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ORIGINAL ARTICLE

Cut-off values of 6-min walk test and sit-to-stand test for determining symptom burden in atrial fibrillation

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Abstract

Background Since symptomatology is a major predictor of quality of life and an endpoint for the management of atrial fibrillation (AF), practical approaches for objectively interpreting symptom burden and functional impairment are needed.

Aims We aimed to provide cut-off values for two frequently used field tests to be able to objectively interpret symptom burden in atrial fibrillation.

Methods One hundred twenty-five patients with AF were evaluated with European Heart Rhythm Association (EHRA) score, 6-min walk test (6MWT), 30 s sit-to-stand test (30 s-STST), Short-Form 36 (SF-36), International Physical Activity Questionnaire-Short Form (IPAQ-SF), and spirometry. Patients with EHRA 1 were classified as "asymptomatic", and those with EHRA 2–4 as "symptomatic". Cut-off values of 6MWT and 30 s-STST for discriminating between these patients were calculated.

Results The optimal cut-off value was "450 m" for 6MWT (sensitivity: 0.71; specificity of 0.79) and "11 repetitions" for 30 s-STST (sensitivity 0.77; specificity of 0.70). Area under ROC curve was 0.75 for both tests ($p < 0.001$). Discriminative properties of the two tests were similar, and they were significantly correlated ($r = 0.58$; $p < 0.001$). Subgroup analysis revealed patients below cut-off values also had worse outcomes in SF-36, IPAQ-SF, and spirometry.

Conclusions In patients with AF, walking < 450 m in 6MWT or performing < 11 repetitions in 30 s-STST indicates increased symptom burden, as well as impaired exercise capacity, quality of life, physical activity participation, and pulmonary function. These cut-off values may help identifying patients who may require adjustments in their routine treatment or who may benefit from additional rehabilitative approaches.

Keywords Atrial fibrillation · EHRA score · Functional impairment · Reference value · Sit-to-stand test · Six-minute walk test · Symptomatology

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting between 2 and 4% of the adults [1]. Cardinal symptoms of AF include dyspnea, fatigue, and palpitations, but patients may also experience exercise intolerance. Almost half of the symptomatic patients report dyspnea on exertion, and 25% of them have reduced exercise capacity. Reduction in exercise capacity may be up to 20% in patients with AF compared to individuals with sinus rhythm [2, 3]. Exercise intolerance leads to a decline in functional status of the patients by limiting their participation in activities of daily living. Functional status is regarded as one of the major predictors of health related quality of life (HRQoL) in patients with AF [4]. Improvement of HRQoL and symptom control

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are the main endpoints in the management of these patients. Therefore, it is important to monitor and address the symptomatology and functional status of these patients properly considering their influence on HRQoL. However, perception of symptoms may vary among patients, and it may be difficult to make clinical judgments based on the reported symptom burden in some patients. In such cases, clinicians may require practical and objective measures for interpreting symptom burden and functional impairment in the clinical practice.

Six-minute walk test (6MWT) is the most commonly used field test for measuring functional status in patients with cardiopulmonary diseases [5]. However, to be able to interpret a single measurement of 6MWT of a patient, the distance walked in 6MWT should be compared to either reference values obtained from healthy individuals or a cut-off value that was specifically determined for that population. Reference values are generally reported based on age groups and gender and it may not be practical to find a value appropriate to the characteristics of a patient being evaluated. On the other hand, cut-off values provide an opportunity to instantly interpret the test result of a patient and consequently, they find a widespread use in the clinical practice. Such cut-off values are present for 6MWT in several cardiopulmonary diseases such as COPD (350 m) [6] and heart failure (300 m) [7] for identifying patients with high mortality risk and/or poor health status, but there is no cut-off value determined in AF. Sit-to-stand tests (STSTs) have become increasingly popular in the clinical practice for measuring physical performance in various cardiopulmonary conditions such as COPD, lung transplantation, and pulmonary hypertension because of their practicality [8–10]. Similar to 6MWT, STSTs require reference or cut-off values for an objective interpretation of a single measurement. In this context, STSTs are even more limited compared to 6MWT, considering the studies investigating cut-off values for these tests are lacking.

