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- Şule TAŞ GÜLEN¹
- Emel CEYLAN¹
- Fisun KARADAĞ¹
- Onur YAZICI¹
- Osman ELBEK²
- İmran KURT OMURLU³

CORRESPONDANCE

Şule TAŞ GÜLEN
Adnan Menderes University, Faculty of Medicine,
Department of Chest Disease, Aydın, Turkey

Phone: 05056919099
e-mail: dr_suletas@yahoo.com.tr

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- ¹ Adnan Menderes University, Faculty of Medicine, Department of Chest Disease, Aydın, Turkey
- ² Kadıköy Florence Nightingale Medical Center, Chest Disease Clinic, İstanbul, Turkey
- ³ Adnan Menderes University, Faculty of Medicine, Department of Biostatistic, Aydın, Turkey

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RESEARCH

THE EFFECT OF COGNITIVE FUNCTIONS ON SPIROMETRIC EVALUATION IN ELDERLY PATIENTS

ABSTRACT

Introduction: Compliance with spirometry may be disturbed among elderly patients, leading to difficulties in diagnosis and treatment. Contradicting studies exist concerning the quality of spirometry measurements, particularly among patients with cognitive disorders. We studied the effect of cognitive functions on spirometry testing time and pulmonary function test (PFT) parameters among patients aged ≥ 65 years.

Materials and Method: The study was conducted in the Pulmonary Function Laboratory of our hospital between January and June 2015. A total of 336 subjects aged >45 years who never underwent PFT were included. Patients were categorized as those aged ≥ 65 years (Group 1) and those aged 45–65 years (Group 2). Mini-Mental State Examination (MMSE) scores of ≥ 24 were considered normal, whereas those of 18–23 indicated mild cognitive dysfunction.

Results: Groups 1 (132 subjects) and 2 (204 subjects) had similar male-to-female ratios. Six (1.8%) patients were excluded because their spirometry was not properly performed. Forced expiratory volume in 1st second (FEV1 % predicted), forced vital capacity (FVC % predicted), FEV1/FVC %, and MMSE results were significantly lower in Group 1 than in Group 2. No significant difference was noted between the groups regarding spirometry testing time and the number of maneuvers. MMSE negatively correlated with age and the number of spirometry maneuvers and positively with FEV1 % and FVC %. The prevalence of obstructive pulmonary disorders was higher in Group 1. Logistic regression analysis revealed age, body mass index, and smoking history as factors affecting obstruction.

Conclusion: Evaluation of cognitive function before performing spirometry testing in elderly patients is essential for accurate and reliable test results.

Keywords: Spirometry; Cognition; Aged; Mental Status and Dementia Tests

ARAŞTIRMA

YAŞLI HASTALARDA KOGNİTİF FONKSİYONLARIN SPIROMETRİK DEĞERLENDİRMeye ETKİSİ

Öz

Giriş: Yaşlı hastalarda spirometriye uyum zor olabilmekte bu da tanı ve tedavide yetersizliklere neden olmaktadır. Özellikle kognitif fonksiyonlardaki bozulmaya bağlı spirometri ölçümlerinin kalitesi ile ilgili çelişkili yayınlar mevcuttur. Çalışmada 65 yaş üzerindeki kişilerde kognitif fonksiyonların spirometri süresi ve solunum fonksiyon testi (SFT) parametreleri üzerine etkisinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya Ocak 2015 ile Haziran 2015 tarihleri arasında hastanemiz solunum fonksiyon laboratuvarına başvuran daha önce SFT yapılmamış olan 45 yaş üzeri toplam 336 olgu alındı. Olguların yaş, kilo, boy, eğitim düzeyi, geçmiş tıbbi öyküleri ve alışkanlıkları, SFT ve standardize mini mental test (MMSE) sonuçları kaydedildi. Olgular 65 yaş üstü (grup 1) ve 45-65 yaş arası (Grup 2) olacak şekilde sınıflandırıldı. MMSE' de 30 puan üzerinden yapılan değerlendirmede 24 puan ve üzeri normal, 18-23 puan arası hafif kognitif bozukluk olarak kabul edildi.

