Reviewer's report

Title: Alcohol consumption and carotid artery structure: a population-based cross-sectional study of Korean adults aged 50 years and older

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Reviewer: Ulf Schminke

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This study aims to investigate the association between subclinical carotid atherosclerosis and alcohol consumption in a population based study in South Korea. Carotid ultrasonography was performed in 4302 subjects at age 50 or older to assess common carotid artery (CCA) intima media thickness IMT, carotid bifurcation (CB) IMT, carotid artery plaques and the diameter of the CCA. Their main findings were that alcohol consumption was inversely associated with CCA-IMT and CB-IMT in men but not in women. In contrast, carotid plaques were positively associated with alcohol consumption of more than 40g/d. Alcohol consumption was further associate with carotid artery enlargement.

Although this is a well-written manuscript, there are some critical issues:

Major compulsory revisions

#1. A major limitation of the study is the low response-rate of the residents of the study area to the invitation to take part in the study. The response rate was 27.9% in women and 19.9% in men, respectively. This is considerably lower than response rate reported in other studies, which is higher than 60% in the some major studies. This limitation needs to be discussed, specifically, since a response rate of less than 30% does not mirror the entire population, anymore. Therefore, the authors should not use the term ‘population-based’ in the introduction and in the discussion (Paragraph on strengths and limitations).

#2. Methods. The authors should describe in more detail, how they have defined never-drinker and former-drinkers, and more importantly, which methods they have used (interview, which questions were asked?; biomarker?) to separate both groups from each other.

#3. Methods, IMT measurement: Which methods were used to measure IMT? Did the authors measure IMT manually or with the use of an automated edge tracking software? If IMT was measured manually, how many measurements were performed in a single arterial segment, e.g., on the CCA far wall? Did the authors perform only a single measurement on each CCA at a point 10mm proximally to the carotid bifurcation or did the authors perform multiple (e.g. 10) measurement in an arterial segment of 10mm in length? If the latter was true, did the authors calculate a mean value out of 10 measurements on each CCA or did they use the maximum value out of 10 measurements per arterial segment and calculate the mean of the maximum values of both CCA to obtain the mean IMT? Reading the present version of the measurement, it seems that only a single
point measurement at each arterial segment was performed. If this true, the single point measurement of the CCA-IMT of each segment is more prone to measurement error compared with an average value out of 10 measurements. Is it possible to re-read the ultrasonography images to perform either manual IMT measurement of at least 10 measurement points per arterial segment or an automatic IMT reading using an edge tracking software? This would improve reproducibility considerably. Otherwise the limitations of a single point measurement have to be discussed. Moreover, only the measurement point of the CCA IMT measurement was explained in the methods section: Where did the authors measure carotid bulb IMT?

#4. Methods, ultrasonography: The authors provide information on the reproducibility of the ultrasonography measurement only for the procedure of IMT measurement. What was the interreader and intrareader variability for the detection of carotid plaques and of the diameter measurement of the CCA? How many technicians were involved in the study? Was the measurement procedure performed by the same technician who performed the scanning procedure?

#5. Methods, ultrasonography: The CCA is a pulsatile vessel. Did the authors perform the diameter measurement ECG-triggered?

#6. Methods. Covariates: Physical exercise was categorized as none, irregular and regular according to which criteria?

#7. Discussion. While carotid IMT and carotid plaques are well-established so-called intermediate risk factors, which have been shown being associated with prevalent vascular risk factors and also prevalent and incident cardiovascular and cerebrovascular diseases, the role of carotid diameter enlargement as a surrogate marker for subclinical atherosclerosis is rather unknown. The authors should provide some information, either in the introduction or in the discussion, on studies, which have investigated associations of carotid diameter enlargement with vascular risk factors and also with prevalent or incident vascular disease such as stroke or myocardial infarction. Specifically, they should elucidate the question why they think that carotid diameter enlargement could play a role as a predictor of future cardiovascular or cerebrovascular events. Are there any reports about this topic in the literature?

#8. Discussion. It is difficult to read if the amount of daily alcohol intake because it is given in some studies as drinks per week, in others as ml per week, and in the present study as g per day. Alcohol consumption should be uniformly expressed in g per day

#9. Discussion. The present study categorized daily alcohol consumption in categories of 0, 1-10g/d, 11 – 20g/d, 20-40g/d, and >40g/d. These categories are different from categories used in other studies. Reference 13 classified alcohol consumption in groups of 0, 1-20g/d, 20-40g/d, 40-60g/d, 60-80g/d and >80g/d. The authors of reference 13 reported a linear decrease of IMT with increasing alcohol consumption up to 60-80g/d. An increase of IMT was reported in the group with an alcohol intake >80g/d. Furthermore, reference 2 reported a protective effect of alcohol against coronary heart disease up to 72g/d, while the harmful effect started at >89g/d. Compared to these studies, the overall daily
alcohol consumption in the population from South Korea was lower. The choice of categories with the highest categories of >40g/d made it impossible to find a J-shaped relationship. On the other hand, the linear decrease in IMT across categories as shown in the present study is still in line with references 2 and 13, because both showed a linear trend towards lower IMT up to an alcohol intake of 40g/d. This problem should be discussed.

10. References. Reference No. 13 and No. 30 are the same.

Minor essential revisions

#1. Page 5. Methods, 5th sentence: ‘….who resides in five dong in the DONG-gu district of the Gwangju Metropolitan City of South Korea, …’ The word ‘dong’ should be translated into English.

#2. Page 7, second paragraph, 4th sentence: ‘The presence of cardiac plaques was recorded, if…’ The word ‘cardiac’ should be replaced by ‘carotid’:

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'