P 1-2

The association between free testosterone level and cognition in elderly women.

Shin Who Park[1*], Won Kim[1†], Kyoung Hyo Choi[1]

Asan Medical Center, University of Ulsan College of Medicine, Department of Rehabilitation Medicine[1]

INTRODUCTION
The human cognitive function can be affected by many factors. Among these factors, testosterone has been thought to play a neuroprotective role in the brain. There have been several studies attempting to correlate cognitive function with testosterone. However, the results of them were inconsistent. The limitation of previous study is that majority of them were conducted in small groups and there have been no study based on Asian data. Furthermore, the effects of physical function on cognition were neglected and unadjusted and there are less studies on female testosterone compared to male.

OBJECTIVE
This study aimed to investigate the association between serum free testosterone (FT) level and cognitive function in elderly women.

METHODS
This is a cross-sectional study using the Korean Frailty and Aging Cohort Study (KFACS) database for the elderly living in a community (1582 females) in the 70-84 age group. Cognitive dysfunction is defined as the below 24 points in Mini-Mental Status Examination in the Korean version of the CERAD Assessment Packet (MMSE-KC) and lower 25% of the value measured by Trail Making Test (TMT), Frontal Assessment Battery (FAB), Digit span, Word list memory, recall and recognition. Lowest quartile groups in skeletal muscle index (appendicular skeletal muscle mass(ASM)/height^2) are defined as sarcopenia and below 9 points of Short Physical Performance Battery (SPPB) are considered poor function group. The duration of education is divided in two groups based on graduation from junior high school or not. Univariate and multivariate logistic regression analyses were performed to investigate the association between FT level and cognitive function.

RESULTS
Low FT level was associated with decreased cognitive function in most of cognitive function test results except Word list recognition task (Table 2, univariate analysis). These associations were maintained in MMSE-KC, TMT, FAB, Word list memory task after

adjusting for all potential confounding factors including skeletal muscle index and SPPB (Table 2, model 2 and 3). Analyses based on four categories in FT level revealed a higher odds ratio (OR) in the lower quartile groups in univariate analysis and multivariate analyses (Table 3).

CONCLUSION

Decreased cognitive function is associated with low FT level in elderly women. And it seems the lower the FT value, the greater the risk of cognitive decline. Additional long term follow up studies are needed to determine the predictability of cognitive disorders with testosterone level.

Table 1. Descriptive data of study variables (N=1582)

Variable	Mean ± S.D.	
Age (years)	75.50	± 3.84
70≤ <75 (%)	42.20	
75≤ <80 (%)	36.30	
80≤ <85 (%)	21.50	
Height (m)	1.51	± 0.05
ASM (kg)	13.52	± 3.78
ASM/Height² (kg/m²)	5.85	± 0.56
SPPB (point)	10.67	± 1.51
Education duration (year)	7.28	± 4.66
> 9 years (%)	23.4	
Free Testosterone (pg/mL)	0.90	± 0.86
MMSE-KC (point)	25.38	± 3.26
≤ 23 (%)	28.60	
> 23 (%)	71.40	
TMT (sec)	90.00	± 64.57
FAB (point)	13.23	± 2.94
Digit span (point)	10.21	± 3.69
Word list (point)		
Memory	16.80	± 4.60
Recall	5.66	± 2.11
Recognition	8.63	± 1.82
Alcohol consumption≥ 2/wk (%)	20.60	
Current smoker (%)	1.00	
Depression (%)	3.70	
Cerebrovascular disease (%)	3.40	

S.D., standard deviation; ASM, appendicular skeletal muscle mass; SPPB, Short Physical Performance Battery; MMSE-KC, Mini-Mental Status Examination in the Korean version of the CERAD Assessment Packet; TMT, Trail Making Test; FAB, Frontal Assessment Battery.

Table 2. Odds ratio of serum free testosterone level for cognitive functio

	Univariate analysis		Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
MMSE-KC	**1.652**	**1.291-2.113**	**1.627**	**1.263-2.096**	1.279	0.936-1.749	**1.337**	**1.013-1.764**
TMT	**1.651**	**1.278-2.133**	**1.622**	**1.243-2.117**	**1.493**	**1.070-2.084**	1.331	0.994-1.781
Digit Span	**1.324**	**1.037-1.691**	**1.294**	**1.009-1.660**	0.972	0.709-1.334	1.091	0.832-1.430
FAB	**1.801**	**1.387-2.337**	**1.781**	**1.365-2.324**	**1.466**	**1.055-2.038**	**1.499**	**1.121-2.003**
Word list								
Memory	**1.749**	**1.368-2.236**	**1.781**	**1.365-2.324**	**1.620**	**1.195-2.196**	**1.499**	**1.121-2.003**
Recall	**1.436**	**1.127-1.829**	**1.410**	**1.096-1.813**	1.179	0.877-1.587	1.281	0.980-1.674
Recognition	1.209	0.953-1.534	1.177	0.925-1.497	1.056	0.798-1.399	1.119	0.869-1.440

The odds of developing cognitive function decrease in the lowest quartile group relative to the rest was analyzed by logistic regression analysis.
Decreased cognitive function was defined by scoring in the lowest quartile on each questionnaire.
P values <0.05 are in boldface.
Model 1 was adjusted for age group.
Model 2 was adjusted for age group, alcohol consumption, smoking, depression, education duration, and ASM/height².
Model 3 was adjusted for age group, alcohol consumption, smoking, depression, education duration, and SPPB.

