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# Patients hospitalized for community-acquired pneumonia present reduced functional performance

Anderson José, Simone D. Corso

**ABSTRACT | Background:** Symptoms of fatigue and dyspnea, treatment with oral corticosteroids, high circulating levels of cytokines, and oxidant/antioxidant imbalance in patients hospitalized with community-acquired pneumonia (CAP) could affect the patients' exercise tolerance and peripheral muscle strength (PMS). **Objective:** To evaluate the functional capacity (FC) of patients hospitalized for CAP and to correlate the FC with length of hospital stay. **Method:** We prospectively evaluated 45 patients ( $49 \pm 16$  years; CAP group) and 20 healthy subjects ( $53 \pm 17$  years; control group). They were randomized to perform, on separate days, a 6-minute walk test (6MWT), a test of PMS, and the Glittre test (GT). Additionally, the SF-36 questionnaire and the MRC scale were completed and evaluated. **Results:** There were significant differences between the groups (CAP and controls) for the 6MWT ( $381.3 \pm 108$  vs.  $587.1 \pm 86.8$  m) and GT ( $272.8 \pm 104.3$  vs.  $174 \pm 39$  sec). The CAP group also presented worse health-related quality of life (HRQoL) scores, reduced strength (quadriceps and biceps), and higher scores of dyspnea. The time required to perform the GT correlated with the length of hospital stay ( $r=0.35$ ,  $P=0.02$ ) and dyspnea ( $r=0.36$ ,  $P=0.02$ ). Significant correlations were observed between GT and 6MWT ( $r=-0.66$ ,  $P=0.0001$ ) and between GT with the physical functioning domain of SF-36 ( $r=-0.51$ ,  $P=0.0001$ ). **Conclusions:** Patients hospitalized for CAP presented with reduced FC, PMS, and HRQoL during hospitalization. In addition, GT performance was related to the length of hospital stay.

**Keywords:** pneumonia; physical therapy; exercise tolerance; quality of life; muscle strength.

## HOW TO CITE THIS ARTICLE

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## ● Introduction

Community-acquired pneumonia (CAP) is one of the most common and serious acute lung diseases. There are 5.6 million cases of CAP are diagnosed annually worldwide, and 1.1 million of these require hospitalization<sup>1-3</sup>. The morbidity and treatment costs of CAP have a substantial social and economic impact<sup>4</sup>.

CAP is an acute inflammatory disease affecting the lungs. The clinical findings are cough, sputum production, chest pain, tachypnea, and fever. Other systemic manifestations, such as generalized myalgia, anorexia, nausea, vomiting, diarrhea, and sensory abnormalities, may also be observed<sup>1,5</sup>. The combination of respiratory and systemic symptoms contributes to malaise and severe prostration. Previous studies have shown that moderate to severe fatigue and dyspnea were the most commonly reported symptoms when CAP was diagnosed. The symptoms remained for seven days and could persist for up to 90 days<sup>6</sup>. High levels of inflammatory markers were found in patients hospitalized with CAP and were related to functional impairment, which was evaluated using a scale of daily activities<sup>7</sup>.

Symptoms of fatigue and dyspnea, treatment with oral corticosteroids, high circulating levels of cytokines, and oxidant/antioxidant imbalance<sup>8</sup> in patients hospitalized with CAP could affect the patients' exercise tolerance and muscle function. Therefore, we designed this study to investigate the functional capacity, peripheral muscle strength (PMS) and health-related quality of life (HRQoL) in patients hospitalized for CAP. In addition, we analyzed the correlation between the functional capacity tests and length of hospital stay.

## ● Method

### Study population

We evaluated 72 patients (44 men) who were hospitalized in a university-affiliated hospital. Inclusion criteria were: CAP as a cause of hospitalization, length of stay of less than 48 hours, over 18 years of age, hemodynamically stable, and an

ability to walk and handle objects unassisted. CAP was diagnosed according to the Brazilian guidelines<sup>5</sup> (newly acquired respiratory symptoms, cough, sputum production, dyspnea, fever, tachypnea, auscultatory findings of abnormal breath sounds and crackles and presence of new lung infiltrate in a chest radiograph). Patients with other pulmonary diseases (chronic obstructive pulmonary disease-COPD, asthma, bronchiectasis or cystic fibrosis) and orthopedic or neurological conditions were excluded. The control group consisted of 20 age- and sex-matched healthy subjects recruited from the community.

