatment failure; low hemoglobin, in particular, was the most important predictor according to multivariate analysis. Conversely, although univariate analysis in our study showed that low serum hemoglobin was associated with a higher rate of colectomy, it was not the most significant predictor according to multivariate analysis. This could be attributed to differences in the patients' conditions between our study and theirs. While the previous study evaluated serum markers after induction therapy, we evaluated serum markers before induction therapy. We believe that serum hemoglobin level at admission was able to evaluate the state of the patient more appropriately than the level after therapy because serum hemoglobin might rise due to treatment, for instance, during blood transfusion after hospitalization.

Low serum albumin level has been reported as one of the significant predictors of colectomy.[2,6,28,29] Chakravarty et al.[2] reported that low serum albumin level, in addition to severe diarrhea, was noted in patients who underwent colectomy. Oshitani et al.[28] demonstrated that nutritive condition, represented by the serum albumin level, was useful as a predictor for controlling UC during the acute phase.

Shiga et al.[6] also demonstrated that relapses and late colectomy were associated with disease activity at diagnosis and lower levels of serum hemoglobin and albumin 4 weeks after the first induction therapy. Mokhele et al.[29] also demonstrated that the serum albumin level on day 3 of corticosteroid therapy was the only predictor of colectomy. In our study, as predictive factors for colectomy were analyzed when the patients were admitted to our hospital, a direct comparison with these studies, which analyzed the predictors after therapy, is difficult. Furthermore, a recent study reported that a CRP-to-albumin ratio of 0.85 on day 3 of intravenous steroid therapy could predict colectomy;[30] again, it is difficult to compare this study with our study because the data in the former were collected after the treatment.

There are some limitations in this study. First, as many patients were referred from middle to small centers, most of these patients were considered to have refractory UC. Second, as the time of admission in our hospital was dependent on previous doctors, the criteria to introduce patients to our hospital are not clearly defined. Third, this study did not include patients who received new therapeutic drugs (such as oral Janus kinase inhibitor [tofacitinib], anti-α4β7 integrin monoclonal antibody [vedolizumab], and an antagonist of the p40 subunit of interleukin-12 and interleukin-23 [ustekinumab]). Further studies must consider these in the future. Finally, as this study is a single-center retrospective study targeting a limited number of patients, a prospective study is necessary to verify our hypothesis.

In conclusion, serum albumin level on admission is the most important predictor for early colectomy in patients with moderate to severe UC. When UC patients present with serum albumin levels below 2.45 g/dL at admission, we should consider presenting the option of surgical treatment. This finding might help determine the early directivity of the treatment and lead to good prognosis for UC patients with a moderate to severe condition.

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