Prevalence of Renal Insufficiency in Individuals with Hypertension and Obesity/Overweight: The FATH Study

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Overweight and obesity are associated with increased cardiovascular risk. Some studies have demonstrated that they also can result in renal damage. The aim of this study was to assess the prevalence of renal insufficiency (RI), defined as a GFR <60 ml/min per 1.73 m², in a cohort of 4585 patients who attended primary care with essential hypertension and a body mass index ≥25 kg/m². The patients were classified as overweight and obese according to body mass index (25 to 29.9 and ≥30 kg/m², respectively). Abdominal obesity was defined as a waist circumference ≥88 and 102 cm in women and men, respectively. Both groups had a high prevalence of metabolic syndrome (Adult Treatment Panel III). The prevalence of RI was high in both the overweight group (22.7%; 95% confidence interval [CI] 20.6 to 24.9) and in the obese group (22.8%; 95% CI 21.0 to 24.7). The presence of diabetes increased the risk for RI (odds ratio 1.83; 95% CI 1.55 to 2.16). The prevalence of RI was greater in patients with abdominal obesity (23 *versus* 17%; $P < 0.001$). In the presence of abdominal obesity, cardiovascular risk factors and components of the metabolic syndrome also were more prevalent. The higher risk for RI with abdominal obesity persisted even after adjustment for dyslipidemia, elevated blood glucose levels, and other variables that are associated with RI (adjusted odds ratio 1.40; 95% CI 0.84 to 2.33). It was concluded that patients who have hypertension and visceral obesity and attend primary care present a higher prevalence of metabolic syndrome and RI.

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Chronic kidney disease (CKD) is a widely known cardiovascular risk factor. Renal insufficiency (RI) and micro- or macroalbuminuria, both manifestations of CKD, are associated with increased cardiovascular morbidity and mortality (1–4).

The application of equations to estimate GFR has revealed an important and growing prevalence of CKD, associated with vascular events both in population-based studies and in patients with cardiovascular risk factors (5,6). Some epidemiologic studies have demonstrated an association between obesity and CKD. A high body mass index (BMI) increases the risk for a reduced GFR in both men and women (7). Obesity can be associated with glomerulosclerosis and also can facilitate a loss of renal function in patients with other kidney diseases (8,9). The risk for presenting RI as defined by a GFR <60 ml/min per 1.73 m² and end-stage renal failure as defined by the need for kidney transplant or dialysis increases with the rise in BMI (10,11).

It therefore is likely that increased prevalence of CKD could be due, at least partially, to an increase in comorbidities such as overweight and obesity and the combination of associated hemodynamic and metabolic disorders that result in metabolic syndrome (MS). Awareness of the association between overweight/obesity and RI is important to adopt preventive and therapeutic measures for this risk factor of CKD. The present study assessed the prevalence of one specific manifestation of CKD, low GFR, in patients with essential hypertension and overweight/obesity seen in primary care.

Materials and Methods

This cross-sectional, multicenter study recruited a total of 4585 patients who attended Spanish primary care centers, previously received a diagnosis of essential hypertension, and a had body mass index (BMI) ≥25 kg/m². Each investigator included four patients with hypertension and overweight (BMI 25 to 29.9 kg/m²) and four patients with hypertension and obesity (BMI ≥30 kg/m²). BP measurements were performed with a validated semiautomatic apparatus (Omron, Banockburn, IL) with a cuff size adapted to the arm circumference. Patients were considered to have hypertension when they had previously received a diagnosis of this condition and/or were taking antihypertensive treatment. The presence of abdominal obesity was defined by a waist circumference ≥88 cm (female) and ≥102 cm (male). Patients were considered to present MS when they fulfilled defining criteria of the Adult Treatment Panel III (12). The comparative data using the criteria established by the International Diabetes Federation also were included (13). Patients were considered to have diabetes when they had previously received a diagnosis of this condition and/or were taking antidiabetic treatment. All patients were asked about their smoking habits and the presence of any previous cardiovascular disease (ischemic heart disease, heart failure, stroke, or peripheral arterial disease)

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and any manifestation of chronic renal disease (renal insufficiency, hematuria, or proteinuria).

Within 7 d, the following parameters were analyzed in plasma after 8 h of fasting: Glucose, HbA_{1c}, cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, and creatinine. GFR was estimated from the serum creatinine using the simplified Modification of Diet in Renal Disease (MDRD) (14) and Cockroft-Gault (C-G) equations (15). The degree of renal function was established according to National Kidney Foundation guidelines (16). RI was defined as a GFR by MDRD <60 ml/min per 1.73 m^2.

The primary objective of the *Factores Adicionales que dificulTan el control en Hipertensos obesos* (FATH) study was to analyze the prevalence of MS in patients with essential hypertension and overweight/obesity. In this *post hoc* substudy, the objective was to study the prevalence of RI in this population.

