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Do Patients with Covid-19 Benefit from Rehabilitation?

Functional outcomes of the first 100 patients in a Covid-19 rehabilitation unit

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ABSTRACT (274/275 words)

Objective: To determine the benefits associated with brief inpatient rehabilitation for Covid-19 patients.

Design: Retrospective chart review.

Setting: A newly created specialized rehabilitation unit in a tertiary care medical center

Participants: Consecutive sample of the first 100 patients with Covid-19 infection admitted to rehabilitation.

Intervention: Inpatient rehabilitation for post-acute care Covid-19 patients

Main Outcome Measures: Measurements, at admission and discharge, comprised a Barthel Activities of Daily Living Index (including baseline value before Covid-19 infection), time to perform 10 sit-to-stands with associated cardio-respiratory changes, and grip strength (dynamometry). Correlations between these outcomes and the time spent in ICU were explored.

Results: Patient characteristics upon admission to rehabilitation were: men 66%, age 66 ± 22 years, mean delay from symptom onset 20.4 ± 10.0 days, BMI 26.0 ± 5.4 kg/m², hypertension 49%, diabetes 29%, with 26% having >50% pulmonary damage on CT-scans. Mean length of rehabilitation stay was 9.8 ± 5.6 days. From admission to discharge, the Barthel index (/100) increased from 77.3 ± 26.7 to 88.8 ± 24.5 ($p<0.001$), without recovering baseline values (94.5 ± 16.2 ; $p<0.001$). There was a 37% improvement in sit-to-stand frequency (0.27 ± 0.16 to 0.37 ± 0.16 Hz; $p<0.001$), a 13% decrease in post-test respiratory rate (30.7 ± 12.6 to 26.6 ± 6.1 ; $p=0.03$), and a 15% increase in grip strength (18.1 ± 9.2 to 20.9 ± 8.9 kg; $p<0.001$). At both

admission and discharge, Barthel score correlated with grip strength ($\rho=0.39-0.66$; $p<0.01$), which negatively correlated with time spent in ICU ($\rho=-0.57$ to -0.49 , $p<0.05$).

Conclusions: Inpatient rehabilitation for Covid-19 patients was associated with substantial motor, respiratory and functional improvement, especially in severe cases, even though there remained mild persistent autonomy loss upon discharge. Following acute stages, Covid-19, primarily a respiratory disease, might convert into a motor impairment correlated with the time spent in intensive care.

Keywords: Covid-19, Pandemic, Rehabilitation

List of abbreviations:

CT-scan: Computerized Tomography scan

D14: Day 14

D24: Day 24

ICU: Intensive Care Unit

IQ: InterQuartile

PM&R: Physical Medicine and Rehabilitation

PT: Physical Therapy

RNA: Ribonucleic Acid

RT-PCR: Reverse Transcriptase Polymerase Chain Reaction

INTRODUCTION

The Covid-19 pandemic forced healthcare systems to rapidly adjust to constantly evolving situations. Traditional acute care units were converted into Covid-19 units with concerns about overwhelming hospital capacities. The rapid development of specific rehabilitation units was essential in response to the high level of dependence observed in many patients and the need to prevent outbreaks in other departments. Several authors have highlighted the need to prepare for post-acute care, but few functional outcomes after Covid rehabilitation have been reported. [1-7]

Covid-19 rehabilitation not only needs to address cardiorespiratory and motor deconditioning, as seen in acute respiratory distress syndrome, but also neurological deterioration, aggravation of comorbidities, and consequences of prolonged bed rest. [8-11]

In this work, we quantified the changes in functional parameters from admission to discharge, for the first 100 patients of a specifically designed Covid-19 rehabilitation unit, comparing non-intensive care unit (ICU) with post ICU patients and those after short vs long prior stay in acute care.

MATERIAL AND METHODS

Creation of the unit - Target patients

A unit of thirty-five single rooms dedicated to Covid rehabilitation was opened to meet the needs of our hospital group during the Spring 2020 epidemic wave, all patients coming from its acute care units. Admission criteria in the rehabilitation unit comprised:

- positive RT-PCR or CT-scan supporting Covid-19 infection (as RT-PCR sensitivity has been reported to range from 66% to 80%, patients having highly evocative clinical signs and CT-scans were considered as Covid-19 patients, as in acute care departments) [12];

- no >6 liters/min oxygen requirement (patients requiring more than 6 liters/min of oxygen were deemed unstable and remained under acute care);

- clinical impression of stability;

- no current endotracheal intubation or tracheotomy;

- and need for rehabilitation and/or extensive social work to optimize a return home.

Nursing and medical care

The ward was organized into sub-units of 8-9 patients, each operated by a team of two physicians, one nurse, two nursing assistants, and two physical therapists. Full personal protective equipment were donned by the staff for patients <14 days after symptom onset. Patients remained in their room at all times, including for their rehabilitation treatments. Following evidence suggesting the persistence of viral RNA on nasopharyngeal swabs for over 20 days, rehabilitation stays were extended up to D24 and further. [13] For >D14 patients, less strict prevention procedures were implemented, involving the sole use of medical masks and hand disinfection with hydro-alcoholic gel.

Logistics and Equipment

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A physiotherapy space was arranged at the floor level for the >D14 patients to minimize patient transportations and to ease access to therapy activities. In addition, individual rehabilitation equipment was made available in each patient room, including dumb-bells, training bands, pedal-boards, hand-cycles, and chairs of standardized height. Eight bicycle-ergometers were available: five for the \leq D14 patient rooms and three for the >D14 physiotherapy space.

Organization of the rehabilitation activities

Two physical therapy (PT) sessions per day were provided for each patient but were kept short (<20 minutes) given the compromised cardio-respiratory condition and high levels of fatigability in post Covid patients. The therapy program primarily included overall motor strengthening with body weight exercises (sit-to-stand, tiptoe stands, squats), elastics and weights, with about three series of ten repetitions for each exercise, according to the patient abilities. Respiratory rehabilitation exercises were associated, including controlled diaphragmatic breathing, with work on the inspiratory and expiratory times. Aerobic work included bicycle-ergometer sessions at submaximal intensity, with monitoring of vital parameters. Finally, an individualized self-rehabilitation program was taught to patients, who were strongly advised to pursue these exercises after discharge, using specific workbooks.

In addition to this PT work, a physical education teacher organized small group sessions for >D14 patients who had become able to handle one-hour long workshops (4 patients at a time, at least 4 meters apart). Two occupational therapists, one speech therapist, and one psychologist were also dedicated to the 35-bed unit. To be medically authorized, speech therapy sessions had to be provided beyond D24, after two consecutive negative RT-PCR tests. The psychologist also cared for the staff.

Discharge process

To consider discharge home, patients had to be >D14 from symptom onset and no longer symptomatic for Covid-19 infection for at least 48h. Suitable home accommodation with temporary possibility of a private space was also required, as well as personal assistance if needed, and no at-risk relative at home. A specific mobile discharge team comprising one PM&R physician, one social worker and one occupational therapist helped detect early and solve any social issues encountered towards returning home. The physician of the mobile discharge team systematically provided tele-consultations after discharge. In addition, a dedicated physiotherapist insured proper execution of the self-rehabilitation exercises by visio-consultations. When discharge home was not possible at D24 from symptom onset, a Covid-free rehabilitation unit was sought.

