Published in final edited form as:
*Aging Male*. 2011 March ; 14(1): 42–47. doi:10.3109/13685538.2010.518179.

# Gonadal Status and physical performance in older men

**Marcello Maggio**[1,2], **Gian Paolo Ceda**[1,2], **Fulvio Lauretani**[2], **Stefania Bandinelli**[3], **E. Jeffrey Metter**[4], **Jack M. Guralnik**[5], **Shehzad Basaria**[5], **Chiara Cattabiani**[1], **Michele Luci**[1], **Elisabetta Dall'Aglio**[1], **Alessandro Vignali**[1], **Riccardo Volpi**[1], **Giorgio Valenti**[1], and **Luigi Ferrucci**[4]

[1] Department of Internal Medicine and Biomedical Sciences, Section of Geriatrics, University of Parma, Italy.

[2] Geriatric Rehabilitation Department, University Hospital of Parma, Parma, Italy

[3] Geriatric Unit, Azienda Sanitaria Firenze, Florence, Italy

[4] Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging Intramural Research Program (NIA-IRP), National Institutes of Health (NIH), Baltimore, MD, USA.

[5] Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging,Bethesda MD, USA.

[6] Boston University School of Medicine, Sections of Endocrinology, Diabetes, and Nutrition.

## Abstract

**Background—**Male aging is characterized by a progressive decline in serum testosterone levels and physical performance. Low testosterone levels may be implicated in the decline of physical performance and consequent mobility disability that occurs with aging. During the recent years many consensus reports have advocated that one of the potential effects of testosterone supplementation is the improvement in mobility. However, to the best of our knowledge no study has fully investigated the relationship between gonadal status and objective measures of physical performance in older men and their determinants.

**Methods—**We evaluated 455 ≥ 65 year old male participants of InCHIANTI study a population based study in two municipalities of Tuscany, Italy with complete data on testosterone levels, hand grip strength, cross-sectional muscle area (CSMA), short physical performance battery (SPPB). Linear models were used to test the relationship between gonadal status and determinants of physical performance.

**Results—**According to baseline serum levels of total testosterone, three different groups of older men were created: 1) severely hypogonadal (N= 23),total testosterone levels ≤230 ng /dl; 2) moderately hypogonadal (N=88), total testosterone >230 and <350 ng/dL), and 3) eugonadal (N=344), testosterone levels ≥350 ng/dL. With increased severity of hypogonadal status, participants were significantly older while their BMI was substantially similar. In the age and BMI adjusted analysis, there was a significant difference in hemoglobin levels, hand grip strength and SPPB score (p for trend<0.001) among −3 groups, with severely hypogonadal men having lower values of hemoglobin, muscle strength and physical performance. We found no association

**Corresponding author**: Marcello Maggio, MD, PhD National Institute on Aging, NIH, NIA-ASTRA unit at Harbor Hospital 3001 S. Hanover Street, Baltimore, MD 21225, USA. Department of Internal Medicine and Biomedical Sciences, Section of Geriatrics, University of Parma, via Gramsci 14, 43100 Parma, Italy. Phone: 0039-0521-703916 marcellomaggio2001@yahoo.it.

**Conflict of interests**: The authors declare that they have no conflict of interest to disclose concerning this manuscript.

**Financial Disclosure:** The InCHIANTI Study was supported as a "targeted project" (ICS 110.1/RS97.71) by the Italian Ministry of Health and in part by the U.S. National Institute on Aging (Contracts N01-AG-916413 and N01-AG-821336) and by the Intramural Research Program of the U.S. National Institute on Aging (Contracts 263 MD 9164 13 and 263 MD 821336).

between testosterone group assignment and calf muscle mass and 4 meter walking speed. In the multivariate analysis grip strength (p for trend=0.004) and haemoglobin (p for trend <0.0001) but not SPPB and other determinants of physical performance were significantly different between the 3 groups.