In this study, we aimed to provide cut-off values for two frequently used exercise tolerance measures in the clinical practice for objectively interpreting the symptom burden and functional impairment of patients with AF. We believe these cut-off values may help identifying the patients who may require adjustments in their routine treatment or those may benefit from new rehabilitative approaches. Accordingly, our main objective in this study was to classify patients as "asymptomatic" and "symptomatic" according to The European Heart Rhythm Association (EHRA) score, then determine cut-off values of 6MWT and 30 s STST (30 s-STST) for discriminating between these patient groups.

Methods

Study design and subjects

A prospective, cross-sectional study was conducted. One hundred twenty-five patients diagnosed with AF who were being treated in the rhythm management clinic of Cardiology Institute of Istanbul University-Cerrahpasa were included in the study between February 2021 and May 2021. Inclusion criterion was diagnosis of paroxysmal, persistent, or permanent AF. Exclusion criteria was diagnosis of heart failure with reduced ejection fraction or any chronic respiratory diseases, recent coronary bypass surgery, previous heart valve surgery, recent acute myocardial infarction, and having a pacemaker. The study was approved by the ethics committee of Izmir Bakircay University (study number: 172/2021), prospectively registered to ClinicalTrials.gov website (registration number: NCT04754360) and carried out according to the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from all patients.

Procedure

Symptomatology of the patients was determined according to the EHRA score. EHRA score is a practical measure for assessing symptom burden and functional impairment in daily activities caused by AF-related symptoms. Six symptom dimensions including palpitations, fatigue, dizziness, dyspnea, chest pain, and anxiety are questioned in four severity categories (EHRA 1–4). While EHRA 1 indicates "no symptoms," i.e., asymptomatic, EHRA 2, 3, and 4 indicates mild, severe, and disabling symptoms, respectively. The maximum category of any of the 6 individual symptoms results in the ultimate EHRA score for the patient [11, 12]. In the present study, the patients having EHRA 1 score were classified as "asymptomatic" and the patients having EHRA 2–4 score were classified as "symptomatic", as in similar studies in the literature [13]. Then, cut-off values of 6MWT and 30 s-STST for discriminating between the symptomatic and asymptomatic patients were determined. For further exploring the discriminative properties of determined cut-off values, patients below and above the cut-off values were compared to each other in terms of exercise tolerance, HRQoL, physical activity level, and pulmonary function.

Outcome measures

Exercise tolerance was assessed using 6MWT and 30 s-STST. All patients performed 6MWT and 30 s-STST consecutively on the same day. The order in which 6MWT and 30 s-STST were applied was decided by random draw. A 15-min resting period was provided between 6MWT and 30 s-STST for avoiding muscle fatigue. 6MWT was conducted in an uninterrupted 30-m long corridor according to the ATS guideline [14]. All participants were informed with standardized statements before testing. The distance walked in 6 min was recorded in meters. 30 s-STST was performed according to the common protocol described in detail for COPD patients [15]. A standard chair with a seating height of 46 cm was used for testing. Patients were instructed to sit on the chair, come forward until their feet are flat on the floor and fold their upper limbs across the chest. Then, they were instructed to stand all the way up and then sit back down as fast as possible for 30 s. The number of completed sit-to-stand repetitions in 30 s was recorded.

Health-related quality of life was assessed using Short Form-36 (SF-36). SF-36 provides scores for 8 domains of HRQoL including physical function, role-physical, role-emotional, vitality, mental health, social functioning, bodily pain, and general health. Each domain is scored between 0 and 100 points, and higher score indicates better HRQoL [16].

Physical activity participation was assessed using The International Physical Activity Questionnaire-Short Form (IPAQ-SF). IPAQ-SF consists of 7 questions measuring the frequency and duration of participation in the physical activities with low, moderate, and vigorous intensities during past week. Physical activity level is reported as continuous data (MET-min/week) and classified into three categories as low (< 600 MET-min/week), moderate (600 – 3000 MET-min/week), or high (> 3000 MET-min/week) physical activity level [17].

