Editorial

J-curve Phenomenon Might Be Inherent: How to Know If It Is Treatment Induced?

Jinho Shin , MD, PhD

Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

OPEN ACCESS

Received: Nov 19, 2017

Accepted: Dec 14, 2017

Correspondence to

Jinho Shin, MD, PhD

Division of Cardiology, Department of Internal Medicine, Hanyang University College of Medicine, 222-1, Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea.

E-mail: jhs2003@hanyang.ac.kr

Copyright © 2018. The Korean Society of Cardiology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Jinho Shin

<https://orcid.org/0000-0001-6706-6504>

Conflict of Interest

The author has no financial conflicts of interest.

The contents of the report are the author's own views and do not necessarily reflect the views of the *Korean Circulation Journal*.

► See the article "The J-curve between Diastolic Blood Pressure and Risk of All-cause and Cardiovascular Death" in volume 48 on page 36.

Excluding the subject with self-reported diagnosis hypertension, Kimm et al.,¹⁾ reported that J-curve phenomenon was observed in a large observational cohort for all-cause mortality, atherosclerotic cardiovascular mortality, and ischemic heart disease mortality. This study went a step farther than the study done by McEvoy et al.,²⁾ which demonstrated J-curve phenomenon in a population cohort trying to exclude the effect of antihypertensive drug treatment. In this study, hypertensive subjects taking antihypertensive medication seems to be excluded at baseline in spite of some limitations.

J-curve phenomenon is a physiologic consequence as the diastolic blood pressure (DBP) is going down below the threshold where myocardial ischemia is induced.³⁾ Myocardial injury related to low DBP was reported in the population.²⁾ The principle is very simple and observed even in placebo group.⁴⁾ And the study by Kimm et al.,¹⁾ is a population version of the J-curve phenomenon observed in placebo group in randomized clinical trial (RCT) which supports that J-curve phenomenon can be inherent to individual's characteristics.

It is very reasonable to compare the hazard of low DBP between treatment group and placebo group to draw true effect of antihypertensive treatment on J-curve phenomenon. If the hazard ratio (HR) is significantly higher than the placebo group, it makes sense to conclude that the J-curve phenomenon is treatment induced. In a recent analysis of RCT data including Systolic Blood Pressure Intervention Trial (SPRINT), Action to Control Cardiovascular Risk in Diabetes (ACCORD), and Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (ONTARGET), J-curve phenomena were noted both in intensive treatment group and standard treatment group but HR was significantly higher not in intensive treatment group but in standard treatment group and the nadir in the intensive treatment group is lower compared with the standard treatment group.⁵⁾

In fact, such comparison between groups was tried for the placebo controlled RCTs. For example, individual patient data arranged for matched-pair analysis showed significant benefit of lowering DBP <70 mmHg in treatment group when compared to the placebo group with matched blood pressure level.⁶⁾ Therefore, it may not be reasonable to down-titrate antihypertensive regimen when DBP <70 mmHg is encountered without considering the hazard reported in those DBP range in the placebo group or less tightly controlled group.

Study of Kimm et al.,¹⁾ suggests that J-curve phenomenon could be inherent. And it will provide a basis to decide whether J-curve phenomenon observed in a treated population is induced or not by testing whether the curve is significantly steeper or not or by testing whether the HR is significantly higher than untreated population or less tightly controlled group.

REFERENCES

1. Kimm H, Mok Y, Lee SJ, Lee S, Back JH, Jee SH. The J-curve between diastolic blood pressure and risk of all-cause and cardiovascular death. *Korean Circ J* 2018;48:36-47.
[PUBMED](#) | [CROSSREF](#)
2. McEvoy JW, Chen Y, Rawlings A, et al. Diastolic blood pressure, subclinical myocardial damage, and cardiac events: implications for blood pressure control. *J Am Coll Cardiol* 2016;68:1713-22.
[PUBMED](#) | [CROSSREF](#)
3. Bellamy RF. Diastolic coronary artery pressure-flow relations in the dog. *Circ Res* 1978;43:92-101.
[PUBMED](#) | [CROSSREF](#)
4. Boutitie F, Gueyffier F, Pocock S, Fagard R, Boissel JPINDANA Project Steering Committee. Individual Data ANalysis of Antihypertensive intervention. J-shaped relationship between blood pressure and mortality in hypertensive patients: new insights from a meta-analysis of individual-patient data. *Ann Intern Med* 2002;136:438-48.
[PUBMED](#) | [CROSSREF](#)
5. Kalkman DN, Brouwer TF, Vehmeijer JT, et al. J curve in patients randomly assigned to different systolic blood pressure targets: an experimental approach to an observational paradigm. *Circulation* 2017;136:2220-9.
[PUBMED](#) | [CROSSREF](#)
6. Wang JG, Staessen JA, Franklin SS, Fagard R, Gueyffier F. Systolic and diastolic blood pressure lowering as determinants of cardiovascular outcome. *Hypertension* 2005;45:907-13.
[PUBMED](#) | [CROSSREF](#)