Universidade de Aveiro Escola Superior de Saúde
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CÍNTIA DIAS DE BARROS

Pontos de corte do teste de 1-minuto sentar-levantar e da força muscular do quadricípite para detetar comprometimento funcional

Cut-offs of the 1-minute sit-to-stand test and quadriceps muscle strength to detect functional impairment

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Dissertação apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Fisioterapia, ramo Musculosquelético, realizada sob a orientação científica da Doutora Alda Marques, Professora Coordenadora da Escola Superior de Saúde da Universidade de Aveiro.

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O júri

Presidente	Professor Doutor Rui Jorge Dias Costa Professor Coordenador da Escola Superior de Saúde da Universidade de Aveiro
Arguente	Professora Doutora Madalena Gomes da Silva Professora Coordenadora da Escola Superior de Saúde do Instituto Politécnico de Setúbal
Orientadora	Professora Doutora Alda Sofia Pires de Dias Marques Professora Coordenadora da Escola Superior de Saúde da Universidade de Aveiro

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Palavras-chave Estado funcional; funcionalidade; pessoas saudáveis; avaliação; intervenção; força muscular.

Resumo

Enquadramento: O declínio do estado funcional está associado ao processo de envelhecimento, e é uma característica identificável, modificável e altamente relevante para a autonomia das pessoas. Contudo, a avaliação do estado funcional não é realizada rotineiramente na prática clínica e a identificação do seu comprometimento é muitas vezes desafiante.

Objetivo: Estabelecer pontos de corte para o teste de sentar-levantar de 1 minuto (1-min STS) e força muscular do quadricípite (FMQ) para identificar comprometimento funcional do membro inferior em pessoas saudáveis.

Métodos: Realizou-se um estudo transversal com pessoas saudáveis, com idade entre os 50 e 89 anos. A capacidade funcional foi avaliada com o teste 1-min STS, o teste de sentar-levantar de 5 repetições (5-STS) e a FMQ. Conduziu-se uma análise de curvas *receiver operating characteristic* (ROC) para explorar a capacidade do 1-min STS e QMS para discriminar o desempenho dos participantes no 5-STS, e calculou-se a área abaixo da curva (AUC).

Resultados: Foram incluídos 341 participantes (71% do sexo masculino; idade média 68 [61; 73] anos; índice de massa corporal 27 [24,7; 30,4] kg/m^2; 6,5% com comprometimento funcional). Os pontos de corte estabelecidos para baixo desempenho foram 25,5 repetições no 1-min STS e 24,8 kgf na FMQ. O 1-min STS teve uma discriminação excecional (AUC = 0,96), com 90% de especificidade, 91% de sensibilidade e precisão de 0,91 para discriminar o desempenho de pessoas saudáveis no 5-STS. A FMQ teve uma excelente discriminação (AUC = 0,79), com 66% de especificidade, 85% de sensibilidade e uma precisão de 0,51.

Conclusão: Os pontos de corte de 25,5 repetições no teste 1-min STS e 24,8 kgf na FMQ discriminam com precisão pessoas saudáveis com comprometimento funcional. Estes pontos de corte poderão auxiliar os profissionais de saúde a tomar decisões rápidas quando planeiam intervenções para prevenir e/ou diminuir a perda de funcionalidade do membro inferior.

Keywords Functional status; functionality; healthy people; assessment; intervention; muscle strength.

Abstract

Background: Functional status decline is associated with the aging process. It is an identifiable, modifiable and highly meaningful trait for people's autonomy. Assessment of functional status is, however, not implemented in routine clinical practice and identification of its impairment is often challenging.

Aim: To establish cut-off values for the 1-minute sit-to-stand test (1-min STS) and for the quadriceps muscle strength (QMS) to identify lower-limb functional impairment in healthy people.

Methods: A cross-sectional study was conducted with healthy people, aged between 50 and 89 years. Functional capacity was assessed with the 1-min STS, the 5-repetition sit-to-stand test (5-STS) and QMS. The receiver operating characteristic (ROC) analysis was used to explore the ability of the 1-min STS and QMS to discriminate participants' performance in the 5-STS, and the area under the curve (AUC) was calculated.

Results: A total of 341 participants (71% male; mean age 68 [61; 73] years; body mass index 27 [24.7; 30.4] kg/m^2; 6.5% with functional impairment) were included. Cut-off values established for low performance were 25.5 repetitions in the 1-min STS and 24.8 kgf for QMS. The 1-min STS had an outstanding discrimination (AUC = 0.96), with 90% specificity, 91% sensitivity and accuracy of 0.91 to discriminate the performance of healthy people in the 5-STS. QMS had an excellent discrimination (AUC= 0.79), with 66% specificity, 85% sensitivity and an accuracy of 0.51.

Conclusion: Cut-off values of 25.5 repetitions in the 1-min STS test and 24.8 kgf in QMS accurately discriminate healthy people with functional impairment. These cut-offs can now be used to help health professionals in their decision-making process when planning to prevent and/or avoid loss of lower-limb functioning.

Abbreviations and/or acronyms

1-min STS – 1-minute sit-to-stand test

5-STS – 5-repetitions sit-to-stand test

ACC – accuracy

ADLs – activities of daily living

AUC – area under the curve

BMI – body mass index

BPAAT – brief physical activity assessment tool

CCI – Charlson comorbidity index

CI – confidence interval

COPD – chronic obstructive pulmonary disease

FEV_1 – forced expiratory volume in one second

FVC – forced vital capacity

HADS – hospital anxiety and depression scale

LR+ – positive likelihood ratio

LR- – negative likelihood ratio

NPV – negative predictive value

PPV – positive predictive value

QMS – quadriceps muscle strength

ROC – receiver operating characteristic analysis

Sens. – sensivity

Spec. – specifity

SpO_2 – peripheral oxygen saturation

STROBE – strengthening the reporting of observational studies in epidemiology

WHO – World Health Organization

WHOQoL-BREF – World Health Organization quality of life questionnaire – short form

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1. Introduction

The World Health Organization (WHO) defines health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (1). During the aging process, even in healthy people, there is a decrease in muscle strength, muscle endurance, balance, flexibility, mobility and cognitive ability, which contribute to a decline in functional status and can be predictive of future health events (2-4).

