

Prediction Index of Total Blood Testosterone Level in Elderly Men

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Abstract

The aim of this study was to obtain a new tool to predict blood testosterone level in elderly men that is safe, easy, and widely affordable. Testosterone level is the exact tool to diagnose andropause. However this examination is not affordable and not accessible by most of the Indonesian as it is expensive and can only be found in big cities. Therefore, it is essential to acquire an index to predict the decrease in blood testosterone level that also considers risk factors affecting blood testosterone level. A Diagnostic test performed in 176 elderly men above 60 years old in Bekasi and Depok. The variables observed were body height, body weight, testosterone level, age, level of education, occupation, monthly spending, multivitamin consumption, lifestyle, exercise. Multivariate analysis shows factors that correlate with the decrease in testosterone level are dietary protein consumption, lifestyle and history of bone fracture.

Diagnostic test between the questionnaire of testosterone level and other risk factors with blood testosterone level show 82.2 % sensitivity and 62.8 % specificity. A Prediction index is obtained with cut off at 6. The prediction index was made in the form of manual and software.

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Introduction

The population of elderly continues to increase globally, including in Indonesia. Currently in Indonesia 17 million people (8%) are over 60 years old. This age group is estimated to grow to 13.5% of the population by 2025.¹ In 2020, the elderly population is expected to reach 29.1 million and 36 million in 2025.² The increase rate of average life expectancy can cause epidemiological transition in health field due to the increase of morbidity caused by degenerative disease. One of the most frequent degenerative disease found in elderly and also the most problematic is osteoporosis. Osteoporosis is marked by the progressive decline in bone mass

due to the decrease of bone mineral and matrix along with changes in the microarchitecture of bone tissue.³

Studies showed that more than 20% of rib fractures and 30 % of pelvic fractures occurs in men, and the mortality rate is 37.5% higher compared to women.⁴ Male osteoporosis is a significant public health problem because of its worse effects compared to osteoporosis in women, with the age of onset and hormonal changes being the two-factor contributing to it. Male osteoporosis have a later age of onset and men do not experience menopause like women do. In menopause, there is a steep and drastic decline of estrogen hormone, so there is also a decline of bone mass in women, whereas, in men, the decline in testosterone hormone (andropause) happens gradually. As the consequence, the impact of osteoporosis in men is more dangerous than it is in women.⁴

Male osteoporosis is affected by testosterone. The decline of testosterone level and the loss of bone mass in a male is in line with the increase of age. Factors that play a role in the declining level of testosterone is aging

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process, hypogonadism, obesity, diabetes mellitus type 2, zinc deficiency, testes malignancy and drug consumption, such as opioids, glucocorticoids and ketoconazole. Other factors contributing to the production of testosterone are protein consumption, physical activity, sun exposure, life style and adequate resting time.^{5,6}

Testosterone production is not produced continuously throughout the day which affects the timing on which the testosterone level is measured. The highest level of testosterone is in the morning before 10.00 AM, thus the measurement of testosterone level have to be done in the morning before 10.00 AM. The declining level of testosterone in men is called andropause, which starts at 40 – 50 years old.⁷ Andropause in men is identical with menopause in women, in both, there is a decline in testosterone hormone. It is known as Androgen decline in the aging male (ADAM).⁸

The use of questionnaire might be of help in diagnosing andropa use. ADAM questionnaire is the most frequently used questionnaire with 88% sensitivity and 60 % specificity, it is simple but effective in identifying andropause in men. One of the shortcomings in the ADAM questionnaire is that it does not consider the severity of the decrease, only the absence or presence of the decrease, hence another questionnaire is made called qADAM questionnaire with 96 % sensitivity but only 30 % specificity.⁸

To establish the diagnosis of andropause, an examination of testosterone is level in blood is needed. The measurement of blood testosterone level is expensive and is not affordable by most of the Indonesian people. To bring health facilities more accessible to Indonesian people who mostly live in villages far from any health facilities and would not be able to afford expensive health facilities, a simple and affordable questionnaire is needed. This new questionnaire will also take into considerations some of the major risk factors involving in the decrease of testosterone levels, like protein consumption, sun exposure, physical activity and another lifestyle suitable for Indonesian people.

