

therefore, conclusions could not be drawn regarding the safety of the zoster vaccine in the population we described. The case reported by Dr Young highlights the need for caution or possibly withholding zoster vaccination in highly immunosuppressed patients.

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<http://dx.doi.org/10.1016/j.mayocp.2016.04.014>

The Different Effects of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers on Mortality



To the Editor: The article by Bangalore et al¹ published in the January 2016 issue of *Mayo Clinic Proceedings* deals with the important topic of cardiovascular protection. In this regard, several recent studies have compared the 2 classes of cardioprotective drugs, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). As highlighted by Bangalore et al, these studies have often reported mortality reduction with ACE inhibitors vs placebo or comparators, while ARBs were not associated with significant effect.

In this new meta-analysis¹ of trials that included patients with diseases ranging from hypertension to myocardial infarction or diabetes, but excluding heart failure, the authors confirmed that ACE inhibitors significantly lower mortality whereas placebo and ARBs do not. Moreover, the authors provided a hypothesis for this difference: ACE inhibitors were discovered and studied in large randomized trials earlier than ARBs.

According to them, in view of the improvement in standard of care over the years, concomitant use of lifesaving drugs such as antiplatelet agents or statins was more likely in patients enrolled in ARB trials. This difference could have contributed to the lower impact of ARBs on mortality. To support this hypothesis, the authors suggested that the rate of mortality and morbidity were higher in the placebo groups of ACE inhibitor trials compared with the placebo groups of ARB trials.

This proposal, however, is not supported by the rate of events in Tables 1 and 2 in their article. Indeed, ACE inhibitor trials lasted on average 3.2 years and ARB trials 3 years. The trials included in their analysis provided a follow-up of roughly 99,836 patient-years for ACE inhibitors and 99,423 patient-years for ARBs. The rate of death was therefore 0.0243 events per patient-year in the placebo arms of ACE inhibitor trials and 0.0299 events per patient-year in the placebo arms of ARB trials. As a consequence, and in contrast with the authors' hypothesis, the rate of death tended to be higher in the placebo groups of ARB trials compared with ACE inhibitor trials.

In addition, my colleagues and I observed in a meta-analysis of studies in patients with hypertension performed since 2000 that ACE inhibitor use was again significantly associated with reduced all-cause mortality by 10% vs the comparator, whereas the ARBs had no such association.^{2,3} Savarese et al⁴ similarly reported a reduction in mortality with ACE inhibitors vs placebo (−9%; $P=.008$), while no significant effect was detected with ARBs. Contrary to the assumption of Bangalore et al, in trials considered in the meta-analysis by Savarese et al, the coprescription of statins or aspirin was higher in the ACE inhibitor trials compared with ARB trials (51% vs 33% for statins and 85% vs 27% for aspirin). Therefore, the different effects

of ACE inhibitors and ARBs cannot be due to different coadministration of lifesaving agents.

In conclusion, it is possible to compare ACE inhibitors and ARBs in a balanced way, at least when restricting the analysis to contemporary trials in patients with hypertension, and in this context, ACE inhibitors are the only class to show a significant reduction of mortality.

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Potential Competing Interests: The author reports receiving honorarium for consultancy from several pharma developing ACE inhibitors or ARBs, including Daiichi Sankyo, Menarini, BMS, Servier, Bayer.

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<http://dx.doi.org/10.1016/j.mayocp.2016.04.021>

In Reply—The Different Effects of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers on Mortality



Dr Mourad contends that the angiotensin-converting enzyme inhibitors (ACEis) are the only drug class to produce a major reduction in