Original Paper

Blood Purification

Blood Purif 2014;38:1–6
DOI: 10.1159/000362862

Published online: September 4, 2014

Impact of BMI on Cardiovascular Events, Renal Function, and Coronary Artery Calcification

Domenico Russo[a] Luigi Francesco Morrone[c] Carmela Errichiello[a]
Maria Grazia De Gregorio[a] Massimo Imbriaco[b] Yuri Battaglia[a]
Luigi Russo[a] Michele Andreucci[d] Biagio Raffaele Di Iorio[e]

Departments of [a]Nephrology and [b]Radiology, University of Naples 'Federico II', Naples, [c]Nephrology Unit, 'G. Rummo' Hospital, Benevento, [d]'Magna Graecia' University, Catanzaro, and [e]Nephrology Unit, 'A. Landolfi' Hospital, Solofra, Avellino, Italy

Key Words
BMI · Cardiovascular events · End-stage renal disease · Coronary calcification progression · Confounders

Abstract
Background/Aims: High BMI increases the risk of cardiovascular events (CVEs) in the general population. Conflicting results have been reported on the role of BMI on CVEs and on decline of renal function in patients with chronic kidney disease not on dialysis (CKD). This study evaluates the impact of BMI on CVEs, dialysis initiation, and coronary artery calcification (CAC) in CKD patients. ***Methods:*** CKD patients were divided in normal-BMI and high-BMI patients. CVEs, initiation of dialysis, and extent and progression of CAC were assessed. Univariate and multivariable analysis were performed (adjustment variables: age, diabetes, hypertension, gender, CKD stage, serum concentration of hemoglobin, parathyroid hormone, calcium, phosphorus, albumin, C-reactive protein, LDL-cholesterol, total calcium score, 24-hour proteinuria). Patients were followed to the first event (CVE, dialysis) or for 2 years. ***Results:*** 471 patients were evaluated. A CVE occurred in 13.5 and 21.3% ($p < 0.05$) of normal-BMI and high-BMI patients, respectively. High BMI did not increase the risk for CVEs in univariate (HR: 1.86; 95% CI: 0.97–3.54; $p = 0.06$) or multivariable analysis (HR: 1.36; 95% CI: 0.57–3.14; $p = 0.50$). High BMI did not increase the risk for initiation of dialysis in univariate (HR: 0.96; 95% CI: 0.58–1.60; $p = 0.9$) or multivariable analysis (HR: 1.77; 95% CI: 0.82–3.81; $p = 0.14$). Adding the interaction term (between BMI and glomerular filtration rate) to other variables, the risk of dialysis initiation significantly increased (HR: 3.06; 95% CI: 1.31–7.18; $p = 0.01$) in high-BMI patients. High BMI was not a predictor of CAC extent or progression. ***Conclusions:*** High BMI was not a predictor of CVEs. High BMI increased the risk for dialysis initiation, but high BMI was not associated to CAC extent and progression. The presence of confounders may underestimate the impact of high BMI on dialysis initiation.

D.R. and L.F.M. contributed equally to this work.

Prof. Domenico Russo
Department of Nephrology, University of Naples 'Federico II'
Via S. Pansini, 5
IT–80131 Napoli (Italy)
E-Mail domenicorusso51@hotmail.com

Luigi Francesco Morrone
Nephrology Unit, 'G. Rummo' Hospital
IT–82100 Benevento (Italy)
E-Mail lfmorrone@gmail.com

KARGER

E-Mail karger@karger.com
www.karger.com/bpu

0253–5068/14/0381–0001$39.50/0

Introduction

The incidence of overweight and obese patients is growing as a worldwide epidemic [1–4]. Patients with high BMI are exposed to higher risk for cardiovascular events (CVEs). Chronic kidney disease (CKD) is an emerging public health problem in all countries and is associated with CVEs [5–11]. Coronary artery calcification (CAC) is regarded as a surrogate marker of atherosclerosis and inflammation, and may increase the risk for CVEs and initiation of dialysis mainly in patients with concomitant CKD [12–15]. Therefore, coexistence of high BMI, CKD, and CAC may multiply the risk for CVEs and progression of CKD.

