

Physical and Functional Impairment During and After Hospitalization in Subjects With Severe COPD Exacerbation

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BACKGROUND: COPD exacerbations are frequent events that have a negative impact on the lives of patients. The aims of this study were to analyze physical and functional impairment during hospital stay in subjects hospitalized due to COPD exacerbation and to assess the physical and functional impact of hospitalization at a 1-month follow-up in patients with severe COPD. **METHODS:** This was a prospective observational study on a sample of 52 subjects hospitalized due to COPD exacerbation. The assessments were performed at baseline, discharge, and 1-month follow-up. The outcome measures were dyspnea, muscle strength, functional capacity, and postural steadiness. **RESULTS:** Quadriceps strength [1.036 ($P = .043$) kg mean difference] and the one-leg stance test [1.04 ($P = .02$) and 0.73 ($P = .032$) s mean difference right and left leg] showed significant impairment during hospitalization. Dyspnea perception improved significantly ($P = .004$) during hospitalization. Additionally, strength in the upper and lower limbs [4.04 ($P = .002$) and 1.23 ($P = .038$) kg mean difference], functional capacity [3.0 number of steps mean difference ($P = .032$)], and the one-leg stance test [2.12 ($P = .006$) and 0.53 ($P = .047$) s mean difference right and left leg] showed significant impairment 1-month follow-up. **CONCLUSIONS:** Hospitalization due to COPD exacerbation leads to physical and functional impairment in patients; impairment is greater at 1-month follow-up. It would be interesting to conduct physical therapy interventions to prevent the impairment. *Key words:* COPD; exacerbation; hospitalized subjects; physical impairment; functional impairment; functional capacity. [Respir Care 2017;62(2):209–214. © 2017 Daedalus Enterprises]

Introduction

COPD is projected to be the fifth leading burden of disease worldwide by the year 2020.¹ A COPD exacerbation

is defined as an acute event characterized by a worsening of the patient's respiratory symptoms.² COPD exacerbations are frequent (mean: 1–4 exacerbations/y)³ and increase in frequency with the severity of the disease. Spencer et al⁴ suggest that frequent exacerbations are related to a worsening of health status.

Several studies^{5,6} support the argument that COPD exacerbations have a negative impact on patients. In addition to the classic symptoms of an exacerbation,⁷ patients may exhibit an impairment in skeletal muscle strength and endurance in both peripheral and respiratory muscles⁸ that can have considerable effects on health status.⁹ It has long been recognized that systemic factors such as inflamma-

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tion, malnutrition, medication, inactivity, age, hypoxemia, and smoking exert strong effects on skeletal muscle performance in patients with COPD.¹⁰

Physical, psychological, and functional impairment during hospital stay in patients with COPD exacerbation is a relevant issue due to the consequences after discharge, such as relocation into nursing homes or caregiver syndrome. Moreover, the increase in the prevalence of COPD and the associated economic burden¹¹ should be taken into account.¹²

Few studies^{13,14} have examined the impact of hospitalization on patients with COPD and patients' lives after discharge. It has been previously shown that hospitalizations result in a decline of functionality in the elderly population.¹⁵ This decline can have a greater impact on patients with more severe COPD. Comprehensive pulmonary rehabilitation^{12,16} for COPD should be included in the care of patients with chronic respiratory impairment to optimize their physical and social performance and autonomy.

The main objectives of the study were (1) to analyze physical and functional impairment during hospital stay in subjects hospitalized due to COPD exacerbation and (2) to assess the physical impact of hospitalization at 1-month follow-up in subjects with severe COPD.

Methods

Study Design

This was a prospective observational study that included assessments at 3 points in time: at baseline, at discharge, and at 1-month follow-up. The study was performed from May to September 2013 in the San Cecilio and Virgen de las Nieves hospitals in Granada, Spain. The study was approved by the hospital ethics committees (approval number 1107). All participants were informed of the objectives of the study and gave their written informed consent before their involvement in the study.

Subjects

Fifty-two subjects were included in this study among those admitted to the hospitals' respiratory care unit with a diagnosis of COPD exacerbation during a 4-month period. Inclusion criteria were: diagnosis of COPD exacerbation according to the criteria of the American Thoracic Society,¹⁷ exacerbations due to respiratory infections only, Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage IV of disease severity,¹⁸ patients >40 y old, and patients free from a hospitalization due to COPD exacerbation in the previous month. Exclusion criteria were: patients with organ failure, cognitive impairment, cancer, or inability to participate. Patients were excluded if their

QUICK LOOK

Current knowledge

COPD exacerbations are frequent events and have a negative impact on the lives of COPD patients. Previous studies confirm that frequent exacerbations are related to a worsening of health status.

