Association of Body Mass Index with Estimated Glomerular Filtration Rate and Incident Proteinuria

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Abstract: Obesity has been one of the most important risk factors of chronic kidney disease (CKD). But the association of body mass index (BMI) with estimated glomerular filtration rate (eGFR) and incident proteinuria has not been studied well. The goal of this study was to elucidate the association of BMI with eGFR and proteinuria using nationwide health examination data. These associations were investigated with data of Korean adults who had undergone health screenings at least three times between 2009 and 2014. eGFR was calculated with Chronic Kidney Disease Epidemiology collaboration equation based on serum creatinine level. The association between BMI and eGFR was analysed with a generalized addictive model adjusting for possible confounders. Similarly, the association between BMI and incident proteinuria was analysed with Cox hazard model adjusting for possible confounders. As a result, a V-shape relationship between BMI and eGFR was observed. The nadir was around 29 kg/m^2. With subgroup analyses for the association between BMI and eGFR, a V-shape association was observed in men and younger age group and an inverse association was observed in women and older age group. A reverse J-shape association between BMI and the adjusted hazard ratio of incident proteinuria was observed. The nadir was approximately estimated around 22 kg/m^2.

1 INTRODUCTION

Obesity has been one of the most important risk factors of Chronic Kidney Disease (Mahmoodnia, 2017). CKD is an emerging health issue because of its high prevalence and incidence worldwide and its association with cardiovascular morbidity and mortality. The relationship between body mass index (BMI), the most representative index of obesity, and estimated glomerular filtration rate (eGFR) has not been studied well. Several studies with small sample size have reported the inverse linear association between BMI and eGFR (Grubbs, 2014). Obesity has been associated with abnormally increased eGFR and decrease of eGFR or measured GFR after successful weight reduction, such as Bariatric surgery is rather well-known (Li, 2016). These observations are not consistent to the observed inverse linear association between BMI and eGFR. Similarly, only a few prospective cohort studies observed an association between overweight and obesity and increased risk of incident proteinuria, and the nature of the relationship between BMI and incident proteinuria has not been reported yet. A cross-sectional study has observed the U-shape association between BMI and prevalent proteinuria (Sato, 2014). Although a sex-specific association of incident proteinuria with underweight and no association with overweight and obesity after 2 years' follow-up has been reported, the follow-up period of that study might not be long enough (Jang, 2014).

The goal of this study was to elucidate the association of BMI with eGFR and incident proteinuria using nationwide health examination data.

2 METHODS

Regular health screening at designated screening hospital across the country is obligatory for adult Koreans. The number of eligible subjects between 2009 and 2014 was between 15,036,607 and 16,456,214. The participation rate was between 66.0% and 74.8% (Cheol, 2016). The data of Korean

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adults (27,448,308 participants) who had undergone health screenings between 2009 and 2014 were analysed. Health screening tests performed on the participants under 20 years old and foreign citizens were excluded (728,569 participants). Subjects with missing information on BMI, eGFR and other confounders were also excluded. For more accurate analysis, we set the minimum time interval between the first health screening of each individual to the next his/her health screening to 6 months. Furthermore, persons who had undergone health screenings at least three times between 2009 and 2014 were included in this study (12,211,062 adults). BMI was calculated from the measured height and weight. The eGFR (mL/min/1.73 m^2) was calculated by the Chronic Kidney Disease Epidemiology Collaboration equation based on serum creatinine level (Inker, 2012). Depending on smoking habit, persons were categorized as non-smoker, ex-smoker, and smoker. Persons who performed moderate or high intensity exercise more than three times a week were classified as 'yes' in the category of regular exercise. Alcohol consumption were categorized as non-drinker, 1~2 times a week, 3~4 times a week and heavy drinker (almost daily).

To observe any differential association between BMI and eGFR according to age or sex, the participants were divided into subgroups by sex and sex-specific median age. The relationship of BMI with eGFR was analysed with a generalized additive model adjusting for possible confounding variables at baseline such as age, sex, systolic blood pressure, fasting serum glucose, serum triglycerides, serum high-density lipoprotein- cholesterol, smoking status, regular alcohol consumption, regular exercise, and known history of medication for diabetes and hypertension. To investigate the association between BMI and incident proteinuria with national health screening data, we analysed the

Table 1: Characteristics according to body mass index categories.

