RESEARCH ARTICLE

The association between serum testosterone and mortality among elderly men on hemodialysis

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Objectives: This study examines the associations between total testosterone levels and dialysis mortality.

Methods: Elderly men who initiate hemodialysis in Taoyuan General Hospital from January 2012 to June 2017 were enrolled. We reviewed clinical characteristics and biochemical data from start of dialysis and followed over a 5-year period after dialysis. Body composition parameters were assessed 3-6 months after dialysis. Skeletal muscle mass index (SMMI) was defined by skeletal muscle mass divided by squared height. We defined those with lowest tertile of testosterone values as low testosterone group. Adjusted hazard ratios (aHRs) and 95% confidence interval (95% CI) for mortality and cumulative survival curves were evaluated by Cox hazards model and Kaplan-Meier method. The discriminative power of SMMI and testosterone levels was calculated according to the area under the curve and the receiver operating characteristic curve (AUROC).

Results: From a total of 137 elderly hemodialysis patients, the range of lowest, middle, and highest tertile of testosterone values was <6.25 nmol/L, 6.25-10.5 nmol/L, and >10.5 nmol/L. After multivariate adjustment other than SMMI, total testosterone levels at baseline were a significant predictor for mortality aHR(95% CI): 0.79 (0.70-0.91). The unadjusted and adjusted c-statistics of SMMI vs testosterone values to predict overall were 770 (0.688-0.852) vs 0.779 (0.691-0.866) and 855 (0.812-0.886) vs 0.812 (0.744-0.856) ($P_s < .05$), whereas the capacity of c-statistics was similar ($\chi^2 = 0.143$ and 2.709, $P_s > .05$).

Conclusions: Total testosterone value was a predictor for mortality. It was noninferior to SMMI in predicting dialysis mortality.

KEYWORDS

body composition, dialysis, low muscle mass, mortality, testosterone

1 | INTRODUCTION

Low muscle mass is common in patients on maintenance dialysis and is associated with poor physical functioning.¹⁻³ Sarcopenia, defined as a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength, and sarcopenic obesity were also risk factors for mortality.^{1,4} It was associated with chronic inflammation,

physical inactivity, malnutrition, and decreased lung function.^{1,5-7} The prevalence of sarcopenia in the elderly is ranged from 0.9% to 24.2%. In Asia, men over 65 years old are more likely to get sarcopenia than women.^{8,9}

Obesity is associated with an increased risk of mortality in general population. Nevertheless, some reports of patients on dialysis have suggested the opposite.^{10,11} There is a U-curve association between body mass index (BMI) and mortality in patients with chronic kidney disease (CKD).¹¹ In those with end-stage renal disease (ESRD), being

Both Hung-Chieh Wu and Lin-Chien Lee contributed equally to this work.

overweight or obese is associated with improved survival whereas being underweight is associated with increased mortality. Indeed, some study had demonstrated the protective effect of high BMI seems limited to high muscle mass, not high fat mass.¹¹ There were several methods to measure lean muscle mass and fat mass, such as dual-energy X-ray absorptiometry (DEXA) and bioimpedance analysis (BIA). However, these methods were not available worldwide and might require repeat measurements.¹²

Low serum testosterone and hypogonadism were highly prevalent in those with CKD.¹³ The rate of decline in testosterone levels is higher in those with CKD, including those on dialysis.¹⁴ It was associated with adipocyte dysfunction, insulin resistance, sarcopenia, and followed by obesity.¹⁵ Besides, it was also linked to endothelial dysfunction, disorder of bone composition, and serum receptor activator of nuclear factor kappa-B ligand (sRANKL) levels.^{16,17} Testosterone inhibited muscle protein degradation and potentiated stem cell differentiation toward myocyte. Testosterone therapy in men with hypogonadism might produce lean muscle mass gain, increased muscle strength and size, as well as weight loss.^{18,19} Hence, testosterone levels were correlated and associated with skeletal muscle mass and low testosterone concentrations might predict long-term survival in those with CKD or dialysis.^{20,21}

The aim of this study was to evaluate prognostic importance of serum testosterone in elderly men with hemodialysis and whether low testosterone levels were superior to low skeletal muscle mass in predicting mortality or not. As testosterone level predicted mortality in male HD patients was largely dependent on age,¹⁴ we restricted our study population to elderly men to minimize the confounding effect of age and analyzed multiple risk factors and comorbid conditions at start of dialysis, including skeletal muscle mass index (SMMI), serum testosterone, BMI, and well-known risk factors for

mortality after dialysis in a regional hospital. The impacts of those factors on mortality in those undergoing dialysis were followed over 5 years.

