

Association of the Glasgow Prognostic Score with Patient-Reported Symptoms in Patients with Gastrointestinal Cancer Undergoing Outpatient Chemotherapy

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Abstract

Purpose

Patients with gastrointestinal cancer receiving chemotherapy frequently experience symptoms that can interfere with eating and contribute to nutritional deterioration. This study examined associations of systemic inflammation and associated nutritional status, assessed using the Glasgow Prognostic Score (GPS), with patient-reported symptoms in patients receiving outpatient chemotherapy, with exploratory analyses performed according to age.

Methods

This cross-sectional observational study involved 120 patients with gastrointestinal cancer who were receiving outpatient chemotherapy at a university hospital in Japan. The GPS was calculated from serum C-reactive protein and albumin concentrations. Patient-reported symptoms and depressive symptoms were assessed using a questionnaire and the Center for Epidemiologic Studies Depression Scale, respectively. Associations between GPS and symptoms were examined in the overall population and separately in patients aged < 65 and ≥ 65 years.

Results

Mean age was 65.2 years, and 70 patients (58.3%) were aged ≥ 65 years. In the overall population, higher GPS was significantly correlated with anorexia, taste changes, dry mouth, and edema. In the multivariable analysis, anorexia remained associated with higher GPS. Among patients aged ≥ 65 years, GPS was correlated with anorexia, taste changes, and diarrhea; anorexia, edema, and diarrhea were retained in the multivariable model. The distribution of GPS-related C-reactive protein/albumin phenotypes did not differ significantly between the age groups.

Conclusion

Patient-reported symptoms, particularly those affecting eating, were associated with GPS in patients with gastrointestinal cancer receiving outpatient chemotherapy. Attention to symptoms such as anorexia, taste changes, and diarrhea alongside objective inflammation-based measures may help identify nutritional problems requiring supportive care, particularly in older patients.

Background

Gastrointestinal cancers constitute a substantial global health burden and are among the leading causes of cancer incidence and mortality worldwide. Colorectal cancer is the third most commonly diagnosed cancer and the second leading cause of cancer-related death worldwide, while gastric, liver, esophageal,

and pancreatic cancers also contribute substantially to cancer morbidity and mortality [1]. These cancers also represent a substantial disease burden in Japan [2]. Advances in systemic anticancer therapy and supportive care have enabled many patients with gastrointestinal cancer to receive chemotherapy in outpatient settings while maintaining their daily lives. Consequently, the maintenance of quality of life (QOL), physical and psychological well-being, and the ability to continue anticancer treatment have become important components of supportive cancer care.

Nutritional care is particularly important in patients with gastrointestinal cancer because both the disease itself and anticancer treatment can have adverse effects on dietary intake, digestion, and nutrient absorption. Nutritional deterioration is associated with impaired physical function, reduced QOL, greater treatment-related toxicity, and difficulties in completing anticancer treatment. Early recognition of nutritional problems and appropriate nutritional support may help patients to maintain dietary intake, physical function, and QOL as well as support the continuation of cancer treatment [3, 4]. Maintaining patients' ability to eat and maintain adequate nutritional status is important not only for eating-related QOL but also for supporting their overall physical and psychological well-being throughout treatment [5]. Moreover, evidence from patient-reported symptom monitoring indicates that systematic recognition and management of symptoms during cancer treatment can improve health-related QOL, facilitate longer continuation of chemotherapy, and may even contribute to better survival outcomes [6].

Patients receiving chemotherapy commonly experience symptoms that can interfere with eating, including anorexia, nausea, taste changes, xerostomia, oral mucosal problems, and diarrhea. Such symptoms are increasingly recognized as nutrition-impact symptoms because they can compromise dietary intake, thereby contributing to nutritional deterioration [5, 7]. Current clinical nutrition guidelines therefore recommend that nutritional assessment in patients with cancer consider not only food intake, body weight, and body mass index but also nutrition-impact symptoms, physical function, muscle mass, and systemic inflammation [3]. This comprehensive approach is particularly relevant to patients with gastrointestinal cancer, for whom disease- and treatment-related factors may simultaneously affect food intake and nutritional status [4].