Bulgular: Olguların 132'si Grup 1'de, 204'ü Grup 2'de idi, her iki grubun erkek ve kadın oranları benzerdi ($p=0.053$). Altı (%1.8) olgunun spirometreleri uygun şekilde yapılmadığından değerlendirmeye alınmadı. Grup 1'de postbronkodilatatör FEV1%, FVC %, FEV1/FVC % değerleri ile MMSE puanları kontrol grubuna kıyasla anlamlı olarak daha düşük bulundu ($p < 0.001$). Spirometri süresi ve manevra sayısı bakımından 2 grup arasında fark saptanmadı. MMSE'nin korelasyon analizinde yaş ve spirometri manevra sayısı ile negatif, FEV1 % ve FVC % değerleri ile pozitif korele olduğu bulundu. Grup 1'de obstrüktif solunum fonksiyon bozukluğu daha fazla idi. Lojistik regresyon analizinde obstrüksiyon için etkili faktörler; yaş, VKİ ve sigara içme öyküsü idi.

Sonuç: Verilerimiz yaşlı olgularda spirometri öncesi kognitif fonksiyonları değerlendirmenin hem spirometri kalitesine hem de spirometri süresine olumlu katkı sağlayacağına işaret etmektedir.

Anahtar sözcükler: Spirometri; Bilişsel durum; Yaşlanma ve Demans testleri



INTRODUCTION

The elderly population is increasing in Turkey as well as worldwide. According to the World Health Organization, the population aged ≥ 65 years is defined as "old" and that aged ≥ 85 years as "very old" (1). The percentage of the elderly population in Turkey was 7.5% in 2012, which increased to 8.3% in 2016. According to population projections, the elderly population is predicted to constitute 10.2% of the total population in 2023, 20.8% in 2050, and 27.7% in 2075 (2).

Various changes in pulmonary functions occur with increasing age, of which the two most important are increased residual volume and decreased vital capacity. Increased functional residual capacity and decreased elastic recoil occur together with aging. Forced expiratory volume in 1st second (FEV1) and forced vital capacity (FVC) show a plateau between ages 18–25 and then decreases by 30 mL/year. This reduction can reach 100 mL/year in smokers (3). In addition, aging may be associated with cognitive function disorders, ranging from mild-to-moderate disorders to dementia. Compared with the younger population, processing and reaction speeds of the elderly are slower during the time-based evaluation of cognitive function. However, this reduction is not so prominent as to affect daily living (4,5). Cognitive function can be assessed using screening tests, such as the Mini-Mental State Examination (MMSE), clock-drawing test, and three-item recall test. Among these, the MMSE is a comparatively short, simple, and global test that can be used in clinical practice and research. The MMSE test is scored over 30 points and measures tendency, attention, memory, motor abilities, and linguistic performance. If the test can be standardized according to age and the educational level, its sensitivity and specificity can reach 82% and 99%, respectively (6,7).

The increased incidence of pulmonary symptoms observed in elderly patients results in an increased requirement of pulmonary function tests (PFT) to distinguish obstructive diseases. In these patients, the presence of a cognitive function disorder can affect the quality of PFT results, thereby influencing the prognosis. Further, elderly patients have difficulties in comprehending spirometry maneuvers and in cooperating with the PFT technician. Thus, spirometry testing time is increased (8). In the present study we determined the effects of cognitive functions on spirometry parameters and testing time using MMSE.

MATERIALS AND METHOD

The study was conducted between January and June 2015 at the Pulmonary Function Laboratory of the Adnan Menderes University Hospital after obtaining ethical committee approval. Subjects were chosen among patients admitted to the laboratory who never underwent spirometry and, thus, were unfamiliar with the maneuvers. A total of 336 patients aged ≥ 45 years provided written consent to participate. Patients diagnosed with chronic obstructive pulmonary disease (COPD), respiratory failure, severe cardiovascular or neurologic disorders were excluded. Subjects were categorized as those aged ≥ 65 (Group 1) and 45–65 (Group 2, controls) years. For all patients, demographic data [age, sex, weight, height, body mass index (BMI), smoking history, socioeconomic and educational status, professional history, medical history], PFT, and standardized MMSE results were recorded.

