

The J Curve Phenomenon is Still Valid in the Era of Primary Revascularization

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Hypertension is a major risk factor for coronary artery disease and is associated with the occurrence of myocardial infarction.¹⁾²⁾ The incidence of ischemic heart disease increases when systolic blood pressure is over 140 mmHg. The 2013 Korean Society of Hypertension guidelines for the management of hypertension recommended a systolic blood pressure cut-off of less than 140 mmHg for coronary artery disease.³⁾ However, it is commonly suggested to control blood pressure more strictly in high risk patients, such as those with ischemic heart disease, by keeping blood pressure lower than 130/80 mmHg.4) The Systolic Blood Pressure Intervention Trial enrolled high risk hypertensive patients, 17% of whom had a previous history of cardiovascular diseases; these patients showed better survival with intensive blood pressure control than a control group with the standard blood pressure cutoff.⁵⁾ In contrast, other studies showed modest and statistically nonsignificant benefits with intensive blood pressure control compared to usual controls.⁶⁾⁷⁾ Also, some recent meta-analyses have reported that the lower blood pressure target for higher-risk patients is not supported by evidence from high-quality, randomized, clinical trials.⁸⁾⁹⁾ Moreover, surrogate marker studies often fail to show the

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benefits of intensive blood pressure control.¹⁰

Thus, controversy remains about specific blood pressure treatment goals for individuals with nascent or active coronary artery diseases even when diagnosis is supported by opposite pathophysiologic hypotheses.¹¹⁾ For example, lower systolic blood pressure targets such as <120 mmHg may be appropriate to reduce myocardial workload. In contrast, excessive lowering of diastolic blood pressure may impair coronary perfusion, especially when coronary artery stenosis remains. However, an attenuated J-curve effect is suggested for patients with coronary artery disease and hypertension after revascularization.¹²

In this edition of the journal, Park et al.¹³⁾ report that patients with acute myocardial infarction show a U curve phenomenon, with the lowest cardiovascular event rate in the quintiles and an average blood pressure of 112.2/73.3 mmHg. The findings of this study showed that even after a successful revascularization procedure, patients with acute MI could still have a residual ischemic burden due to several causes, including untreated segments of target vessels, other untreated non-target vessels, or ischemia due to microvascular causes even when no significant residual coronary arterial stenosis was apparent. In such circumstances, blood pressure that is too low can easily cause ischemic symptoms and lead to additional revascularization procedures during clinical follow-up.

However, we should pay attention to the possibility of reverse causality. In observational studies like the KAMIR registry, even if various statistical techniques are applied to remove confounding factors, unmeasured or imprecisely measured confounders prevent causal inferences being drawn from associations due to reverse causality.¹⁴⁾ Although the former is typically acknowledged in reports of such studies, the latter appears to be less well-understood and, therefore, is more often overlooked as a potential explanation for apparent, often unexpected, associations between risk factors and adverse outcomes.¹⁵⁾ For example, the J-curve may represent a more severe and debilitating underlying chronic condition such as frailty or malignancy and the low blood pressure may be a mere epiphenomenon of this illness, thereby resulting in greater mortality.¹⁶⁾

In conclusion, even in the era of total revascularization, blood pressure controlled to less than 140/90 mmHg is still a valid goal for the secondary prevention of cardiovascular events in hypertensive patients with coronary artery disease. And, if there is no evidence of impaired perfusion, more strict blood pressure control can further improve cardiovascular outcomes in selected, healthy patients with coronary artery disease, including previous myocardial infarction.

References

- Shin J, Park JB, Kim KI, et al. 2013 Korean Society of Hypertension guidelines for the management of hypertension: part l-epidemiology and diagnosis of hypertension. *Clin Hypertens* 2015;21:1. eCollection 2015.
- 2. Lee SH, Kim JH, Jeong MH, et al. Clinical characteristics and outcomes of acute ST-segment elevation myocardial infarction in younger Korean adults. *Korean Circ J* 2015;45:275-84.
- 3. Shin J, Park JB, Kim KI, et al. 2013 Korean Society of Hypertension guidelines for the management of hypertension: part III-hypertension in special situations. *Clin Hypertens* 2015;21:3. eCollection 2015.
- 4. Rosendorff C, Black HR, Cannon CP, et al. Treatment of hypertension in the prevention and management of ischemic heart disease: a scientific statement from the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention. *Circulation* 2007;115:2761-88.
- SPRINT Research Group, Wright JT Jr., Williamson JD, et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med* 2015;373:2103-16.
- Lonn EM, Bosch J, Lopez-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med 2016;374:2009-20.

- ACCORD Study Group, Cushman WC, Evans GW, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010;362:1575-85.
- Rosendorff C, Lackland DT, Allison M, et al. Treatment of hypertension in patients with coronary artery disease: a scientific statement from the American Heart Association, American College of Cardiology, and American Society of Hypertension. *Hypertension* 2015;65:1372-407.
- Bangalore S, Kumar S, Volodarskiy A, Messerli FH. Blood pressure targets in patients with coronary artery disease: observations from traditional and Bayesian random effects meta-analysis of randomised trials. *Heart* 2013;99:601-13.
- Moon SH, Moon JC, Heo DH, et al. Increased pulse wave velocity and augmentation index after isometric handgrip exercise in patients with coronary artery disease. *Clin Hypertens* 2015;21:5. eCollection 2015.
- 11. Messerli FH, Mancia G, Conti CR, et al. Dogma disputed: can aggressively lowering blood pressure in hypertensive patients with coronary artery disease be dangerous? *Ann Intern Med* 2006;144:884-93.
- 12. Lu W. Could intensive anti-hypertensive therapy produce the "J-curve effect" in patients with coronary artery disease and hypertension after revascularization? *Eur Rev Med Pharmacol Sci* 2016;20:1350-5.
- Park H, Hong YJ, Cho JY, et al. Blood pressure target and clinical outcome in patients with acute myocardial infarction. *Korean Circ J* 2017;47:446-54.
- 14. Youn JC, Han S, Ryu KH. Toward a new heart failure registry in Korea. *Korean Circ J* 2017;47:316-7.
- 15. Sattar N, Preiss D. Reverse causality in cardiovascular epidemiological research: more common than imagined? *Circulation* 2017;135:2369-72.
- Lee SE, Lee HY, Cho HJ, et al. Clinical characteristics and outcome of acute heart failure in Korea: results from the Korean acute heart failure registry (KorAHF). *Korean Circ J* 2017;47:341-53.