Unresolved inflammation during hospitalization is associated with post-discharge institutionalization and mortality in geriatric rehabilitation inpatients: The RESORT cohort

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ABSTRACT

Background: Inflammation contributes to adverse health outcomes in community-dwelling populations. Little is known about inflammation in hospitalized older adults and its association with adverse outcomes. This study aimed to evaluate the association of the inflammatory markers C-reactive protein (CRP) and albumin measured during acute and geriatric rehabilitation hospitalization with institutionalization and mortality in geriatric rehabilitation inpatients.

Methods: Within the RESTORing health of acutely unwell adultTs (RESORT) cohort, CRP and albumin were measured as part of usual care during acute and geriatric rehabilitation hospitalization. Inflammatory markers are presented as median, peak (CRP: maximum; albumin: minimum), variation (interquartile range) and direction of change (increased CRP or decreased albumin: positive or negative difference between last measurement and median of preceding measurements). Logistic regression was used to determine the associations between inflammatory markers and institutionalization at three-month and all-cause mortality at three- and twelve-month post-discharge.

Results: Geriatric rehabilitation inpatients (n = 1846) with a median age of 83.3 years (interquartile range 77.6–88.3) and 56.6% of female were included. Increased CRP during geriatric rehabilitation was associated with institutionalization. Higher median, peak and increased levels of CRP during geriatric rehabilitation but not during acute hospitalization were associated with higher mortality. Lower CRP variation during acute hospitalization but higher CRP variation during geriatric rehabilitation was associated with higher mortality. Lower median level of albumin during both hospitalizations were associated with higher mortality.

Conclusions: Inflammation characterized by lower albumin during acute hospitalization and, higher CRP and lower albumin during geriatric rehabilitation was associated with mortality in geriatric rehabilitation inpatients. Increased CRP during geriatric rehabilitation was associated with institutionalization. Unresolved inflammation in geriatric rehabilitation might indicate ongoing disease activity leading to adverse outcomes.

1. Introduction

After acute hospitalization, 35% of geriatric patients experience functional decline and loss of independence (Covinsky et al., 2003), which is associated with hospital readmissions, institutionalization and mortality (Barnes et al., 2013; Brown et al., 2016; Tonkikh et al., 2016;
Inflammation is a risk factor for hospitalization in community-dwelling older adults (de Gonzalo-Calvo et al., 2012). C-reactive protein (CRP) and albumin (Alb) measurements from a representative patient during acute or geriatric rehabilitation hospitalization can resolve, persist or increase after acute hospitalization and could influence subsequent recovery from disease (Bateman et al., 2009; Griffith et al., 2016).

Geriatric rehabilitation after acute hospitalization plays an important role in restoring patients’ function and preserving the ability of self-management in older adults (Achterberg et al., 2019). In older post-stroke rehabilitation patients, high CRP and low albumin were associated with poor functional performance at discharge (Yoshimura et al., 2018). On the other hand, high CRP but not low albumin measured in acutely hospitalized older adults, higher CRP and lower albumin at admission has been associated with post-discharge institutionalization and short- and long-term all-cause mortality in geriatric rehabilitation inpatients.

This study aimed to investigate whether the median, peak, variation and change of CRP and albumin during acute and geriatric rehabilitation hospitalization are associated with post-discharge institutionalization and short- and long-term all-cause mortality in geriatric rehabilitation inpatients.

2. Methods

2.1. Study design

REStORing health of acutely unwell adulTs (RESORT) is a prospective, observational, and longitudinal inception cohort of geriatric rehabilitation inpatients (Clark et al., 2020). Older and frail adults who had multimorbidity and required comprehensive rehabilitation care were admitted to geriatric rehabilitation wards at the Royal Melbourne Hospital (Melbourne, Victoria, Australia) for recovery following acute illness. Patients were excluded if they were transferred back to acute care before consent was obtained, or received palliative care at admission, or were unable to provide consent and had no nominated proxy. A total of 1890 patients who were admitted from 16th, October 2017 and 31st, March 2020 were included in the RESORT cohort. All patients provided written informed consent or, if a patient could not provide informed consent (e.g., due to severe dementia, delirium), their designated proxy provided informed consent. In the present analysis, patients were excluded if they died during geriatric rehabilitation hospitalization (n = 36), or had no CRP and albumin measurements during hospitalization (n = 8) (Fig. 1). Only the index admission was included in the analysis for patients who were readmitted to hospital. This study was approved by the Melbourne Health Human Research Ethics Committee.
### Table 2
Inflammatory markers during acute and geriatric rehabilitation hospitalization.

