

# Low Testosterone in Male Patients with Cancer is Associated with Decreased Physical Function



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## Background

- Male patients with cancer often present with serum testosterone concentrations below the normal range.<sup>1</sup>
- Many cancer-related symptoms including weight loss, pain and fatigue have been associated with low serum testosterone concentrations.<sup>2-3</sup>
- Little is known, however, about the impact of extremely low serum testosterone concentrations on physical function in patients with cancer.

## Objective

- To determine whether an extremely low serum free testosterone concentration is associated with reduced physical function in male patients with cancer.

## Methods

### Population

- Our patient population was derived from 176 male patients with cancer who were consecutively evaluated at the Cancer Nutrition Rehabilitation (CNR) clinic of the McGill University Health Centre between January 10, 2007 and September 8, 2010.
- All male patients with solid tumours were included in the study, except patients with prostate, brain or breast cancer.

### Procedures

- The patients' demographic and clinical information, and results of evaluations performed by the CNR team of health professionals were recorded in a computerized database.
- Part of the patient evaluation included a routine blood test and a functional assessment by a physiotherapist.
- The following data was extracted from the database for analysis:

#### Blood Test Results

- Serum Free Testosterone (FT) Concentration**
  - measured by radioimmunoassay using a commercial kit
  - normal range = 31.2 – 162.9 pmol/L

#### Functional Assessment Results

- Six-Minute Walk Distance (6-MWD)**
  - Patients were instructed to cover as much distance as possible in 6 minutes by walking back and forth along a 15 m hallway.
- Gait Speed**
  - Patients were instructed to walk as fast as possible over a total distance of 10 meters. Time was recorded with a stop watch for the middle 5 meters to ensure a constant speed.

### Statistical Analyses

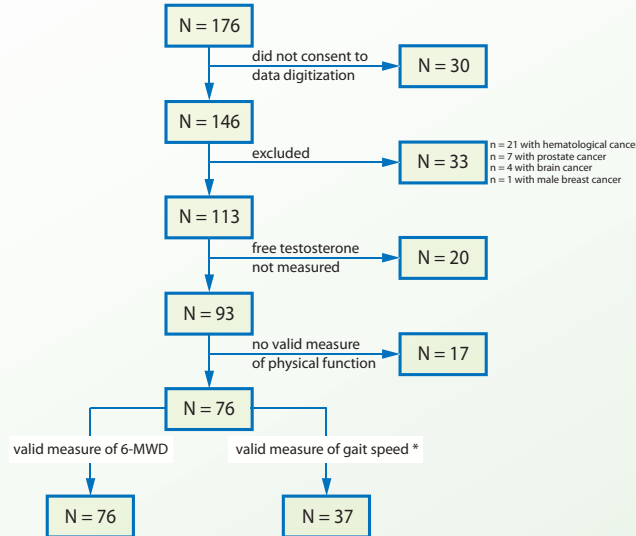
- Independent *t*-tests were used to compare 6-MWD and gait speed between patients in the lowest free testosterone quartile (L) and upper three free testosterone quartiles (U).
- Multivariate linear regression analysis was used to investigate the effect of free testosterone level (L vs. U) on 6-MWD and gait speed, controlling for age.

## Discussion

- Patients with an extremely low serum free testosterone concentration had a significantly lower 6-MWD and gait speed than patients with a mildly low to normal concentration, independently of age.
- Increasing age was associated with reduced 6-MWD in our population, but in contrast to what has been reported in the literature<sup>4</sup>, it did not affect gait speed.
- Serum free testosterone level (L vs. U) and age only explained a small percentage of the variability of physical function in our population. The contribution from other factors such as stage of disease, physical activity level and symptoms like pain and fatigue should be tested in future larger scale studies.

## Results

Figure 1. Patient Flow Diagram of Study Inclusion



\*Gait speed was not initiated as part of the physiotherapist's functional assessment until December 3, 2008.

Figure 2. Six-Minute Walk Distance in Patients in the Lowest Quartile vs. Upper Three Free Testosterone Quartiles (N = 76)

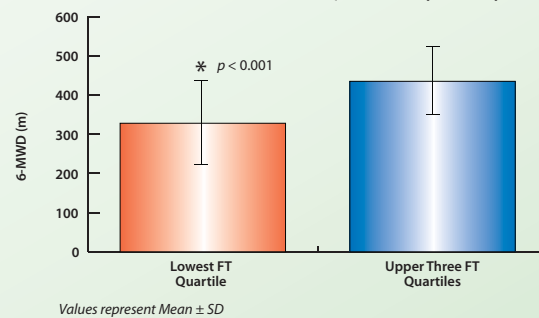


Figure 2 shows that patients in the lowest quartile had a significantly lower 6-MWD than patients in the upper three free testosterone quartiles.