All subjects signed the consent form, and the study was approved by the Ethics Committee on Research of Universidade Nove de Julho, São Paulo, SP, Brazil, protocol number 273811/2009.

Study design

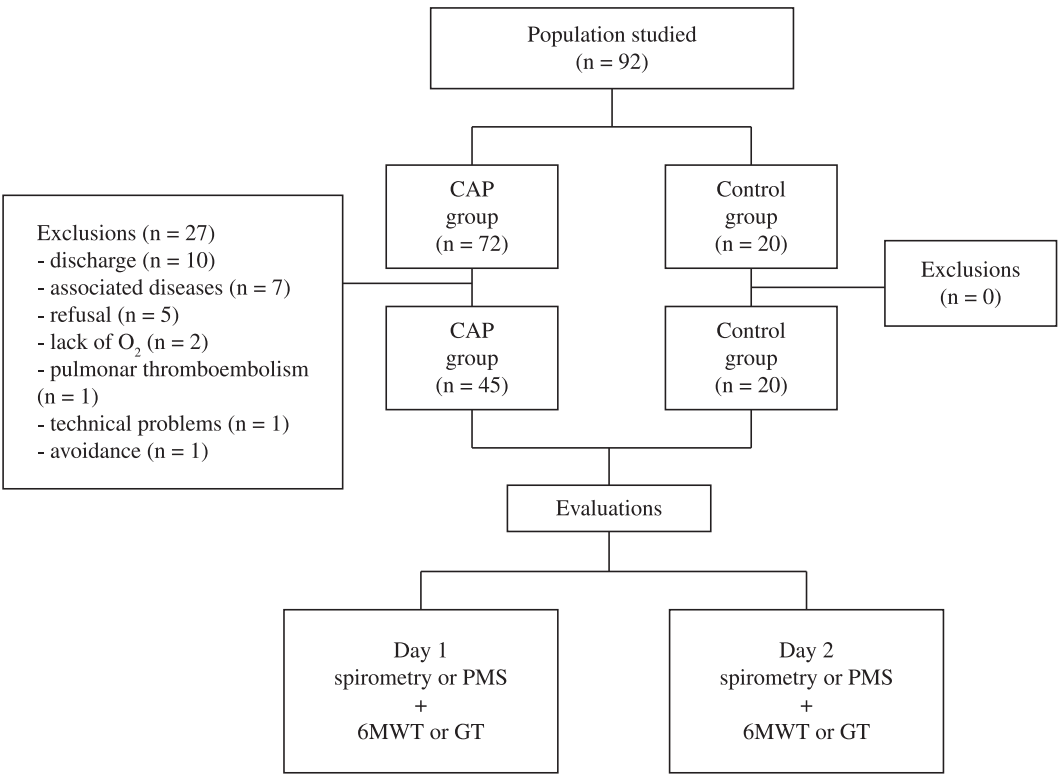
This was a cross-sectional controlled study conducted on two consecutive days. On the first day, patients answered the Medical Research Council scale (MRC)<sup>9</sup> and Short-Form 36 questionnaire (SF-36)<sup>10</sup>, and their CRB-65 scores<sup>11</sup>

were recorded. Subsequently, patients performed either a spirometry<sup>12,13</sup> or peripheral muscle strength (PMS) test, as well as either the 6-minute walk test (6MWT)<sup>14,15</sup> or the Glittre test (GT)<sup>16</sup>. On the second day, patients underwent the tests not performed on the previous day (spirometry or PMS and 6MWT or GT). The order of the tests was randomized (Figure 1).

Assessments

Peripheral muscle strength

We obtained the dominant-limb strength of the quadriceps femoris (QF) and biceps brachii (BB) using the maximum voluntary isometric contraction (MVIC) assessed with a dynamometer (model DLC/DN, Kratos, São Paulo, Brazil). Patients did three repetitions of MVICs maintained for 5 seconds, with a minute rest between them. If the difference in strength of the three contractions exceeded 5%, we conducted another measure of MVIC<sup>17</sup>. The highest value was recorded for analysis. For the QF, patients sat on a chair with the hip and knee at 90° flexion and were requested to extend the knee; for BB, the elbow joint was positioned at 90° flexion, and then elbow



**Figure 1.** Study flow diagram. CAP: community-acquired pneumonia; PMS: peripheral muscle strength; 6MWT: six minute walk test; GT: Glittre test.

flexure was requested. The PMS measurement was performed in a subgroup of patients (n=28).