Statistical Analyses

Variables are expressed as the mean (SD) or frequency (95% confidence interval [CI]). Patients were classified by BMI into overweight or obese patients and by waist circumference into abdominal obesity/no abdominal obesity. The χ^2 test was used to compare proportions of overweight and obese patients. Comparison of means between overweight and obese patients and between abdominal obesity or not was done using the *t* test. Consistency between GFR by MDRD and by C-G was estimated using the Bland-Altman method. Logistic regression was applied to estimate the risk of GFR <60 ml/min per 1.73 m^2 as a result of the presence of abdominal obesity before and after adjustment for other covariates. Two-tailed comparisons were made throughout, and $P < 0.05$ was considered statistically significant. The analysis was carried out using SPSS for Windows (version 12.0; SPSS, Chicago, IL).

Results

A total of 2206 men and 2379 women with a mean age of 61.9 yr (10.6 yr) were studied. Of these, 32.9% (95% CI 30.7 to 33.4) had previously received a diagnosis of diabetes; 3.6% (95% CI 3.10 to 4.2%) were aware that they had chronic renal disease. Table 1 shows the characteristics of patients who were classified according to BMI into overweight or obese patients. The mean values of waist circumference were higher in the obese group, who also presented higher plasma glucose concentrations and a higher degree of dyslipidemia. The prevalence of MS by Adult Treatment Panel III criteria was 80.2% (95% CI 78.01 to 82.26) and 92.83% (95% CI 91.5 to 94.5) in the overweight and obese groups, respectively ($P < 0.0001$) and when International Diabetes Federation criteria were applied was 85.37 (95% CI 83.4 to 87.18) and 95.12 (95% CI 94.01 to 96.01) of the overweight and obese patients, respectively. There was a higher prevalence of diabetes in the obesity group. The overweight patients had similar systolic BP and diastolic BP values to those of the obese patients. There was a higher prevalence of smokers in the overweight group (28.9 *versus* 23%; $P < 0.0001$). The GFR by C-G was higher than that calculated by MDRD with a mean difference of 4.72 ml/m per 1.73 m^2 in the overweight group and 24.7 ml/m per 1.73 m^2 in the obesity group (Figure 1).

There were no significant differences in the prevalence of renal insufficiency (GFR <60 ml/m per 1.73 m^2) between overweight and obese patients (23% [95% CI 21 to 25%] *versus* 23% [95% CI 21 to 25%]; Table 2). In both the overweight and the obese groups, patients with diabetes had a higher prevalence of RI (30.1% [95% CI 24.4 to 32.9] *versus* 19.2% [95% CI 17.6 to 20.8; $P < 0.0001$] in the obese group and 29.1% [95% CI 24.6 to 33.9] *versus* 20.1% [95% CI 18.0 to 22.9] in the overweight patients). The risk for a GFR 30 to 60 ml/m per 1.73 m^2 was 83% greater (odds ratio 1.83; 95% CI 1.55 to 2.16) in the presence of diabetes. When the distribution of GFR along quartiles of waist circumference was analyzed, there was a larger proportion of patients with GFR >90 ml/m per 1.73 m^2 in the higher percentiles of waist circumference ($P = 0.008$ for the trend). A higher preva-

Table 1. Characteristics of the patients[a]

Variable	Overweight (BMI 25 to 29.9 kg/m^2) (n = 2060)	Obesity (BMI ≥30 kg/m^2) (n = 2525)	P
Age (yr)	61.9 (10.5)	61.9 (10.7)	NS
Male (%)	51.8	45.0	<0.0001
BMI (kg/m^2; mean [SD]	27.8 (1.3)	35.1 (4.1)	<0.0001
Waist (cm; mean [SD])			
male	101.1 (10.5)	113.6 (11.5)	<0.0001
female	94.2 (10.7)	107.9 (12.9)	<0.0001
SBP (mmHg; mean [SD]	145.75 (17.4)	145.84 (18.2)	NS
DBP (mmHg; mean [SD]	85.01 (10.3)	85.5 (10.8)	NS
Glucose (mg/dl; mean [SD]	110.0 (28.9)	117.7 (34.1)	<0.0001
HDL cholesterol (mg/dl; mean [SD]	53.6 (15)	51.3 (13.2)	<0.0001
Triglycerides (mg/dl; mean [SD]	148.0 (68)	161.7 (78)	<0.0001
Diabetes	26.04 (24.1 to 27.9)	37.03 (10.9 to 13.5)	<0.0001
MS 1 (% [95% CI])	80.2 (78.0 to 82.2)	92.8 (91.5 to 94.0)	<0.0001
MS 2 (% [95% CI])	85.4 (83.4 to 87.2)	95.1 (94.0 to 96.0)	<0.0001

[a]BMI, body mass index; CI, confidence interval; DBP, diastolic BP; MS 1, metabolic syndrome (Adult Treatment Panel III criteria); MS 2, metabolic syndrome (International Diabetes Federation criteria); SBP, systolic BP.