**Conclusions—**In older men, gonadal status is independently associated with some determinants (hemoglobin and muscle strength) of physical performance.

### Keywords

testosterone; physical performance; older men

## Introduction

Male aging is characterized by a progressive decline in serum testosterone levels with 30% to 50% of men over 70 and 80 years considered hypogonadic (1).

Over the last few years there has been a serious effort to define and operationalize clinical and biochemical characteristics of the testosterone deficiency syndrome (2-7). Noteably, specific symptoms associated with low serum levels of testosterone in older persons may negatively affect the quality of life and contribute to deterioration of function of organs and systems (7). Main characteristics include decrease of libido, carbohydrate metabolism disorders, sarcopenia, and adverse changes in mood and cognition.

Because of these multiple effects it has been postulated that low testosterone may participate in the causal pathway that leads to disability in older men. This hypothesis is supported by several studies. We previously demonstrated that low testosterone levels predict the development of anaemia in both older men and women (8) which is a strong correlate of physical performance in the older population (9). Older men with lower bioavailable testosterone have a higher fall risk (10) and lower physical strength and poor functional outcomes (11). The link between testosterone and physical performance emerges from studies performed in patients affected by prostate cancer and undergoing androgen deprivation therapy (ADT) (12-14). This category of patients, with a treatment goal of achieving serum testosterone levels less than 50 ng/ dl (six-times lower than the lower limit of normal in young men) experience a significant reduction in upper body strength and walking speed and a poorer performance in comparison to those not undergoing ADT (12-14).

Despite the increasing number of documents developed to create a definition of hypogonadism useful in clinical practice, the relationship between determinants and objective measures of physical performance and gonadal status in older men has not been fully addressed.

Using data from the InCHIANTI study, we hypothesized that older men with different gonadal status would differ significantly on parameters that are critical for physical function.

## METHODS

### Study sample

The study population included 601 men randomly selected from all male residents 65 years and older in the CHIANTI catchment Area, Invecchiare nel CHIANTI (InCHIANTI) study, Tuscany, Italy with complete data on total testosterone, fasting insulin, glucose, interleukin-6 (IL-6), haemoglobin, cross-sectional muscle area ($mm^2$), short physical performance battery score, grip strength and major chronic disease diagnoses.

## Exclusions

From the initial 601 men aged ≥ 65 years old, 126 participants were excluded because they did not donate a blood test and 10 subjects were excluded because they had missing values for serum total testosterone. The Italian National Institute of Research and Care on Aging Institutional Review Board ratified the study protocol. Participants consented to participate and to have their blood samples analyzed for scientific purposes (15).

## Biological Samples

Blood samples were obtained from participants after a 12-hour fast, and after a 15-minute rest. Aliquots of serum were stored at −80C° and were not thawed until analyzed.

## Laboratory Measures and Test Characteristics

Total testosterone was assayed using commercial radioimmunologic kits (Diagnostic Systems Laboratories, Webster, TX). For total testosterone, the MDC was 0.03 nmol/L; intra-assay and inter-assay CVs for 3 different concentrations were 9.6%, 8.1%, and 7.8%, and 8.6%, 9.1%, and 8.4%, respectively.

Serum interleukin-6 (IL-6) was measured in duplicate by high-sensitivity enzyme-linked immunsorbent assay (ELISA) (BIOSOURCE, Camarillo, CA). The lowest detectable concentration was 0.1pg/mL, and the interassay CV was 4.5%.

Plasma insulin level was determined with a double-antibody, solid-phase radioimmunoassay (intra-assay CV = 3.1 + 0.3%; Sorin Biomedica, Milan, Italy). Cross-reactivity with human proinsulin was 0.3%. Serum glucose level was determined by using an enzymatic colorimetric assay (Roche Diagnostics, Mannheim, Germany) and a Roche-Hitachi 917 analyzer. Plasma insulin was determined using a commercial double-antibody, solid phase radioimmunoassay (Sorin Biomedica, Milan, Italy) with an intra-assay coefficient of variation ±standard deviation (SD) of 3.1 ± 0.3%.