### Glittre test

The GT was undertaken as previously described<sup>16</sup>. The test was conducted in a 10-meter-long hallway in the hospital. Two tests were performed an hour apart on the same day to minimize the learning effect previously demonstrated in patients with COPD<sup>16</sup>. The test with shorter duration was used for the analysis. Heart rate (HR), oxygen saturation (SpO<sub>2</sub>), dyspnea, and leg fatigue were measured at rest and at the end of the test. The time spent performing the test was recorded and was the main outcome for this test.

### Analysis

We performed statistical analysis using SPSS for Windows version 17.0 (SPSS, Chicago, Illinois). We used the Kolmogorov-Smirnov test to verify the adherence of the data distribution to a normal curve. The parametric data (age, BMI, 6MWT, GT, PMS, pulmonary function and domains of physical functioning, bodily pain, general health perception, vitality, social functioning and mental health of the SF-36 questionnaire) were expressed as means and standard deviations (SD). Nonparametric data (length of hospital stay, MRC scale and the domains of physical role functioning and emotional role functioning of the SF-36 questionnaire) were expressed as medians and interquartile ranges. We performed parametric variable comparisons between the CAP and control groups using Student's t-test for independent samples. We compared the nonparametric variables with the Mann-Whitney test. Correlations between variables were performed using Pearson's correlation test. The probability of a type I error was set at 5% (P<0.05).

## Results

### Sample characteristics

From a sample of 72 patients with CAP, 27 were excluded, including 10 patients who were discharged before completing the survey, 7 who had other associated lung diseases (asthma and tuberculosis), 5 who decided to withdraw from the study, 3 who experienced technical problems during some evaluations, one who progressed to pulmonary thromboembolism and one who left the hospital before completing the study. No volunteers were excluded from the control group. Therefore, 65 subjects were surveyed in total, including 45 patients in the CAP group (28 men) and 20 subjects in the control group (10 men). There were no significant differences between the groups regarding age and BMI. Patients in the CAP group showed a restrictive pattern in lung function (Table 1).

All hospitalized patients took antibiotics. In addition, 39 patients received gastric protectors, 20 used inhaled bronchodilators, 17 received corticosteroids, 16 received antihypertensive medications, 11 received antiplatelet medications, 8 received insulin, 6 received diuretics, and 9 received other medications. Four patients were given oxygen during the tests. The CRB-65 scores were 0 and 1 for 34 and 11 patients, respectively. Within the CAP group, 43 patients were discharged and two died.

### Functional capacity and peripheral muscle strength

Patients with CAP walked less in the walking test and took longer to perform the GT (Table 2). Additionally, they had lower maximum heart rates. We observed a significant difference in SpO<sub>2</sub> between the CAP and control groups. Compared to the control

**Table 1.** Characteristics of the CAP and control groups.

Variables	CAP group (n=45)	Control group (n=20)	P
Age, years	49±16	53±17	0.42
BMI, Kg/m <sup>2</sup>	25.4±4.1	27.4±4.5	0.10
FVC, L	2.0±0.7	3.3±0.9	<0.001
FVC, % predicted	54.6±17.2	89.8±11.2	<0.001
FEV <sub>1</sub> , L	1.7±0.7	2.8±0.7	<0.001
FEV <sub>1</sub> , % predicted	57.8±17.8	92.9±11	<0.001
FEV <sub>1</sub> /FVC, %	86.0±9.8	83±4.5	0.09
Length of hospital stay, days	13 (8.5-18)	-----	-----

CAP: community-acquired pneumonia; BMI: body mass index; FEV<sub>1</sub>: forced expiratory volume in one second; FVC: forced vital capacity.

group, CAP patients showed reduced PMS for biceps (15.9±5.6 vs. 12.4±4.9 Kgf, P=0.031) and quadriceps (29±6.4 vs. 19±7.2 Kgf, P<0.001).

Dyspnea and health-related quality of life

Patients in the CAP group had high scores for dyspnea and reduced HRQoL compared to the control group (Table 3).