The objective of this study is to produce a more accurate, easier and effective prediction index for the blood testosterone level which will be used as a screening instrument for an early prevention of the fatal continuation of the

decrease of testosterone level, which is the decrease of bone density and bone fracture.

Materials and methods

This study was conducted in Bekasi and Depok, West Java, with 176 elderly men above 60 years old as subjects. The research protocol was approved by The Faculty of Dentistry Universitas Indonesia Ethical Committee and Faculty of Medicine Ethical Committee Universitas Indonesia prior to data collection.

This study was a diagnostic test with cross-sectional design to acquire a novel and more accurate instrument to predict testosterone level. The variables observed were body height, body weight, testosterone level, age, level of education, occupation, monthly spending, multivitamin consumption, lifestyle, exercise, physical activity, food texture and history of bone fracture. All datas acquired from the questionnaires except total testosterone level was measured using immunoassay method.

Six questionnaires were developed in this study, which are questionnaires about protein consumption, calcium consumption, exposure to sunlight, physical activity, lifestyle and the decrease of testosterone level. The questionnaires themselves are new. Therefore, validity and reliability tests are conducted before the use of the questionnaires. Dietary profile of food containing protein and calcium used food frequency method. Questionnaire about the decrease of testosterone level consisted of nine questions with three options of answers with an emphasis on the severity of symptoms. Below is the Questionnaire of Testosterone Level. (table.1)

No.	Question	Often	Sometimes	Never
1.	Do you feel a decrease in libido/sex drive lately?			
2.	Do you feel easily fatigued?			
3.	Is there a decrease in muscle strength?			
4.	Is there a decrease in height?			
5.	Do you feel a decrement in enjoying life (feeling happy)?			
6.	Do you feel sad or easily irritated?			
7.	Do you feel a decrease in erection strength?			
8.	Do you feel sleepy after dinner?			
9.	Is there a decline in productivity?			

Table 1. The questionnaire of testosterone level.

The result of validity testing shows that the correlation between items in each of the components ranges from weak to very strong with coefficient correlation 0.00 – 0.99 while the correlation between the item and the total component is also weak to very strong with coefficient correlation 0.02 – 0.94. The result of reliability testing of the questionnaire shows the internal consistency is weak until very strong with alpha- Cronbach's score is 0.03 – 0.86. Chi-square analysis was performed to find the relationship between testosterone level and risk factors followed by multivariate analysis to find the dominant risk factors that affects the testosterone level of elderly men with $p < 0.05$.

Result

The testosterone level of subjects based on The Questionnaire of Testosterone Level is shown in Table 2. Majority of subjects had decreased testosterone level based on questionnaire (60.8%).

Questionnaire of the Testosterone Level	n (%)
Good ≤ 8	69 (39,2%)
Decrease > 8	107 (60,8%)

Table 2. Testosterone level of subjects based on The Questionnaire of Testosterone Level.

Risk Factors		Testosterone level Good (86)		Testosterone level Decreased (90)		p-value
		n	%	n	%	
Questionnaire	Good ≤ 8	50	72.5	19	27.5	0.00*
	Decrease > 8	36	33.6	71	66.4	
Age	≤ 70 y.o	52	60.5	54	60	0.95
	> 70 y.o.	34	39.5	36	40	
Education	High	72	83.7	70	77.80	0.32
	Low	14	16.3	20	22.20	
Multivitamin	Yes	31	36	36	40	0.59
	No	55	64	54	60	
Food texture	Hard	72	83.7	67	74.40	0.13*
	Soft	14	16.3	23	25.60	
Lifestyle	Good	76	88.4	86	95.60	0.08*
	Poor	10	11.6	4	4.4	
Calcium intake	Adequate	38	44.2	48	53.30	0.23*
	Deficient	48	55.8	42	46.70	
Protein intake	Adequate	61	70.9	34	37.80	0.00*
	Deficient	25	29.1	56	62.20	
Sunlight Exposure	Adequate	45	52.3	42	46.70	0.45
	Deficient	41	47.7	48	53.30	
Physical Activity	Adequate	46	53.5	41	45.60	0.29
	Lacking	40	46.5	49	54.40	
History of bone fracture	No	82	95.3	81	90	0.18*
	Yes	4	4.7	9	10	
Monthly expenses (Rp)	> 1.5 mill	32	37.2	31	34.40	0.70
	≤ 1.5 mill	54	62.8	59	65.60	
Body mass index	Normal	48	55.8	45	50	0.44
	Low	38	44.2	45	50	

