demonstrated that rituximab is effective for AAV, especially renal AAV. This is the first case of DLBCL-related AAV with biopsy-proven crescentic glomerulonephritis, and although R-CHOP did not provide lymphoma remission, renal function improved. Thus, rituximab could be effective for improving renal function in AAV. Clinicians should consider the possibility of AAV occurring as a complication in DLBCL.

Informed consent was obtained from the patient for the publication of this article.

REFERENCES

1. Bilici A, Yapici HS, Ercan S, Seker M, Ustaalioglu BB, Salman T, et al. The prevalence and significance of autoantibodies in patients with non-Hodgkin's lymphoma: are they correlated with clinicopathological features? J Buon. 2012;17:502–7.
2. Hamidou MA, El Kouri D, Audrain M, Grolleau JY. Systemic antineutrophil cytoplasmic antibody vasculitis associated with lymphoid neoplasia. Ann Rheum Dis. 2001;60:293–5, http://dx.doi.org/10.1136/ard.60.3.293.
3. Tsuda M, Nakashima Y, Ikeda M, Shimada S, Nomura M, Matsushima T, et al. Intravascular large b-cell lymphoma complicated by anti-neutrophil cytoplasmic antibody-associated vasculitis that was successfully treated with rituximab-containing chemotherapy. J Clin Exp Hematop. 2015;55:39–43.
4. Shinkawa Y, Hatachi S, Yagita M. Intravascular large B-cell lymphoma with a high titer of proteinase-3-anti-neutrophil cytoplasmic antibody mimicking granulomatosis with polyangiitis. Mod Rheumatol. 2019;29:195–7, http://dx.doi.org/10.1080/14397595.2016.1205798.
5. Sugiyama A, Kobayashi M, Daizo A, Suzuki M, Kawashima H, Kagami SI, et al. Diffuse cerebral vasoconstriction in a intravascular lymphoma patient with a high serum MPO-ANCA level. Intern Med. 2017;56:1715–8, http://dx.doi.org/10.2169/internalmedicine.56.8051.
6. Muto G, Takahashi Y, Yamashita H, Mimori A. A patient with intravascular lymphoma presenting with cerebral infarction and a high serum MPO-ANCA level. Mod Rheumatol. 2011;21:207–10, http://dx.doi.org/10.1007/s10165-010-0361-z.
7. Zuckerman KK, Leventhal L, Wynne C. Positive c-ANCA in a patient with lymphoma and without vasculitis. J Clin Rheumatol. 1997;3:279–81, http://dx.doi.org/10.1097/00124743-199710000-00007.
8. Stone JH, Merkel PA, Spiera R, Seo P, Langford CA, Hoffman GS, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med. 2010;363:221–32, http://dx.doi.org/10.1056/NEJMoa0909905.
9. Jones RB, Tervaert JW, Hauser T, Luqmani R, Morgan MD, Peh CA, et al. Rituximab versus cyclophosphamide in ANCA-associated renal vasculitis. N Engl J Med. 2010;363:211–20, http://dx.doi.org/10.1056/NEJMoa0909169.

Taro Horino[a,*], Osamu Ichii[b]

[a] *Department of Endocrinology, Metabolism and Nephrology, Kochi Medical School, Kochi University, Kohasu, Oko-cho, Nankoku, Kochi 783-8505, Japan*

[b] *Laboratory of Anatomy, Department of Basic Veterinary Sciences, Faculty of Veterinary Medicine, Hokkaido University, Kita 18, Nishi 9, Kita-Ku, Sapporo 060-0818, Japan*

[*] *Corresponding author.*
E-mail address: horinott@yahoo.co.jp (T. Horino).

https://doi.org/10.1016/j.nefro.2020.04.017

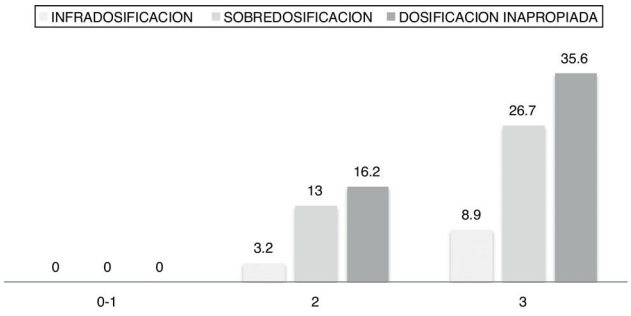
Predictor factors of inappropriate rivaroxaban dosage using the Ckd-Epi equation☆