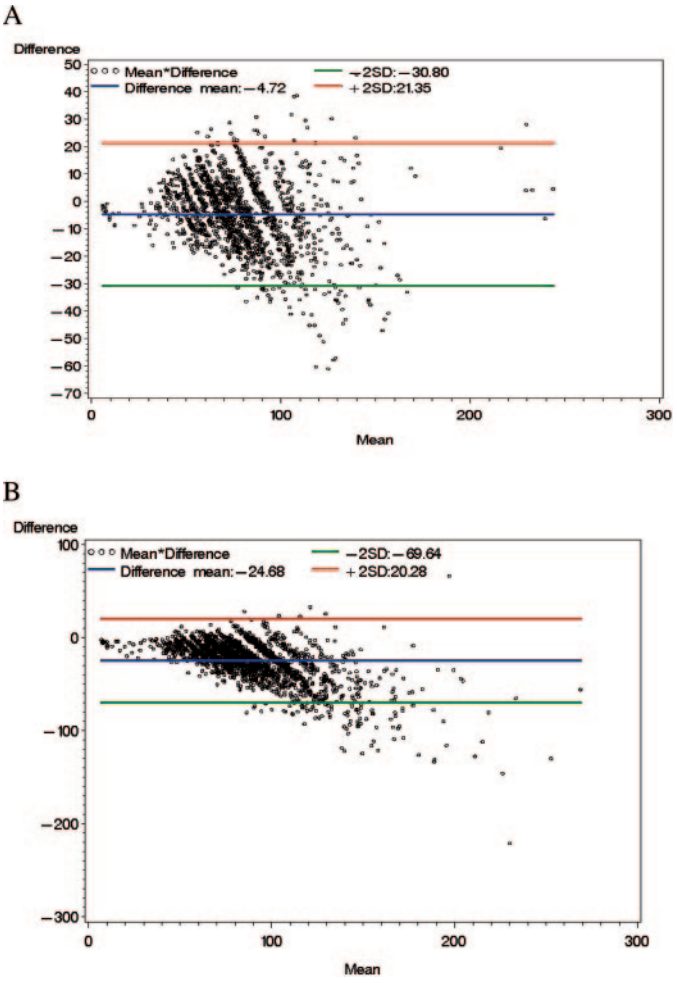

Figure 1. Bland-Altman plot comparing two methods to estimate the GFR (Cockroft-Gault and MDRD) in overweight (A) and obese (B) hypertensive patients.

lence of RI was observed in patients with abdominal obesity (Table 2). The distribution of risk factors in patients with abdominal obesity is shown in Table 3. Patients with abdominal obesity tended to be older and to present more metabolic alterations and obesity (BMI ≥30 kg/m^2). The presence of abdominal obesity increased the risk for presenting a GFR <60 ml/min per 1.73 m^2 by 55%. After adjustment for all of the components of the MS, this risk was only slightly reduced (odds ratio 1.51; 95% CI 1.13 to 2.01).

Discussion

This study shows a very high prevalence (23%) of RI (GFR by MDRD <60 ml/m per 1.73 m^2) in a relatively large cohort of adult hypertensive patients with overweight/obesity. Given the difficulties with accurate estimation of GFR and the limitations of calculating GFR on the basis of serum creatinine alone, there is an increased interest in the use of equations (MDRD and C-G). These equations include variables such as age, weight, gender, and race and show a good correlation with accurate markers of GFR (17). When comparing both equations, the GFR values that were obtained with the C-G method were higher, and the differences were larger with higher BMI values. Other studies have shown that, in the presence of obesity/overweight, the C-G method overestimates GFR and consider the MDRD equation, especially in cases of reduced GFR, to be more accurate (18,19).

In the Spanish population pilot study, the prevalence of GFR <60 ml/m per 1.73 m^2 was 5.1% (20), similar to that (5% of the population) performed in >500,000 patients in a Canadian population (21). However, when patients with hypertension are studied, there is a greater prevalence of RI. In a cohort of 721 patients who had essential hypertension, a mean age of 56 yr, and a BMI of 28.9 kg/m^2 and attending a hospital clinic, a GFR <60 ml/min per 1.73 m^2 was observed in 16.2% of the patients (22). In another recently published study (23), the prevalence of a GFR <60 ml/min per 1.73 m^2 by MDRD in 13,687 patients who had hypertension and were seen in primary care in Spain was 27.7%. Patients who were included in this study were of similar characteristics to our study group. Most of them were overweight or obese, only 17% had normal body weight, and 30.6% had diabetes. The older age (mean 68.1 yr) could explain the higher prevalence of RI than that observed in our population. In the MicroAluminuria en pacientes con glucemia Basal ALterada (MAGAL) study published in this issue (24), the prevalence of RI in patients with hypertension and microalbuminuria was 19.9%, but 10% of these patients had BMI <25 kg/m^2.

