Editorial

Statin therapy for heart failure: to prescribe or not?

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Submitted Sep 21, 2015. Accepted for publication Oct 10, 2015.

doi: 10.3978/j.issn.2072-1439.2015.10.49

View this article at: http://dx.doi.org/10.3978/j.issn.2072-1439.2015.10.49

Since the publication of the first large randomised trial (1), the overwhelming body of evidence has demonstrated significant benefits of statins in patients with atherosclerotic cardiovascular disease (ASCVD). Despite strong recommendations of statins in ASCVD (2,3), controversy exists in patients with heart failure (HF). Although numerous observational studies have demonstrated favorable prognosis in HF patients treated with statins, two landmark randomized trials with rosuvastatin, GISSI-HF and CORONA studies (4,5), have not confirmed any marked reduction of all-cause mortality and non-fatal myocardial infarction (MI) and stroke in HF patients. Therefore, current guidelines do not explicitly recommend the use of statins in HF patients (1,2). However, a meta-analysis by Preiss and co-workers has further fuelled this debate (6).

Preiss *et al*. have examined the effects of statins on the risk of HF hospitalization and HF death by analyzing all primary and secondary randomized controlled trials with statins between 1994 and 2014. In 17 trials conducted over 4.3 years with 132,538 participants without HF at baseline, statins reduced low-density lipoprotein cholesterol (LDL-C) by 0.97 mmol/L, resulting in a 26% reduction of non-fatal MI. For the first time, the authors observed that statins modestly reduced the risks of non-fatal HF hospitalization and a composite HF outcome (HF death or non-fatal HF hospitalization) with no demonstrable difference in risk reduction between those who suffered an MI or not. Interestingly, despite a clear reduction in LDL-C and non-fatal MI in all participants, these effects of statin therapy were not related to the risk of first non-fatal hospitalization or the composite HF outcomes (6).

Statin therapy has been well-documented to reduce the risk of ASCVD in primary- and secondary prevention populations. The cardioprotective effects of statins are primarily derived from their cholesterol-lowering effects (1,2). However, non-lipid-modulation effects of statins, termed as pleiotropic effects, have been implicated in their cardioprotection, including anti-inflammation and anti-oxidation, endothelium protection, immunomodulation, and so on (7). Of note, no relationship was observed by Preiss *et al*. between reduction of non-fatal MI or LDL-C by statins, and risk of non-fatal HF hospitalization or the composite HF outcome (6). It indicates that the potential benefits of statins on HF could be associated with their pleiotropic effects rather than cholesterol-lowering effects. Interestingly, in GISSI-HF and CORONA trials, reduction of hs-CRP by rosuvastatin have not contributed to lower major events in HF patients (4,5). However, rosuvastatin has been proven to reduced hs-CRP levels resulting in significant lower incidence of major cardiovascular events (8). Therefore, it implicates that anti-inflammation is not one of candidate pleiotropic effects of statin protection against HF. The underlying mechanism of statins on HF remains to be identified.

Unlike the subjects with symptomatic HF (New York Heart Association class II, III, or IV) in GISSI-HF and CORONA trials (4,5), this meta-analysis included the participants without HF at baseline (6). It could be a principal explanation for their discrepancies about HF outcomes by statins. According to the classification system of HF stages (9), the participants with symptomatic HF in GISSI-HF and CORONA trials should be at Stage C or Stage D of HF. In contrast, the majority of the patients in this meta-analysis are at the first 2 stages (A and B) of HF. There are two plausible reasons to further explain the difference of HF outcomes between the subjects in these two trials and those in the meta-analysis. Firstly, HF is considered as a progressive pathological condition (9).

During the development and progression of HF, cholesterol, served as an essential component for human body, will be consumed for biosynthesis of various hormones and maintenance of cell membranes. Thus, HF patients have lower total cholesterol and LDL-C as compared with non-HF patients. In contrast to patients without HF, a low total cholesterol portends a poor prognosis in patients with HF (1). It is therefore not surprising that more reduction of LDL-C will not result in lower incidence of HF events in patients with established HF (6). Secondly, the cause of death in patients with coronary artery disease without HF is different from those with HF. Non-HF patients die primarily from acute MI and ventricular fibrillation, whereas HF patients are more likely to die from progressive HF and stroke (10). Therefore, no reduction of HF events were observed in all participants despite a marked reduction in non-fatal MI. Similarly, no relationship was indicated between reduction of MI or LDL-C by statins, and risk of HF events (6).

Despite controversy about the role of statins in patients with symptomatic HF, it is recommendable that statin therapy should be used in HF related to ischemic heart disease because coronary heart disease is acknowledged as the first cause of HF and incident HF always carries a dismal clinical prognosis (9). More importantly, the study by Preiss and co-workers reminds us that prevention of new-onset HF and HF hospitalization can be achieved by statins particularly in patients with coronary heart disease.

Acknowledgements

None.

Footnote

Provenance: This is a Guest Editorial commissioned by the Section Editor Yue Liu (Department of Cardiology, the First Affiliated Hospital of Harbin Medical University, Harbin, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. European Association for Cardiovascular Prevention & Rehabilitation, Reiner Z, Catapano AL, et al. ESC/EAS Guidelines for the management of dyslipidaemias: the Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Eur Heart J 2011;32:1769-818.
2. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014;129:S1-45.
3. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-9.
4. Gissi-HF Investigators, Tavazzi L, Maggioni AP, et al. Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. Lancet 2008;372:1231-9.
5. Kjekshus J, Apetrei E, Barrios V, et al. Rosuvastatin in older patients with systolic heart failure. N Engl J Med 2007;357:2248-61.
6. Preiss D, Campbell RT, Murray HM, et al. The effect of statin therapy on heart failure events: a collaborative meta-analysis of unpublished data from major randomized trials. Eur Heart J 2015;36:1536-46.
7. Blum A, Shamburek R. The pleiotropic effects of statins on endothelial function, vascular inflammation, immunomodulation and thrombogenesis. Atherosclerosis 2009;203:325-30.
8. Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008;359:2195-207.
9. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation 2009;119:e391-479.
10. Pereira-Barretto AC, Bacal F, de Albuquerque DC. Most Heart Failure Patients Die from Pump Failure: Implications for Therapy. Am J Cardiovasc Drugs 2015. [Epub ahead of print].

Cite this article as: Huang XS, Zhao SP. Statin therapy for heart failure: to prescribe or not? J Thorac Dis 2015;7(10):1702-1703. doi: 10.3978/j.issn.2072-1439.2015.10.49