In this cohort study the impact of BMI on either CVEs or initiation of dialysis was evaluated as the primary aim. In addition, the impact of BMI on presence, extent, and progression of CAC was evaluated as a secondary aim. To the best of our knowledge, no previous study has addressed these evaluations in the same study population.

Subjects and Methods

This was a cohort study of out- and inpatients who had been evaluated from 2002 to 2009 at a single nephrology unit (Department of Nephrology, University of Naples). Eligibility criteria were age >18 years and having at least 6 months of follow-up prior to the evaluation for the study. Exclusion criteria were symptoms of heart failure or coronary artery disease, previous history of myocardial infarction, coronary bypass surgery, angioplasty, stroke, rapidly progressive renal disease, or arrhythmia (to avoid motion artifacts during assessment of CAC). Diabetic patients were those on regular use of insulin or oral hypoglycemic drugs. The procedures were followed in accordance with the ethical standards of the institution.

Patients were divided in two subgroups for statistical purposes: normal-BMI (BMI: 18.5–24.9 kg/m^2) and high-BMI patients, the latter consisting of overweight (BMI: 25.0–29.9 kg/m^2) and obese (BMI >30.0 kg/m^2) patients. Further division of patients was made on the basis of CKD (stages 1–5, as reported by K-DOQI guidelines).

Patients underwent a full clinical examination, medical history, and routine blood chemistry, and were followed up to the first event (either CVE or initiation of dialysis, whichever occurred first) or to 2 years from enrolment. The primary event was either a CVE (fatal and not fatal myocardial infarction, sudden death, coronary revascularization) or dialysis initiation. The secondary aim was presence, extent and progression of CAC.

BMI was computed as weight (in kilograms) divided by the square of the height (in meters). Glomerular filtration rate (GFR) was given by 24-hour measured creatinine clearance, and estimated GFR was calculated with the MDRD formula.

Intact parathyroid hormone (iPTH) was assayed by the chemiluminescent immunometric method (Diagnostic Products, Los Angeles, Calif., USA). The presence of CAC was assessed by a multislice computed tomography (CT) scan. CT scans were performed at a single radiology department (University of Naples) and analyzed by a radiologist (M.I.) who was unaware of the clinical classification of patient. Calcifications within the coronary artery tree above a threshold of 130 HU were included and summed to obtain the total calcium score (TCS). TCS was measured both in Agatston units (AU) and volume in patients with presence of coronary calcification above zero at the baseline CT scan. TCS was measured at enrollment and regarded as baseline TCS; TCS measured either closest to the event or at the end of observation period was regarded as follow-up TCS. Changes of TCS over time were presented as annualized progression, with the following formula: [TCS (follow-up) – TCS (baseline)]/days of follow-up × 365 [16]. The annualized progression of TCS was categorized in absent (≤25th percentile), moderate (25th–75th percentile), and accelerated (>75th percentile) progression according to distribution of progression in the overall population of the study [17, 18].

Continuous data are reported as means ± SD. Frequency data are reported as numbers and percentages. The assumption of normal distribution of data was tested using the Kolmogorov-Smirnov test. Categorical variables were evaluated with a χ^2 test. Student's t test or a Mann-Whitney U test was used to compare continuous data distribution between two independent samples, as appropriate. Correlations between continuous variables were tested by a Pearson or Spearman test depending on normality of variable distribution. Multivariable survival analysis was performed by Cox's proportional hazard model and the adjustment variables were age, diabetes, hypertension, gender, CKD stage, serum hemoglobin, iPTH, serum calcium, serum phosphorus, serum albumin, C-reactive protein, LDL-cholesterol, TCS, and 24-hour proteinuria. Risk adjustment variables were selected a priori based on previous research and were maintained in the models irrespective of statistical significance. Interaction (product) terms were sought and added to Cox's models as adjustment covariates if statistically significant at $p < 0.05$. Baseline TCS ≥100 AU and ≥400 were used in logistical regression, and were regarded as the cutoff of increased cardiovascular risk [17].

Tests were two-tailed and statistical significance was set at $p < 0.05$. Analyses were performed using SPSS, version 19.