Pulmonary Function Testing (PFT)

The test was conducted at our laboratory with the patient in a sitting position, according to the 2005 ATS/ERS criteria, using a Jaeger Master Scope spirometer. Subjects were tested eight

times or until they could not continue the test, and the three best results were recorded. All measurements were performed by the same Certified Pulmonary Function Technician. The bronchodilation test was conducted with an inhaler device. At 15 min after the inhalation of four puffs of salbutamol (400 µgr), FEV1 (%), FVC (%), and FEV1/FVC (%) values were recorded. Results that were not acceptable according to the ATS/ERS 2005 criteria or those not reproducible were excluded. According to these criteria, post-bronchodilator FEV1/FVC values of <70% indicated obstruction and FEV1 and FVC values of <80% with a normal FEV1/FVC ratio indicated restriction. The test testing time and number of maneuvers were recorded (9).

Mini-Mental State Examination (MMSE)

MMSE was developed in 1975 in English language. Its standardized form was translated to Turkish in 1997, and we used this version to evaluate cognitive functions (Figure 1), including attention, memory, motor skills, and linguistic abilities. MMSE was scored over 30 points, including 10 for time and space orientation, 6 for memory (3 for registration and 3 for recall), 5 for attention, 8 for linguistic abilities, and 1 for visual-spatial functions. Scores of ≥ 24 points indicated normal, those of 18–23 indicated mild, and those of ≤ 17 indicated severe cognitive impairment (10).

Statistical analysis

For the statistical analysis of the data, SPSS (Statistical Package for Social Sciences, for Windows Release 16.0 licensed to University of California Davis USA) software package was utilized. Descriptive statistics of categorical measures (gender, educational status, group, etc.) were expressed as frequency (percentage).

Kolmogorov–Smirnov test was used to assess the normality of numeric variables. Mann–Whit-

ney U test was used to compare the two groups for all non-normally distributed numeric variables, and descriptive statistics were presented as median (interquartile range). χ^2 test was used to analyze categorical data, and descriptive statistics were represented as frequency (%). Spearman's ρ correlation analysis was used to determine correlations between numeric variables. Logistic regression (LR) with a forward stepwise variable selection was used to determine factors affecting obstruction. $p < 0.05$ was considered statistically significant.

RESULTS

Of the 336 subjects [mean age, 62.14 ± 9.32 (range, 45–89) years; 174 (51.8%) males], 273 (81.3%) had received education for < 5 years [62 (18.5%) were illiterate and 211 (62.8%) were primary school graduates] and 23 (6.8%) were university graduates. Mean BMI was 29.28 ± 6.29 (17.51–61.73), and 161 (47.9%) subjects had no smoking history. Six (1.8%) subjects were eliminated because their spirometric tests did not match the 2005 ATS/ERS criteria (three each from groups 1 and 2; $p = 0.683$).

Among the remaining 330 patients, PFT results indicated obstruction in 145 (43.2%) and restriction in 56 (16.7%). The mean number of maneuvers was 3.60 ± 1.26 , and mean PFT testing time was 19.01 ± 5.00 min. Median MMSE was 21.50 (19–24) points. MMSE results indicated severe dementia in 18.8% of the subjects, mild dementia in 43.5%, and normal function in 37.8%.

Mean BMI was statistically significantly lower in Group 1 than Group 2 (26.80 versus 30.08, $p < 0.001$). Median MMSE scores were 19 (17–22) and 23 (20–25) in groups 1 and 2 and differences were statistically significant ($p < 0.001$). Educational level and medical and smoking histories are shown in Table 1.



The prevalence of mild and severe cognitive impairment was 42.4% and 37.9%, respectively, in Group 1 and 44.6% and 5.9%, respectively, in Group 2 ($p < 0.001$). Among subjects who scored < 24 points, 100 (75%) in Group 1 and 97 (47.5%) in Group 2 were either illiterate or primary education graduates. There were no significant differences in spirometry testing time and the number of maneuvers between the groups ($p=0.352$ and $p=0.603$). The level of postbronchodilator FEV1/FVC %, FEV1 % predicted and FVC % predicted were found significantly lower in group 1 ($p<0,001$). Obstructive pulmonary dysfunction was noted in 58.1% and 34.8% of patients in groups 1 and 2, respectively ($p<0.001$). However, the difference in the rate of restrictive pulmonary dysfunction between the groups was not significant ($p=0.166$; Table 2).

