Journal of Geriatric Cardiology JGC
EDITORIAL
J Geriatr Cardiol 2024; 21(7): 713–715

Interpretation of Chinese Expert Consensus on the Diagnosis and Management Strategy of Patients with Statin Intolerance: A guiding file for helping to lipid management for Chinese population

Jian-Jun LI✉

Cardiometabolic Center, National Center for Cardiovascular Disease, Chinese Academy of Medical Science, Fuwai Hospital, Beijing, China

✉ Correspondence to: lijianjun938@126.com

https://doi.org/10.26599/1671-5411.2024.07.006

ABSTRACT It is well-known that elevated low-density lipoprotein cholesterol (LDL-C) is a causal risk factor for atherosclerotic cardiovascular disease (ASCVD), statins are cornerstone drugs for the cause-based treatment of ASCVD, which has created a new era for ASCVD therapy. However, statin intolerance is not clinically uncommon, which there are several issues with confusion and misunderstandings. Hence, a file named Chinese Expert Consensus on the Diagnosis and Management Strategy of Patients With Statin Intolerance, like a navigator, has recently been published written by a team of experts from the Cardiovascular Metabolic Medicine Professional Committee, Expert Committee of the National Center for Cardiovascular Diseases aiming to enhance the standardized clinical application of statins and improve the prevention and clinical outcome. In this article, author briefly summarized the key points of above consensus in order to helping to comprehending the content of the consensus suggestions.

Atherosclerotic cardiovascular disease (ASCVD) is the number one killer of human health and life. Abnormal cholesterol metabolism, especially elevated levels of low-density lipoprotein cholesterol (LDL-C), is a pathogenic risk factor for ASCVD.[1] Therefore, lowering LDL-C treatment is referred to as the pathogenesis treatment of ASCVD. The clinical application of statins, a class of drugs not available in the 1980s, has ushered in a new era of pathogenesis treatment for ASCVD.

Over 40 years of extensive research on statins suggests that statins have clinical value in reducing the incidence and events of ASCVD for both primary and secondary prevention, and they are the cornerstone drugs recommended by numerous guidelines at home and abroad for lipid management and the prevention and treatment of ASCVD.[2] At the same time, as chemical drugs with a clear molecular structure and target, statins also have certain adverse reactions. Against the background of the continuous emergence of new lipid-lowering drugs, the phenomenon of statin intolerance (referred to as statin intolerance) has gradually attracted attention, with certain precision control issues in diagnosis and management. In this context, the Cardiovascular Metabolism Committee of the National Cardiovascular Experts Committee organized experts in related fields in China to formulate the Chinese expert consensus on the clinical diagnosis and management of statin intolerance (hereinafter referred to as the statin intolerance expert consensus), which was published in domestic and foreign journals,[3,4] aiming to provide clinical guidance for the diagnosis and management of statin intolerance based on data from the Chinese population in a comprehensive and systematic manner.

First, the consensus of statin intolerance experts comprehensively reviewed the safety data of statins in the Chinese population, especially safety data from randomized controlled studies in the Chinese population. It is well known that the overall safety of statins is good, but there are racial differences in tolerability, and there is a lack of detailed analysis

of data related to the Chinese population. The consensus of statin intolerance experts addresses this deficiency. Overall, the incidence of statin-related adverse reactions in the Chinese population is 7.46%, with rates of liver and muscle symptoms both below 1.5%.[5] Studies have shown that there is no significant difference in the incidence of adverse reactions to statins between Chinese and non-Chinese populations.

Next, a historical review of the identification and definition of statin intolerance was conducted by the experts on statin intolerance. It showed the expert recommendations on the diagnostic criteria and management of statin intolerance from various academic groups worldwide. The analysis of the differences in definitions played a role in summarizing, concluding, and comparative analysis, contributing to a macro understanding of the global research status of statin intolerance. In fact, the official documents related to statin intolerance originated from the National Lipid Association Statin Intolerance Panel in 2014. They initially defined the basic concept of statin intolerance as having appropriate scientific evidence to prove clinical or laboratory adverse experiences related to statin therapy, manifested as pain, injury, or risk, with discontinuation or dose reduction being confirmed as reasonable. Subsequently, expert consensus on statin intolerance was published in Taiwan (China), Japan, Canada, and other countries and regions,[6-8] highlighting the biggest difference in diagnostic criteria among these consensus statements.