## Co morbidity and other variables

**Diseases—**Diseases were ascertained by an experienced clinician according to pre-established criteria that combines information from self-reported physician diagnoses, current pharmacological treatment, medical records, clinical examinations and blood tests. Diseases included in the current analysis were coronary heart disease (including angina and myocardial infarction), congestive heart failure, stroke, Parkinson's disease.

## Body Size, Composition, and Physical function

Weight and height were measured by using standard techniques. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m2). A right leg pQCT scan was performed on all participants by a recent generation device (XCT 2000; Stratec, Pforzheim, Germany) to evaluate the cross-sectional muscle and fat areas of the calf. The pQCT technology, an increasingly used imaging method in research has been shown to be highly reproducible for the assessment of body composition parameters (16).

A short physical performance battery (SPPB) based on the lower-extremity performance tests used in the Established Populations for the Epidemiologic Studies of the Elderly (EPESE) was used to summarize physical performance. The SPPB consisted of walking speed, ability to stand from a chair, and ability to maintain balance in progressively more challenging positions. Walking speed was defined as the best performance (time in seconds) of two 4 m walks at usual pace along a corridor. Participants were allowed to use canes or walkers. To test the ability to stand from a chair, participants were asked to stand up and sit

down as quickly as possible in a chair five times with their hands folded across their chest; time (in seconds) to complete the test was recorded. For the standing balance test, participants were asked to stand in three progressively more difficult positions for 10 seconds each: a side-by-side position, a semitandem position, and a full-tandem position. Each physical performance measure was categorized into a five-level score, with 0 representing inability to do the test and 4 representing the highest level of performance. The three measures were then added to create a summary physical performance measure ranging from 0 (worst) to 12 (best) (17).

Handgrip strength was measured using a handheld dynamometer (hydraulic hand "BASELINE"; Smith & Nephew, Agrate Brianza, Milan, Italy). Participants were asked to perform the task twice with each hand. The average of the best result obtained with each hand was used for these analyses.

Physical activity in the year before the interview was coded as: 1) sedentary: completely inactive or light-intensity activity less than 1 h/wk; 2) light physical activity: light-intensity activity 2–4 h/wk; and 3) moderate-high physical activity: light activity at least 5 h/wk or more or moderate activity at least 1–2 h/wk.

### Health Behaviors

Smoking history was determined from self-report and dichotomized in the analysis as "current smoking" versus "ever smoked" or "never smoked". Education was assessed as years of school.

### Statistical Analysis

Variables are reported as mean values ± standard deviations (SD), medians and inter-quartile ranges or number and percentages. To approximate normal distributions, log-transformed values for IL-6 and insulin were used in the analysis and back-transformed for data presentation.

Generalized linear models by class were used to test the relationship between determinants of physical performance and gonadal status in a Model 1 adjusted for Age and BMI, and Model 2: Model 1 plus Log (IL-6), Physical activity, Log (Insulin), Parkinson Disease, CHF, Stroke. All the analyses were performed by the SAS statistical package, version 9.1 (SAS Institute Inc., Cary, North Carolina).

## Results

According to baseline serum levels of total testosterone, older men were divided in 3 different groups: A) Severely hypogonadal (N= 23): total testosterone ≤230 ng /dl; B) Moderately hypogonadal (N=88): 230 > total testosterone and <350 and C) Eugonadal (N=344): total testosterone ≥ 350 ng/dl.

Figure 1 shows the conceptual model used for this study. Low testosterone may affect parameters that are important for mobility disability in older persons.

Table 1 shows the characteristics of the population according to gonadal status. There was a significant difference in age ($p<0.001$) with participants in the severe hypogonadal group more likely to be older.

