RESEARCH LETTER

LESS IS MORE

Evaluating the PEN-FAST Clinical Decision-making Tool to Enhance Penicillin Allergy Delabeling

Patient-reported penicillin allergy is associated with inappropriate prescribing, antibiotic resistance, and adverse outcomes.[1] Various clinical decision-making tools for penicillin allergy have been developed to guide antibiotic selection and delabeling strategies,[1-3] yet further validation is required to promote their use. PEN-FAST is a clinical decision-making tool with a high negative predictive value (NPV) that can identify patients with low-risk penicillin allergy who do not require skin testing prior to oral penicillin challenge.[1] We aimed to validate PEN-FAST in risk stratification of reported penicillin allergies at a large tertiary health care system outside of the country in which it was developed to further promote PEN-FAST use and enhance global penicillin allergy delabeling.

Supplemental content

Methods | A retrospective medical record review was performed for nonpregnant patients with reported penicillin allergies who underwent penicillin allergy testing from October 9, 2020, to July 7, 2022, in allergy and immunology outpatient clinics of a large US tertiary referral health care system. The Yale University institutional review board approved the study and waived the requirement for informed consent because the data were deidentified. This cohort study followed the STROBE reporting guideline.

Allergy testing consisted of skin prick and intradermal testing with oral challenge after skin testing or direct oral challenge (DC) without skin testing. The PEN-FAST (eFigure in Supplement 1) scores were compared with outcomes based on positive penicillin allergy test results, which were defined as positive skin test results or allergic reaction to oral challenge within 60 minutes. Sensitivity, specificity, NPV, and positive likelihood ratio were calculated for each PEN-FAST score in predicting penicillin allergy, and the area under the receiver operating characteristic curve was calculated to assess overall diagnostic performance. Data were analyzed using Stata, version 14.2 (StataCorp).

Results | The study included 120 patients (median [IQR] age, 54 [37.3-67.0] years; 95 females (79.2%). Direct challenge was performed in 16 patients (13.3%) (**Table 1**). Patients who received DC had PEN-FAST scores of 0 (5 patients [4.2%]) or 1 (11 patients [9.2%]), and none had immune- or nonimmune-mediated reactions. Eighty-eight patients (73.3%) had PEN-FAST scores of 2 or less, indicating low risk, and all had negative test results. Four patients (3.4%) had positive penicillin test results: 2 had positive skin test results (PEN-FAST score, 3), and 2 had negative skin test results but failed oral challenges (PEN-FAST scores, 3 and 5). In predicting penicillin allergy, PEN-FAST scores of 2 or less had sensitivity, specificity, NPV, and a positive likelihood ratio of 100% (95% CI,

Table 1. Clinical Characteristics of Patients With Penicillin Allergy Evaluation and Testing Outcomes According to PEN-FAST Scores

Characteristic	Patients, No. (%) (N = 120)	Tested positive on PEN-FAST, No. (%)	Tested negative on PEN-FAST, No. (%)
Age, median (IQR), y	54 (37.3-67.0)	NA	NA
Female, No. (%)	95 (79.2)	NA	NA
History of atopy, No. (%)	73 (60.8)	NA	NA
Asthma	28 (23.3)	NA	NA
Allergic rhinitis	48 (40.0)	NA	NA
Atopic dermatitis	3 (2.5)	NA	NA
Hymenoptera venom allergy	2 (1.7)	NA	NA
Food allergy	27 (22.5)	NA	NA
Penicillin skin testing, No. (%)	104 (86.7)	NA	NA
Oral challenge, No. (%)	118 (98.3)	NA	NA
Oral challenge following skin test	102 (85.0)	NA	NA
Direct oral challenge	16 (13.3)	NA	NA
PEN-FAST score			
0	21 (17.5)	0	21 (17.5)
1	60 (50.0)	0	60 (50.0)
2	7 (5.8)	0	7 (5.8)
3	30 (25.0)	3 (2.5)	27 (22.5)
4	0	0	0
5	2 (1.7)	1 (0.8)	1 (0.8)

Abbreviation: NA, not applicable.

Table 2. Performance of Each PEN-FAST Score in Predicting Penicillin Allergy

Performance Measure	Cutoff PEN-FAST score				
	0 vs 1-5	0-1 vs 2-5	0-2 vs 3-5	0-3 vs 4-5	0-4 vs 5
Sensitivity, % (95% CI)	100 (39.8-100)	100 (39.8-100)	100 (39.8-100)	25.0 (0.6-80.6)	25.0 (0.6-80.6)
Specificity, % (95% CI)	18.1 (11.6-26.3)	69.8 (60.6-78.0)	75.9 (67.0-83.3)	99.1 (95.3-100)	99.1 (95.3-100)
Positive predictive value, % (95% CI)	4.0 (1.1-10.0)	10.3 (2.9-24.2)	12.5 (3.5-29.0)	50.0 (1.3-98.7)	50.0 (1.3-98.7)
Negative predicative value, % (95% CI)	100 (83.9-100)	100 (95.5-100)	100 (95.9-100)	97.5 (92.7-99.5)	97.5 (92.7-99.5)
Positive likelihood ratio (95% CI)	1.22 (1.12-1.33)	3.31 (2.51-4.37)	4.14 (3.00-5.72)	29.00 (2.18-385.17)	29.00 (2.18-385.17)
Negative likelihood ratio (95% CI)	0	0	0	0.76 (0.43-1.33)	0.76 (0.43-1.33)
Accuracy, % (95% CI)	20.8 (14.0-29.2)	70.8 (61.8-78.8)	76.7 (68.1-83.9)	96.7 (91.7-99.1)	96.7 (91.7-99.1)

39.8%-100%), 75.9% (95% CI, 67.0%-83.3%), 100% (95% CI, 95.9%-100%), and 4.14 (95% CI, 3.00-5.72), respectively (**Table 2**). The area under the receiver operating characteristic curve was 0.88 (95% CI, 0.84-0.92).

Discussion | Penicillin allergy is a public health issue; however, less than 10% of reported penicillin allergy is confirmed by formal testing.[4] Clinical decision-making tools encourage the use of penicillin allergy evaluations and DC with greater frequency and accuracy. This study focused on PEN-FAST, a user-friendly tool that has been successfully validated, with an NPV of 93% to 100%.[1,5] Our study showed PEN-FAST had an NPV of 100% in identifying patients with a low-risk penicillin allergy history who could safely proceed to DC and ultimately penicillin allergy delabeling.

Other tools have been developed to risk stratify patients with penicillin allergy. However, some of these tools are limited by their generalizability and lack of external validation.[3,6] A benefit of PEN-FAST is its simplicity, which allows for greater use among allergists and potentially primary care clinicians, particularly in areas without easy access to allergists.

Limitations of this study include its retrospective design, referral bias, and single study site. The findings support those of a previous study[1] and subsequent validation in a European single-center study,[5] and advocate for the use of PEN-FAST as an accurate clinical decision-making tool to enhance penicillin allergy evaluations and promote greater use of direct penicillin challenge.

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