Supplementary Online Content

De Lott LB, Burke JF; Michigan Neuro-Ophthalmology Research Consortium. Use of laboratory markers in deciding whether to perform temporal artery biopsy. *JAMA Ophthalmol*. Published online February 5, 2015. doi:10.1001/jamaophthalmol.2014.5861.

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Statistical Analysis

ESR was adjusted for patient age and sex because ESR is known to be higher in women and increases with age even in normal individuals.[1] The upper limit of normal for ESR was generated using the following formulas:

Women: (Age + 10) / 2

Men: Age/2

Descriptive statistics for patient characteristics were calculated and differences by TAB result were assessed using bivariate logistic regression for continuous and categorical variables. Multiple imputation using chained equations was used to address the issue of missing CRP (n=98), platelet (n=101), and ESR (n=15) observations, because relying only on complete-case analysis can lead to biased estimates of regression coefficients and standard errors in a multiple logistic regression model in the context of missing data.[2, 3] CRP and adjusted ESR were imputed using a series of logistic regression models, and platelets were imputed using a series of ordinary least squares regression models with sex, age, biopsy result, and institution as additional independent variables. Using this approach, 50 imputed data sets were generated and summary estimates were generated using conventional techniques.

eAppendix 2. Supplemental Discussion

When optimally integrated, there are certain situations in which CRP, platelets, and age may notably influence risk and biopsy decisions for individual patients. The predictions outlined in eTable 4 are not meant to represent exact individual risk predictions for these 2 hypothetical patients, but instead to emphasize this point. For example, according to this model, the risk of biopsy-proven GCA in a 60 year old woman with elevated ESR and platelets, but a normal CRP,

is 16.4%. Risk increases slightly to 24.5% if CRP is elevated. Although this is interesting information, many would argue that both patients should be biopsied because a 16% or 25% chance of missing this diagnosis is too high when weighed against the risk of harm if the patient is untreated.

More compelling is that in the same 60 year old woman with an elevated ESR and CRP, the risk of GCA might be 8% or nearly 25% depending on whether or not her platelets are elevated. If the 60 year-old woman in this example were a person with uncontrolled diabetes or multiple co-morbidities, the risk of empiric treatment with corticosteroids and/or biopsy might outweigh an 8% risk of GCA, but not a 25% risk. Furthermore, if she were 80 years old with an elevated ESR, elevated CRP, and normal platelets, the risk of biopsy-proven GCA would be more than twice that of a 60 year-old woman with the same laboratory results. Understanding how these individual factors may influence risk is important in making appropriate treatment decisions for individual patients.

eReferences

1. Miller A, Green M, Robinson D. Simple rule for calculating normal erythrocyte sedimentation rate. *British medical journal (Clinical research ed.)*. 1983;286:266
2. Rubin DB. Multiple imputation after 18+ years. *Journal of the American Statistical Association*. 1996;91:473-489
3. Cummings P. Missing data and multiple imputation. *JAMA pediatrics*. 2013;167:656-661

eTable 1. Temporal artery biopsy result by institution (n=404).

Study site, n (%)	Positive (n=90)	Negative (n= 314)
Ann Arbor	25 (23.2)	83 (76.9)
Michigan City	1 (10.0)	9 (90.0)
Bethesda	4 (57.1)	3 (42.9)
Ramat Gan	9 (36.0)	16 (64.0)
Jerusalem	5 (38.5)	8 (61.5)
Baton Rouge	3 (23.1)	10 (76.9)
Marshfield	38 (17.5)	179 (82.5)
Lexington	5 (45.5)	6 (54.6)

eTable 2. Missing data by temporal artery biopsy result.

Missing Variable	Temporal artery biopsy result	
	Positive, n=90 (% of total positive)	Negative, n=314 (% of total negative)
ESR	5 (5.6)	10 (3.2)
CRP	10 (11.1)	88 (28.0)
Platelet count	18 (20.0)	83 (26.4)

eTable 3. Multiple logistic regression model predicting temporal artery biopsy result using imputed adjusted ESR, CRP, and platelet count (n=404).

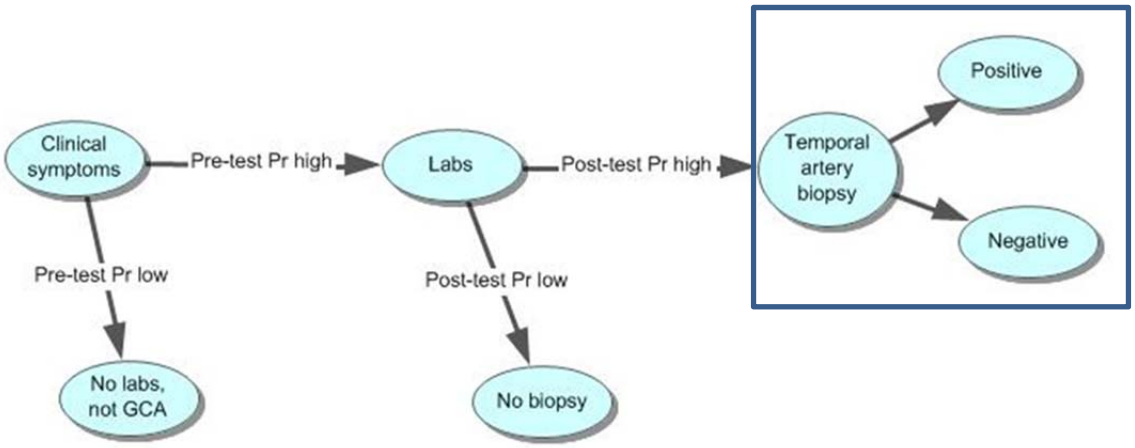
Covariate	OR (95% CI), *P* value
Age	1.06 (1.04, 1.08), *P*<0.001 for 1 year increase
Female	0.75 (0.41, 1.38), *P*=0.35
Adjusted ESR	1.10 (0.79, 1.53), *P*=0.56
Platelets	1.01 (1.00, 1.01), *P*<0.001 for 1 K/mm3 increase
CRP	1.55 (0.92, 2.63), *P*=0.10

eTable 4. Predicted probabilities of biopsy-proven giant cell arteritis for 2 hypothetical women with elevated erythrocyte sedimentation rate.

	Baseline predicted probability % (95% CI)[a]	CRP	Platelet count (K/mm3)	Predicted probability % (95% CI)
60 year old	5.0 (0.6, 9.5)	↑	200	8.2 (3.1, 13.3)
		↑	450	24.5 (12.4, 36.5)
		↓	200	5.1 (0.3, 10.0)[b]
		↓	450	16.4 (4.8, 28.1)
80 year old	13.7 (4.4, 23.1)	↑	200	21.1 (7.0, 35.3)
		↑	450	49.3 (32.4, 66.2)
		↓	200	14.0 (0.6, 27.4)[b]
		↓	450	37.2 (16.9, 57.5)

[a]Predicted probability of biopsy positive giant cell arteritis based on age and sex, assuming non-elevated erythrocyte sedimentation rate and CRP, with platelet count = 200 K/mm3.
[b]Predicted probability of biopsy positive giant cell arteritis assuming elevated erythrocyte sedimentation rate only
↑= "elevated" and ↓="not elevated" for dichotomous variables; CRP= C-reactive protein

eFigure. Conceptual Model



After accounting for clinical signs/symptoms (pre-test probability) and laboratory results (post-test probability), only those patients with a post-test probability deemed high enough to warrant temporal artery biopsy (TAB) were included in this study (box). Pr = probability.