Reply

Reply to the comment on “Effects of long term angiotensin II AT-1 receptor blockade on survival, hemodynamics and cardiac remodeling in chronic heart failure in rats”


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We read with interest the comments by Willenheimer [1] on our paper recently published in Cardiovascular Research [2]. Willenheimer states that (a) collagen density being the same in untreated MI rats and in irbesartan-treated MI rats, and (b) heart weight/body weight ratio being decreased in irbesartan-treated vs. untreated MI rats, the absolute myocardial collagen content is reduced in the irbesartan-treated animals. In our opinion, this assumption is questionable since fibrosis development is not an evenly distributed process. Hence, subendocardial fibrosis (which we evaluated) does not necessarily reflect what happens in other myocardial layers, and therefore cannot be extrapolated to the whole myocardium. Now regarding a possible antifibrotic effect of irbesartan, our data show that the pathological process of fibrosis development which is clearly evidenced by the increase of collagen density in untreated MI rats (5.26±0.60) as compared to sham rats (2.17±0.09) was neither prevented nor even slightly reduced in the irbesartan-treated group (5.15±0.48). Willenheimer also postulates that the MI rats surviving at 7.5 months might be those with the least degree of fibrosis, thus leading to an underestimation of fibrosis in these rats with, as a result, an underestimation of the antifibrotic effect of irbesartan in the rats treated with this drug. It is true that in a previous study [3], we showed that subendocardial collagen density decreases with survival duration (from 4.28±0.22 for animals deceased between 0 and 3 months after coronary ligation down to 2.01±0.10 for animals deceased between 9 and 12 months after coronary ligation), but in this study the ACE inhibitor trandolapril displayed a true antifibrotic effect (collagen density 1.49±0.26 for rats deceased between 9 and 12 months).

In summary, even if an apparent antifibrotic effect of irbesartan could be inferred from a reduction in the absolute myocardial collagen content, we feel that with irbesartan (and in contrast with trandolapril) no true antagonist effect vs. the pathological process of fibrosis development in heart failure was evidenced.

References


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