Letters to the Editors

Comments on the giant cell arteritis probability score

Sirs,
We reviewed the probability score for giant cell arteritis (GCA) (1) with interest and present the following queries and alternatives:

1. The dataset with 23 GCA cases out of 122 patients is small. Is not overfitting of the model a strong possibility, especially since 17 predictors were employed?

2. The scoring system arbitrarily assigns integer values to each predictor, but the predictors are not of equal importance. (Fig. 1). The incremental risk of continuous variables such as age and C-reactive protein, and binary variables such as sex may not be appropriately represented by single unit integer changes.

3. The information for the probability score is to be provided by general practitioners. At the time of referral, alternative pathologies may not be known. We wonder if fever or the symptoms of polymyalgia rheumatica are specific enough to be weighed identically with the other more robust criteria. It may be difficult for a general practitioner to differentiate fever of unknown origin from GCA from low-grade infection or lymphoma. It may be problematic for a general practitioner to distinguish polymyalgia rheumatica from fibromyalgia, osteoarthritis flare, or rotator cuff syndrome.

4. The manual addition of 17 data items is not easier compared to entering the data on a risk calculator via smart phone or computer terminal at the point of care (https://goo.gl/THCnuU).

5. Future iterations of the probability score can incorporate the guidelines for the transparent reporting of a multivariable prediction model for individual prognosis of diagnosis (TRIPOD) (2).

Two prediction rules (3, 4) have recently been published with 5 to 13X more GCA cases. These TRIPOD-compliant, multicentre studies examined consecutive temporal artery biopsies of patients referred from rheumatology, ophthalmology as well as primary care. Age and bloodwork values were maintained as continuous variables to improve statistical power. These studies found that:

i) Platelets were a strong predictor of GCA, compared to C-reactive protein or erythrocyte sedimentation rate (Fig. 1).
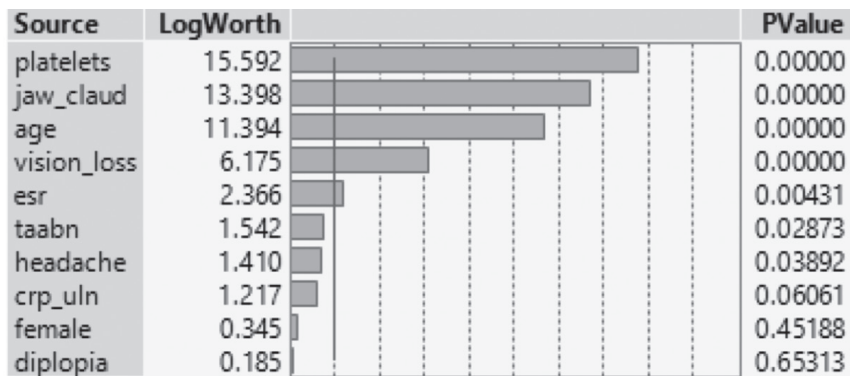

Fig. 1. The relative importance of predictor variables for giant cell arteritis from a logistic regression analysis of 1,201 patients undergoing temporal artery biopsy and 300 biopsy-proven cases.
The logworth statistic is defined as the –log (p-value). Typically, if the logworth is greater than 2, then the variable is considered important in the statistical model.
jaw_claud: jaw claudication; taabn: temporal artery tenderness or pulselessness; esr: erythrocyte sedimentation rate in millimeters/hour; crp_uln: C-reactive protein divided by its upper limit of normal.

ii) Age had an exponential risk curve past 65 years of age (https://docs.google.com/document/d/1wM5oTTsE1MuvSEchQRRmFj49IJxNQKPkIjyihamCM4s/edit?usp=sharing) which is not adequately expressed in the GCAPS proforma.

iii) Gender was not a statistically significant risk factor for GCA. Women did not have a higher risk for GCA on multivariable analysis.

Doppler ultrasound (US) of the temporal artery may detect the mural inflammation or luminal changes of GCA, but requires high quality studies, and expertise in interpretation. Conway et al. recently reported that US had a sensitivity of 53% and specificity of 72% for the clinical diagnosis of GCA (5). They emphasised that the interpretation of ultrasound results requires knowledge of the performance characteristics in the target population.

In closing we appreciate that no prediction algorithm for GCA is foolproof. However, combining the pretest probability from an externally validated prediction model for biopsy-proven GCA with US, or perhaps non-invasive ocular blood flow tests (5), or future genetic markers may improve the accuracy of risk stratification.

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