Figure 3. Gait Speed in Patients in the Lowest Free Testosterone Quartile vs. Upper Three Free Testosterone Quartiles (N = 37)

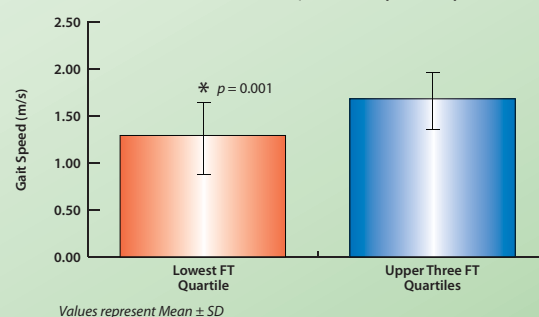


Figure 3 shows that patients in the lowest quartile had a significantly lower gait speed than patients in the upper three free testosterone quartiles.

## Limitations

- This study was limited by its small sample size, and retrospective design.
- Our patients represented a biased population as they were referred to the CNR clinic for complex issues such as severe fatigue, weight loss, and reduced functional capacity.

## References

- Fleishman SB, Khan H, Homel P, et al: Testosterone levels and quality of life in diverse male patients with cancers unrelated to androgens. *J Clin Oncol* 28:5054-60, 2010
- Skipworth RJ, Moses AG, Sangster K, et al: Interaction of gonadal status with systemic inflammation and opioid use in determining nutritional status and prognosis in advanced pancreatic cancer. *Support Care Cancer* 19:391-401, 2011
- Greenfield DM, Walters SJ, Coleman RE, et al: Quality of life, self-esteem, fatigue, and sexual function in young men after cancer: a controlled cross-sectional study. *Cancer* 116:1592-601, 2001
- Bohannon RW: Comfortable and maximum walking speed of adults aged 20-79 years: reference values and determinants. *Age Ageing* 26:15-9, 1997

## Acknowledgements

We wish to thank S. Amdouni, N. Aubin, S. Carney, M. Chasen, M. Eades, P. Di Dio, J. Lemoignan, N. MacDonald, and S. Schulman for their contribution to the success of the CNR program.

Table 1. Patient Characteristics (N = 76)

	Lowest FT Quartile (n = 19)	Upper 3 FT Quartiles (n = 57)
Age (yrs): Mean (SD)	66.9 (12.5)	57.9 (11.8)
Cancer Diagnosis: n (%)		
Head & Neck	1 (5.3)	19 (33.3)
Lung	--	4 (7.0)
Upper Gastrointestinal	3 (15.8)	9 (15.8)
Hepato-biliary	2 (10.5)	6 (10.5)
Pancreatic	5 (26.3)	7 (12.3)
Colorectal	6 (31.6)	5 (8.8)
Other	2 (10.5)	7 (12.3)
Stage: n (%)		
I-II	--	9 (15.8)
III-IV	19 (100)	48 (84.2)
Serum FT (pmol/L)*: Mean (SD) [Range]	6.6 (3.5) [0.1 – 11.8]	23.3 (11.6) [12.1 – 68.9]

\*Normal Serum Free Testosterone Range = 31.2 – 162.9 pmol/L

Patients in the lowest quartile were older and more likely to have colorectal or pancreatic cancer than patients in the upper three free testosterone quartiles.

Table 2. Multivariate Linear Regression of Free Testosterone Level (Lowest Quartile vs. Upper Three Quartiles) and Age on Six-Minute Walk Distance (N = 76)

Outcome: 6-MWD (m)	R <sup>2</sup> = 0.31; p < 0.001	
Predictors:	regression coefficient (95 % CI)	p-value
Serum FT (L vs. U)	-99 (-151 – -9)	<0.001
Age (yrs/10)	-27 (-45 – -9)	0.004

Table 2 shows that patients in the lowest quartile walked 99 m less on average than patients in the upper three free testosterone quartiles, controlling for age.

For every 10 year increase in age, patients walked 27 m less when controlling for free testosterone level.

Table 3. Multivariate Linear Regression of Free Testosterone Level (Lowest Quartile vs. Upper Three Quartiles) and Age on Gait Speed (N = 37)

Outcome: Gait Speed (m/s)	R <sup>2</sup> = 0.28; p = 0.004	
Predictors:	regression coefficient (95 % CI)	p-value
Serum FT (L vs. U)	-0.36 (-0.61 – -0.11)	0.006
Age (yrs/10)	-0.05 (-0.15 – 0.05)	0.317

Table 3 shows that patients in the lowest quartile walked 0.36 m/s slower on average than patients in the upper three free testosterone quartiles, controlling for age.

Age did not influence the average gait speed in our patient population.

## Conclusion

- Our study shows that in male patients with cancer, an extremely low serum free testosterone concentration is associated with significantly decreased physical function, independently of age.
- It remains to be determined whether reduced physical function in male patients with cancer can be overcome with testosterone-replacement therapy.