Given the coexistence of hypertension and overweight/obesity in our patients, it is difficult to establish the significance of each of these in the development of kidney damage. Both in hypertension and in overweight/obesity, as well as in diabetes, glomerular hyperfiltration can occur, which, over time, can contribute to kidney damage (25,26). Ribstein *et al.* (26) demonstrated in a comparative study in patients with hypertension that the presence of obesity causes a higher filtration fraction and, consequently, more microalbuminuria, thus confirming that the increase in weight intensifies hypertensive renal damage. Microalbuminuria was not measured in our study. Nonetheless, the greater prevalence of GFR >90 ml/m per 1.73 m^2 in patients in the highest percentile of waist circumference suggest the presence of hyperfiltration, at least at some point during the renal life of patients with hypertension and obesity, a hyperfiltration that contributes to a steady decline of renal function. In the Hypertension Detection and Follow-Up Program (27), the incidence of chronic renal disease at 5 yr, defined by proteinuria and/or GFR <60 ml/min per 1.73 m^2, was higher in patients with obesity and overweight (31 and 34%, respectively) than in hypertensive patients with ideal weight (28%).

No differences in prevalence of RI were observed between overweight or obese patients who were classified according to BMI in our study. A possible explanation is that a cutoff point of 25 kg/m^2 in hypertensive patients with other risk factors already defines the increased risk for RI. Besides, BMI indicates only body corpulence, and it might be hypothesized that hypertensive patients with BMI between 25 and 29.9 kg/m^2 have more body fat than nonhypertensive overweight individuals. Furthermore, it has been reported that hypertensive patients

Table 2. GFR and prevalence of renal insufficiency (GFR <60 ml/min per 1.73 m^2) according to BMI group and abdominal obesity

Parameter	Mean GFR (ml/min per 1.73 m^2)	Proportion of Patients with GFR <60 ml/min per 1.73 m^2
BMI		
overweight	77.1 (26)[b]	22.7 (20.6 to 24.9)[c]
P	NS	NS
obesity	77.5 (25)[b]	22.8 (21.0 to 24.7)[c]
Abdominal obesity[a]		
absent	81 (27)[b]	17 (14 to 20)[c]
P	<0.0001	<0.001
present	77 (25)[b]	23 (22 to 26)[c]

[a]Cut point 88 and 102 cm for men and women, respectively.
[b]Mean (SD).
[c]% (95% CI).

Table 3. Proportion of patients with cardiovascular risk factors according to abdominal obesity

Variable	Abdominal Obesity (%)		*P*
	Yes	No	
Age ≥65 yr	46	39	0.0003
SBP ≥130 mmHg	82	84	0.178
Diabetes	33	27	0.0003
Reduced HDL cholesterol[a]	32	21	<0.0001
Triglycerides ≥ 150 mg/dl	48	45	0.079
Glucose ≥ 110 mg/dl	44	37	<0.0001
BMI ≥ 30 kg/m^2	66	14	<0.0001

[a]<40 mg/dl in men and <40 mg/dl in women.

had more visceral adipose tissue accumulation, measured by multiscan magnetic resonance imaging, than nonhypertensive control subjects for a similar fat mass (28). In fact, our study shows that patients with abdominal obesity have a significantly lower GFR and that there are more patients with CKD compared with non(abdominal)obese patients, supporting the relevance of abdominal obesity in kidney damage. A study to assess body fat and its association with BMI in hypertensive patients is warranted. On the other side, it has been shown in patients without diabetes that, regardless of BMI, central distribution of fat (abdominal obesity) increases the risk for a reduction of GFR (29). The greater prevalence of RI in hypertensive patients with abdominal obesity could be due to the different metabolic alterations that frequently are associated with this type of obesity and that constitute the MS. A greater prevalence of metabolic alterations was seen in patients with abdominal obesity, although they still have a high risk for RI after adjustment for these variables. Therefore, other factors that were not determined in this study, such as hyperinsulinemia, increased sympathetic activity, renin-angiotensin system activation, inflammatory mediators, and other adipocyte-derived products, could play a role in the development of RI that is associated with abdominal obesity and MS (30). As expected, in the presence of diabetes, the prevalence of RI increased significantly in both overweight and obese patients.

Conclusion

Our study reveals that patients who have hypertension and overweight/obesity and are seen in a primary care setting show a high prevalence of MS and RI in which abdominal obesity plays an important role. Stepping up of preventive and therapeutic measures to control these frequent and important vascular risk factors therefore should be considered.