Functional status is defined as an individual's ability to carry out the usual daily activities necessary to meet basic needs, fulfil usual functions and maintain health and well-being (5). It includes functional capacity, i.e., an individual's maximum capacity to perform daily life activities in a standardized environment; and functional performance, i.e., the activities people actually do during the course of their daily life (5). Functional capacity is related to what an individual can do in a 'standardised' environment, usually in a test situation, and hence reflects the environmentally adjusted ability of an individual (5, 6). Functional performance is defined as the physical, psychological, social, occupational, and spiritual activities that people do in the normal course of their daily life. These activities are the outcome of individual choice, i.e., they are activities people feel they need and want to perform, subject to the limits imposed by capacity, and generally requiring less than the functional capacity to be accomplished. The gap between capacity and performance provides a useful guide regarding what can be done to the environment of the individual to improve performance (7).

Functional decline is a term used to reflect the loss of an individual's ability to perform activities of daily living (ADLs) independently and safely (usually at home, in the community) and can be assessed with functional capacity or functional performance measures (3, 8-10). Functional decline can progress to functional limitations and eventually lead to disability (10, 11). In healthy people, the decline in functional status has been associated with an increased number of falls and fractures, hospitalizations and risk of mortality (2, 8, 9, 12). Therefore, functional status is highly meaningful for people's daily life and its impairment can be early identified and modified. It is known that, in particular, the decline in muscle strength has a direct impact on functional status and can lead to loss of independence in ADLs and decreased quality of life (2, 12). There is evidence of a decline in muscle strength (13) that may be attributable to age-related changes in neuromuscular contributors to strength, including decreased motor unit recruitment and increased fatty infiltration of muscle. Lower extremity function, as indicated by timed gait over a measured course and/or the ability and time to complete five repeated chair-stands, gives insight on the health status and disability risk of individuals (14, 15).

The 5-repetitions sit-to-stand test (5-STS) is a well-established and widely used measure to assess functional status (16). It can be quickly performed in any healthcare setting, requires minimal resources, is reproducible and provides information about an individual's functional prognosis (2, 16-20). The sit-to-stand movement is destabilizing in nature and mechanically demanding for the balance system, as the body quickly changes from a stable state sitting position to a position with a relatively small base of support and a high centre of mass, requiring the muscles of the lower limbs to be strengthened. It is, therefore, a task difficult to perform by many older healthy people, who are often seen to need a long time to perform the test (21, 22). A cut-off of 12.1 seconds for low performance in the 5-STS has been determined (16). The 5-STS has been applied in different contexts, namely with frail people, in a hospital context and with community-dwelling elderly people (17). This test has also shown an important role in predicting mortality risk in other populations, such as people with respiratory and Parkinson diseases (23-26). Evidence has, however, shown that the 5-STS has a potential ceiling effect in healthy people (27, 28). Therefore, other measures are needed to determine functional status impairment in this population.

The ability to get up from a sitting position is one of the most important measures of physical function, it is an essential activity for daily life and one of the most biomechanically demanding functional tasks (19, 20, 29, 30). Thus, other more demanding sit-to-stand tests might be an alternative measure to detect functional impairment in healthy people. The use of the 1-minute sit-to-stand test (1-min STS) as a measure of functional status has been increasing in research and clinical practice because it is also easy to implement and requires only limit space and equipment (18). It has been shown that the 1-min STS is a more stressful test to the cardiorespiratory system and demands a higher physical effort than the 5-STS (31), which might help to overcome the ceiling effect of the 5-STS in healthy people. However, there is no cut-off value available to identify functional impairment in the 1-min STS.

Moreover, quadriceps muscle strength (QMS) has been identified as the most important factor limiting an individual's ability to get up from a chair and is crucial for the performance of a variety of other ADLs (2, 32). In fact, muscle strength measures have been associated with loss of functional status and independence (2, 16, 18, 32-34). The literature has shown a decline in QMS and mobility in men and women from baseline to up to 3 years, and these parameters were predictors of increase in number of falls and mortality (35). Nevertheless, cut-off values to identify functional impairment through QMS are also missing.

Thus, this study aimed to establish the cut-off values for the 1-min STS and QMS to identify functional status impairment in healthy people.

2. Methods

This study is part of a large study entitled “GENIAL – genetic and clinical markers in COPD trajectory”, which was conducted in people with chronic obstructive pulmonary disease (COPD) and age and gender-matched healthy controls between September 2016 and June 2019.

2.1. Ethical considerations

Ethical approval was obtained from the ethics committees of the University of Aveiro (13APR’2016:8/2015), Administração Regional de Saúde do Centro, I.P. (3NOV’2016:64/2016), Centro Hospitalar do Baixo Vouga (22MAR’2017:777638), Hospital Pedro Hispano (17FEB’2017:10/CE/JAS), Hospital Distrital da Figueira da Foz (18JUL’2017) and Hospital da Misericórdia da Mealhada (9NOV’2018), and from the National Data Protection Committee (8828/2016). All participants provided written informed consents before any data collection. This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (36).

2.2. Study design

A secondary analysis of a cross-sectional study was conducted.

2.3. Participants

For the purposes of this study, only healthy controls, with an age between 50 and 89 years, and no missing data in the 5-STS were analysed.

Healthy people, older than 18 years old and presenting no chronic respiratory diseases were recruited from the community (e.g., day centres, civil parishes). People with the most prevalent age-related conditions, such as controlled arterial hypertension, dyslipidaemia and diabetes, were included to ensure maximum representativeness from community-dwelling people (37). This is in accordance with the World Health

Organization's definition of 'health' as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (38).

Exclusion criteria included: i) history of an acute cardiac or respiratory condition in the previous month; ii) presence of cardiac, musculoskeletal or neuromuscular diseases that impaired the ability to perform the assessments (e.g., amputation, Parkinson's disease); iii) signs of cognitive impairment and iv) history of neoplasic or immunological disease.

2.4. Data collection

Data collection was performed by trained staff (physiotherapists) with experience in collecting the outcome measures.