Correlations between FC, PMS and HRQoL

The time spent performing the GT was the only outcome that presented correlations with the length of hospital stay and MRC scale, as both variables did not show correlations with 6MWT (Figure 2). Longer times taken to perform the GT were correlated with lower distances walked in the 6MWT (r=−0.66; P=0.0001). Additionally, the GT correlated with the

physical functioning domain of the SF-36 (r=−0.51, P<0.001) and with lung function (FEV<sub>1</sub>: r=−0.56, P=0.002; FVC: r=−0.53, P=0.0001).

The 6MWT showed significant correlation with lung function (FEV<sub>1</sub>: r=0.56 and FVC: r=0.54; both P=0.0001). 6MWT also correlated positively with PMS (quadriceps: r=0.40, P=0.03) and HRQoL (bodily pain: r=0.43, P=0.004; physical functioning: r=0.35, P=0.02).

• Discussion

CAP is a serious disease of high prevalence and is a major cause of hospitalization around the world. It generates high costs and is the leading cause of death from infectious diseases<sup>1-5</sup>. CAP’s mortality rate has been the main focus of previous studies. However, its impact on functional status is rarely studied. The

Table 2. Results of 6MWT and GT.

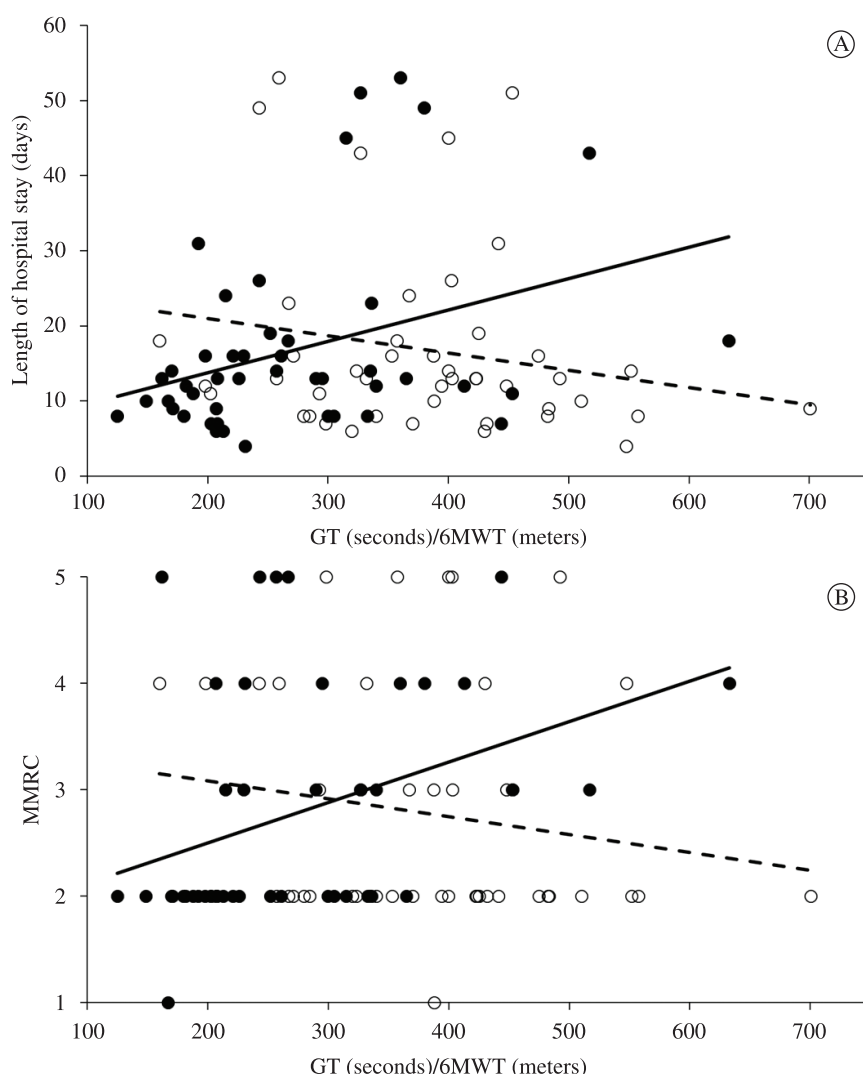
Variables	CAP group (n=45)	Control group (n=20)	P
6MWT			
distance, m	381.3±108	587.1±86.8	<0.001
distance, % predicted	66.2±17.0	107.7±13.9	<0.001
Peak HR, bpm	112±20	128±25	0.015
HR, % max	65.2±9.7	76.4±12.8	0.002
SpO2 at peak exercise, %	92.4±5.0	96.5±2.3	<0.001
GT			
time, s	272.8±104.3	174±39	<0.001
Peak HR, bpm	122.4±19.4	134.4±24	0.058
HR, % max	71.6±10.2	80.1±11.1	0.006
SpO2 at peak exercise, %	93.8±3.9	95.7±2.0	0.012