It has been confirmed that statin intolerance can be divided into partial intolerance and complete intolerance. The former refers to the inability to tolerate any type or dose of statin drugs, while the latter refers to the inability to tolerate certain doses of certain statins. The expert consensus on statin intolerance is based on the past suggestions of Chinese scholars, which have clarified the definition, classification, diagnostic criteria, and management recommendations for statin intolerance in the Chinese population.[9] The definition states that patients experience one or more statin-related adverse reactions after taking statin drugs, which can be improved by dose reduction or discontinuation of statins, but reappear after re-starting. The diagnostic criteria must simultaneously meet the following four elements: (1) clinical manifestations: subjective symptoms (such as muscle pain, weakness) and/or abnormal levels of liver and muscle standard indicators in laboratory tests; (2) types and doses of statin drugs used: patients cannot tolerate more than two types of statin drugs, one of which is at the lowest daily dose; (3) timing and causality: adverse reactions occur after starting or increasing the dose of statins, subside after discontinuation, and reappear upon re-administration; and (4) exclusion of other possible causes: the likelihood of being related to other diseases or drug interactions is low.

Regarding the treatment of statin intolerance, the expert consensus on statin intolerance fully combines the basic characteristics and data of the Chinese population, and proposes a processing flowchart with Chinese characteristics. The core spirit is to strictly grasp the diagnostic criteria, exclude possible subjective feelings, cognition, and the impact of the nocebo effect, and preserve the application of statin drugs as much as possible, such as switching to low doses, natural statins, etc. Emphasizing the standardization and individualization of treatment, distinguishing between partially intolerant and completely intolerant use of statins. The combination of low-dose statins with cholesterol absorption inhibitors is considered the most practical and simplest way to deal with it.[10]

In conclusion, the author firmly believes that in the real-world clinical practice, despite the many challenges related to statin intolerance, this expert consensus resembles a "navigator" for lipid management in the Chinese population. It can help improve people's scientific understanding of statin intolerance, standardize the clinical use of statins, and enhance the rate of lipid control and the prevention and treatment level of ASCVD in our country.

DISCLOSURE

Acknowledgements

We would like to thank all the experts who actively participated in and provided valuable suggestions for the development of the Chinese expert consensus on the diagnosis and management of statin intolerance.

Fundings

This article was supported by CAMS Innovation

Fund for Medical Sciences (CIFMS, 2021-I2M-C&T-B-030).

Conflict of Interests

There is no conflict of interest in the consensus of experts on statin intolerance and in this interpretation.

REFERENCES

[1] Li JJ, Liu HH, Li S. Landscape of cardiometabolic risk factors in Chinese population: a narrative review. *Cardiovasc Diabetol* 2022; 21: 113.
[2] Yang C, Qian J, Li JJ. Landscape of statin as a cornerstone in atherosclerotic cardiovascular disease. *Rev Cardiovsc Med* 2023; 24: 373.
[3] Li J-J, Zhao S-P, Zhao D, *et al*. 2023 Chinese guidelines for lipid management. *Front Pharmacol* 2023; 14: 1190934.
[4] National Cardiovascular Disease Experts Committee Cardiovascular Metabolic Medicine Professional Committee. [Clinical diagnosis and management of statin intolerance expert consensus in China]. Chinese Circulation Journal 2024; 39: 105-115. [Article in Chinese].
[5] Cheeley MK, Saseen JJ, Agarwala A, *et al*. NLA scientific statement on statin intolerance: a new definition and key considerations for ASCVD risk reduction in the statin intolerant patient. *J Clin Lipidol* 2022; 16: 361–375.
[6] Chien SC, Chen PS, Huang YH, *et al*. 2019 Taiwan Society of Lipids and Atherosclerosis expert consensus statement on statin intolerance. *J Formos Med Assoc* 2019; 118: 1385–1392.
[7] Kajinami K, Tsukamoto K, Koba S, *et al*. Statin intolerance clinical guide 2018. *J Atheroscler Thromb* 2020; 27: 375–396.
[8] Mancini GB, Baker S, Bergeron J, *et al*. Diagnosis, prevention, and management of statin adverse effects and intolerance: Canadian Consensus Working Group update (2016). *Can J Cardiol* 2016; 32(7 Suppl): S35-S65.
[9] Li JJ, Liu HH, Wu NQ, *et al*. Statin intolerance: an updated, narrative review mainly focusing on muscle adverse effects. *Expert Opin Drug Metab Toxicol* 2020; 16: 837–851.
[10] Liu J, Luo S-H, Qing P, *et al*. Comparative study of high-dose Xuezhikang and low-dose Xuezhikang plus Ezetimibe on pro- and anti-inflammatory markers. *Clin Lipidol* 2013; 8: 151–157.

Please cite this article as: LI JJ. Interpretation of Chinese Expert Consensus on the Diagnosis and Management Strategy of Patients with Statin Intolerance: A guiding file for helping to lipid management for Chinese population. *J Geriatr Cardiol* 2024; 21(7): 713–715. DOI: 10.26599/1671-5411.2024.07.006