Ethics

The local ethics committee approved the study (UPEC IRB 0011558 n°2020-064). Non-opposition to utilization of patient data was systematically pursued.

Study design and participants

A retrospective chart review of the first 100 patients admitted to the Covid-19 rehabilitation department was conducted since its opening on March 25, 2020.

Inclusion criteria included age ≥ 18 years, and the ability and willingness to participate in two daily PT sessions five days a week. Among included patients, functional outcome criteria were analyzed for lengths of stay ≥ 72 hours.

Demographics and clinical characteristics were recorded, including age, sex, date of admission, medical history, Covid-19 severity factors, clinical signs, biological and radiological data from the acute stay, drug treatments, date of discharge, length of stay, destination at discharge, and personal assistance at home if any. The following outcomes were assessed by only two physiotherapists to limit variability:

- Barthel Index of Activities of Daily Living (also retrospectively assessed before the Covid episode by questioning the patient or family); [14,15]

- Time to perform 10 full sit-to-stands as quickly as possible from a standardized 40-cm height chair, arms folded over the chest, with respiratory rate, oxygen saturation, heart rate, and Borg scale of perceived exertion, recorded before and after. [16-18] When 10 sit-to-stands could not be completed, the number of completions in one minute was collected;

- Hand grip strength, using dynamometry. The forearm was resting on the thigh, palm upwards, elbow to the body at 90° flexion. The best result of two tries was kept for each side. [19,20]

Changes in these outcomes from admission to discharge were measured in all patients, and then compared between:

- Patients who stayed in ICU *versus* patients who did not.

- Patients who stayed in acute care longer than the median length of stay *versus* those who stayed less.

Correlations between outcomes were also explored.

Data analysis

Descriptive statistics were used for quantitative continuous variables using mean±SD or median (IQ). Qualitative data were compared using χ^2 -tests. Comparisons between admission and discharge values were carried out by paired sample *t*-tests or Wilcoxon signed ranked tests. Correlations between Barthel total score and other functional tests, and between functional scores and time spent in acute care were explored by Spearman or Pearson tests. Between-group comparisons were made using independent samples *t*-tests or Mann-Whitney U tests. Patients with missing data, upon admission or discharge, were excluded from the statistical analysis for the relevant parameter. All statistical analyses were performed according to conditions of normality on Shapiro-Wilk tests. SPSS v25 software was used, with a significance set at 0.05.

RESULTS

Population description

The descriptive characteristics of the 100 patients are presented in Table 1. On admission, median age was 66 (41% were >70) with 66% men; mean BMI was 26 kg/m²; mean delay post-onset was 20.4±10.0 days. At the time of diagnosis, the main clinical symptoms were dyspnea with fever and 26% had >50% pulmonary damage on CT-scans. There was a high prevalence of hypertension (48%) and diabetes (29%). In terms of prior drug treatment, 37% had received hydroxychloroquine, 9% had received liponavir, 5% had received tocilizumab and 6% had received corticosteroids.

23% of patients had been admitted to intensive care and 77% had needed oxygen. Upon admission in rehabilitation, 58% still required oxygen, administered with nasal cannula (*Table 2*). The severity of admitted patients worsened over the course of the epidemic wave as the proportion of ICU and intubated patients gradually increased to reach 60% and 50% respectively by May 15, 2020, the date of the admission of the 100th patient. Of note, there was a discrepancy between the number of patients hospitalized in intensive care and those who were intubated (*Supplemental Figure 1*). Indeed, the general consensus was to limit orotracheal intubation to a strict minimum to avoid complications related to this procedure. [21] In parallel, the number of days since the onset of infection at admission also gradually increased (*Supplemental Figure 1A*). The number of weekly admissions followed the spring pandemic's curve, peaking at 25 (*Supplemental Figure 1B & 2*).

The mean length of stay in the rehabilitation unit was 9.8±5.6 days, with 79% of discharges home or to a relative's and 15% transfers to Covid-free units for further inpatient rehabilitation. The proportion of patients needing personal assistance at home increased by

26% ($p<0.001$) as compared with before the infection, and 3% of patients still needed oxygen at discharge (*Table 2*).

Overall functional outcomes

- The total Barthel score improved from admission to discharge (77.3 ± 26.7 vs 88.8 ± 24.5 respectively; $p<0.001$), in particular in terms of personal care and motor skills (transfers, walking, and use of stairs). However, independence for personal tasks of daily living at discharge remained lower than prior to infection (88.8 ± 24.5 vs 94.5 ± 16.2 respectively; $p=0.001$) (*Figure 1*).

- Sit-to-stand frequency increased by 37% (0.27 ± 0.16 to 0.37 ± 0.16 Hz; $p<0.001$; *Figure 2A*);

- Post sit-to-stand test respiration rate dropped by 9% (30.1 ± 12.0 to 28.0 ± 7.5 ; $p=0.029$; *Figure 2A*);

- Borg exertion score after the sit-to-stand test improved by 30% (3.0 ± 2.4 to 2.1 ± 1.5 ; $p=0.023$; *Figure 2B*);

- Grip strength among right-handed people (92% of patients) increased by 15% (18.1 ± 9.25 to 20.9 ± 8.9 kg, $p<0.001$; *Figure 2C*).

Correlations between length of acute stay, motor parameters and functional autonomy

Barthel total score correlated with sit-to-stand frequency, both at admission and discharge ($\rho=0.66$, $p<0.001$ and $\rho=0.53$, $p<0.001$ respectively; *Figure 3A*) and with grip strength both at admission and discharge ($\rho=0.43$, $p=0.003$ and $\rho=0.39$, $p=0.007$ respectively;

Figure 3B). Grip strength was negatively correlated with the number of days spent in ICU, both at admission and discharge ($\rho=-0.49$, $p=0.053$ and $\rho=-0.57$, $p=0.021$ respectively; *Figure 3C*), as was post-test Borg at discharge ($\rho=-0.51$, $p=0.042$).

Between-group comparisons

Prior to admission into rehabilitation, the median length of stay in acute care was 14 days. The patient groups considered for comparison were therefore: 1) ICU *versus* non-ICU stays; 2) ≥ 14 days *versus* <14 in acute care. The mean length of stay in the Covid rehabilitation department was not different between these groups: post-ICU patients ($n=23$) had spent 9.4 ± 4.2 days in our unit *versus* 9.9 ± 5.3 days in non-ICU patients ($n=77$) ($p=0.86$), and patients who spent ≥ 14 days in acute care ($n=50$) had spent 10.1 ± 5.1 days in our unit *versus* 9.5 ± 5.0 days for those who spent <14 days in acute care ($n=50$) ($p=0.54$). There was also no difference in functional parameters upon admission into rehabilitation between these same groups, including for grip strength and Barthel index. Yet, comparisons of changes in functional outcomes from admission to discharge revealed two differences between the groups:

- Grip strength improved more in post-ICU patients ($+3.3\pm 3.1$ kg; $n=13$) *versus* patients who did not require ICU ($+0.99\pm 3.7$ kg; $n=31$; $p=0.049$; data not shown);
- The score for transfers on the Barthel Index improved more in patients who stayed ≥ 14 days in acute care ($+30.0\pm 60.7\%$; $n=45$) than in patients who stayed <14 days ($+8.7\pm 22.3\%$, $n=45$; $p=0.041$; data not shown).