Cancer-related nutritional deterioration is also closely linked to systemic inflammation. The Glasgow Prognostic Score (GPS), which is calculated from serum C-reactive protein (CRP) and albumin concentrations, is a simple and objective systemic inflammation-based score [8]. The GPS has been extensively investigated across different cancer types and clinical settings, and higher GPS values have been associated not only with poorer survival but also with weight and muscle loss, poorer performance status, and treatment-related complications [9, 10]. Thus, assessing patient-reported symptoms together with GPS may provide clinically relevant information regarding the interplay among treatment-related symptoms, systemic inflammation, and nutritional status during chemotherapy.

The relationship between nutritional status and treatment-related symptoms may be particularly important in older patients. Older adults with cancer constitute a heterogeneous population with age-related vulnerabilities that may not be captured by routine oncological assessment. The American

Society of Clinical Oncology recommends geriatric assessment for patients aged ≥ 65 years receiving systemic cancer therapy and identifies nutrition, along with physical and cognitive function, emotional health, comorbidities, polypharmacy, and social support, as a key domain requiring assessment [11]. Similarly, the ESMO/SIOG Cancer in the Elderly Working Group emphasizes the importance of assessing nutritional status as part of geriatric assessment and recognizes that treatment-related symptoms, including nausea and loss of appetite, can adversely affect nutritional status during systemic cancer therapy [12]. These recommendations suggest that even when older patients do not necessarily have poorer nutritional status compared with younger patients, careful assessment of nutritional status in addition to treatment-related symptoms may be of particular importance for identifying age-related vulnerabilities during chemotherapy.

Although the prognostic significance of the GPS has been extensively investigated, less is known about how systemic inflammation assessed using the GPS is associated with patient-reported symptoms in patients with gastrointestinal cancer receiving outpatient chemotherapy. Furthermore, whether the patterns of these associations differ according to age remains insufficiently understood. Clarifying these relationships may help to identify symptoms that warrant closer attention during nutritional and supportive care and thereby facilitate the early identification of patients who may be vulnerable to nutritional deterioration.

Therefore, this study investigated the associations of systemic inflammation and associated nutritional status, assessed using the GPS, and patient-reported symptoms among patients with gastrointestinal cancer receiving outpatient chemotherapy. In addition, exploratory age-stratified analyses were conducted to characterize the patterns of these associations in patients aged ≥ 65 years.

This study examined the associations of systemic inflammation and associated nutritional status, assessed using the GPS, with patient-reported symptoms in patients receiving outpatient chemotherapy, and explored the patterns of these associations in older patients.

Methods

Study design and participants

This cross-sectional observational study was conducted at Tohoku University Hospital between July 30 and September 30, 2018. Patients with gastrointestinal cancer receiving outpatient chemotherapy were consecutively recruited. Eligibility criteria were age ≥ 18 years, the ability to provide informed consent, and sufficient cognitive capacity to complete self-administered questionnaires. Clinical and pathological data such as demographic characteristics, cancer type, and treatment regimen were obtained from medical records.

Assessment of systemic inflammation and nutritional status

Systemic inflammation and associated nutritional status were assessed using the Glasgow Prognostic Score (GPS), an inflammation-based score derived from serum C-reactive protein (CRP) and albumin concentrations. According to the original GPS criteria, patients with CRP $\leq$ 1.0 mg/dL and albumin $\geq$ 3.5 g/dL were assigned a GPS of 0; those with either CRP > 1.0 mg/dL or albumin < 3.5 g/dL were assigned a GPS of 1; and those with both CRP > 1.0 mg/dL and albumin < 3.5 g/dL were assigned a GPS of 2 (Forrest et al., 2003; McMillan, 2013).

For the descriptive analyses, patients were further classified into the following four inflammation–nutrition phenotypes according to the individual CRP and albumin components of the GPS: normal CRP and albumin (CRP $\leq$ 1.0 mg/dL and albumin $\geq$ 3.5 g/dL); hypoalbuminemia without elevated CRP (CRP $\leq$ 1.0 mg/dL and albumin < 3.5 g/dL); elevated CRP without hypoalbuminemia (CRP > 1.0 mg/dL and albumin $\geq$ 3.5 g/dL); and combined elevated CRP and hypoalbuminemia (CRP > 1.0 mg/dL and albumin < 3.5 g/dL). These phenotypes corresponded to GPS scores of 0, 1, 1, and 2, respectively. Note that this classification was used to characterize the biochemical patterns underlying the GPS and was not intended as a clinical diagnosis of malnutrition, pre-cachexia, or cachexia.