Spirometry was performed according to the guideline of American Thoracic Society (ATS) and European Respiratory Society (ERS) [18]. Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), and peak expiratory flow (PEF) were measured and expressed as percentages of the predicted values. ERS'93 prediction equations were used for calculation of the predicted values [19]. Maximum inspiratory (MIP) and expiratory (MEP) pressures were measured using a mouth pressure meter (MicroRPM; MicroMedical, UK) according to the guideline of ATS/ERS [20]. A maximum value of three efforts that vary less than 5% was recorded for inspiratory and expiratory pressures.

Statistical analysis and sample size

Data was analyzed using SPSS v.20 (IBM Corp., Armonk, N.Y.). Receiver operating characteristics (ROC) curve analysis was performed to explore the ability of 6MWT and 30 s-STST to discriminate between the patients with preserved and reduced functional status. Youden's index was used to determine the optimal cut-off values for 6MWT and 30 s-STST. Areas under the ROC curve (AUC) of 6MWT and 30 s-STST were compared to each other using Hanley-McNeil method for exploring which test has better discriminative ability for identifying the patient's functional status. In addition, Pearson correlation analysis was conducted for investigating the relationship between 6MWT and 30 s-STST. As a sub-group analysis, exercise tolerance, HRQoL, physical activity level, and pulmonary function were compared between the patients below and above the cut-off values using independent samples *t*-test for continuous variables and chi-square test for categorical variables. $P < 0.05$ was considered statistically significant.

Sample size was calculated using G-Power 3.1 (Universitat Dusseldorf, Germany) [21]. In the literature, we were unable to find a study that compares the functional measures between patients in EHRA 1 and EHRA ≥ 2 for estimating a possible effect size and consequently, a sample size for our study. However, in a study implementing a similar measure, i.e., NYHA classification, significant differences with effect sizes ranging from 0.58 to 1.7 are reported between the AF patients with and without functional impairment (NYHA 1 vs NYHA ≥ 2) in terms of subgroups scores indicating functional status in SF-36 (physical function, role limitations-physical, and physical component summary score) [22]. Consequently, we hypothesized to detect a significant difference with an effect size of at least 0.58 between the patients below and above the cut-off values of 6MWT and 30 s-STST in terms of functional status and quality of life in our study. In the literature, approximately 30% of patients with AF report no subjective symptoms [4], which means that if a cohort of AF patients are classified as symptomatic and asymptomatic according to a symptom measure, groups would include unequal number of patients. Considering this inequality, the sample size was calculated specifying the allocation ratio as 30%:70% in the software. Then, it was calculated that minimum of 114 participants are needed in the study to be able to detect a significant difference with an effect size of at least 0.58 between the patients below and above the cut-off values with 80% power at 95% confidence level.

Results

One hundred and sixty-nine patients diagnosed with AF were invited to participate in the study. Seventeen patients did not agree to participate. Twenty-seven patients were excluded for not meeting the inclusion/exclusion criteria. Remaining 125 patients were included in the study. Thirty-four patients (27%) were EHRA 1, 64 patients (51%) were EHRA 2, 23 patients (19%) were EHRA 3, and 4 patients (3%) were EHRA 4. Consequently, 34 patients were classified as "asymptomatic" (27%) and the rest as "symptomatic" (73%). None of the patients were actively participating in a structured exercise training program. All patients were able to perform exercise performance tests and spirometry. There was no missing data. Demographic and clinical characteristics of entire cohort ($n = 125$) and asymptomatic ($n = 34$) and symptomatic

($n = 91$) patients are shown in Table 1. Asymptomatic patients had significantly better 6MWT and 30 s-STST compared to symptomatic patients ($p < 0.001$). Rest of the variables did not differ between asymptomatic and symptomatic patients (excluding EHRA scores).