Factores de predicción de dosificación inadecuada de rivaroxabán utilizando la ecuación de CKD-EPI

Dear Editor,

Rivaroxaban is approved for preventing stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (NVAF), with one or more risk factors. It is recommended that the Cockcroft-Gault (CG) equation be used for the dosing of this drug.[1] However, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is the method of choice for determining kidney function and is the equation used by the majority of laboratories in Spain.[2] There are discrepancies in values calculated using the two equations which may cause errors in prescribed doses of rivaroxaban.[3,4] Prescription of inappropriate doses is linked to an adverse cardiovascular

DOI of original article:
https://doi.org/10.1016/j.nefro.2020.04.016.
☆ Please cite this article as: Pérez Cabeza AI, Górriz JL, Bravo Marqués R, Chinchurreta Capote PA, López Tejero S, González Correa JA, et al. Factores de predicción de dosificación inadecuada de rivaroxabán utilizando la ecuación de CKD-EPI. Nefrologia. 2021;41:216–218.



Se construye una escala de riesgo de prescripción de dosis inapropiada de rivaroxabán al aplicar la ecuación CKD-EPI con las variables edad ≥ 75 años, CKD- EPI < 70 ml/min/1,73 m2 y peso extremo (≤ 60 o ≥ 85 kg). Cada variable puntúa 0 (ausencia de la categoría) o 1 (presencia). La suma de cada variable permite un cómputo de 0 a 3 (eje de abscisas). En el eje de ordenadas se expresan los porcentajes de dosis bajas inapropiadas, sobredosificaciones y dosificaciones inapropiadas de rivaroxabán en función del valor de la escala de riesgo. Se considera la ecuación CG el patrón oro.

Fig. 1 – Percentage of patients with inappropriate rivaroxaban dosage prescription based on the number of factors on the risk scale.

prognosis.[5] The objective of our study was to identify groups of patients in whom the CKD-EPI and CG equations can be used indiscriminately with a low risk of prescription error.

An observational, retrospective study was conducted of patients with atrial fibrillation or atrial flutter seen at a cardiology clinic between November 2012 and December 2014. Patients with metal stent implantation or moderate to severe rheumatic mitral stenosis, for whom serum creatinine levels in the past 12 months were not available, or for whom body weight was not recorded at the clinic, were excluded.

A total of 571 patients were enrolled, with a mean age of 69 years (±13.6 years), CHA_2DS_2VASc 2.8 ± 1.7 and HAS-BLED 1.2 ± 0.8. (CHA_2DS_2VASc is: **C**ongestive heart failure, **H**ypertension, **A**ge, **D**iabetes mellitus **S**troke **V**ascular disease, **A**ge, **S**ex.HAS-BLED is: **H**ypertension, **A**bnormal renal and liver function, **B**leeding, **L**abile INRs, **E**lderly, **D**rugs or alcohol.) Table 1 shows the patients' baseline characteristics

Using the CKD-EPI equation, 41 patients (7.2%) would receive inappropriate dosing of rivaroxaban (nine due to underdosing and 32 due to overdosing). In particular, 509 (89.1%) would receive 20 mg daily, 59 (10.3%) would receive 15 mg daily and three (0.5%) would have a contraindicated prescription. Using the Cockcroft-Gault formula (CG), 487 individuals (85.3%) would receive a daily dose of 20 mg, 80 (14.0%) would receive a daily dose of 15 mg and four (0.7%) would have a contraindicated prescription.