|                         | Acute hospitalization | Geriatric rehabilitation | p value |
|-------------------------|-----------------------|--------------------------|---------|
|                         | n | Freq | Value | n | Freq | Value |         |
| CRP, mg/L               |   |      |       |   |      |       |         |
| Median                  | 1354 | 2 [1–5] | 32.4 [9.3–80.6] | 1132 | 2 [1–3] | 17.5 [5.7–40.3] | <0.001 |
| Peak                    | 1354 | 2 [1–5] | 50.9 [11.8–149.0] | 1132 | 2 [1–3] | 23.4 [7.1–63.6] | <0.001 |
| Variation               | 923 | 4 [2–7] | 24.8 [6.5–59.3] | 662 | 3 [2–5] | 12.0 [3.6–36.0] | <0.001 |
| Albumin, g/L            |   |      |       |   |      |       |         |
| Median                  | 1704 | 4 [2–8] | 30.5 [27.0–34.0] | 1644 | 3 [2–5] | 31.0 [28.0–33.0] | <0.001 |
| Peak                    | 1704 | 4 [2–8] | 29.0 [24.0–33.0] | 1644 | 3 [2–5] | 29.0 [26.0–32.0] | <0.001 |
| Variation               | 1363 | 5 [3–9] | 2.0 [1.3–3.5] | 1235 | 3 [2–6] | 1.5 [1.0–2.5] | <0.001 |
| CRP/albumin ratio       |   |      |       |   |      |       |         |
| Median                  | 1253 | 2 [1–4] | 1.1 [0.3–3.1] | 1053 | 2 [1–3] | 0.6 [0.2–1.5] | <0.001 |
| Peak                    | 1253 | 2 [1–4] | 1.6 [0.3–5.3] | 1053 | 2 [1–3] | 0.8 [0.2–2.3] | <0.001 |
| Variation               | 757 | 4 [2–7] | 1.0 [0.2–2.4] | 552 | 3 [2–5] | 0.4 [0.1–1.25] | <0.001 |

Abbreviations: Freq: Frequency; CRP: C-reactive protein; IQR: Interquartile range.

n: The number of patients who had available measurements of CRP and albumin.

The p values represent the comparison of the CRP, albumin and CRP/albumin ratio values between acute and geriatric rehabilitation hospitalization.

CRP/albumin ratio only includes the simultaneous measurements of CRP and albumin within each patient.

### 2.2. Patient characteristics

A standardized Comprehensive Geriatric Assessment (CGA) was performed within 48 h of admission to geriatric rehabilitation. Age and sex were extracted from medical records. The smoking status, living status and use of a walking aid was collected using a self-reported survey completed by the patient and/or their care. If the patient or their carer could not complete the survey, data was extracted from medical records. The primary reason for hospital admission was extracted from medical records and classified into musculoskeletal, neurologic, infections, cardiovascular, gastrointestinal, respiratory and other diseases. Length of stay of acute and geriatric rehabilitation hospitalization were extracted from medical records. Body mass index (BMI) was calculated using height (m) and weight (kg). Standing height was measured without footwear if patients were able to stand; if patients were unable to stand, height was calculated from the measured knee height using the Longitudinal Aging Study Amsterdam (LASA) formula (Ghulamea et al., 1985). Weight was measured by a weighing scale, chair or hoist, depending on the patient’s mobility. Malnutrition risk was assessed using the Malnutrition Screening Tool (MST) (Ferguson et al., 1999). Frailty status was assessed by the Clinical Frailty Scale (CFS), which scores frailty from 1 (very fit) to 9 (terminally ill) (Rockwood et al., 2005). Activities of Daily Living (ADLs) (Katz et al., 1963) and Instrumental Activities of Daily Living (IADLs) (Lawton and Brody, 1969) were measured to assess patients’ self-care ability. Katz index was used to assess ADLs with a score ranging from 0 to 6, while Lawton and Brody scale was used to assess IADLs with a score ranging from 0 to 8. Higher scores represent greater dependency in both assessments. Morbidity was examined by the Cumulative Illness Rating Scale (CIRS) in which higher sum of scores in all organ systems represents higher disease severity (Linn et al., 1968). Cognitive impairment was defined by a dementia diagnoses or a standardized Mini-Mental State Examination (sMMSE) < 24 score (Folstein et al., 1975) or a Montreal Cognitive Assessment (MoCA) < 26 score (Nasreddine et al., 2005) or a Rowland Universal Dementia Assessment Scale (RUDAS) < 23 score out of 30 (Storey et al., 2004). Anti-inflammatory medications use (corticosteroids, antibiotics, immunosuppressants, anti-neoplastic agents, anti-rheumatic products) during hospitalization was extracted from medical records.