Assessment sessions took place in the Respiratory Research and Rehabilitation Laboratory (Lab3R), at the School of Health Sciences of University of Aveiro (ESSUA), or in the participating institutions. Initially, a brief description of the study purpose was provided by the researcher and time was given for the participant to read the information sheet, clarify any doubts and sign the informed consent. Then, a code was assigned to each participant to guarantee the confidentiality of their information.

A structured questionnaire was first used to collect sociodemographic (age and sex), anthropometric (height and weight measurements to compute body mass index – BMI) and general clinical (smoking habits, self-reported medication and comorbidities) data to characterise the sample. The severity of comorbid diseases was recorded and scored according to the Charlson comorbidity index (CCI) (39) and interpreted as: mild (CCI scores of 1–2), moderate (CCI scores of 3–4) or severe (CCI scores ≥5).

2.4.1. Patient reported outcome measures (PROMs)

All PROMs were applied using a supervised self-administration method, preceded by a brief explanation about the aim of each questionnaire or scale. Before applying the PROMs, formal permission for using the questionnaires was provided by each developer.

Brief physical activity assessment tool (BPAAT)

Self-reported physical activity level was assessed with the Portuguese version of the brief physical activity assessment tool (BPAAT), which comprises two questions regarding the frequency and duration of moderate and vigorous physical activity undertaken in a usual week (40, 41). Each question is rated in a 0–4 scale. A total score was calculated (range 0 to 8) and interpreted as "insufficiently active" (scores<4) or "sufficiently active" (scores≥4) (40). The BPAAT showed moderate inter-rater reliability (k=0.53, 95%CI: 0.33 – 0.72) in adult people (40) and moderate correlations ($0.394 \leq \rho \leq 0.435$, $p< 0.05$) with accelerometry (41).

Quality of life questionnaire – short form (WHOQoL-BREF)

The WHOQoL-BREF is a short version of the WHOQoL-100 for use in situations where time is restricted. It is a cross-cultural measure of subjective perspectives which consists of 26 questions and assesses four domains of quality of life: physical, psychological, social and environmental. Each item is measured from 1 to 5 on a Likert scale with varying scale response anchors, where higher values represent higher quality of life. One example of item is “How much do you enjoy life?”, rated on the following response options: (1) not at all, (2) a little, (3) a moderate amount, (4) very much, and (5) an extreme amount. The scores are transformed on a scale from 0 to 100 to enable comparisons to be made between domains composed of unequal numbers of items (42).The WHOQoL-BREF is one of the most known generic questionnaires for the assessment of quality of life in both healthy and ill populations (43, 44). It presented “almost very good” to goodness of fit (comparative fit index = 0.949 and Tucker-Lewis index = 0.943) and an adequate internal consistency in elderly people in the community when comparing in between WHOQoL-BREF domains (Cronbach’s α = 0.64-0.90; composite reliability: 0.59-0.88) (42, 45).

Hospital anxiety and depression scale (HADS)

Symptoms of anxiety and depression were assessed using the Portuguese version of the HADS (46). This scale contains 14 questions, seven questions measuring symptoms of anxiety (HADS-A) and seven measuring symptoms of depression (HADS-D). Each question has four possible answers ranging from 0 to 3, so the possible scores range from 0 (the individual has no depression or anxiety) to 21 (maximum depression/anxiety reported by the individual). Scores inferior to 8 were considered “normal values”, between 8 and 10 were interpreted as “mild values”, between 11 and 14 as “moderate values” and between 15 and 21 as “ severe values” of anxiety and depression symptoms (46, 47). The scale has shown to have a good test-retest reliability ($ICC_{2,1}$=0.71-0.90) and be valid when compared with The Beck Depression Inventory (r=0.73) and Spielberger’s State and Trait Anxiety Inventory (r=0.71) within the general population in primary care (48).

2.4.2. Clinical measurements

Vital signs and peripheral oxygen saturation (SpO_2) were initially assessed to establish baseline safety and monitor participants. Blood pressure was measured using a portable automatic sphygmomanometer which also provided the heart rate (Medel Elite, S.Polo di Torrile, Italy); SpO_2 was monitored using a pulse oximeter (Konica Minolta, Pulsox-300i, United Kingdom), and the respiratory rate was assessed using a stopwatch by counting the number of respiratory cycles taken in one minute.

Lung function was assessed with a portable spirometer (MicroLab 3535, CareFusion, Kent, UK) according to standardized guidelines (49). The most frequently measurements considered in spirometry, i.e., forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and FEV_1/FVC ratio were registered (50).

The isometric handgrip strength was measured as recommended by the American Society of Hand Therapists using a hydraulic-hand dynamometer (Model 12-0241 Lite, Fabrication Enterprises Inc., White Plains, NY, USA) (51). This is a measurement of mobility and quality of life in healthy people (52). Handgrip strength was assessed at the dominant hand with the elbow at 90º flexion (Figure 1). Three attempts were performed and the highest value was retained for analysis and was interpreted according to reference values for this population (53, 54).

Figure 1 - Demonstration of the isometric handgrip strength using the hydraulic-hand dynamometer.

Additionally, to assess lower-extremity muscle strength in older adults, QMS was assessed as peak torque during an isometric contraction of the quadriceps using a hand-held dynamometer (Hoggan MicroFET2 Muscle Tester, Model 7477, Pro Med Products, Atlanta, GA), accordingly to the proposed protocol (32). Participants were asked to sit on a chair with the knee flexed at 70º. The hand-held dynamometer was placed in the anterior tibia region, 5 cm above the lateral malleolus form the dominant lower limb, and the participant was instructed to stretch the knee over a 4-5 second period against the resistance applied (Figure 2). QMS measurements were evaluated on participants' dominant side; three attempts were performed with a recovery period of 30 seconds to avoid fatigue, and the highest value was retained for analysis (32). These values were interpreted according to the reference values for this population (32). This measure has shown excellent test-retest reliability ($ICC_{3,1}$=0.932-0.984) in older adults (55) and be valid when compared with isometric Biodex System 3 dynamometer (r = 0.57-0.86; p <0.05) (56) .

Figure 2 - Demonstration of the quadriceps muscle strength assessment using the hand-held dynamometer.

