Certain antihypertensive compounds, beyond blood pressure (BP) reduction, might directly have beneficial effects on vascular homeostasis, including the improvement of endothelial function. In this issue of American Journal of Hypertension, Tomiyama and colleagues evaluated the impact of treatment with two different angiotensin receptor blockers telmisartan (40 mg/d) and valsartan (80 mg/d), on forearm reactive hyperemia (RH) and plasma levels of asymmetric dimethylarginine (ADMA), considered two markers of endothelial function, in a 12-week study with a cross-over design. Reactive hyperemia was found to be greater, whereas plasma levels of ADMA were lower after telmisartan as compared with valsartan treatment, despite a similar BP reduction exerted by both compounds. Worth noting, changes in RH were inversely related to changes in ADMA. Considering RH a nitric oxide (NO)-dependent phenomenon and because ADMA is the endogenous inhibitor of NO synthase, the investigators suggest that reduction of ADMA and consequent amelioration of NO-dependent vasodilation might explain the observed specific beneficial effect of telmisartan on forearm resistance arteries.

The present study is of interest and further supports the possibility that drugs, even belonging to the same pharmacologic class, might have a different impact on endothelial dysfunction in hypertensive patients. Because endothelium-dependent vasodilation is an accepted marker of cardiovascular events, it might be extrapolated that treatment with telmisartan might better improve clinical prognosis of hypertensive patients as compared with valsartan. However, these conclusion should be taken with caution. First, the investigators consider RH as a marker of NO-dependent vasodilation, whereas NO plays a minimal role in determining RH. In contrast, RH is an established method to assess microvascular vasodilatory reserve, which is also influenced by structural changes. Thus, mechanisms different from NO may mediate the beneficial effect of telmisartan. This possibility is also in agreement with the large body of evidence indicating that the blockade of the renin-angiotensin system has a limited effect on endothelium-dependent vasodilation in the forearm microcirculation of hypertensive patients. Furthermore, when endothelial function is evaluated, it is crucial not only to demonstrate that a treatment is associated with an improvement in vasodilation, but also that this effect is exerted by restoring NO availability. Despite these limitations, forearm RH can represent an important vascular parameter in hypertensive patients.

Another interesting aspect of the study is the greater effect of telmisartan as compared with valsartan in reducing circulating ADMA. This difference might be explained by the greater activation of peroxisome proliferator activated receptor (PPAR)-γ, as it can reduce oxidative stress or increase ADMA degradation. However, the clinical significance of ADMA in hypertensive patients is not established and, in addition, the present study lacks of a control group to ascertain whether its plasma levels are increased in the enrolled group of hypertensive patients. On the other hand, because ADMA plays a pathologic role in certain populations, including patients with renal failure, it would be of interest to confirm this effect of telmisartan in hypertension.

The open questions raised from the present study can be answered by future long-term prospective studies on large numbers of hypertensive patients evaluating whether the beneficial effects of telmisartan are mediated by increased NO availability or whether the PPAR-γ agonist effect contributes to the improvement in RH and reduction of ADMA levels.

References
2. Tomiyama H, Yamada J, Koji Y, Shiina K, Yoshida M, Yamashina A: Effect of telmisartan on forearm postschematic hyperemia and

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