Groups 1 and 2 were divided into subgroups based on normal (≥ 24 points) and abnormal MMSE scores. FEV1 % predicted, FVC % predicted and FEV1/FVC % values were significantly lower in Group 1 ($p=0.01, 0.001, 0.003$, respectively), whereas there was no significant difference between PFT testing time and the number of maneuver.

MMSE negatively correlated with age and the number of spirometry maneuvers and positively with FEV1 % predicted and FVC % predicted values (Table 3, Graphs 1 and 2).

Logistic regression analysis, performed to determine factors contributing to obstructive disorders, revealed age, BMI, and smoking history as factors affecting obstruction (specificity, 77.3%; sensitivity, 60.0%; accuracy, 69.7%; Table 4).

Table 1. Demographic data of the case and control groups.

Variable	Group 1 (≥ 65 years) (n=132)	Group 2 (control) (n=204)	p
Sex (M/F) %	58.3/41.7	47.5/52.5	0.053
BMI (kg/m^2) (% percentile)	26.80 (23.53–31.23)	30.08(25.76–33.74)	<0.001
Education			
Illiterate + Primary Education (%)	114 (86.4)	159 (77.9)	0.074
Secondary + Post-Sec. (%)	18 (13.6)	45 (22.1)	
Medical history			
With comorbidities (%)	85 (64.4)	122 (59.8)	0.398
Without comorbidities (%)	47 (35.6)	82 (40.2)	
Smoking history (%)	72 (54.5)	103 (50.5)	0.467
Evaluable PFT (%)	129 (97.7)	201 (98.5)	0.683
MMSE score (% percentile)	19 (17–22)	23 (20–25)	<0.001

Abbreviations: BMI: body mass index, PFT: pulmonary function test

Table 2. Comparison of MMSE and PFT parameters of the case and control groups.

Variables	Group 1 (n=132)	Group 2 (n=204)	p
MMSE, ≥24 points (%)	26 (19.7)	101 (49.5)	
MMSE, 18–23 points (%)	56 (42.4)	91 (44.6)	<0.001
MMSE, ≤17 points (%)	50 (37.9)	12 (5.9)	
PFT testing time (min)	17.5 (16–21)	18 (16–21)	0.352
# PFT maneuvers	3 (3–4)	3 (3–4)	0.603
Obstruction (%)	75 (58.1)	70 (34.8)	<0.001
Restriction (%)	27 (20.9)	29 (14.4)	0.166
FEV1/FVC (%)	67.48 (58.39–75.24)	74.40 (66.51–79.58)	<0.001
FEV1 (% predicted)	67.80 (54.15–86.80)	86.50 (72.40–100.15)	<0.001
FVC (% predicted)	82.50 (71.65–94.85)	96.10 (83.75–109.85)	<0.001

Abbreviations: MMSE: Mini-Mental State Examination, PFT: pulmonary function test, FEV1: forced expiratory volume–1st s, FVC: forced vital capacity, # PFT maneuvers: number of PFT maneuvers.

Table 3. Relationship of MMSE with age and the number of spirometry maneuvers.

Variable	Mental Test	
	r	p
Age (years)	–0.421	<0.001
# spirometry maneuvers	–0.160	0.003

Abbreviations: # spirometry maneuvers: number of spirometry maneuvers

Table 4. Results of logistic regression analysis for factors affecting obstruction.

Risk factor	OR	95% Confidence Interval for OR		p
		Lower	Upper	
Age (years)	1.053	1.025	1.082	<0.001
BMI (kg/m ²)	0.928	0.887	0.970	0.001
Smokinghistory (packets/year)	3.251	1.956	5.401	<0.001

