Original Article

Role of Serum Proteinase 3 Antineutrophil Cytoplasmic Antibodies in the Diagnosis, Evaluation of Disease Severity, and Clinical Course of Ulcerative Colitis

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Background/Aims: Proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA) is a serologic marker for granulomatosis with polyangiitis. However, recent studies have also shown their role as diagnostic markers for ulcerative colitis (UC). This study was performed to investigate the clinical roles of PR3-ANCAs in the disease severity, disease extension, and clinical course of UC.

Methods: Serum PR3-ANCAs were measured in 173 UC patients including 77 patients with new-onset patients UC diagnosed within 1 month, 110 patients with Crohn's disease, 48 patients with other intestinal diseases, and 71 healthy controls. Associations between the PR3-ANCA titer and clinical data, such as disease severity, disease extension, and clinical course, were assessed. The clinical utility of PR3-ANCA measurement was evaluated by receiver operating characteristic (ROC) analysis.

Results: PR3-ANCA ≥3.5 U/mL demonstrated 44.5% sensitivity and 95.6% specificity for the diagnosis of UC in all patients. PR3-ANCA positivity was more prevalent in the 77 new-onset UC patients (58.4%). In this group, the disease severity and extension were more severe in PR3-ANCA positive patients than in PR3-ANCA negative group (p<0.001). After treatment, the partial Mayo scores were significantly decreased with the PR3-ANCA titers. The proportion of patients who required steroids for induction therapy was significantly higher among PR3-ANCA positive than negative group. ROC analysis revealed that PR3-ANCA ≥3.5 U/mL had 75% sensitivity and 69.0% specificity for steroid requirement in new-onset UC patients.

Conclusions: Our results indicate that PR3-ANCA measurement is useful not only for diagnosing UC but also for evaluating disease severity and extension and predicting the clinical course. **(Gut Liver 2022;16:92-100)**

Key Words: Colitis, ulcerative; Proteinase 3 antineutrophil cytoplasmic antibody; Disease severity; Clinical course

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory disease of intestines consisting of Crohn's disease (CD) and ulcerative colitis (UC).[1] CD and UC are diagnosed by characteristic endoscopic and histological findings.[2] However, disease-specific serologic markers for CD and UC can reportedly avoid the risks by invasive diagnostic examinations as endoscopy and gastrointestinal series.[3,4] Several serologic markers have been established as diagnostic markers for CD, including anti-*Saccharomyces cerevisiae* antibodies (ASCAs),[5,6] anti-*Pseudomonas fluorescens*-associated sequence I2 antibodies,[7] anti-*Escherichia coli* outer membrane porin C antibodies,[8] anti-bacterial flagellin antibodies,[9] and anti-CD peptide antibodies.[10] Conversely, only perinuclear-antineutrophil cytoplasmic

antibodies (p-ANCAs) have been established as diagnostic markers for UC.[5,11] Although the association between p-ANCAs and UC has been proven in previous studies, corresponding antigens of p-ANCAs are still unclear.[12,13]

ANCAs include p-ANCAs and cytoplasmic ANCAs (c-ANCAs), the latter of which are specific serologic markers of granulomatosis with polyangiitis.[14] Proteinase 3 (PR3), which is a serine protease in azurophilic granules, is an antigen of c-ANCAs. Saadah and Al-Mughales[15] showed that c-ANCAs were positive in only 5.3% of IBD patients (7/131) and were not specific for UC (4 UC and 3 CD). Despite the fact that few reports have described an association between c-ANCAs and IBD, Arias-Loste et al.[16] and Mahler et al.[17] were the first to demonstrate that PR3-ANCA measurement is useful for the diagnosis of UC. Our previous study also revealed that the manufacturer's cutoff value (3.5 U/mL) of PR3-ANCA measurement by chemi-luminescence enzyme immunoassay had 39.2% sensitivity and 96.1% specificity for a diagnosis of UC.[18] Furthermore,

recent studies have shown that PR3-ANCA measurement is useful in the diagnosis of UC worldwide.[19-21] These studies have shown that PR3-ANCAs are the serologic marker in the diagnosis of UC; however how PR3-ANCAs affect the disease severity, disease extension, and clinical course of UC remains unclear.