Participants' functional capacity was assessed with the 5-STS and the 1-min STS tests. A straight-backed armless chair (floor to seat height 48 cm), with a hard seat, stabilized against a wall and knees and hips flexed to 90º was used to perform both tests (19). For the 5-STS, participants were instructed to sit on the chair, cross their arms at the chest and then stand up all the way and sit down, as fast as possible, for five times without using the arms (Figure 3), according to the proposed protocol (21). The 5-STS has shown an excellent test-retest reliability ($ICC_{3,1}$ 0.957) (16). A cut-off of 12.1 seconds in the 5-STS has been established for impaired performance and was used to classify participants in our study as having (i.e., 5STS>12.1 seconds) or not having (i.e., 5STS≤12.1 seconds) impairment (15).

Figure 3 – Demonstration of the 5-repetition sit-to-stand test.

In the 1-min STS, participants were instructed to place their hands stationary on the hips, without using the hands or arms to assist movement, and were instructed to stand up all the way and sit down, as many times as possible, for 1 minute (Figure 4), as previously proposed and was interpreted according to reference values (18). The 1-min STS has shown a good test-retest reliability ($ICC_{3,1}$ 0.80-0.98) (19). In both sit-to-stand tests, the best performance of three trials was considered for the analysis.

Figure 4 – Demonstration of the 1-minute sit-to-stand test.

2.5. Data analysis

Statistical analyses were performed using IBM SPSS Statistics version 28.0 (IBM Corporation, Armonk, NY, USA) and plots created using GraphPad Prism version 8.0 (GraphPad Software, Inc., La Jolla, CA, USA). The level of significance was set at 0.05. Descriptive statistics (i.e., absolute and relative frequencies, mean±standard deviation and median [interquartile range]) were used to describe the sample. Normality of data distribution was explored with the Kolmogorov-Smirnoff test. Then, independent t tests, Mann-Whitney U tests and chi-squared tests were used to compare sociodemographic, anthropometric and general clinical characteristics between the healthy controls performing the 5-STS equal or below 12.1 seconds and those above the cut-off.

The ability to discriminate participants' performance in the 5-STS was assessed for the 1-min STS and QMS using receiver operating characteristic analysis (ROC). The area under the curve (AUC), sensitivity, specificity, positive predictive value, negative predictive value, accuracy, positive likelihood ratio and negative likelihood ratio were calculated (57, 58). Sensitivity is defined as the proportion of positives which are identified correctly as such, or the probability of a positive test, also known as the true-positive rate. Specificity is defined as the proportion of negatives which are identified correctly as such, or the probability of a negative test, also known as the true-negative rate. When evaluating the success of a test, the positive predictive value is the probability that the condition is present when the test is positive. Similarly, the negative predictive value is the probability that the condition is not present when the test is negative. Accuracy is the proportion of true results from the total number of participants tested (57, 58). All these calculations are described in Table 1. The discriminative ability of the ROCs was interpreted as: AUC=0.5 - "no discrimination", 0.5<AUC≤0.6 – "poor discrimination", 0.6<AUC≤0.7 – "acceptable discrimination", 0.7<AUC≤0.8 – "excellent discrimination", AUC>0.9 – "outstanding discrimination" (59). The optimal cut-off values were identified by the highest Youden index (57).

Table 1 - Equations used to calculate different parameters related to the quality of the analysis of the ROC curves.

$$\text{Sens.} = \frac{\text{true positives}}{[\text{true positives } + \text{ false negative}]}$$
$$\text{Spec.} = \frac{\text{true negatives}}{[\text{ true negatives } + \text{ false positives}]}$$
$$\text{PPV} = \frac{\text{true positives}}{[\text{true positives } + \text{ false positives}]}$$
$$\text{NPV} = \frac{\text{true negatives}}{[\text{true negatives } + \text{ false negatives}]}$$
$$\text{ACC} = \frac{[\text{true positives } + \text{ true negatives}]}{[\text{true positives } + \text{ false positives } + \text{ false negatives } + \text{ true negatives}]}$$
$$\text{LR+} = \frac{\text{sensitivity}}{1 - \text{specificity}}$$
$$\text{LR}- = \frac{1 - \text{sensitivity}}{\text{specificity}}$$

Legend: ACC – accuracy; NPV – negative predictive value; PPV – positive predictive value; LR+ –positive likelihood ratio; LR- – negative likelihood ratio; Sens.- sensitivity; Spec. – specificity.

3. Results

Four hundred and two healthy participants were recruited for the GENIAL study. From these, forty were excluded since they did not match the inclusion/exclusion criteria and three dropped out the assessment. Hence, in total three hundred and fifty-nine healthy people were included. For this study, ten participants were excluded due to their age and eight participants due to missing data. A total of three hundred and forty-one participants met the inclusion criteria for this analysis. A flow diagram of the recruited and included sample is provided in Figure 5.

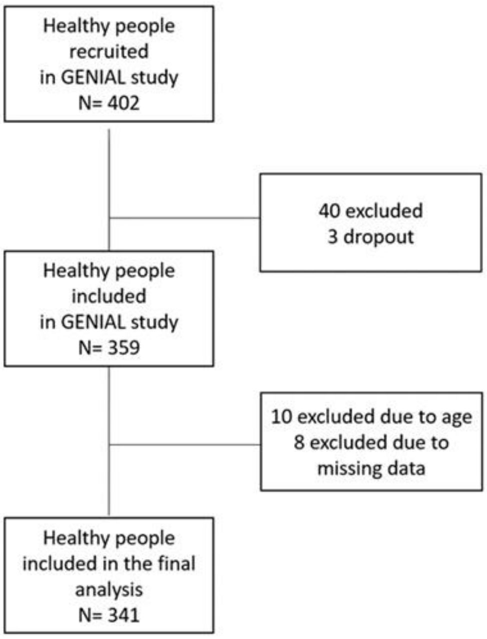

Figure 5 – Flow diagram of participants in the GENIAL study and included in the analysis.