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Miguel, Garcia Campillo Joan Manuel, Garcia Sabater Joaquin, Garcia Cabarcos Jose Antonio, Garcia Hernández Luis, Garcia Cobelo Maria Emma, Garcia Prieto Mariano, Garcia-Reyes Ramos Mercedes, Garcia Conejero Olga, Garcia Peñafiel Rafael, Garcia Ochoa Rocío De Vicente, García García Alberto, García Vallano Isaac, García Allas Isabel, García Norro Javier, García Pérez Jordi, García Hidalgo José, García Aparicio Judit, García López Manuel, García Bernal Manuela, García Callejas Ricardo, García Urendez Jose, Garrido Sampedro Manuel, Gasalla Rodríguez Concepción, Gascó García Plácido, Gaspar Hernández Andrés, Gene García Jose R., Gené García Pedro, Gil Monje Maria, Gimenez Navarro María Antonia, Giménez Palop Olga, Giner Garrigues Francisco, Giner Lacuesta Isabel, Gippini Pérez Antonio, Girón Daviña Marta, Gispert Servitge Adria, Goikoetxea Arrillaga Alejandro, Gomara Sonia, Gómez Ruiz Javier, Gómez Gonzalez Laureano, Gómez Mendicuti Manuel, Gómez Fumero Sonsoles, Gómez Aguinaga Juan Manuel, Gómez Ribelles Rafael, Gonzalez López Belén, Gonzalez Gago Jose Antonio, Gonzalez Gonzalez Juana, Gonzalez Cuber Lamberto, González Lorrio Francisco, Gonzalez Gonzalez Luis, Gonzalez López Arce Luis, Gonzalez Moreiras Manuel, Gonzalez Cabrera Marcos, González Álvarez Antonio, González Galán Concepción, González Acuña Eduardo, González González Javier, González Rodríguez Luis, González Rodríguez Manuel, González Candela Rosario, Gonzalo Carlos, Gorriz Santamaría Elena, Gorrotxtegi Ereño Jesús, Goterris Pinto Marian, Granado Sanchez Francisco José, Gras Balaguer Santiago, Guardiola Grau Begoña, Guerrero Reina Salvador, Guillen Garcia Francisco, Guillen Hdez. Monserrat, Gutiérrez Delgado Eduardo, Gutiérrez Méndez José Luis, Guzmán Martí Juan A., Guzon Méndez Fernando, Helguera Jose Luis, Heredia Cabrera Francisco, Hernaez Cabañas Luis F., Hernández Pérez Ana, Hernández Surroca Daniel, Hernández Díaz Francisco, Hernández Gutiérrez Juana Isabel, Hernández Moreno Julio, Hernández Pedro, Hernández García Concepción, Hernández Rico Filomena, Hernández Iglesias Juan José, Hernández Rodríguez Maria Dolores, Hernández Herrera Ricardo, Herran Oteruelo Luis Ángel, Herrera Hernández Eduardo, Hevia Rodríguez Eduardo, Hidalgo Santiago Juan Carlos, Hinojosa Gallardo Juan Luis, Ibor Vidal Encarnación, Iglesias Fernandez Federico, Imaz Pérez Francisco, Inesta Mena Claudia, Iraola Sierra Begoña, Irizabal Navas Juan Cruz, Jane Jaures Antoni, Jiménez Cámara Antonio, Jiménez Rodríguez Maria Ángeles, Jiménez Jerez Maria Del Carmen, Jiménez Cámara Valentín, Jiménez Garijo Diego, Jiménez Herrera José María, Jiménez Notario Manuel, Jiménez Samper Milagros, Jorge Sanchez Ramón J., Juan Alberola Vicente, Kern Volcy Edouard José, Laborda Esteruelas Montse, Laiseca Sagardui Javier, Lalinde Herrero Martín, Lamarca Roca Angels, Lara Fornelino Luis Felipe, Lasso Oria Virginia, Latorre Atienza Marco A., Leal Correa Bartolome, Leira Paz Gloria, Lemus Gallego Juan Luis, Lezaun Indurain Ana, Lillo Gallego Paco, Linares Lorenzo Francisco, Llenares Orts José F., Llorente Gómez De Segura Iñaki, Lluna Gasco Carlos, López Abietar María Isabel, López García Celia, López Serrano Beatriz, Lopez Varela Carmen, López De La Iglesia Jaime, López Vázquez Jose Luis, López Toledo Mª Luisa, López Quintero Purificación, López Luque Santiago Rafael, López Mitxelena Teresa, López Aisa Blanca, López Ortiz Francisco, López Cambeses Rosario, López Crespo Yolanda, Lozano Cobos Antonio, Luengo Agüero Jesus, Macia Pérez Ramón, Madero Ambrojo Emilio, Magadalena Belio José Félix, Mahiques García Elvira, Malagas Ferrera Herminio, Mansilla Rodríguez Calixta, Marco Segarra Emili, Marín De La Cueva Juan Antonio, Marín Ibáñez Alejandro, Marín Osorio Carmen, Marion Navasa Gonzalo,

