

## Letters

### RESEARCH LETTER

## Residual Inflammatory Risk in Outcomes of Chinese Patients After Percutaneous Coronary Intervention



Inflammation contributes to the pathogenesis of coronary heart disease (CHD). Routine clinical practice includes assessing residual risks of cholesterol and thrombosis in patients with CHD. The importance of lowering residual inflammatory risk (RIR) in patients after percutaneous coronary intervention (PCI) remains uncertain. RIR has gained much interest with the success of the CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcome Study) and the large-scale outcome trials with colchicine.<sup>1,2</sup> In Western populations, high RIR is defined by high-sensitivity C-reactive protein (hsCRP) level  $\geq 2$  mg/L.<sup>3</sup> Although hsCRP has demonstrated value as a predictor of CHD, hsCRP concentrations have ethnic differences, with especially lower levels in East Asian populations. The median of hsCRP level in patients with CHD who underwent PCI in Japan and South Korea was 0.9 mg/L in retrospective studies.<sup>4,5</sup> The definition of high RIR in the East Asian population requires additional clinical exploration.

This single-center, prospective cohort study was approved by the Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology ([2021]0191) and was registered on ClinicalTrials.gov (A Prospective Study of Residual Inflammatory Risk and the Impact on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Interventions; [NCT05131750](https://clinicaltrials.gov/ct2/show/study?term=NCT05131750)). Written informed consent was obtained from all patients. This study included patients aged 18-80 years who completed planned PCI. Patients with influencing factors on hsCRP detection were excluded. The primary endpoint was major adverse cardiovascular and cerebrovascular events (MACCEs), which were defined as the composite of all-cause death, nonfatal myocardial infarction,

nonfatal stroke, and revascularization due to ischemia. All patients completed at least 12 months of follow-up. This study collected clinical endpoints that occurred within 12 months of follow-up after PCI. Patients who experienced the primary endpoint during 1 month of follow-up were excluded.

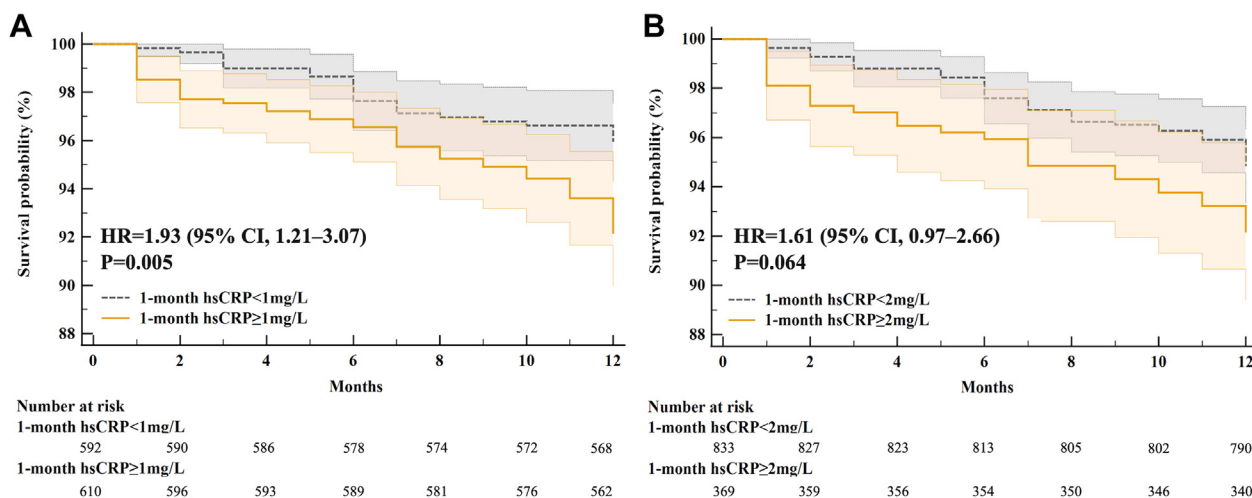
Continuous variables that were not normally distributed are presented as median and IQR. Categorical variables are described as n (%). To check for differences of continuous variables with non-normally distributed, we used Mann-Whitney *U* test. A Kaplan-Meier survival curve was used to compare the risk of MACCEs among patients stratified by hsCRP. All the statistical tests were performed using SPSS 26.0.

From May 6, 2021, to November 18, 2022, a total of 1,408 patients were enrolled, and 1,202 patients completed the 12-month follow-up. The mean age of the total cohort was  $59.5 \pm 9.9$  years; 301 of 1,202 (25.0%) were female, 778 of 1,202 (64.7%) had hypertension, 394 of 1,202 (32.8%) had diabetes mellitus, 822 of 1,202 (68.4%) had previous CHD, 108 of 1,202 (9.0%) had previous stroke, 122 of 1,202 (10.1%) had heart failure, and 74 of 1,202 (6.2%) had chronic kidney disease. MACCEs, the primary endpoint, were observed in 72 (6.0%) patients.

The median baseline hsCRP level was 1.2 mg/L and the median 1-month hsCRP level was 1.0 mg/L, which were much lower than the value previously reported for the RIR (2 mg/L). At baseline, the hsCRP levels (1.4 [IQR 0.8-5.6] mg/L vs 1.2 [IQR 0.5-3.4] mg/L,  $P = 0.053$ ) were not significantly different between patients with and without MACCEs. However, at the 1-month follow-up, the levels of hsCRP (1.3 [IQR 0.8-4.3] mg/L vs 1.0 [IQR 0.5-2.4] mg/L,  $P = 0.014$ ) were significantly greater in patients with MACCEs than those without MACCEs.

