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Response to Letter to the Editor

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Dear Editor

We would like to thank Drs Ugurlu and Egeli for their interest in our article and their relevant comments.

Several studies suggest that the soluble form of triggering receptor expressed on myeloid cells-1 (TREM-1) receptor engagement contributes to the pathology of both infectious and sterile inflammatory diseases. Recently, the role of TREM-1 in atherosclerosis development has been identified, promoting monocyte recruitment within the intima and increasing lipid uptake through up-regulation of CD36 expression. In addition, TREM-1 promotes deleterious post-ischaemic cardiac remodelling through the modulation of myeloid cell trafficking, specifically in ischaemic heart tissue. In the French registry of Acute ST-segment-elevation and non-ST-segment-elevation myocardial infarction (FAST-MI) cohort of nearly 1000 patients managed with acute coronary disease, plasma levels of sTREM-1 predicted the risk of 2 yr death, after adjusting for cardiovascular risk factors, treatments and C-reactive protein (CRP) levels.[1]

Moreover, in rheumatoid arthritis (RA), we recently showed that plasma levels of sTREM-1 correlated with disease activity (i.e. CRP levels) and also with clinical joint inflammation, suggesting a specific role in RA synovitis pathogenesis.[2] Nevertheless, as the authors pointed out, the implications of TREM-1 are extremely various, including septic shock, ischaemia/reperfusion injury, immuno-inflammatory conditions and cancer. The mechanisms that drives TREM-1 activation remain partially unknown.

Next, Ugurlu and Egeli suggest that age and sex may be potential confounding factors in our study. Such an hypothesis is supported by a recent study reporting a significant correlation between sTREM-1 levels and creatinine levels in myeloperoxidase anti-neutrophil cytoplasmic antibody-associated renal vasculitis and in acute community-acquired pneumonia.[3,4] However, in our study, increased levels of plasma creatinine and kidney failure may also reflect disease severity. Although we cannot exclude an impact of impaired renal function on serum sTREM-1 levels, it remains possible that the sTREM-1 level is an independent biomarker of amyloidosis. This finding needs to be confirmed in larger studies.

A positive relationship between age and serum sTREM-1 level has also been previously reported in patients with RA. We believe that such an association could also be explained by more severe systemic inflammation, as well as mild renal impairment in aged patients.

These challenging questions need to be further explored in the future in studies including a larger number of patients allowing multivariate analysis. Finally, a better understanding of the TREM-1 signalling pathway will help us to deepen our understanding of inflammatory disease pathophysiology in order to identify patients who may benefit from therapeutic strategies targeting TREM-1.

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