The Humble Relation of Hypersensitivity-Associated Acute Coronary Syndrome (Kounis Syndrome) and Acute and Sub-Acute Triggers of Cardiovascular Events

In the very interesting paper published in *The American Journal of Cardiology,*[1] several acute and subacute triggers of cardiovascular events were described including physical, emotional and/or mental, community and/or wide events, and toxins. Although air pollution and takotsubo (stress) cardiomyopathy were included in this list, the authors have omitted to refer to the Kounis hypersensitivity-associated acute coronary syndrome that includes endothelial dysfunction leading to coronary vasospastic angina,[2] atheromatous plaque erosion or disruption inducing coronary thrombosis,[3] and hypersensitivity events associated with stent thrombosis.[4] Indeed, in a recent report,[5] it was found that the above 3 types of the disease can lead to cardiac arrest (6.3%), death (2.9%), cardiogenic shock (2.3%), and ventricular fibrillation (1.1%). Kounis syndrome as cardiovascular event trigger. In 2 Japanese hospitals the annual incidence of Kounis syndrome at the emergency department from 2012 to 2017 was 2% (2 of 100) in the first and from 2013 to 2017 2.2% (3 of 138) in the second.[6]

Furthermore, disproportionality analysis of the FDA Adverse Event Reporting System (2004 to June 2016), which constitutes a consolidated pharmacovigilance source to monitor rare but serious adverse triggers such as Kounis syndrome, has shown that out of 499 spontaneous reports of drug-induced Kounis syndrome, 236 cases (47%) were attributed to a single trigger drug.[7] The authors of the above report were referred to air pollution and takotsubo (stress) cardiomyopathy as triggers of cardiovascular events. Indeed, air pollution as antigen carrier and takotsubo as stress cardiomyopathy have been already associated with Kounis syndrome.[8,9]

Therefore, searching, recognizing, diagnosing, and discovering new acute and subacute triggers of cardiovascular disease would have important implications for prevention, protection, and therapy of these so dangerous types of diseases.

Conflict of interest

None

Nicholas G. Kounis, MD, PhD*
Ioanna Koniari, MD, PhD
Grigorios Tsigkas, MD, PhD
George D. Soufras, MD, PhD
Periklis Davlouros, MD, PhD
George Hahalis, MD, PhD
Department of Cardiology, University of Patras School of Medicine, Patras, Greece
2 December 2018
10 December 2018

1. Schwartz BG, Kloner RA, Naghavi M. Acute and sub-acute triggers of cardiovascular events. *Am J Cardiol* 2018.
2. Rich MW. Is vasospastic angina an inflammatory disease? *Am J Cardiol* 2005;96:1612.
3. Kounis NG, Cervellin G, Koniari I, Bonfanti L, Dousdampanis P, Charokopos N, Assimakopoulos SF, Kakkos SK, Ntouvas IG, Soufras GD, Tsolakis I. Anaphylactic cardiovascular collapse and Kounis syndrome: systemic vasodilation or coronary vasoconstriction? *Ann Transl Med* 2018 Sep;6:332. https://doi.org/10.21037/atm.2018.09.05.
4. Ferreira RM, Villela PB, Almeida JCG, Sampaio PPN, Albuquerque FN, Pinheiro FMC, França Filho W, Salles JABE, Mansur Filho J. Allergic recurrent coronary stent thrombosis: a mini-review of Kounis syndrome. *Cardiovasc Revasc Med* 2018. https://doi.org/10.1016/j.carrev.2018.03.00. pii: S1553-8389(18)30090-3.
5. Abdelghany M, Subedi R, Shah S, Kozman H. Kounis syndrome: a review article on epidemiology, diagnostic findings, management and complications of allergic acute coronary syndrome. *Int J Cardiol* 2017;232:1–4.
6. Yanagawa Y, Kondo A, Ishikawa K, Nagasawa H, Takeuchi I, Jitsuiki K, Ohsaka H, Omori K. Kounis syndrome should be excluded when physicians treat patients with anaphylaxis. *Ann Allergy Asthma Immunol* 2017;119:392.
7. Raschi E, Fertonani Affini L, Antonazzo IC, Diemberger I, Poluzzi E, De Ponti F. Drug-induced Kounis syndrome: a matter of pharmacovigilance. *Int J Cardiol* 2019;274:381.
8. Hahalis G, Kounis GN, Soufras GD, Kouni SA, Kounis NG. Diesel exhaust, thrombus formation, and Kounis syndrome: a potential association. *Inhal Toxicol* 2009;21:431–432.
9. García Núnez I, Algaba Mármol MA. A minimum difference between 2 syndromes. *J Investig Allergol Clin Immunol* 2017;27:201–202.

https://doi.org/10.1016/j.amjcard.2018.12.001

National Trends of Percutaneous Coronary Intervention in Patients ≥70 Years of Age

Over the past few decades, there has been an increase in life expectancy and elderly have been constituting a bigger subset of patients with coronary artery disease (CAD).[1] Coronary arteries involvement in elderly has a peculiar pathophysiology, with increased calcification, left main coronary involvement and more diffuse disease.[2,3] In addition to the increased burden of co-morbidities, elderly patients with CAD tend to present late.[4] Available data on the trend and outcomes of PCI in elderly patients with CAD are limited, and comes mainly from single centered or small multicentered registries.[1,2] In this study, we examined the largest national administrative database to evaluate the temporal trends in the utility of PCI in the older patients as well their in-hospital mortality.

We queried the Nationwide Inpatient Sample (NIS) database from 1998 to 2013 to identify hospitalizations of patients aged ≥70 years with International Classification of Diseases, Ninth Edition procedure code for PCI, either with bare-metal (36.06) or drug-eluting stents (36.07). We aimed at evaluating the temporal trends of PCI procedures as well as all-cause in-hospital mortality in patients aged ≥70 years. Statistical analyses were performed using SPSS Statistics 22. We analyzed data from the national estimates using the new trend weights provided by the NIS.[10] Time series analyses were performed in R 3.1.3[5] using the nlme package.[6]

Over a 16-year period (1998 to 2013), a total of 3,597,119 patients with age ≥70 years underwent PCI across the United States. In those, 2,435,203 were 70 to 79 years, 1,089,789 were 80 to 89 years and 72,127 were ≥90 years. From 1998 to 2013, there was an increase in comorbidities burden in elderly receiving PCI. Baseline characteristics are described in Table 1. Overall, the number of PCIs performed in patients aged ≥70 in 1998 was 151,752 compared with 165,260 cases in 2013. From 1998