Included participants were mostly male (71%), had a median age of 68 [61; 73] years old and a median BMI of 27 [24.7; 30.4] kg/m^2, a mild CCI total score (51.6%) and were mostly insufficiently active (64%). A small part of the sample took more than 12.1 seconds to perform the 5-STS (n=22; 6.5%) and were therefore classified has having functional impairment. People performing the 5-STS in more than 12.1 seconds were significantly older, presented a higher BMI and CCI total score, were more anxious (although not within clinically relevant values), had worse self-perceived physical health and social relationships, lower muscle strength and a worse performance in the 1-min STS than those performing the 5-STS in less or equal to 12.1 seconds. Participants' characteristics are summarized in table 2.

Table 2 – Sample characterization for the total sample and for each subgroup, according to the performance in the 5-repetition sit-to-stand test.

	Total sample (n=341)	5STS ≤ 12.1s (n=319)	5STS > 12.1 s (n=22)	p
Age, years	68.0 [61.0; 73.0]	67.0 [60.0; 73.0]	74.0 [69.0; 83.0]	**<0.001**
Sex (male), n (%)	241 (70.7%)	230 (72.1%)	11 (50%)	**0.032**
BMI, kg/m2	27.3 [24.7; 30.4]	27.2 [24.6; 29.9]	30.2 [27.3; 33.0]	**0.005**
Lung function				
FEV_1, %predicted	102.0 [90.5; 113.0]	103.0 [92.0; 113.0]	95.5 [84.0; 105.0]	0.085
FVC, %predicted	96.0 [85.0; 109.0]	96.0 [86.0; 109.0]	93.0 [78.0; 105.0]	0.235
CCI, total score	2.0 [2.0; 3.0]	2.0 [2.0; 3.0]	4.0 [3.0; 4.0]	**<0.001**
Comorbidities, n (%)				
Arterial hypertension	167 (49.0%)	157 (49.2%)	10 (45.5%)	0.827
Diabetes	59 (17.3%)	54 (16.9%)	5 (22.7%)	0.558
Dislipidemia	137 (40.2%)	128 (40.1%)	9 (40.9%)	1.000
BPAAT (sufficiently active), n (%)	156 (46.0%)	147 (46.2%)	9 (42.9%)	0.824
HADS anxiety score	5.0 [3.0; 7.0]	5.0 [3.0; 7.0]	8.0 [5.0; 10.0]	**0.003**
HADS depression score	4.0 [2.0; 7.0]	4.0 [2.0; 7.0]	5.0 [3.0; 9.0]	0.148
WHOQoL-Bref score				
Physical health	56.0 [56.0; 63.0]	56.0 [56.0; 63.0]	50.0 [44.0; 56.0]	**0.001**
Psychological health	69.0 [56.0; 75.0]	69.0 [63.0; 75.0]	66.0 [56.0; 72.0]	0.181
Social relationships	75.0 [56.0; 81.0]	75.0 [56.0; 81.0]	56.0 [50.0; 75.0]	**0.006**
Environmental health	69.0 [63.0; 81.0]	69.0 [63.0; 81.0]	69.0 [59.5; 75.0]	0.129
Handgrip strength, kg	36.0 [28.0; 44.0]	37.0 [30.0; 44.0]	28.0 [18.0; 32.0]	**<0.001**
QMS, kgf	27.6 [22.0; 34.5]	27.9 [22.8; 34.8]	19.6 [15.1; 24.1]	**<0.001**
5-STS, seconds	7.5 [6.2; 9.3]	7.4 [6.2; 9.0]	14.3 [13.6; 15.8]	**<0.001**
1-min STS, repetitions	34.0 [28.0; 41.0]	35.0 [30.0; 42.0]	20.0 [14.0; 22.0]	**<0.001**

Data are presented as median [Q25; Q75] or number (percentage). Bold denotes a statistically significant difference between people taking ≤ 12.1s or > 12.1s in the 5-STS.

Legend: 1-min STS, 1-minute sit-to-stand; 5-STS, 5-repetition sit-to-stand; BMI, body mass index; BPAAT, Brief physical activity assessment tool; CCI, Charlson comorbidity index; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; HADS, hospital anxiety and depression scale; QMS, quadriceps muscle strength; WHOQoL-Bref, World Health Organization quality of life questionnaire – short form.

The 1-min STS test presented an outstanding discriminative ability (AUC = 0.96) for the performance in the 5-STS test (Figure 6).

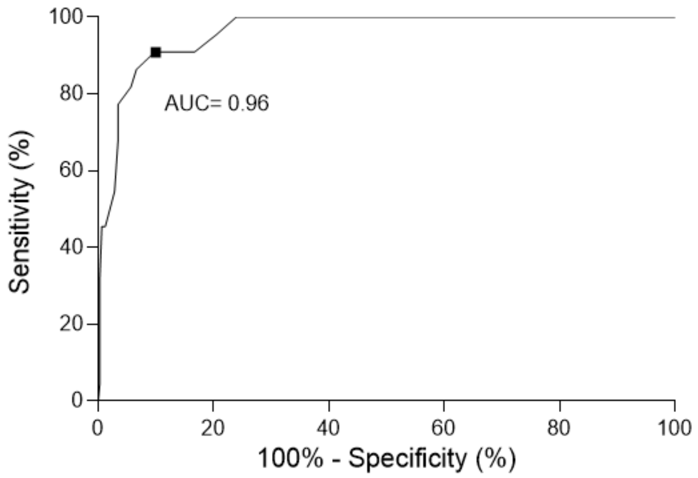

Figure 6 – Receiver operating characteristics (ROC) curve demonstrating the ability of the 1-minute sit-to-stand test to discriminate between healthy people with and without functional impairment (>12.1s or ≤12.1s) in the 5-repetitions sit-to-stand test. The point identifies the optimal cut-off identified by the Youden index.

A cut-off of 25.5 repetitions showed 90% specificity, 91% sensitivity and an accuracy of 0.91 to discriminate between people performing ≤12.1s or >12.1s in the 5-STS test (Table 3).

