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Original Article

On-treatment lipid profiles to predict the cardiovascular outcomes in ASCVD patients comorbid with chronic kidney disease — The multi-center T-SPARCLE registry study

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KEYWORDS
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Secondary prevention

Background: The aim of this study is to determine the relationship between the on-treatment lipid profiles and the CV events in CKD and non-CKD population.
Method: This study was a multi-center observational registry, the Taiwanese Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) Registry. This study follows up patients with CV diseases in Taiwan who have secondary prevention therapies. The primary outcome is the time of first occurrence of a major adverse cardiac events (MACEs).
Result: 5388 patients with ASCVD were included and 1478 (27.4%) had CKD without dialysis. CKD patients had higher TG and lower LDL-C levels. The incidence of recurrent MACEs per 1000 person-years in CKD patients was 19.5 (95% CI 15.5—24.9), compared with 9.1 (95% CI 7.4—11.1) in non-CKD patients. In patients with statin therapy, there were no differences in MACE risk between each level of on-treatment LDL-C, TG and HDL-C level. Higher on-treatment non-HDL-C level was a significant predictor for higher MACE risk in patients without CKD, and borderline significant in CKD patients under statin therapy. Heart failure history was also associated with higher MACE risk in both group. Lower body mass index (BMI < 23 kg/m^2) was associated with higher MACE risk in CKD patients.
Conclusion: In ASCVD patients, on-treatment LDL-C was not a good CV outcome predictor. Instead, on-treatment non-HDL-C was a better predictor. Heart failure history was also associated with higher MACE risk in both group of patients. Lower BMI (<23 kg/m^2) was associated with higher recurrent MACE risk in CKD patients.

Introduction

Atherosclerotic cardiovascular diseases (ASCVD), such as coronary artery disease (CAD), cerebrovascular disease (CVD), peripheral artery disease (PAD) and prior myocardial infarction (MI), are common in general population. Patients with ASCVD may have higher risks of further cardiovascular (CV) events. Risk-reduction therapies, such as quit smoking, blood pressure control, lipid and diabetes management, weight management, physical activity and certain medications use, are proven to be beneficial to the CV outcomes.[1]

Chronic kidney disease (CKD) is an independent risk factor of ASCVD.[2] Patients with CKD and preexisting ASCVD are associated with higher risks of CV events and poorer outcomes.[3,4] However, traditional risk factors still have more predictability for stratifying CV risk than CKD.[5] Therefore, risk-reduction therapies in CKD patients are very important.

Evidences show serum low-density lipoprotein cholesterol (LDL-C) level and other lipid risk factors, such as triglycerides and low HDL cholesterol (HDL-C), and non-HDL-C result in ASCVD and further CV events.[6—8] Statins have been shown to reduce CV events and all-cause mortality with large-scaled studies in patients with dyslipidemia. However, most statin clinical trials were not designed to include patients with CKD, and most evidences of the statins use in CKD patients were from the post-hoc subgroup analyses. Besides, there is no trial to compare on-treatment lipid profiles with the CV outcomes in CKD patients. Therefore, the aim of this study is to determine the relationship between the on-treatment lipid profiles and the CV events in the ASCVD patients comorbid with/without CKD.

Method

This study was conducted from a multi-center observational registry, the Taiwanese Secondary Prevention for patients with AtheRosCLErotic disease (T-SPARCLE) Registry, from 14 teaching hospitals in Taiwan.[6—8] This registry-type prospective observational study recruits and follows up a large population of patients with CV diseases in Taiwan who have been receiving secondary prevention therapies.

Inclusion criteria

Adult patients ($>$18 year-old) who had stable symptomatic ASCVD, including CAD, CVD or PAD, were recruited. Patients with CAD was defined as those who had significant coronary artery stenosis ($\geq$50%), or had a history of MI, or who had angina showing ischemic electrocardiographic changes or positive response to stress tests. Patients with CVD were defined as those with cerebral infarction, intra-cerebral hemorrhage, transient ischemic attack due to cervical or intracranial large artery stenosis ($\geq$50%). PAD was defined as peripheral atherosclerosis with symptoms of ischemia and confirmed by ankle-brachial index, Doppler ultrasound, or angiography. CKD was defined as estimated glomerular filtration rate (eGFR) $<$60 ml/min, which based on serum creatinine level, age and sex. Comorbid hypertension was defined as home systolic blood pressure exceeding 140 mmHg or a diastolic pressure over 90 mmHg, or having anti-hypertensive medication concurrently according to the medical records. Comorbid diabetes was defined as HbA1c $\geq$ 6.5% or having glucose lowering agents concurrently according to the medical records. Comorbid heart failure was defined as Framingham's criteria and the heart failure diagnosis in the medical records.

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