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## Brief Communication

### Current Status and Residual Risks of the Patients with Atherosclerotic Cardiovascular Disease in Taiwan – Data from the T-SPARCLE Study

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#### SUMMARY

Cardiovascular (CV) disease is a leading cause of death worldwide, with unique disease burden in East Asians. However, Asian cohort of CV disease is insufficient. Therefore, a prospective, multicenter observational registry study, Taiwanese Secondary Prevention for patients with Atherosclerotic disease (T-SPARCLE) Registry, has been run since 2010 to document treatment and outcome of CV disease in Taiwan. We identified several region-specific issues, including treatment patterns, general and residual risk factors, which might be valuable for guiding patient care.

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#### 1. Cardiovascular disease in East Asians and Taiwan

Cardiovascular (CV) disease remained the leading cause of death in the past decade. The epidemiology of CV events and management is unique in East Asia.<sup>1,2</sup> In addition to genetic and lifestyle differences, healthcare system may contribute to the regional differences in CV outcome.

The study protocol of Taiwanese Secondary Prevention for patients with Atherosclerotic disease (T-SPARCLE) has been published previously.<sup>3</sup> As of June, 2020, nine analyses from our cohort have been published (Table 1). Currently, we are still following up the participants and enrolling new patients.

#### 2. Risk factors control

In Taiwan, only 54.8% of patients with a previous CV event had low-density lipoprotein cholesterol (LDL-C) controlled below 100 mg/dL, and 55.9% reached their blood pressure (BP) goal.<sup>4</sup>

Statin was used in about 70% of these patients, and it was the most important factor for reaching LDL-C target. Other factors associated with both better lipid and BP control included older age, male gender, history of diabetes mellitus (DM), and history of myocardial infarction (MI) or coronary artery disease (CAD). Additional factors for predicting poorer lipid control included chronic kidney disease (CKD) and higher waist-hip ratio (WHR).<sup>5–7</sup>

Anti-thrombotic agent is critical for secondary prevention of CV events. However, in our registry, only about 85% of the patients received anti-thrombotic agent, and only 71% of those with cerebro-

vascular disease received the medication.<sup>4</sup>

#### 3. Overview of predicting major adverse cardiovascular events (MACE)

In patients under treatment for atherosclerotic cardiovascular disease (ASCVD), there were still remaining factors, known as residual risk, that predicted worse outcome. The most important ones included the lipid profile after treatment, diabetes, CKD and heart failure.<sup>8</sup> Of note, although the BP target remained suboptimal in Taiwan, hypertension was not a residual risk factor for the patients under treatment for secondary prevention.

#### 4. Lipid control and MACE

For lipid management, it is uncertain whether the intensity of statin treatment or the target LDL-C level achieved is more important for CV outcome.<sup>2,9</sup> We demonstrated that LDL-C level, but not statin intensity, was associated with further MACE in patients with ASCVD in Taiwan.<sup>8</sup>

However, from these studies, we are not yet able to provide a clear guide about the optimal LDL-C target for the ASCVD patients in Taiwan. In our studies,<sup>10,11</sup> for patients with additional risk factors such as DM or CKD, there seemed no further benefit to lower LDL-C to < 70 mg/dL as compared to target at 70–99 mg/dL. Only 3–5% of our patients received high-intensity statin. This is in contrast to current western guidelines, which recommend initiating a high-intensity statin and very low LDL-C target of < 55 mg/dL.<sup>2,9</sup> Our study results afford more evidence for the lipid treatment guideline announced by the Taiwan National Health Insurance Department in 2013, but not the one in 2019.<sup>12</sup> One previous Asian trial showed

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**Table 1**  
Studies from T-SPARCLE registry.

| Author                   | Year | Residual risk (under statin) analysis                     | Other major findings   |
|--------------------------|------|---|--|
| Yin et al. <sup>3</sup>  | 2012 | No  | Methodology.   |
| Chen et al. <sup>7</sup> | 2013 | No  | Less lipid goal attainment in women.   |
| Lin et al. <sup>14</sup> | 2014 | No  | Less lipid goal attainment in CKD patients.  |
| Ho et al. <sup>5</sup>   | 2015 | No  | Statin therapy was the independent factor for achieving LDL-C goal.  |
| Jeng et al. <sup>4</sup> | 2015 | No  | Only about half achieved BP and LDL-C goals.<br>Independent factors: statin use, sex, cerebrovascular disease. |
| Yeh et al. <sup>8</sup>  | 2017 | Borderline residual risk factor of LDL-C < 100            | Controlled LDL-C level, but not statin use, was associated with MACEs.   |
| Lin et al. <sup>10</sup> | 2017 | Residual risk in DM: LDL-C ≥ 130, non-HDL ≥ 100, TG ≥ 250 | Risk factors for MACE:<br>1. DM: HF, CKD, beta-blocker, non-HDL-C.<br>2. Non-DM: HF, CKD, MI.                  |
| Ho et al. <sup>11</sup>  | 2018 | Residual risk in CKD: non-HDL ≥ 130, TG ≥ 200             | Risk factors for MACE:<br>1. CKD: non-HDL-C, HF, BMI.<br>2. Non-CKD: non-HDL-C, HF.                            |
| Tsai et al. <sup>6</sup> | 2019 | No  | Patients with higher WHR were less likely to achieve the lipid goals.  |

Abbreviations: BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; HF, heart failure; LDL-C, low-density lipoprotein cholesterol; MACE, major adverse cardiovascular events; MI, myocardial infarction; Non-HDL-C, non-high-density lipoprotein cholesterol; WHR, waist-hip ratio.

similar findings.<sup>13</sup> However, it is possible that our studies may not have enough power to detect the benefit of lowering LDL-C target to < 70 mg/dL.

Non-HDL-C was shown to be a better marker than LDL-C for predicting MACE in patients under statin treatment in our studies.<sup>10</sup> This is different from current guidelines that focus on LDL-C level.<sup>2,9</sup> The results are noteworthy because about half of our patients in T-SPARCLE registry had on-treatment non-HDL-C > 130 mg/dL.<sup>14</sup> This residual risk was particularly significant for DM patients.<sup>10</sup>

## 5. Residual risk factors in special groups

Diabetes continued to be a significant risk factor even after blood glucose control. In patients with DM, we found that heart failure, CKD, higher non-HDL-C and without beta-blocker use were significant predicting factors for further CV events.<sup>10</sup>

In our studies, CKD was an independent risk factor for future MACE, and those with more advanced stage of CKD were at a greater risk.<sup>8</sup> In patients with CKD, we found that heart failure and very low body mass index (BMI) were associated with future CV events.<sup>11</sup>

## 6. Conclusion

In our studies, some residual risk factors continued to predict MACE even under well medical support in Taiwan. There were some important differences noted between our results and the guidelines from western countries. This cohort allowed us to better understand the individual's risk and might help to develop local guidelines in a more precise way.

## Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article.

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