2 | MATERIALS AND METHODS

2.1 | Subjects

This is a retrospective observational cohort study that included 245 adult male patients receiving dialysis in Taoyuan General Hospital from January of 2012 to June of 2017. The subjects were followed up until September 30, 2017. We reviewed clinical characteristics and biochemical data from start of renal replacement therapy (RRT) and followed over a 5-year period after dialysis. Body composition parameters, including overhydration (OH), fat tissue mass index (FTI), extracellular water (ECW), intracellular water (ICW), and SMMI, were assessed 3-6 months after dialysis. BMI was defined as body weight (kg) divided by height square (m^2). Dialysis dose (Kt/V) was estimated by urea kinetic modeling formulas.²² Those with dialysis vintage less than 3 months ($n = 6$), those on peritoneal dialysis ($n = 19$), those with lack of demographic and biochemical data ($n = 11$), those undergoing dialysis with ventilator dependency ($n = 2$), and those younger than 65 years old were excluded ($n = 70$) (Figure 1). Consequently, a total of 137 eligible male patients were included for analysis.

2.2 | Ethics

This study was conducted in accordance with the Declaration of Helsinki (2000) of the World Medical Association, and the protocol was approved by the institutional review board of Taoyuan General Hospital (TYGH.106011). This study was investigated in a single

FIGURE 1 Data flow

regional hospital, and all patients in the study were directly diagnosed and followed up at Taoyuan General Hospital.

2.3 | Outcome ascertainment

Demographic data, comorbidities, clinical characteristics, biochemical data, and all-cause mortality as well as the date and possible etiology of death were recorded according to electronic medical records. Participants lost to follow-up without death confirmation were censored at the last date of follow-up. Participants who survived over the administration censor date were censored on September 30, 2017. In addition to all-cause mortality, cardiovascular death (CV death) was defined as death due to coronary heart disease, sudden cardiac death, peripheral arterial occlusive disease, and stroke.²⁰

2.4 | Body composition measurements

Body composition parameters were measured by bioimpedance spectroscopy using physiological models and mixture equations (Cole-Cole plot and Hanai formulas) (body composition monitor (BCM), Fresenius Medical Care, Germany). FTI and SMMI were defined by fat tissue mass and skeletal muscle mass divided by squared height (FTM/Ht^2 and SMM/Ht^2).¹ Skeletal muscle mass (SMM) was calculated after the following bioimpedance analysis equations: Skeletal muscle mass (kg) = $\{(0.401 \times \text{height}^2/\text{Resistance}) + (3.825 \times \text{gender}) - (0.071 \times \text{age}) + 5.102\}$, where height was in centimeter, resistance was in ohms, men = 1 and women = 0, and age was in years.²³ As it was reported 70% of muscle mass and 20% of fat mass were made up of water, volume of overhydration (OH) was defined by total body water minus water from muscle mass and fat mass.²⁴ Fluid overload, reflected by $OH/ECW \geq 15\%$, was estimated and adjusted in the study.²⁵ Sarcopenia was defined as $SMMI < 8.87$ in Asian men.⁹ Body composition parameters measured by bioimpedance spectroscopy had been validated by gold standard methods, such as bromide dilution method for ECW, total body potassium method for ICW, DEXA for lean muscle mass and fat mass, and clinical assessment and ultrafiltration volume for fluid overload.²⁴

2.5 | Comorbidity ascertainment and laboratory data measurement

All laboratory measures were performed by laboratory department in Taoyuan General Hospital using standardized and automated methods. Serum creatinine values were measured by an enzymatic IDMS traceable method (Beckman Coulter AU640 analyzer, Brea, California), whereas CRP was measured by latex assay (AU system, Beckman, Brea, California). Serum albumin was determined using bromocresol green (BCG) assay (AU640, Beckman Coulter, Brea, California). Total testosterone (reference range: 8.36–28.7 nmol/L (241–827 ng/dL)) was measured by chemiluminescence immune assay (CLIA, Centaur, SIEMENS, Munich, Germany). Based on previous studies, low testosterone values could be defined as lowest tertile, lowest quartile among dialysis population, or serum testosterone levels