After adjusting for age, the three testosterone groups differed significantly by hemoglobin levels (p for trend <.001), hand grip strength (p for trend <.001) and SPPB score (p for trend <.001). Participants in the severe hypogonadal group had a higher prevalence of chronic

heart failure (p=0.01), compared to the other two groups. There was no significant difference in calf muscle area (p= 0.49) and 4 meter walking speed (p= 0.73). After further adjustment for BMI, hemoglobin (p for trend <.001), hand grip strength (p for trend <.001) and SPPB score (p for trend <.001) remained significantly different between the three testosterone groups. We also found no significant difference in calf muscle area (p= 0.49) and 4 meter walking speed (p= 0.73).

After further adjustment for log (IL-6), log (Insulin), physical activity, Parkinson's disease, CHF, and stroke, there was a still significant difference in hemoglobin levels (p for trend <0.0001) and muscle strength (p for trend <0.0001) between testosterone status groups while SPPB scores (p=0.34) were no longer significantly different. In the multivariate analysis we also confirmed that 4-m walking speed, muscle mass, were not different between the 3 groups. Hemoglobin levels (p for trend <0.0001) and muscle strength (p for trend <0.0002) were still significantly different between the three groups when the analysis was restricted to participants free of any disability in activities of daily living.

## Discussion

In a representative sample of older Italian men, we found a significant difference in hemoglobin levels and muscle strengths between individuals with different testosterone status, namely severely hypogonadal, moderately hypogonadal and eugonadal.

To our knowledge, this is the first study that has fully investigated whether determinants and measures of physical performance are significantly different across testosterone levels independent of age and confounders.

Interestingly, in doing the analysis for this manuscript, we grouped participants based on the most recent recommendations on clinical values that should be used for treatment and monitoring of late-onset hypogonadism in aging males (7). According to these guidelines testosterone levels below 230 ng/dL identify patients that need to be treated. Because of its peculiar design, it is difficult to compare this study with others. Zitzman et al that tried to relate testosterone-related symptoms in elderly men to concentrations of androgen levels in an attempt to explain increasing prevalence of these symptoms with aging (18). They found that psychosomatic complaints and metabolic risk relate to testosterone in a symptom-specific manner. However no information on physical performance was provided in their study.

There is a complex pathway by which Testosterone may affect physical function. We found that only hemoglobin levels and muscle strength were significantly different in the 3 categories of participants in a first model adjusted for age and BMI. These findings are not completely unexpected. A relationship between testosterone levels and hemoglobin has been established previously in this same population (8). In the present analysis participants in the three testosterone status groups were significantly different in hemoglobin levels after adjusting for confounders including IL-6, Fasting insulin, physical activity, and wasting diseases. Interestingly, in a recent intervention study hemoglobin levels increased significantly in a linear, dose-dependent fashion in both young and older men in response to graded doses of testosterone hypothesizing a dose dependent effect of testosterone on anemia (19).

Since anemia is one of the most powerful markers and frailty and disability (9) this mechanism should be considered in future studies addressing the effects of testosterone on these parameters.

The second determinant of physical function significantly associated with gonadal status was the grip strength. It is well known that testosterone affects muscle function and quality (20) and several randomized controlled studies conducted with testosterone in men show a direct effect of this hormone on muscle strength, in hypogonadal and frail older men (21,22). A recent meta-analysis including data from 11 randomized-clinical trials suggests that, in older men, testosterone or dihydrotestosterone therapy produced a moderate increase in muscle strength compared with placebo (23). However, as reported by Storer et al the relationship between testosterone and muscle strength does not imply an immediate effect on physical function (24).

Despite the robust relationship between testosterone and muscle mass in the literature (21) we did not find any significant difference in this parameter among 3 groups. This finding may be explained by the partial and much localized measure of muscle mass that was used in our study.