What this paper contributes to our knowledge

In the present study, physical status in subjects with severe COPD exhibited a significant impairment during hospital stay. Additionally, physical impairment was greater at 1-month follow-up.

cognitive impairment or their condition prevented them from performing the assessment.¹⁹

During the hospitalization, subjects were administered the standard medical and pharmacologic treatment, including inhaled bronchodilators, systemic steroids, and oxygen therapy. No additional interventions were performed during the hospitalization.

Assessment

For descriptive purposes, age, body mass index, and smoking habit were recorded. The Charlson comorbidity index was used to assess comorbidities.²⁰ The Barthel index²¹ was used to measure subjects' level of dependence. The St George Respiratory Questionnaire was administered to assess subjects' perceived quality of life in the last year.²² The SenseWear arm band (BodyMedia, Pittsburgh, Pennsylvania) was used to count the number of steps walked in 24 h during the hospital stay. Subjects wore the device during 3 different days. The SenseWear arm band was placed on the back of each patient's upper left arm (ie, the triceps).^{23,24} A spirometry test was carried out with a portable spirometer (Micro Spirometer, CareFusion, Basingstoke, United Kingdom) according to the criteria of the American Thoracic Society.²⁵ Oxygen saturation was assessed with a pulse oximeter (Pulsox-1, Konica-Minolta, Tokyo, Japan).

Outcome Measures

Dyspnea, muscle strength, functional capacity, and postural steadiness were assessed at baseline (the second day of hospitalization), at discharge (the last day of hospitalization), and at 1-month follow-up (subjects were called on the telephone and given an appointment for the assessment).

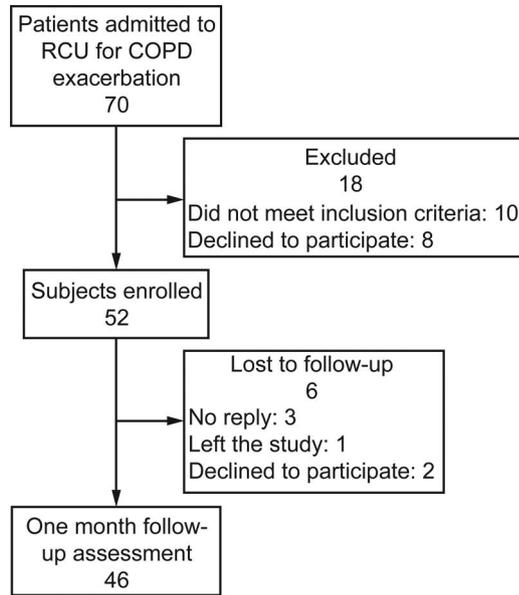


Fig. 1. Flow chart. RCU = respiratory care unit.

Dyspnea Perception

Dyspnea perception was assessed at rest using the modified Borg scale.²⁶ Subjects classified their breathlessness from 0 to 10.

Muscle Strength

Lower- and upper-limb strength was assessed using a dynamometer. Quadriceps strength was assessed with a portable dynamometer (hand-held dynamometer manual muscle test system model 01163, Lafayette Instrument Company, Lafayette, Indiana). The test was performed as reported previously.²⁷ Quadriceps weakness is a surrogate marker for subjects' reduced generalized performance status. A reduction in muscle strength implies a worsening in work capacity in patients with COPD.

Handgrip measurement is a reliable marker of peripheral muscle strength. A handgrip dynamometer (TEC-60, Technical Products, Clifton, New Jersey) individually adjusted to the size of the subject's handgrip was used as reported previously by Shephard et al.²⁸

Functional Capacity

The 2-min step-in-place test is a useful alternative to the 6-min walk test when there are space limitations.²⁹ Subjects were asked to raise their knees alternatively, and the number of full steps completed in 2 min was recorded.

