Aortic Stiffness Does Not Mediate the Relation Between Pulse Pressure and CRP

To the Editor:

Dr Yasmin et al have described a positive correlation between C reactive protein level and arterial stiffness in individuals selected at random from local general practice lists. From these data the authors suggest that inflammation may be involved in arterial stiffening. As quoted by Yasmin et al, we have reported in population based sample (891 subjects randomly selected from the electoral rolls whom 13% with treated hypertension), a positive correlation between pulse pressure and c reactive protein independent of carotid-femoral pulse wave velocity. This correlation remained after exclusion of patients with treated risk factors. Also, we showed in a post hoc analysis of a randomized trial (the REASON project) that the greater the decrease in pulse pressure, the greater the decrease in the proportion of patients with high c reactive protein levels. These results suggest that pulse pressure per se may modulate CRP secretion. There are several plausible mechanisms by which pulse pressure could increase inflammation levels, and in particular CRP levels, which provides a downstream integration of overall cytokines activation. Indeed, it has been demonstrated that shear stress was associated with increased production of reactive oxygen species and of cytokines such as tumor necrosis alpha or interleukin. Therefore, in addition to the hypothesis raised by Yasmin et al, our findings argue a causal relationship leading from pulse pressure to inflammation.

Jacques Amar
Jean Bernard Ruidavets
Jean Ferrieres

Hôpital Rangueil
INSERM 558
Toulouse, France


Pulse Pressure and CRP: An Inflammatory Issue

In response:

We thank Amar et al for their interest in our recent article demonstrating, for the first time, a relationship between inflammation and arterial stiffness in apparently healthy individuals. They revisit their own, as yet unproven, hypothesis, speculating that an increase in pulse pressure leads to inflammation, perhaps due to an increase in oxidative stress. Although we are grateful to Amar et al for highlighting this, we are somewhat unclear as to what their recent letter adds to the debate, because it appears to contain no new information, just that already presented in their previous article. Indeed, we were disappointed that Amar et al did not take the opportunity to extend their original analyses to determine more fully the factors influencing aortic pulse wave velocity (PWV). Moreover, the hypothesis that increased pulse pressure is proinflammatory was originally proposed by Schillaci et al, which Amar et al fail to cite.

We have taken this opportunity to investigate, retrospectively, the factors predicting C-reactive protein (CRP) levels in our own cohort, using stepwise multiple regression analysis. Interestingly, neither pulse pressure nor aortic PWV were independently correlated with CRP levels, which is contradictory to the data presented by Amar et al. One potential explanation for this discrepancy is the statistical approach used by Amar et al. As we have already noted, other explanations include the fact that 10% of patients studied by Amar et al were receiving antiinflammatory agents, 13% were being treated for dyslipidemia, and a further 13% were taking antihypertensive therapy. In contrast, we specifically excluded patients with cardiovascular disease or those receiving any medication.

These contradictory results clearly have the potential to inflame the issue further. Rather than do this on the basis of little supporting evidence, we would strongly suggest that what is now required is calm reflection and some well-designed mechanistic studies. Only this will advance the debate and potentially bring clinical benefit for our patients in the future.

John R. Cockcroft

Wales Heart Research Institute
University Hospital, Cardiff, UK

Yasmin

Clinical Pharmacology Unit, University of Cambridge
Addenbrooke’s Hospital, Cambridge, UK

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Jacques Amar, Jean Bernard Ruidavets and Jean Ferriere

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