We did not detect any significant difference in 4-meter walking speed among 3 groups. In contrast was found a significant difference in SPPB in the age and BMI adjusted model but not in fully adjusted models. Since the physical performance is an integration of different stimuli, the decline in physical function with age is unlikely to be explained by one single factor (25). In addition in older especially frail men physical function tests also tend to be confounded, by the presence of neuropathy, vascular disease, visual and hearing impairment, cognitive impairment, and arthritis. Consistently, a recent intervention study with testosterone performed in intermediate-frail and frail elderly men did not find a significant improvement of physical performance assessed by 6-minute walking test and physical performance test at 6-month assessment (vs. baseline) in the testosterone group (22).

## Limitations

Our study has some limitations. This is a preliminary analysis with a cross-sectional design and therefore no causality can be determined. The analysis accounted only for a limited number of determinants of physical performance and potential confounders. We did not use testosterone as continuous variable but this was not the aim of this analysis. Finally, given the small number of severely hypogonadal participants (N= 20), further studies including larger number of this category of patients are required.

## Strengths of the Study

The limitations are offset by important strengths. This is the first attempt in a very well designed population study to apply guidelines of hypogonadism addressing the crucial issue of physical performance in older population. To make this investigation of clinical translational relevance we used the same thresholds commonly used in the clinical practice. Second, information concerning the inflammatory cytokines and the covariates used in the multivariate analysis cannot be easily found in other epidemiological studies.

## Perspective

There is need of longitudinal studies to define critical testosterone thresholds predicting the decline in physical performance in older men. From the gerontological perspective, the group of -moderately hypogonadal -participants, so called “grey zone” where a real disease is not present should deserve particular attention in future observational studies. Clinical trials targeting mobility or physical performance as main outcome of testosterone in older men.

In conclusion, in older men, gonadal status is independently associated with some determinants (hemoglobin and muscle strength) of physical performance

## Acknowledgments

The InCHIANTI Study was supported as a “targeted project” (ICS 110.1/RS97.71) by the Italian Ministry of Health and in part by the US National Institute on Aging (Contracts N01-AG-916413 and N01-AG-821336), and by the Intramural Research Program of the US National Institute on Aging (Contracts 263 MD 9164 13 and 263 MD 821336). None of the sponsoring institutions interfered with the collection, analysis, presentation, or interpretation of the data reported here.