Table 3 - Cut-off values, specificity, sensitivity and accuracy

Cut-off	AUC	95%CI	p	Sens.	Spec.	PPV	NPV	Acc.	LR+	LR-
1-min STS 25.5	0.96	0.94; 0.99	<0.001	0.91	0.90	0.41	0.99	0.91	9.28	0.10
QMS 24.8	0.79	0.69; 0.89	<0.001	0.85	0.66	0.08	0.99	0.51	2.46	0.23

Legend: 1-min STS, 1-minute sit-to-stand; 95%CI, 95% confidence interval; Acc., Accuracy; AUC, area under the curve; LR+, Positive likelihood ratio; LR-, Negative likelihood ratio; NPV, Negative predictive value; PPV, Positive predictive value; QMS, quadriceps muscle strength; Sens., sensitivity; Spec., specificity.

An excellent discriminative ability (AUC = 0.79) for functional performance was found with the QMS (Figure 7).

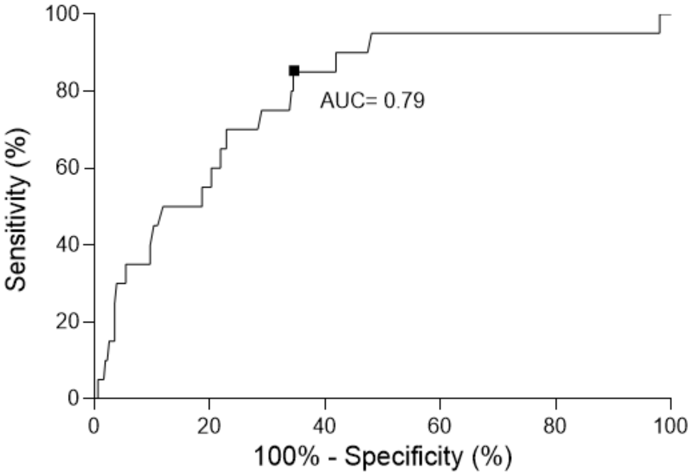

Figure 7 – Receiver operating characteristics (ROC) curve demonstrating the ability of quadriceps muscle strength to discriminate between healthy people with and without functional impairment (>12.1s or ≤12.1s) in the 5-repetitions sit-to-stand test. The point identifies the optimal cut-off identified by the Youden index.

A cut-off of 24.8 kgf was found to have 66% specificity, 85% sensitivity and an accuracy of 0.51 to discriminate between people performing ≤12.1s or >12.1s in the 5-STS test (Table 2).

4. Discussion

This study investigated the cut-off values of the 1-min STS and QMS to determine functional impairment in healthy people. Our study provides important evidence of the potential of the 1-min STS and QMS to be used as measures to help identifying people with functional status impairment. The optimal cut-off values found were less than 25.5 repetitions for the 1-min STS and less than 24.8 kgf for QMS.

In the present study, we explored whether the 1-min STS and QMS were adequate measures to identify functional impairment in healthy people. Both measures showed excellent results in the ROC analysis, however, the 1-min STS test yielded the highest AUC (AUC = 0.96). This was expected since there is a good discriminative power between repetitions-based (5-STS) and time-based (1-min STS) sit-to-stand tests (29), while only moderate to weak associations have been described between the 5-STS test and QMS in different populations (26, 60).

Although cut-off values have never been determined for healthy people, the cut-off value found for the 1-min STS test (25.5 repetitions) is consistent with the lower limit of normality (21 to 23 repetitions, depending on age and gender) found in a previous study that established reference values for the 1-min STS test (61), strengthening the use of our cut-off and its applicability to populations other than the Portuguese.

For the QMS, cut-off values of 18kg for men and 16kg for women have been proposed to identify sarcopenia in healthy people aged 60 and over (62). The cut-off found in our study was higher (24.8 kgf) but it was established for functional status, not for sarcopenia. Sarcopenia is defined by age-associated loss of muscle mass and function, but functional impairment may appear before sarcopenia occurs (63). Other relevant cut-offs for isometric QMS have been established for people with chronic respiratory diseases – 14.8kg in women and 25.3kg in men (64). Our cut-off values are similar to those proposed for men and, indeed, our sample was mostly composed of men.

Participants with functional impairment were found to be older, have a higher BMI, more comorbidities and symptoms of anxiety, worse self-perception of physical health and social relationships, lower muscle strength and worse performance in the 1-min STS. Similar findings have been previously reported (61). Since most of these characteristics are preventable and modifiable, attention to interventions in this population should be given. In fact, preventive strategies against loss of functional status have shown excellent results with healthy elderly people in the community (65-68). Intervention programs, centred on multicomponent and progressive aerobic, endurance, balance and flexibility exercises, have shown preventive effects in loss of independence, functional decline, social participation and quality of life, and even in preventing the syndrome of fragility (68-75). It is, therefore, important that health professionals assess functional status and use the cut-off values found to establish the individuals who need intervention or prevention programs, which should include different types of stimuli, such as to improve muscle strength and mass, cardiovascular function, gait and balance ability, and cognitive ability, in order to promote a greater increase in independence and capacity to perform daily activities (72, 74, 76, 77).

Moreover, the decline in the 1-min STS test and QMS has been associated with physical disability in ADLs and functional limitations (35, 64), and impacts the number of falls and fractures and the risk of mortality (35, 78). These findings show how meaningful and impactful functional status impairments might be for people's daily life, which reinforces the need to assess this domain routinely in clinical practice. We found cut-off values for the healthy population aged 50 to 89 years that allow healthcare professionals to identify functional impairment simply and easily, in any setting, and guide appropriate care and/or preventive interventions to minimise or avoid loss of independence. Nevertheless, we must remember that functional status is a multidimensional outcome and, thus, a comprehensive assessment is important.

4.1 Strengths and limitations

This study presents some strengths and limitations that need to be acknowledged. First, we have included a relatively large and healthy sample size (only 22 people presented functional status impairment according to the cut-off established for the 5-STS), which reinforces the power of our results. Second, we did not stratify the analysis by sex or age decade (e.g., 50-59, 60-69, 70-79 and 80-89 years old) hence, it is uncertain if the proposed cut-off values remain the same for male and female or across decades. In fact, our sample was matching a group of people with COPD, hence only around 30% of participants were women, it is therefore possible that our results are more suitable for men. Nevertheless, the cut-off value of the 5-STS that was used as an anchor is a general cut-off value, not stratified by age or sex. Lastly, being healthy was self-reported by participants according to how they felt, which is in line with the WHO's definition (1). Although there was no formal medical evaluation and comorbidities and medication were self-reported, the satisfactory results obtained in all tests and questionnaires (within normality) certify the health status of the population.