Table 1. Characteristics of the Sample at Baseline

Variables	Values (N = 52)
Age, mean ± SD y (range)	75.87 ± 6.14 (65–88)
BMI, mean ± SD kg/m ² (range)	26.46 ± 6.49 (15–38)
Length of hospital stay, mean ± SD d (range)	12.17 ± 5.17 (6–23)
Charlson Comorbidity Index, mean ± SD (range)	5.3 ± 1.6 (3–11)
Barthel index, mean ± SD (range)	77.39 ± 27.03 (30–100)
SGRQ symptoms, mean ± SD (range)	61.54 ± 19.39 (19.7–96)
SGRQ activity, mean ± SD (range)	78.99 ± 25.63 (6.29–100)
SGRQ impact, mean ± SD (range)	58.46 ± 14.35 (29–79)
SGRQ total score, mean ± SD (range)	65.21 ± 15.50 (33–84)
Steps during hospital stay, mean ± SD steps (range)	705.84 ± 104.5 (11–1,075)
FVC, mean ± SD L (range)	1.13 ± 0.74 (0.69–1.28)
FVC, mean ± SD % predicted (range)	27.35 ± 5.48 (23.69–31.4)
FEV ₁ , mean ± SD L (range)	0.52 ± 0.38 (0.31–0.84)
FEV ₁ , mean ± SD % predicted (range)	34.16 ± 8.5 (29.47–38.4)
S _{pO₂} , mean ± SD % predicted (range)	87.09 ± 3.25 (82–93)
Borg scale, mean ± SD (range)	6.46 ± 2.24 (3–10)
Female sex, n (%)	3 (4.54)
Ex-smokers, n (%)	60 (90.9)

BMI = body mass index
SGRQ = St George Respiratory Questionnaire

Postural Steadiness

The one-leg stance test assesses postural steadiness in a static position.³⁰ Subjects were asked to raise one leg and keep the leg raised as long as possible. The time that the subjects stood on each leg was measured in seconds using a stopwatch.

Statistical Analyses

EPIDAT 3.1 software (Dirección Xeral de Saúde Pública (Xunta de Galicia)) was used to calculate sample size. The sample size calculation was based on the estimation of quadriceps muscle strength impairment values^{14,31} and the impairment expected in handgrip dynamometry (1 kg) (1.2 ± 0.33 and -1.5 ± 0.82). Hence, to have 80% power using a 2-sided α = 0.05 and a hypothetical dropout rate of 15%, 52 subjects were required to show statistically significant differences during hospitalization.

Descriptive statistics (mean ± SD) were used to determine participants' characteristics. The Kolmogorov-Smirnov test was used to assess the normality of the continuous data. The statistical distribution of the data was initially analyzed using the Shapiro-Wilks test. An analysis of variance measure repeated was used to compare the outcomes during hospitalization, at discharge, and at follow-up. Data

Table 2. Clinical Variables at Baseline, Discharge, and 1-Month Follow-Up

Variables	Baseline	Discharge	1-Month Follow-up	Mean Difference Between Baseline and Discharge (95% CI)	<i>P</i>	Mean Difference Between Discharge and Follow-up (95% CI)	<i>P</i>
FVC, % predicted	27.35 ± 5.48	30.81 ± 7.9	28.90 ± 4.36	3.46 ± 6.32 (4.054–5.278)	.041	2.10 ± 5.84 (–3.21 to 2.34)	.17
FEV ₁ , % predicted	34.16 ± 8.5	39.07 ± 11.2	36.49 ± 9.12	5.11 ± 9.62 (3.018–6.573)	.02	3.42 ± 10.07 (–4.17 to 1.58)	.043
Borg scale	6.48 ± 2.28	3.61 ± 2.18	4.45 ± 3.55	2.870 ± 1.984 (2.280–3.459)	.004	0.38 ± 2.81 (–5.17 to –0.658)	.41
2MSP, steps	13.82 ± 18.17	14.23 ± 20.4	12.4 ± 15.49	0.42 ± 19.54 (–4.040 to 1.858)	.36	3.0 ± 2.13 (–0.531 to –4.02)	.032

Results are mean ± SD. An analysis of variance measure repeated was used to compare the outcomes at hospitalization, discharge, and follow-up. 2MSP = 2-min step-in-place test

Table 3. Physical Variables at Baseline, Discharge, and 1-Month Follow-Up

Variables	Baseline	Discharge	1-Month Follow-Up	Mean Difference Between Baseline and Discharge (95% CI)	<i>P</i>	Mean Difference Between Discharge and 1-Month Follow-Up (95% CI)	<i>P</i>
Handgrip strength, kg	17.96 ± 10.75	17.16 ± 10.7	13.12 ± 11.52	0.403 ± 9.44 (–0.53–6.75)	.92	4.04 ± 3.82 (–0.78 to –6.12)	.002
Quadriceps strength, kg	9.45 ± 3.29	7.4 ± 3.11	6.17 ± 3.54	1.036 ± 2.58 (–3.301 to –1.571)	.043	1.23 ± 3.35 (–4.30 to –1.82)	.038
OLS right leg, s	3.94 ± 5.59	2.92 ± 4.78	1.87 ± 2.53	1.04 ± 3.52 (–4.53 to –0.094)	.02	2.12 ± 3.65 (–2.59 to –0.67)	.006
OLS left leg, s	2.73 ± 3.14	2.03 ± 3.65	1.50 ± 2.09	0.73 ± 2.87 (–2.626 to –0.041)	.032	0.53 ± 2.88 (0.047–1.37)	.047