The ROC curve analysis revealed that both 6MWT and 30 s-STST have discriminative values for identifying the asymptomatic and symptomatic patients ($p < 0.001$), with an AUC of 0.744 and 0.746, respectively, suggesting "acceptable" discrimination for symptomatology (Fig. 1). The optimal cut-off value was "450 m" for 6MWT, which had a sensitivity of 0.71 and a specificity of 0.79, and "11 repetitions" for 30 s-STST, which had a sensitivity of 0.77 and a specificity of 0.70.

Comparison between AUCs of 6MWT and 30 s-STST yielded no significant difference (difference between areas: 0.002; standard error of difference: 0.057; $z = -0.035$; $p = 0.972$) which indicates that both tests have similar discriminative properties in identifying the symptomatology of the patients. In addition, Pearson product-moment correlation revealed that a significant relationship is present between 6MWT and 30 s-STST ($r = 0.579$; $p < 0.001$).

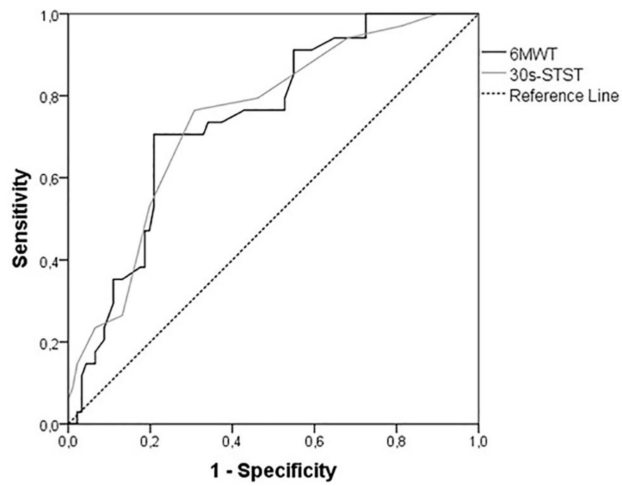

Fig. 1 Receiver operating characteristics curve for 6MWT and 30 s-STST for identifying the asymptomatic and symptomatic patients

According to the cut-off value calculated for 6MWT, 48 patients (38%) walked ≥ 450 m and 77 patients (62%) walked < 450 m. Comparison of exercise tolerance, HRQoL,

Table 1 Demographic and clinical characteristics of entire cohort, and asymptomatic and symptomatic patients according to the EHRA score

	Entire cohort ($n = 125$)	Asymptomatic patients ($n = 34$)	Symptomatic patients ($n = 91$)
Age (years)	65.02 ± 6.84	63.56 ± 6.32	65.56 ± 6.99
Gender (*n*)			
Female	61 (49%)	12 (35%)	49 (54%)
Male	64 (51%)	22 (65%)	42 (46%)
EHRA score (*n*)			
I	34 (27%)	34 (%100)	
II	64 (51%)		64 (70%)
III	23 (19%)		23 (25%)
IV	4 (3%)		4 (5%)
AF type (*n*)			
Permanent	76 (61%)	19 (56%)	57 (63%)
Persistent	27 (22%)	6 (18%)	21 (23%)
Paroxysmal	22 (17%)	9 (26%)	13 (14%)
AF duration (years)	6.49 ± 6.07	6.32 ± 6.09	6.55 ± 6.10
LVEF (%)	57.14 ± 6.48	57.65 ± 6.66	56.95 ± 6.44
BMI (kg/m^2)	30.47 ± 5.01	30.63 ± 4.94	30.41 ± 5.06
Comorbidities (*n*)			
Hypertension	84 (67%)	21 (62%)	63 (69%)
Dyslipidemia	83 (66%)	22 (65%)	61 (67%)
Diabetes mellitus	47 (38%)	11 (32%)	36 (40%)
Exercise tolerance			
6MWT (m)	407 ± 96	462 ± 67[a]	387 ± 98[a]
30 s-STST (reps)	10.18 ± 2.64	11.85 ± 2.57[b]	9.55 ± 2.40[b]