In this study, we investigated the diagnostic potential of PR3-ANCAs in 173 UC patients and 77 new-onset UC patients at two centers and analyzed the association between the PR3-ANCA titer and the disease severity, disease extension, and clinical course.

MATERIALS AND METHODS

1. Subjects

Our study was conducted at Fukuoka University and Kurume University from July 1, 2015 to June 30, 2020. Blood samples from UC patients (n=173) were used. Blood samples from 96 UC patients were collected randomly during the clinical course and they from 77 new-onset UC patients were collected at the first or second visit to our hospitals. The diagnosis of UC was confirmed by the clinical data and the findings of endoscopy and histopathology. Clinical data were collected from patients' medical information. The disease severity of UC was defined according to the partial Mayo score (0–1, remission; 2–4, mild; 5–6, moderate; 7–9, severe) in 173 patients and Mayo score (0–2, remission; 3–5, mild; 6–10, moderate; 11–12, severe) in 135 UC patients who underwent colonoscopy around 2 weeks before and after blood sampling. Table 1 summarized the clinical characteristics of UC patients.

As control, blood samples from CD (n=110), other intestinal diseases (n=48), and healthy controls (n=71) were collected. The diagnosis of CD was confirmed by the clinical data and the findings of endoscopy and histopathology. In 110 CD patients including 17 patients with ileitis, 75 with ileocolitis, and 18 with colitis. Forty-eight patients with other intestinal diseases including 28 infectious colitis and 20 other colon disease, and 71 age-matched, healthy volunteers were collected. Table 2 summarized the clinical characteristics of the subjects.

Table 1. Clinical Characteristics of Ulcerative Colitis Patients

Characteristics	No. (%)
No. of patients	173
Mean age, yr	40.4
Sex, F/M	83/90
Mean disease duration, yr	5.83
Disease extent	
Proctitis	17 (9.8)
Left colitis	44 (25.4)
Pancolitis	112 (64.7)
Severity (partial Mayo score)	
Remission (0-1)	24 (13.9)
Mild (2-4)	55 (31.8)
Moderate (5-6)	54 (31.2)
Severe (7-9)	40 (23.1)
Therapy	
No treatment	31 (17.9)
5-ASA	134 (77.5)
Steroids	56 (32.4)
Immunomodulators	17 (9.8)
Tacrolimus	4 (2.3)
Anti-TNF-α	4 (2.3)

F, female; M, male; 5-ASA, 5-aminosalicylic acid; TNF, tumor necrosis factor.

Table 2. Characteristics of the Subjects Studied

Characteristics	Ulcerative colitis	Crohn's disease	Intestinal control	Healthy control
No. of patients	173	110	48	71
Sex, F/M	83/90	38/72	20/28	41/30
Mean age, yr	40.4	37.8	38.9	36.8
PR3-ANCA positive, No. (%)	77 (44.5)	8 (7.3)	1 (2.1)	1 (1.4)
MPO-ANCA positive, No. (%)	17 (9.8)	0	0	0

F, female; M, male; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody; MPO, myeloperoxidase.

This study was approved by the ethical review committee of both Fukuoka University (approval number: 2018M043) and Kurume University (approval number: 15213). Written informed consent was waived by an opt-out method, because of the retrospective design.

2. Autoantibody assays

Serum PR3- and myeloperoxidase (MPO)-ANCA titers were examined using chemiluminescence enzyme immunoassay kits (STACIA MEBLux test; Medical and Biological Laboratories, Aichi, Japan) as previously described.[18] Briefly,
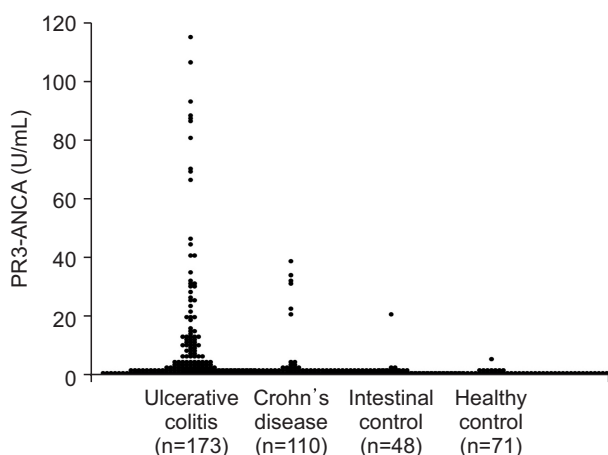

