Comment
Retinal macroaneurysm are localised dilatations of retinal arterioles. Hypertensive women in the sixth or seventh decade have a predilection. The most common clinical symptom is decline in central visual acuity due to retinal oedema, exudation or haemorrhage.[5] Direct laser photocoagulation of the macroaneurysm may be considered if the lipid exudates coming from it threaten the fovea. Treatment when haemorrhage is present is fraught with difficulties.

The present case would not have benefited from laser photocoagulation due to the severity of macular oedema and presence of retinal haemorrhages. Although spontaneous resolution is known occur, in the present case, bevacizumab might not only have hastened the decrease in retinal thickness but also provided superior visual outcome. Intravitreal bevacizumab is also well tolerated and no adverse effects were observed. The results observed in this case are provocative and require additional investigation.

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Sir,

Plasma metalloproteinase-9 in age-related macular degeneration

Chau *et al*[1] described raised plasma metalloproteinase-9 (MMP-9) in age-related macular degeneration (ARMD), hypothesising that if atherosclerosis and ARMD share a common mechanism, then systemic MMP-9 and MMP-2 may be increased in patients with ARMD. While it is a plausible hypothesis, it is unclear why they have not tested it in a simple cross-sectional analysis of two groups—one with ARMD but no atherosclerosis and another group with atherosclerosis but no ARMD. Instead, each of their three sample groups includes patients with or without a history of symptomatic atherosclerosis (eg, myocardial infarction) as well as risk factors (eg, hypertension). This is pertinent as cardiovascular disease and its risk factors substantially affects MMP levels.[2,3]

The authors state 'no statistically significant differences in clinical data related to atherosclerosis were observed between subjects in the three groups included in the study'. As they offer no statistical test or data in support of this statement, it is unclear to us how they can make this assertion. The authors provide no power calculation to assure the reader that the risks of statistical error types 1 and 2 have been addressed and minimised, given the small numbers in each subject group. We wonder whether in fact the failure to find a difference between data sets is because of a small number error (ie, false negative).

Chau *et al*[1] choose to present their data as SEM, which denies the reader a simple estimate to the distribution of the data—many would argue that the correct measure of variance is SD.[4] One of their results is a mean of 740 ng/ml with SE 494 ng/ml. We submit that these data are likely to have a strong non-normal distribution and so convention states that it should be presented as median and interquartile range. We wonder which other indices also have a non-normal distribution, which could be determined by a test of statistical normality (eg, the Anderson–Darling test). The importance of distribution is that it governs the method of analysis. Differences in three or more data sets with a normal distribution should be sought using analysis of variance (ANOVA), as the authors have used. However, if their data contain at least one data set with a non-normal distribution, then the correct analysis would be a test such as the Kruskall–Wallis test. In addition, neither ANOVA nor the Kruskall–Wallis test tell us of differences between individual groups. A *post hoc* test is necessary to probe for such intergroup differences should have been performed; student's *t*-test is inappropriate. We will appreciate it if the authors can provide these analyses, as well as a power calculation.

While we do not doubt the accuracy of the raw data derived from the plasma, we have difficulty with their analysis and presentation of the results. They may find a different story with their data, the findings of which could be important.

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Sir,

Reply to Drs Blann and Lip

We would like to thank Drs Blann and Lip for their interest in our paper.[1] We believe that the association of atherosclerosis and age-related macular degeneration (AMD) is a complex one,[2] it is likely that they share a common mechanism but local factor might dictate the final disease process. It is possible that they share similar risk factors. The suggestion of a cross-sectional analysis of the two groups, one with AMD but without atherosclerosis and one with atherosclerosis but no AMD, suffers selection bias and it is not practically possible to say who are without atherosclerosis, at least in an eye clinic. In our study design, we included consecutive patients and normal controls, using a medical questionnaire to correct, for potential alternations in MMP levels. As the method of acquisition is identical, it reduces bias and also allowed us to study the interaction of atherosclerosis and AMD.

The rest of the concern of Drs Blann and Lip was on our statistical analysis. The mere reason that there are so many different statistical tests is that no one can really agree on the best test to be used in different circumstances. Although I do agree with their comments, the threefold increase of MMP-9 levels in AMD patients will be significant, no matter how you want to analyse the data.

As for the specific comment, the statistical analysis of the clinical data was summarised in Table 1 in the published paper. This is a pilot study as the number of patients was small, as we have mentioned in the original paper, and we need a larger study (which is underway) to confirm our findings and the current data set has allowed us to perform more accurate study size calculation.

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