

LETTER TO THE EDITOR

Response to Letter by Drs. Mohammed Abbas, Maria Sessa, and Francesco Corea

To the Editor:

We thank Mohammed Abbas, Maria Sessa, and Francesco Corea for their interest in our manuscript. Dr. Mohammed Abbas and colleagues, in their letter to the journal, included important discussion points concerning our recent publication (Milio G et al., *Arch Med Res* 2006;37:342–347).

In our investigation and according to previous study (1,2), we have considered high IgG antibody levels as markers of previous infections. Accordingly, several cross-sectional investigations observed a relationship between Cp IgG seropositivity (3,4), HP IgG and CMV IgG and asymptomatic carotid atherosclerosis (5).

We would like to underline that patients included in our study were selected from a total number of about 1100 patients, all referred to our Unit of Cardiovascular Prevention for a clinical evaluation, but one potential confounding variable not evaluated in the present study that could influence our conclusions is the impact of socioeconomic status (SES). Unfortunately, we cannot address this issue definitively because the information related to SES was not obtained as part of the database.

However, several considerations make this possibility unlikely. First, most of the patients in this investigation lived in Palermo, which has a very ethnically homogeneous population primarily of European descent.

Moreover, all study participants had some degree of access to health care, as evidenced by the fact that all had, by definition, clinical evaluation at study inception; hence, extremes of SES probably play no role in outcome.

Regarding the ultrasonographic examination, we agree with Dr. Mohammed Abbas and colleagues that the assessment of IMT on three different approaches (anterior, posterior and lateral) for each studied segment (distal CCA, bifurcation, proximal ICA) is the correct procedure and this information must be clearly specified in the text.

Regarding the percentage of missing data, we observed that IMT in ICA is more difficult to visualize and the main disadvantage of including ICA IMT as the outcome measure is the potential for more missing data that in our study was about 38%.

We agree with Dr. Mohammed Abbas and colleagues that the functional resistive index (RI) is an important marker of atherosclerosis, but in our study a retrospective

analysis with risk factors is not applicable. Nevertheless, the present study suggested the existence of an association between increased carotid IMT and the presence of traditional cardiovascular risk factors or new emerging factors, including markers of infection and inflammation.

We confirmed the role of these emerging risk factors in another recently published work (6) where we showed a role of markers of infection and inflammation beyond traditional cardiovascular risk factors, in influencing the cardio- and cerebrovascular outcome in patients with early stages of atherosclerosis, such as in asymptomatic patients with carotid IMT. Infection may contribute to the process promoting vessel wall injury initiated by oxidized LDL, smoking-derived oxidants, hypertensive shear stress, or diabetes glyoxidized molecules. Inflammation and immune reactions in response to infections may exacerbate and act synergistically with all of the above-mentioned vasculotoxic factors. Further research, both *in vitro* and *in vivo*, is required to answer these questions. We confirm that flogosis and its mediators may have an important role in the pathogenesis of atherosclerosis and its complications perhaps by favoring instability or break of plaque. In fact, a common element of *Helicobacter pylori*, *Chlamydia pneumoniae* and cytomegalovirus infection and the atherosclerosis complications can be the chronic inflammatory and/or autoimmune conditions determined by these infections, as the release of cytokines and the activation of the coagulative cascade. Locally, a chronic flogosis can cause instability of plaque inducing thrombotic complications and interacting with traditional risk factors. Although antibiotic treatment of infections in CAD patients had no impact on mortality in large prospective trials, promising data are coming from smaller studies, and further studies are needed to investigate the possibility for this category of high-risk patients to undergo therapeutic approaches for primary prevention. Regarding inflammation, the available prospective data are highly consistent and provide strong evidence that inflammatory markers such as C-reactive protein and fibrinogen are independent risk factors for coronary disease. Moreover, clinical evidence relating inflammation to vascular risk complements a large body of basic laboratory and experimental studies demonstrating a fundamental role of inflammation in vascular disease. The strength of these observations suggests that ongoing work evaluating

therapies that interfere with the inflammatory component of atherosclerosis is a potentially important line of study.

References

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