DISCUSSION

In this retrospective study on the first 100 patients with Covid-19 infection admitted into a specialized rehabilitation unit, inpatient therapy was associated with substantial functional, motor, and cardio-respiratory improvement, particularly in those patients who had undergone severe acute disease. Nonetheless, loss of autonomy and motor weakness persisted at discharge, which occurred about a month after the onset of Covid-19.

Usefulness of a Covid rehabilitation unit

To our knowledge, the present article is the first to report quantified, systematically collected data on rehabilitation effects in such a large cohort of Covid patients. It is worth mentioning that this work came in the midst of a trend to convert many rehabilitation facilities into acute departments in several countries. [22] In that context, the present study still suggests the importance of early inpatient Covid rehabilitation, within 3 weeks of disease onset, including sustained motor exercises. Our findings confirmed early reports from around the world: a recent Japanese case report showed a comparable improvement on grip strength and Barthel index in one patient with early rehabilitative care, while an Italian review of post Covid clinical status upon admission into rehabilitation also observed low Barthel Index total scores (<50, see below). [23,24] More recently, two studies compared functional data between admission and discharge from a specialized rehabilitation unit, from smaller sample sizes. The first study mainly provided respiratory data for 23 subjects, while the second provided other functional data for 41 patients. As in the present work, both studies showed an improvement

in Barthel index and suggested that the neurological consequences of Covid infection could be long-lasting. [6,7]

In this study, most patients admitted to the rehabilitation unit were elderly, male, with a high prevalence of cardiovascular comorbidities, all characteristics consistent with Covid-19 infection risk and severity factors previously reported. [25-27] The estimated Barthel index prior to the episode was >90/100, showing that these patients were free of prior limitation of daily activities. Barthel at admission in rehabilitation was thus notably low (77.3 ± 26.7), 5% of the patients having even lost all autonomy for daily activities (i.e. Barthel <30). Upon admission, there was marked motor weakness in this non-geriatric population mostly free of pre-morbid neurological disability, with a mean grip strength and a sit-to-stand frequency both at 80% of normal values in that age range. At discharge, mean grip strength remained 10% below normal. [17,18,28] Therefore, in this study much of the post-acute functional consequences seemed to be motor. The question may arise as to whether such motor impairment may be attributable to sole deconditioning in patients who were hospitalized for several days, or to direct Covid-19 aggression of neurological pathways. [29-33]

Any impact of Covid-19 on the nervous system is being scrutinized in the literature. A literature review with meta-analysis outlines possible neurological symptomatology. [34] The sole known neurological disorders observed in the present series were probable ICU-acquired weakness – unfortunately however, electroneuromyography was not systematically performed in the present cohort – and few post-intubation swallowing disorders. We did not note any emerging confusion related to the Covid-19 infection in a context where some of our patients did have pre-existing cognitive impairments. One patient suffered from an acute stroke for

which he was initially hospitalized and was then incidentally diagnosed with Covid-19. In the presence of other risk factors, this stroke was not attributed to the ongoing Covid infection. Most of the rehabilitative therapy involved motor exercises and few pure respiratory exercises. Accordingly, motor progression was dramatic during the hospital stay and functional autonomy highly correlated with motor performance. This made sense since the sit-to-stand test and grip strength have been shown to correlate with overall strength and global physical functioning, thus assumingly with the Barthel Index. [15,17] The mean length of rehabilitation stay (9.8 ± 5.0 days) was notably shorter than in a traditional inpatient rehabilitation setting. This may have resulted from both the intensity of the rehabilitative care provided and the effectiveness of the mobile team specifically dedicated to accelerate the discharge process.

Recovery was incomplete at discharge, which may imply the need to continue with outpatient rehabilitation beyond discharge. To this end, since outpatient physiotherapy was forbidden during the spring pandemic, patients were taught guided self-rehabilitation exercises and were provided with a workbook containing an individualized program, similarly to what exists in other indications [35]. A more prolonged stay might have allowed a more complete recovery.

Effect of motor rehabilitation on severe Covid cases

The findings suggest that an ICU or longer acute stay did not hamper responsiveness to rehabilitation. In fact, responsiveness was even enhanced for some outcomes in these severely affected patients. Admittedly, motor function may have started from lower values in these cases, even though differences upon admission into rehabilitation were not statistically significant between the groups. Nevertheless, these findings are reassuring, since they support

the reversibility of much of the motor consequences of longer stays in acute care or of ICU stays.

Study limitations

The present study is not controlled. In the context of the health crisis of the Spring 2020, it was not considered ethical to carry out a clinical trial of rehabilitation *versus* a "sham rehabilitation" control group. The lack of hindsight in this disease and the emergencies that professionals were faced with also made it impossible to design a control group with a real but different rehabilitation protocol. Another limitation was the proportion of missing functional data (*see Tables & Figures*). Due to rapid patient turnover, functional assessments could not be always carried out. Data were however sufficient to show pre-post and between-group statistical differences. Respiratory data was also incomplete although these would have allowed to better characterize and follow up patients: spirometry was not assessed as there was concern about the infectious risk of its use, and Pa/FiO₂ measurements were not possible since patients admitted in rehabilitation were not ventilated, as per inclusion criteria.

Conclusions

When the Covid-19 health crisis began, a number of reports emphasized the need to be prepared for post-acute care management. [1-5] The objective, quantified functional improvement from admission to discharge suggests the usefulness of rehabilitation in a specialized unit after Covid-19 infection, with even greater improvement for some outcomes

in patients who had undergone ICU or stayed longer in acute care. However, the consequences of severe Covid-19 infection on dependence appear to be long lasting and predominantly related to motor limitation. Once the acute hospital situation has subsided, prospective and randomized blinded studies comparing the effectiveness of different types of rehabilitation and including specific respiratory assessments may further knowledge on Covid rehabilitation.

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Declaration of interests

The authors declare no competing interests.

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Figure 1. Changes in Barthel index (n=89)

A. Barthel index items; Items laid out in order to highlight motor tasks. **B.** Barthel index total score. Data expressed in mean±SEM.

* p<0.05; ** p<0.01; *** p<0.001

Figure 2. Functional data upon admission and at discharge

A. Sit-to-stand parameters; **B.** Borg scale before and after Sit-to-stand test; **C.** Grip strength in right-handed patients. Data expressed in mean±SEM.