### 2.3. Inflammatory markers

Blood samples were drawn based on clinical indication during the acute and geriatric rehabilitation hospitalization. CRP was measured in serum using the immunoturbidimetric method (Abbott Diagnostics, Chicago, Illinois, USA) with a detection limit of 0.1 mg/L. Serum albumin was measured using the Bromocresol Purple (BCP) assay (Abbott Diagnostics, Chicago, Illinois, USA) with a detection limit of 0.3 g/L. Both CRP and albumin were analysed on the ARCHITECT c16000 clinical chemistry analyzer (Abbott Diagnostics, Chicago, Illinois, USA). All tests were performed within the pathology department of the Royal Melbourne Hospital by trained staff.

The inflammatory markers CRP, albumin and CRP/albumin ratio were expressed as median, peak (CRP and CRP/albumin ratio: maximum value; albumin: minimum value) and variation (interquartile range (IQR)). If geriatric rehabilitation patients had an inter-hospital transfer defined as a transfer back to an acute ward and coming back to geriatric rehabilitation, data of the acute hospitalization period was treated as part of the geriatric rehabilitation. The CRP value less than 10 mg/L and albumin value more than 35 g/L were considered as normal levels (McMillan, 2008). To indicate the direction of change of inflammatory markers during acute and geriatric rehabilitation hospitalization, respectively, the difference between the last measurement and the median level of preceding measurements was calculated (change = last measurement - median of preceding measurements). CRP and CRP/albumin ratio were considered to be increased if the change > 0; albumin was considered to be decreased if the change < 0. Non-increased CRP and CRP/albumin were defined as reference groups if the change ≤ 0; non-decreased albumin was defined as the reference group if the change ≥ 0 (Fig. 2).

To test whether the change in CRP and albumin from acute to geriatric rehabilitation hospitalization was associated with mortality, patients who had CRP and/or albumin measurements during both acute and geriatric rehabilitation hospitalization were grouped based on the median values of CRP median and albumin median during acute stay (Macute) and geriatric rehabilitation (MGk). The categories of change were defined as: low-low (values ≤ Macute and ≤ MGk), low-high (values ≤ Macute and > MGk), high-low (values > Macute and ≤ MGk) and high-high (values > Macute and > MGk).

### 2.4. Institutionalization and mortality

The incidence of institutionalization was defined as a new admission
to a nursing home within three months post-discharge from geriatric rehabilitation. Institutionalization data was collected by follow-up phone calls performed by researchers or extracted from medical records if the patient and/or carer could not be contacted. Patients were excluded from the institutionalization analyses if they were nursing home residents before their hospital admission (n = 51), died within three-month follow-up (n = 168), or had missing data (n = 125). Overall, 1511 patients were included in institutionalization analyses (n = 9 were nursing home residents who died within three-month follow-up). Mortality data was obtained from the Registry of Births, Deaths and Marriages Victoria on 24th, July 2020 and medical records and included all-cause mortality. If the follow up for mortality was less than twelve months from discharge, patients were excluded from the mortality analyses (n = 497) (Fig. 1).

2.5. Statistical analyses

Data are presented as medians and IQR for skewed distributed continuous variables. Categorical variables are presented as frequencies with percentages. Wilcoxon signed-rank test was applied to compare the median, peak and variation levels of inflammatory markers between acute and geriatric rehabilitation hospitalization.