[a],[b]Statistically significant difference *($p < 0.001$)*, *AF* atrial fibrillation, *BMI* body mass index, *EHRA* score European Heart Rhythm Association symptom classification, *LVEF* left ventricular ejection fraction, *6MWT* 6-min walk test, *30 s-STST* 30 s sit-to-stand test

physical activity level, and pulmonary function between the patients walked below and above of 450 m in 6MWT is shown in Table 2. Patients walked < 450 m in 6MWT had significantly worse performance in 30 s-STST, worse scores in all 8 sub-scales of SF-36 except "mental health", lower physical activity level, and worse pulmonary function compared to patients walked ≥ 450 m.

According to the cut-off value calculated for 30 s-STST, 56 patients (45%) performed ≥ 11 repetitions and 69 patients (55%) performed < 11 repetitions. Comparison of exercise tolerance, HRQoL, physical activity level, and pulmonary function between the patients performed below and above of 11 repetitions in 30 s-STST is shown in Table 3. Patients performed < 11 repetitions in 30 s-STST had worse performance in 6MWT, worse scores in all 8 sub-scales of SF-36 except "mental health", lower physical activity level, and worse pulmonary function except FVC and FEV_1.

6MWT classified 38% of patients as asymptomatic and 62% of patients as symptomatic. Although this ratio was 45 to 55% for 30 s-STST, McNemar test revealed that it did not significantly differ between 6MWT and 30 s-STST ($\chi^2 = 1.750$, $p = 0.186$), further supporting the fact that both tests have similar discriminative properties for identifying the symptomatology of patients.

Discussion

Our study demonstrated that walking less than 450 m in 6MWT or performing less than 11 repetitions in 30 s-STST indicates increased symptom burden and functional impairment in patients with AF. Exercise tolerance, HRQoL, physical activity level, and pulmonary function are significantly impaired in patients below these cut-off values, compared to those above the values. 6MWT and 30 s-STST have similar discriminative ability in identifying the symptomatology of patients. In this study, we proposed two practical measures for objectively determining symptom burden and functional status in patients with AF.

Functional status is a multidimensional concept that can be defined as an individual's ability to provide necessities of daily life without symptoms [23]. It is an important determinant of HRQoL in patients with AF [4, 13]. In the literature, various instruments were used for evaluating functional status and symptomatology in these patients, including EHRA score, NYHA functional classification, Canadian Cardiovascular Society classification, or the Duke Activity Scale Index. Studies also propose that objective approaches such as 6MWT or cardiopulmonary

Table 2 Comparison between the patients who walked ≥ 450 m and < 450 m in 6MWT

	Patients who walked ≥ 450 m in 6MWT (n = 48)	Patients who walked < 450 m in 6MWT (n = 77)	P value
30 s-STST (reps)	11.90 ± 1.98	9.10 ± 2.44	< 0.001
SF-36 (0–100)			
Physical function	76.04 ± 17.50	49.81 ± 22.92	< 0.001
Role-physical	85.94 ± 31.33	51.62 ± 46.65	< 0.001
Role-emotional	96.53 ± 12.38	72.73 ± 42.48	< 0.001
Vitality	62.71 ± 15.64	51.75 ± 21.18	0.002
Mental health	67.33 ± 1 5.80	62.44 ± 17.18	0.113
Social functioning	92.27 ± 14.47	75.57 ± 27.88	< 0.001
Bodily pain	79.19 ± 17.90	69.48 ± 26.79	0.017
General health	62.17 ± 17.31	51.97 ± 16.67	0.001
Physical activity			
MET.min/week	1215 ± 1204	737 ± 836	0.011
Low PA level (n)	12 (25%)	44 (57%)	0.002
Moderate PA level (n)	32 (67%)	30 (39%)	$\chi^2 = 12.434$
High PA level (n)	4 (8%)	3 (4%)	
Spirometry			
FVC (%)	91.10 ± 16.08	82.62 ± 20.33	0.017
FEV_1 (%)	92.31 ± 18.90	83.57 ± 21.93	0.025
PEF (%)	79.72 ± 18.31	67.85 ± 25.65	0.003
MIP (cmH_2O)	72.02 ± 25.63	59.19 ± 19.82	0.004
MEP (cmH_2O)	90.38 ± 28.21	75.03 ± 20.57	0.001

