



## Perioperative stroke and hyperhomocysteinemia: a possible pathogenic link

Maurizio Acampa<sup>1</sup>, Pietro Enea Lazzerini<sup>2</sup>, and Giuseppe Martini<sup>1</sup>

<sup>1</sup>Department of Neurological and Sensorineural Sciences, University Hospital of Siena, "Santa Maria alle Scotte" General Hospital, <sup>2</sup>Department of Medical Sciences, Surgery and Neurosciences, University of Siena, Siena, Italy

We have read with interest the review by Ko [1], focused on pathophysiological mechanisms of perioperative stroke. The author examined different risk factors for perioperative stroke, including conventional vascular risk factors and specific mechanisms related to the type of surgery.

In addition to these mechanisms, we suggest that hyperhomocysteinemia (HHcy) may represent a relevant pathogenic factor in the development of perioperative stroke, especially in specific cardiac surgical procedures [2,3].

High homocysteine levels can lead to an ischemic stroke through multiple mechanisms and are associated with the occurrence of atrial fibrillation (AF) and a prothrombotic state [3]. HHcy has an acute and direct effect on atrial ionic channels (inhibition of the transient outward potassium current and ultra-rapid delayed-rectifier K<sup>+</sup> currents, increase of inward-rectifier K<sup>+</sup>-current, increased Na<sup>+</sup> currents) that produce early after depolarization and cause focal ectopic/triggered activity [3]. Moreover, HHcy may promote atrial fibrosis (atrial structural remodeling) that causes slow and heterogeneous atrial conduction (with increased P wave dispersion on the electrocardiogram),

favoring the appearance of a vulnerable reentrant substrate [4]. These atrial electrical and structural alterations represent a well-known substrate for AF, resulting in an increased risk of cardioembolic stroke. HHcy may also contribute to a prothrombotic state through different mechanisms (increased tissue factor expression, attenuated anticoagulant processes, enhanced platelet reactivity, increased thrombin generation, augmented Factor V activity, impaired fibrinolytic potential), resulting in increased risk of atrial thrombosis and possible subsequent ischemic embolic stroke [3].

In patients undergoing cardiac surgery who develop HHcy, an appropriate homocysteine-lowering treatment [5] could represent a preventive strategy to prevent the occurrence of AF and reduce the risk of ischemic stroke.

### ORCID

Maurizio Acampa, <https://orcid.org/0000-0003-4149-1785>

Pietro Enea Lazzerini, <https://orcid.org/0000-0001-6721-1214>

Giuseppe Martini, <https://orcid.org/0000-0002-1176-3463>

### References

1. Ko SB. Perioperative stroke: pathophysiology and management. *Korean J Anesthesiol* 2018; 71: 3-11.

Corresponding author: Maurizio Acampa, M.D., Ph.D.

Department of Neurological and Sensorineural Sciences, University Hospital of Siena, "Santa Maria alle Scotte" General Hospital, 17, Viale Bracci, Siena 53100, Italy

Tel: 39-0577585408, Fax: 39-0577586294, Email: [m.acampa@ao-siena.toscana.it](mailto:m.acampa@ao-siena.toscana.it)

ORCID: <https://orcid.org/0000-0003-4149-1785>

Received: February 19, 2018. Accepted: February 27, 2018.

*Korean J Anesthesiol* 2018 August 71(4): 332-333

<https://doi.org/10.4097/kja.d.18.00046>

© This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © The Korean Society of Anesthesiologists, 2018

Online access in <http://ekja.org>

2. Acampa M, Lazzarini PE, Martini G. Postoperative atrial fibrillation and ischemic stroke: the role of homocysteine. *Eur Stroke J* 2018; 3: 92-3.
3. Acampa M, Lazzarini PE, Guideri F, Tassi R, Martini G. Ischemic stroke after heart transplantation. *J Stroke* 2016; 18: 157-68.
4. Acampa M, Lazzarini PE, Guideri F, Rechichi S, Capecchi PL, Maccherini M, et al. Homocysteine and P wave dispersion in patients with heart transplantation. *Clin Transplant* 2011; 25: 119-25.
5. Spence JD, Yi Q, Hankey GJ. B vitamins in stroke prevention: time to reconsider. *Lancet Neurol* 2017; 16: 750-60.