

Author's Reply

To the Editor,

We would like to thank the authors for their scientific comments related to our recently published article (1) entitled "Vagal denervation in atrial fibrillation ablation: A comprehensive review." published in *Anatol J Cardiol* 2017; 18:142-8. As mentioned by the authors, the inferior vena cava-left atrium fat pad (namely also ganglion C) located around the coronary sinus mainly provides vagal innervations and selectively innervates the atrioventricular node in humans (2, 3). Furthermore, this ganglion contains much more neurons than other ganglia (4). On the basis of this anatomical background, we only targeted ganglion C and performed the procedure using selective right atrial approach in patients with functional atrio-ventricular block (5, 6). Our selective right atrial approach was successful in six of seven patients. Considering the clinical features of failed case, this patient was the oldest patient in the study population. Therefore, we speculated that fibrosis of the conduction system due to advanced age may be the reason of unsuccessful ablation.

In their study, Xhaet et al. (3) tried to reveal the importance of fat pads in the vagal control of the atrio-ventricular node. The study demonstrated that parasympathetic innervations of atrio-ventricular node were mainly provided by the integrity of the vagal ganglia but not directly by the right vagus nerve. This study may be a starting point for well-designed studies to clarify selective or integrative innervations principles of cardiac parasympathetic system.

We thoroughly agree with the authors' comments that there are some difficult questions that should be answered:

(1) Which is the best method to define the exact location of vagal ganglia?

(2) How can we achieve complete and permanent ablation?

(3) Is there any importance of long-term effect of unrequited sympathetic activity after denervation?

Future studies are needed to clarify all these dilemmas in patients with atrial fibrillation.

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References

1. Aksu T, Güler TE, Mutluer FO, Oto MA. Vagal denervation in atrial fibrillation ablation: A comprehensive review. *Anatol J Cardiol* 2017; 18: 142-8.
2. Hou Y, Scherlag BJ, Lin J, Zhang Y, Lu Z, Truong K, et al. Ganglionated plexi modulate extrinsic cardiac autonomic nerve input: ef-

fects on sinus rate, atrioventricular conduction, refractoriness, and inducibility of atrial fibrillation. *J Am Coll Cardiol* 2007; 50: 61-8.

3. Xhaet O, DE Roy L, Floria M, Deceuninck O, Blommaert D, Dormal F, et al. Integrity of the Ganglionated Plexi Is Essential to Parasympathetic Innervation of the Atrioventricular Node by the Right Vagus Nerve. *J Cardiovasc Electrophysiol* 2017; 28: 432-7.
4. Armour JA, Murphy DA, Yuan BX, Macdonald S, Hopkins DA. Gross and microscopic anatomy of the human intrinsic cardiac nervous system. *Anat Rec* 1997; 247: 289-98.
5. Aksu T, Gölcük SE, Güler TE, Yalın K, Erden I. Functional permanent 2:1 atrioventricular block treated with cardioneuroablation: Case report. *HeartRhythm Case Rep* 2015; 29: 58-61.
6. Aksu T, Gölcük E, Yalın K, Güler TE, Erden I. Simplified cardioneuroablation in the treatment of reflex syncope, functional AV block, and sinus node dysfunction. *Pacing Clin Electrophysiol* 2016; 39: 42-53.

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Ibuprofen-induced Kounis syndrome with diffuse ST segment depression and atrial fibrillation

To the Editor,

Kounis syndrome is defined as acute coronary events associated with allergy, anaphylaxis, or anaphylactoid reactions (1). In this syndrome, many inflammatory mediators, such as histamine, chymase, tryptase, thromboxane, prostaglandins, leukotrienes and its derivatives, as well as different cytokines and chemokines play a major role together with the activation of mast cells, lymphocytes, macrophages, and eosinophils (1, 2). Many factors, such as foods, different drugs, environmental exposures, and coronary stents, may trigger allergic reactions (1, 2). We presented a case of ibuprofen-induced Kounis syndrome with diffuse ST segment depression with ST segment elevation in aVR lead and atrial fibrillation.