below 10.4 nmol/L.^{20,26,27} We defined those with lowest tertile of testosterone levels (<6.25 nmol/L) as low testosterone group regarding sample size and study power, whereas those with testosterone levels ≥ 6.25 nmol/L were defined as non-low testosterone group. The interassay coefficient of variability in serum testosterone was 19.5%, 12.7%, and 7.4% in low (1.8–4.1 nmol/L), middle (9.5–17.7 nmol/L), and high pool (21.7–36.8 nmol/L). After commencing dialysis, most blood samples were collected predialysis, except postdialysis BUN. Postdialysis BUN was obtained to calculate dialysis dose using urea kinetics modeling formula.²² Laboratory data such as albumin, creatinine (SCr), hemoglobin (Hb), C-reactive protein (CRP), and dialysis dose (Kt/V) were measured at start of RRT. Not only body composition parameters but also total testosterone were measured concomitantly at 3–6 months after dialysis. Diagnosed comorbidities were also recorded at start of dialysis, such as diabetes (DM), hypertension (HTN), history of cancer, coronary artery disease (CAD), and congestive heart failure (CHF). CHF was defined according to the New York Heart Association (NYHA) Functional Classification, whereas CAD was defined as elevated serum troponin I and the need for revascularization.

2.6 | Statistical analysis

Continuous variables with a normal distribution were summarized as mean $\pm$ SD unless otherwise stated. Variables with a non-normal distribution are expressed as a median (interquartile range (IQR)). Normality was assessed by Kolmogorov-Smirnov test. Pearson's chi-square test, Fisher's exact test, Student's independent t test, or Mann-Whitney U test is used to determine the differences in the demographic data, the laboratory variables, and clinical characteristics between 2 groups. Spearman's rank correlation (ρ) was used to determine correlations of testosterone with other variables. All-cause mortality and cardiovascular mortality were recorded and calculated using Kaplan-Meier method. Cumulative survival curves for mortality in hemodialysis patients with different groups were performed according to the log-rank test. The hazard ratios (HRs) and 95% confidence intervals (CIs) for all-cause mortality were calculated using Cox proportional hazards model. The fit of the Cox proportional hazard model was tested by Schoenfeld residuals test. The prognostic values of low testosterone levels were tested by several models: model 1, adjusted with age and BMI; model 2, adjusted with age, BMI, comorbidities (DM and HTN), and biochemical data; model 3, adjusted with all variables including body composition parameters; and model 4, adjusted with all variables except SMMI. Calculations and comparisons in competing risk data ratio for all-cause and cardiovascular death were conducted using Fine and Gray's proportional subhazard models. We chose "Enter" method for multivariable adjustment; thus, all variables were entered together. The discriminative ability of SMMI and testosterone to predict mortality was determined using the area under the curve for the receiver operating characteristic (AUROC) curve. C-statistic was calculated using predicted probabilities variable produced by binary logistic regression as the test value in ROC graph procedure. All statistical analyses were performed using PASW Statistics 18 (SPSS

Inc., Chicago, IL, USA) and STATA 14.0 (StataCorp. College Station, Texas, USA). Because of the good correlation between SMMI and testosterone, we compared *c*-statistics using method developed by Delong.²⁸ A two-tailed *P* value of <.05 was considered statistically significant.

3 | RESULTS

3.1 | Demographic data

The cohort of the 137 elderly men were followed up for a median of 23.4 months, ranged from 4 to 60 months, since commencing dialysis. None of these patients received organ transplantation. The median age for the patients was 72 years. The most common causes of ESRD were diabetes (37.9%) and chronic glomerulonephritis (24.1%). The majority (~88%) of serum testosterone values were obtained before noon (89.1% of low testosterone group vs 86.8% of non-low testosterone group; *P* = .790). The range of lowest, middle, and highest tertile of testosterone values was <6.25 nmol/L, 6.25-10.50 nmol/L, and >10.50 nmol/L, whereas the proportion of sarcopenia in different tertiles was 54.3%, 4.5%, and 2.2%,

respectively (*P* < .001). The mortality rate at the end of the 5-year study period was 44.5% (*n* = 61). The median time to mortality after dialysis was 24 months. The common cause of mortality during the 5-year cohort period was cardiovascular events (59.0%).

