[e] *Servicio de Nefrología, Hospital Central de la Defensa Gómez Ulla, Madrid, Spain*

[*] *Corresponding author.*
E-mail addresses: fvalga@hotmail.com (F. Valga), taniarmv@msn.com (T. Monzón), nvegdia@gmail.com (N. Vega-Diaz), sruisan@gobiernodecanarias.org (S. Ruiz-Santana), saraaladrosara@gmail.com (S. Aladro), rassoul.1011@gmail.com (R. Diallo-Saavedra),. josedelaflor81@yahoo.com (J.C. De la Flor), josecarlos.rodriguez@ulpgc.es (J.C. Rodriguez-Perez)

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Including KDIGO cardiovascular risk stratification into SCORE scale could improve the accuracy to better stratify cardiovascular risk

Incluir la estratificación de riesgo KDIGO en la escala SCORE podría mejorar la exactitud para estratificar mejor el riesgo cardiovascular

Dear Editor,

Chronic kidney disease (CKD) is a common condition worldwide;[1] however, it is vastly underdiagnosed as it frequently remains asymptomatic until reaching advanced stages.[2] Thus, a recent database study performed in Spain has shown that in adults, the prevalence of identified CKD reaches only 5% of the population, which is far from previous nation-wide, population-based studies.[3] The CKD prevalence is expected to increase in the next future, as people will be

Table 1 – Cardiovascular risk stratification according to 2019 ESC and KDIGO guidelines.

	2019 ESC	KDIGO
Very high risk	• Documented ASCVD • T2DM with TOD[a] or ≥3 major risk factors, or T1DM of long duration (>20 years) • Severe CKD (eGFR < 30 mL/min/1.73 m^2) • SCORE ≥ 10% • FH with ASCVD or another major risk factor	• eGFR < 30 mL/min/1.73 m^2 or eGFR 30–44 mL/min/1.73 m^2 with UACR ≥ 30 mg/g or eGFR 45–59 mL/min/1.73 m^2 with UACR > 300 mg/g
High risk	• Markedly elevated single risk factors (TC >310 mg/dL, LDL-C > 190 mg/dL, or BP ≥ 180/110 mmHg) • Patients with FH without other major risk factors • Patients with DM without TOD[a], with DM duration ≥10 years or another additional risk factor • Moderate CKD (eGFR 30-59 mL/min/1.73 m^2) • SCORE ≥5% and <10%	• eGFR 30–59 mL/min/1.73 m^2 with UACR < 30 mg/g or eGFR 45–59 mL/min/1.73 m^2 with UACR 30–300 mg/g or eGFR ≥ 60 with UACR > 300 mg/g
Moderate risk	• SCORE ≥1% and <5% • Young patients (T1DM < 35 years; T2DM < 50 years) with DM duration < 10 years, without other risk factors	• eGFR ≥ 60 mL/min/1.73 m^2 with UACR 30–300 mg/g[b]
Low risk	• SCORE < 1%	• eGFR > 60 mL/min/1.73 m^2 with UACR < 30 mg/g

[a] Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy.
[b] Modified from original KDIGO as ESC includes 45–59 GFR as high risk category.
ASCVD: atherosclerotic cardiovascular disease; BP: blood pressure; CKD: chronic kidney disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; ESC: European Society of Cardiology; FH: familial hypercholesterolemia; KDIGO: Kidney Disease: Improving Global Outcomes; LDL-C: low-density lipoprotein cholesterol; SCORE: Systematic Coronary Risk Estimation; T1DM: type 1 DM; T2DM: type 2 DM; TC: total cholesterol; TOD: target organ damage.

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Table 2 – Cardiovascular risk stratification of CKD patients according to 2019 ESC guidelines and with the KDIGO modification.