Additional clinical variables included body mass index, demographic and disease-related characteristics, and treatment regimen.

Assessment of patient-reported symptoms

Treatment-related symptoms were assessed based on the patients' subjective perceptions. Symptom items were selected with reference to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), ver. 5.0 [13]. However, symptom severity was rated by the patients themselves and was not graded by clinicians according to the CTCAE. Patients rated each symptom on an 11-point scale ranging from 0 to 10, with higher scores indicating greater perceived symptom severity.

The assessed symptoms were loss of appetite, taste changes, nausea, oral mucositis, dry mouth, fatigue, constipation, diarrhea, numbness of the hands and feet, skin symptoms of the hands and feet, and edema. Patients could also report other symptoms not included in the predefined items.

Psychological assessment

Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item self-report instrument developed by Radloff [14]. Participants rated the frequency of depressive symptoms experienced during the previous week on a four-point scale, yielding a total score ranging from 0 to 60. A score $\geq$ 16 was used to indicate clinically relevant depressive symptoms. The CES-D has demonstrated acceptable reliability and validity in patients with cancer [15].

Statistical analysis

Descriptive statistics were used to summarize participant demographic and clinical characteristics. Categorical variables are presented as numbers and percentages. The chi-squared test was used to assess differences in the distribution of GPS categories (GPS 0, 1, and 2) according to demographic and clinical characteristics, treatment-related variables, the presence or absence of patient-reported symptoms, and depressive symptoms.

Correlations between GPS and the severity of individual patient-reported symptoms and CES-D scores were examined using Spearman's rank correlation coefficient. Correlation analyses were performed for the overall study population and separately for patients aged < 65 years and ≥ 65 years.

As an exploratory multivariable analysis, stepwise multiple linear regression analysis was performed with GPS as the dependent variable. Candidate explanatory variables included patient-reported symptom severity scores, the number of patient-reported symptoms, CES-D scores, and demographic and clinical characteristics, including cancer site, history of surgery, and treatment-related characteristics. Regression analyses were performed for the overall study population and separately for patients aged < 65 years and ≥ 65 years. Variance inflation factors were examined to assess multicollinearity among variables retained in the final models.

All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS Statistics ver. 21 (IBM Corp., Armonk, NY).

Ethical considerations

This study was approved by the Institutional Review Board of Tohoku University School of Medicine (approval no. 2018-1-176). All participants provided written informed consent prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki [16] and the Ethical Guidelines for Medical and Health Research Involving Human Subjects in Japan [17].

Results

Valid responses were obtained from 120 patients with gastrointestinal cancer. Mean age was 65.2 ± 9.6 years; 50 patients were aged <65 years and 70 were aged ≥65 years. Based on CRP and albumin concentrations, 70 patients had normal CRP/albumin levels, 32 had low albumin only, 6 had elevated CRP only, and 12 had both elevated CRP and low albumin. The distribution of inflammation–nutrition phenotypes did not differ significantly between the two age groups ($\chi^2 = 2.78$, $p = 0.43$) (Table 1). No significant differences in GPS distribution were observed according to cancer type. However, the distribution of inflammation–nutrition phenotypes varied across cancer sites, with abnormal CRP and/or albumin patterns appearing more frequently in some gastrointestinal cancer groups (Figure 1).

The most frequently reported symptoms were fatigue ($n = 99$, 83.9%), numbness of the hands and feet ($n = 88$, 73.3%), and taste changes ($n = 85$, 70.8%) (Table 2). GPS was not significantly associated with the demographic or clinical characteristics examined. In the overall population, GPS was positively correlated with the severity of anorexia ($\rho = 0.26$, $p = 0.004$), taste changes ($\rho = 0.26$, $p = 0.005$), dry

mouth ($p = 0.18$, $p = 0.049$), and edema ($p = 0.22$, $p = 0.018$). CES-D scores were not significantly correlated with GPS (Table 3).