Results

Five hundred and forty-two patients were screened; 71 patients were not evaluated because of follow-up <6 months prior to enrollment (n = 30), BMI <18.5 kg/m^2 (2 patients with normal renal function and 1 patient with stage 2 CKD), poor compliance to diet or drugs prescriptions (n = 15), and transfer of medical care to another clinic (n = 23). A complete evaluation was performed in 471 patients (250 were outpatients and 221 inpatients). The causes of hospitalization were hypertensive nephrosclerosis (35%), unknown causes (27%), chronic glomerulonephritis (23%), diabetic nephropathy (10%), and interstitial nephropathy (5%). Follow-up lasted 39 ± 27

Table 1. Clinical characteristics and baseline biochemistry

Variable	Overall patients	Normal BMI	High BMI	Obesity
Number (%)	471	156 (33.1)	196 (41.6)	119 (25.3)
Age, years	53±13	50±15	53±13	56±12
Male gender, %	75.5	75.6	78.6	70.3
Diabetes, %	19.1	16	16	28
Hypertension, %	87	84	85	95
CAC, %	44	38	44	53
Stage 1 CKD, %	34	27	36	39
Stage 2 CKD, %	22	25	22	18
Stage 3 CKD, %	28	29	28	26
Stage 4 CKD, %	11	14	8	11
Stage 5 CKD, %	5	5	5	5
GFR, ml/min	70±36	65±35	72±37	74±38
Estimated GFR (MDRD)	59±33	57±33	60±33	59±32
PTH, pg/ml	83±87	85±85	86±95	78±80
Serum calcium, mg/dl	9.4±0.6	9.3±0.8	9.5±0.5	9.5±0.5
Serum phosphorus, mg/dl	3.6±0.8	3.7±0.9	3.6±0.8	3.8±1.0
TCS, AU	156±439	108±106	107±250	300±715
TCS, volume	144±400	95±264	100±231	283±663
BMI, kg/m^2	27.5±4.8	23.0±1.4	27.0±1.4	34.2±4.1
Hemoglobin, g/dl	13.8±1.7	13.6±1.8	14.1±1.7	13.7±1.8
C-reactive protein, mg/dl	0.5±0.9	0.5±1.0	0.51±0.83	0.66±1.07
Serum fetuin-A, g/l	0.52±0.25	0.57±0.30	0.51±0.24	0.47±0.22
Serum homocysteine, μmol/l	19.9±10.5	21.1±13.4	19.2±9.0	19.3±7.6
Fibrinogen, mg/dl	363±115	344±121	365±116	387±99
Serum albumin, mg/dl	4.3±0.4	4.3±0.5	4.4±0.45	4.4±0.4
24-hour urinary protein excretion, mg/dl	868±1,575	865±1,559	869±1,690	870±1,430
24-hour urinary phosphorus excretion, mg/dl	749±313	663±268	783±319	791±336
Triglycerides, mg/dl	138±76	118±53	147±87	147±77
Total cholesterol, mg/dl	189±41	187±39	190±43	192±42
LDL-cholesterol, mg/dl	112±37	113±34	109±39	113±37
Phosphate binder use, %	11	13	8	11

Values are means ± SD unless otherwise indicated.

months. Clinical characteristics and blood chemistry of the patients are reported in table 1.

There were 156 cumulative events. In detail, 88 patients (18.7%) had a CVE and 68 patients (14.4%) initiated dialysis. Occurrence of a CVE and initiation of dialysis according to BMI and to CKD stage are reported in table 2. CVEs were registered in 21 (13.5%) and 67 (21.3%) patients with normal and high BMI, respectively ($p < 0.05$). In detail, CVEs were recorded in 34 overweight (17.3%) and 33 obese (27.7%) patients ($p < 0.05$). Dialysis initiation was reported in 26 (16.7%) and 42 (13.3%) patients ($p = 0.33$; n.s.) with normal and high BMI, respectively. In detail, initiation of dialysis was observed in 29 overweight (14.8%) and 13 obese (10.9%) patients ($p = 0.3$; n.s.). No differences were found when analysis was performed in patients divided according to CKD stage.

