Osteoporosis International (2019) 30:1529–1531
https://doi.org/10.1007/s00198-019-04925-8

SHORT SCIENTIFIC COMMUNICATION

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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Received: 5 February 2019 / Accepted: 1 March 2019 / Published online: 18 March 2019

Abstract

Purpose T_{50} is a novel serum-based marker that assesses the propensity of calcification in serum. Shorter T_{50} indicates greater propensity to calcify and it has been associated to cardiovascular disease (CVD) and mortality among patients with kidney disease. In the general population, neither the correlates of T_{50} nor the relationships of T_{50} with bone mineral density (BMD) are known.

Methods We performed a nested cross-sectional study selecting 150 individuals at random among participants from the Osteoporotic Fractures in Men (MrOS) Study, a study of community-living older men. We categorized individuals into tertiles of T_{50} and compared demographics and disease indicators across tertiles. We utilized linear regression to evaluate the cross-sectional association between T_{50} and hip and spine BMD in multivariable models.

Results Older age was associated with shorter T_{50}. Kidney function tended to be lower in those with shorter T_{50} and the prevalence of CVD and peripheral arterial disease in those with shorter T_{50}, albeit these findings did not achieve statistical significance. We found no statistically significant associations between T_{50} and total hip or total spine BMD in either unadjusted or multivariable adjusted models.

Conclusions T_{50}, a novel indicator of serum calcification propensity, is not associated with BMD in community-living older men. Future larger studies should determine if T_{50} may give insights to CVD in the general population above and beyond traditional risk factors.

Keywords Bone mineral density · Calcification propensity score

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 moieties 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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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 USA [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 measurements were more prevalent 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 either unadjusted models, or 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 of community-living older men from the MrOS study. 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 peripheral arterial disease marked by the ankle-brachial index in community-living men. These

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/week) ± 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. 73 m^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

	Beta (95% CI)	*P* value
Total hip BMD (g/cm^2)		
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

findings were not statistically significant in the small studysample evaluated here 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.

Funding information Dr. Alexander L. Bullen was supported by a Ruth L. Kirschstein training grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK; T32DK104717). Dr. Joachim H. Ix was supported by a midcareer mentoring award from the NIDDK (K24DK110427). Measurements were supported from an award from the American Heart Association to Dr. Joachim H. Ix (14EIA18560026).

The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: the National Institute on Aging (NIA), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Center for Advancing Translational Sciences (NCATS), and NIH Roadmap for Medical Research under the following grant numbers: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128.

Compliance with ethical standards

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.

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