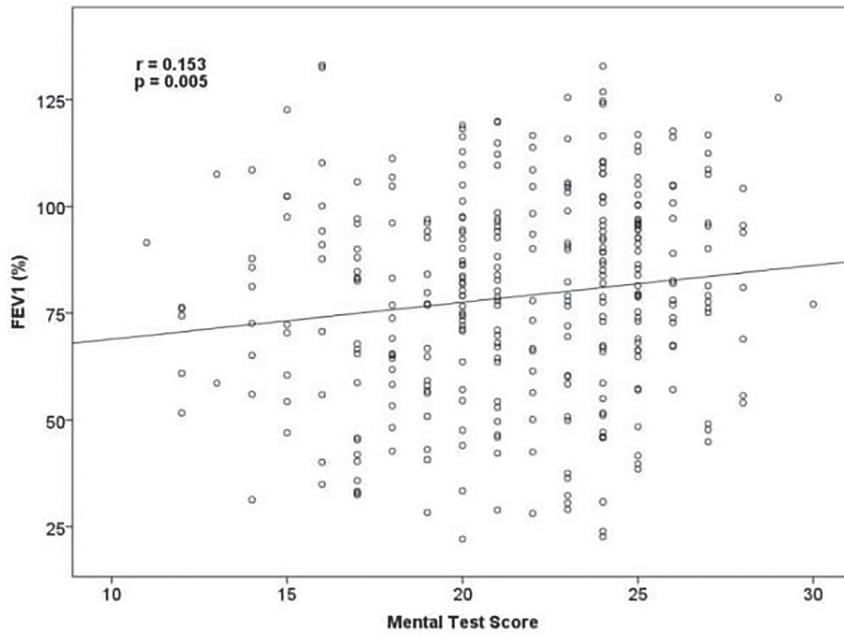


Figure 1. Relationship between MMSE Score and FEV1%.

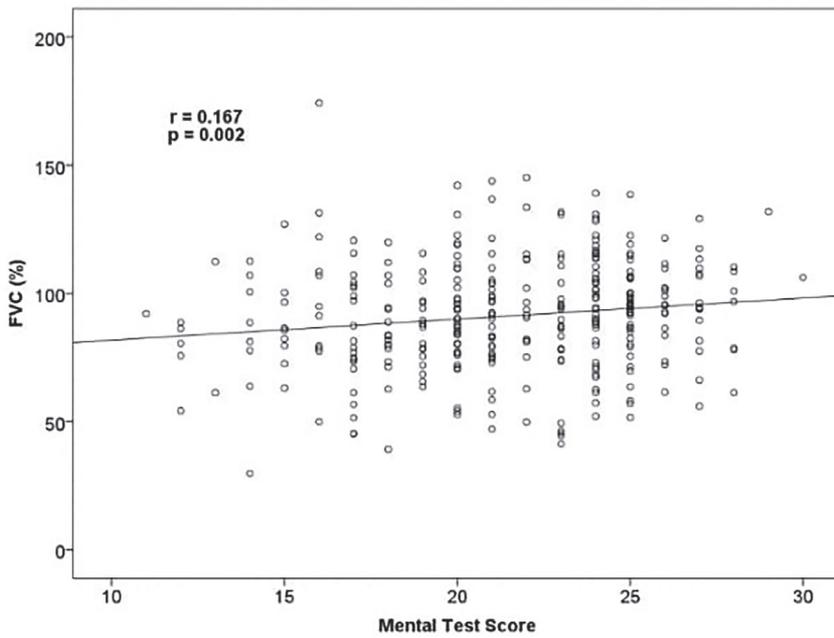


Figure 2. Relationship between MMSE Score and FVC%.

DISCUSSION

Our study indicated that cognitive functions declined with age and as they declined, FEV1 and FVC values decreased and the number of spirometry maneuvers increased. Age, BMI, and smoking history were determined to be factors affecting obstructive pulmonary dysfunction.

Six (1.8%) of our subjects were excluded because they did not comply with the 2005 ATS/ERS criteria. Similarly, in the spirometry study conducted by Czajkowska-Malinowska et al. (8), 29 (2.3%) of 1271 subjects aged 65–94 years were excluded. Bellia et al. (11) evaluated 1622 subjects aged ≥ 65 years and excluded spirometry results of 103 (6.4%). The reason why our study had a lower ratio of excluded subjects may be because of the younger subject group in our study compared with other studies.