	Total (n = 56,435)			Women (26,955)			Men (29,480)		
	2019 ESC	KDIGO	P	2019 ESC	KDIGO	P	2019 ESC	KDIGO	P
Very high risk, n (%)	19,572 (34.7)	20,702 (36.7)	<0.001	7682 (28.5)	8289 (30.8)	<0.001	11,890 (40.3)	12,413 (42.1)	<0.001
Documented ASCVD	16,425 (29.1)	16,425 (29.1)	1.0	6095 (22.6)	6095 (22.6)	1.0	10,330 (35.0)	10,330 (35.0)	1.0
T2DM with TOD[a] or ≥3 major risk factors, or T1DM of long duration (>20 years)	11,380 (20.2)	11,380 (20.2)	1.0	4620 (17.1)	4620 (17.1)	1.0	6760 (22.9)	6760 (22.9)	1.0
Severe CKD (eGFR <30 mL/min/1.73 m^2)	4008 (7.1)	NA	<0.001	2295 (8.5)	NA	<0.001	1713 (5.8)	NA	<0.001
eGFR < 30 mL/min/1.73 m^2 or eGFR 30–44 mL/min/1.73 m^2 with UACR ≥ 30 mg/g or eGFR 45–59 mL/min/1.73 m^2 with UACR > 300 mg/g	NA	6680 (11.8)		NA	3825 (14.2)		NA	2855 (9.7)	
SCORE ≥ 10%	NA	NA	–	NA	NA	–	NA	NA	–
FH with ASCVD or another major risk factor	581 (1.0)	581 (1.0)	1.0	292 (1.1)	292 (1.1)	1.0	289 (1.0)	289 (1.0)	1.0
High risk, n (%)	25,565 (45.3)	26,755 (47.4)	<0.001	13,316 (49.4)	13,750 (51.0)	<0.001	12,249 (41.6)	13,005 (44.1)	<0.001
Markedly elevated single risk factors (TC > 310 mg/dL, LDL-C > 190 mg/dL, or BP ≥ 180/110 mmHg)	6147 (10.9)	5826 (10.3)	0.002	3254 (12.1)	3125 (11.6)	0.085	2893 (9.8)	2701 (9.2)	0.007
Patients with FH without other major risk factors	12,728 (22.6)	12,580 (22.3)	0.291	6384 (23.7)	6325 (23.5)	0.549	6344 (21.5)	6255 (21.2)	0.371
Patients with DM without TOD[a], with DM duration ≥10 years or another additional risk factor	17,042 (30.2)	16,890 (29.9)	0.324	8436 (31.3)	8375 (31.1)	0.571	8606 (29.2)	8515 (28.9)	0.409
Moderate CKD (eGFR 30–59 mL/min/1.73 m^2)	12,364 (21.9)	NA	<0.001	6852 (25.4)	NA	0.214	5512 (18.7)	NA	<0.001
eGFR 30-59 mL/min/1.73 m^2 with UACR < 30 mg/g or eGFR 45–59 mL/min/1.73 m^2 with UACR 30–300 mg/g or eGFR ≥60 with UACR >300 mg/g	NA	14,182 (25.1)		NA	6978 (25.9)		NA	7204 (24.4)	
Score ≥5% and < 10%	NA	NA	–	NA	NA	–	NA	NA	–
Moderate risk, n (%)	9183 (16.3)	7565 (13.4)	<0.001	4829 (17.9)	4077 (15.1)	<0.001	4354 (14.8)	3488 (11.8)	<0.001
Score ≥1% and < 5%	6069 (10.8)	5780 (10.2)	0.005	3223 (12.0)	3070 (11.4)	0.040	2846 (9.7)	2710 (9.2)	0.055
Young patients (T1DM < 35 years; T2DM < 50 years) with DM duration <10 years, without other risk factors	5215 (9.2)	5113 (9.1)	0.292	2532 (9.4)	2483 (9.2)	0.468	2683 (9.1)	2630 (8.9)	0.446
eGFR ≥ 60 mL/min/1.73 m^2 with UACR 30–300 mg/g[b]	NA	4076 (7.2)	–	NA	1901 (7.1)	–	NA	2175 (7.4)	–
Low risk, n (%)	2115 (3.7)	1413 (2.5)	<0.001	1128 (4.2)	839 (3.1)	<0.001	987 (3.3)	574 (1.9)	<0.001
Score < 1%	2115 (3.7)	1413 (2.5)	<0.001	1128 (4.2)	839 (3.1)	<0.001	987 (3.3)	574 (1.9)	<0.001
eGFR >60 mL/min/1.73m^2 with UACR < 30 mg/g	NA	0	–	NA	0	–	NA	0	–

[a] Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy.
[b] Modified from original KDIGO as ESC includes 45–59 GFR as high risk category.
ASCVD: atherosclerotic cardiovascular disease; BP: blood pressure; CKD: chronic kidney disease; DM: diabetes mellitus; eGFR: estimated glomerular filtration rate; ESC: European Society of Cardiology; FH: familial hypercholesterolemia; KDIGO: Kidney Disease: Improving Global Outcomes; LDL-C: low-density lipoprotein cholesterol; SCORE: Systematic Coronary Risk Estimation; T1DM: type 1 DM; T2DM: type 2 DM; TC: total cholesterol; TOD: target organ damage.