## References

1. Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. Baltimore Longitudinal Study of Aging. J Clin Endocrinol Metab. 2001; 86:724–731. [PubMed: 11158037]
2. Valenti G, Bossoni S, Giustina A, Maugeri D, Motta M, Vigna GB, Fellin R, Corica F, Corsonello A, Paolisso G, Barbagallo M, Dominguez L, Denti L, Ceda G, Ferrari E, Pontiggia B, Strollo F. Italian Study Group on Geriatric Endocrinology. Consensus Document on substitution therapy with testosterone in hypoandrogenic elderly men. Aging Clin Exp Res. Dec; 2002 14(6):439–64. Review. [PubMed: 12674485]
3. Morales A, Lunenfeld B. Investigation, treatment and monitoring of late-onset hypogonadism in males. Official recommendations of ISSAM. International Society for the Study of the Aging Male. International Society for the Study of the Aging Male. Aging Male. 2002; 5(2):74–86. [PubMed: 12198738]
4. Petak SM, Nankin HR, Spark RF, Swerdloff RS, Rodriguez-Rigau LJ. American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients--2002 update. American Association of Clinical Endocrinologists. Endocr Pract. Nov-Dec; 2002 8(6):440–56. [PubMed: 15260010]
5. Practice Committee of the American Society for Reproductive Medicine. Treatment of androgen deficiency in the aging male. Fertil Steril. May; 2004 81(5):1437–40. [PubMed: 15136135]
6. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, Montori VM. Testosterone therapy in adult men with androgen deficiency syndromes: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2006; 91(6):1995–2010. Erratum in: J Clin Endocrinol Metab. 2006 Jul;91(7):2688. [PubMed: 16720669]
7. Wang C, Nieschlag E, Swerdloff RS, Behre H, Hellstrom WJ, Gooren LJ, Kaufman JM, Legros JJ, Lunenfeld B, Morales A, Morley JE, Schulman C, Thompson IM, Weidner W, Wu FC. ISA, ISSAM, EAU, EAA and ASA recommendations: investigation, treatment and monitoring of late-onset hypogonadism in males. Aging Male. 2009; 12(1):5–12. [PubMed: 18763169]
8. Ferrucci L, Maggio M, Bandinelli S, Basaria S, Lauretani F, Ble A, Valenti G, Ershler WB, Guralnik JM, Longo DL. Low testosterone levels and the risk of anemia in older men and women. Arch Intern Med. 2006; 166(13):1380–8. [PubMed: 16832003]
9. Chaves PH. Functional outcomes of anemia in older adults. Semin Hematol. 2008; 45(4):255–60. [PubMed: 18809096]
10. Orwoll E, Lambert LC, Marshall LM, Blank J, Barrett-Connor E, Cauley J, Ensrud K, Cummings SR. Osteoporotic Fractures in Men Study Group. Endogenous testosterone levels, physical performance, and fall risk in older men. Arch Intern Med. 2006; 166(19):2124–31. [PubMed: 17060543]
11. Araujo AB, Travison TG, Bhasin S, Esche GR, Williams RE, Clark RV, McKinlay JB. Association between testosterone and estradiol and age-related decline in physical function in a diverse sample of men. J Am Geriatr Soc. 2008; 56(11):2000–8. [PubMed: 19016935]
12. Bylow K, Mohile SG, Stadler WM, Dale W. Does androgen-deprivation therapy accelerate the development of frailty in older men with prostate cancer?: a conceptual review. Cancer. 2007; 110(12):2604–13. Review. [PubMed: 17960609]
13. Basaria S, Lieb J 2nd, Tang AM, DeWeese T, Carducci M, Eisenberger M, Dobs AS. Long-term effects of androgen deprivation therapy in prostate cancer patients. Clin Endocrinol (Oxf). 2002; 56(6):779–86. [PubMed: 12072048]

14. Clay CA, Perera S, Wagner JM, Miller ME, Nelson JB, Greenspan SL. Physical function in men with prostate cancer on androgen deprivation therapy. Phys Ther. 2007; 87(10):1325–33. [PubMed: 17684084]
15. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc. 2000; 48:1618–1625. [PubMed: 11129752]
16. Cesari M, Pahor M, Lauretani F, Zamboni V, Bandinelli S, Bernabei R, Guralnik JM, Ferrucci L. Skeletal muscle and mortality results from the InCHIANTI Study. J Gerontol A Biol Sci Med Sci. 2009; 64(3):377–84. [PubMed: 19181709]
17. Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol A Biol Sci Med Sci. 1994; 49:M85–M94.
18. Zitzmann M, Faber S, Nieschlag E. Association of specific symptoms and metabolic risks with serum testosterone in older men. J Clin Endocrinol Metab. 2006; 91(11):4335–43. [PubMed: 16926258]
19. Coviello AD, Kaplan B, Lakshman KM, Chen T, Singh AB, Bhasin S. Effects of graded doses of testosterone on erythropoiesis in healthy young and older men. J Clin Endocrinol Metab. 2008; 93(3):914–9. [PubMed: 18160461]
20. Chaves PH. Functional outcomes of anemia in older adults. Semin Hematol. 2008; 45(4):255–60. [PubMed: 18809096]
21. Ferrando AA, Sheffield-Moore M, Yeckel CW, Gilkison C, Jiang J, Achacosa A, Lieberman SA, Tipton K, Wolfe RR, Urban RJ. Testosterone administration to older men improves muscle function: molecular and physiological mechanisms. Am J Physiol Endocrinol Metab. 2002; 282:E601–E607. [PubMed: 11832363]
22. Onder G, Della Vedova C, Landi F. Validated treatments and therapeutics prospectives regarding pharmacological products for sarcopenia. J Nutr Health Aging. 2009; 13(8):746–56. Review. [PubMed: 19657562]
23. Srinivas-Shankar U, Roberts SA, Connolly MJ, O'Connell MD, Adams JE, Oldham JA, Wu FC. Effects of testosterone on muscle strength, physical function, body composition, and quality of life in intermediate-frail and frail elderly men: a randomized, double-blind, placebo-controlled study. J Clin Endocrinol Metab. 2010; 95(2):639–50. [PubMed: 20061435]
24. Ottenbacher KJ, Ottenbacher ME, Ottenbacher AJ, Acha AA, Ostir GV. Androgen treatment and muscle strength in elderly men: A meta-analysis. J Am Geriatr Soc. 2006; 54:1666–73. [PubMed: 17087692]
25. Storer TW, Woodhouse L, Magliano L, Singh AB, Dzekov C, Dzekov J, Bhasin S. Changes in muscle mass, muscle strength, and power but not physical function are related to testosterone dose in healthy older men. J Am Geriatr Soc. Nov; 2008 56(11):1991–9. [PubMed: 18795988]
26. Webber SC, Porter MM, Menec VH. Mobility in Older Adults: A Comprehensive Framework. Gerontologist. Feb 9.2010