3.2 | Comparisons between low vs non-low testosterone groups

Table 1 showed the comparisons between low and non-low testosterone group at start of dialysis. The age was similar between matched groups (73.0 years vs 71.0 years). The group of low testosterone values consisted of higher proportion of CV death (51.0% vs 18.3%), higher proportion of sarcopenia (54.3% vs 6.6%), and higher level of CRP (142.7 nmol/L vs 89.4 nmol/L). The low testosterone group also consisted of lower levels of BMI (23.0 vs 23.4), lower levels of skeletal muscles reflected by SMMI (7.8 kg/m² vs 9.7 kg/m²), lower level of serum creatinine (0.81 mmol/L vs 0.91 mmol/L), and lower ECW and ICW (13.9 L vs 17.0 L and 18.4 L vs 20.0 L) (all *P*s < .05). There was no difference between 2 groups in age, length of hemodialysis, serum albumin, hemoglobin, Kt/V, overhydration, FTI, and underlying disease.

TABLE 1 Baseline characteristics of study population

Parameters	Low testosterone N = 46	Non-low testosterone N = 91	P value
Age (y)	73.0 (65.0-79.0)	71.0 (66.0-78.0)	.330
Length of HD (mo)	23.0 (11.0-42.0)	23.4 (8.0-48.0)	.603
BMI (kg/m ²)	22.8 (22.0-25.1)	24.9 (23.1-27.3)	<.001*
Cause of death (n) (CVE/sepsis/others)	23/4/11	13/4/6	<.001*
Comorbidity			
DM (n)	17	35	1.000
Hypertension (n)	30	59	1.000
CHF (n)	5	9	1.000
History of cancer (n)	5	5	.303
CAD (n)	10	16	.646
Biochemical data at first trimester of dialysis			
Albumin (g/dL)	32.0 (29.0-35.0)	35.0 (33.0-39.0)	.053
Creatinine (mmol/L)	0.81 (0.73-0.91)	0.91 (0.78-1.04)	<.001*
Hemoglobin (g/L)	88.0 (80.0-92.0)	94.0 (84.0-102.0)	.096*
C-reactive protein (nmol/L)	142.7 (119.2-193.3)	89.4 (57.1-135.5)	<.001*
Total testosterone (nmol/L)	4.82 (3.96-5.76)	10.9 (8.60-14.30)	<.001*
Kt/V	1.51 (1.35-1.77)	1.45 (1.28-1.60)	.082
OH (L)	2.1 (1.6-2.3)	1.9 (1.4-2.3)	.857
SMMI (kg/m ²)	7.8 (6.9-8.6)	9.7 (8.8-10.9)	<.001*
FTI (kg/m ²)	10.8 (8.1-14.0)	12.4 (8.8-14.6)	.200
ECW (L)	13.9 (9.8-16.4)	17.0 (13.1-20.3)	.041*
ICW (L)	18.4 (16.1-19.8)	20.0 (17.6-21.6)	.015*

*P < .05, data were percentage, mean ± standard deviation, and median (interquartile range (IQR)).

BMI, body mass index; CVE, cardiovascular event; HD, hemodialysis; DM, diabetes mellitus; CHF, congestive heart failure; CAD, coronary artery disease; OH, overhydration; SMMI, skeletal muscle mass index; FTI, fat tissue mass index; ECW, extracellular water; ICW, intracellular water.

TABLE 2 Univariate correlations between serum testosterone and other variables

Variables	Spearman ρ	P
Age (per year)	-0.131	.171
C-reactive protein (per nmol/L)	-0.304	<.001*
Hemoglobin (per mg/dL)	0.307	.001*
Albumin (per g/dL)	0.377	<.001*
Creatinine (per mg/dL)	0.275	.004*
BMI (per kg/m ²)	0.203	.033*
FTI (per kg/m ²)	-0.127	.188
SMMI (per kg/m ²)	0.773	<.001*
ICW (per L)	-0.002	.981
OH/ECW (per %)	-0.356	<.001*

*P < .05, by Spearman's rank test.

