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Comment on

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Published in:
Rheumatology advances in practice

DOI:
[10.1093/rap/rkac041](https://doi.org/10.1093/rap/rkac041)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2022

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

van Nieuwland, M., Brouwer, E., Neuman, L. M., van Bon, L., & Alves, C. (2022). Comment on: Validation of the Southend giant cell arteritis probability score in a Scottish single-centre fast-track pathway. *Rheumatology advances in practice*, 6(2), [rkac041]. <https://doi.org/10.1093/rap/rkac041>

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Letter to the Editor (Matters arising from published papers)

Rheumatology Advances in Practice 2022;00:1–2
<https://doi.org/10.1093/rap/rkac041>
Advance Access Publication 19 May 2022

Comment on: Validation of the Southend giant cell arteritis probability score in a Scottish single-centre fast-track pathway

DEAR EDITOR, We read with interest the publication by Melville *et al.* [1] on the external validation of the GCA probability score (GCAPS). This article reflects the greatly needed external validation of the GCAPS, which was originally developed by Laskou *et al.* [2]. The GCAPS might aid in pre-test identification of patients with a high risk for GCA. The authors of the current publication emphasize the ability of the GCAPS to exclude patients referred with a low risk of GCA, according to the GCAPS, from further diagnostic workup as one of their key messages. We would like to comment on this article as we gathered data that indicate using these risk stratification groups with more caution.

In our cohort regarding external validation, we found the receiver operating characteristics (ROC) curve as well as the risk stratification proposed by Sebastian *et al.* [3–5]. Our EULAR abstract was cited by the authors of the current publication [1, 4]. The retrospective cohort consisted of 135 patients suspected of GCA who had their diagnostic workup in our fast-track clinic. Similar to the current article, our results showed good discrimination of the GCAPS, with an area under the ROC curve of 0.83 (interquartile range 0.75–0.91). Also, the prevalence of GCA increases from low- to high-risk groups. However, in contrast to the current publication, not all GCA cases were exclusively classified as intermediate and high risk using risk stratification criteria as proposed by Sebastian *et al.* Our results show that 5 of 40 (12.5%) patients with a final diagnosis of GCA were classified as low risk (GCAPS <9). The optimal cut-off value (maximum combined sensitivity and specificity) also differs between cohorts (≥ 13 vs > 10.5 in our cohort). In the original Southend Hospital cohort, the optimal cut-off value was > 9.5 [2].

While it is undesirable to overlook GCA patients given the risk of severe complications, unnecessary diagnostic workup should also be avoided, considering healthcare costs and distress for elderly patients. Therefore there is a need for a proper trade-off when determining the cut-off value to exclude GCA patients. The authors suggest to adopt a GCAPS binary cut-off based on the low-risk category for accepting or rejecting referrals for specialist

review, as none of the patients in their cohort with GCAPS <9 were diagnosed with GCA. However, when using this cut-off in our cohort to exclude GCA, 12.5% of GCA cases would be wrongfully classified as non-GCA. Differences in risk stratification and cut-off values could be attributed to different patient populations and to varying incidences of GCA between countries [6]. Furthermore, referral procedures in different countries influence the diagnostic workup of suspected GCA patients. To illustrate this, the NHS Lanarkshire clinical practice, where the validation study by Melville *et al.* [1] was conducted, rejected 30% of referrals following telephone consultation on the grounds of clinical implausibility, and therefore the GCAPS algorithm was not tested on all patients referred to the clinic. It might be possible that GCA patients with an atypical presentation were overlooked. These patients would probably classify as low risk in the GCAPS. For example, 5% of GCA patients have normal levels of inflammatory markers in the Netherlands and a varying percentage of normal levels are found worldwide [7, 8]. Furthermore, GCAPS modifications might influence the stratification of patients, as the parameter extracranial artery abnormalities was not available in our cohort. However, this variable was not associated with GCA, as described in the current publication by Melville *et al.* [1].

GCAPS can be an excellent tool to prioritize fast referral and diagnostic workup for patients suspected of GCA by stratification into risk groups. Differences between cohorts illustrate that the binary cut-off value based on low-risk stratification by Sebastian *et al.* should not instantly be used to exclude GCA broadly in practice. The particular GCAPS cut-off value of <9 could be relevant to exclude GCA in the NHS Lanarkshire clinical practice and Southend Hospital, as none of the patients in the low-risk group in these separate studies ultimately had GCA [1, 5]. However, varying incidences and referral strategies likely impact the application of risk stratification in different populations and countries. We propose caution when using the risk stratification as a way to exclude patients from further diagnostic workup in other populations than described in the NHS Lanarkshire clinical practice and Southend Hospital. We would advise taking into account the underlying incidence and referral strategies when implementing risk stratification based on the GCAPS.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement

The data underlying this article will be shared upon reasonable request to the corresponding author.

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Accepted 22 March 2022

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