

Testosterone serum levels in elderly fall-prone men do not correlate with age or performance in the 30 seconds chair stand test

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Background & aims. Multiple studies have shown associations between low testosterone, declining physical function and cognition, metabolic syndrome, depression, falls, and even mortality, and the benefits of reestablishing the level of testosterone in elderly men with deficiency. The purpose of the study was to decide who of such men might benefit from further geriatric assessment, intervention by training, testosterone injections, and how to get in touch with these gentlemen.

Method. Testosterone was measured in men above 70 years old who experienced a decline in safety of mobility. Participants were recruited through advertisements in local newspapers. Men who walk unsteadily, are about to fall or have been falling, who experience that they are getting weaker or have deteriorated physical health, were questioned about symptoms and diseases, supplied with total testosterone measurements and a 30 seconds chair stand test.

Results. 177 men were screened. Mean age 77.7 (70-95). Total testosterone mean value = 12.1 (4.3-17.0 nmol/l). Chair stand tests did not correlate with testosterone levels, $p = 0.98$, neither did testosterone levels correlate with age, $p = 0.65$, (Spearman).

Conclusions. The important fact is that the gentlemen themselves experience a physical decline confirmed through a thorough conversation. We still do not know for sure how to identify men who might profit from further examination but a testosterone blood test and a chair stand test in men above 70 years old who experience increasing frailty will be a start.

Key words: nutrition, metabolism

INTRODUCTION

Lack of testosterone contributes to several physical diseases and has a negative influence on cognition and mood as well ¹. Low testosterone contributes to anemia due to reduced stimulation of the production of erythropoietin and seems to increase the risk of cardiovascular disease, metabolic syndrome, and to influence inflammatory markers like c-reactive protein (CRP) and erythrocyte sedimentation ¹. Furthermore, testosterone deficiency is associated with sarcopenia, mobility limitations, and low physical performance ¹⁻³. Overall lack of testosterone correlates with poor physical and social function and overall health, and is associated with falls in older men ^{1,2}. Several studies have demonstrated the safety and benefits of testosterone treatment, also including potential risks of prostate

Received: December 3, 2019
Accepted: January 4, 2021

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Conflict of interest

The Authors declare no conflict of interest

How to cite this article: Midttun M, Overgaard K, Skovgaard Rasmussen R. Testosterone serum levels in elderly fall-prone men do not correlate with age or performance in the 30 seconds chair stand test. *Journal of Gerontology and Geriatrics* 2021;69:98-102. <https://doi.org/10.36150/2499-6564-N285>

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cancer and cardiovascular events^{1,4-7}. Intramuscular testosterone seems to be more effective than transdermal administration for increasing lean body mass and improving muscle strength in middle-aged and old men, particularly in the lower extremities⁸. Besides the inconvenience and risk of severe injury for the patient, all causes of frailty are costly to the healthcare systems and therefore it is important to identify and prevent testosterone deficiency in old fall prone men⁹.

In the present study, the primary aim was to find out who might benefit from further geriatric assessment, intervention and possibly from testosterone injections, and how to get in touch with them. Is it sufficient to publish an advertisement in a local paper stating that frail gentlemen at least 70 years old are needed for a research study, or are other tools needed? Furthermore, how do we identify those gentlemen who probably will profit from further geriatric assessment and testosterone treatment?

MATERIAL AND METHODS

This investigation complies with the Helsinki Declaration, and was approved by the Danish Data Protection Agency and the relevant Scientific Ethics Committee (protocol no.: H-16020521). ClinicalTrials.gov Identifier: NCT02873559.

Through advertisements in local newspapers in the suburbs of Copenhagen we were searching for “men 70 years and older who walk unsteadily, are about to fall or have been falling, who experience that they are getting weaker, or that their physical health deteriorates”. 177 men responded by email or by telephone after having read the advertisements in the local paper. In some cases, their relatives contacted us.

The trial participants had a thorough interview about their health and symptoms with focus on falls or problems walking safely, their experience of physical decline, and they were asked if they used any kind of walking aid. A few tests were made to try and identify those who might profit from further geriatric assessment and/or possibly testosterone injections. The Chair Stand Test was performed, and the total testosterone (blood test) was measured¹⁰. These two tests were supplied with another thorough interview including questions about other diseases. In case of insulin dependent diabetes, a PSA (prostate-specific antigen) level above 5 µg/l, prostatic cancer, or any other active cancer or severe heart disease participants were excluded from the trial. Chair Stand Test performance above 12 in 30 seconds, a total testosterone above 12.9 nmol/l together with the medical history were used as cut off. The 30-Second Chair Stand Test was used to measure improvement of general strength and power in lower extremities. The

number of times the participant can rise from a chair in 30 seconds with arms crossed over the chest and returning to a sitting position between each repetition is counted by a test leader. Repetitions are only counted as successful if full extension of the hips and knees is achieved for each rise. The back does not need to touch the backrest of the chair when returning to a sitting position but contact with the seat must be made. This test has a satisfactory correlation ($r = 0.78$) with leg press exercise abilities¹⁰ and an acceptable test retest reliability has been found¹¹. It has recently been scientifically proven that the ability of elderly persons to perform a slightly different version (timing of 5 chair-stands) of this simple test correlates with the risk of serious fall injuries¹².