4.2 Future work

Future studies that explore the external validity of these cut-offs are needed, namely in other cohorts and exploring its utility in predicting other meaningful outcomes. Moreover, functional status is a multidimensional outcome and, therefore, a comprehensive assessment is required since individuals might present impairment in only a part of its components. Future studies should explore the inclusion of other measures of functional status, such as the timed up and go test, gait speed or short physical performance battery, which have been shown to be valid measures to identify deficits in balance and functional mobility in older adults, and appear to be related with independence (79-81). This more comprehensive assessment could further be explored in combination with the cut-offs found in this study to potentially developed an algorithm to help health professionals identifying individuals with functional status impairment or at risk of impairment, hence guiding the use of rehabilitation of preventive measures.

5. Conclusions

In summary, the present study established the cut-off values for the 1-min STS test (25.5 repetitions) and QMS (24.8 kgf) to identify functional impairment in healthy adults. An excellent to outstanding discriminative ability to identify people with low performance with these simple and quick functional status measures was found. These cut-off values will help health professionals to detect functional impairment in healthy people through quick, easy, and resource-saving tests. Cut-off values can now be used in any setting to guide clinical-decision making to optimise this treatable trait, so that appropriate care and/or preventative interventions can be provided.

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Appendix I – Participant information sheet

Folha de informação ao participante

O Sr./Sra. está a ser convidado/a para participar no estudo de investigação clínica intitulado: "GENIAL – Marcadores genéticos e clínicos na trajetória da DPOC". Mas, antes de decidir, é importante que compreenda porque é que a investigação está a ser realizada e o que é que a mesma envolve. Por favor, leia a informação com atenção e discuta a sua participação com outros, se assim o entender. Se houver algo que não esteja claro para si ou necessitar de informação adicional, por favor pergunte aos investigadores (contactos no final deste documento). Use o tempo que precisar para decidir se deseja ou não participar.

Muito obrigado desde já por ler a informação.

Qual é o propósito do estudo?

Este estudo visa determinar o papel das mutações genéticas associadas ao desenvolvimento e trajetória da Doença Pulmonar Obstrutiva Crónica (DPOC) e identificar os marcadores clínicos (e.g., dispneia; número de exacerbações; função pulmonar; tolerância ao exercício) capazes de detetar episódios de exacerbações agudas da DPOC (episódios de agravamento dos sintomas respiratórios que é acima da sua variação normal do dia-a-dia e leva à alteração da medicação).

A suscetibilidade para desenvolver DPOC varia consideravelmente entre indivíduos, sugerindo que outros fatores de risco para além do tabaco (principal fator de risco) podem influenciar o desenvolvimento da doença. Estudos recentes demonstraram que a suscetibilidade genética pode desempenhar um papel determinante na patogénese da DPOC. Contudo, pouco se sabe acerca desta relação entre o desenvolvimento da doença e o perfil genético dos pacientes. Da mesma forma, sabe-se que a deterioração clínica dos pacientes é altamente dependente da frequência e gravidade das exacerbações agudas, e que pacientes com função pulmonar semelhante apresentam níveis diferentes de incapacidade/suscetibilidade às exacerbações agudas. Assim, os resultados deste estudo irão potencialmente contribuir para melhorar o conhecimento sobre a DPOC e informar sobre as estratégias para prevenir, detetar precocemente e gerir as exacerbações agudas. Para que seja possível alcançar estes objetivos vimos então solicitar a sua participação neste estudo que será realizado na Escola Superior de Saúde da Universidade de Aveiro/iBiMED, centros de saúde e centro hospitalar do Baixo Vouga, Centro Hospitalar do Médio Ave e Hospital Pedro Hispano.

Porque é que fui escolhido?

Foi escolhido/a porque é uma pessoa saudável, com doença pulmonar obstrutiva crónica em fase estável ou cuidador/a de uma pessoa com esta doença. Para o estudo, precisamos de dados de aproximadamente 400 pessoas, com uma condição clínica semelhante à sua, que aceitem participar.

Tenho de participar?

A decisão de participar, ou não, é completamente sua. Se decidir participar vai-lhe ser pedido que assine um formulário de consentimento informado mas, é totalmente livre de desistir a qualquer momento, sem que para tal tenha de dar qualquer justificação. A decisão de desistir ou de não participar, não afetará a qualidade dos serviços de saúde ou qualquer outro, que lhe são prestados agora ou no futuro.

O que me acontecerá caso decida participar?

Se decidir participar, após assinar e entregar aos investigadores o consentimento informado, será feita uma avaliação do seu estado de saúde geral. Primeiro, serão gravados os sons dos seus pulmões durante aproximadamente 20 segundos (3 repetições), com um microfone, como se fosse um estetoscópio, que está ligado a um computador portátil. Seguidamente, ser-lhe-á medido o peso e a altura numa balança. Depois, ser-lhe-á avaliada a força dos seus músculos da respiração e a capacidade respiratória, através de dois testes que consistem em inspirar e soprar para um equipamento. A avaliação da força dos seus músculos da coxa e braço realizar-se-ão de seguida através de um aparelho que se encosta à região do corpo em teste, é-lhe pedido que realize o máximo de força que conseguir e em breves segundos, o aparelho indica a força daquele músculo. Veremos também a sua tolerância ao exercício através do teste de sentar e levantar de uma cadeira. Ser-lhe-á também pedido para colocar um bocadinho de saliva para um copo (semelhante

ao que utiliza quando realiza análises clínicas) para posterior análise. Mediremos também a quantidade de oxigénio no seu sangue e a sua frequência cardíaca através de um oxímetro (aparelho pequeno que se coloca no seu indicador e nos dá a informação desses valores em segundos). De seguida avaliaremos a sua frequência respiratória observando a sua região abdominal e mediremos a tensão arterial com um medidor de tensão arterial digital. Por último, ser-lhe-á pedido que responda a um questionário para avaliar o seu nível de atividades física e um outro para avaliar o impacto da sua doença no seu dia-a-dia. Se for cuidador de um doente com DPOC ou residir com o mesmo, ser-lhe-á também pedido que use um acelerómetro por 1 semana. Nenhum dos testes realizados provoca qualquer dor ou desconforto. A duração da avaliação será de aproximadamente 45 minutos e poderão ser realizadas em sua casa ou possivelmente num gabinete do Hospital Pedro Hispano, de acordo com a sua preferência.