Fig. 1. Serum proteinase 3 antineutrophil cytoplasmic antibodies (PR3-ANCAs) were measured in ulcerative colitis, Crohn's disease, intestinal control, and healthy control. The PR3-ANCA titers were significantly higher in ulcerative colitis compared to those in Crohn's disease, intestinal control, and healthy control (p<0.001 for all the other groups).

serum samples were mixed with PR3- or MPO-conjugated beads. The serum samples with beads were incubated and washed several times. Next, alkaline phosphatase-conjugated goat anti-human IgG (H+L) was added in samples and incubated for 5 minutes at 37℃. CDP-Star was added and PR3- and MPO-ANCA titers were measured. The cutoff value was >3.5 U/mL.

3. Statistical analysis

Data were analyzed by JMP Pro version 16 statistical analysis software (SAS Institute Inc., Cary, NC, USA). The student t-test, analysis of variance, Mann-Whitney U test, Kruskal-Wallis test, chi-square test, Fisher exact test, paired t-test, and Wilcoxon signed-rank test were used where appropriate. PR3-ANCA positive and PR3-ANCA negative groups were compared using the analysis of covariance adjusting for study stratification factors, such as age, gender, disease extent, disease severity, and treatment. The strength of a correlation is measured by the correlation coefficient (r). A receiver operating characteristic (ROC) curve was analyzed to determine whether the PR3-ANCA titer was a predictive factor for a steroid requirement during induction therapy for UC. Statistical significance was set at p<0.05.

RESULTS

1. Differences in clinical characteristics between PR3-ANCA positive and negative groups with UC

The clinical characteristics of UC patients are shown

Table 3. Comparison of Clinical Characteristics between PR3-ANCA Positive and PR3-ANCA Negative Groups in Ulcerative Colitis Patients

Characteristics	PR3-ANCA positive group (n=77)	PR3-ANCA negative group (n=96)	p-value
Mean age, yr	40.8	40.1	0.128
Sex, F/M	33/44	50/46	0.347
Disease extent, No. (%)			0.338
Proctitis	4 (5.2)	13 (13.5)	
Left colitis	20 (26.0)	24 (25.0)	
Pancolitis	53 (68.8)	59 (61.5)	
Severity (partial Mayo score), No. (%)			<0.001
Remission (0–1)	1 (1.3)	23 (24.0)	
Mild (2–4)	18 (13.4)	37 (38.5)	
Moderate (5–6)	32 (41.5)	22 (22.9)	
Severe (7–9)	26 (33.8)	14 (14.6)	
Mean±SD	5.27±2.44	3.12±2.84	<0.001
Treatment, No. (%)			
No treatment	17 (22.1)	14 (14.6)	0.418
5-ASA	58 (75.3)	76 (79.2)	0.877
Steroids	26 (33.8)	30 (31.3)	0.842
Immunomodulators	9 (11.7)	8 (8.3)	0.567
Tacrolimus	3 (3.9)	1 (1.0)	0.313
Anti-TNF-α	1 (1.3)	3 (3.1)	0.785

PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody; F, female; M, male; 5-ASA, 5-aminosalicylic acid; TNF, tumor necrosis factor.

