Among patients with established HFrEF and diabetes, sudden death followed by HF death are the most common causes of CV death. In addition, ethnic variations among patients with and without diabetes were observed regarding the risk of cause-specific CV mortality. Future studies focusing on the prevention of sudden death and HF death should be prioritized among patients with HFrEF and diabetes.

*Abhinav Sharma, MD, PhD
Carolyn S.P. Lam, MBBS, PhD
Wan Ting Tay, BSc
Jonathan Yap, MBBS, MPH
Michael R. MacDonald, MBChB
Amir Razaghizad, MSc
Lauren B. Cooper, MD
Christopher O'Connor, MD
David J. Whellan, MD, MHS
Inder S. Anand, MD, PhD†
Jasper Tromp, MD, PhD
Robert J. Mentz, MD

*Division of Cardiology
McGill University Health Centre
1001 Decarie Boulevard
Montreal H4A 3J1, Quebec, Canada
E-mail: Abhinav.Sharma@mcgill.ca

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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TO THE EDITOR

Homocysteine and Thrombophilia in Pulmonary Hypertension

In a recent issue of *JACC: Asia*, Lian et al[1] reported on thrombophilia in patients with thromboembolic pulmonary hypertension. They did not study plasma total homocysteine nor genetic factors that predispose to hyperhomocysteinemia, such as the T allele of methylenetetrahydrofolate reductase (MTHFR). Both hyperhomocysteinemia and the T allele of MTHFR are more common in China than elsewhere,[2] and are more common than the hereditary clotting factors that they studied.

Can the authors tell us the prevalence of hyperhomocysteinemia and the allele distribution of MTHFR and of other genes that predispose to hyperhomocysteinemia, such as cystathionine gamma lyase (CTH/CGL), methionine synthase (MTR), and methionine synthase reductase (MTRR)?

*J. David Spence, MD

*Stroke Prevention and Atherosclerosis Research Centre
Robarts Research Institute
Western University
1400 Western Road
London, Ontario N6G 2V4, Canada
E-mail: dspence@robarts.ca

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REPLY: Homocysteine and Thrombophilia in Pulmonary Hypertension

We thank Dr Spence for his interest in our study of congenital thrombophilia in patients with chronic thromboembolic pulmonary hypertension (CTEPH).[1] The study is a continuation of our research of congenital thrombophilia in patients with pulmonary embolism (PE),[2] in which we found that the prevalence of congenital thrombophilia in Chinese patients with PE is 7.2%, with a predominance of anticoagulant protein deficiency. We are therefore interested in the prevalence of thrombophilia in CTEPH, which is considered a rare sequela of PE.

As Dr Spence mentioned in his letter, hyperhomocysteinemia is much more common in Chinese patients with venous thromboembolism (VTE). Zhang[3] showed that the prevalence of hyperhomocysteinemia in Chinese patients with PE was 34.57%, significantly higher than that in healthy control subjects (10%; $P < 0.001$). Hyperhomocysteinemia increased the risk of PE (OR: 5.146; 95% CI: 1.945-13.617; $P = 0.001$). A study by Lu et al[4] similarly showed that total plasma homocysteine levels were significantly higher in patients with PE than in healthy control subjects (16.6 ± 1.8 μmol/L vs 12.5 ± 1.5 μmol/L; $P < 0.01$), and hyperhomocysteinemia was an independent risk factor for PE in the Chinese population. Wang et al[5] studied the genotype distribution of MTHFR C667T in Chinese patients with VTE, and the distribution of T/T, C/T, and C/C genotypes in the VTE group was 29.3%, 48.3%, and 22.4%, respectively.

We are very concerned about the impact of VTE risk factors in patients with CTEPH. The prevalence and clinical characteristics of antiphospholipid antibody syndrome[6] and congenital thrombophilia[1] in Chinese patients with CTEPH have been reported. Additional issues for investigation, as noted by Professor Spence, are the prevalence of hyperhomocysteinemia and polymorphisms of genes that predispose to hyperhomocysteinemia in patients with CTEPH. We plan to publish the epidemiologic and genetic data of hyperhomocysteinemia, as well as the interaction model for multiple VTE risk factors in CTEPH patients, in future research.

Tian-Yu Lian, MD
Yu-Ping Zhou, MD
Yong-Jian Zhu, MD
Fan Guo, MD
***Zhi-Cheng Jing, MD**

*Department of Cardiology
State Key Laboratory of Complex Severe and Rare Diseases
Peking Union Medical College Hospital
Chinese Academy of Medical Sciences and
Peking Union Medical College
No. 1, Shuaifuyuan
Dongcheng District, Beijing 100730, China
E-mail: jingzhicheng@vip.163.com
Twitter: @Jing_ZhiCheng

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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