In the age-stratified analysis, among patients aged ≥ 65 years, GPS was positively correlated with the severity of anorexia ($p = 0.29$, $p = 0.016$), taste changes ($p = 0.26$, $p = 0.030$), and diarrhea ($p = 0.27$, $p = 0.023$) (Table 3).

In the exploratory stepwise multiple linear regression analysis, anorexia was associated with higher GPS in the overall population ($B = 0.093$, $p = 0.002$; $R^2 = 0.069$). Among patients aged < 65 years, edema was associated with higher GPS ($B = 0.143$, $p = 0.002$; $R^2 = 0.145$). Among patients aged ≥ 65 years, anorexia ($B = 0.191$, $p < 0.001$), number of patient-reported symptoms ($B = -0.197$, $p < 0.001$), edema ($B = 0.093$, $p = 0.021$), and diarrhea ($B = 0.098$, $p = 0.022$) were retained in the final model ($R^2 = 0.287$, $p < 0.001$) (Table 4).

Discussion

This study examined the associations between the Glasgow Prognostic Score (GPS), an inflammation-based measure derived from serum CRP and albumin concentrations, and patient-reported symptoms in patients with gastrointestinal cancer receiving outpatient chemotherapy. In the overall population, there was a positive correlation of anorexia, taste changes, dry mouth, and edema with GPS, and anorexia remained associated with higher GPS in the exploratory multivariable analysis. Among patients aged ≥ 65 years, anorexia, taste changes, and diarrhea were correlated with GPS, and anorexia, edema, and diarrhea were retained in the multivariable model. In contrast, the distribution of GPS-related CRP/albumin phenotypes did not differ significantly between younger and older patients. These findings suggest that attention to specific patient-reported symptoms, particularly those that can interfere with eating, may provide clinically relevant information when considered alongside objective inflammation-based measures. Anorexia may reduce food intake and contribute to nutritional deterioration, whereas cancer-related systemic inflammation may itself contribute to anorexia and metabolic alterations. Thus, the observed associations are likely to reflect complex and potentially bidirectional relationships among systemic inflammation, nutritional status, and patient-reported symptoms rather than a simple causal pathway from symptoms to poor nutrition [3, 18]. Therefore, focusing on symptoms may serve as an opportunity to recognize difficulties with eating that may not be fully captured by laboratory or nutritional measures alone.

This perspective is particularly relevant to patients with gastrointestinal cancer, for whom eating, obtaining adequate nutrition, and recovering from treatment may be affected by multiple interacting factors. Cancer itself, previous gastrointestinal surgery, systemic therapy, systemic inflammation, and physical and psychological factors can all have an effect on food intake, digestion, absorption, and daily functioning [3, 19]. Surgery may result in persistent anatomical or functional changes, while chemotherapy can cause anorexia, nausea, taste changes, oral symptoms, diarrhea, and fatigue. These problems may be especially relevant in pancreatic cancer, which was relatively common in the present

population. Importantly, physical symptoms and psychological well-being may also be interrelated. In our previous longitudinal study of patients undergoing pancreatic tumor resection, depressive symptoms were associated with patient-reported physical and gastrointestinal symptoms, and these relationships changed during postoperative recovery [20]. Although CES-D scores were not significantly associated with GPS in the present study, this does not exclude the potential importance of psychological well-being in eating, recovery, or nutritional care. Therefore Patient-reported symptoms during outpatient chemotherapy should not necessarily be regarded solely as adverse effects of chemotherapy but may reflect the cumulative effects of disease, previous surgery, ongoing treatment, inflammation, and physical and psychological factors.

The age-stratified findings further suggest the importance of considering symptoms within the broader vulnerability of older patients. Although patients aged ≥ 65 years did not have a significantly poorer distribution of GPS-related CRP/albumin phenotypes, associations of GPS with anorexia, taste changes, and diarrhea were observed in this group. These findings should not be interpreted as demonstrating differences between age groups, given that no formal interaction analyses were performed. Nevertheless, older adults may be more vulnerable to the combined effects of reduced intake, treatment-related symptoms, physical inactivity, loss of muscle mass, and functional decline. Current American Society of Clinical Oncology guidelines recommend multidimensional geriatric assessment of older adults receiving systemic cancer therapy, including physical and cognitive function, emotional health, comorbidities, polypharmacy, nutrition, and social support [11]. Cancer nutrition guidelines similarly emphasize assessing nutritional intake together with muscle mass and physical function [3]. Our findings therefore support incorporating patients' own symptom experiences into such multidimensional assessment rather than relying on chronological age or laboratory measures alone.