in Table 1. In 173 UC patients, there were 90 men and 83 women, with a mean age of 40.4 years (range, 12 to 84 years). In 110 CD patients, 72 were men and 38 were women, with a mean age of 37.8 years (range, 12 to 67 years). Table 2 shows PR3-ANCA positivity was high in UC compared to CD, intestinal control, and healthy control. Sensitivity (UC vs non-UC) was 44.5% and specificity (UC vs non-UC) was 95.6%. In MPO-ANCA, sensitivity was 9.8% and specificity was 100%. The PR3-ANCA titers
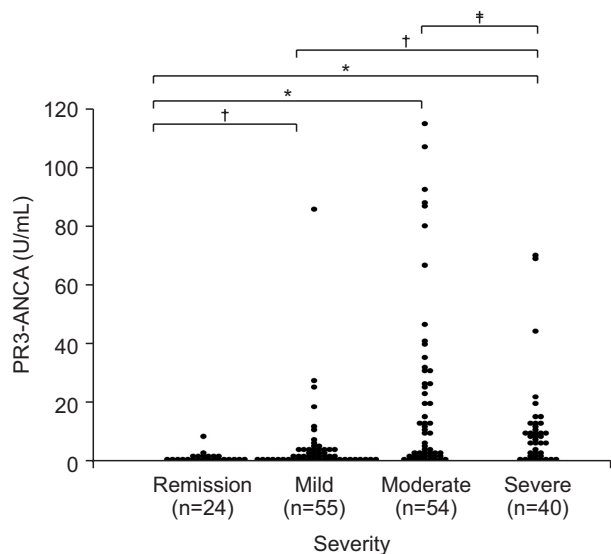
in each group were shown in Fig. 1. The PR3-ANCA titers in UC patients were much higher than them in other groups. In CD, eight patients including two with colitis, six with ileocolitis were PR3-ANCA positive. Furthermore, we investigated the differences in clinical characteristics between PR3-ANCA positive and negative groups (Table 3). The disease severity according to partial Mayo score was significantly different between PR3-ANCA positive and negative groups (5.27 vs 3.12, p<0.001). Fig. 2 shows the PR3-ANCA titers for each disease severity according to the partial Mayo scores. A significant association was present between the PR3-ANCA titer and the disease severity with the exception of moderate and severe disease. Furthermore, we investigated the correlation between the PR3-ANCA titers and Mayo scores in 135 patients who underwent colonoscopy around 2 weeks before and after blood sampling. Fig. 3 shows that there was a mild correlation between the PR3-ANCA titers and Mayo scores (r=0.356, p<0.001). No significant differences were found in disease extension between PR3-ANCA positive and negative groups. There were not any association between the MPO-ANCA titer and clinical data, because the number of MPO-ANCA positive group was small (data not shown).

Fig. 2. Significant differences were observed in the proteinase 3 anti-neutrophil cytoplasmic antibody (PR3-ANCA) titers among different disease severities in 173 ulcerative colitis patients with the exception of moderate and severe (p=0.57). *p<0.001, †p<0.01, ‡p=0.57.

2. Differences in clinical characteristics between PR3-ANCA positive and negative groups in new-onset UC

Next, we investigated 77 patients with a diagnosis of UC within 1 month who were either untreated or treated with 5-aminosalicylic acid (5-ASA) alone to exclude bias caused by therapeutic factors (Fig. 4). Forty-five (58.4%) in 77 new-onset UC patients were PR3-ANCA positive. Thus, PR3-ANCA was highly positive in the treatment-naïve group as previously shown,[18] suggesting that PR3-
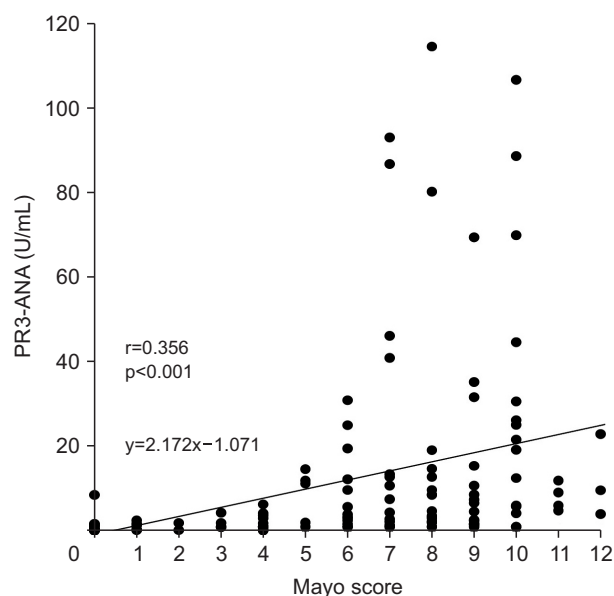