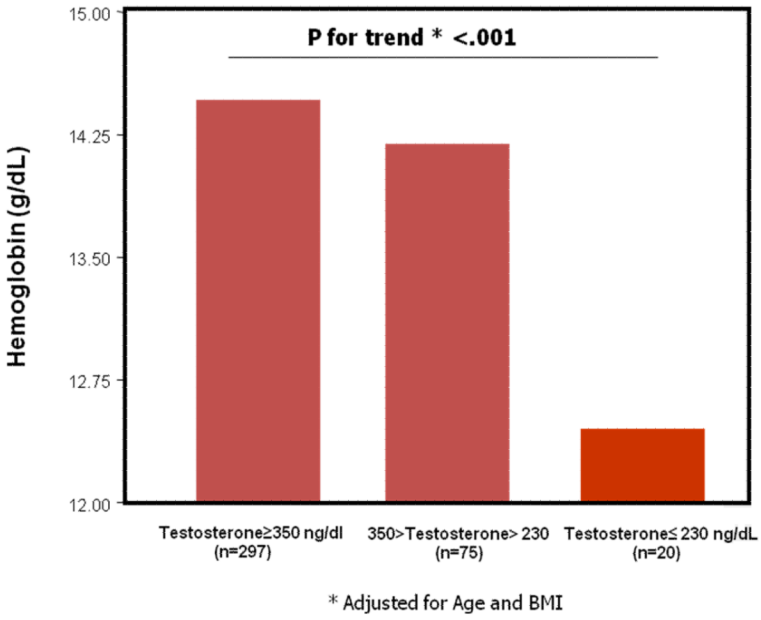


**Figure 1.**

Hemoglobin levels according to gonadal status in older men. The trend of Hemoglobin levels across these groups was significant after adjusting for age and BMI ($p<0.001$)

