

Point-by-point response

C1: As at present, the SERVE-HF trial demonstrated the most valuable findings in the field of CSA in association with heart failure, the beneficial effects of CSA on maintaining or even improving the cardiac function should be argued more extensively quoting not only the paper published by the current author but also the appropriate historical literatures.

R1: I added explanation regarding the beneficial effects of CSA toward patients with heart failure in page 9-10.

C2: Although the reviewer knows that this may not be the focus in this editorial, the readers in WJR will also have much interest in the issue of whether OSA should be actively treated by the PAP therapy (CPAP) in patients concurrently having OSA and heart failure. The large-scale, long-term SAVE trial published in NEJM in 2016 addressed this issue. They concluded no benefit of CPAP treatment on the primary endpoints of cardiovascular mortality and frequency of hospital admission. The results obtained from the SAVE trial (for OSA) are qualitatively the same as those reported by the SERVE-HF (for CSA), indicating that irrespective of the type of sleep apnea (either CSA or OSA), the expensive, active PAP therapy has no clinical benefit at all on the most important endpoint of improving the survival rate in patients with sleep apnea (CSA and/or OSA) and heart failure. These points should be discussed and included in the text.

R2: Descriptions regarding treatment of OSA by CPAP in patients with cardiovascular disease (not focusing on heart failure) is beyond the scope of this editorial. Nevertheless, we added brief descriptions regarding results of the SAVE trial in page 13.

C3: The study design introduced by the ADVENT-HF trial is of great interest for the reviewer, because this design is essentially different from and unique in comparison with the designs employed by many other studies performed in the past, i.e., the ADVENT-HF trial targets both the heart-failure patients with CSA-predominant SAS and those with OSA-predominant SAS, resulting in that the ADVENT-HF does not separate the patients having heart failure and CSA from those having heart failure and OSA. The reviewer is quite convinced that the basic consideration adopted by the ADVENT-HF is essentially valid, because the subjects with significant CSA forcibly express OSA, as well. This is because

the depression of respiratory center neurons during emergence of CSA concurrently inhibits the pharyngeal muscles opening the upper airway, leading to the upper airway collapse (i.e., occurrence of OSA). Therefore, the reviewer thinks that it is indispensable for estimating the treatment effect of sleep apnea without separating CSA and OSA in patients with heart failure. Based on these facts, the reviewer would require the authors to explain the unique design taken by the ADVENT-HF not superficially but more deeply.

R3: As the reviewer pointed, it is impossible to separate OSA and CSA since CSA may lead upper airway collapses. We added texts regarding mechanisms why OSA coexists with CSA and enhanced the uniqueness of the study design of ADVENT-HT trial in page 12.

C4: The abbreviation of “ADHD” seems to be not explained in the text (p. 10)

R4: I have corrected the abbreviation.