In the univariate analysis, variables linked to a higher likelihood of receiving inappropriate dosing were the CHA_2DS_2-VASc scale ($p < 0.001$), HAS-BLED ≥3 (17.6% versus 6.5%; $p = 0.028$), creatinine ($p < 0.001$); age ($p < 0.001$), weight ($p < 0.001$) and CKD-EPI ($p < 0.001$). Among patients with dosing discrepancies, CKD-EPI values were 56.44 ± 10.93 ml/min/1.73 m^2 (p10 = 43.6; p90 = 68.9). In the multivariate analysis, significant predictive factors for receiving inappropriate dosing were extreme weight ≤60 kg or ≥85 kg (2.5 95% confidence interval [CI] 1.2–5.3; $p = 0.013$), age ≥75 years (7.4 95% CI 2.7–20.4; $p < 0.001$) and CKD-EPI <70 ml/min/1.73 m^2 (23.1 95% CI 6.9–77.7; $p < 0.001$).

Table 1 – Clinical data corresponding to the sample ($n = 571$).

Male sex	302 (52.9)
Age (years)	69 ± 13.6
Age ≥75 years	228 (39.9)
CHA_2DS_2VASc (score)	2.8 ± 1.7
CHA_2DS_2VASc score	
0–1	136 (23.8)
≥2	435 (76.2)
HAS-BLED (score)	1.2 ± 0.8
HAS-BLED score	
0–2	537 (94)
≥3	34 (6)
Weight (kg)	79.3 ± 16.1
Body weight (kg)	
≤60	75 (13.1)
1–84	306 (53.6)
≥85	190 (33.3)
Atrial fibrillation	509 (89.2)
Atrial flutter	75 (13.2)
CKD-EPI (ml/min/1.73 m^2)	79.6 ± 22.6
>50 ml/min/1.73 m^2	508 (89)
30–49 ml/min/1.73 m^2	48 (8.4)
15–29 ml/min/1.73 m^2	12 (2.1)
<15 ml/min/1.73 m^2	3 (0.5)
CKD-EPI <70 ml/min/1.73 m^2	176 (30.8)
Cockcroft-Gault (ml/min)	90.1 ± 40.5
>50 ml/min	483 (84.6)
30–49 ml/min	73 (12.8)
15–29 ml/min	11 (1.9)
<15 ml/min	4 (0.7)
Hypertension	375 (65.7)
Diabetes mellitus	138 (24.2)
Stroke, transient ischaemic attack (TIA) and/or peripheral embolism	47 (8.3)
Vascular disease¶	55 (9.6)
Heart failure or LVEF <40%	59 (10.3)
LVEF (%)	60.5 ± 6.8
Hypertensive heart disease	118 (20.7)
Cardiomyopathy	26 (4.6)
Severe left valvular heart disease	42 (7.4)
Ischaemic heart disease	55 (9.6)
Coronary revascularisation	
PCI with stents	30 (5.2)
Coronary surgery	15 (2.7)
Lung disease	85 (14.9)
Liver disease	17 (3)

Qualitative variables are expressed in terms of *n* (%). Quantitative variables are expressed in terms of mean ± standard deviation. PCI: Percutaneous coronary intervention. LVEF: Left ventricular ejection fraction. (CHA_2DS_2VASc is: **C**ongestive heart failure, **H**ypertension, **A**ge, **D**iabetes mellitus **S**troke **V**ascular disease, **A**ge, **S**ex.HAS-BLED is: **H**ypertension, **A**bnormal renal and liver function, **B**leeding, **L**abile INRs, **E**lderly, **D**rugs or alcohol.)

§ A single patient may present atrial fibrillation and atrial flutter.

¶ Peripheral artery disease, myocardial infarction and/or atheromatous plaques in aorta.

A scale was constructed with these variables wherein one point was assigned to each value present (Fig. 1). A score ≥2 identified patients susceptible to receiving inappropriate dosing with a sensitivity of 100%, a specificity of 70.2%, a positive predictive value (PPV) of 20.6% and a negative predictive value (NPV) of 100%. The receiver operating characteristic (ROC) curve was 0.88 (95% CI 0.85–0.92) ($p < 0.001$). In these patients, estimated creatinine clearance (eCrCl) and estimated

glomerular filtration rate (eGFR) should be determined and, in the event that such discrepancy is confirmed, more specific testing should be done (24-h urine creatinine clearance) and the risk/benefit ratio individually assessed of selecting a high or low dose or a different direct oral anticoagulant (DOAC) with no dosing discrepancies depending on the formula used.[6] In individuals with less than two criteria, the CKD-EPI and CG equations can be used indiscriminately. Hence, using this scale, calculation using the CG equation could be limited to 34.9% of patients.