From a clinical perspective, these findings highlight the importance of asking not only whether body weight or laboratory parameters have deteriorated but also whether patients are experiencing symptoms that interfere with eating. Maintaining the ability to eat is important not only for energy and nutrient intakes but also for the enjoyment of food, eating-related QOL, and overall physical and psychological well-being. This is particularly relevant during outpatient chemotherapy, when changes in appetite, taste, oral condition, bowel function, fatigue, and food intake may develop between scheduled visits. Systematic attention to patient-reported symptoms may enable emerging problems to be identified and supportive care to be initiated before substantial nutritional or functional deterioration occurs. Randomized evidence has shown that systematic monitoring of patient-reported symptoms during cancer treatment can improve QOL and allow chemotherapy to be continued for longer [6, 21]. In addition, malnutrition has been associated with poorer compliance with postoperative chemotherapy in patients with gastric cancer [22]. Although the present study did not evaluate the association of symptom management and nutritional intervention with treatment continuation, these findings reinforce the clinical importance of recognizing and responding to symptoms. Assessment should therefore extend beyond laboratory and anthropometric measures to include what patients themselves experience as barriers to eating.

Recognizing these difficulties should lead to timely and individualized supportive care. For patients with gastrointestinal cancer, nutritional support should address not only inadequate intake but also the symptoms and problems that interfere with eating. For example, physicians and nurses can identify disease- and treatment-related symptoms; dietitians can assess dietary intake and provide individualized nutritional strategies; and pharmacists can contribute to the management of treatment-related symptoms. Support for physical activity and function may also be incorporated according to individual patient needs. In older patients with advanced pancreatic or non-small-cell lung cancer, the NEXTAC-ONE study demonstrated the feasibility of an early multimodal intervention integrating nutritional support and exercise during chemotherapy [23]. In patients with pancreatic cancer after pancreatectomy, supervised exercise therapy combined with adjuvant chemotherapy was feasible and was associated with a high treatment-completion rate, together with improvements in measures of frailty, muscle mass, and nutritional status [24]. Although these studies did not establish that nutritional or exercise interventions improve survival, they do illustrate a future direction in which nutritional care is integrated with support for physical function during cancer treatment. Taken together, our findings support a multidisciplinary approach in which patient-reported symptoms and nutritional problems are identified early and linked to appropriate symptom management and nutritional care, with support for physical activity and function incorporated when needed. Such care may help patients maintain their ability to eat, remain physically active, and continue their daily lives during anticancer treatment.

Limitations

This study has several limitations that should be noted. First, the cross-sectional, single-center design precludes conclusions regarding temporal or causal relationships between patient-reported symptoms and GPS. The observed relationships might be bidirectional and possibly reflect disease activity or other unmeasured factors. Second, several gastrointestinal cancer types and treatment regimens were included, and pancreatic cancer was relatively overrepresented because recruitment was conducted mainly through surgical outpatient clinics and an outpatient chemotherapy center, potentially limiting generalizability. Third, symptoms were assessed using 0–10 numerical rating scales for items selected with reference to the CTCAE rather than a validated multidimensional patient-reported outcome instrument. Fourth, GPS is an inflammation-based prognostic score and not a comprehensive measure of nutritional status; therefore, dietary intake, weight change, body composition, muscle mass, and physical function should also be considered in nutritional assessment [3, 22]. Finally, the age-stratified and stepwise regression analyses were exploratory; subgroup sample sizes were limited; and GPS was treated as a continuous dependent variable despite its ordinal nature. The negative coefficient for the number of patient-reported symptoms in the older subgroup should therefore not be interpreted as a protective association and requires confirmation in larger prospective studies.