Results are mean ± SD. An analysis of variance was used to compare the outcomes at hospitalization, discharge, and follow-up. OLS = one-leg stance test

were analyzed with SPSS 20.0 (SPSS, Chicago, Illinois). A *P* value of <.05 was considered to be significant.

Results

The final sample was composed of 52 subjects. The distribution of participants is shown in Figure 1. Descriptive data of the sample at baseline are shown in Table 1.

The mean age of participants was 75.87 ± 6.14 y (range 65–88 y), and 4.54% (*n* = 3) of the subjects were women. The mean length of hospital stay was 12.17 ± 5.17 d. Most of the subjects were independent but needed help in the bathroom and getting dressed or undressed. In the sample, 90.9% of the subjects were ex-smokers with a mean of 18.27 ± 14.71 y without smoking.

The values presented in Table 1 show that dyspnea perception at baseline was 6.46 ± 2.24 in the modified Borg scale. All of the subjects had severe COPD (GOLD IV), with spirometric values of FEV₁ of 0.52 ± 0.38 L and FVC of 1.13 ± 0.74 L.

Dyspnea perception (*P* = .004), FVC (*P* = .041), and FEV₁ (*P* = .02) improved significantly from baseline to discharge (Table 2). Significant differences were observed between discharge (*P* = .032) and follow-up (*P* = .043) in FEV₁ and functional capacity.

Quadriceps strength (*P* = .043) and the one-leg stance (*P* = .02 for right leg and *P* = .032 for left leg) test showed significant differences from baseline to discharge (Table 3). Additionally, strength in the upper (*P* = .002)

and lower (*P* = .038) limbs and the one-leg stance test showed significant differences between discharge and follow-up (*P* = .006 for right leg and *P* = .047 for left leg).

Discussion

The objectives of the study were (1) to analyze physical and functional impairment during hospital stay in hospitalized subjects due to COPD exacerbation and (2) to assess the physical and functional impact of hospitalization at 1-month follow-up in subjects with severe COPD.

Our results showed that muscle strength and postural steadiness significantly deteriorated during hospital stay and at 1-month follow-up. We also observed impairment in physical function at 1-month follow-up.

Previous studies³²⁻³⁴ have described the impairment caused by COPD: Elderly subjects with COPD exhibit a substantial impairment, depending on the severity of airway obstruction. However, few studies¹⁴ have focused on the impact of COPD exacerbations on the physical and functional state of patients.

Overall, our results showed that subjects exhibited a marked physical impairment in global muscle strength due to inactivity and the exacerbation situation, which implies immobility during hospitalization. It has been shown previously that the mean number of steps per day is 2,237 in subjects with COPD. Subjects included in our study walked a mean of 705.84 ± 104.5 steps during 24 h of hospital stay.

Pitta et al¹⁴ showed that COPD exacerbations have a negative impact on exercise capacity and physical activity and lead to impairment in muscle strength in subjects with COPD. Spruit et al³¹ found that subjects with COPD had significantly less muscle strength during COPD exacerbations when compared with subjects with COPD with a stable disease. In a study conducted by Spruit et al,³¹ lower-limb strength decreased during hospitalization and was partially recovered 3 months after discharge. Our results are in line with those of previous studies^{14,31} and confirm that after a hospital stay for a COPD exacerbation, subjects exhibited a physical impairment that persisted and increased significantly at 1-month follow-up; this important impairment can be explained by the severity of the condition of our subjects.

In adults, hospitalization is considered to be a critical transitional event that has deleterious effects in older people.³⁵ In patients with COPD, hospitalizations are frequent and increase with the severity of the disease. However, the impacts of hospitalization on patients' functionality have not been widely explored so far. Lower-muscle strength is reflected in a decrease in the ability to perform activities of daily living. It has been shown previously that hospitalization leads to a significant physical impairment in subjects admitted to the hospital due to pneumonia and that impairment increases with age.³⁵ The main risk factors for functional decline associated with hospitalization are age, immobility, cognitive impairment, and functional status before admission.³⁶ Our results confirm the effects of hospitalization on physical function; they highlight the priority of implementing in-hospital rehabilitation programs with patients with COPD due to their age range, their vulnerability to functional decline, and the chronicity of the disease, which implies a functional impairment before admission.