CAP: community-acquired pneumonia; 6MWT: 6-minute walk test; HR: heart rate; GT: Glittre test.

Table 3. Comparison between the CAP and control groups for dyspnea and HRQoL.

Variables	CAP Group (n=45)	Control Group (n=20)	P
MRC	2 (2-4)	1 (1-1)	<0.001
SF-36			
Physical functioning	57.1±24.6	85.5±18.4	<0.001
Physical role functioning	0 (0-50)	100 (81.25-100)	<0.001
Bodily pain	39.6±20.4	73.4±25.2	<0.001
General health perception	57.1±20.3	79±21	<0.001
Vitality	53.0±17.9	77±15.4	<0.001
Social functioning	56.7±27.1	85.4±17.1	<0.001
Emotional role functioning	0 (0-100)	100 (100-100)	<0.001
Mental health	70.7±17.8	82.4±15.6	0.01

CAP: community-acquired pneumonia; HRQoL: health-related quality of life; MRC: Medical Research Council dyspnea scale.



**Figure 2.** Correlations between the length of hospital stay and GT/6MWT (A) and between MRC scale and GT/6MWT (B). A) Glitter test: black circles, solid line ( $r=0.35$ ,  $P=0.02$ ), 6MWT: white circles, dashed line ( $r=-0.2$ ,  $P=0.19$ ). B) Glitter test: black circles, solid line ( $r=0.36$ ,  $P=0.02$ ), 6MWT: white circles, dashed line ( $r=-0.16$ ,  $P=0.28$ ).

present study shows a reduction in FC, PMS, and HRQoL in patients hospitalized for CAP.

To the best of our knowledge, this is the first study that objectively evaluates functional capacity by performance-based tests such as the GT and 6MWT and peripheral muscle function by the maximum voluntary contraction in patients hospitalized for CAP.

6MWT is the most frequently used test of FC in patients with respiratory diseases because it has established reference values<sup>14-15,18</sup> and has been considered the best marker of inactivity in daily living for patients with COPD<sup>19</sup>. However, the GT has been suggested as being more appropriate to assess functional status in patients with COPD because

while the 6MWT evaluates only a single isolated activity, the GT involves unsupported arm activities, rising from a chair, walking, and climbing stairs<sup>20</sup>.

It has been demonstrated that GT performance time in patients with COPD is longer in comparison with a control group<sup>21</sup>. The time spent by patients with COPD to perform the GT was 60% greater than that in a control group<sup>21</sup>, which is similar to the percentage (64%) difference found in our study when comparing the CAP and control groups. It is interesting to note that our patients with CAP had similar times for performing the GT compared with patients with COPD in this other study<sup>16</sup> (272.8 sec and 280.2 sec, respectively). Therefore, CAP patients demonstrate difficulties in performing simple and routine activities



similar to activities of daily living (ADL). The poor performance of our younger patients ( $49 \pm 16$  yrs) with better lung function ( $FEV_1$ :  $57.8 \pm 17.8\%$  of predicted) could be attributed to the acute clinical condition of patients hospitalized with CAP as compared to stable COPD patients ( $61 \pm 8$  yrs,  $FEV_1$ :  $48 \pm 15\%$  of predicted)<sup>16</sup>.