Conclusion

Among patients with gastrointestinal cancer who were receiving outpatient chemotherapy, several patient-reported symptoms, particularly anorexia, were associated with GPS, with additional

associations observed in exploratory analyses of patients aged ≥ 65 years. These findings highlight the importance of paying attention to symptoms that may interfere with eating and considering them together with objective inflammation-based measures. Supporting patients with gastrointestinal cancer involves more than monitoring laboratory values or body weight; it also requires understanding the symptoms and difficulties that affect their ability to eat and maintain their daily lives. Early identification of these problems may facilitate timely symptom management and nutritional support, with support for physical activity and function incorporated when needed. Therefore, a multidisciplinary approach may provide an important framework for supporting patients' nutritional, physical, and psychosocial well-being during anticancer treatment.

Declarations

Clinical trial number

not applicable.

Competing Interests

The authors declare no competing interests.

Ethics approval

This study was approved by the Ethics Committee of Tohoku University Graduate School of Medicine (approval no. 2018-1-176) and was conducted in accordance with the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all participants prior to their participation in the study.

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Author Contribution

NS and FM contributed to the study conception and design. Data collection was performed by NS, FM, HI, and HS. Statistical analysis was performed by NS and MS. The first draft of the manuscript was written by NS. MS contributed to the review and refinement of the manuscript. MS, CI, and MU critically reviewed and revised the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 to 4 are available in the Supplementary Files section.

Figures

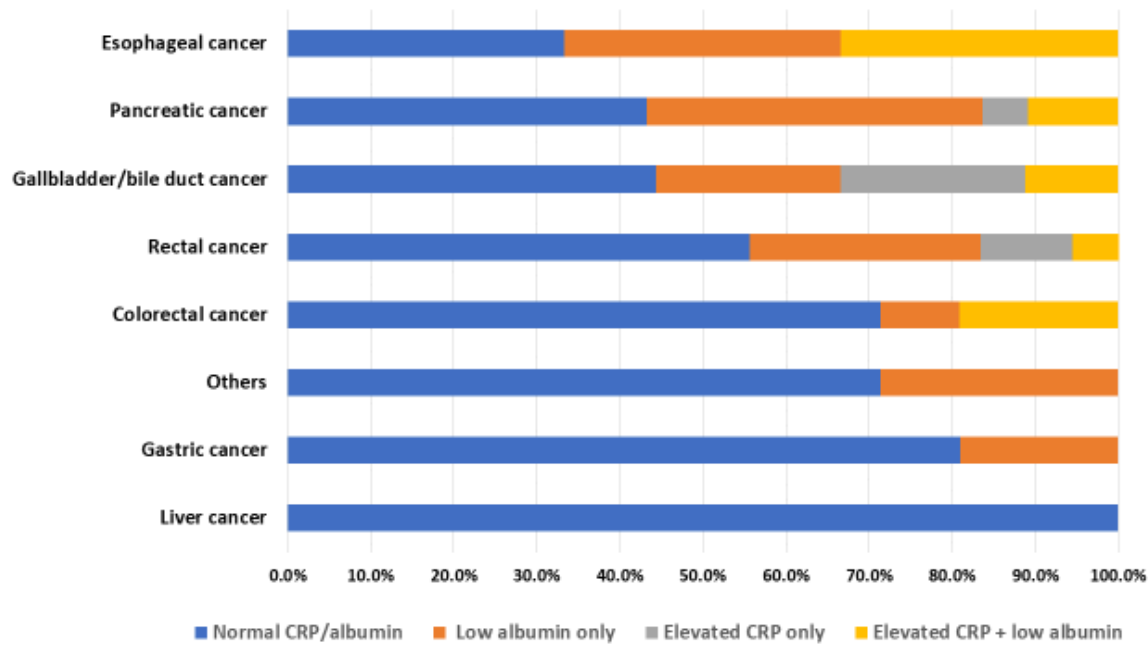


Figure 1. Distribution of inflammation–nutrition phenotypes according to cancer type

Figure 1

Distribution of inflammation–nutrition phenotypes according to cancer type.

Inflammation–nutrition phenotypes were classified according to CRP and albumin concentrations as normal CRP/albumin (CRP ≤1.0 mg/dL and albumin ≥3.5 g/dL), low albumin only (CRP ≤1.0 mg/dL and albumin <3.5 g/dL), elevated CRP only (CRP >1.0 mg/dL and albumin ≥3.5 g/dL), and elevated CRP + low albumin (CRP >1.0 mg/dL and albumin <3.5 g/dL). CRP, C-reactive protein.

Supplementary Files

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