Fig. 3. Pearson correlation coefficient between the proteinase 3 anti-neutrophil cytoplasmic antibody (PR3-ANCA) titers and Mayo scores in 135 ulcerative colitis patients who underwent colonoscopy.
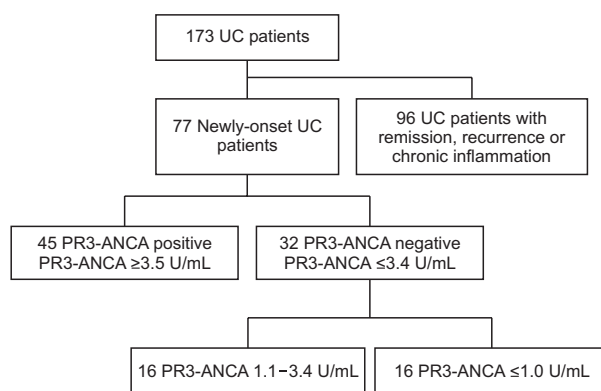

Fig. 4. Flow diagram of the ulcerative colitis (UC) patients included in our analysis cohort.
PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody.

Table 4. Comparison between PR3-ANCA Positive and PR3-ANCA Negative Groups in UC Patients with a Diagnosis of UC within 1 Month Who Were Either Untreated or Treated with 5-ASA Alone

Characteristics	PR3-ANCA positive group (n=45)	PR3-ANCA negative group (n=32)	p-value
Mean age, yr	32.9	34.5	0.827
Sex, F/M	20/25	12/20	0.295
Disease extent, No. (%)			0.029
Proctitis	1 (2.2)	7 (21.9)	
Left colitis	10 (22.2)	5 (15.6)	
Pancolitis	34 (75.6)	20 (62.5)	
Severity (Mayo score), No. (%)			<0.001
Remission (0-2)	0	0	
Mild (3-5)	3 (6.7)	13 (40.6)	
Moderate (6-10)	35 (77.8)	19 (59.3)	
Severe (11-12)	7 (15.6)	0	
Mean±SD	8.24±2.52	5.69±2.60	<0.001
Treatment, No. (%)			0.726
5-ASA	29 (64.4)	18 (56.3)	
Non treatment	16 (35.6)	14 (43.7)	

PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody; UC, ulcerative colitis; ASA, 5-aminosalicylic acid; F, female; M, male.
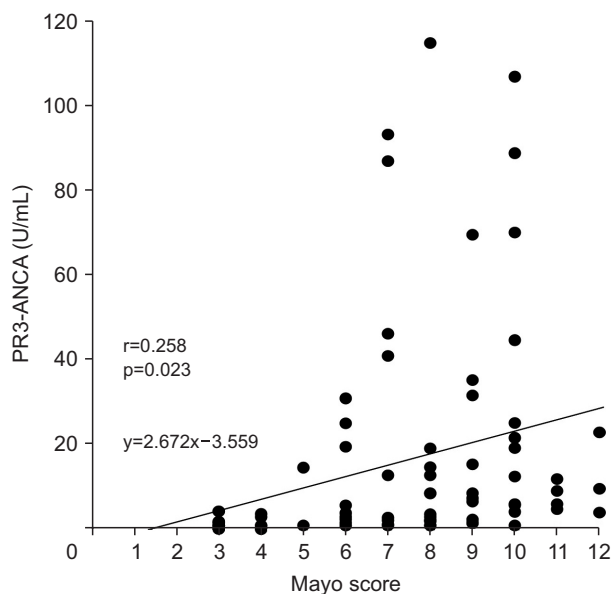

Fig. 5. The pearson correlation coefficient between the proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA) titers and Mayo scores in 77 new-onset ulcerative colitis patients.

r=0.258
p=0.023

y=2.672x−3.559

Fig. 6. (A) Partial Mayo scores and (B) the proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA) titers before and after treatment in 21 PR3-ANCA positive group are shown. After treatment, both the partial Mayo scores and the PR3-ANCA titers were significantly decreased.

