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Correlates of T_{50} and Relationships with Bone Mineral Density in Community-Living Older Men: The Osteoporotic Fractures in Men (MrOS) Study

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Keywords

Calcification propensity score; bone mineral density

Osteoporosis is a major cause of morbidity and mortality in older persons [1]. While prevalence is particularly high in women, osteoporosis is also common in men, and risk factors may be unique [2]. T_{50} is a novel serum-based marker that assesses the propensity to calcification [3].

When calcium and phosphate precipitation is initiated in serum, there is formation of primary calciprotein particles (CPPs) which are rich in calcium and phosphate and contain small quantities of proteins including albumin and fetuin-A. With time, these moeties transition to larger secondary CPPs that differ in calcium, phosphate, and protein content from the primary CPPs. Calciprotein particle maturation time (T_{50}) is a measure of the time to transition from primary to secondary CPPs in serum in vitro [3]. Shorter T_{50} suggests greater propensity to calcify. A shorter T_{50} has been associated with risk of cardiovascular disease (CVD) and all-cause mortality in kidney transplant recipients [4] and CKD patients [5]. No study to our knowledge has evaluated the relationship of T_{50} with bone disease in those without kidney disease. This study was designed to examine the correlates of T_{50} and relationship to bone mineral density (BMD) in community-living older men.

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CONFLICTS OF INTEREST

Andreas Pasch is an inventor of the T_{50}-Test and co-founder, stock-holder, and employee of Calciscon Ltd., Nidau, Switzerland, which commercializes the T_{50}-Test. Dr Orwoll has received research support from Lilly and Mereo Biopharma, and has provided consulting for Bayer. Alexander L Bullen, Cheryl A.M Anderson, Elizabeth R. Hooker, Deborah M. Kado, and Joachim H. Ix declare that they have no conflict of interest.

We measured T_{50} among participants from The Osteoporotic Fractures in Men (MrOS) Study (http://mrosdata.sfcc-cpmc.net), a prospective observational cohort study of 5994 men at six sites across the US [6,7]. We took a random sample of 150 individuals, one had missing blood specimens, bringing our analytic sample to 149. We categorized individuals into tertiles of T_{50}, and compared demographics and disease indicators across tertiles using analysis of variance and chi square tests, as appropriate. We utilized linear regression to evaluate the cross-sectional association between T_{50} and hip and spine BMD. The mean T_{50} was 336 ± 52 min. All participants were men, mean age was 74 ± 5 years, and 19% (n=29) had CVD. Participant demographics and clinical characteristics, stratified by tertile of T_{50} concentration, are shown in Table 1. Older men were more likely to have shorter T_{50}. Kidney function tended to be lower in those with shorter T_{50}, and the prevalence of CVD and low ankle brachial index were higher in this group, albeit these findings did not reach statistical significance. We found no statistically significant associations between T_{50} and total hip or total spine BMD in analyses adjusted for variables including age, BMI, kidney function, vitamin D, and PTH. (Table 2)

In conclusion, T_{50}, a novel indicator of serum calcification propensity was not associated with BMD in a random sample from the MrOS study of community-living older men. Shorter T_{50} is a robust indicator for soft tissue calcification and cardiovascular disease in high risk populations. We observed non-significant trends between shorter T_{50} and higher prevalence of CVD and lower ankle brachial index in community-living men. These findings were not statistically significant but should be re-evaluated in larger study samples in future studies to determine if T_{50} may give insights to cardiovascular disease risk above and beyond traditional risk factors in the general population.

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Table 1.

Selected characteristics[a] by T_{50} tertiles in community-living older men (MrOs) (random sub-cohort only, n=149)

	T_{50} Tertile I	T_{50} Tertile II	T_{50} Tertile III	*P*-value[c]
T_{50} range (min)	206–314	314–361	361–477	
N	50	50	49	
Age (years) ± SD	75.1 (±5.8)	73.3 (±4.7)	72.3 (±4.3)	0.02
Black, N (%)	4 (8.0)	2 (4.0)	2 (4.1)	0.15
Clinical Center, N (%)				
Birmingham	21 (42.0)	19 (38.0)	22 (44.9)	0.78
Portland	29 (58.0)	31 (62.0)	27 (55.1)	
> High school education, N (%)	42 (84.0)	43 (86.0)	35 (71.4)	0.14
BMI (kg/m^2) ± SD	27.7 (±3.9)	27.8 (±3.8)	27.0 (±3.5)	0.48
Alcohol intake (drinks/wk) ± SD				
<1 drink/week	24 (48.0)	26(53.1)	24 (50.0)	0.88
1+ drinks/week	26 (52.0)	23 (46.9)	24 (40.0)	
Smoking status, N (%)				
Never	10 (20.0)	21 (42.0)	20 (40.8)	0.15
Former	37 (74.0)	27 (54.0)	27 (55.1)	
Current	3 (6.0)	2 (4.0)	2 (4.1)	
Physical activity score ± SD	146.5 (±83.7)	159.3 (±84.6)	161.2 (±66.5)	0.60
Prevalent CVD, N (%)	10 (20.0)	13 (26.0)	6 (12.2)	0.22
ABI, N (%)				
<0.9	7 (14.0)	2 (4.1)	1 (2.0)	0.11
0.9 to <1.4	42 (84.0)	47 (95.9)	47 (95.9)	
>=1.4	1 (2.0)	0	1 (2.0)	
Hypertension, N (%)	21 (42.0)	23 (46.0)	19 (38.8)	0.77
Diabetes, N (%)	6 (12.0)	11 (22.0)	0	<0.01
eGFR (ml/min/1.73m^2) ± SD	75.5 (±18.2)	82.6 (±15.1)	82.3 (±18.0)	0.07
Calcium (mg/dL) ± SD	9.3 (±0.4)	9.2 (± 0.4)	9.3 (±0.4)	0.43
Phosphate (mg/dL) ± SD	3.2 (±0.5)	3.2 (± 0.4)	3.1 (±0.4)	0.13
PTH (pg/ml) ± SD	33.4 (±16.3)	31.2 (±13.2)	29.2 (±9.9)	0.32
25(OH) Vitamin D (ng/ml) ± SD	22.9 (±8.3)	23.7 (±7.5)	24.3 (±6.8)	0.65
Mean total hip BMD (g/cm^2) ± SD	0.9 (±0.2)	0.9 (+0.1)	0.9 (±0.1)	0.44
Mean total spine BMD (g/cm^2) ± SD	1.0 (±0.2)	1.0 (±0.2)	1.0 (±0.2)	0.99

[a]Variables from baseline (not available at dental visit 1): education level, PASE score, CVD (stroke or MI), ABI, hypertension, diabetes, eGFR, Calcium, Phosphate, history of any fracture, history of hip fracture.

Table 2.

Linear regression of the association between T_{50} and total hip and total spine BMD

Total hip BMD (g/cm^2)		**Beta (95% CI)**	***P*-value**
	Model 1	0.000009 (−0.0004, 0.0004)	0.97
	Model 2	<–0.0001 (−0.0005, 0.0005)	1.00
Total spine BMD (g/cm^2)			
	Model 1	−0.0002 (−0.0007, 0.0004)	0.50
	Model 2	<–0.0001 (−0.0007, 0.0006)	0.91

Model 1: Unadjusted

Model 2: Adjusted for age, race, clinical center, BMI, physical activity, PTH, vitamin D, eGFR, Calcium, and Phosphate