	Total (n=12,211,062)	BMI[1] < 18.5 kg/m² (n=415,403)	18.5kg/m² ≤ BMI < 25kg/m² (n=7,841,447)	BMI ≥ 25 kg/m² (n=3,954,212)	P-value
Age (years)	46.9 ± 13.6	39.3 ± 14.9	46.4 ± 13.6	48.56 ± 13.0	<.001
Sex					
Male	5,541,961 (45.4%)	280,406 (67.5%)	3,783,941 (48.3%)	1,477,614 (37.4%)	<.001
Female	6,669,101 (54.6%)	134,997 (32.5%)	4,057,506 (51.7%)	2,476,598 (62.6%)	
SBP[2] (mmHg)	122.2 ± 14.8	113.0 ± 13.5	120.3 ± 14.3	127.1 ± 14.4	<.001
FSG[3] (mg/dL)	96.9 ± 22.4	90.2 ± 17.9	95.2 ± 20.9	101.0 ± 24.9	<.001
TG[4] (mg/dL)	132.6 ± 91.9	82.1 ± 49.1	119.2 ± 80.4	164.7 ± 106.6	<.001
HDL[5] (mg/dL)	55.0 ± 13.6	63.0 ± 14.3	56.4 ± 13.7	51.3 ± 12.4	<.001
Smoking					
Never	7,366,297 (60.3%)	297,972 (71.7%)	4,892,862 (62.4%)	2,175,463 (55%)	<.001
Formal	1,821,408 (14.9%)	27,479 (6.6%)	1,073,589 (13.7%)	720,340 (18.2%)	
Current	3,023,357 (24.8%)	89,952 (21.7%)	1,874,996 (23.9%)	1,058,409 (26.8%)	
Regular exercise[6]					
Yes	2,926,581 (24%)	60,088 (14.5%)	1,867,823 (23.8%)	998,670 (25.3%)	<.001
No	9,284,481 (76%)	355,315 (85.5%)	5,973,624 (76.2%)	2,955,542 (74.7%)	
Alcohol consumption[7]					
None	6,234,122 (51.1%)	234,699 (56.5%)	4,078,439 (52%)	1,920,984 (48.6%)	<.001
1 ~ 2	4,383,086 (35.9%)	143,920 (34.6%)	2,793,094 (35.6%)	1,446,072 (36.6%)	
3 ~ 4	1,155,360 (9.5%)	25,504 (6.1%)	693,639 (8.8%)	436,217 (11%)	
> 4	438,494 (3.6%)	11,280 (2.7%)	276,275 (3.5%)	150,939 (3.8%)	
Anti-HT[8]					
Yes	1,679,739 (13.8%)	13,916 (3.3%)	829,837 (10.6%)	835,986 (21.1%)	<.001
No	10,531,323 (86.2%)	401,487 (96.7%)	7,011,610 (89.4%)	3,118,226 (78.9%)	
Anti-Diabetic[9]					
Yes	556,411 (4.6%)	5,543 (1.3%)	291,845 (3.7%)	259,023 (6.6%)	<.001
No	11,654,651 (95.4%)	409,860 (98.7%)	7,549,602 (96.3%)	3,695,189 (93.4%)	

[1] Body mass index; [2]Systolic blood pressure; [3] Fasting serum glucose; [4] Serum triglycerides; [5] Serum high-density lipoprotein-cholesterol; [6] Regular exercise: moderate or high intensity exercise, more than three times per week; [7] Number of alcohol consumption per week; [8] History of anti-hypertensive medication; [9] History of anti-diabetic medication

Note: Number (percentage %) for categorical variables; Mean ± standard deviation for continuous variables.

P-value was calculated by ANOVA-test for continuous variables and Pearson's chi-squared test for categorical variables. P-values < 0.05 denote statistical significance.

data of participants who had eGFR 60 mL/min/1.73 m^2 or above and normo-proteinuria at baseline (11,559,520 adults). Incident proteinuria was defined as the occurred event when the result of urine dipstick test showed a protein 1+ or higher during the follow-up period in each individual who had negative result in urine dipstick test at the first health screening.