Table 3. Relationship Between Blood Testosterone Level and the Questionnaire of Testosterone Level and Other Risk Factors.

Chi Square Analysis, * $p < 0.25$ to be included in multivariate analysis.

The bivariate analysis between blood testosterone level and the questionnaire of the decline in testosterone level and other risk factors is shown in Table 3. Bivariate analysis and chi-square analysis between blood testosterone level and the questionnaire of testosterone level and other risk factors have shown a significant difference in two variables, which are the questionnaire of testosterone level and nutrition intake containing protein ($p < 0.05$). However, variables such as food texture, lifestyle, food intake containing calcium, history of bone fracture with $P < 0.25$ were included in the multivariate analysis.

The multivariate analysis results show that the factors correlated with the decrease in testosterone level are the questionnaire of testosterone level, food intake containing protein, lifestyle, and history of bone fracture. (table. 4)

	B	S.E.	Wald	Df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Questionnaire	1.68	0.36	21.04	1	0.00	5.37	2.61	11.01
Protein	1.44	0.35	16.54	1	0.00	4.23	2.11	8.50
Lifestyle	-0.97	0.68	2.01	1	0.15	0.37	0.09	1.44
History of Bone Fracture	0.89	0.68	1.73	1	0.18	2.45	0.64	9.33
Constant	-1.63	0.35	21.34	1	0.00	0.19		

Table 4. Final model multivariate analysis between testosterone level and the questionnaire of testosterone level and other risk factors.

Risk Factors	Code	Weight	Score (code x weight)
Questionnaire Good: 8 Decrease > 8	0	5	
	1		
Protein Intake ≤ 145.79 gr/mg > 145.79 gr/mg	1	4	
	0		
Good Lifestyle Poor Lifestyle	1	1	
	0		
History of Bone Fracture 'yes' no	1	1	
	0		
Total score			

Table 5. Index of the decrease of testosterone level in elderly men.

Score 0-6 normal testosterone level.

Score 7-11 decline of testosterone level.

The scoring system is a more simple way to predict risk factors of the decrease in testosterone level. From this study, a scoring model is created based on the final model of multivariate analysis. The scoring model, with the name "Index of the Decrease of Testosterone Level in Elderly Men" is shown in table 5. The score ranges from 0 -11 with cut off 6, meaning

that score from 0-6 implies a normal testosterone level, and the score ranging from 7 -11 implies a decline in testosterone level. If the results show a decline in testosterone level, then the patient must be referred to a specialist.

Discussion

Testosterone plays an important role in regulation bone turnover and bone mass in men by promoting bone formation. A reduced of testosterone level leads to an increase of alveolar bone loss and changes of trabecular pattern as well as a decrease in bone mineral density of skeletal tissue. Combination of bone mineral density and testosterone level might have more impact for tooth loss prediction.⁹ It is important for dentist to predict testosterone level in men to prevent tooth loss. The result of this study concludes that factors correlated with the decline in testosterone level are questionnaire of testosterone level, protein intake, lifestyle, and history of bone fracture.

