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Handgrip strength shows no improvements in geriatric patients with persistent inflammation during hospitalization

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ABSTRACT

Purpose: Hospital-associated deconditioning due to a combination of illness and inactivity is a serious problem for elderly adults. Here we investigate whether persistence in inflammatory status affects changes in physical function during short-term hospitalization.
Methods: This was a prospective observational study in elderly medical patients at a geriatric department. Measurements were obtained at admission and one week after admission and included de Morton Mobility Index (DEMMI) test, 30-second chair stand test (30-s CST), 4-m gait speed (4-m GST) test, handgrip strength, activity levels determined with ActivPALs, and concentrations of circulating C-reactive protein (CRP) from blood samples. Only patients with inflammation (C-reactive protein levels ≥ 10 mg·L^{-1}) at admission were included in this study. They were divided into those with continued inflammation (CI: CRP remained ≥ 10 mg·L^{-1}) and those that became non-inflammatory (BN: CRP decreased to < 10 mg·L^{-1}) after one week of admission.
Results: On admission 214 patients (67% female) with a median (IQR) age of 86 (81–91) years were categorized as inflammatory. There were no baseline differences in physical function between CI (n = 138, 67% female) and BN (n = 76, 68% female). DEMMI-score increased similarly in both groups ($P < 0.05$). When normalized to days between tests, only changes in handgrip strength were significantly different between the CI- and BN-group (-0.05 [-0.27–0.28] vs. 0.16 [-0.10–0.41] kg·day^{-1}, respectively, $P < 0.01$). There was a positive association between changes in CRP and length of hospital stay ($r_s = 0.30$, $P < 0.001$).
Conclusion: Hospitalized geriatric patients admitted with inflammation showed only moderate improvement of general mobility during hospital stay, regardless of changes in their inflammatory status. However, handgrip strength increased only in those patients who became non-inflammatory during hospitalization.

1. Introduction

Hospital-associated deconditioning due to a combination of illness and inactivity is a serious problem for elderly adults. Previous studies have shown that the systemic level of the inflammatory biomarker C-reactive protein (CRP) (Ticinesi et al., 2016) is predictive of both length of hospital stay and readmission rates (Brown et al., 2012; Hogarth et al., 1997). Moreover, systemic inflammation is significantly associated with recovery of physical function in elderly recuperative care patients (Dennis et al., 2012). Consequently, geriatric patients admitted with systemic inflammation have poorer muscle function compared to patients with normal CRP. In addition, patients with elevated CRP do

not seem to improve their muscle function during hospitalization, despite being medically treated (Bautmans et al., 2005).

We recently found a negative association between changes in muscle mass in response to resistance training and the level of systemic CRP in geriatric patients during hospitalization (Norheim et al., 2017). Thus, patients displaying signs of inflammation during their hospital stay may be more prone to hospital-associated deconditioning. Since in that study CRP was only measured at one or two time-points, with no detail about the potential changes in CRP during hospital stay, it remains unknown whether changes in inflammatory status during hospitalization is predictive of changes in functional performance.

We therefore aimed to investigate whether geriatric patients with

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continuous inflammation differed in functional changes during hospitalization compared to patients who were inflammatory at admission and in whom inflammation resolved during their stay. We hypothesized that patients presenting persistent inflammation would show poorer recovery of physical function compared to patients who became non-inflammatory during their hospital stay.

2. Methods

2.1. Participants

The current study was a prospective observational study performed from May 2014 to December 2015 at the Geriatric ward at Bispebjerg Hospital, Denmark. All patients who were admitted due to acute illness and with elevated circulating levels of inflammation markers (i.e. CRP ≥ 10 mg·L^{-1}) (Bautmans et al., 2005) were included. Patients in isolation, delirious patients, patients who could not understand Danish and patients with terminal cancer were excluded from the study. Based on the initial examination of the patient by the clinical doctor, it was estimated whether the stay at the department would be very short or not. Patients with an expected stay at the hospital of < 3 days were excluded. Also, patients that were unable to complete the physical tests were excluded. Trained researchers conducted all physical tests. The study was approved by the Regional Human Ethical Research Committee of the Hospital Region of Copenhagen (No. H-15005016).

2.2. Measurements

2.2.1. Functional performance

The included patients were assessed on two occasions, separated by a median of 7.0 (5.0–8.0) days; at admission and at discharge with at least two consecutive days between tests. Mobility was assessed with the de Morton Mobility Index (DEMMI) (DeMorton et al., 2008), which includes 15 items giving total scores that range from 0 (poor mobility) to 100 (independent mobility). A 30 second chair stand test (30-s CST) (Jones et al., 1999) and a 4-meter gait speed test (4-m GST) (Studenski et al., 2011) were used to assess lower extremity physical function. The 30-s CST involves rising from an armless chair (height: 46 cm) with hands crossed over the chest for as many times as possible in 30 s. The 4-m GST measures the time it takes for the patient to walk 4 m in their usual pace and from a standing start. Handgrip strength was measured with a digital Jamar® hand held dynamometer (Mathiowetz et al., 1985) with the patients seated in a chair with their elbow flexed at ~ 90° and resting on the arm of the chair. A minimum of three trials with each hand was completed and the patients continued until the highest attempt was followed by a weaker attempt. The highest value was recorded and the value from the same hand was used to investigate changes over time in the post-assessments. New Mobility Score (NMS) (Parker and Palmer, 1993) served as descriptive variable.

