Reviewer’s report

Title: The underlying mechanism for development of hypertension in the metabolic syndrome

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Reviewer: Wen-Yuan Lin

Reviewer’s report:

This is an interesting review to describe the underlying mechanism for development of hypertension in the metabolic syndrome. The author found that insulin resistance, sympathetic overactivity, oxidative stress, endothelial dysfunction, activated renin-angiotensin system, increased inflammatory mediators and obstructive sleep apnea were the possible factors to develop hypertension in the metabolic syndrome. It wrote good, however, there are some points should be addressed in this review article.

Major Compulsory Revisions:

1. As we knew, the main underlying pathophysiologic feature of metabolic syndrome was central obesity and insulin resistance. Elevated blood pressure was one of the abnormal metabolic factors in the definition of metabolic syndrome. Central obesity will induce the elevation of blood pressure. The author had described the effect of insulin resistance on the development of hypertension in the metabolic syndrome. I think if the author could demonstrate the possible mechanism of central obesity on the development of hypertension in metabolic syndrome. It will be much better.

2. In page 4, the author found that insulin resistance induces anti-natriuretic effect which stimulates renal sodium re-absorption. Finally, it caused elevated blood pressure and hypertension. Could you describe more evidences to prove the causal relation, especial in the metabolic syndrome? If someone with metabolic syndrome but the blood pressure is normal now. If he/she has higher chance to become hypertension in the future than people who are not metabolic syndrome?

3. In page 5, it would be better to collect more evidences regarding the development of hypertension in metabolic syndrome via sympathetic overactivity. In this paragraph, the author suggested that central obesity and insulin resistance were closed related to sympathetic overactivity. I think if we should focus on the development of hypertension in the metabolic syndrome.

4. In page 6, I think author should find some cohort studies to demonstrate the effect of endothelial dysfunction on the development of hypertension.

5. In page 8(regarding to inflammatory mediators), it would be better to describe some common inflammatory factors such as hsCRP.. to prove the development of hypertension in the metabolic syndrome.

6. In page 9(OSA), I think these descriptions were not enough to convince me to
believe that OSA is the underlying mechanism of development of hypertension in the metabolic syndrome. Most of these studies were cross-sectional design. Dose author suggest any mechanism between OSA and hypertension? I think it wound be better to describe the pathophysiologic mechanism, not the epidemiologic data.

Minor Essential Revisions

1. In page 3, line 7-9. If the author added the AHA/NHLBI definition of metabolic syndrome followed the IDF definition. It will be better.
2. In page 4, line 9-11. The author described that oxidative stress is associated with sodium retention and salt sensitivity. I think this sentence is not appropriate to show in this paragraph. It should be moved to the paragraph "Oxidative stress and endothelial dysfunction"
3. In page 7, line 8, angiotensionogen should be angiotensinogen.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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