In univariate Cox analysis, high BMI was not associated with increased risk for a CVE (HR: 1.86; 95% CI: 0.97–3.54; $p = 0.06$). After adjustment for a priori selected risk adjustment variables (age, diabetes, hypertension, gender, stage CKD, serum concentration of hemoglobin, PTH, calcium, phosphorus, albumin, C-reactive protein, LDL-cholesterol, value of TCS, and 24-hour proteinuria), the lack of association persisted in multivariable Cox analysis (HR: 1.36; 95% CI: 0.57–3.14; $p = 0.50$).

In univariate Cox analysis, high BMI was not associated with increased risk for initiation of dialysis (HR: 0.96; 95% CI: 0.58–1.60; $p = 0.9$). After adjustment for the above risk adjustment variables, the lack of association persisted (HR: 1.77; 95% CI: 0.82–3.81; $p = 0.14$). Assessment of presence and effects of interactions between some adjustment variables showed significant interaction

Table 2. CVEs and initiation of dialysis in the whole cohort and in different stages of CKD according to normal BMI and high BMI

	Whole cohort		Stages 1–2 CKD		Stage 3 CKD		Stages 4–5 CKD	
	N-BMI	H-BMI	N-BMI	H-BMI	N-BMI	H-BMI	N-BMI	H-BMI
Patients, n	156	315	81	184	45	85	30	46
CVEs, n (%)	21 (13.5)	67* (21.3)	7 (8.6)	31 (16.8)	8 (17.8)	23 (27.0)	6 (20.0)	13 (28.3)
Dialysis initiation, n (%)	26 (16.7)	42 (13.3)	1 (1.2)	1 (0.5)	6 (13.3)	19 (22.3)	19 (63.3)	22 (47.8)

* $p < 0.05$ vs. normal BMI. N-BMI = Normal BMI; H-BMI = high BMI.

Table 3. Logistic regression model for basal TCS and progression of TCS for BMI (high BMI vs. normal BMI) as the explanatory variable

	Basal TCS ≥100 AU			Basal TCS ≥400 AU			TCS progression		
	HR	95% CI	p	HR	95% CI	p	HR	95% CI	p
Univariate analysis	1.23	0.79–1.91	0.37	1.50	0.76–2.98	0.25	1.05	0.59–1.87	0.87
Multivariable analysis	1.04	0.53–2.05	0.91	1.22	0.47–3.15	0.68	0.91	0.41–2.07	0.83

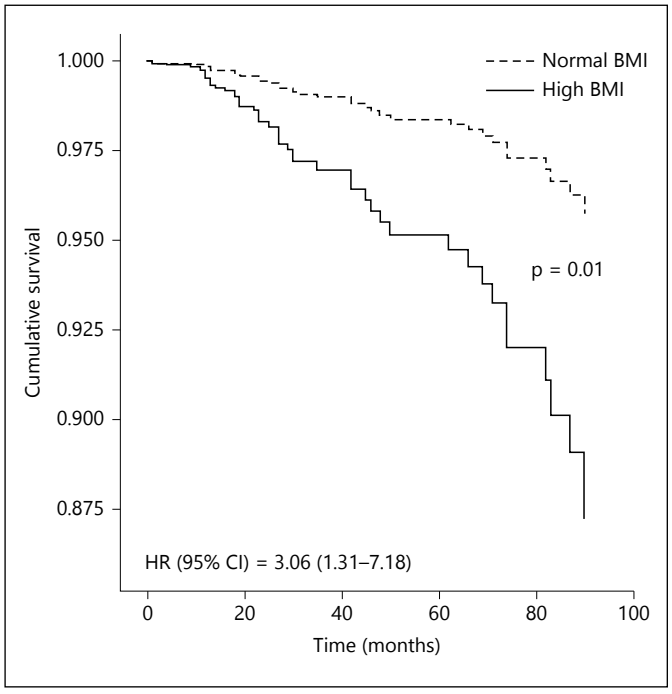

Fig. 1. Multivariable-adjusted Cox proportional-hazard model for initiation of dialysis. Explanatory variable: BMI status (high BMI vs. normal BMI). Adjustment variables: age, diabetes, hypertension, gender, CKD stage, hemoglobin concentration, iPTH, serum calcium, serum phosphorus, C-reactive protein, serum albumin, LDL-cholesterol, 24-hour urinary protein excretion, TCS, interaction (product) term between BMI and GFR.