Marti Corominola Andreu, Martín Peces Blanca, Martín Pérez Enrique, Martín Sanchez Jose, Martín Jiménez Juan Antonio, Martín Collado Manolo, Martín Blázquez Mercedes, Martín Fresneda Soledad, Martín Alegre Amparo, Martín Ruiz Aurelio, Martín Domenech Ignacio, Martín Lafoz Juan Carlos, Martín Gonzalez Luis, Marín Moros José María, Martínez Garcia Agustín, Martínez Ruiz Andrés, Martínez Rosselló Antonio, Martínez Bravo Bernardino, Martínez Quess Dulce, Martínez Ortega Francisco, Martínez Piquer Joaquín, Martínez Orozco Marino, Martínez Llarena Marisa, Martínez Mercedes, Martínez Fernandez Montserrat, Martínez Pardo Rafael, Martínez Luque Francisco Javier, Martínez Martínez Mª Jesús, Martos Calzado José, Massana Toro Pere, Matellanes Matellanes Ángel, Mateos Freire Sergio, Mato Marcos Fernando, Matoses Nacher Daniel, Mayques Alos José Luis, Medina Maya Jose Antonio, Medina Cuenca Pedro, Melo Faus Juan Bta, Mena Garcia Candido, Mena Pena Maria, Méndez Gómez Begoña, Méndez Robles Jesús, Méndez Delagado Manuel, Merina Sanchez Rafael, Mesa Pedrero Carlos, Minchero Alberto, Mingo Belloso Yolanda, Minuesa Cortijo Francisco Javier, Miñana Aguado Sandra, Miñano Fernández Pilar, Molina Molina Felipe, Molina De Heras Miguel, Monblan Díaz Eva, Monge García José Manuel, Monraba Ferrer Jose M., Monroy Fuenmayor Nieves, Montalvillo Montalvillo Jose Luis, Montesinos E., Moñivas Lijaro Mariano, Morales Navarro Fernando, Morales Aranjuez Isabel María, Moralez Pérez Lola, Moreno Andújar Dolores, Moreno Moreno Eugenio, Morillo Vázquez Álvaro, Mulero Garcia Maria José, Munguia Alcalde Vicente, Muñoz Peláez Carmen, Muñoz Rodríguez J.A., Muñoz Galán Maria Dolores, Murguizu Garcia Ana, Murie Roig Ana, Muriel Díaz Paz, Murillo Torrado Diego, Murillo Torrado Mariano, Nader Ramirez Roberto, Nasser Rifai Adel, Navalón Martínez Amparo, Navalón Gómez Pascual, Navarro Navarrete Carmen, Navarro Pérez Jorge, Navarro Sanz Juan José, Navarro Villena Manuel, Nicolau Rerrer Francisca, Nieto Fernandez Arroyo Manuel, Nieto Hortal Pepe, Nieto Cervera Rafael, Nogales Rebollo Gregorio J., Noguera Bennaser Juan, Ocaña Cazalilla Carmelo, Ogallas Raya Fuensanta, Olalde Quintana Rafael, Oliva Gomez Fco Jose, Olivares Bautista Mari Carmen, Oliveras Montse, Oliveras Deulofeu Victor, Olmedo Peñaranda Javier, Orio Segura Esperanza, Orquín Vera Abelardo, Ortega Cantero Ángel, Ortega Cutillas Mariano, Ortega Jiménez Victor, Ortiz De Santa Maria Jose, Ortiz-Villajos Serrano Carmen, Osca Pellicer David, Osuna Dominguez José, Otero Toral Ángel, Otero Coton Jose, Otero Rodríguez Rocío, Paches Porcar Maria Dolores, Palacios Villanueva Cayetano, Palomares Moral Eduardo, Panero Alejandro, Pardo Otero Felipe, Paredes Saura José, Parralejo Cano Francisco, Pascual Fuster Vicente, Pastor Mira Percebal Isidro, Paz Rodríguez Fabiola, Pazos González Pilar, Peco Bermúdez Benjamín, Pedraza Sánchez Sonia, Pellicer Muñoz Mónica, Pellit Ramil Ignacio, Pensado Pousa José, Peña Díaz Dolores, Perea Mostajo Janeth, Pereira Cuello Jesús, Pérez Pérez Carlos, Pérez Gil Javier S., Pérez Cebrian Maria José, Perez Mira Maria José, Pérez Zamora Susana, Pérez Fernández Aurelia, Pérez González Guillermo, Pérez Boronat Luis, Pérez Palmes Mari Paz, Pérez Rivero Miguel A., Perona Pagan Miguel, Picazo Romero Emilio, Piury Alonso Carlos, Pizarro López Mar, Ponce Martín Jose, Ponce Bejarano Manuel, Ponz Callen Antonio, Prat Mireia, Prieto Girón Jesús, Prieto Díaz Miguel A., Prieto Prieto Raquel, Puchades