older and the proportion of hypertension and diabetes, the leading causes of CKD, are growing.[2] CKD increases morbidity and mortality, particularly cardiovascular (CV) disease.[2,3] The 2019 European Society of Cardiology (ESC) guidelines of dyslipidemia classify severe CKD (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2), and moderate CKD (eGFR 30–59 mL/min/1.73 m^2), as very high and high CV risk, respectively, without requiring SCORE estimation.[4] However, it is well known that the risk of CV outcomes does not only depend on renal function, but also on albuminuria.[3] Thus, the Kidney Disease, Improving Global Outcomes (KDIGO) guidelines include both parameters in the stratification of CV disease.[5] As 2019 ESC guidelines included eGFR, but not albuminuria for risk stratification, it would be important to analyze the impact of updating SCORE scale with KDIGO CV risk stratification.

For this purpose, data from BIG-PAC®, a database with information from non-selected 1.8 million persons of primary health care centers and referral hospitals within the Spanish national health system were analyzed.[1] Adult patients, with ≥1 diagnostic code of CKD or having laboratory results meeting the definition of CKD, were included. CKD stages were defined according to the eGFR (CKD-EPI) and the urine albumin-to-creatinine ratio (UACR) criteria, as follows: CKD stage 1: eGFR ≥ 90 mL/min/1.73 m^2 and UACR ≥30 mg/g; CKD stage 2: eGFR 60–89 mL/min/1.73 m^2 and UACR ≥ 30 mg/g; CKD stage 3a: eGFR 45–59 mL/min/1.73 m^2; CKD stage 3b: eGFR 30–44 mL/min/1.73 m^2; CKD stage 4: eGFR 15–29 mL/min/1.73 m^2; and CKD stage 5: eGFR < 15 mL/min/1.73 m^2.[1] CV risk was classified according to SCORE.[4] Moreover, this scale was updated by adding the KDIGO criteria into SCORE scale (Table 1).[4,5] Categorical variables were described by their absolute and relative frequencies and were compared with the Chi-square test or the Fisher exact test, when appropriate.

A total of 56,435 (4.91%) patients had CKD, of whom 26,955 (47.8%) were women. According to 2019 ESC guidelines, 34.7%, 45.3%, 16.3% and 3.7% of patients had very high, high, moderate and low CV risk, respectively (80.0% very high/high CV risk). After updating risk stratification with KDIGO criteria, these numbers were 36.7%, 47.4%, 13.4% and 2.5%, respectively; $P < 0.001$ in all cases (84.1% very high/high CV risk). Therefore, the introduction of the KDIGO criteria within the SCORE scale translated into more patients classified as very high and high CV risk patients, respectively (absolute difference: +2.0% and +2.1%; relative difference: +5.8% and +4.6%, respectively; both $P < 0.001$). This occurred in women and men, similarly (Table 2).

These data indicate that including albuminuria into SCORE may improve the accuracy of this scale to better stratify CV risk. Of note, preventing strategies for the development and progression of CKD (renal function and albuminuria) with renin–angiotensin system inhibitors, and more recently, with sodium glucose cotransporter-2 inhibitors, have also shown a positive impact on CV disease.[6–9] Therefore, an improved CV risk stratification may be helpful to better identify those patients that would benefit more from these therapies. In fact, the 2021 ESC guidelines on CV disease prevention have also include albuminuria in addition to renal function for CV risk stratification.[10]

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Ana Cebrian[a], Carlos Escobar[b,*], Unai Aranda[c], Beatriz Palacios[c], Margarita Capel[c], Antoni Sicras[d], Aram Sicras[d], Antonio Hormigo[e], Nicolás Manito[f], Manuel Botana[g], Roberto Alcázar[h]

[a] *Primary Care Center Cartagena Casco, Cartagena, Murcia, Spain*
[b] *University Hospital La Paz, Madrid, Spain*
[c] *AstraZeneca, Spain*
[d] *Health Economics and Outcomes Research, Atrys Health, Barcelona, Spain*
[e] *Primary Care Center Salud Puerta Blanca, Malaga, Spain*
[f] *Hospital de Bellvitge, Hospitalet de Llobregat, Barcelona, Spain*
[g] *Hospital Universitario Lucus Augusti, Lugo, Spain*
[h] *University Hospital Infanta Leonor, Madrid, Spain*

[*] *Corresponding author.*
E-mail address: escobar_cervantes_carlos@hotmail.com (C. Escobar).

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