Acta Cardiol Sin 2019;35:615–617
Editorial Comment
doi: 10.6515/ACS.201911_35(6).20191028A

# A Bridge Still Too Far

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Atherothrombosis is the foremost cause of premature mortality and of disability-adjusted life years worldwide. Low-density lipoprotein cholesterol (LDL-C) is one of the modifiable risk factors of the development and the progression of atherothrombosis. Abundant evidence from experimental, epidemiological, genetic studies, and randomized clinical trials has unequivocally suggested that the reduction in atherothrombotic events tracks with the LDL-C reduction with no interaction by treatments.[1]

Pooled data from these trials have also demonstrated that the relative cardiovascular benefits from the LDL-C reduction, mostly with statin treatment, was consistent — a 22% relative risk reduction for major vascular events and a 20% relative risk reduction in coronary death by every 1-mmol/dL reduction in the LDL-C level — regardless of the baseline LDL-C level.[2] With the emerging evidence from nonstatin treatment, we now learn that there is no lower limit of the LDL-C level that is known to be genuinely unsafe.[3] As a result, the guidelines on both sides of the Atlantic have advocated a more aggressive and stringent goal in patients at higher risk for atherothrombosis.[4,5]

Despite guidelines advocates and the greater use of statin treatment in patients at higher risk for atherothrombosis,[6] attaining the LDL-C goal in those patients still represents an obstacle. In this issue of the Journal, Tsai, et al., showed this phenomenon again.[7] Using data from the Taiwanese Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) registry, they reported that patients with established atherosclerotic disease were less likely to attain a LDL-C level less than 100 mg/dL if having an increasing waist-hip ratio. In addition to LDL-C goal attainment, any increases in those anthropometric markers, including the body mass index, simple waist circumference, and the waist-hip ratio, were associated with a lower likelihood of attaining the high-density lipoprotein cholesterol (HDL-C) goal and the triglyceride goal.

Their main finding was comparable to what we have learned from other studies. Those with an elevated body mass index, waist circumference, and/or waist-hip ratio, are more likely to have an unfavorable metabolic profile that, in itself, defines metabolic syndrome when the low HDL-C level and/or the high triglyceride level presents. Although patients with metabolic syndrome are at higher risk for atherothrombosis, the likelihood of receiving statin treatment for them was low and, therefore, they were more unlikely to attain their LDL-C goal.[6] In our prior study, around 64% of patients with abdominal obesity (indexed by an increase in waist circumference) who failed to attain their LDL-C goal were still very likely to receive the same lipid-lowering regimen from their physicians.[8]

The recent data suggested the LDL-C goal attainment rate in patients with high risk for atherothrombosis increased from 16% to more than 50% over the first 10 years of this century (Table 1). What do these data add to our understanding of the LDL-C control in Taiwan? The series of their findings should be reviewed in conjunction with data from the Taiwan Acute Coronary Syndrome-Full Spectrum Data Registry and from the Acute Coronary Syndrome-Diabetes Mellitus Registry of Taiwan Society of Cardiology.[9,10] Altogether, they point out that there is still a long road ahead in the realm of secondary prevention of atherothrombosis. In the more modern T-SPARCLE registry, the mean baseline LDL-C level was 99.6 ± 33.2 mg/dL, with 69% of patients receiving statin treatment; whereas, the mean baseline LDL-C level was 112.3 ± 37.4 mg/dL, with 50% of patients receiving statin treatment at discharge, in the Taiwan Acute Coronary Syndrome-Full Spectrum Data Registry. It can be expected that more patients would require more potent statin treatment and/or

Received: October 23, 2019 Accepted: October 28, 2019
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**Table 1.** The low-density lipoprotein cholesterol goal attainment rate in recent registries that included Taiwan

| | Enrollment | | Referenced guidelines | Patient no. | | Goal attainment rate in high risk patients* | |
|---|---|---|---|---|---|---|---|
| | Period | Country | | Overall | Taiwan | Overall | Taiwan |
| REALITY-Asia[15] | July 2002 through December 2004 | China, Korea, Malaysia, Singapore, Taiwan, and Thailand | NCEP ATP III guidelines | 2622 (66% high risk, 100% with statin) | 500 (36% high risk, 100% with statin) | 38% | 16% |
| LTAP 2[16] | September 2006 through April 2007 | Brazil, Canada, France, Korea, Mexico, the Netherlands, Spain, Taiwan, and United States | NCEP ATP III guidelines | 9955 (59% high risk, 75% with statin) | 966 (78% high risk, 83% with statin) | 67% | Not reported |
| CEPHEUS Pan-Asian[17] | April 2008 through December 2008 | Hong Kong, Indonesia, Korea, Malaysia, Philippines, Taiwan, Thailand, and Vietnam | NCEP ATP III guidelines 2004 update | 7281 (81% high risk, 94% with statin) | 999 (76% high risk, 93% with statin) | 55% | 69% |
| T-SPARCLE[18] | January 2010 through February 2011 | Taiwan | Not reported | 3316 (100% high risk, 69% with statin) | 3316 (100% high risk, 69% with statin) | 55% | 55% |

* A low-density lipoprotein cholesterol level lower than 100 mg/dL.
CEPHEUS, Centralized Pan-European Survey on the Under-treatment of Hypercholesterolemia; LTAP 2, Lipid Treatment Assessment Project 2; NCEP ATP III, National Cholesterol Education Program Adult Treatment Panel III; REALITY-Asia, Return on Expenditure Achieved for Lipid Therapy in Asia; T-SPARCLE, Taiwanese Secondary Prevention for Patients with Atherosclerotic Disease.

additional nonstatin treatment when answering our latest guidelines advocate, a LDL-C level lower than 70 mg/dL in patients with coronary heart disease and/or acute coronary syndrome.[11] Given that the healthcare reimbursement policy has effects on the LDL-C goal attainment rate in Taiwan,[12] we should be ready to set off the new voyage of triumphing over atherothrombosis in 2019 when our healthcare system starts reimbursing statin treatment by a new threshold, which should not be treated as the end but rather as the beginning where the contemporary evidence now further lowers the LDL-C bar down to lower than 50 mg/dL.[13,14]

## FUNDING SOURCE

None.

## DISCLOSURE

Tzung-Dau Wang has no relevant disclosure.

Kang-Ling Wang has received honoraria from Bayer, Boehringer Ingelheim, Daiichi-Sankyo, Novartis, Orient EuroPharm, and Pfizer.

Chern-En Chiang has been on the speaker bureau for AstraZeneca, Bayer, Boehringer Ingelheim, Daiichi-Sankyo, Merck Sharp & Dohme, Novartis, Pfizer, Sanofi, and Servier.

## DISCLAIMER

This article reflects the views of the authors only.

## CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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