2.2.2. Physical activity level

Activity levels were measured using triaxial ActivPAL accelerometers (PAL Technologies, Glasgow, Scotland) attached anterior on the mid-thigh of each subject. Recordings started after the pre-tests had been completed and stopped before the post-tests began. Data were stored in the 32 MB memory of the ActivPAL and subsequently downloaded using ActivPAL software (version 6.3.0). Microsoft Excel 2010 (Redmond, WA) was used for the data analysis. Only full days of recording (24 h) were included in the analysis, producing a median of 5.0 (3.0–6.0) days measured. Activity level was divided into hours per day spent sedentary (lying or sitting) or active (standing or walking).

2.2.3. Biochemistry and categorization

Blood samples were taken, as part of normal hospital procedures, after an overnight fast at approximately 8 am on the first or second day of admission. Blood levels of haemoglobin (Hb) and leukocytes, and

plasma levels of C-reactive protein (CRP) and albumin were determined by the Department of Clinical Biochemistry at Bispebjerg Hospital. CRP was analyzed with enzyme-linked immunosorbent assay (ELISA) kit (DuoSet DY1707). Circulating CRP levels were used to categorize patients into inflammatory or non-inflammatory using a cut-off value of 10 mg·L^{-1}, as described by Bautmans et al. (2005). Moreover, CRP levels were recorded both at admission (days 1–2) and after 1 week (days 6–8) of hospitalization to classify patients into those who were either continuously inflammatory, continuously non-inflammatory or displayed a shift in their inflammatory status during the duration of the hospitalization.

2.3. Statistics

All continuous data were tested for normality and equal variance using the Shapiro-Wilk test and Brown-Forsynthe test, respectively. Differences in C-reactive protein and functional performance between groups were analyzed with a two-way analysis of variance (ANOVA) for repeated measures. Differences from pre to post were analyzed with the Wilcoxon signed rank test, while differences between groups were analyzed with the Mann-Whitney U test. Spearman's rho (r_s) was used to determine correlations between two variables. Because geriatric patients are often unable to rise from a chair without support (Bodilsen et al., 2015), we used the McNemar's test to investigate the probability of transitioning from one state (unable) to another state (able) during the hospitalization. Data are presented as medians (interquartile range [IQR]) unless otherwise indicated. Significance was set a priori at $P < 0.05$. Analyses were performed in SigmaPlot version 13.0 for Windows (Systat Software, Inc., San Jose, California).

3. Results

3.1. Patients and categorization

One thousand thirty-one patients were hospitalized during the study period, whereof 616 were excluded from the study and 112 did not complete both pre- and post-assessments. The main reasons for exclusion were not being able to complete the physical tests and too short hospital stay (< 3 days). Out of the 303 patients (72% female) who completed both pre- and post-assessments, 89 patients (83% female) were categorized as non-inflammatory on admission. Therefore, 214 patients (67% female) with inflammation were included in the present study. These patients had a median length of stay of 10 (7–14) days and a median NMS of 4 (3–7), and 90% of them required a walking aid. The patients displayed the following admission diagnoses: respiratory and infectious diseases (23%), musculoskeletal diseases and injuries (28%), genitourinary and digestive diseases (16%), endocrine and immunological diseases (1%), cardiovascular and neurological diseases (17%), and other (15%) (Karlsen et al., 2016). One week after admission 138 (67% female) patients remained inflammatory, while 76 (68% female) became non-inflammatory.

3.2. Persistence of inflammation

Baseline characteristics of the included patients, i.e. those who were inflammatory at admission and either stayed inflammatory (continuous inflammation: *CI*) or became non-inflammatory (became non-inflammatory: *BN*) after one week of admission, are presented in Table 1. The CI group had a 3 days longer length of stay and thus showed more days between tests compared to the BN-group ($P < 0.05$). Haemoglobin and albumin levels were significantly lower in the CI group at admission ($P < 0.05$). Changes in CRP and functional performance during hospital stay are presented in Table 2. Plasma levels of CRP were significantly higher in the CI- compared to the BN-group both at admission ($P < 0.05$) and after one week ($P < 0.05$), and both groups demonstrated a significant ($P < 0.05$) reduction in CRP levels from