(p = 0.001) between BMI and GFR (as 24-hour measured creatinine clearance) for initiation of dialysis; the interaction was significant (p = 0.001) even when GFR was calculated with the MDRD formula. Adding the interaction term to other adjustment variables, the risk of dialysis initiation significantly increased (HR: 3.06; 95% CI: 1.31–7.18; p = 0.01) in high-BMI patients compared to normal-BMI patients (fig. 1). Baseline data both on presence and extent (as TCS) of CAC are reported in table 1.

Annualized TCS progression was faster in high-BMI patients (206 ± 448 AU per year) compared to normal-BMI patients (100 ± 101 AU per year), but the difference was not significant. Absent progression was found in 55.1% of normal-BMI patients and in 53.8% of high-BMI patients, and accelerated progression was observed in 27.3% of high-BMI patients and in 20.3% of normal-BMI patients; these differences were not significant. High BMI was not an explanatory factor of either the extent of TCS (≥100 and ≥400 AU) or progression of TCS (table 3).

Discussion

In the present study the impact of high BMI on CVEs, initiation of dialysis, and presence, extent, and progression of CAC was evaluated. The occurrence of a CVE was

more frequent among patients with high BMI. Nonetheless, high BMI was not predictive of CVEs in multivariable analysis.

Other studies have reported conflicting results concerning the effect of high BMI on the occurrence of CVEs. Indeed, a strong direct association has been observed between BMI and CVEs in the general population [2–4, 19]; however, the occurrence of myocardial infarction and fatal coronary heart disease was lower in obese patients with nonadvanced stages of CKD [20]. A plausible explanation for the lack of association between high BMI and CVEs in our study population may be the fact that high-BMI patients had marginal dyslipidemia and inflammation, and no derangements of mineral metabolism. Indeed, only serum concentration of triglycerides and fibrinogen was significantly higher in high-BMI patients compared to normal-BMI patients; concentration of other markers of inflammation as well as of PTH, calcium, and phosphorus was not different between normal- and high-BMI patients. This may indicate that a high BMI does not influence the occurrence of CVEs in the absence of comorbidities.

The present study shows significant association between high BMI and initiation of dialysis. We hypothesize that hemodynamic changes may explain the increased risk of dialysis initiation observed in our study population. High BMI causes glomerular hypertrophy and consequent hyperfiltration that may be responsible for more rapid decline of renal function and for faster dialysis initiation. This may be the reason why the risk of dialysis initiation was three times higher in our patients with high BMI compared to those with normal BMI. However, it is important to underline that the association between high BMI and CKD has been debated. Indeed, while results of some studies [8, 21–28] are in keeping with those of the present one, BMI was not responsible for progression of CKD in diabetic patients [7] and no difference was observed in the rate of annual progression of estimated GFR comparing normal, overweight, and obese nondiabetic patients with stage 3 CKD [29].

Based on the findings of the present study, we may assume that the conflicting results concerning the association between BMI and dialysis initiation may be due to the significant interaction existing between BMI and GFR. Likely, BMI-dependent hyperfiltration may mask the association between BMI and GFR. Indeed, in preliminary analysis no association was found between high BMI and dialysis initiation in our study population. However, BMI was a significant predictor of dialysis initiation when the interaction between BMI and GFR was entered in the final model as a variable of adjustment.

The data on the potential association between BMI with presence, extent, and progression of CAC are scarce. The process leading to CAC formation and progression seems linked to atherosclerosis, inflammation, and deranged mineral metabolism. Therefore, a higher incidence and faster progression of CAC should be expected in patients with high BMI and concomitant CKD. However, this hypothesis was not confirmed by the data of the present study. Indeed, the percentage of patients with basal CAC was higher in high-BMI compared to normal-BMI patients, but the difference was not significant. TCS was not different between patients with normal and high BMI. Finally, high BMI did not predict progression of CAC. A comparison of our results with previous ones on this issue is rather difficult because of different study aims, different analytic strategies, and multiethnicity of the examined population [30–33]. For instance, high BMI increased the risk of CAC progression in a large cohort of asymptomatic patients [30]. However, in that study many patients did not have CKD and no value of BMI was reported. In a small cohort of patients with stages 3–4 CKD, BMI was a predictor of vascular calcification evolution only in the nondiabetic group [32]. Higher BMI was associated with higher PTH in overweight and obese veterans with stages 2–5 CKD, suggesting an association between high BMI with secondary hyperparathyroidism [33], but unfortunately vascular calcification was not evaluated.