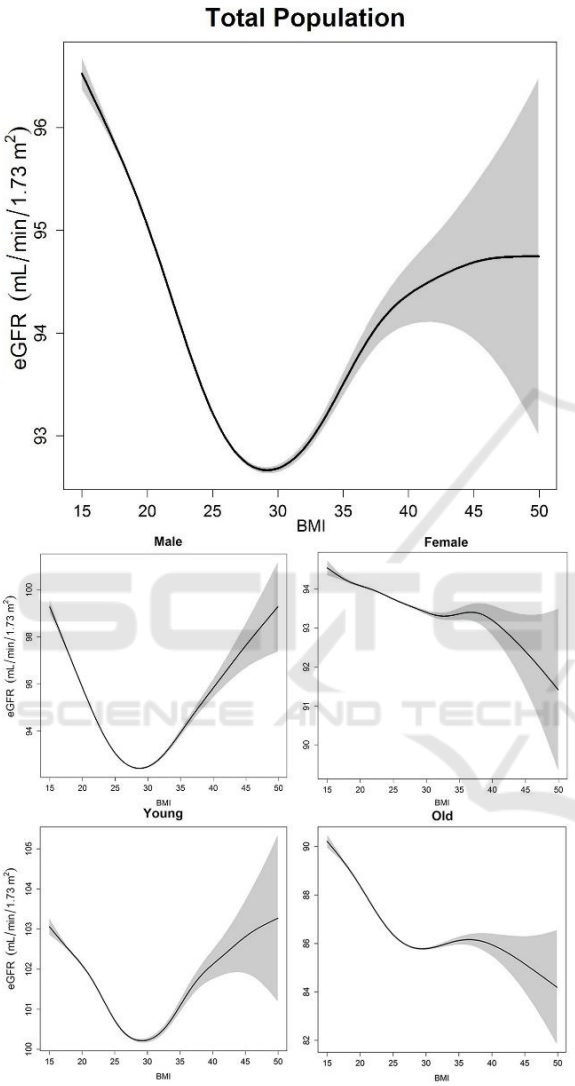

Figure 1: The relationship between body mass index and estimated glomerular filtration rate was evaluated with a general additive model with adjustment for age, sex, smoking status, regular exercise, regular alcohol consumption, known history of diabetes or hypertension medication, systolic blood pressure, fasting serum glucose, serum triglycerides, and serum high-density lipoprotein-cholesterol at baseline. Estimated glomerular filtration rate was calculated with Chronic Kidney Disease Epidemiology Collaboration equation based on serum creatinine. The shaded area represents 95% confidence interval.

The Cox hazard model was used to analyze the association between BMI and incident proteinuria with the adjustment of possible confounding variables at baseline, such as age, sex, fasting serum glucose, serum triglycerides, serum high-density lipoprotein-cholesterol, systolic blood pressure, known history of diabetes or hypertension medication, smoking status, regular alcohol consumption, and regular exercise. To visualize the association of BMI with eGFR and incident proteinuria, penalized splines as the smoothing were implemented by the R function *pspline* in package survival (degree of freedom set as default).

3 RESULTS

As shown in figure 1, the V-shape association between BMI and eGFR was observed in the analysis of total population. The nadir was around 29 kg/m^2. With subgroup analyses, the V-shape association was observed only in men and younger age group (sex-specific median age; 44 years old in men, 49 years old in women). In women and older age group, the inverse association between BMI and eGFR was observed.

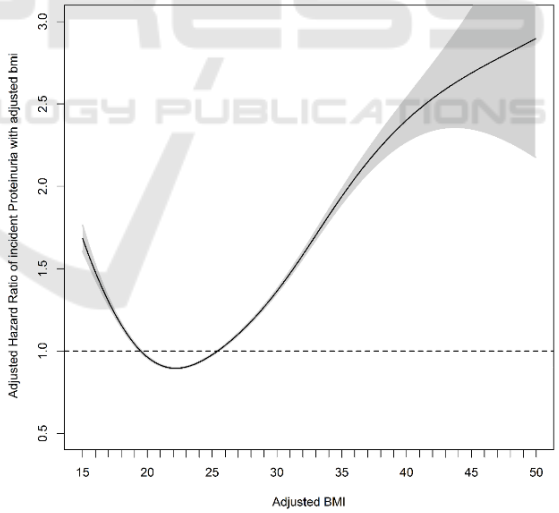

Figure 2: The association between body mass index and incident proteinuria in total population. A reverse J-shape association between body mass index and adjusted hazard ratio of incident proteinuria was observed with adjustment for age, sex, smoking status, regular exercise, regular alcohol consumption, known history of diabetes or hypertension medication, systolic blood pressure, fasting serum glucose, serum triglycerides, and serum high-density lipoprotein-cholesterol at baseline. The shaded area represents 95% confidence interval.