ANCA measurement is useful in the diagnosis of UC. Table 4 shows the differences in the clinical characteristics between the PR3-ANCA positive and negative groups. The disease severity according to Mayo score and extension were significantly different between the PR3-ANCA positive and negative groups ($p<0.001$). Furthermore, there was a significant correlation between the PR3-ANCA titer and disease severity (Fig. 5), although the correlation coefficient was lower than that of Fig. 3 because this study did not include UC patients with remission. Among the eight patients with proctiti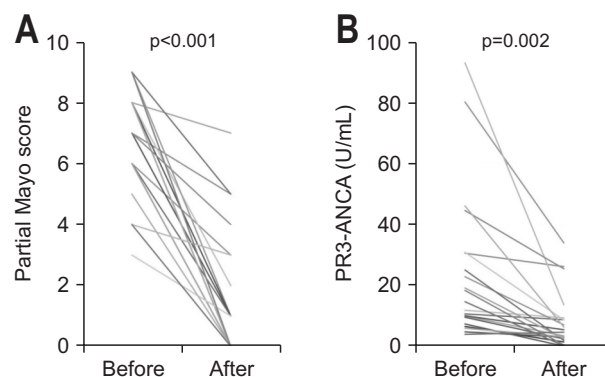s, only one (12.5%) was PR3-ANCA positive, whereas among the 54 patients with pancolitis, 34 (63.0%) were PR3-ANCA positive. Thus, the disease extension was significantly different between PR3-ANCA positive and negative groups ($p=0.029$).

3. PR3-ANCA titer represents disease severity of UC in an individual patient

We assessed the partial Mayo scores and PR3-ANCA titers before and after treatment in PR3-ANCA positive UC patients. In 173 patients, 21 patients including 15 new-onset patients, were measured PR3-ANCA again more than 1 year later, were evaluated for the change of the partial Mayo scores and PR3-ANCA titers during the course of treatment. Of the 21 patients, two were treated with 5-ASA only, 15 with the combination of 5-ASA and steroid, and four with the combination of 5-ASA, steroid, and molecu-

Table 5. Comparison of Treatment by PR3-ANCA Titer in New-Onset Ulcerative Colitis Patients

Therapy	PR3-ANCA, U/mL			p-value
	≤1.0	1.1–3.4	≥3.5	
Steroid therapy				<0.001
Treatment	4 (25.0)	8 (50.0)	36 (80.0)	
None	12 (75.0)	8 (50.0)	9 (20.0)	
Molecular targeted & immunosuppressive therapy				0.227
Treatment	2 (12.5)	2 (12.5)	15 (33.3)	
None	14 (87.5)	14 (87.5)	30 (66.7)	

Data are presented as the number (%).
PR3-ANCA, proteinase 3 antineutrophil cytoplasmic antibody.
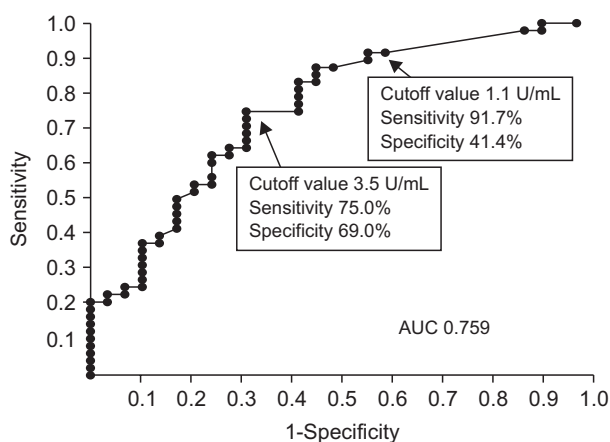

Fig. 7. The clinical utility of proteinase 3 antineutrophil cytoplasmic antibody (PR3-ANCA) measurement was evaluated in the steroid requirement during induction therapy in ulcerative colitis (UC) patients by receiver operating characteristics analysis. Sensitivity and specificity were calculated using the clinical data obtained from 48 patients with UC treated with steroids and 29 patients with UC not treated with steroids.
AUC, area under the curve.

lar targeted or immunosuppressive therapy. Fig. 6 showed the changes in the partial Mayo scores and PR3-ANCA titers in 21 patients. The PR3-ANCA titers decreased as the partial Mayo scores improved in most of the 21 patients. The PR3-ANCA titers were significantly decreased after treatment (p=0.002). This result demonstrated that the PR3-ANCA titer represents the disease severity at the time of examination in an individual UC patient.