After grouping patients according to hsCRP  $\geq 1$  mg/L or hsCRP  $\geq 2$  mg/L, the influence of hsCRP at the 1-month follow-up on MACCEs was explored using Kaplan-Meier curve analysis and the log-rank test. For hsCRP at the 1-month follow-up, the survival probability of patients with hsCRP  $\geq 1$  mg/L was lower than that in patients with hsCRP  $< 1$  mg/L (HR: 1.93; 95% CI: 1.21-3.07;  $P = 0.005$ ; [Figure 1A](#)). However, the survival probability of patients with 1-month hsCRP  $\geq 2$  mg/L was not significantly different

**FIGURE 1** Kaplan-Meier Curves for MACCEs Stratified by hsCRP at 1-Month Follow-Up



(A) Kaplan-Meier curve stratified by 1-mo hsCRP  $\geq 1$  mg/L. (B) Kaplan-Meier curve stratified by 1-mo hsCRP  $\geq 2$  mg/L. hsCRP = high-sensitivity C-reactive protein; MACCE = major adverse cardiac and cerebrovascular event.

compared with those with 1-month hsCRP  $< 2$  mg/L (HR: 1.61; 95% CI: 0.97-2.66;  $P = 0.064$ ) (Figure 1B).

This study revealed the details of the RIR in Chinese patients after PCI and proposed the following points: 1) the 1-month hsCRP levels after PCI conveyed prognostic implications; and 2) an hsCRP level  $\geq 1$  mg/L appeared more suitable than the traditional RIR standard (hsCRP  $\geq 2$  mg/L) for predicting MACCEs in Chinese patients after PCI.

Miao Yu, MD, PhD<sup>a,b,c</sup>

Yuan-Fan Yuan, MD<sup>a,b,c</sup>

Fen Yang, MD, PhD<sup>a,b,c</sup>

Jia-Hao Xu, MD<sup>a,b,c</sup>

Mei-Lin Liu, MD, PhD<sup>a,b,c</sup>

Shao-Fang Nie, MD, PhD<sup>a,b,c</sup>

Yu-Yan Xiong, MD, PhD<sup>a,b,c</sup>

Peter Libby, MD, PhD<sup>d</sup>

\*Xiang Cheng, MD, PhD<sup>a,b,c</sup>

\*Department of Cardiology

Union Hospital

Tongji Medical College

Huazhong University of Science and Technology

1277# Jie-Fang Avenue

Wuhan, Hubei 430022, China

E-mail: [nathancx@hust.edu.cn](mailto:nathancx@hust.edu.cn)

From the <sup>a</sup>Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; <sup>b</sup>Hubei Key Laboratory of Biological Targeted Therapy, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology,

Wuhan, China; <sup>c</sup>Hubei Provincial Engineering Research Center of Immunological Diagnosis and Therapy for Cardiovascular Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; and <sup>d</sup>Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.

This work was supported by grants from the National Key Research and Development Program (2021YFC2500500 and 2022YFC2503501), Chinese Society of Cardiology's Foundation (HFCSC2019B02), National Natural Science Foundation of China (82030016 and 82230011), and Hubei Natural Science Foundation (2020CFA020) to Dr Cheng. This work was also supported by grants from The National Heart, Lung, and Blood Institute (1R01HL134892 and 1R01HL163099-01), the RRM Charitable Fund, and the Simard Fund to Dr Libby. Dr Libby is an unpaid consultant to, or involved in clinical trials for Amgen, AstraZeneca, Baim Institute, Beren Therapeutics, Esperion Therapeutics, Genentech, Kancera, Kowa Pharmaceuticals, Medimmune, Merck, Moderna, Novo Nordisk, Novartis, Pfizer, and Sanofi-Regeneron. Dr Libby is a member of the scientific advisory board for Amgen, Caristo Diagnostics, Cartesian Therapeutics, CSL Behring, DalCor Pharmaceuticals, Dewpoint Therapeutics, Eulucid Bioimaging, Kancera, Kowa Pharmaceuticals, Olatec Therapeutics, Medimmune, Novartis, PlaqueTec, TenSixteen Bio, Soley Therapeutics, and XBiotech, Inc. Dr Libby's laboratory has received research funding in the last 2 years from Novartis, Novo Nordisk, and Genentech. Dr. Libby is on the Board of Directors of XBiotech, Inc. Dr Libby has a financial interest in Xbiotech, a company developing therapeutic human antibodies, in TenSixteen Bio, a company targeting somatic mosaicism and clonal hematopoiesis of indeterminate potential (CHIP) to discover and develop novel therapeutics to treat age-related diseases, and in Soley Therapeutics, a biotechnology company that is combining artificial intelligence with molecular and cellular response detection for discovering and developing new drugs, currently focusing on cancer therapeutics. All other authors have reported that they have no relationships related to the contents of this paper to disclose.

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](#).

## REFERENCES

1. Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med*. 2017;377:1119-1131.

2. Fiolet ATL, Opstal TSJ, Mosterd A, et al. Efficacy and safety of low-dose colchicine in patients with coronary disease: a systematic review and meta-analysis of randomized trials. *Eur Heart J*. 2021;42:2765-2775.
3. Kalkman DN, Aquino M, Claessen BE, et al. Residual inflammatory risk and the impact on clinical outcomes in patients after percutaneous coronary interventions. *Eur Heart J*. 2018;39:4101-4108.
4. Takahashi N, Dohi T, Endo H, et al. Residual inflammation indicated by high-sensitivity C-reactive protein predicts worse long-term clinical outcomes in Japanese patients after percutaneous coronary intervention. *J Clin Med*. 2020;9:1033.
5. Ahn JH, Tantry US, Kang MG, et al. Residual inflammatory risk and its association with events in East Asian patients after coronary intervention. *JACC Asia*. 2022;2:323-337.