FVC forced vital capacity, *FEV_1* forced expiratory volume in 1 s, *MIP* maximum inspiratory pressure, *MEP* maximum expiratory pressure, *PA* physical activity, *PEF* peak expiratory flow, *SF-36* Short Form-36, *6MWT* 6-min walk test, *30 s-STST* 30 s sit-to-stand test

Table 3 Comparison between the patients who performed ≥ 11 repetitions and < 11 repetitions in 30 s-STST

	Patients who performed ≥ 11 repetitions in 30 s-STST ($n = 56$)	Patients who performed < 11 repetitions in 30 s-STST ($n = 69$)	*P* value
6MWT (m)	469 ± 66	357 ± 88	< 0.001
SF-36 (0–100)			
Physical function	76.25 ± 16.30	46.59 ± 21.99	< 0.001
Role- physical	82.59 ± 32.31	50.36 ± 48.03	< 0.001
Role- emotional	91.07 ± 24.20	74.40 ± 42.06	0.010
Vitality	62.95 ± 16.34	50.29 ± 20.82	< 0.001
Mental health	65.93 ± 15.39	63.01 ± 17.82	0.336
Social functioning	90.92 ± 15.33	74.73 ± 28.73	< 0.001
Bodily pain	83.79 ± 16.89	64.62 ± 25.82	< 0.001
General health	61.77 ± 16.84	51.12 ± 16.79	0.001
Physical activity			
MET.min/week	1071 ± 932	779 ± 1058	0.002
Low PA level (*n*)	17 (30%)	39 (57%)	0.010
Moderate PA level (*n*)	36 (65%)	26 (37%)	$\chi^2 = 9.146$
High PA level (*n*)	3 (5%)	4 (%6)	
Spirometry			
FVC (%)	88.64 ± 17.38	83.53 ± 20.44	0.143
FEV_1 (%)	90.00 ± 20.06	84.32 ± 21.89	0.140
PEF (%)	79.11 ± 19.48	66.77 ± 25.63	0.004
MIP (cmH_2O)	73.76 ± 22.79	56.01 ± 19.94	< 0.001
MEP (cmH_2O)	88.50 ± 26.72	75.03 ± 20.57	0.002

FVC forced vital capacity, *FEV_1* forced expiratory volume in 1 s, *MIP* maximum inspiratory pressure, *MEP* maximum expiratory pressure, *PA* physical activity, *PEF* peak expiratory flow, *SF-36* Short Form-36, *6MWT* 6-min walk test, *30 s-STST* 30 s sit-to-stand test

exercise test (CPET) may be used to evaluate functional status despite they are not an exact measure of functional status [11, 24]. EHRA score, Canadian Cardiovascular Society classification or NYHA functional classification provides an instant discrimination between the patients having different degrees of symptom burden and functional impairment, which may help clinical decisioning. However, perception of symptoms may vary from patient to patient. For example, females may tend to perceive their symptoms more intensely than men. Lower social status, poor self-assessed health, and high levels of chronic distress are also associated with worse symptom perception [25]. In our study, 73% of our patients were symptomatic according to EHRA score. However according to objective measures, i.e., 6MWT and 30 s-STST, 62% and 55% of patients were symptomatic, respectively. This finding suggests that subjective measures may overestimate the symptomology of patients.