Chilet Ángeles, Pueyo Martínez Manuel, Pujol Dakme Pere, Quintana Ortíz Javier, Rabanal Carrera Sandra, Raigda Igada Guerra Antonio, Ramirez Marent Jose Ignacio, Ramírez Canca María Teresa, Ramírez González Rosa Mª, Ramos Rodriguez Consuelo, Ramos Martín Vidal, Razón Angulo Emilio, Regueiro Antonio, Requena Marín Carmen, Retuerta García María Dolores, Rey Gonzalez Pilar, Ribes Albert Jose, Riuas Alcázar Guillermo, Rivero Moreno Antonio, Roberto Echevarri Enrique, Robre Oriete Mariano, Roca Guanter Enric, Rodondo Rico Inmaculada, Rodriguez Arce Angeles, Rodríguez López Elisa, Rodríguez Vicente Isabel, Rodriguez Inchaustegui Jose Luis, Rodríguez Pino Jose Manrique, Rodríguez Sanchez Juan José, Rodríguez Apresa Mª Dolores, Rodríguez Solureano Maria Antonia, Rodríguez Rodríguez Miguel Ángel, Rodríguez Hernández Vidal, Rodríguez Poncela Antonio, Rodríguez López Mercedes, Roldán Sanchez Juan Jose, Romaní Del Castillo Javier, Romero González Elena, Romero Atanes Jesús, Romero Martín Julia, Rosa Gil Luis, Rubio Hernández Jose Félix, Rudolphi Carralero Teodoro, Ruiz Comellas Anna, Ruiz Diez Dolores, Ruiz Ferrando Ernestina, Ruiz Franzi Ignacio, Ruiz De Gordeguela Julio, Ruiz Pastor Luis, Ruiz Fernandez Manuel, Ruiz Aragón Rosalía, Ruvira Martínez Ernesto, Sacristán Rubio Alberto, Sáenz Galeano Antonio, Sainz Salazar Mª Félix, Saiz Jose Antonio, Salas Fernando, Salas Tomas, Salgado Cachofeiro José Alfonso, Salgado Nieto Vicente, Sanchez Calso Antonio, Sanchez Garcia Fernado, Sanchez Mate Isabel, Sanchez Moran Isabel, Sanchez Viel Isabel, Sanchez Prieto Jaime, Sanchez Coureiro Manuel, Sanchez Santos Natividad, Sánchez Berbel Baldomero, Sánchez Carrillo Santiago, Sancho Soriano Natividad, Saniger Herrera José Manuel, Sanmartín Almenar Ana, Sansano Trives Rosario, Santana Benítez Jesús, Santiago Sáez Andrés, Santiago Antonio, Santos Altozano Carlos, Santos Bueso Isabel María, Santos Godoy Rafael, Sanz Rebollo Gloria, Sanz García Juan José, Sanz Bailón Luis, Sarria Ferrada Jesús, Segarra Codina Ramon, Segrera Manzano Silvia, Serrano Contreras Benjamín, Serrano Valverde Leticia, Serrano-Guerra Librero Fco. Javier, Silva Silva Manuela, Simón Gutierrez Raul, Sirvent Antolin Luis, Sorli Guerola Jose Vicente, Soubriet Velasco Ángel, Suárez Hernández Hector, Suárez Castro Nicanor Enrique, Suárez Fernández Eusebio, Tarradellas Bancus Jose María, Tejero Puerto Francisco, Tisaire Sanchez Javier, Tola Gutiérrez Beatriz, Toldos Villegas Gregorio, Torner Perarnau Lluis, Torres Izquierdo Jesus, Torres Exposito Juan, Trujillano Gerardo, Úbeda Pastor María, Valeriola Julvez José María, Valero Barcelo Carmen, Valero Lance Maria Pilar, Valladares Mateu Lluis Carles, Vargas Negrín Francisco, Vázquez Rojo Carlos, Vázquez García María Dolores, Velasco Escobar Pablo, Velayos Jiménez Enrique, Velazquez Ferro Juan Jesús, Ventura Rodriguez Silvestre, Vergara Martín Jesús, Vicente Arroyo Manuel J., Vigil-Escalera Francisco, Vila Villarte Carme, Vilano Vives Jordi, Villa Estebanez Rubén, Villahoz Castrillejo Rosa, Villalva Quintana Elena, Villanueva Budia Guillermo, Villanueva Gómez Isabel, Villanueva Telleria Jerusalén, Villanueva Rebollo José Manuel, Villanueva Zarate Jose Ramón, Villar Rivera Marcos, Villarte Perez Ofelia, Villena Machuca Maria Luisa, Viudes Plaza Emilio, Vizuete Gala Carmen, Zamorano Martín Juan Carlos, Zapata Medin Luisa, Zeloro González Tomás, Zuazagoitia Nubla Jose Félix, Zubiri Sáenz Félix, Zugaza Gurruchaga Lucrecia.