There were some limitations in this study that should be mentioned. One limitation was that FGF-23 was not assayed. This represents a limitation considering the strong effect of FGF-23 on CVEs and on progression of vascular calcification. However, it should be taken into account that the present study started in 2002 and very few data on clinical relevance of FGF-23 were available at that time. In addition, routine assay of FGF-23 is still not suggested in clinical practice despite the large body of evidence that has accumulated in recent years on the association of FGF-23 with CVEs.

Conclusion

In a cohort of patients representative of the population commonly evaluated in the nephrology clinic, high BMI was not a predictive risk factor for CVE. High BMI significantly increased the risk for initiation of dialysis

when interaction factors were taken into account, indicating that confounders may underestimate the impact of high BMI on dialysis initiation. High BMI was not associated with presence, extent, or progression of CAC.

Disclosure Statement

All authors declare to have no relationships with companies that may have a financial interest in the information contained in the manuscript. All authors declare to have no financial interest. All authors declare to have no conflict of interest.

References

1 Marx J: Cellular warriors at the battle of the bulge. Science 2003;299:846–849.
2 Hill JO, Wyatt HR, Reed GW, Peters JC: Obesity and the environment: where do we go from here? Science 2003;299:853–855.
3 Hostetter TH, Lising M: National kidney disease education program. J Am Soc Nephrol 2003;14(suppl 2):S114–S116.
4 Ford ES, Giles WH, Dietz WH: Prevalence of the metabolic syndrome among US adults: findings from the Third National Health and Nutrition Examination Survey. JAMA 2002; 287:356–359.
5 Wang Y, Chen X, Song Y, Coballero B, Cheskin LJ: Association between obesity and kidney disease: a systematic review and meta-analysis. Kidney Int 2008;73:19–33.
6 Abrass CK: Obesity: what does it have to do with kidney disease? J Am Soc Nephrol 2004; 15:2768–2772.
7 Bagby PS: Obesity-initiated metabolic syndrome and the kidney: a recipe for chronic kidney disease? J Am Soc Nephrol 2004;15: 2775–2791.
8 Gelber RP, Kurth T, Kausz AT, Manson JE, Buring JE, Levey AS, Gaziano JM: Association between body mass index and CKD in apparently healthy men. Am J Kidney Dis 2005;46: 871–880.
9 Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D: Predictors of new-onset kidney disease in a community-based population. JAMA 2004;291:844–850.
10 Hall YN, Hsu CY, Iribarren C, Darbinian J, McCulloch CE, Go AS: Body mass index and risk for end-stage renal disease. Ann Intern Med 2006;144:21–28.
11 Iseki K, Ikemiya Y, Kinjo K, Inoue T, Iseki C, Takishita S: Body mass index and the risk of development of end-stage renal disease in a screened cohort. Kidney Int 2004;65:1870–1876.
12 Russo D, Corrao S, Miranda I, Ruocco C, Manzi S, Elefante R, Brancaccio D, Cozzolino M, Biondi ML, Andreucci VE: Progression of coronary artery calcification in predialysis patients. Am J Nephrol 2007;27:152–158.
13 Di Lullo L, Floccari F, Santoboni A, Rivera RF, Morrone L, Russo D: Progression of cardiac valve calcification and decline of renal function in CKD patients. J Nephrol 2013;26:739-744.
14 Russo D, Morrone LF, Imbriaco M, Pota A, Russo L, Scognamiglio B, Sorrentino R: Coronary artery calcification and outcomes in diabetic patients with and without chronic kidney disease. Blood Purif 2013;36:17–20.
15 Russo D, Bellasi A, Pota A, Russo L, Di Iorio B: Effects of phosphorus restricted diet and phosphate binding therapy on outcomes in patients with chronic kidney disease. J Nephrol 2014, Epub ahead of print.
