Excessive accumulation of visceral fat and the risk of developing proteinuria in the general population

Young Su Kim[1], Jeon Yong Deok[2], Jwa-Kyung Kim[1], Sung Gyun Kim[1], Hyung Jik Kim[1]

Department of Internal Medicine & Kidney Research Institute, Hallym University Sacred Heart Hospital, Korea
[2]Department of Internal Medicine, National Medical Center

Objectives

- Obesity is recognized as an independent risk factor for the development of chronic kidney disease (CKD). A reduction in body weight (BW) can improve proteinuria, and glomerular filtration rate (GFR). Hence, emphasis has recently been placed on the importance of optimal obesity management, and the control of the fat mass.
- Further, the predictive ability of abdominal or central obesity to identify individuals with increased health risks might be more evident. Visceral obesity is closely associated with various metabolic and cardiovascular complications and even mortality above and beyond that associated with total adiposity.
- Although a few limited number of studies have evaluated the association between visceral adipose tissue and albuminuria, most analyses were conducted as a cross-sectional design.

Methods

- In this longitudinal cohort study of the general Korean population, the effects of baseline VFM as well as 4-year changes in VFM (ΔVFM) on proteinuria development were prospectively evaluated.
- Individuals who participated in two health screening check-ups separated by a 4-year period (2008–2012, 2009–2013) were analyzed. Subjects with the following criteria were excluded (n = 198); pre-existing proteinuria at the baseline exam (n = 48); previous history of urologic malignancy (n = 6); glomerulonephritis (n = 12); CKD or undergoing dialysis (n = 51); and missing data at baseline (n = 81).
- Body composition data were obtained using a multifrequency bioelectrical impedance analyzer (Zeus 9.9 PLUS; Jawon Medical, Korea). The data about fat mass (FM), percentage of body fat (PBF, %), and VFM (kg) were obtained.
- Subjects were divided into 3 groups by gender-specific tertile of the baseline VFM and ΔVFM.

Results

- The mean age was 51.9±7.7 years, and 23.4% were men. Men were significantly older and had higher systolic and diastolic blood pressure (BP) and BMI than women. As expected, bioimpedance analysis revealed markedly higher PBF and VFM in men.
- Over the 4-year follow-up, 1258 (52.5%) subjects experienced a decline in VFM, whereas 870 (36.4%) gained VFM. The remaining 235 (11.1%) participants experienced no changes in VFM. The median value of ΔVFM
- was – 0.10 (interquartile range [IQR]: -0.4, 0.2) and 0.00 (IQR: -0.2, 0.2) in men and women, respectively.
- The incidence of proteinuria development was 3.9% (n=93), and was significantly higher in men than women (6.1% vs. 3.2%, p = 0.001).

Table 1. Factors associated with proteinuria development.

Variables	Men, proteinuria development			Women, proteinuria development		
	+ (n = 34, 6.1%)	- (n = 527)	p	+ (n = 59, 3.2%)	- (n = 1776)	p
Age, years	58.9 ± 9.3	53.9 ± 7.7	< 0.001	54.5 ± 8.7	51.1 ± 7.4	0.001
SBP, mmHg	129.7 ± 15.4	122.6 ± 14.9	0.014	128.1 ± 18.6	117.1 ± 15.1	<0.001
DBP, mmHg	83.2 ± 9.2	77.6 ± 10.3	0.003	79.0 ± 15.0	72.2 ± 11.0	<0.001
Smoking, n (%)	14 (41.1)	97 (18.4)	0.084	10 (16.9)	51 (2.8)	0.031
BMI	26.8 ± 3.3	24.5 ± 2.6	<0.001	24.3 ± 3.4	23.3 ± 2.8	0.011
Creatinine (mg/dL)	1.04 ± 0.22	0.92 ± 0.19	<0.001	0.82 ± 0.21	0.74 ± 0.13	<0.001
eGFR (mL/min/1.73m^2)	80.2 ± 19.4	91.7 ± 16.2	<0.001	84.6 ± 18.8	92.4 ± 14.6	<0.001
hs_CRP	-2.00 ± 0.91	-2.36 ± 0.91	0.067	-2.41 ± 1.15	-2.73 ± 0.084	0.015
WC	91.2 ± 9.5	83.4 ± 9.3	<0.001	80.1 ± 9.9	76.7 ± 7.9	0.001
Δ WC	1.93 ± 5.86	-1.2 ± 6.21	0.030	2.10 ± 5.78	-0.87 ± 6.02	0.001
VFM (kg)	3.38 ± 1.36	2.42 ± 0.81	<0.001	2.45 ± 1.0	2.02 ± 0.7	0.003
Δ VFM (kg)	0.07 ± 0.62	-0.11 ± 0.49	0.039	0.16 ± 0.68	-0.04 ± 0.39	<0.001
PBF (%)	27.4 ± 4.68	25.1 ± 4.67	0.005	30.1 ± 5.6	28.4 ± 4.3	0.036
Δ PBF (%)	0.01 ± 3.37	-0.70 ± 3.06	0.084	0.02 ± 3.79	-0.30 ± 2.59	0.058