No caso de ter DPOC, poderá ainda realizar alguns exames complementares de diagnóstico (pletismografia, DLCO e/ou TAC) se o seu médico considerar relevante. Terá também a possibilidade, no caso de experienciar uma exacerbação do seu estado de saúde, de realizar uma intervenção no sentido de melhorar o seu estado de saúde e ter a sua condição monitorizada durante 3 semanas.

Quais são os efeitos secundários, desvantagens e riscos se eu resolver participar?

Não existem efeitos secundários, desvantagens ou riscos de participar no estudo.

Quais são os possíveis benefícios se eu resolver participar?

Toda a informação clínica recolhida será fornecida aos participantes para que seja do seu conhecimento e, no caso de sofrer um agravamento dos sintomas, beneficiará de um acompanhamento semanal do seu estado de saúde prestado por um fisioterapeuta respiratório qualificado. Para além disso, a informação obtida neste estudo, através da sua participação, poderá ajudar a melhorar o conhecimento sobre a patogénese da DPOC e, a prevenção, diagnóstico precoce e gestão das exacerbações agudas, uma doença crónica que afeta cerca de

800.000 portugueses.

A minha participação será confidencial?

Toda a informação recolhida no decurso do estudo será mantida estritamente confidencial e mantido o anonimato. Os dados recolhidos serão salvaguardados com um código e palavra-passe, para que ninguém o/a possa identificar. Apenas os investigadores do projeto terão acesso aos seus dados.

O que acontecerá aos resultados do estudo?

Os resultados do estudo serão analisados e incorporados em Dissertações de Mestrado e Teses de Doutoramento e alguns serão publicados em Jornais Científicos. No entanto, em nenhum momento o Sr./Sra. será identificado/a. Se gostar de obter uma cópia de qualquer relatório ou publicação, por favor diga ao investigador com quem contactar.

Quem é que está a organizar e a financiar o estudo?

Este estudo foi financiado pelo Programa Operacional Competitividade e Internacionalização - COMPETE, através do Fundo Europeu de Desenvolvimento Regional - FEDER (POCI-01-0145-FEDER-016701), e pela Fundação para a Ciência e Tecnologia (PTDC/DTP-PIC/2284/2014). Este estudo foi também parcialmente apoiado pelo COMPETE através do FEDER e da FCT através do projeto UID/BIM/04501/2013. O estudo decorre na Universidade de Aveiro em colaboração com o ACES e Centro Hospitalar do Baixo Vouga, Centro Hospitalar do Médio Ave e Hospital Pedro Hispano.

Contactos para mais informações sobre o estudo

Alda Marques (Investigadora Responsável)

Escola Superior de Saúde da Universidade de Aveiro,

Telefone 234 372 462

e-*mail:* *amarques@ua.pt*

Appendix II – Scientific outputs developed under the scope of this dissertation

Poster discussion:

Dias C., Machado A., Paixão C., Mendes MA., Ferreira PG., Marques A**.** (2022) "Functional impairment in people with ILD: is one measure enough?" Pulmonol. 2022;28 Supl Congr 3:43 (IF: 9.216, 5 years IF: 7.845, RESPIRATORY SYSTEM: Q1) URL: https://www.journalpulmonology.org/en-pdf-X2531043722034190

Dias C., Machado A., Mendes MA., Ferreira D., Martins V., Simão P., Marques A. (2022) "Cut-off points of the one-minute sit-to-stand test to detect functional impairment and mortality risk in people with COPD" Pulmonol. 2022;28 Supl Congr 3:50 (IF: 9.216, 5 years IF: 7.845, RESPIRATORY SYSTEM: Q1) URL: https://www.journalpulmonology.org/en-pdf-X2531043722034190

Exposed poster:

Machado A., **Dias C.**, Gonçalves AP., Mendes AM., Martins V., Simão P., Burtin C., Marques A. (2022) "Cut-off scores of the mMRC and CAT to predict short-term exacerbations in people with COPD" Pulmonol. 2022;28 Supl Congr 3:141 (IF: 9.216, 5 years IF: 7.845, RESPIRATORY SYSTEM: Q1) URL: https://www.journalpulmonology.org/en-pdf-X2531043722034200

Oral communications:

Rebelo P., Santos ES., Rodrigues G., Grave A., **Dias C.,** Oliveira AC., Moura MJ., Rijo AS., Brooks D., Marques A. (2022) "Intensity and safety of community-based physical activities for people with COPD" Pulmonol. 2022;28 Supl Congr 3:26-27 (IF: 9.216, 5 years IF: 7.845, RESPIRATORY SYSTEM: Q1) URL: https://www.journalpulmonology.org/en-pdf-X2531043722034180

Almeida S., Rebelo P., Rodrigues G., Santos E.S., Monteiro C., Grave A., **Dias C.**, Santos C., Simões A., Rodrigues C., Marques S., Oliveira A.C., Rijo A.S., Moura M.J., Mendes M.A., Marques A. "Impact of pulmonary rehabilitation on the social support of people with COPD" European Respiratory Journal 2022 60: 954; DOI: 10.1183/13993003.congress-2022.954

Paper:

Dias C., Machado A., Paixão C., Marques A. “Cut-off of the 1-minute sit-to-stand test and quadriceps muscle strength to detect functional impairment” Annals of Physical and Rehabilitation Medicine *(under review)*

Machado A., **Dias C.**, Rebelo P., Souto-Miranda S., Mendes M.A., Ferreira D., Martins V., Simão P., Burtin C., Marques A. “Functional status in people with COPD and its relationship with disease severity – a cross-sectional study with matched controls” Pulmonology Journal *(under review)*