OR, odds ratio; CI, confidence interval; MMSE-KC, Mini-Mental Status Examination in the Korean version of the CERAD Assessment Packet; TMT, Trail Making Test; FAB, Frontal Assessment Battery; ASM, appendicular skeletal muscle mass; SPPB, Short Physical Performance Battery.

Table 3. Odds ratio of each quartile of serum free testosterone level for cognitive function

		Univariate analysis		Model 1		Model 2		Model 3	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
MMSE-KC	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	**1.411**	**1.004-1.984**	**1.498**	**1.057-2.124**	**1.653**	**1.076-2.539**	**1.644**	**1.124-2.404**
	Q3	**1.680**	**1.204-2.344**	**1.732**	**1.231-2.438**	1.476	0.966-2.255	**1.599**	**1.100-2.325**
	Q4	**2.234**	**1.612-3.096**	**2.267**	**1.622-3.168**	**1.744**	**1.153-2.638**	**1.889**	**1.312-2.720**
TMT	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	0.815	0.572-1.163	0.839	0.582-1.211	0.843	0.525-1.353	0.834	0.558-1.247
	Q3	1.214	0.868-1.698	1.235	0.872-1.748	1.161	0.743-1.814	1.137	0.775-1.668
	Q4	**1.659**	**1.198-2.297**	**1.654**	**1.181-2.318**	1.499	0.976-2.303	1.317	0.909-1.907
Digit Span	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	1.222	0.885-1.685	1.274	0.918-1.768	1.333	0.875-2.031	1.270	0.887-1.817
	Q3	**1.458**	**1.064-1.999**	**1.484**	**1.076-2.047**	**1.573**	**1.045-2.367**	1.319	0.927-1.875
	Q4	**1.617**	**1.183-2.210**	**1.611**	**1.172-2.214**	1.265	0.840-1.906	1.310	0.927-1.850
FAB	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	0.937	0.651-1.349	0.968	0.668-1.404	0.930	0.592-1.463	0.870	0.582-1.301
	Q3	1.095	0.768-1.561	1.099	0.767-1.576	0.897	0.574-1.403	1.001	0.679-1.476
	Q4	**1.819**	**1.302-2.543**	**1.821**	**1.295-2.561**	1.378	0.905-2.099	**1.454**	**1.007-2.100**
Word list Memory	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	1.106	0.793-1.541	1.170	0.831-1.648	1.372	0.913-2.062	1.169	0.813-1.680
	Q3	1.166	0.839-1.619	1.186	0.845-1.664	1.005	0.664-1.522	1.091	0.761-1.565
	Q4	**1.906**	**1.391-2.612**	**1.926**	**1.391-2.666**	**1.806**	**1.218-2.679**	**1.649**	**1.166-2.331**
Word list Recall	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	0.959	0.697-1.320	1.004	0.721-1.397	1.007	0.692-1.466	1.006	0.711-1.423
	Q3	1.226	0.899-1.671	1.249	0.905-1.723	0.977	0.672-1.421	1.218	0.868-1.708
	Q4	**1.521**	**1.121-2.063**	**1.525**	**1.111-2.093**	1.172	0.809-1.699	1.395	0.998-1.948
Word list Recognition	Q1	Ref.		Ref.		Ref.		Ref.	
	Q2	1.057	0.781-1.432	1.091	0.802-1.484	1.102	0.778-1.561	1.063	0.773-1.460
	Q3	1.234	0.915-1.664	1.247	0.922-1.689	1.184	0.837-1.674	1.231	0.900-1.684
	Q4	1.324	0.984-1.782	1.306	0.967-1.765	1.158	0.816-1.644	1.235	0.902-1.691

The odds of developing cognitive function decrease in the respective quartile group relative to the 1st quartile group were analyzed by logistic regression analysis. The quartile groups were numbered in descending order.
P values <0.05 are in boldface.
Model 1 was adjusted for age group.
Model 2 was adjusted for age group, alcohol consumption, smoking, depression, education duration, and ASM/height².
Model 3 was adjusted for age group, alcohol consumption, smoking, depression, education duration, and SPPB.

OR, odds ratio; CI, confidence interval; Qn, nth quartile group of free testosterone level; Ref.,reference; MMSE-KC, Mini-Mental Status Examination in the Korean version of the CERAD Assessment Packet; TMT, Trail Making Test; FAB, Frontal Assessment Battery; ASM, appendicular skeletal muscle mass; SPPB, Short Physical Performance Battery.