Revista Portuguesa de Cardiologia 41 (2022) 811–812

Portuguese Society of CARDIOLOGY

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

LETTER TO THE EDITOR

Reply to Letter to the editor regarding the article: ''Inflammation and ischemic heart disease: The next therapeutic target?''

Resposta a Carta ao editor referente ao artigo: Inflamação e doença cardíaca isquémica: o próximo alvo terapêutico?

We would like to thank the author for the interesting comments regarding our review as well as for exploring several important topics concerning inflammation in ischemic heart disease (IHD), which are of relevance when addressing current data.[1,2] Notably, over the years the assessment of the pathophysiological mechanisms underlying the complex interplay between inflammation and IHD has been an area where remarkable progress has been made.[3] In this regard, we agree on the relevance of the role of the immune system as a potential major player.[3,4] While this point should be further underscored, there are still several hindrances concerning the immune response modulation, a highly promising albeit complex field where advances from other areas may help in unlocking its potential, as recently illustrated by Engelen et al.[4]

In terms of the use of biomarkers to assess inflammatory status in IHD patients, it should be further recalled that, as explored in our review, while some parameters (such as high-sensitivity C-reactive protein (hs-CRP)) have been instrumental in enabling a more comprehensive view of atherogenesis, their clinical impact in terms of therapeutic modulation is still not fully understood.[1,5] Indeed, and as expertly alluded to by the author, some of these caveats have been addressed in the European Society of Cardiology (ESC) guidelines, as well as in a dedicated contemporary review by the United States Preventive Services Task Force.[5,6] As detailed in our review, the fact that while in some studies (such as JUPITER and CANTOS) hs-CRP levels were present as an inclusion criterion and decreased in the intervention group, whereas in others (such as COLCOT) they were not, should also be mentioned.[1,7] Nonetheless, and while there is still a long road ahead, the insights provided by the assessment of these biomarkers should be acknowledged, as these have also increased the scope of our understanding of the interplay between cardiovascular disease (CVD) and other entities.[8,9] Interestingly, in terms of the inter-relationship between CVD and cancer, a topic where data have increasingly shown that shared risk factors should be considered, a study has reported an increased risk of cancer in smokers with CVD who had elevated hs-CRP levels, further showing the possible interest of these markers in the context of an integrative framework.[8,9]

We would also like to thank the author for the elegant remarks concerning different therapeutic approaches to inflammation in this setting. As discussed in our article, over recent decades there have been several pivotal steps in the quest for inflammatory modulation to reduce risk in IHD.[1,7] While we agree that, when compared to other settings across the cardiovascular continuum, translational progress in this specific area has been difficult and overshadowed by both uncertainties, as well as by the complexity brought about by breakthroughs in our basic understanding of the overall inflammatory response, some of the recent data from large randomized controlled trials have begun to enable us to gain a better understanding of the role of inflammatory modulation.[1,3,7,10,11] This paradigm shift is illustrated by the recently updated ESC guidelines on CVD prevention in clinical practice, which have incorporated the potential consideration of the use of low-dose colchicine in select high-risk individuals, as a class IIb (level A) recommendation.[5] While we agree that further data (especially long-term safety and overall side effects) are needed, and that there are still several important unaddressed issues in this field (as also discussed in the guidelines), these data could support a cautiously optimistic outlook in this setting.[5,12] Finally, and as mentioned above, we also view with great interest and attention the developments in the domain of immune modulation as a means for more personalized and possibly broader therapies for atherosclerotic disease.[2,4] Indeed, this could open the field up to vaccination approaches to CVD, somewhat changing the contemporary management paradigm of these diseases.[13,14] Of note, and while this perspective is also under study for other facets of CVD, there are still several issues which need to be addressed in this setting prior to potential clinical applications.[3,14–16]

As such, and while keeping in mind the myriad pitfalls in this field, as well as the diverse and protean hurdles which need to be crossed prior to the generalization of the present findings, current data support the role of inflammation not only in the pathogenesis of IHD, but also as a potentially valuable therapeutic strategy.[3–5] The coming years will be of paramount importance in the definition of the relative role

https://doi.org/10.1016/j.repc.2022.07.001

of these interventions in the integrated pragmatic approach to risk reduction in IHD.

Conflicts of interest

The authors have no conflicts of interest to declare.

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