The reverse J-shape association between BMI and the adjusted hazard ratio of incident proteinuria was observed. The nadir was approximately estimated around 22 kg/m^2 as shown in figure 2. With subgroup analyses, there was no difference according to sex and age (sex-specific median age; 44 years old in men, 49 years old in women).

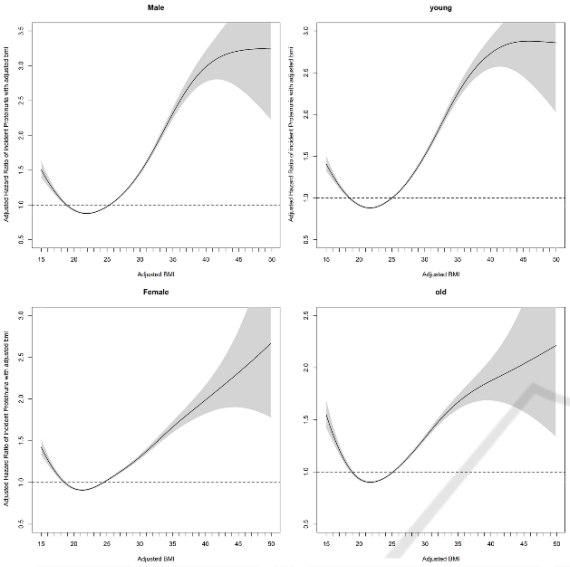

Figure 3: The association between body mass index and incident proteinuria in subgroups; A reverse J-shape association between body mass index and the adjusted hazard ratio of incident proteinuria was not differential according to sex and age with adjustment for age, sex, smoking status, regular exercise, regular alcohol consumption, known history of diabetes or hypertension medication, systolic blood pressure, fasting serum glucose, serum triglycerides, and serum high-density lipoprotein-cholesterol at baseline. The shaded area represents 95% confidence interval.

4 CONCLUSIONS

The association of BMI and eGFR was not linear and differential according to sex and age. Between BMI and incident proteinuria, the reverse J-shape association was observed and its nadir between 22 and 23 kg/m^2. It is necessary to consider non-linear association of BMI and eGFR and incident proteinuria when the association of obesity with renal function or incident proteinuria is evaluated. Clinical implications of these observations need to be studied with future studies.

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REFERENCES

Grubbs, V., Lin, F., Vittinghoff, E., Shlipak, M., et al. (2014). Body Mass Index and Early Kidney Function Decline in Young Adults: A Longitudinal Analysis of the CARDIA (Coronary Artery Risk Development in Young Adults) Study. *American Journal of Kidney Diseases*, 63(4), pp.590-597.

Hobbs, H., Farmer, C., Irving, J., et al. (2011). Is high body mass index independently associated with diminished glomerular filtration rate? An Epidemiological study. *Journal of Renal Care*, 37(3), pp.148-154.

Inker LA, Schmid CH, Tighiouart H, et al. (2012). Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*.;367:20-29.

Li, K., Zou, J., Ye, Z., Di, J., et al. (2016). Effects of Bariatric Surgery on Renal Function in Obese Patients*: A Systematic Review and Meta Analysis. PLOS ONE*, 11(10), p.e0163907.

Mahmoodnia, L. and Tamadon, M. (2017). On the occasion of world kidney day 2017; obesity and its relationship with chronic kidney disease. *Journal of Nephropathology*, 6(3), pp.105-109.

Kawamoto, R., Kohara, K., Tabara, Y., Et Al. (2008). An Association between Body Mass Index and Estimated Glomerular Filtration Rate. *Hypertension Research*, 31(8), pp.1559-1564.

Kansui, Y., Ohtsubo, T., Goto, K., et al. (2012). Association of Body Mass Index with Glomerular Filtration Rate in Japanese: A Cross-Sectional Study in Work-Site Population. *Clinical and Experimental Hypertension*, 34(2), pp.140-144.

Cheol Seong, S., Kim, Y., Khang, Y., et al. (2016). Data Resource Profile: The National Health Information Database of the National Health Insurance Service in South Korea. *International Journal of Epidemiology*, p.dyw 253.

Sato, Y., Fujimoto, S., Konta, T., Iseki, K., et al. (2013). U-shaped association between body mass index and proteinuria in a large Japanese general population sample. *Clinical and Experimental Nephrology*, 18(1), pp.75-86.

Jang, C., Hyun, Y., Lee, K. and Kim, H. (2014). The association between underweight and the development of albuminuria is different between sexes in relatively healthy Korean subjects. *Nephrology Dialysis Transplantation*, 29(11), pp.2106-2113.