The associations of the median, peak, variation levels and direction of change of CRP, albumin and CRP/albumin ratio with institutionalization and mortality were assessed using multiple logistic regression analyses and expressed as odds ratios (OR) with 95% confidence intervals (CI). The categories of change of CRP or albumin from acute to geriatric rehabilitation hospitalization with mortality was analysed by Cox regression analysis expressed as hazard ratios (HR) with 95% CIs and adjusted survival curves. The high-high CRP and low-low albumin groups were used as references in their respective analyses. All analyses included a crude model and a model adjusted for age, sex, length of stay of the acute or geriatric rehabilitation hospitalization, cognitive impairment, cardiovascular disease, chronic renal failure, diabetes, chronic obstructive pulmonary disease, cancer, and autoimmune disease. To investigate if the association between inflammatory markers and the outcomes was independent of infections as the primary reason for hospital admission, multiple logistic regression analyses were conducted excluding patients with infections as the primary reason for hospitalization (n = 114). The area under the curve (AUC) from receiver operating characteristics (ROC) was calculated to assess the discriminatory ability of inflammatory markers for mortality. The AUC > 0.9 was considered as high accuracy, 0.7 ≤ AUC ≤ 0.9 as moderate accuracy, 0.5 < AUC < 0.7 as low accuracy and AUC ≤ 0.5 as chance result (Fischer et al., 2003). A p-value less than 0.05 was considered significant. Statistical analyses were conducted by the Statistical Package for the Social Sciences (SPSS) 26.0 (IBM Corp, Armonk, NY, USA).

3. Results

3.1. Patient characteristics

Overall, 1846 patients with a median age of 83.3 years (IQR: 77.6–88.3) and 56.6% females were included in this analysis (Table 1). The patients had a median frailty score of 6 (IQR: 5–7), a median ADL score of 2 (IQR: 1–3) and a median IADL score of 1 (IQR: 0–2). The primary reasons for hospital admission were mainly musculoskeletal diseases (47.5%). The median CIRS score was 12 (IQR: 9–16). The length of stay during acute hospitalization was 7.1 days (IQR: 3.9–12.5) and 19.9 days (IQR: 13.2–31.7) during geriatric rehabilitation.

3.2. Inflammatory markers

A total of 9628 CRP tests were taken from 1594 patients and 17,750 albumin tests from 1838 patients during their entire hospital stay. The median number of CRP tests performed was 2 (IQR: 1–5) during acute stay (n = 1354) and 2 (IQR: 1–3) during geriatric rehabilitation (n = 1132). The median number of albumin tests taken was 4 (IQR: 2–8) during acute stay (n = 1704) and 3 (IQR: 2–5) during geriatric rehabilitation (n = 1644). Overall, 79.9% of CRP tests and 87.2% of albumin

Table 3

Assocation of inflammatory markers during acute and geriatric rehabilitation hospitalization with institutionalization at three-month post-discharge.

| Event/total | Acute hospitalization | | | Geriatric rehabilitation | | |
|---|---|---|---|---|---|
| | Crude model | Adjusted model | | Crude model | Adjusted model |
| | OR (95% CI) | p value | OR (95% CI) | p value | OR (95% CI) | p value |
| CRP, mg/L | | | | | | |
| Median | 1112 | 0.998 | 0.158 | 0.999 | 0.158 | 0.999 | 0.239 |
| Peak | 1112 | 0.999 | 0.064 | 0.999 | 0.064 | 0.999 | 0.236 |
| Variation | 200/ | 0.998 | 0.213 | 0.999 | 0.213 | 0.999 | 0.465 |
| CRP/albumin ratio | 743 | 0.995 | 0.001 | 0.995 | 0.001 | 0.995 | 0.002 |
| Increased, yes | 200/ | 0.843 | 0.324 | 0.887 | 0.324 | 0.887 | 0.512 |
| CRP, mg/L | 743 | 0.600 | 1.184 | 0.619 | 1.270 | 0.620 |
| Albumin, g/L | | | | | | |
| Median | 1395 | 1.009 | 0.458 | 0.994 | 0.458 | 0.994 | 0.676 |
| Peak | 1395 | 1.009 | 0.381 | 0.994 | 0.381 | 0.994 | 0.645 |
| Variation | 290/ | 1.011 | 0.778 | 1.044 | 0.778 | 1.044 | 0.293 |
| Decreased, yes | 290/ | 1.211 | 0.166 | 1.122 | 0.166 | 1.122 | 0.438 |
| CRP/albumin ratio | 1112 | 0.924 | 1.589 | 0.838 | 1.503 | 0.838 |
| CRP, mg/L | | | | | | |
| Median | 1028 | 0.962 | 0.139 | 0.972 | 0.139 | 0.972 | 0.303 |
| Peak | 1028 | 0.972 | 0.070 | 0.982 | 0.070 | 0.982 | 0.307 |
| Variation | 173/ | 0.917 | 0.046 | 0.931 | 0.046 | 0.931 | 0.129 |
| increased, yes | 173/ | 0.799 | 0.245 | 0.780 | 0.245 | 0.780 | 0.227 |
| CRP/albumin ratio | 616 | 0.842 | 2.998 | 0.849 | 2.998 | 0.849 |
| Albumin, g/L | | | | | | |
| Median | 1279/2,976 | 1.951 | 0.002 | 2.115 | 0.002 | 2.115 | 0.001 |
| Peak | 1279/2,976 | 1.951 | 0.150 | 2.115 | 0.150 | 2.115 | 0.001 |
| Variation | 1,350–3,313 | 1.951 | 0.002 | 2.115 | 0.002 | 2.115 | 0.001 |
| Decreased, yes | 1,350–3,313 | 1.951 | 0.002 | 2.115 | 0.002 | 2.115 | 0.001 |