One way of interpreting a single measurement of 6MWT is to compare the distance walked by a patient to a reference value obtained from healthy individuals. However, these reference values may significantly differ. For example, reference value of 6MWT for healthy adults is reported as 631 m by Troosters et al. [26], and 571 m by Casanova et. al. [27]. More specific reference values are reported for various age groups and genders, but it may be difficult to find a value that is appropriate to demographical characteristics of an individual being evaluated. On the other hand, cut-off values calculated for specific diseases enable instant and practical interpretation of a single measurement of 6MWT. Most of the studies investigating such values aimed to provide a practical way for identification of the patients at high risk of morbidity or mortality. Pinto-Plata et al. showed that in patients with severe COPD, walking < 300 m in 6MWT indicates higher risk of mortality and higher chance of being hospitalized [28]. In the BODE index, which is developed for prediction of mortality in patients with COPD, the level of impairment in exercise capacity is determined according to cut-off values of 350 m, 250 m, and 150 m in 6MWT [29]. Similarly in patients with heart failure, first Bittner et al. and then Rostagno et al. showed that 6MWT distance of < 300 m indicates higher risk of morbidity and mortality [7, 30]. In this study, we aimed to determine cut-off values for functional impairment, and we found that walking < 450 m in 6MWT indicates worse functional status. It will not be appropriate to directly compare our cut-off value of 450 m to those determined for various prognostic events. However, it is seen that the cut-off values indicating high risk of mortality or morbidity are much lower than 450 m. Cardiorespiratory fitness is one of the major determinants of general health. Higher cardiorespiratory fitness is directly associated with lower risk of all-cause mortality and cardiovascular disease-related events [31]. A decrease in the cardiopulmonary fitness that is able to significantly affect mortality risk will have a more pronounced impact on 6MWT. This may explain why prognostic cut-off values in the literature are much lower compared to 450 m of our study. On the other hand, studies that investigated cut-off values for identifying impaired functional status report findings similar to ours. Morales et al. [32] demonstrated that walking below 450 m in 6MWT is associated with severely reduced exercise capacity (VO_2peak < 14 ml/kg/min) in patients with heart failure. In addition, they reported AUC of 0.83 for the discriminative ability of 6MWT. Similarly, Pulz et al. [33] showed that a cut-off value of 490 m in 6MWT is indicative of severely reduced exercise capacity. AUC reported for discriminative ability of 6MWT was 0.89 in their study. AUC for the discriminative ability of 6MWT and 30 s-STST in our study was 0.75 for both tests which is slightly lower compared to those obtained in heart failure patients. This is not surprising since in those studies authors investigated the ability of 6MWT in predicting another objective measure, i.e., CPET. It is expected that association between two objective measures will be much stronger compared to that between an objective and a subjective measure, as in our study. Nevertheless, both 6MWT and 30-s STST had "acceptable" discrimination for asymptomatic and symptomatic patients.

Sit-to-stand tests have become increasingly popular in both clinical and research setting for quantifying the physical performance in various cardiopulmonary diseases due to their practicality. Among them, COPD is the most common condition in which STSTs are utilized [8]. We detected a "moderate" relationship between 30 s-STST and 6MWT in patients with AF with a correlation coefficient of 0.58, which is similar to those reported in patients with COPD (0.65) [15] and pulmonary hypertension (0.66) [10]. Additionally, 30 s-STST and 6MWT yielded similar AUCs for discriminating the symptomatology of the patients. Both findings support the fact that 30 s-STST and 6MWT will provide results in parallel with each other when applied for evaluating functional impairment in patients with AF. However, interpreting a single measurement is also a problem for STSTs, as in 6MWT. There are several studies that investigated the reference or cut-off values for 30 s-STST, but the literature is rather limited in this context. Reference values of 30 s-STST are reported as 12–17 repetitions for women and 14–19 repetitions for men in healthy adults aged 60–65 years [34]. It is also demonstrated that performing below these average values (< 12 for women and < 14 for men) is associated with increased risk of fall. Another study reports that performing > 15 and > 17 repetitions in 30 s-STST by women and men, respectively, is required for maintaining physical independence later in life [35]. Again, comparing our cut-off value of 11 repetitions to those reported for heathy individuals will not be ideal. However, it is seen that average of 30 s-STST of our entire cohort is 10 repetitions, which is way lower than recommend values for maintaining physical independence in healthy individuals. This could be interpreted as AF patients in general are already at risk for an impairment in their functionality. In addition to this, performing under 11 repetitions in 30-s STST may further increase this risk in patients with AF. We believe that STSTs recently have become more important for clinicians and researchers. As a result of the COVID-19 pandemic, many management and follow-up strategies for chronic diseases are transitioning into remote models. A recent study calling for action for cardiac telerehabilitation during COVID-19 era emphasizes the importance of remote patient assessment for setting rehabilitation goals [36]. Preliminary results support that STSTs are feasible and reliable to be applied remotely in home-setting [37]. These tests may be remotely applied to patients with AF as well to monitor their functional status at home, and the cut-off value of 11 repetitions may be considered as an important risk indicator while interpreting test results.