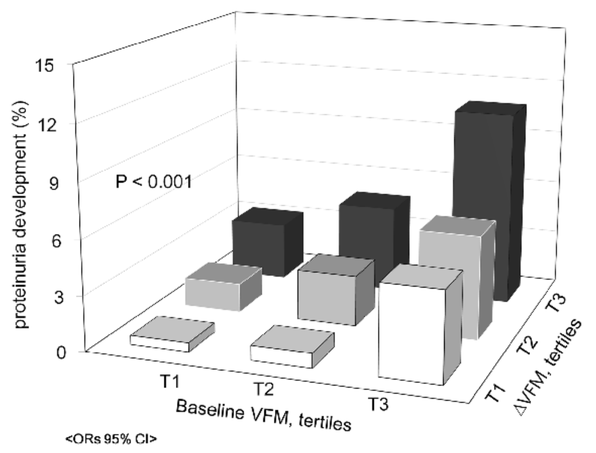
- At baseline, increased age and various obesity-related cardiometabolic parameters including higher BP, increased WC, and higher levels of VFM and PBF were significantly associated with future proteinuria development. Serum hs-CRP levels were also higher in subjects with proteinuria development.
- In addition, subjects who developed proteinuria exhibited a significant increase in ΔVFM, whereas those without proteinuria development experienced a decrease in ΔVFM during the 4 years.

Table 2. OR for proteinuria development stratified by tertiles of baseline VFM and ΔVFM

Parameters	Men (n = 561)				Women (n = 1832)			
	Total	Proteinuria development	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)	Total	Proteinuria development	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Baseline VFM								
T1	186	5 (2.7)	1 (reference)	1 (reference)	610	10(1.6)	1 (reference)	1 (reference)
T2	187	8 (4.3)	1.61 (0.52-5.01)	1.19 (0.37-3.83)	611	16 (2.6)	1.61 (0.73-3.58)	1.17 (0.52-2.64)
T3	188	21 (11.2)	4.55 (1.67-12.34)	3.43 (1.22-9.67)	611	33 (5.4)	3.42 (1.67-7.01)	2.01 (1.05-4.15)
ΔVFM during 4 years								
T1	185	7 (3.8)	1 (reference)	1 (reference)	610	12 (1.9)	1 (reference)	1 (reference)
T2	186	8 (4.3)	1.03 (0.31-2.44)	1.02 (0.35-2.90)	612	17 (2.8)	1.44 (0.67-2.21)	1.85 (0.85-4.00)
T3	190	19 (10.0)	2.45 (1.05-5.76)	2.92 (1.22-6.99)	610	30 (4.9)	2.65 (1.34-5.23)	3.16 (1.56-6.39)

- Subjects in the highest baseline VFM and ΔVFM tertiles had a significantly increased the risk of proteinuria development in both genders. Even after adjustment for age, smoking, systolic and diastolic BP, serum creatinine, and hs-CRP levels, each of the highest tertiles of baseline VFM and ΔVFM were independent predictors of proteinuria development.

Figure 1. The incidence of proteinuria development according to baseline VFM and ΔVFM tertiles



<ORs 95% CI>

Baseline VFM / ΔVFM	T1	T2	T3
T1	1 (reference)	1.49 (0.13-16.51)	10.06 (1.33-76.14)*
T2	3.06 (0.35-26.38)	5.64 (0.70-45.49)	11.66 (1.49-91.22)*
T3	6.46 (0.81-51.46)	9.70 (1.25-75.25)*	23.41 (3.15-98.11)*

Subjects in the highest baseline VFM and ΔVFM tertiles exhibited the greatest risk of proteinuria development, which suggested the additive harmful effects of the two factors.

Table 3. Comparisons of WC and VFM for predicting the risk of proteinuria development

Variables		Multivariate analysis			
		VFM		WC	
		OR (95% CI)	P	OR (95% CI)	P
Age	1 year increase	1.06 (1.02-1.10)	0.003	1.05 (1.02-1.09)	0.005
Gender	male	1.03 (0.65-1.85)	0.422	1.16 (0.61-2.22)	0.636
Smoking	presence	1.02 (0.75-2.22)	0.545	1.03 (0.71-2.89)	0.449
SBP	1 mmHg increase	1.02 (1.01-1.04)	0.038	1.02 (1.01-1.04)	0.041
baseline creatinine	1 mg/dL increase	2.67 (2.19-7.11)	0.001	3.98 (2.23-10.16)	0.002
hs-CRP	1 mg/L increase	1.23 (0.94-1.59)	0.124	1.22 (0.94-1.59)	0.135
VFM or WC	T1 (reference)	-	-	-	-
	T2	1.81 (0.81-2.41)	0.143	1.11 (0.77-1.76)	0.233
	T3	2.66 (1.44-4.94)	0.002	2.07 (0.96-4.49)	0.064
ΔVFM or ΔWC	T1 (reference)	-	-	-	-
	T2	1.79 (1.01-3.53)	0.048	1.85 (0.99-3.44)	0.053
	T3	3.49 (2.01-6.06)	<0.001	2.60 (1.31-5.17)	0.006

- **Following adjustment of both parameters, both the highest baseline VFM and ΔVFM tertile were significant determinants of future proteinuria development in multivariate analysis.**
- **Then, to compare the effectiveness as a predictor of proteinuria development between WC and VFM, we reanalyzed our data with WC.**
- **As a result, as expected, the highest tertile of Δ WC was an independent predictor of proteinuria development (OR 2.60, 95% CI 1.31-5.17, p=0.006) in multivariate analysis. However, the predictive role of highest tertile of baseline WC for proteinuria development was marginally significant (OR2.07, 95% CI 0.96-4.49, p=0.064).**

Conclusions

- **(1) during the 4 years, the incidence of proteinuria development was 3.9%, and it was significantly higher in men compared to women.**
- **(2) Baseline VFM and greater increase in ΔVFM were both important risk factors for developing proteinuria in the general population**
- **(3) Appropriate education and interventions to prevent accumulation of VFM should be the major focus of preemptive strategies.**

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