* p<0.05; ** p<0.01; *** p<0.001

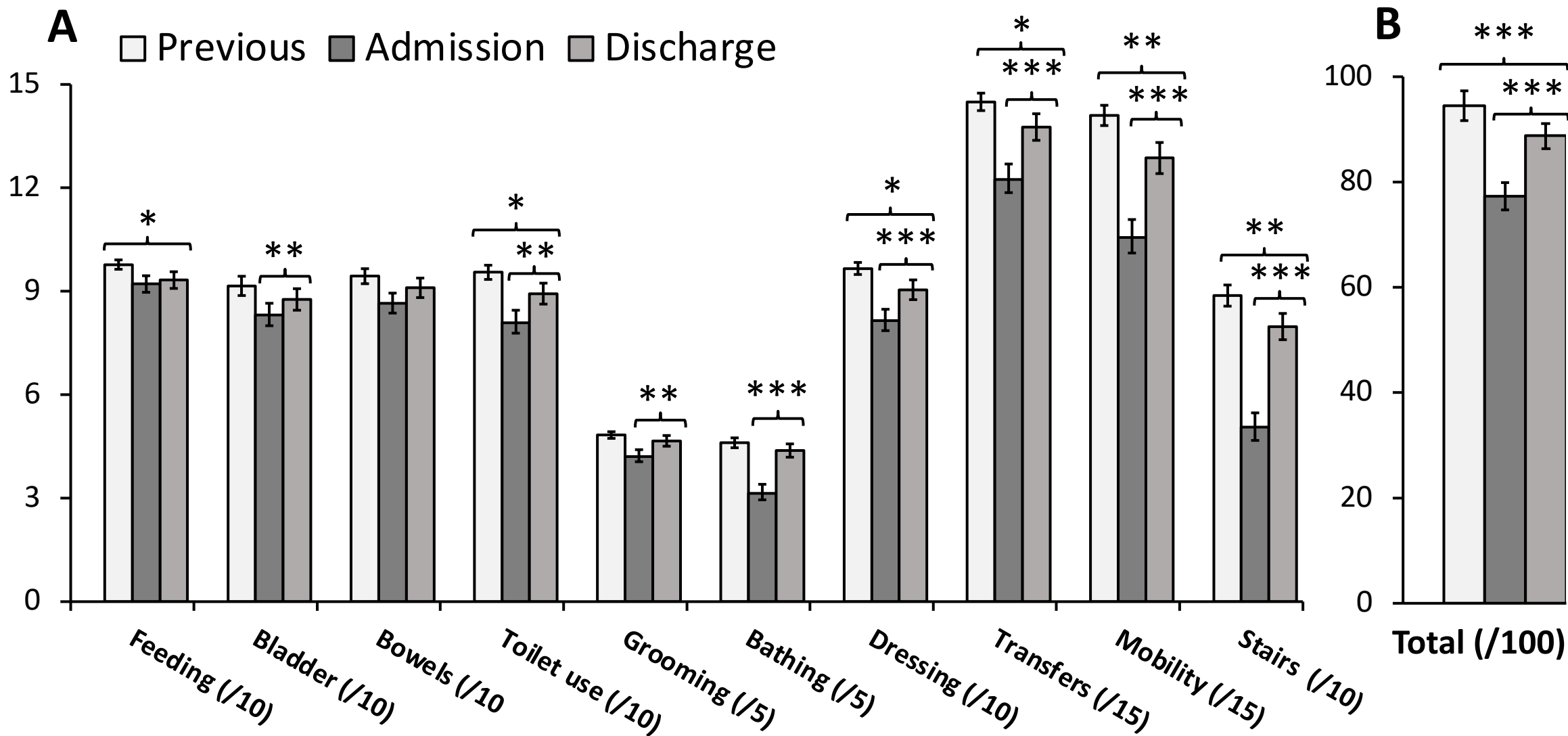
Figure 3. Correlations between motor/functional tests and Barthel index or number of ICU days

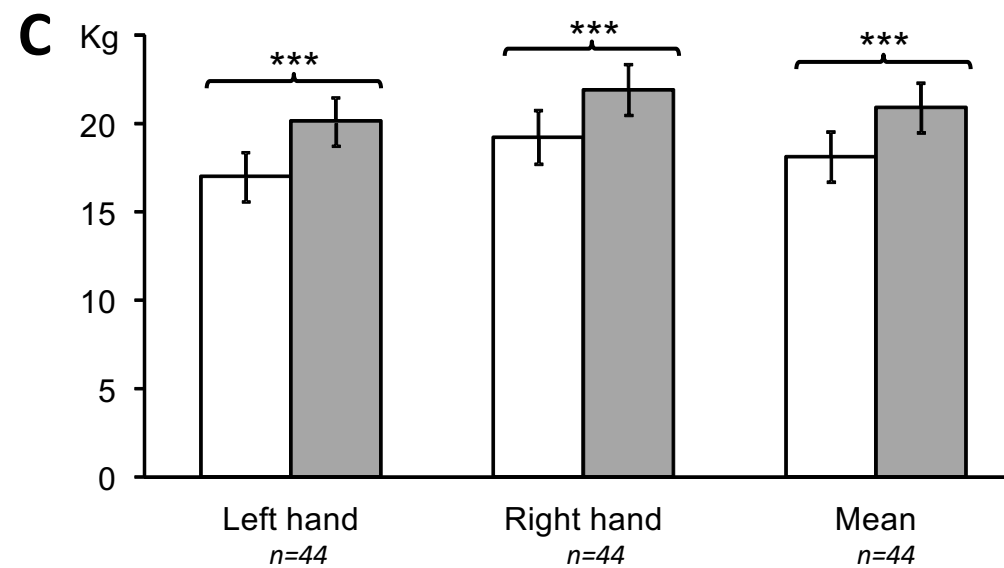
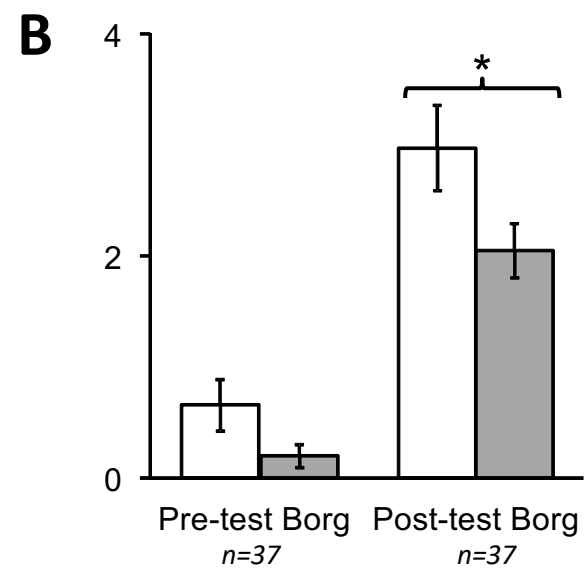
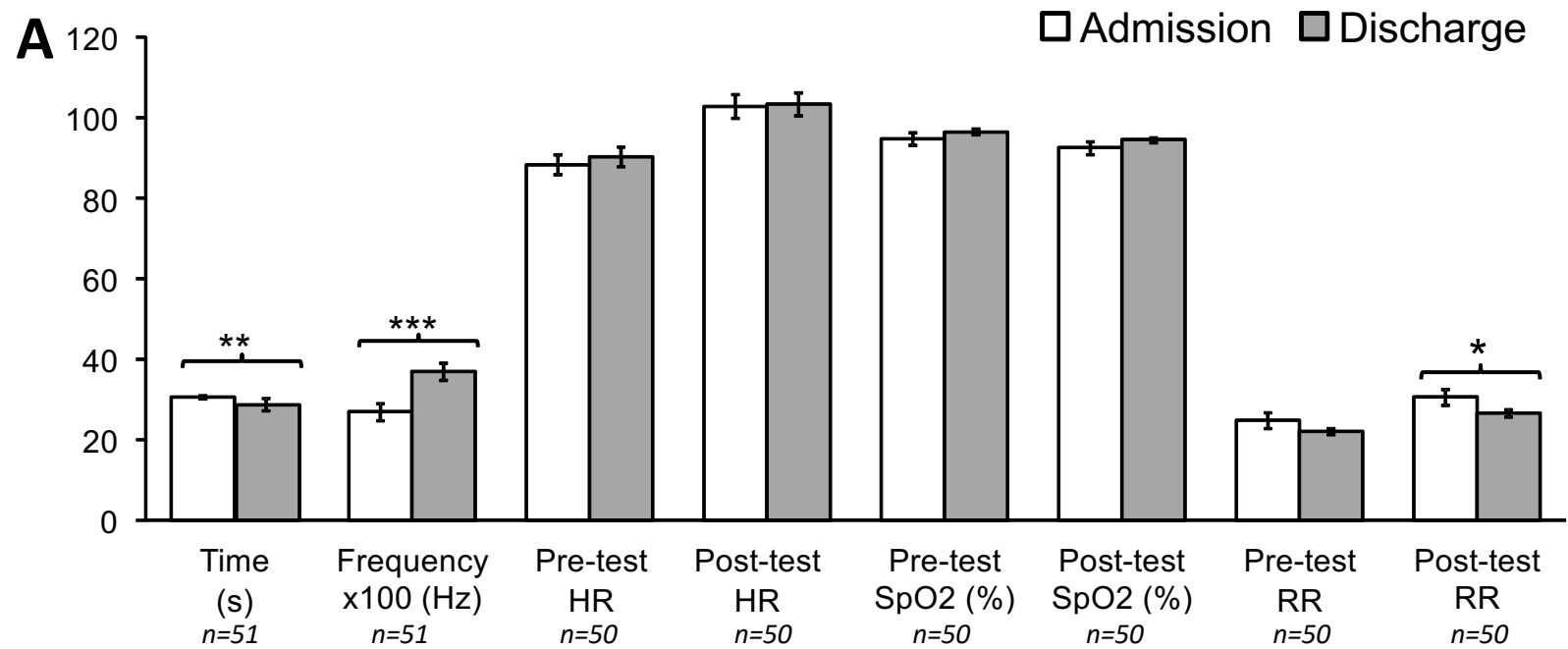
A. Barthel total score and Sit-to-stand frequency at admission and at discharge.