Abbreviations: OR: Odds ratio; 95% CI: 95% Confidence interval; CRP: C-reactive protein.

Adjusted model: adjusted for age, sex, length of stay for acute hospitalization or geriatric rehabilitation, cognitive impairment, cardiovascular disease, chronic renal failure, diabetes, chronic obstructive pulmonary disease, cancer, and autoimmune disease. Event/Total: The number of patients institutionalized at three-month follow-up out of the total number of patients included in the analysis. Bold values indicate statistically significant results (p < 0.05).
tests were abnormal. The median, peak and variation levels of CRP and CRP/albumin ratio were significantly higher during acute stay than geriatric rehabilitation (all p < 0.001). The median and peak of albumin were lower and variations of albumin higher during acute hospitalization than geriatric rehabilitation (all p < 0.001) (Table 2).

### 3.3. Inflammation and institutionalization

The incidence of institutionalization at three-month follow-up was 25.4% (n = 384/1511). CRP, albumin and CRP/albumin ratio during acute hospitalization were not associated with institutionalization (Table 3). During geriatric rehabilitation, CRP (increased) was associated with institutionalization in both crude and adjusted models (adjusted OR: 1.008, 95% CI: 1.005–1.012, p < 0.001). Albumin (median, peak) values were associated with institutionalization in the crude model (OR: 0.967, 95% CI: 0.936–0.999, p = 0.004; adjusted OR: 0.962, 95% CI: 0.937–0.989, p = 0.005), but not in the adjusted model. CRP/albumin ratio during geriatric rehabilitation were not associated with institutionalization (Table 3). After excluding patients with infections as the primary reason for hospitalization, CRP (peak) and CRP/albumin ratio (variation) during acute hospitalization were associated with institutionalization (Table A.1).

### 3.4. Inflammation and all-cause mortality

The mortality rate was 9.1% (n = 168/1846) at three-month and 21.1% (n = 285/1349) at twelve-month follow up. During acute hospitalization, lower variation of CRP was associated with higher three-month mortality (adjusted OR: 0.994, 95% CI: 0.989–0.999, p = 0.027) (Table 4). Lower albumin median was not associated with three-month mortality (Table 4) but higher twelve-month mortality (adjusted OR: 0.967, 95% CI: 0.936–0.999, p = 0.046) (Table 5). Lower variation of CRP, albumin and CRP/albumin ratio was associated with higher twelve-month mortality (adjusted OR: 0.994, 95% CI: 0.989–0.998, p = 0.004; adjusted OR: 0.901, 95% CI: 0.818–0.993, p = 0.036; adjusted OR: 0.852, 95% CI: 0.760–0.955, p = 0.006) (Table 5).

During geriatric rehabilitation, CRP (median, peak, variation, increased) values were associated with three-month mortality (adjusted ORs: 1.008 (95% CI: 1.005–1.012, p < 0.001), 1.009 (95% CI: 1.004–1.014, p < 0.001), 2.610 (1.651–4.126, p < 0.001). Albumin (median, peak, decreased) values were associated with three-month mortality (adjusted ORs: 0.890 (95% CI: 0.854–0.927, p < 0.001), 0.884 (0.851–0.918, p < 0.001) and 1.021 (1.008–1.035, p < 0.001)). CRP/albumin ratio (median, peak, variation, increased) values were associated with three-month mortality (all p < 0.010) (Table 4). These associations remained significant for twelve-month mortality (all p < 0.010) (Table 5). After excluding patients with infections as the primary reason for hospitalization, the significance for CRP variation during acute hospitalization on mortality at three-month follow up (all p < 0.046).

