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Reply to "Reflections on Vascular Ageing and Microvascular Pulsatility"

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To the Editors of

Journal of Hypertension

Dearest,

as you suggested through e-mail on April 17th, we produced a reply to McDonnell et al. commenting our paper on the December 2013 issue.

We hope it is suitable for publication and it is a valid contribution to clarify the raised issues.

Thank you very much

Dr. Francesco Stea

Pisa

Reply to letter : “Reflections on Vascular Ageing and Microvascular Pulsatility”

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We thank McDonnell et al. for their interest in our work (1). In their letter, they question that the positive correlation between wave reflection and renal resistive index (RI) in the interlobar arteries of hypertensive patients proves whether wave reflection is protective or not for the microvasculature. Furthermore, a number of limitations were proposed.

We agree that aging and hypertension might have influenced the relationship between RI and wave reflection with its effect on the microcirculation. To better elucidate the confounding effect of aging, we re-analyzed our data splitting the population along the median of age – that is, conveniently, 53.5 years. As expected, in the older subgroup all the correlations found in the whole of the population are confirmed and even stronger. However, no sign of an opposite trend is apparent in the younger subgroup, despite a reasonable hypothesis that the younger half would have a shorter duration of hypertension with less vascular damage and remodelling. We are aware that the conclusions drawn in our study cannot be extended to the general population or to populations with different cardiovascular risk, as acknowledged in the article (Stea, Sgro et al. 2013). Nevertheless, our study can give useful information about hypertensive patients coming from a daily life clinical setting, since this is a population in which changes in arterial function and structure have a crucial role. Second, given the continuous distribution of blood pressure values in the general population, it seems implausible that normo- and hypertensive subjects would have a completely opposite behaviour.

The cited studies by McDonnell et al. (2, 3) are of extreme interest, but comparisons or comments are difficult since the results were presented uniquely as abstracts. Nevertheless, despite retinal and renal RI are known to be correlated (4), some relevant differences should be acknowledged. Renal interlobar arteries are larger and their RI might mostly reflect global atherosclerotic burden and stiffness and pulsatility of large arteries (hence the correlation with PWV and central PP)(1, 5), while retinal arteries are smaller and further downstream in the circulation branching, thus their RI could more closely reflect structural damage and the real transmission of pulsatility to the microcirculation. However, the clinical significance of renal RI has been extensively documented, much more than that of retinal pulsatility (6, 7). We would also like to point out that in our study

results similar to those of RI were obtained when eGFR or UACR, established markers of hypertensive renal damage, were considered.

Furthermore, glyceril trinitrate has a distinct and peculiar effect on the pulse wave (8), but such high doses (500 mcg) (3) might have significant effects on global hemodynamics, so that they can't be considered only as a manipulation of wave reflection, an effect occurring at much lower doses (8).

We acknowledge that chronic antihypertensive treatment (9) may have differentially reduced the capacity of muscular arteries to dampen the highly pulsatile flow wave travelling through the system and reaching the peripheral microvasculature in organs with low resistance to flow. However, in our study we have shown similar results in the treated and untreated cohorts, and found no statistical significance of therapy in the multivariate analysis. We can add that, as mentioned above, the younger half doesn't show a different behaviour, and they have a lower proportion of treated subjects (chi-square P=0.014).

A noteworthy collateral finding in our cohort is also a positive correlation between reflection magnitude and age (R=0.36, p<0.001, without difference under or over 53.5 years). This finding, in accordance with previous studies (10), suggests that the known plateau shown plotting augmentation index against age is due to shifts in reflection sites rather than to a decrease of wave reflection with age.

Therefore, considering the limitations already acknowledged in our manuscript and those discussed here following the suggestion of McDonnell et al., we conclude that the hypothesis of peripheral wave reflection having a significant protective role for the microcirculation of low resistance vascular beds is still far to be proven. As already mentioned in our conclusions, studies with a combination of prospective design and examination of different vascular beds could possibly help, clarifying the cross-talk between the micro and macrocirculation and the pathophysiological role of wave reflections.

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