16 Achenbach S, Ropers D, Pohle K, Leber A, Thilo C, Knez A, Menendez T, Maeffert R, Kusus M, Regenfus M: Influence of lipid-lowering therapy on the progression of coronary artery calcification. Circulation 2002;106: 1077–1082.
17 Russo D, Corrao S, Battaglia Y, Andreucci M, Caiazza A, Carlomagno A, Lamberti M, Pezone N, Pota A, Russo L, Sacco M, Scognamiglio B: Progression of coronary artery calcification and cardiac events in patients with chronic renal disease not receiving dialysis. Kidney Int 2011;80:112–118.
18 Russo D, Bellasi A, Pota A, Russo L, Di Iorio B: Effects of phosphorus-restricted diet and phosphate-binding therapy on outcomes in patients with chronic kidney disease. J Nephrol 2014, Epub ahead of print.
19 Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH: The disease burden associated with overweight and obesity. JAMA 1999;282:1523–1529.
20 Elsayed EF, Tighiouart H, Weiner DE, Griffith J, Salem D, Levey AS, Sarnak MJ: Waist-to-hip ratio and body mass index as risk factors for cardiovascular events in CKD. Am J Kidney Dis 2008;52:49–57.
21 Wahba IM, Mak RH: Obesity and obesity-initiated metabolic syndrome: mechanistic links to chronic kidney disease. Clin J Am Soc Nephrol 2007;2:550–562.
22 Chalmers L, Kaskel FJ, Bamgbola O: The role of obesity and its bio-clinical correlates in the progression of chronic kidney disease. Adv Chronic Kidney Dis 2006;13:352–364.
23 Shen WW, Chen HM, Chen H, Xu F, Li LS, Liu ZH: Obesity-related glomerulopathy: body mass index and proteinuria. Clin J Am Soc Nephrol 2010;5:1401–1409.
24 Ryu S, Chang Y, Woo HY, Kim SG, Kim DI, Kim WS, Suh BS, Choi NK, Lee JT: Changes in body weight predict CKD in healthy men. J Am Soc Nephrol 2008;19:1798–1805.
25 Navarro-Díaz M, Serra A, López D, Granada M, Bayés B, Romero R: Obesity, inflammation, and kidney disease. Kidney Int Suppl 2008;74(suppl 111):S15–S18.
26 Mallamaci F, Ruggenenti P, Perna A, Leonardis D, Tripepi R, Tripepi G, Remuzzi G, Zoccali C: ACE inhibition is renoprotective among obese patients with proteinuria. J Am Soc Nephrol 2011;22:1122–1128.
27 Kramer H, Luke A, Bidani A, Cao G, Cooper R, McGee D: Obesity and prevalent and incident CKD: the Hypertension Detection and Follow-Up Program. Am J Kidney Dis 2005; 46:587–594.
28 Mohsen A, Brown R, Hoefield R, Kalra PA, O'Donoghue D, Middleton R, New D: Body mass index has no effect on rate of progression of chronic kidney disease in subjects with type 2 diabetes mellitus. J Nephrol 2012;25: 384–393.
29 Othman M, Kawar B, El Nahas AM: Influence of obesity on progression of non-diabetic chronic kidney disease: a retrospective cohort study. Nephron Clin Pract 2009;113:16–23.
30 Mohsen A, Brown R, Hoefield R, Kalra PA, O'Donoghue D, Middleton R, New D: Risk factors for the progression of coronary artery calcification in asymptomatic subjects. Circulation 2007;115:2722–2730.
31 Kestenbaum BR, Adeney KL, de Boer IH, Ix JH, Shlipak MG, Siscovick DS: Incidence and progression of coronary calcification in chronic kidney disease: the Multi-Ethnic Study of Atherosclerosis. Kidney Int 2009;76: 991–998.
32 Stavroulopoulos A, Porter CJ, Pointon K, Monaghan JM, Roe SD, Cassidy MJ: Evolution of coronary artery calcification in patients with chronic kidney disease stages 3 and 4, with and without diabetes. Nephrol Dial Transplant 2011;26:2582–2589.
33 Kovesdy CP, Ahmadzadeh S, Anderson JE, Kalantar-Zadeh K: Obesity Is associated with secondary hyperparathyroidism in men with moderate and severe chronic kidney disease. Clin J Am Soc Nephrol 2007;2:1024–1029.