Our sub-groups analysis revealed that cut-off values of 6MWT and 30 s-STST also provide a significant discrimination in terms of HRQoL, physical activity participation, and pulmonary function in patients with AF. As we discussed earlier, symptom burden and functional status are the major predictors of HRQoL. As the EHRA score of patients increases, HRQoL decreases [13]. Consequently, it is not surprising to detect a significant difference in HRQoL between the patients above and below our cut-off values. Similar to HRQoL, physical activity level of symptomatic patients is significantly lower compared to asymptomatic patients. Health benefits of physical activity for both general population and chronic conditions are well established in the literature. Higher level of physical activity is associated with better general health. On the other hand, individuals with better health condition are more willing to participate in physical activity [38]. This suggests that there may be a two-way relationship between physical activity and general health, which may also help explaining why symptomatic AF patients had lower physical activity level in the study. AF guidelines recommend that patients should be encouraged to undertake moderate-intensity exercise and remain physically active in their lives [1]. Our cut-off values may help identifying patients who need to be encouraged to participate in physical activity. AF is not regarded as a disease with direct pulmonary consequences. However, several studies report that AF may hinder pulmonary function of lungs by hemodynamic alterations that result in an increased backward pressure and congestion of the lungs [39]. Also, pulmonary function is another major factor dictating exercise tolerance and general health. In our study, spirometric variables are in their normal predicted ranges in the entire AF cohort. However, when we classify patients according to the cut-off values, it is seen that symptomatic patients also had worse pulmonary function. This finding supports the importance of pulmonary function in functionality and general health status of an individual. These significant differences of HRQoL, physical activity participation, and pulmonary function between the patients above and below the cut-off values further contribute to the discriminative ability of our cut-off values.

Limitations

In our study, we aimed to provide cut-off values for an objective and practical interpretation of the current symptomatology and functional impairment of AF patients. Consequently, cross-sectional design of this study did not allow us to investigate the ability of these cut-off values for predicting possible prognostic events, as in other studies in the literature. For example, EHRA score ≥ 2 is found to be associated with higher risk of hospitalization and bleeding episodes [13]. Future studies may investigate whether these cut-off values provide insights on the risks of such prognostic events.

Conclusion

In this study, we proposed cut-off values for interpreting the results of two frequently used functional tests in the clinical practice. In patients with AF, walking < 450 m in 6MWT or performing < 11 repetitions in 30 s-STST indicates increased symptom burden and functional impairment. Patients below these values have worse exercise tolerance, HRQoL, physical activity level, and pulmonary function, compared to those above the values. These values may help identifying the patients who may require adjustments in their routine treatment or those may benefit from additional rehabilitative approaches such as exercise training. In addition, patients may be motivated into becoming more physically active by objectively showing them their physical impairment via these cut-off values. Although 6MWT and 30 s-STST have similar discriminative ability for identifying the functional impairment in these patients, 30 s-STST is a much simpler test that can also be applied remotely in home-setting. This may place 30 s-STST in a more advantageous position considering telerehabilitation has especially raised during the era of COVID-19.

Declarations

Ethics approval The study was approved by the ethics committee of Izmir Bakircay University (study number: 172/2021), prospectively registered to ClinicalTrials.gov website (registration number: NCT04754360) and carried out according to the ethical guidelines of the 1975 Declaration of Helsinki.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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