The diagnostic test between questionnaire of testosterone level and level of testosterone showed sensitivity and specificity of the questionnaire were 78.9% and 58.1 % respectively. This questionnaire will be used as screening tool due to high sensitivity. This result is in accordance with several other studies using ADAM questionnaire. ADAM questionnaire had sensitivity of 88-97% suggesting its utility as a screening test. Despite a high sensitivity, the ADAM questionnaire is reported to have a specificity of only 24-60%, suggesting that its use beyond an initial assessment maybe limited. ADAM test lacks specificity, so it is not recommended as an alternative for blood serum examination of free testosterone to identify androgen deficiency in elderly men.¹⁰

Wing Chu et al. investigated the validity of the ADAM questionnaire chinese version as a screening for androgen deficiency in Chinese men.¹¹ The statistical analysis showed that Chinese ADAM Questionnaire has a high sensitivity (88%) but low specificity (32 %).¹¹ This study is also in line with the study conducted by Balliet and Burke. They found that there was an increase in testosterone level of the male subjects who gradually increased their protein consumption following the low calories diet intervention.¹² Aging and modifiable lifestyle factors such as tobacco and alcohol use,

caffeine intake, psychosocial stress, obesity are associated with testosterone levels. Diet and exercise have also shown influences on Sex Hormone Binding Globulin, thereby affecting the bioavailable pool of testosterone.¹³

This study concluded that the risk of men with the history of the bone fracture to have a decline in testosterone level is 2.5 times larger than men with no history of bone fracture. This study is in accordance with the result of a study conducted by Risto, et al. They proved that the group with history of bone fracture had a significantly lower bone density and free androgen index compared to the group without history of bone fracture. The study also found that the total testosterone level in the group with history of bone fracture is lower than the group without history of bone fracture although results from statistical analysis found that it was not significant.¹⁴ A study from Meier, et al. also showed a similar result¹⁵

Testosterone level decreased significantly with the increasing smoking habit. Testosterone level were found to be significantly lower among heavy smoking-severe oligo/azoosperma patients as compared to non smoking-normozoosperma controls ($p < 0.00$).¹⁶ A double-blind cross-study conducted by Beaven, et al. who investigated the acute effect of caffeine on the increased exercise of professional rugby athlete correlated with testosterone and cortisol level. The study concluded that the higher a given dose of caffeine, the higher the increase of the athletes' testosterone level. All of these results showed the same result with this study in proving that elderly men who consume coffee and smoke have a lower decline in testosterone level compared to elderly men who do not consume coffee and smoke.¹⁷

Shun Chueh in his study comparing the AMS scale (Aging Male Symptoms) with ADAM questionnaire in detecting androgen deficiency. The result of his study concluded that both AMS scale and ADAM questionnaire have enough sensitivity and specificity to detect androgen deficiency of elderly men. Both tools (AMS scale and ADAM questionnaire) can be used for screening purposes, but thorough physical and biochemical examination have to be done in patients with high risk or suspected of having androgen deficiency.¹⁸

Diagnostic test of the questionnaire of testosterone level compared to total blood

testosterone level in this study shows a more accurate result with 78.9 % sensitivity and 58.1 % specificity, and so this questionnaire is qualified as an early diagnostic tool for the decrease in testosterone level. Testosterone level examination is needed as an exact diagnosis. Diagnostic examination between the questionnaire of testosterone level and other risk factors compared to total testosterone level was also conducted in this study because the decline in testosterone level is affected by many risk factors.

The result of the diagnostic examination showed 82.2 % sensitivity and 62.8% specificity, qualifying this questionnaire as the screening tool for elderly men suspected of suffering from the decline in testosterone level. This study also created an index to predict the decrease in testosterone level. The use of the questionnaire and this prediction index will increase the accuracy in predicting the decrease in testosterone level and so will be more accurate as a screening tool in predicting the decrease in total testosterone level

Conclusions

A questionnaire of testosterone level and an index to predict the decrease of testosterone level in elderly men in a form of a simple scoring model were developed based on multivariate analysis of risk factors. This scoring model is a very significant screening tool so initial preventive measurements could be done to prevent the decrease in testosterone level and decline in bone density.

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Declaration of Interest

The authors report no conflict of interest.

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