Within the regulation of blood pressure, the renin-angiotensin system (RAS) plays an essential role with AngII causing vasoconstriction, which increases the blood pressure. AngII is formed after \( \text{ACE} \) is cleaved by AngI. We hypothesize that the blunting of AngII production with concomitant exercise reduces improvements in metabolic fitness by removing an important stimulus for capillary growth in exercised muscles. The aim of this research was to expose the pathway by which AngII and \( \text{ACE} \) are implied in exercise-induced capillary growth of human muscle. We show that highest increases in indices of metabolic strain are observed after high intense exercise bouts and that the increase in AngII is \( \text{ACE} \) genotype dependent. Furthermore, subjects with the ACE-II genotype had a significant higher capillary perfusion in the finger after exercise. Our findings of our ACE inhibition study support the view that an angiotensin-regulated mechanism affects the hypoxia-specific gene response in peripheral muscle to endurance exercise and support the notion that the muscle’s transcript regulation by ACE inhibition is related to muscle oxygenation during exercise. This indicates that there is a shift in the activation of the gene program from muscle fibres to the surrounding interstitium after ACE inhibition. In a training study we observed a significant correlation between increases in \( \hat{\text{V}}\text{O}_2\text{max} \) and the changes in capillary-to-fibre-ratio. We further observed that variability in the cardiovascular response, based on \( \hat{\text{V}}\text{O}_2\text{max} \) and heart rate at rest, was related to the \( \text{ACE} \) I/D genotype. Our findings that physiological improvements after exercise are dependent on \( \text{ACE} \) levels, both due to different \( \text{ACE} \) genotypes and to taking \( \text{ACE} \) inhibitors may have clinical repercussions. It may explain the individual variation in the response to exercise rehabilitation in aerobic power and oxygen uptake. These differences in exercise-induced improvements have rarely been valued in pharmacological studies of hypertension and exercise rehabilitation.