Comment on: Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis

Sir, Salvarani et al. [1] recently published an article on risk factors for severe cranial ischaemic events (CIEs) in GCA. Some words of caution are warranted regarding the results of the study and their interpretation.

First, 33/38 included patients (87%) with CIE had visual loss, mostly due to anterior ischaemic optic neuritis. These patients largely outweigh those with cerebrovascular accidents and whether the results apply to the latter is unknown. Hence, this work should be viewed as a study on risk factors for visual loss, rather than CIE, in GCA.

Secondly, it is especially worrying to read a claim of causation in the second key message, stating that ‘anti-platelet or anti-coagulation therapy did not reduce the risk of cranial ischaemic events in GCA’. The positive association between anti-thrombotic therapy and CIE probably reveals the unsurprising fact that antecedent diseases treated with anti-thrombotic agents are associated with an increased risk of thrombotic events.

Likewise, the conclusive causal statement that ‘a lower inflammatory state appears to contribute to the development of severe CIE in GCA’ is premature. Elderly patients without visual loss need cranial symptoms, systemic manifestations or unexplained inflammation in order to suspect GCA. It was therefore expected that these features would be more prevalent in the group of patients without visual loss at diagnosis.

Thirdly, the discussion and the first key message focus on the results of the multivariable analysis, which should be interpreted very cautiously. The multivariable model was built on 120/180 patients at most, because CRP levels were available for only 16/38 patients (42%) with CIE and 104/142 patients (73%) without CIE. We are not informed if patients with CRP results were similar to those without CRP results and why much fewer CRP results were available for patients with CIE than for those without. Moreover, with only 16 patients available in the CIE group and four predictor variables, this logistic regression model is far from having the required 10 outcome events for each predictor variable [2]. These issues threaten the validity of the multivariable analysis.

Even if these methodological concerns are ignored, the authors should have concluded that no variable was associated with CIE in multivariate analysis since all P-values are >0.05. The lack of statistical significance should have precluded any discussion on the clinical meaning of these results.

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Comment on: Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis: reply

Sir, We have read with interest the comments of Steichen on our article [1]. Cerebrovascular accidents are a rare complication of GCA. Hence, as several studies have done previously we considered cerebrovascular accidents and visual loss together. We agree that visual loss represents the main contributor of cranial ischaemic events (CIEs) in our cases, but we are also convinced that cerebrovascular accidents are part of the spectrum of cranial ischaemic events and they should be considered together with visual loss. Furthermore, because of their rare occurrence, it is difficult to identify an adequate number of cases with cerebrovascular accidents for a separate analysis in a population-based study.

We observed that patients treated with anti-platelet/anti-coagulation therapy had a higher risk of developing GCA-related severe CIEs, differently from two recent retrospective studies that found that anti-platelet/anti-coagulation therapy reduced the risk of CIEs [2, 3].

We agree that the increased risk observed in our study may in part be related to the fact that antecedent diseases treated with anti-thrombotic agents are associated with an increased risk of thrombotic events. However, the three studies were similarly planned, and anti-platelet/anti-coagulant therapy was administered before GCA diagnosis for similar medical conditions. Therefore we consider appropriate our second key message stating that ‘anti-platelet or anti-coagulation therapy did not reduce the risk of CIEs in GCA’, which reflects the results of our study in comparison to the different results of the two studies mentioned above.

Several studies have clearly shown that a low inflammatory response is associated with a higher risk of developing severe CIEs, as our study also found [4, 5]. Patients with cranial signs/symptoms, but not with systemic manifestations, usually have a high diagnostic suspicion of arteritis [6].

We agree that the results of the multivariable analysis should be interpreted cautiously however, although the P value was at the limit of significance, the very high OR appeared to validate our results. Furthermore, the results of multivariable analysis were supported by the analysis of categorical data using chi-square test.

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1 Steichen O. Comment on: Risk factors for severe cranial ischaemic events in an Italian population-based cohort of patients with giant cell arteritis. Rheumatology 2009;48:1180.