The sample size was small, especially in patients with stage 3–5 kidney disease, and this might have limited the statistical power. Larger studies will be needed to confirm the external validity of our results.

Funding

Alejandro Isidoro Pérez Cabeza and Francisco Ruiz Mateas declare that they have received consulting fees from Bayer Hispania, S.L.

REFERENCES

1. Steffel J, Verhamme P, Potpara TS, Albaladejo P, Antz M, Desteghe L, et al. The 2018 European Heart Rhythm Association practical guide on the use of non-vitamin antagonist oral anticoagulants in patients with atrial fibrillation. Eur Heart J. 2018;39:1330–93.
2. https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf [accessed 05.04.19].
3. Manzano-Fernández S, Andreu-Cayuelas JM, Marín F, Orenes-Piñero E, Gallego P, Valdés M, et al. Comparison of estimated glomerular filtration rate equations for dosing new oral anticoagulants in patients with atrial fibrillation. Rev Esp Cardiol. 2015;68:497–504.
4. Pérez Cabeza AI, Chinchurreta Capote PA, González Correa JA, Ruiz Mateas F, Rosas Cervantes G, Rivas Ruiz F, et al. Discrepancies between the use of MDRD-4 IDMS and CKD-EPI equations, instead of the Cockcroft-Gault equation, in the determination of the dosage of direct oral anticoagulants in patients with non-valvular atrial fibrillation. Med Clin (Barc). 2018;150:85–91.
5. Yao X, Shah ND, Sangaralingham LR, Gersh BJ, Noseworthy PA. Non-vitamin K antagonist oral anticoagulant dosing in patients with atrial fibrillation and renal dysfunction. J Am Coll Cardiol. 2017;69:2779–90.
6. Eppenga WL, Kramers C, Derijks HJ, Wensing M, Wetzels JFM. De Smet PAGM drug therapy management in patients with renal impairment: how to use creatinine-based formulas in clinical practice. Eur J Clin Pharmacol. 2016;72:1433–9.

Alejandro Isidoro Pérez Cabeza[a,*], José Luis Górriz[b], Rafael Bravo Marqués[a], Pedro Antonio Chinchurreta Capote[a], Sergio López Tejero[a], José Antonio González Correa[c], Fidel Ernesto Mesa Prado[a], Almudena Valle Alberca[a], Francisco Ruiz Mateas[a]

[a] *Servicio de Cardiología, Hospital Costa del Sol, Marbella (Málaga), Spain*
[b] *Servicio de Nefrología, Hospital Clínico Universitario, INCLIVA, Universidad de Valencia, Valencia, Spain*
[c] *Departamento de Farmacología, Facultad de Medicina, Universidad de Málaga-IBIMA, Málaga, Spain*

[*] *Corresponding author.*
E-mail addresses: alejandroipc@hotmail.com, alejandro.perez.cabeza@juntadeandalucia.es (A.I. Pérez Cabeza).

https://doi.org/10.1016/j.nefroe.2021.04.002

Syndrome of inappropriate antidiuretic hormone as the initial presentation of COVID-19: A novel case report

Síndrome de Hormona Antidiurética Inapropiada como la Presentación Inicial de COVID-19: Un nuevo informe de un caso

Dear Editor:

The rapid and unprecedented spread of severe acute respiratory syndrome coronavirus disease 2019 (COVID-19) has significantly limited our understanding of this disease. As the pandemic continues to evolve,[1] cardio-pulmonary symptoms predominate, however new atypical manifestation of COVID are increasingly recognized.

To alert clinicians regarding a novel presentation of COVID-19. We present the first reported case of SARS-COV2 induced syndrome of inappropriate diuretic hormone (SIADH) manifesting as new-onset seizures.

A previously healthy 75-year-old man presents with a witnessed episode of new-onset seizures. Per family accounts,

DOI of original article: https://doi.org/10.1016/j.nefro.2020.04.016.