RESULTS

DATA ANALYSIS

Data was not assumed to be normally distributed and non-parametric statistics were used. Spearman's rank-order correlation test was used for ranked pairs. Fisher's exact probability test was used for categorical data comparisons that resulted from classifying data in two different ways. P-values below 0.05 were considered statistically significant.

All 177 trial participants had a history of falling, being about to fall, insecure walking, impaired physical functions, or loss of independency. About 20% had been falling previously to the contact and 44 (24%) used walking aid. Their mean age was 77.7 (70-95 years), and mean serum testosterone levels was 11.7 nmol/l ranging from 1.2 to 24.8. Table I shows results for difference age groups.

Also chair stand test performance did not correlate with age ($p = 0.58$, Spearman). In 57 men prostate-specific antigen (PSA) levels were investigated and ranged from 0.1 to 47 µg/l, but PSA levels did not correlate with testosterone levels, age or chair stand test performance ($0.20 < p < 0.58$).

Of the 177 men, 110 (64%) had a testosterone below 13 nmol/l, and 30% (64 men) had a testosterone below 10 nmol/l.

Denmark is a small country with 5.806.000 inhabitants (measured in the third quarter of 2018 by Statistics of Denmark), with 465.238 inhabitants in the suburbs of Copenhagen, 26.284 men are between 70-100 years old. Level of education is not registered for men older than 69 years, therefore figures for the group of men between 65-69 years old were used. Suburbs of Copenhagen for the men included were the municipalities of Herlev, Gentofte, Ballerup, Gladsaxe, Lyngby-Taarbæk, Rødovre, Frederiksberg, and Egedal. Levels of education are illustrated in Table II.

Table I. Age group characteristics.

Characteristics	70-79 years	80-89 years	90 + years	All
Men (N)	100	71	6	177
Mean testosterone levels (nmol/l)	11.7	11.7	12.2	11.7
Chair Stand Test performance (in 30 sec)	10	10	12	10

Among these fall-prone men, chair stand test performance did not correlate with testosterone levels ($p = 0.98$, Spearman), and neither did testosterone levels correlate with age ($p = 0.65$, Spearman).

Table II. Levels of education.

Suburbs of Copenhagen Level of Education	Engineers or technical education	Skilled craftsmen
All men (n = 26284)	374 (1.4%)	3781 (14%)
Screened men (n = 177)	23 (13%)	22 (12%)

Compared to the normal population of men age 70 or older in the suburbs of Copenhagen and their level of education, the trial participants consisted of more engineers and men with technical education than skilled craftsmen ($p < 0.01$, Fisher). Trial participants thus were biased toward having higher technical educations.

DISCUSSION

In the present investigation testosterone levels and Chair Stand Test performances were measured in 177 men at least 70 years old who experienced a decline in safety of mobility, had been falling or were about to fall, were walking unsteadily, experienced impaired physical functions or a loss of independency.

They were all citizens from the surroundings of Copenhagen, and all responded to advertisements in the local papers, in some cases their wife or children responded for them. They were interested in participating in a trial made for reducing risk of falls in frail men age 70 or older. The majority of the participants were between 70 and 80 years old (57%), only six (3.4%) were above 90 years old. About 20% had been falling previously to the contact, and 24% used a walking aide, mainly walking stick. Despite quite serious symptoms including falls, only 64% of the men had a testosterone below 13 nmol/l. Thirty percent (52 men) had a testosterone below 10 nmol/l, which is rather low even for at 80-years old man.

Chair stand test performances did not correlate with testosterone serum levels. In previous studies Vanderput³ did not find any association between total testosterone and lean mass in older men (mean age 76), and in a previous study by Roy et al.¹³ free testosterone was found a better predictor of arm and leg strength than total testosterone in aging men. Chair Stand Test performance, leg extension power, and lean muscle mass are not directly comparable, but different expressions of muscle function. Chair stand test is a test of rapidity and balance as well as muscle strength, and even of cognition as the subject must understand the instruction to

perform properly. In spite of not being significant, the chair stand test is important as a supportive test to confirm the need for further geriatric examination, possibly training and/or possibly testosterone.

Testosterone deficiency is associated with reduced cognitive function, increased depressive symptoms, fatigue, metabolic syndrome, and institutionalization, hospitalization, loss of muscle mass, decline in physical function, osteoporosis, and mortality, and the testosterone level is influenced by various factors such as severe infections, and fractures^{1,2}. Overall testosterone is a very important hormone, but low testosterone is not the only cause of all symptoms of frailty, and it is therefore of great importance to differ between those who may, and those who may not need other kinds of treatment than probably testosterone and/or physical training.