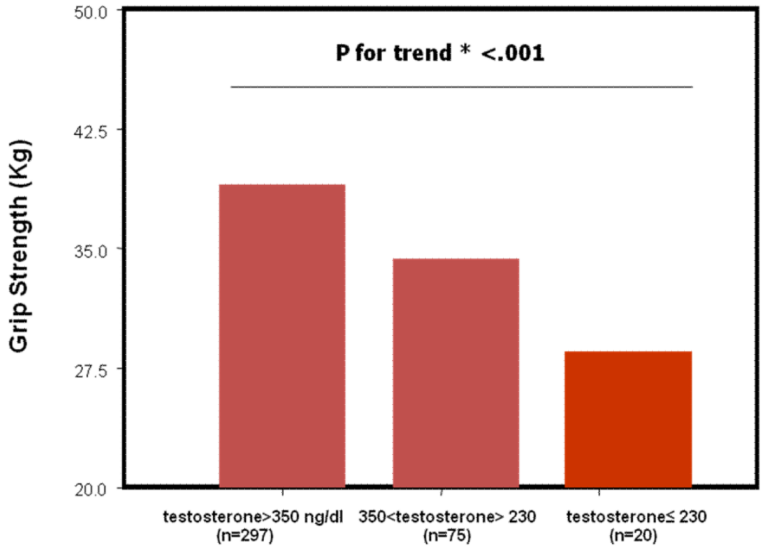


**Figure 2.**
Muscle strength according to gonadal status. The trend of hand grip strength across these groups was significant after adjusting for age and BMI ($p<0.001$).

## TABLE 1

Characteristics of the Study population according to gonadal status[a].

| | Eugonadal testosterone >350 ng/dl | Moderately Hypogonadal 350>testosterone> 230 ng/dl | Severely Hypogonadal testosterone ≤ 230 | P* for trend |
|---|---|---|---|---|
| | N=344 | N=88 | N=23 | |
| Age | 73.8 ± 6.3 | 76.1 ± 7.4 | 82.0 ± 8.4 | <0.001 |
| BMI(Kg/m$^2$) | 26.6 ± 3.4 | 26.9 ± 3.4 | 27.5± 3.2 | 0.39 |
| Smoking (never) n (%) | 98 (28%) | 26 (29%) | 7 (30%) | 0.34 |
| Education (years) | 6.2 ± 3.6 | 6.1 ± 3.2 | 6.4 ± 3.7 | 0.54 |
| Fasting Insulin (mIU/L) | 9.5 [4.5-14.6] | 10.4 [6.9-14.3] | 9.5 [6.8-14.0] | 0.24 |
| IL-6 | 1.6 [1.1-3.0] | 1.5 [0.9-2.2] | 1.6 [0.9-2.7] | 0.53 |
| Hemoglobin (g/dl) | 14.5 ± 1.3 | 14.3 ± 1.2 | 12.5 ± 2.1 | **<.0001** |
| Cross-sectional Muscle Area (mm$^2$) | 6999.9 ± 1228.6 | 6951.2 ± 1111.8 | 6515.3 ±1202.1 | 0.51 |
| 4-m Walking Speed (m/sec) | 1.1 ± 0.3 | 1.0 ± 0.26 | 0.9 ± 0.4 | 0.53 |
| Short Physical performance Battery Score (m/sec) | 10.7 ± 2.7 | 10.0 ± 3.1 | 7.6 ± 4.2 | **0.04** |
| Grip strength (Kg) | 38.8 ± 10.5 | 34.2 ± 9.7 | 27.7 ± 10.5 | **0.02** |
| Physical activity, n ( %) | | | | 0.39 |
| Sedentary Moderate High | 50 (14) | 14 (16) | 5 (5) | |
| Moderate | 264 (77) | 68 (77) | 16 (70) | |
| High | 30 (9) | 6 (7) | 2 (8) | |
| P-arkinson n ( %) | 23 (5) | 0 (0) | 0 (0) | 0.11 |
| CHF, n ( %) | 9 (3) | 4 (15) | 10 (10) | **0.01** |
| Stroke, n ( %) | 18 (4) | 5 (15) | 0 (0) | 0.96 |

[a] Values are expressed as means ± SD (^) unless otherwise indicated.

* Age-adjusted

## Table 2

Differences in determinants and measures of physical performance according to gonadal status.

| Variable | P for trend * |
|---|---|
| Handgrip | **0.004** |
| SPPB | 0.34 |
| 4-m walking Speed | 0.80 |
| Muscle Mass | 0.71 |
| Muscle mass | 0.71 |
| Hemoglobin | **<0.0001** |

* Each line refers to a multivariate analysis adjusted for Age, BMI, Smoking, Education, Physical Activity , Log (IL-6), Log (Insulin), Parkinson's Disease, Chronic heart failure, Stroke.