B. Barthel total score and mean grip strength at admission and at discharge.

C. Grip strength and the number of days spent in ICU at admission and at discharge.

Spearman or Pearson tests were used according to conditions of normality on Shapiro Wilk tests. Outliers beyond 2SD on Z-tests were excluded.





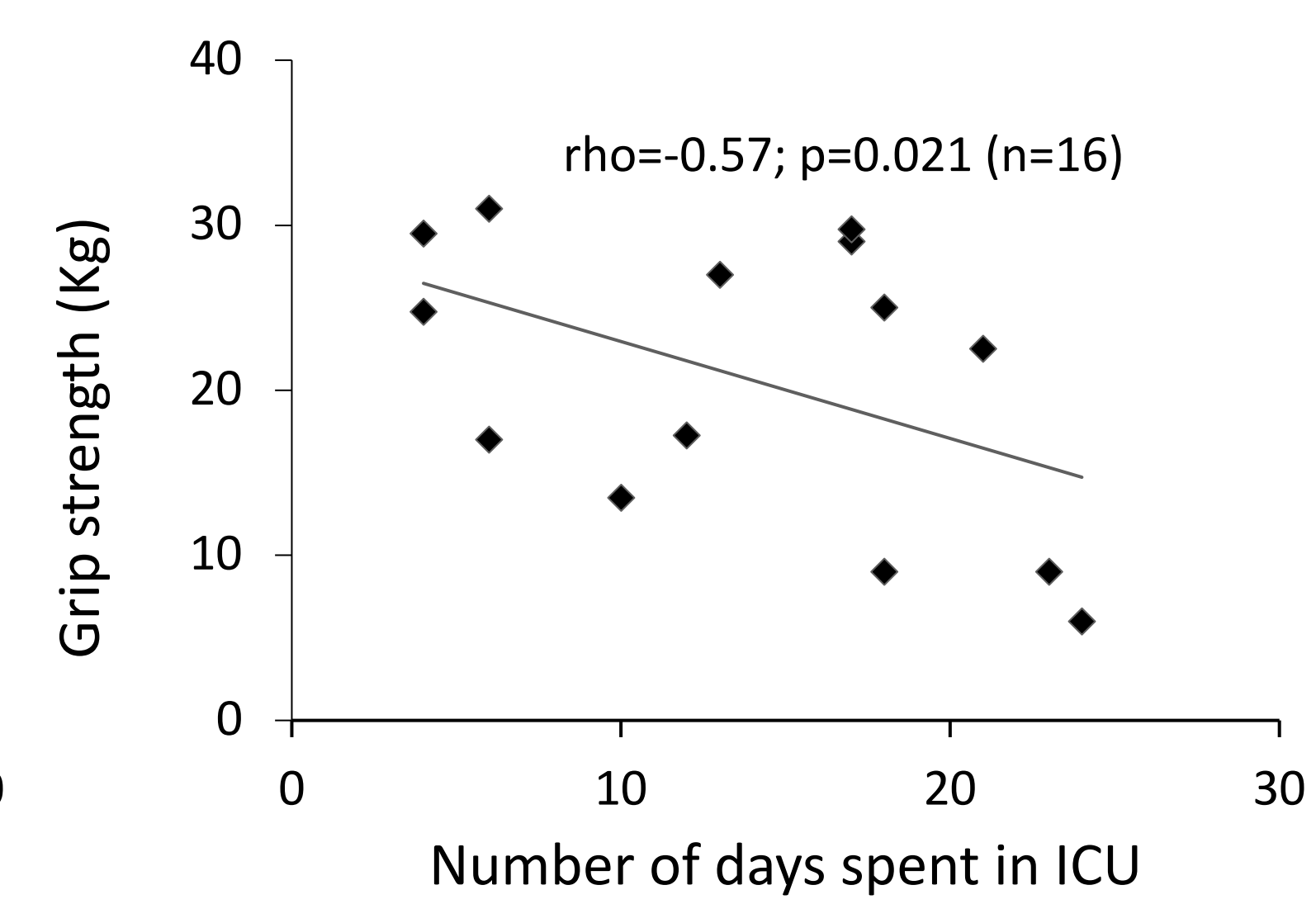
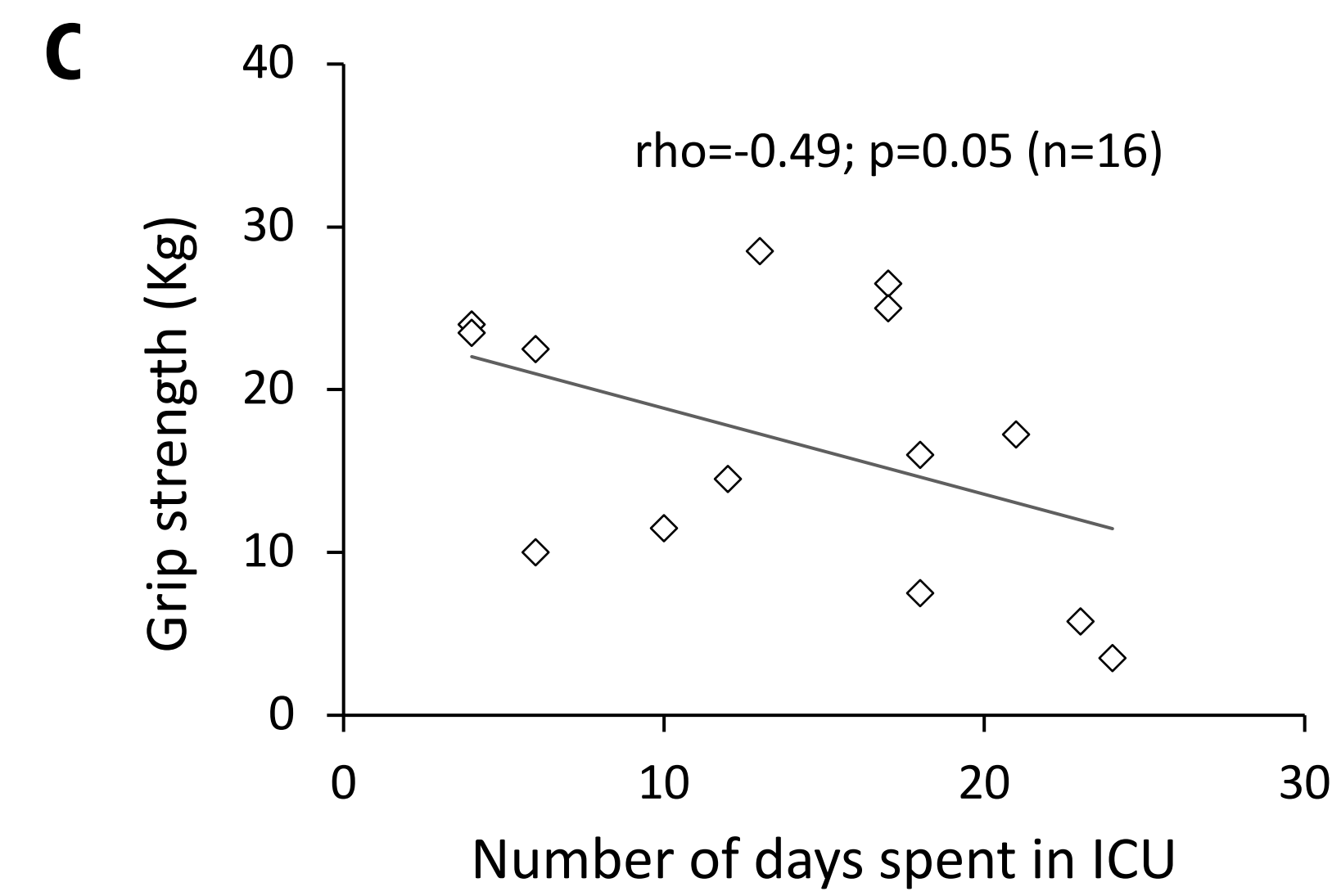