4. Association between the PR3-ANCA titer and clinical course

Next, we investigated the clinical course in 77 new-onset UC patients. Fig. 4 showed the number of UC patients classified by their PR3-ANCA titer. We found that 80.0% (36/45) of patients with a PR3-ANCA titer of ≥3.5 U/mL required steroids for induction therapy, whereas 50% (8/16) of those with a PR3-ANCA titer of 1.1 to 3.4 U/mL and 25% (4/16) of those with a PR3-ANCA titer of ≤1.0 U/mL required ste-

roids for induction therapy (Table 5). A high PR3-ANCA titer was significantly associated with a steroid requirement. In addition, 33.3% (15/45) of patients with a PR3-ANCA titer of ≥3.5 U/mL required molecular targeted therapy (anti-tumor necrosis factor-α antibodies) or immunosuppressive therapy (tacrolimus with steroids), whereas 12.5% (4/32) of PR3-ANCA negative group required such therapy. However, there was no significant association between the PR3-ANCA titer and the requirement for molecular targeted or immunosuppressive therapy. Moreover, the clinical utility of the PR3-ANCA titer was evaluated in the steroid requirement during induction therapy in UC patients by ROC analysis. Fig. 7 showed an area under the ROC curve of 0.759 (95% confidence interval, 0.647 to 0.871) and demonstrated that a PR3-ANCA titer of ≥3.5 U/mL had 75.0% sensitivity and 69.0% specificity. A PR3-ANCA titer of ≥1.1 U/mL had a higher sensitivity (91.7%) and lower specificity (41.4%). Therefore, a PR3-ANCA titer of ≥3.5 U/mL in UC patients is a predictive marker for a steroid requirement during the clinical course.

DISCUSSION

Serum biomarkers are expected to be useful not only in differentiating among CD, UC, other intestinal diseases, and an absence of intestinal disease but also in predicting the disease severity and clinical course. Calabresi et al.[22] first reported that p-ANCAs positivity was 75% in 24 UC patients in 1961. In Western countries, the positivity of p-ANCAs is higher in UC patients than in those with CD or healthy controls.[23] Prideaux et al.[24] showed that p-ANCAs positivity was lower in Asian UC patients (33%) compared with Caucasian UC patients (70%). This difference between Asia and Western countries is consistent with previous studies from Hong Kong (44%),[25] China (43%),[26] Japan (35%),[27] and Korea (22%).[28] Furthermore, p-ANCAs are detected in CD patients who have UC-like colonic inflammation.[29] Therefore, ASCAs have been used as serum

biomarkers to exclude CD with UC-like colonic inflammation from UC. A meta-analysis of 60 studies revealed that a p-ANCA positive/ASCA negative status was a most sensitive combination for UC diagnosis, which had 50.5% sensitivity and 94.7% specificity.[30] Additionally, PR3-ANCAs were recently revealed to be a diagnostic biomarker for UC. In Western countries, PR3-ANCAs were detected more in UC patients than CD patients (sensitivity, 52.1%; specificity, 97.3%).[16] In 61 pediatric patients in Switzerland, PR3-ANCAs had a high sensitivity and specificity in the diagnosis of UC (58% and 93%, respectively).[19] In China, PR3-ANCAs had a sensitivity of 57.1% and specificity of 98.9%. This study also showed that the positivity of PR3-ANCAs was 58.4% in new-onset UC patients. Therefore, PR3-ANCAs have shown high sensitivity and specificity in the diagnosis of UC worldwide.

