Evaluating a Penicillin Allergy Clinical Decision-Making Tool to Enhance Penicillin Allergy De-labeling

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Background

- Patient-reported penicillin allergy is associated with
  - inappropriate prescribing
  - increased antibiotic resistance
  - adverse patient outcomes
- 95-98% of patients with documented penicillin allergy were de-labeled after testing
- PEN-FAST is a clinical decision-making tool that consists of three clinical criteria:
  - time from penicillin allergy (2 points for ≤ 5 years)
  - phenotype (2 points for anaphylaxis, angioedema, or severe cutaneous reaction)
  - treatment required (1 point for any treatment required)
- A score of ≤2 has been shown to have a 95-100% negative predicative value in predicting positive penicillin allergy testing results

Objective

We aim to further validate the PEN-FAST tool in risk stratifying reported penicillin allergies for penicillin allergy de-labelling.

Questions

Does a low PEN-FAST score (≤2) have a high specificity and negative predictive value to predict tolerance to penicillin per testing?

Methods

- Study design: retrospective cohort study
- Patient population: patients with reported penicillin allergies who underwent penicillin allergy testing from 10/9/2020-7/10/2022 at a single tertiary-referral healthcare system
- PEN-FAST scores were compared to testing results
- Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, and accuracy was calculated for each PEN-FAST score (0-5) in predicting positive penicillin testing results
- Data was analyzed using STATA, version 14.2 (StataCorp)

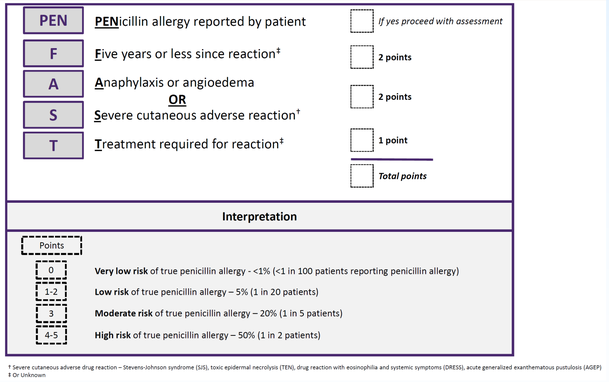

Figure 1: The PEN-FAST Clinical Decision-Making Tool
a. Includes unknown
b. Forms of severe cutaneous adverse reactions include potential Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis. Patients with a severe delayed rash with mucosal involvement should be considered to have a severe cutaneous adverse reaction

Results

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)

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

	Cutoff PEN-FAST score				
Performance Measure	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)

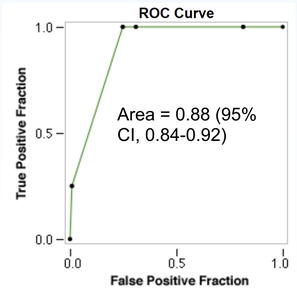

Figure 2: Area Under the Receiver Operating Curve of PEN-FAST Score in Predicting Positive Penicillin Allergy

Summary

Penicillin allergy is a public health issue; however, less than 10% of reported penicillin allergy is confirmed by formal testing.

Clinical decision-making tools encourage the use of penicillin allergy evaluations and direct oral challenge (DC) with greater frequency and accuracy. Various 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.

This study focused on PEN-FAST, a user-friendly tool that has been successfully validated, with an NPV of 93% - 100%. Its simplicity allows for greater use among allergists and primary care clinicians.

Our study showed a PEN-FAST score of ≤2 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 de-labeling.

Limitations

- Retrospective design
- Referral bias
- Single study site

Conclusions

DC are underutilized in penicillin allergy evaluations despite most histories being low risk in tested patients. A PEN-FAST score of ≤2 is associated with a high negative predictive value in our cohort and can be used to encourage DC and enhance penicillin allergy de-labeling.