



Reply to: World allergy organization anaphylaxis guidance 2020

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Anaphylaxis is the most severe clinical presentation of acute systemic allergic reactions. It is a potentially fatal reaction, whose prevalence is increasing. We want to thank Cardona et al for updating the World Allergy Organization (WAO) anaphylaxis guidance,¹ which has a global impact in increasing global awareness of anaphylaxis. However, as we recommended to the European Academy of Allergy and Clinical Immunology (EAACI), Food Allergy, anaphylaxis guidelines group,² we suggest authors to include Kounis syndrome (KS) in the next WAO guideline update of anaphylaxis.

Mast cells are present in cardiac tissue and coronary arteries so that they can constitute primary targets in anaphylaxis. Inflammatory mediators released during the allergic reaction, such as histamine, platelet-activating factor, and eicosanoids, contribute to vasoconstriction and coronary artery spasm. KS is an acute coronary syndrome (ACS) secondary to anaphylaxis that can occur as vasospastic angina caused by endothelial dysfunction (type 1), myocardial infarction (type 2) or stent thrombosis with an occluding thrombus (type 3A) or stent restenosis (type 3B). KS can also involve cerebral, mesenteric and peripheral

arteries.^{3,4} KS appears in 1-2% of anaphylaxis^{5,6} and associates an in-hospital mortality of 7.0% vs 0.4% compared to the anaphylaxis non-KS group.⁵ Early recognition and prompt, adequate intervention are critical in reducing morbidity and mortality in KS. Patients with acute coronary syndrome should be managed according to the ACS guidelines. Unfortunately, these guidelines lack specific details regarding the management of ACS due to KS. Some review articles^{7,8} have proposed that type I should be treated with intravenous corticosteroids, and the use of calcium channel blockers, nitrates, and nitroglycerin should be considered. Type II patients should be treated for ACS, adding corticosteroids. In this case, the use of epinephrine is controversial because ischemia and coronary vasospasm could get worse. Type III patients would need an urgent aspiration of intrastent thrombus and histological examination of material and staining for eosinophils (hematoxylin and eosin) and mast cells (Giemsa).

In conclusion, due to the significant impact of the WAO anaphylaxis guidance¹ on healthcare professionals around the world, we would like to suggest that Cardona et al consider including KS in the following guideline update to expand

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and homogenizing the knowledge of this underestimated and life-threatening entity that is part of the clinical picture of some anaphylaxis.

Abbreviations

ACS, acute coronary syndrome; KS, Kounis syndrome; WAO, World Allergy Organization.

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Author contributions

B.B. and J.S. were involved in manuscript drafting. A.G.L., D.B., and M.V.M. were involved in the revision of the text and the approval of the final version of the document.

Ethics approval

The article has not required approval from the ethics committee.

Authors' consent for publication

All authors consent to the publication of the article.

Declaration of competing interest

J.S. reports having served as a consultant to Thermofisher, MEDA, Novartis, Sanofi, Leti, FaesFarma, Mundipharma, and GSK; having been paid lecture fees by Novartis, GSK, Stallergenes, Leti, Sanofi, and FaesFarma; as well as having received grant support for research from Thermofisher, Sanofi, and ALK. B.B. reports having received personal lecture fees from Roxall outside of the submitted work. D.B. reports having received grant support for research from Instituto Carlos III and having served as a consultant to

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REFERENCES

1. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *WorldAllergyOrgan J.* 2020 Oct 30;13(10):100472.
2. Barroso B, Gómez-López A, Betancor D, Valverde-Monge M, Sastre J. Reply to "European academy of allergy and clinical immunology, food allergy, anaphylaxis guidelines group. EAACI guidelines: anaphylaxis (2021 update)". *Allergy.* 2024 Jan 12. <https://doi.org/10.1111/all.16018>. Epub ahead of print. PMID: 38214139.
3. Goto M, Matsuzaki M, Fuchinoue A, et al. Chronic atherosclerotic mesenteric ischemia that started to develop symptoms just after anaphylaxis. *Case Rep Gastroenterol.* 2012;6:300-308.
4. González-de-Olano D, Alvarez-Twose I, Matito A, et al. Mast cell activation disorders presenting with cerebral vasospasm-related symptoms: a "Kounis-like" syndrome? *Int J Cardiol.* 2011;150:210-211.
5. Desai R, Parekh T, Patel U, et al. Epidemiology of acute coronary syndrome co-existent with allergic/hypersensitivity/anaphylactic reactions (Kounissyndrome) in the United States: a nationwide inpatient analysis. *Int J Cardiol.* 2019;292:35-38.
6. Zisa G, Panero A, Re A, Mennuni MG, Patti G, Pirisi M. Kounis syndrome: an underestimated emergency. *Eur Ann Allergy Clin Immunol.* 2023;55(6):294-302.
7. Poggiali E, Benedetti I, Vertemati V, et al. Kounis syndrome: from an unexpected case in the Emergency Room to a review of the literature. *Acta Biomed.* 2022 Mar 14;93(1), e2022002.
8. Abdelghany M, Subedi R, Shah S, et al. Kounis syndrome: a review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. *Int J Cardiol.* 2017 Apr 1;232:1-4.