### 3.5. Discrimination of prediction models

The discriminatory abilities of all measures of CRP, albumin and CRP/albumin ratio during geriatric rehabilitation were considered as low accuracy (0.5 < AUC < 0.7) for both three- and twelve-month mortality (Table A.4).

The adjusted survival curves for the categories of change of CRP or...
Inflammation is associated with loss of skeletal muscle mass and strength (Tuttle et al., 2020), poor physical performance (Brinkley et al., 2009), functional decline (Washida et al., 2021; Yaku et al., 2020), loss of living dependence (Abete et al., 2019; Aiello et al., 2008), and cognitive impairment (Sartori et al., 2012), all of which are risk factors of institutionalization (Han et al., 2016; Kvael et al., 2017). High CRP levels are associated with a composite of rehabilitation outcomes including a transfer to acute hospital, in-hospital mortality and institutionalization in geriatric rehabilitation inpatients (Aquilani et al., 2020). However, our study did not identify associations of median or peak of CRP and albumin during both hospitalization but increased CRP during geriatric rehabilitation with institutionalization, indicating that patients who were discharged with unresolved inflammation were more likely to be institutionalized regardless of the inflammation level per se. This highlights the importance of recovery from inflammation during geriatric rehabilitation.

Several studies have demonstrated an association between high CRP and low albumin at hospital admission with high mortality in older patients during acute illness (Akirov et al., 2017; Eckart et al., 2020; Marsik et al., 2008). The median of albumin but not CRP in acute hospitalization were associated with three- and twelve-month mortality. This might be because albumin in blood has a longer half-life than CRP and it not only indicates inflammation but also malnutrition (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018). When inflammation is not resolved and the acute phase serves as the first-line of defence against pathogens and injuries (Sproston and Ashworth, 2018).
hospitalizations. Increased CRP and decreased albumin during geriatric rehabilitation had better survival compared to high CRP or low albumin during both hospitalizations. This might be beneficial from the anti-oxidative property and abilities of albumin to maintain vascular barrier and bind toxins (Alphonsus and Rodseth, 2014; Ha and Bhagavan, 2013).

To our knowledge, this is the first study to investigate the association of inflammation in acute and geriatric rehabilitation hospitalization with short- and long-term adverse health outcomes. The Glasgow Prognostic Score (GPS) also combines CRP and albumin to assess systemic inflammation as a prognostic indicator in various conditions and diseases such as heart failure (Matsuo et al., 2021), post stroke (Yoshimura et al., 2018), and cancer (Mcmillan, 2013). However, the GPS is usually being used at one time point, e.g. at hospital admission (Yoshimura et al., 2018), diagnose of diseases (Forrest et al., 2003), or initiation of a treatment (Ishihara et al., 2016). This study focused on overall inflammation level during hospitalization instead of a certain time point. The limitations of this study are that patients had varying lengths of stay in hospital, irregularly measured inflammatory markers during hospitalization, and infections acquired during hospitalization was not controlled for, which hinder the application of more comprehensive statistical models (e.g., group-based trajectory modelling). Although we used median, peak, variation and direction of change to capture the levels of inflammatory markers during hospitalization multi-dimensionally, the AUC analysis indicates these values fail to adequately identify patients at risk of mortality. Information about smoking status, living status and use of a walking aid was self-reported. Furthermore, results are not generalizable to other cohorts of older adults in acute hospital or community settings.

5. Conclusions

In conclusion, measures of CRP and albumin throughout geriatric rehabilitation were associated with all-cause mortality in geriatric rehabilitation inpatients. Albumin during acute hospitalization was associated with mortality, whereas CRP was not. Recovery from high CRP and low albumin during rehabilitation was associated with lower mortality. Unresolved inflammation during geriatric rehabilitation revealed as increased CRP was associated with institutionalization. Despite statistically significant associations of inflammation with mortality, inflammatory markers have low accuracy to be used in clinical practice. Further studies that examine anti-inflammatory interventions that could improve outcomes in geriatric rehabilitation population should be tested.

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Declaration of competing interest

All authors declare no conflict of interest.

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