References

1. Manjunath G, Tighiouart H, Coresh J, Macleod B, Salem DN, Griffith JL, Levey AS, Sarnak MJ: Level of kidney function as a risk factor for cardiovascular outcomes in the elderly. *Kidney In* 63: 1121–1129, 2003
2. Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S: Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: The HOPE randomized trial. *Ann Intern Med* 134: 629–636, 2001
3. Arnlov J, Evans JC, Meigs JB, Wang TJ, Fox CS, Levy D, Benjamin EJ, D'Agostino RB, Vasan RS: Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: The Framingham Heart Study. *Circulation* 112: 969–975, 2005
4. Madison JR, Spies C, Schatz IJ, Masaki K, Chen R, Yano K, Curb JD: Proteinuria and risk for stroke and coronary heart

disease during 27 years of follow-up: The Honolulu Heart Program. *Arch Intern Med* 166: 884–889, 2006
5. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351: 1296–1305, 2004
6. Foley RN, Wang C, Collins AJ: Cardiovascular risk factor profiles and kidney function stage in the US general population: The NHANES III study. *Mayo Clin Proc* 80: 1270–1277, 2005
7. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D: Predictors of new-onset kidney disease in a community-based population. *JAMA* 291: 844–850, 2004
8. Kambham N, Markowitz GS, Valeri AM, Lin J, D'Agati VD: Obesity-related glomerulopathy: An emerging epidemic. *Kidney Int* 59: 1498–1509, 2001
9. Bonnet F, Deprele C, Sassolas A, Moulin P, Alamartine E, Berthezene F, Berthoux F: Excessive body weight as a new independent risk factor for clinical and pathological progression in primary IgA nephritis. *Am J Kidney Dis* 37: 720–727, 2001
10. 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* 46: 871–880, 2005
11. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS: Body mass index and risk for end-stage renal disease. *Ann Intern Med* 144: 21–28, 2006
12. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 285: 2486–2497, 2001
13. Alberti KG, Zimmet P, Shaw J: Metabolic syndrome: A new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med* 23: 469–480, 2006
14. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D: A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 130: 461–470, 1999
15. Cockcroft DW, Gault MH: Prediction of creatinine clearance from serum creatinine. *Nephron* 16: 31–41, 1976
16. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G: National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Ann Intern Med* 139: 137–147, 2003
17. Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P: Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. *J Am Soc Nephrol* 16: 763–773, 2005
18. Cirillo M, Anastasio P, De Santo NG: Relationship of gender, age, and body mass index to errors in predicted kidney function. *Nephrol Dial Transplant* 20: 1791–1798, 2005
19. Rigalleau V, Lasseur C, Perlemoine C, Barthe N, Raffaitin C, Liu C, Chauveau P, Baillet-Blanco L, Beauvieux MC, Combe C, Gin H: Estimation of glomerular filtration rate in diabetic subjects: Cockcroft formula or modification of Diet in Renal Disease study equation? *Diabetes Care* 28: 838–843, 2005
20. de Francisco AL, Otero A: Occult chronic renal failure: EPIRCE study. *Nefrologia* 25[Suppl 4]: 66–71, 2005
21. Garg AX, Mamdani M, Juurlink DN, van Walraven C; Network of Eastern Ontario Medical Laboratories (NEOMeL): Identifying individuals with a reduced GFR using ambulatory laboratory database surveillance. *J Am Soc Nephrol* 16: 1433–1439, 2005
22. Jabary NS, Martin D, Munoz MF, Santos M, Herruzo J, Gordillo Bustamante J: Serum creatinine and creatinine clearance to estimate renal function in essential hypertension. *Nefrologia* 26: 64–73, 2006
23. Redon J, Cea-Calvo L, Lozano JV, Fernandez-Perez C, Navarro J, Bonet A, Gonzalez-Esteban J; Investigators of the ERIC-HTA 2003 Study: Kidney function and cardiovascular disease in the hypertensive population: The ERIC-HTA study. *J Hypertens* 24: 663–669, 2006
24. Redon J, Morales-Olivas F, Galgo A, Brito MA, Mediavilla J, Marin R, Rodriguez P, Tranche S, Lozano JV, Filozof C; the MAGAL group: Urinary albumin excretion and glomerular filtration rate across the spectrum of glucose abnormalities in essential hypertension. *J Am Soc Nephrol* 17[Suppl 3]: 236–245, 2006
25. Chagnac A, Weinstein T, Korzets A, Ramadan E, Hirsch J, Gafter U: Glomerular hemodynamics in severe obesity. *Am J Physiol Renal Physiol* 278: F817–F822, 2000
26. Ribstein J, du Cailar G, Mimran A: Combined renal effects of overweight and hypertension. *Hypertension* 26: 610–615, 1995
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* 46: 587–594, 2005
28. Sironi AM, Gastaldelli A, Mari A, Ciociaro D, Positano V, Postano V, Buzzigoli E, Ghione S, Turchi S, Lombardi M, Ferrannini E: Visceral fat in hypertension: Influence on insulin resistance and beta-cell function. *Hypertension* 44: 127–133, 2004
29. Pinto-Sietsma SJ, Navis G, Janssen WM, de Zeeuw D, Gans RO, de Jong PE; PREVEND Study Group: A central body fat distribution is related to renal function impairment, even in lean subjects. *Am J Kidney Dis* 41: 733–741, 2003
30. Kurella M, Lo JC, Chertow GM: Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults. *J Am Soc Nephrol* 16: 2134–2140, 2005