3.3 | The discriminative power and associations between testosterone values and death

In Table 2, serum testosterone values decreased with CRP and fluid status (OH/ECW), and moved in the same direction as albumin, hemoglobin, SCr, BMI, and SMMI. The correlation between SMMI and testosterone levels was good (correlation coefficient 0.77). In univariate analysis for continuous variables using Cox proportional hazards model, albumin, SMMI, CRP, BMI, and serum testosterone values were significant predictors for all-cause mortality (Data S1). After adjusting for BMI, comorbidities (DM and hypertension), laboratory data, and biocomposition parameters other than SMMI, testosterone value remained a predictor for all-cause death and cardiovascular mortality (adjusted HRs and 95% CI: 0.79 (0.70-0.91) and 0.88 (0.77-0.99))(Ps < .05). Compared to non-low testosterone

group, the low testosterone group had strong associations with either all-cause death or cardiovascular mortality (adjusted HRs and 95% CI: 3.39 (1.67-6.86) and 6.13 (2.27-16.53)) (Model 4) (Table 3). The association between low testosterone values and all-cause mortality was independent of general obesity, albumin, and inflammation. However, after adjusting for SMMI, the prognostic value of testosterone level was not persisted in neither all-cause nor cardiovascular death (Model 3). Figure 2 shows the survival curves for those on dialysis between low and non-low testosterone groups at baseline. The mortality was different for low vs non-low testosterone groups (82.6% vs 25.3%, log-rank $\chi^2 = 36.15$, $P < .001$). As cardiovascular mortality might be confounded by competing risk of other etiologies of death, we calculated and compared cumulative incidence in competing risk data ratios. The cumulative incidence of cardiovascular and all-cause death was 33.6% and 44.5%, whereas the cumulative incidence difference of cardiovascular and all-cause death between low and non-low testosterone groups after 5 years was 29.1%(11.7%-46.4%) and 56.4%(37.7%-75.0%, $P_s < .01$). Because potential mechanism of low testosterone values in predicting dialysis death was associated with low skeletal muscle mass, we also compared the discriminative power, c-statistics, of SMMI to that of serum testosterone values. The unadjusted c-statistics of SMMI vs testosterone values to predict overall survival were 0.770 (0.688-0.852) vs 0.779 (0.691-0.866), whereas those for CV death were 0.724 (0.620-0.828) vs 0.721 (0.609-0.833)($P_s < .05$). The capacity of 2 unadjusted c-statistics was similar ($\chi^2 = 0.143$ and 0.003, $P_s > .05$). Adding age, BMI, comorbidities, laboratory data, and other body composition parameters into the model did not change the result. The adjusted c-statistics of SMMI vs testosterone values to predict overall survival were 0.855 (0.812-0.886) vs 0.812 (0.744-0.856), whereas those for CV death were 0.736

TABLE 3 Crude and adjusted all-cause and cardiovascular death of low testosterone group^a

Models	All-cause mortality		Cardiovascular death	
	HR (95% CI)	P value	HR (95% CI)	P value
Crude	3.71 (2.17-6.30)	<.001*	4.71 (2.28-9.72)	<.001*
Model 1				
Age + BMI	3.83 (2.17-6.76)	<.001*	4.88 (2.24-10.66)	<.001*
Model 2				
Model 1 + DM + HTN + biochemical data ^b	3.27 (1.60-6.67)	<.001*	6.54 (2.37-18.01)	<.001*
Model 3				
Model 2 + body composition	0.95 (0.41-2.26)	.911	1.56 (0.50-4.90)	.447
Model 4				
Model 3 - SMMI	3.39 (1.67-6.86)	<.001*	6.13 (2.27-16.53)	<.001*

^aCompared to non-low testosterone group.

^bBiochemical data include serum albumin, creatinine, hemoglobin, C-reactive protein, and testosterone.

*P < .05.

DM, diabetes; HTN, hypertension; BMI, body mass index; SMMI, skeletal muscle mass index.

FIGURE 2 Cumulative survival curves after commencing dialysis over 5 y for low vs non-low testosterone group Both P s < .05 (A) all-cause death (B) cardiovascular death

(0.675-0.812) vs 0.683 (0.592-0.806) (P s < .05). The capacity of 2 adjusted c-statistics was not different ($\chi^2 = 2.709$ and 2.542, P s > .05) (Figure 3).

4 | DISCUSSION

This retrospective observational cohort study demonstrated that not only skeletal muscle mass index but also low testosterone values at baseline was associated with mortality after multivariable adjustment. Low testosterone values were associated with low skeletal muscle mass. There was no difference between the discriminative power of SMMI and testosterone in predicting death. Baseline testosterone values were noninferior to SMMI in predicting dialysis death.