Regarding postural steadiness, the study conducted by Tudorache et al³⁷ showed that the presence of COPD with stable or exacerbation phases is associated with impairment in postural steadiness. Our results showed that hospitalization led to impairment in postural steadiness. The impairment was shown to increase in both legs after 1-month follow-up. Finally, dyspnea perception improved significantly during hospitalization due to the pharmacologic and medical treatment.

Limitations and Strengths

Our study has several limitations that should be considered. First, there are some recognized prognostic indices that can be used to predict the probability of recovery, dependence, or death after hospitalization in older people.^{38,39} Although there are no indices specifically designed for patients with COPD, the variables we collected are all valid tools to obtain data on functional status. Second,

although data on functional status are not always routinely collected in hospitalized patients, our variables are simple to collect, and there is substantial evidence⁴⁰ that functional status is a key predictor of a wide range of outcomes. The main strength of this study is that the focus on COPD exacerbation is novel as well as the depth of clinical assessments for strength/function.

Conclusions

Hospitalization leads to physical and functional impairment, including decreased muscle strength and postural steadiness, in subjects hospitalized due to a severe COPD exacerbation; impairment increases between discharge and follow-up. To prevent this significant impairment, it would be interesting to implement a pulmonary rehabilitation program with these patients to decrease their physical and functional impairment.

REFERENCES

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997;349(9064):1498-1504.
2. Rodríguez-Roisin R. Toward a consensus definition for COPD exacerbations. *Chest* 2000;117(5 Suppl 2):398S-401S.
3. Miravittles M, Guerrero T, Mayordomo C, Sánchez-Agudo L, Nicolau F. Factors associated with increased risk of exacerbation and hospital admission in a cohort of ambulatory COPD patients: a multiple logistic regression analysis: the EOLO Study Group. *Respiration* 2000;67(5):495-501.
4. Spencer S, Calverley PM, Burge PS, Jones PW. Impact of preventing exacerbations on deterioration of health status in COPD. *Eur Respir J* 2004;23(5):698-702.
5. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005;60(11):925-931.
6. Groenewegen KH, Schols AM, Wouters E. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. *Chest* 2003;124(2):459-467.
7. Donaldson GC, Wedzicha JA. COPD exacerbations. 1: Epidemiology. *Thorax* 2006;61(2):164-168.
8. Martínez-Llorens JM, Orozco-Levi M, Masdeu MJ, Coronell C, Ramírez-Sarmiento A, Sanjuas C, et al. Disfunción muscular global durante la exacerbación de la EPOC: un estudio de cohortes [Global muscle dysfunction and exacerbation of COPD: a cohort study]. *Med Clin (Barc)* 2004;122(14):521-527.
9. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbations on quality of life in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1998;157(5):1418-1422.
10. Kim HC, Mofarrah M, Hussain SN. Skeletal muscle dysfunction in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2008;3(4):637-658.
11. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting patients after discharge from the hospital. *Ann Intern Med* 2003;138(3):161-167.
12. Dal Negro R. Optimizing economic outcomes in the management of COPD. *Int J Chron Obstruct Pulmon Dis* 2008;3(1):1-10.