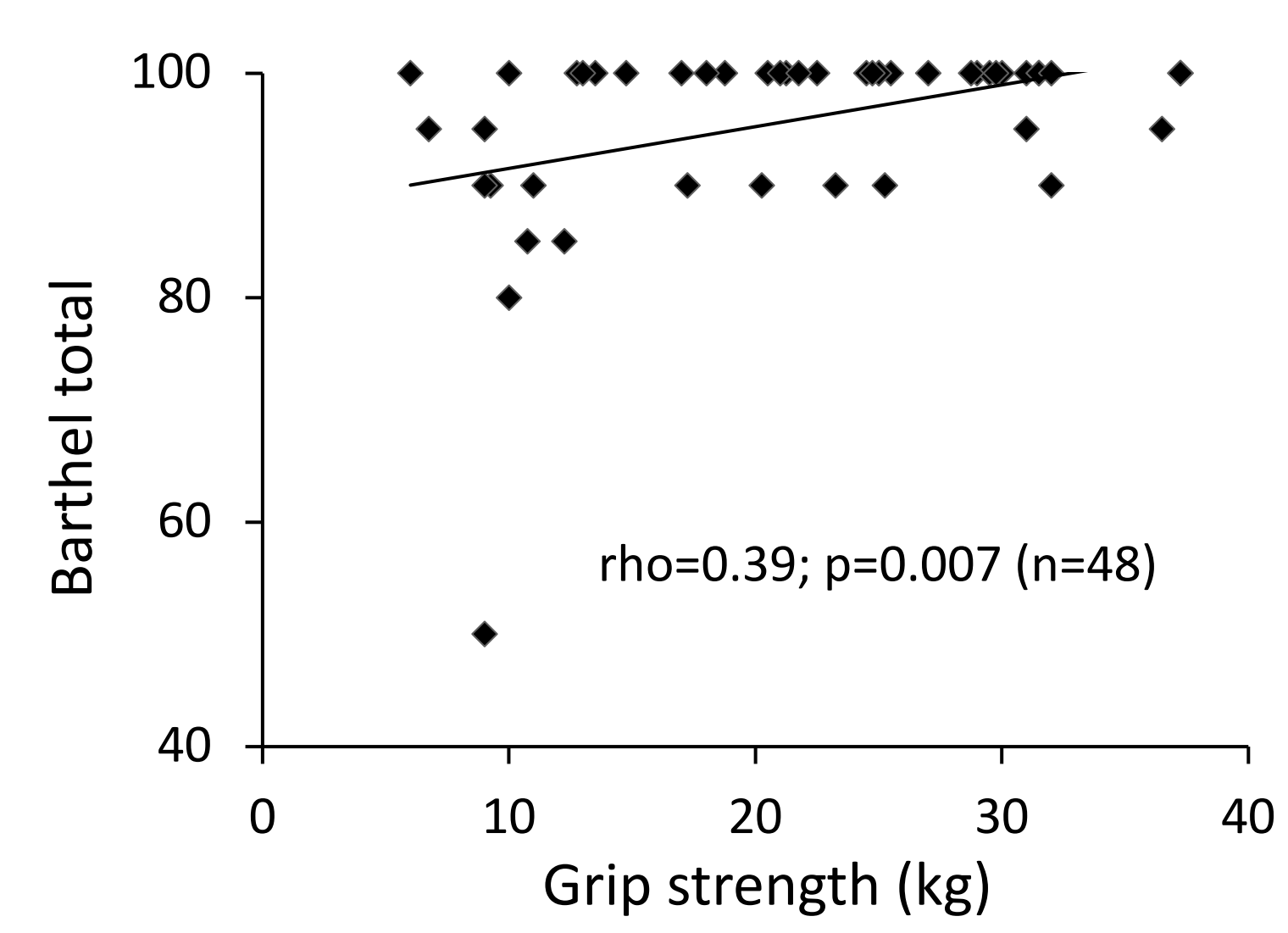
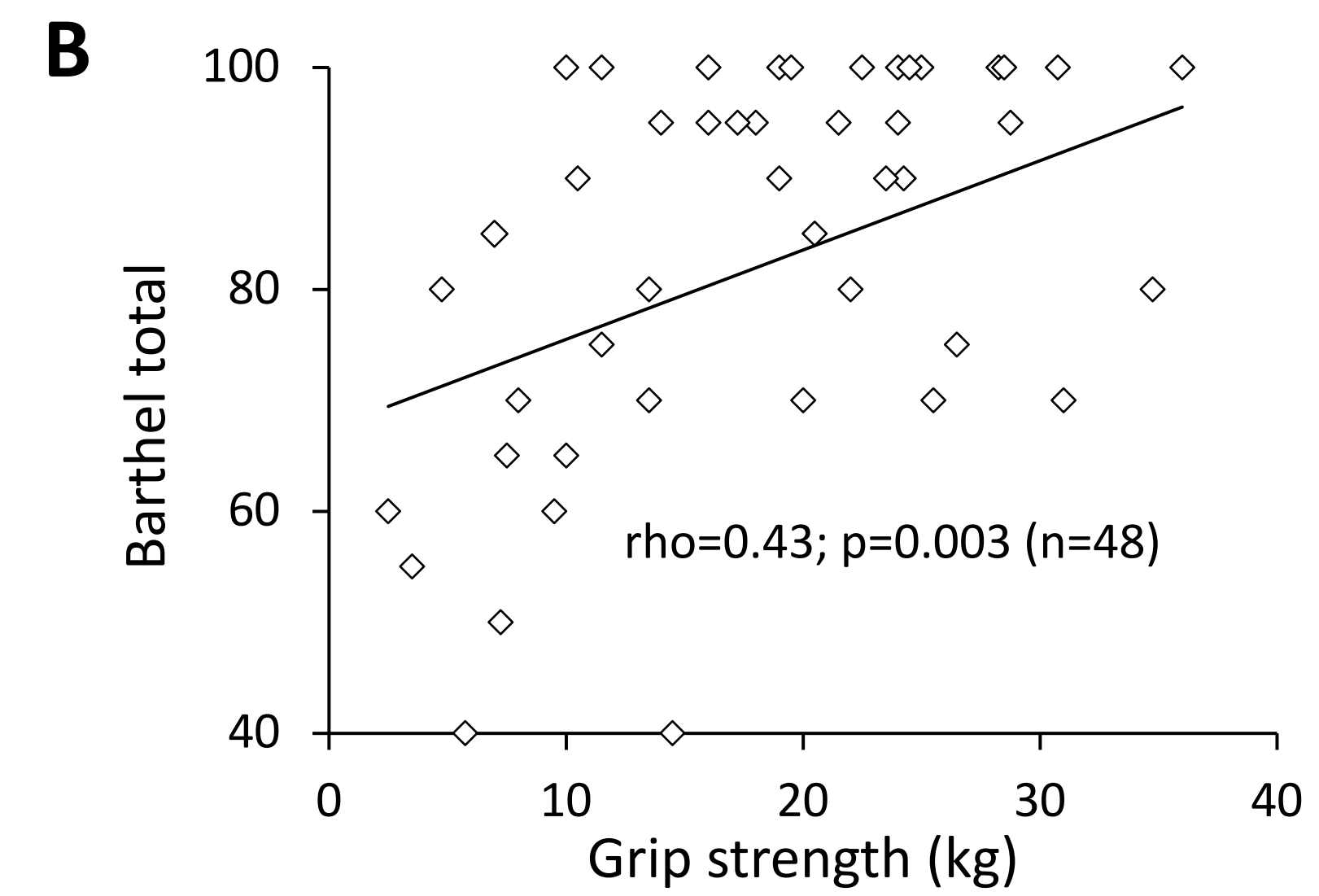
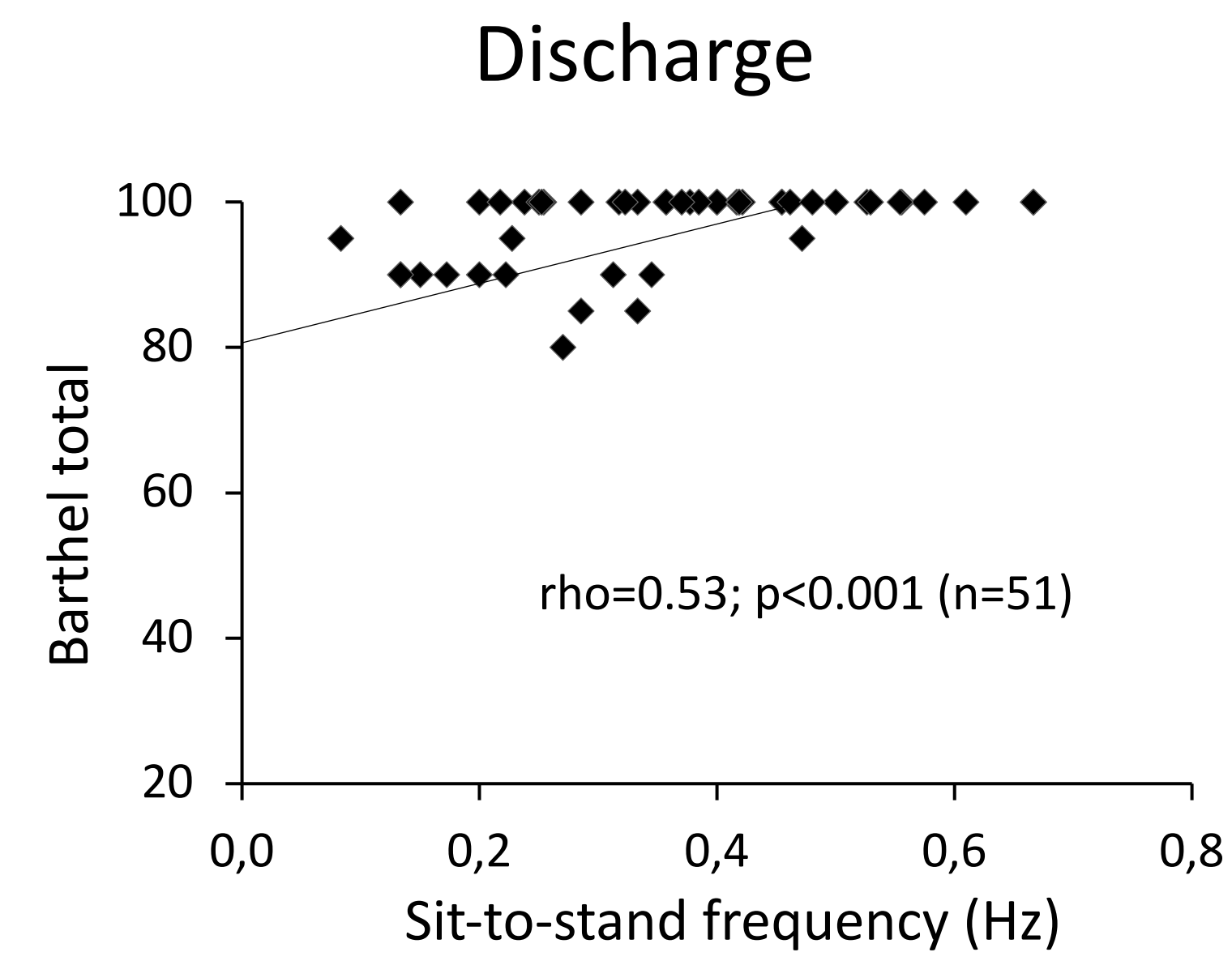
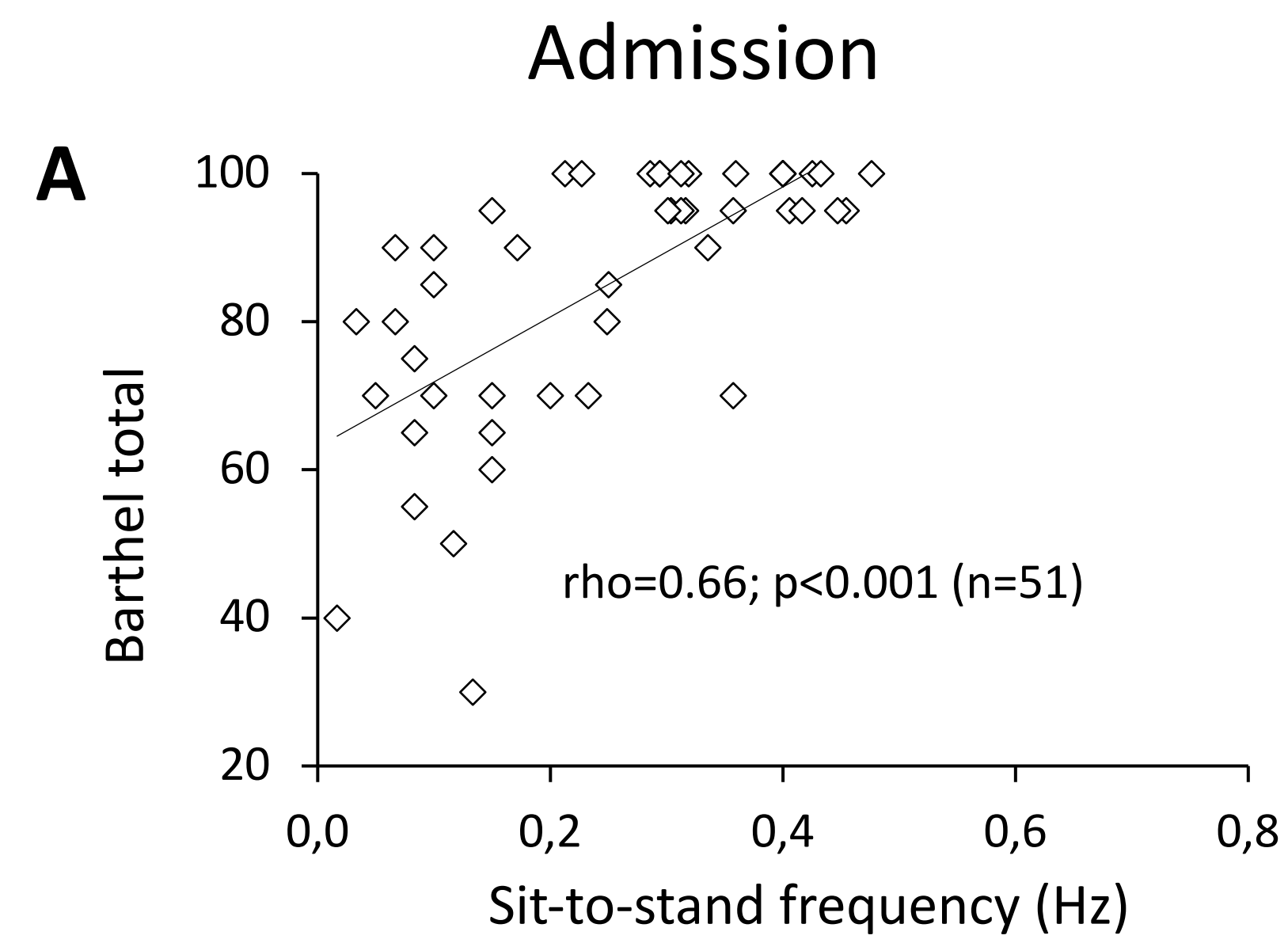