Cognitive functions decline because of age-dependent reductions in cerebral blood flow and oxygen and glucose consumptions. Also, educational level, comorbidities, and/or age-related decrease in physical activity are influential factors (12). MMSE scores were found lower in the elderly than in the controls, although levels of education, comorbidity, and smoking history were found similar between the groups, suggesting that age affects cognitive functions regardless of the educational level or comorbidities.

Studies evaluating pulmonary and cognitive functions in the elderly, without any obstructive lung disease such as asthma or COPD, are limited in the medical literature. Carvalhaes-Neto et al. (6) studied 208 subjects aged >65 years measuring cognitive functions using MMSE and found that 60.5% had severe, 17.3% mild dementia, and 22.1% had normal function. In our study, 18.8% of subjects had severe and 43.5% had mild dementia and 37.8% had normal function. One of the factors affecting cognitive functions is the educational level and it should be taken into consideration. However, Carvalhaes-Neto et al. (6) did not mention educational levels of their subjects. In our study, 62 (18.5%) sub-

jects were illiterate and MMSE scores were lower among subjects with ≤ 5 years of education.

Feng et al. (13) studied 2450 patients aged >55 years and evaluated spirometry parameters together with cognitive functions using MMSE, taking educational level into consideration. Mean MMSE scores were 27.00 ± 3.45 , and 1167 (47.6%) subjects had ≥ 7 years of education. In our study, mean MMSE score for the entire sample was 21.36 ± 3.86 and 273 (81.3%) subjects were educated for <5 years [62 (18.5%) were illiterate]. This finding suggested that the difference in MMSE scores between the two studies was related to educational level. Illiterate subjects were evaluated using standardized MMSE for literate adults because no standardized MMSE for illiterate adults was available in Turkey at the time our study was conducted. We suggest further studies using standardized MMSE studies for illiterate individuals.

Bellia et al. (11) evaluated 638 patients with obstructive diseases and 984 control subjects, all with similar age, sex, and educational levels. MMSE scores were significantly lower in the case group. Similarly, in our study, although educational levels were not significantly different, the elderly group had lower MMSE scores, suggesting that age affects cognitive functions.

Pulmonary functions decline with age (3). Most elderly subjects (particularly subjects aged >75 years) have difficulty in performing forced spirometry maneuvers (FEV1 and FVC), which becomes even more difficult when cognitive function is affected (14–16). Haynes (15) evaluated spirometry and diffusion capacity (DLCO) performances in 150 subjects aged ≥ 80 years, together with 178 control subjects aged 40–50 years, and determined that FEV1/FVC lower limits of normal were similar in the elderly and control groups. However, DLCO (% predicted) was significantly lower (15). In our study, we found higher rates of obstructive PFT results in the elderly group compared to the controls, whereas the rates of restrictive PFT results were found similar in both



groups. There was no significant difference between the groups regarding spirometry testing time and the number of maneuvers. Factors associated with obstructive PFT results were smoking history [odds ratio (OR)=3.25], age (OR=1.05), and BMI (OR=0.92). Luoto et al. (17) studied 2025 subjects aged 65–100 years for the incidence of airway obstruction and found that age, active smoking (OR=1.75), smoking history (OR=1.36), and male sex (OR=0.95) were affecting factors and that ages 70–79 years were 1.90-fold effective and ages 80–89 and 90–100 years were 3.15- and 2.84-fold effective, respectively, for obstructive pulmonary dysfunction.

Although we found no difference between the groups regarding spirometry testing time and the number of maneuvers, correlation analysis revealed that older age is associated with impaired cognitive functions. Impaired cognitive function in individuals of advanced age can lead to more spirometry maneuvers, suggesting that the technician will have to spend more time for spirometric tests. Further, FEV1 and FVC values decreased with the deterioration of cognitive functions. The literature indicates that

DLCO, body plethysmography, helium dilution volumetry, and standard forced oscillation techniques can be used to evaluate pulmonary functions in cognitive-impaired elderly individuals when spirometry does not suffice. However, further studies are required regarding this subject (6,14).

In conclusion, cognitive functions deteriorate with age and physiological changes and functional cognitive disorders affect spirometry parameters and the number of maneuvers. Our data indicated that evaluating cognitive functions before undergoing spirometry can improve the quality and testing time of spirometry in the elderly. For the elderly with cognitive impairment, further studies investigating alternative methods to assess pulmonary functions are needed.