13. Seemungal TA, Donaldson GC, Bhowmik A, Jeffries DJ, Wedzicha JA. Time course and recovery of exacerbations in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2000;161(5):1608-1613.
14. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Physical activity and hospitalization for exacerbation of COPD. *Chest* 2006;129(3):536-544.
15. Inouye SK, Wagner DR, Acampora D, Horwitz RI, Cooney LM Jr., Tinetti ME. A controlled trial of a nursing-centered intervention in hospitalized elderly medical patients: the Yale Geriatric Care Program. *J Am Geriatr Soc* 1993;41(12):1353-1360.
16. Martín-Valero R, Rodríguez-Martínez MC, Cantero-Tellez R, Villanueva-Calvero E, Fernández-Martín F. Advances in comprehensive pulmonary rehabilitation for COPD patients. In: Panos R, editor. *COPD clinical perspectives*. Rijeka, Croatia: InTech; 2014. doi: 10.5772/57563.
17. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;152(5 Pt 2):S77-S121.
18. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med* 2007;176(6):532-555.
19. Torres-Sánchez I, Valenza MC, Sáez-Roca G, Cabrera-Martos I, López-Torres I, Rodríguez-Torres J. Results of a multimodal program during hospitalization in obese COPD exacerbated patients. *COPD*. 2016;13(1):19-25.
20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987;40(5):373-383.
21. Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. *Md State Med J* 1965;14:61-65.
22. Jones PW. St. George's Respiratory Questionnaire: MCID. *COPD* 2005;2(1):75-79.
23. Watz H, Waschki B, Meyer T, Magnussen H. Physical activity in patients with COPD. *Eur Respir J* 2009;33(2):262-272.
24. Patel SA, Benzo RP, Slivka WA, Sciruba FC. Activity monitoring and energy expenditure in COPD patients: a validation study. *COPD* 2007;4(2):107-112.
25. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A. Standardisation of spirometry. *Eur Respir J* 2005;26(2):319-338.
26. Borg GA. Psychophysical basis of perceived exertion. *Med Sci Sports Exerc* 1982;14(5):377-381.
27. Martin HJ, Yule V, Syddall HE, Dennison EM, Cooper C, Aihie Sayer A. Is hand-held dynamometry useful for the measurement of quadriceps strength in older people? a comparison with the gold standard Biodex dynamometry. *Gerontology* 2006;52(3):154-159.
28. Shephard RJ, Montelpare W, Plyley M, McCracken D, Goode RC. Handgrip dynamometry, Cybex measurements and lean mass as markers of the ageing of muscle function *Br J Sports Med* 1991;25(4):204-208.
29. Jones CJ, Rikli RE. Measuring functional fitness of older adults. *J Active Aging* 2002;24-30. <http://www.dsnm.univr.it/documenti/OccorrenzaIn/matdid/matdid182478.pdf>. Accessed August 19, 2016.
30. Michikawa T, Nishiwaki Y, Takebayashi T, Toyama Y. One-leg standing test for elderly populations. *J Orthop Sci* 2009;14(5):675-685.
31. Spruit MA, Gosselink R, Troosters T, Kasran A, Gayan-Ramirez G, Bogaerts P, et al. Muscle force during an acute exacerbation in hospitalised COPD patients and its relationship with CXCL8 and IGF-1. *Thorax* 2003;58(9):752-756.
32. Viegi G, Pistelli F, Sherrill DL, Maio S, Baldacci S, Carrozzi L. Definition, epidemiology and natural history of COPD. *Eur Respir J* 2007;30(5):993-1013.
33. Oga T, Nishimura K, Tsukino M, Sato S, Hajiro T, Mishima M. Longitudinal deteriorations in patient reported outcomes in patients with COPD. *Respir Med* 2007;101(1):146-153.
34. Peruzza S, Sergi G, Vianello A, Pisent C, Tiozzo F, Manzan A, Coin A, Inelmen EM, Enzi G. Chronic obstructive pulmonary disease (COPD) in elderly subjects: impact on functional status and quality of life. *Respir Med* 2003;97(6):612-617.
35. Martín-Salvador A, Torres-Sánchez I, Sáez-Roca G, López-Torres I, Rodríguez-Alzueta E, Valenza MC. Age group analysis of psychological, physical and functional deterioration in patients hospitalized for pneumonia. *Arch Bronconeumol* 2015;51(10):496-501.
36. Osuna-Pozo CM, Ortiz-Alonso J, Vidán M, Ferreira G, Serra-Rexach JA. Review of functional impairment associated with acute illness in the elderly. *Rev Esp Geriatr Gerontol* 2014;49(2):77-89.
37. Tudorache E, Oancea C, Avram C, Fira-Mladinescu O, Petrescu L, Timar B. Balance impairment and systemic inflammation in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2015;10:1847-1852.
38. Barnes DE, Mehta KM, Boscardin WJ, Fortinsky RH, Palmer RM, Kirby KA. Prediction of recovery, dependence or death in elders who become disabled during hospitalization. *J Gen Intern Med* 2013;28(2):261-268.
39. Covinsky KE, Palmer RM, Counsell SR, Pine ZM, Walter LC, Chren MM. Functional status before hospitalization in acutely ill older adults: validity and clinical importance of retrospective reports. *J Am Geriatr Soc* 2000;48(2):164-169.
40. Boyd CM, Ricks M, Fried LP, Guralnik JM, Xue QL, Xia J. Functional decline and recovery of activities of daily living in hospitalized, disabled older women: the Women's Health and Aging Study I. *J Am Geriatr Soc* 2009;57(10):1757-1766.