TABLE 1 Population characteristics (n=100)

n≥95 for all collected data. Delays expressed in days.

n [%] unless specified otherwise.

Demographics	
Age [median±IQ]	66±22
Sex (Male)	66 [66%]
Mean delay post-onset at admission	20.4±10.0
Mean delay post-onset at discharge	32.7±10.7
BMI [mean±SD]	26.0±5.4
Clinical characteristics at time of diagnosis	
Dyspnea	79 [79%]
Asthenia	76 [76%]
Fever	73 [73%]
Cough	64 [64%]
Myalgia	33 [33%]
Diarrhea	25 [25%]
Ageusia	16 [16%]
Headache	14 [14%]
Anosmia	13 [13%]
Pulmonary embolism	4 [4%]
Thrombosis	1 [1%]
Background and comorbidities	
High blood pressure	48 [48%]
Age >70	41 [41%]
Diabetes	29 [29%]
BMI >30	17 [17%]
Renal failure	13 [13%]
Coronaropathy	1 [1%]
Stroke	9 [9%]
Immunosuppression	3 [3%]

TABLE 2 Characteristics of hospital stays (n=100)

n≥99 for all collected data. Duration and lengths of stay expressed in days.
n [%] unless specified otherwise.

Acute care	
Prior intensive care	23 [23%]
Intubation	13 [13%]
Duration of intubation [mean±SD]	8.2±8.5
Nasal O2 at admission	77 [77%]
Nasal O2 at discharge	58 [58%]
Overall length of stay in acute care [mean±SD]	14.4±8.7
In intensive care [mean±SD]	13.8±9.0
In acute care after ICU [mean±SD]	10.22±4.87
In acute care if no ICU stay [mean±SD]	11.65±6.48
Rehabilitation care	
Length of stay [mean±SD]	9.8±5.1
Deaths	2 [2%]
At discharge	
Overall duration of O2 dependency [mean±SD]	17.4±11.1
O2 dependency at discharge	3 [3%]
Discharge home	75 [75%]
Discharge to a relative's home	4 [4%]
Transfer to a Covid-free rehabilitation unit	15 [15%]
Transfer to acute care	8 [8%]
Personal assistance before Covid	19 [19%]
Personal assistance after Covid	24 [24%]