The GT is composed of a circuit of functional activities that the patient needs to accomplish as fast as possible. These activities were developed to represent essential activities that are common in everyday life and known to be problematic for patients with pulmonary disease, particularly patients with COPD. In our study, the GT was the only test that correlated with the length of hospital stay and dyspnea evaluated by the MRC scale. In Skumlien's study, significant relationships were observed between the GT and disease stage ( $r = -0.61$ ;  $p < 0.01$ ), hospitalization rate in the past year ( $r = 0.35$ ;  $p < 0.01$ ), exercise capacity ( $r = -0.82$ ;  $p < 0.01$ ), reported activity restrictions ( $r = 0.43$ ;  $p < 0.01$ ), dyspnea during daily activities ( $r = 0.35$ ;  $p < 0.01$ ) and BMI ( $r = -0.57$ ;  $p < 0.01$ )<sup>16</sup>. Additionally, patients with longer GT times had a five times the risk of three or more serious exacerbations compared to those with shorter GT times. Thus, the authors suggested that the GT yields information complementary to the 6MWT<sup>16</sup>. This seems reasonable because the 6MWT uses only the act of walking, which is not representative of the metabolic expenditure and dyspnea induced by the different ADL provided by the GT<sup>21</sup>. Based on these considerations, it is possible that the GT is more suitable for the FC evaluation in patients hospitalized for CAP. Although our findings demonstrate that the GT was the only test of FC that correlated with length of stay, future studies are recommended to confirm whether this test is more sensitive in detecting the reduction of FC with this condition.

Patients hospitalized for CAP presented lower performance on the 6MWT (66% of predicted), indicating a reduction in FC, as previously demonstrated in patients with stable COPD<sup>22-24</sup>. In a study by Solh et al.<sup>7</sup>, elderly patients hospitalized for CAP showed a decline in functional capacity as assessed by an ADL scale. This decline was related to the level of tumor necrosis factor (TNF- $\alpha$ ) and the severity of the CAP. Persistent FC decline was observed after three months and was associated with hospital readmission and death, which leads us to infer that exercise training should be applied early to minimize the loss of FC and PMS during hospitalization. In our sample, the CRB-65 scores were low, such that the patients could perform all the proposed assessments. Consequently, the majority

of patients evolved favorably, culminating with discharge from the hospital.

Our study is the first to evaluate PMS in patients hospitalized for CAP. We were interested in studying this outcome because patients with CAP have high levels of inflammatory cytokines<sup>7,25-27</sup> and unbalanced oxidant/antioxidant ratios in favor of the oxidants<sup>8</sup>, which are not related to the disease severity scores<sup>28</sup>. It is possible that inflammatory and oxidative stress are involved in the development of peripheral muscle weakness during hospitalization in patients with CAP, as previously demonstrated in patients with COPD<sup>29-31</sup>.

Reduced FC and PMS led to difficulty in performing ADL, compromising all domains measured by the SF-36 questionnaire. Our results are in agreement with those of Metlay et al.<sup>6</sup>, who evaluated the SF-36 in patients with CAP and found similar scores for all SF-36 domains except the vitality and emotional role functioning.

### Implications of the study

Our results highlight the need to assess FC and PMS not only in patients with COPD hospitalized due to acute exacerbation but also in patients with acute pulmonary disease, in order to diagnose their FC and muscle impairment. Strategies to minimize the functional and peripheral muscle impairment through resistance training should be tested in patients with CAP, as resistance training has been effective in preventing the deleterious impact of exacerbations on peripheral muscle function in patients with COPD<sup>32</sup>.

### Limitations of the study

This study has some relevant limitations. Patients did not undergo an evaluation before discharge or in the period after hospital discharge. However, comparisons with the control group allowed us to confirm impairments of FC, PMS, and HRQoL in patients hospitalized with CAP. It is possible that the reductions in FC could have been overestimated, as the control group was composed of healthy individuals instead of hospitalized controls. However, it is difficult to establish a hospitalized healthy control group because any reason for hospitalization could indicate a prior reduction of the outcomes evaluated in our study. We did not objectively measure patients' physical activity during hospitalization with any activity monitors, nor did we measure their inflammatory status, both of which could explain the reduced PMS in our patients.

## ● Conclusion

Patients hospitalized for CAP have reduced functional capacity, peripheral muscle strength, and health-related quality of life during hospitalization. The GT was the only functional capacity test that demonstrated a correlation with the length of hospital stay. New therapeutic approaches applied to hospitalized patients should be studied to maintain and/or restore functional capacity and peripheral muscle strength in these patients.

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