



# Reply to “The impact of hyperlipidemia and carotid atherosclerosis”

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## DEAR EDITOR,

We would like to thank Yang et al. for their interest in our work.<sup>1</sup> In their Letter to the Editor, they summarized our most important findings and also raised several concerns about our work.<sup>2</sup> Listed below are our responses for their concerns.

For the first concern, the study subjects of our work were recruited from two community-based cohorts.<sup>2</sup> During the enrollment period, we provided extracranial carotid artery ultrasound scans to whom had voluntarily provided informed consent, completed questionnaire interviews, and received physical examinations and blood sampling. There was no indication for an ultrasound scan and all measurements, including questionnaire interviews, physical examinations, blood sampling, and ultrasound scans were performed at the communities.

For the second concern, the enrollment of cohort members was conducted by batches. The duration of each batch was 4–5 months. All eligible volunteers completed questionnaire interviews, received physical examinations, and had their blood drawn for biochemical determinations at the date they provided informed consent. Due to the limitation of the capacity of ultrasound scans, not all enrollees received ultrasound scans at the same date of physical and biochemical examinations. The mean (standard deviation) interval between the dates of physical and biochemical examinations and ultrasound scans was 29.4 (24.5) days. Approximately 90% of the intervals were less than 60 days. Seven (0.9%) subjects had an interval of 91–113 days, and 403 (49.3%), 330 (40.4%), and 77 (9.4%) subjects had an interval of 0–30, 31–60, and 61–90 days, respectively. It is unlikely that the short intervals between the dates of physical and biochemical examinations and ultrasound scans would introduce significant effects on the likelihood of the presence and progression of carotid atherosclerosis.

For the third concern, Yang et al. pointed out that the uses of anti-hypertensive, antidiabetic, and antihyperlipidemic medications are critical confounding factors.<sup>1</sup> Indeed, in the study, the definitions of hypertension, diabetes mellitus (DM), and hyperlipidemia included subjects who currently use antihypertensive, antidiabetic, and antihyperlipidemic medications, respectively. However, the uses of these medications are not qualified as confounders. To be a confounder in case-control studies, the extraneous factor must be fulfilled two criteria: (1) the extraneous factor is associated with the study factor in

the control subjects, and (2) the extraneous factor is associated with the disease in the nonexposed subjects.<sup>3</sup> It is unlikely that healthy subjects will receive antidiabetic or antihyperlipidemic medications. Therefore, these extraneous factors, that is, antidiabetic, antidiabetic, or antihyperlipidemic medications, will not introduce confounding effects. Our findings, including (1) hyperlipidemia was not significantly associated with carotid atherosclerosis in multi-variable analyses and (2) the adjusted odds ratios of carotid atherosclerosis for hyperlipidemia alone and DM alone were close to the null value 1.0 in the combinatory analyses, are not the results of confounding.<sup>2</sup> Furthermore, among a handful etiological studies which contemporarily explored the effects of hypertension, DM, and hyperlipidemia on carotid atherosclerosis, the findings for hypertension and DM were consistent, whereas it was inconsistent for hyperlipidemia.<sup>4–7</sup> More researches on the relationships between hyperlipidemia and carotid atherosclerosis seem necessary.

The last, in our study, the prevalence rate of hypertension was higher than those of DM and hyperlipidemia. Approximately three-quarters of hyperlipidemic subjects and more than two-thirds of DM patients are also affected with hypertension. Moreover, in the combinatory analyses, the adjusted odds ratios of having carotid atherosclerosis for hypertension with or without hyperlipidemia or DM were significantly elevated. But, it was close to the null value for hyperlipidemia alone or DM alone. The potential impacts of controlling blood pressure should be larger than those of controlling blood lipids and glucose.

We would like to thank Yang et al. again and hope that our responses could be of help.

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