Although there is no disagreement that antihypertensive treatment improves clinical outcomes, the blood pressure (BP) level for optimal benefit remains unclear. Among individuals without apparent cardiovascular disease, progressively lower BP levels are associated with improved cardiovascular outcomes down to a level of at least 115/75 mm Hg⁴; however, in the very large group of patients with comorbidities such as coronary artery disease, diabetes, and peripheral arterial disease, there is debate about how low BP should be reduced. A critically important concern relates to the adequacy of myocardial perfusion at these lower BP levels because data from multiple observational-type studies have suggested an increase in cardiac ischemic events at these lower levels (Figure).²⁻⁵ This is an issue because many of these patients also have coronary microvascular dysfunction, which could potentiate any harmful effects associated with very low BP.

A provocative report in this issue provides coronary flow data to assess the impact of antihypertensive BP level.⁶ Before addressing this novel study, it is appropriate to review concepts underlying coronary flow reserve (CFR), which was the measure used in this study. CFR is the ratio of coronary flow at near maximal hyperemia relative to basal flow. Although there is some controversy about what the specific lower threshold should be, a CFR <2.0 generally indicates an important limitation in coronary blood flow and, in the absence of an epicardial coronary stenosis, implies that the limitation is in the coronary microvasculature.⁷ Such limitations have the potential to result in myocardial ischemia and related adverse consequences. CFR, however, is complex, since it is usually obtained by Doppler (either via intracoronary or transthoracic transducer) and expressed as a blood flow velocity ratio. As such, it does not provide absolute (ml/gm myocardium) blood flow that can be obtained noninvasively by positron emission tomography or cardiac magnetic resonance imaging. Thus, CFR may be reduced simply as a result of an increased basal flow. Nevertheless, a low CFR has been associated with an increased risk for adverse cardiovascular events in many disorders⁸ and, thus, generally implies coronary microvascular dysfunction.

Microvascular dysfunction is prevalent in patients with hypertension: CFR <2.0 has been documented in about a third of such patients and in about a fifth of those with prehypertension.⁹ In many, microvascular dysfunction is present even without other evidence of organ damage, such as left ventricular hypertrophy.¹⁰ Thus, microvascular dysfunction likely represents an early sign of vascular dysregulation and an attractive diagnostic and therapeutic target. Long-term treatment with calcium antagonists and angiotensin-converting enzyme inhibitors improves microvascular dysfunction among individuals with hypertension¹¹,¹²; however, uncertainty remains about what the optimal BP level should be among individuals with hypertension with documented microvascular dysfunction.

Attempting to fill this void, Mizuno et al compared CFR values according to the mean treated BP level achieved.⁶ They enrolled patients with never-treated hypertension and compared findings with normotensive subjects. Individuals with coronary artery disease, diabetes, left ventricular dysfunction, or other significant comorbidities were excluded. Patients were started on antihypertensive therapy, and BP was carefully recorded every 2 to 4 weeks. After 12 months of treatment, patients were categorized into 3 groups according to achieved mean systolic blood pressure (SBP): (1) ≤140 mm Hg; (2) 120 to 139 mm Hg; or (3) <120 mm Hg. Transthoracic echocardiography with Doppler was employed to assess CFR of the left anterior descending artery, using dipyridamole to augment flow.

At baseline, mean CFR was 3.1 among controls and ≤2.4 among patients with hypertension. After 12 months of antihypertensive therapy, mean CFR increased to 2.7 among patients with hypertension who achieved a SBP <120 mm Hg (mean=114 mm Hg). Within this low SBP group, patients with mean diastolic blood pressure of 76 mm Hg had a greater increase in CFR than patients with mean diastolic blood pressure of 69 mm Hg. In contrast, CFR remained similar (2.3) among those who achieved mean SBP of 120 to 139 mm Hg (mean=135 mm Hg), and CFR decreased (2.1) among those who achieved mean SBP ≥140 mm Hg (mean=144 mm Hg).

The authors are to be congratulated on conducting a study to help determine what the optimal BP should be in the management of microvascular dysfunction. At first interpretation, a lower SBP would appear to be preferential; however, certain aspects of the study deserve comment. Although most patients were treated with an angiotensin-converting enzyme inhibitor/angiotensin receptor blocker and/or calcium antag-
Figure. The figure illustrates a disproportionate increase in the hazard for adverse outcomes among patients with low systolic blood pressure who have concomitant peripheral arterial disease (PAD) and coronary artery disease. Adapted from Bavry AA et al. 

onist, we were not provided with the number of agents or dosage required in each group. Patients who achieved SBP <120 mm Hg might represent a group with easier-to-control hypertension, despite use of relatively few agents, or could represent a group where success was achieved at the cost of multiple high-dose antihypertensive agents. Similar logic holds for those who only achieved SBP ≥140 mm Hg: Were these patients treated to a lesser degree, or did they just have refractory hypertension and more advanced microvascular disease? If the latter, CFR would likely remain low even with optimal BP treatment. It is possible that low BP is better unless severe microvascular dysfunction is present.

In addition to CFR, the index of microcirculatory resistance can also be used to study the microcirculation. Mechanistic studies can be designed to examine circulating blood cells liberated from endothelium as a measure of microvascular health. Lastly, randomized trials are needed to determine with better certainty what the optimal BP should be among patients with microvascular dysfunction. Among certain populations of patients, such as individuals with diabetes, a randomized clinical trial has already begun to define what the lower level of BP should be.13

In conclusion, this study suggests that treating SBP to <120 mm Hg is preferential as long as diastolic blood pressure remains >70 mm Hg. Until randomized antihypertensive studies that include conventional and lower BP targets can be conducted, advice would dictate that lower BP to a point is better.

Disclosures
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References

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