There are limitations for our study. Because no standardized MMSE for illiterate adults was available at the time of the study, these subjects were evaluated using standardized MMSE for literate adults in our study. Also, very elderly group could not be evaluated because of low number of participants.

REFERENCES

1. Allen SC, Baxter M. A comparison of four tests of cognition as predictors of inability to perform spirometry in old age. *Age Ageing* 2009;38 (5):537-41. (PMID:19553358).
2. Allen SC, Charlton C, Backen W, Warwick-Sanders M, Yeung P. Performing slow vital capacity in older people with and without cognitive impairment-is it useful? *Age Ageing* 2010;39:588-91. (PMID:20625184).
3. Bellia V, Pistelli R, Catalano F, et al. Quality Control of Spirometry in the Elderly. The S.A.R.A. Study. *Respiratory Health in the Elderly. Am J Respir Crit Care Med* 2000;161(4 Pt 1):1094-100. (PMID:10764296).
4. Carvalhaes-Neto N, Lorino H, Gallinari C, et al. Cognitive function and assessment of lung function in the elderly. *Am J Respir Crit Care Med* 1995;152(5 Pt 1):1611-5. (PMID:7582303).
5. Coskun F. Aging and changes in anatomy and physiology of the respiratory system. *Turkiye Klinikleri J Pulm Med-Special Topics* 2017;10(3):145-7. Available from: <http://www.turkiyeklinikleri.com/article/en-yaslanma-ile-solunum-sistemi-anatomi-ve-fizyolojisinde-degisimler-80310.html>. Accessed: 29.01.2018.
6. Czajkowska-Malinowska M, Tomalak W, Radliński J. Quality of spirometry in the elderly. *Pneumonol Alergol Pol* 2013;81:511-7. (PMID:24142780).
7. Dustman RE, Emmerson R, Shearer D. Physical activity, age, and cognitive-neuropsychological function. *J Aging Phys Act* 1994;2:143-81. [Internet] Available from: <https://doi.org/10.1123/japa.2.2.143>. Accessed: 29.01.2018.

8. Feng L, Lim ML, Collinson S, Ng TP. Pulmonary function and cognitive decline in an older Chinese population in Singapore. *COPD* 2012;9(5):555-62. (PMID:22909131).
9. Gungen C, Ertan T, Eker E, Yasar R, Engin F. Reliability and validity of the Standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. *Turkish Journal of Psychiatry* 2002;13(4):273-81. (PMID:12794644).
10. Haynes JM. Pulmonary function test quality in the elderly: a comparison with younger adults. *Respiratory Care* 2014;59(1):16-21. (PMID:23801784).
11. Luoto JA, Elmståhl S, Wollmer P, Pihlsgård M. Incidence of airflow limitation in subjects 65-100 years of age. *Eur Respir J* 2016;47(2):461-72. (PMID:26677939).
12. Miller MR, Hankinson J, Brusasco V, et al. ATS/ERS Task Force. Standardisation of spirometry. *Eur Respir J* 2005;26(2):319-38. (PMID:16055882).
13. Petersen RC, Stevens JC, Ganguli M, Tangalos EG, Cummings JL, DeKosky ST. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001;56(9):1133-42. (PMID:11342677).
14. Sink KM, Yaffe K. Cognitive Impairment and Dementia. In: Landefeld CS, Palmer RM, Johnson MA, et al. (Eds). *Current Geriatric Diagnosis and Treatment*. McGraw Hill, New York 2004, pp 60-73.
15. Small SA, Stern Y, Tang M, Mayeux R. Selective decline in memory function among healthy elderly. *Neurology* 1999;52(7):1392-6. (PMID:10227623).
16. The uses of epidemiology in the study of the elderly. Report of a WHO Scientific Group on the Epidemiology of Aging. *World Health Organ Tech Rep Ser* 1984;706:1-84. (PMID:6437089).
17. Turkish Statistical Institute. Elderly with Statistics, 2016. Turkey Statistical Institute Newsletter 2017;24644. [Internet] Available from: www.tuik.gov.tr/PrehaberBultenleri.do?id=24644. Accessed: 29.01.2018.