A 57-year-old man presented with complaints of nausea, vomiting, itching, dyspnea, and retrosternal chest pain after taking ibuprofen+pseudoephedrine combination cold medication. He had no known systemic disease or prior drug use. He had taken two tablets of the same drug 15 days ago. Physical examination findings were as follows: cold, sweaty, blood pressure of 80/50 mm Hg, and pulse rate of 120 bpm. Isotonic sodium chloride infusion, dexamethasone, and pheniramine were administered, and subsequently, blood pressure increased. In the first 10 min of the ongoing chest pain, electrocardiography was performed, which showed diffuse ST depression with ST elevation in aVR lead. Cardiac troponin-I levels were 19.5 (normal range, 0.0-0.1)

ng/mL, and mass CK-MB was 15.6 (normal range, 0.0–3.2) ng/mL. Echocardiography revealed mild hypokinesia of the left ventricle. Follow-up electrocardiography revealed improvement in ST depressions as well as atrial fibrillation. Coronary angiography showed normal arteries. Atrial fibrillation spontaneously recovered. Diltiazem, ketotifen, and acetylsalicylic acid were administered, and the patient was discharged with recommendations.

Ibuprofen is a widely used nonsteroidal anti-inflammatory drug that rarely causes allergic reactions (3). Kounis syndrome was first described by Kounis in 1991 and occurs in people of all age groups; however, because most cases remain undiagnosed, frequency is less often indicated in literature (1, 2). It is seen more frequently Southern Europe, especially Turkey, Greece, Italy, and Spain. Climate, environmental factors, and gene-environment interactions play a role in the development of this syndrome, and heterozygous E148Q mutation is frequently observed in Kounis syndrome (1). The diagnosis depends on clinical suspicion, symptoms, and signs as well as laboratory, electrocardiographic, echocardiographic, and angiographic evidence (1, 2). This syndrome has different subtypes: Kounis syndrome type 1 is an acute myocardial infarction associated with a mediator-induced coronary spasm in the normal coronary artery; type II is associated with atheromatous plaque stimulated by mediators; and type III is associated with sten t thrombosis (1, 2). According to findings, our case is of a type I variant. Although myocardial ischemia due to systemic hypotension has been previously reported, in our case, symptoms continued despite improvements in hypotension (4). Many triggers have been reported in the literature, but association with ibuprofen is rarely reported. Our case is of an unusual ibuprofen-associated Kounis syndrome suspected to be related to the left main coronary artery occlusion based on electrocardiographic findings, with atrial fibrillation occurring afterward.

There is no common consensus about treatment of this syndrome, but the treatment target is subtype dependent. Mast

cell-stabilizing drugs, steroids, ketotifen, nedocromil sodium, and sodium cromoglycate may be helpful in managing allergic reactions. Exposure of the patient to trigger mediators should be avoided (1, 5). Vasodilators (non-dihydropyridine calcium-channel blockers and nitrates) should be initiated for coronary vasospasms (1, 2, 5). In subtypes II and III, the coronary events should also be treated (1, 2).

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References

1. Kounis NG. Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management. *Clin Chem Lab Med* 2016; 54: 1545–59. [\[CrossRef\]](#)
2. Fassio F, Almerigogna F. Kounis syndrome (allergic acute coronary syndrome): different views in allergologic and cardiologic literature. *Intern Emerg Med* 2012; 7: 489–95. [\[CrossRef\]](#)
3. Kumar A, Berko NS, Gothwal R, Tamarin F, Jesmajian SS. Kounis syndrome secondary to ibuprofen use. *Int J Cardiol* 2009; 137: e79–80. [\[CrossRef\]](#)
4. Antonelli D, Koltun B, Barzilay J. Transient ST segment elevation during anaphylactic shock. *Am Heart J* 1984; 108: 1052-4. [\[CrossRef\]](#)
5. Keskin M, Hayiroğlu Mİ, Onuk T, Keskin Ü, Ekmekçi A. Kounis syndrome presenting with acute inferior wall myocardial infarction and cardiogenic shock secondary to intravenous ampicillin/sulbactam administration. *Anatol J Cardiol* 2016; 16: 893-4. [\[CrossRef\]](#)

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