Several studies had demonstrated the association among low testosterone values, risk of cardiovascular disease, and mortality.^{14,15,29} However, the comparisons between skeletal muscle mass and testosterone values in predicting mortality have not been well investigated. Low testosterone values were associated with sarcopenia, low muscle strength, and physical inactivity.^{15,30} There was also dose-response relationship between testosterone therapy and gain of muscle mass as well as muscle strength.¹⁸ Testosterone potentiated differentiation of pluripotent stem cell toward myogenic lineage and inhibited muscle protein degradation. There was also bidirectional relationship between low testosterone values and obesity as well as metabolic syndrome.²⁹ Hence, serum testosterone values provided survival information through associations with low skeletal muscle mass and obesity. It was also linked to endothelial dysfunction, erythropoietin-stimulating

FIGURE 3 The discriminative power of SMMI vs testosterone for mortality over 5 y (A) all-cause death (B) cardiovascular death

agents hyporesponsiveness, disorder of bone composition, inflammation, and serum receptor activator of nuclear factor kappa-B ligand levels.^{16,17,31,32} Testosterone might work as hemopoietic growth factor through improving iron bioavailability via the hepcidin pathway.³¹ Moreover, testosterone was inversely correlated with the progress of atherosclerosis in aorta and carotid artery.^{33,34} Undoubtedly, serum testosterone levels can predict mortality. The incidence of protein-energy wasting, which was a predictor of dialysis death, was higher in subjects with sarcopenic obesity rather than that in subjects with low muscle mass only.¹ Not surprisingly, serum testosterone, which might be an indicator of sarcopenic obesity in elderly men, was noninferior to SMMI in predicting dialysis death. In present study, we demonstrated that baseline testosterone values were noninferior to SMMI in predicting all-cause and cardiovascular death. The prognostic value of testosterone values was not persisted after adjusting for SMMI. Serum testosterone values might provide survival information for those on maintenance dialysis.

In the study, the incidence of low testosterone values was similar to previous study (50% ~ 70%).^{13,20} There were several explanations for high prevalence of low testosterone values in those with CKD. One of them was dysfunction of hypothalamic-pituitary-gonadal axis, which resulted in decreased synthesis and secretion of serum testosterone. It was also reported low testosterone levels might predict

mortality in those with advanced CKD, whereas the predictability was unclear in general population.³⁵ Besides, some testosterone might be removed by hemodialysis. Moreover, diurnal change and high variance of testosterone levels were also reported.³⁶ Low testosterone values could not be explained by increased clearance only. In the study, more than 80% of testosterone levels were measured before the noon and all blood samples were obtained before the dialysis sessions. The effect of diurnal change and in-person variance would be minimized. Although we had only single measurement of total testosterone levels, it might be reliable and representative for long-term hormone milieu in men.^{37,38} After adjusting for demographic data, body composition parameters except SMMI, and biochemical data, baseline total testosterone levels remained a significant predictor for dialysis death.

In those on dialysis, whether serum testosterone was superior to SMMI in predicting mortality was unclear. The strength of the study was to measure lean body mass precisely using body composition monitor and compare the discriminative power between serum testosterone values and SMMI in predicting dialysis death. Although the discriminative power of testosterone levels in predicting mortality was less than that of SMMI, there was no difference between the capacities of adjusted and unadjusted c-statistics (both P s > .05). However, there were several limitations in present study. First, it was a retrospective observational study within one medical center; therefore, the external validity was limited. Second, single measurement of total testosterone values was not representative for longitudinal and long-term testosterone levels. However, total testosterone levels declined in those on maintenance dialysis and those with normal testosterone at baseline might be reclassified nondifferentially into non-low or low testosterone groups at follow-up. The misclassification might underestimate the prevalence of androgen deficiency and biased to the null difference; thus, our finding will be more significant without misclassification. Third, SMMI measured by bioimpedance analysis was easily influenced by overhydration. We had adjusted for overhydration values to reduce the bias. Finally, estradiol levels were not measured. Estradiol level was a surrogate for visceral fat and might be associated with cardiovascular death.¹⁸ Nonetheless, it was less strongly associated with cardiovascular death than testosterone.³⁹

In summary, baseline total testosterone value was a predictor for mortality after multivariate adjustment. It was noninferior to SMMI in predicting death among elderly men on dialysis. Endogenous testosterone might be a simple marker for biocomposition parameters and a cardiovascular risk factor for those on dialysis. The associations between the anabolic effect of exogenous testosterone therapy and mortality were not clear. This study was limited by the retrospective nature and sample size. A multicenter randomized control trial is warranted to confirm the association between exogenous testosterone supplement and dialysis survival.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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