Only few tests were made to try and identify those men who might profit from further and thorough geriatric examination because of their functional problems. Thorough examination and tests of for example BMI, liver- and renal function etc. were not included in this investigation, because participants were only screened for eligibility for participation in a trial. Therefore, available characteristics for participants were limited and present a limitation to this investigation.

The most import finding was that the gentlemen themselves experienced a physical decline. If their symptoms of physical decline are supported by a low testosterone they might profit from further examination by a geriatrician, for example in a fall clinic, and testosterone supplementation therapy may prevent or reduce a rapid progression of their symptoms.

Who responded to the advertisement in the local papers? Did we get the right subjects for the trial? Previous research has shown that participation in clinical research is influenced by as well socioeconomic, racial, as ethical factors¹⁵. Some people chose to participate in research studies because they hope to obtain medical or personal benefit, because they want to help others or to make an important contribution to society^{15,16}. The topic of the study has an influence on the number of responders as well. In the article by A. Saliba and P. Ostojic¹⁷ it was concluded that some personality types are predisposed to participate in studies irrespectively of the selection criteria. For instance, personality types

described with “intuition” (characteristic for those who more often will grasp an opportunity) seem to have a key predisposing factor in favor of volunteering. And the dominating personality types were those described with “intuition and feeling” and “intuitive, logic and analysis”. “Warmth and sympathy” towards the researcher/other participants or the chance to apply “logic and analysis” may further drive “intuitive-feeling-types” to volunteer whereas the chance to apply “logic and analysis” to an innovative concept may provide additional attraction for the intuitive types who were logic and analytic as well to agree to participate in such a study. The latter may explain the high percentage of well-educated gentlemen and especially the high percentage of engineers who applied for the present study, (13 versus 1.4% in the background population).

Furthermore, the way information on a research topic is presented to potential volunteers may influence their decision to participate. The “one size fits all” approach may not be optimal. Instead, presenting information on the future possibilities of a project would be expected to appeal to the personality types described as “Intuitives”, whereas providing factual data on the likely outcome/benefits of the research should be more attractive to “sensitives”. These observations partly explain why our first very small (and free) article in the newspaper, and a bigger one on Facebook did not provide the expected results, because we did not connect with the target group. Through a Facebook advertisement, we expected to obtain contact with the subjects through their children or grandchildren, but that failed completely. This seems to imply that research studies that rely on volunteers are skewed in favor of volunteers having the above-mentioned personalities regardless of the selection criteria or recruitment methods.

Apart from belonging to certain personality types the gentlemen described above have signed up for the trial because they experience different kinds of frailty, they still must be rather strong and in a relatively good health, or they would not have the strength to even think of participating in a research study. This proves what we already know that it requires great reserves of cognition and energy to sign up on your own initiative as a participant in a research study.

How do we identify those gentlemen who will most probably profit from further geriatric assessment and probably testosterone treatment? We still do not know for sure but taking a testosterone blood test in all men above 70 years old who turn to their GP or are referred to a fall clinic due to increasing frailty will be a start, supplied with a Chair Stand Test and a thorough interview. It is furthermore crucial to screen all those referred to the department of geriatrics as well because there you will surely find the frailest of the frail, those who do not

have the strength to sign up for a trial announced in a free newspaper and who may profit from testosterone treatment as a supplement to the standard treatment they receive.

CONCLUSIONS

Lack of testosterone is associated with sarcopenia, mobility limitations, poor physical and social function and overall health, and in older men it is associated with falls, and besides the inconvenience for the patient, all causes of frailty are costly to the healthcare systems. Therefore, it is important to identify aging men with testosterone deficiency. The participants were recruited through announcements in local papers, and 177 men signed up and were tested with a thorough interview, Chair Stand Test, and a testosterone blood test. Through this kind of announcing we did not get in contact with the frailest patients, thus supporting evidence from other investigations where investigators found that volunteers are skewed and show certain strength and personalities – such as being intuitive, logic and analytic regardless of the selection criteria, or recruitment method

Neither age nor 30 seconds Chair Stand Test performance correlated with serum levels of testosterone. The important fact is that the participants themselves experienced a physical decline and increased risk of falls confirmed through a thorough interview. Therefore, a chair stand test performance nor a testosterone blood test can stand alone. The chair stand test is a test of muscle strength, rapidity, and balance and may be used to confirm the need for further examination, possibly including therapy such as physical exercises and testosterone supplementation.

ACKNOWLEDGEMENTS

The investigation was funded by Helsefonden, Marie og Børge Kroghs Fond, The Beckett Foundation, Any and Richard Sperling Foundation, Fondation Juchum, and the Velux Foundation. Besides providing funding, no source of funding had any involvement in the investigation.

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