Previous studies have shown that serum biomarkers are not sufficient to assess the disease severity and predict the response to treatment in IBD patients.[31] Indeed, there was no association between p-ANCAs positivity and the disease severity of UC.[32] In 601 patients with UC, p-ANCA and ASCA titers were not associated with the disease severity, disease extension, or colectomy.[33] Kovacs et al.[34] found that titers of serum biomarkers were not associated with the disease severity and that the positive rates were stable during the clinical course. Thus, most studies have shown no correlation between p-ANCAs and the disease severity in UC patients.[23] In several studies, however, high titers of p-ANCA were detected in patients with active UC.[35,36] A recent study, which demonstrated that p-ANCA titers in UC patients were correlated with the concentration of fecal calprotectin, indicated that the change in the p-ANCA titers during the clinical course was associated with the disease severity.[37] Although p-ANCA measurement is useful for the diagnosis of UC, its use in the evaluation of the disease severity is still controversial. However, we demonstrated that the PR3-ANCA titer was correlated with the disease severity and was higher positivity in patients with pancolitis than in other types of colitis. Furthermore, the change in the PR3-ANCA titer was associated with the disease severity during the clinical course in individual patients. Our results reveal that the PR3-ANCA titer is a serologic marker of UC for the diagnosis, the assessment of the disease severity, and disease extension.

In a European cohort of 432 UC patients, Høie et al.[38] found that p-ANCAs were associated with a risk of both first relapse and the total number of relapses. However, most studies have shown no associations between p-ANCAs and the disease severity and the risk of colectomy in UC patients.[33,39] Furthermore, a recent study revealed that there were no associations between the p-ANCA titer

at diagnosis and the clinical course in 120 IBD patients.[37] Although the PR3-ANCA titer has been reported to be a diagnostic biomarker for UC, the relevance of the PR3-ANCA titer to the clinical course remains unclear. In this study, we showed that 80% (36/45) of patients with UC who had a PR3-ANCA titer of ≥3.5 U/mL required steroids for remission induction. In contrast, only 25% (4/16) of those with a PR3-ANCA titer of ≤1.0 U/mL required steroids for remission induction. We also found that 33.3% (15/45) of patients with UC who had a PR3-ANCA titer of ≥3.5 U/mL required molecular targeted or immunosuppressive therapy in addition to steroids, which was not significantly different from patients with a titer of ≤3.4 U/mL (12.5%, 4/32). Our ROC analysis of the PR3-ANCA titer as a predictive factor for a requirement for steroid induction in patients with UC showed that a PR3-ANCA titer of 3.5 U/mL had 75.0% sensitivity and 69.0% specificity, suggesting that the PR3-ANCA titer may be predictive of the clinical course.

This study has several limitations. Intestinal inflammation in UC patients was not assessed by fecal calprotectin or serum C-reactive protein. In addition, patients who required colectomy were excluded. We investigated the PR3-ANCA titer for the clinical course from diagnosis to subsequent treatment, however, we have not evaluated other clinical courses such as the time to relapse, steroid-free period, surgery, and admission rate. The changes in the PR3-ANCA titer before and after treatment were assessed in only 21 patients. The correlation between the PR3-ANCA titer and Mayo score was mild, although disease severities were significantly higher in PR3-ANCA positive group than it in negative group. In the future, it is necessary to evaluate the correlation between the PR3-ANCA titer and the disease severity using various methods and various clinical courses and to investigate the change of the PR3-ANCA titer associated with the disease severity and treatment in a prospective study of patients across multiple races and ethnicities.

In conclusion, PR3-ANCA positivity was high in new-onset UC patients. The PR3-ANCA titer was associated with the disease severity, extension of disease, and clinical course. Our results suggest that PR3-ANCAs are useful serological markers not only for diagnosing UC but also for evaluating the disease severity and disease extension and predicting the clinical course.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Study design: S.I., H.T. Data collection: S.I., H.T., K.T., M.M., N.K., K.A., S.F., H.I., S.Y. Data analysis: S.I., H.T., K.M., H.S. Drafting of the manuscript: S.I., H.T. Critical revision of the manuscript: K.M., T.T., F.H. All authors have read and agreed to the published version of the manuscript.

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