

Reliability of skin test results when read at different time points

Sara Marian Seibert, M.S.,¹ Tonya S. King, Ph.D.,² David Kline, M.S.,² Cathy Mende, C.N.P.,³ and Timothy Craig, D.O.³

ABSTRACT

Percutaneous skin testing to determine allergies is usually read 15–20 minutes after placement, but the time to reading may be prolonged because of clinic duties or emergencies. The objective of the study was to compare skin-prick testing (SPT) wheal and flare reactions at 10, 30, and 40 minutes with the standard 20 minutes to determine if extended time from placement to reading skin tests interferes with clinical significance. Fifty-three subjects undergoing routine aeroallergen SPT for allergy symptoms were tested with allergen extracts, histamine, and a negative control solution. Based on these results, SPTs can be read up to 40 minutes after placement but are more reliable when read between 20 and 30 minutes after placement. Skin testing to determine IgE-mediated or immediate hypersensitivity can be read up to 30 minutes without significant loss of reliability.

(Allergy Asthma Proc 32:203–205, 2011; doi: 10.2500/aap.2011.32.3436)

ImmEDIATE hypersensitivity skin testing is commonly used to clinically assess patient sensitivity to antigens to determine triggers causing allergic symptoms.^{1,2} Skin-prick tests (SPTs) are usually placed and the immediate reaction (wheal and erythema) is read within 15–20 minutes of placement. However, because of clinical care responsibilities and emergencies reading is often deferred until much later or may be performed before 15 minutes. Previous literature has identified various operator-controlled variables in skin testing including allergen extract concentration, skin test device, interpretation methodology, and result documentation.^{3,4} The literature still has to address if variation in time to SPT reading compromises the validity of the test. It is the aim of this study to determine if skin tests are still reliable to use as clinical data at 10, 30, and 40 minutes in comparison with the standard 20 minutes.

METHODS

Study Design

Eligible participants in the prospective observational study were patients scheduled to undergo routine skin testing at the Penn State Milton S. Hershey Medical Center Outpatient Allergy Clinic from June 30, 2009 to August 7, 2009. All were aged ≥ 18 years, had no dermatographia, and had a positive reaction to the positive control SPT (Duo Tip-Test II; Lincoln Diagnos-

tics, Decatur, IL). The study was approved by the Penn State Human Subjects Protection Office.

Subject Population

The study group consisted of 57 volunteers (16 men and 41 women) between the ages of 19 and 82 years (mean age, 36 years [SD, ± 13.9 years]). Four patients were excluded because of dermatographia.

Study Protocol

A panel of 38 standard aeroallergens was used including 10 trees (American elm, birch mix, red alder, red oak, box elder, white ash, cottonwood eastern, red mulberry, hickory/pecan mix, and black walnut pollen), 3 grasses (grass mix, Bermuda grass, and Timothy grass), 6 weeds (ragweed, dock/sorrel mix, Russian thistle, lamb's quarter, pigweed, and English plantain), 10 animal allergens (feather mix, cockroach mix, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat hair, dog epithelia, dog hair, mouse epithelia, rat epithelia, and ladybug), and 9 molds (*Alternaria alternata*, *Cladosporium/Hormodendrum*, *Penicillium notatum*, *Aspergillus fumigatus*, *Helminthosporium solani*, *Epicoccum nigrum*, *Fusarium* mix, *Cephalosporium acremonium*, and *Stemphylium solani*). Additional food allergens were tested based on the patient's individual clinical need.

Percutaneous skin testing was performed according to previously established clinical methods.⁵ Test sites containing allergen extracts were compared with a positive and negative control, histamine (10 mg/mL) and glycerinated saline, respectively. The forearm test site was cleansed with alcohol and allowed to dry. The test sites were marked, and tests were placed 5-cm apart. Duo-Tip Test II lancets were used to puncture the epidermis and expose it to the standard allergen and selected allergen food extracts. The tests were measured at 10, 20, 30, and

From the ¹College of Medicine, ²Department of Public Health, and ³Section of Allergy Asthma and Immunology, Penn State University, Hershey, Pennsylvania

The authors have no conflicts to declare pertaining to this article

Address correspondence and reprint requests to Timothy Craig, D.O., Section of Allergy Asthma and Immunology, Department of Medicine, Penn State University, 500 University Drive, Hershey, PA 17033

E-mail address: tcraig@psu.edu

Copyright © 2011, OceanSide Publications, Inc., U.S.A.

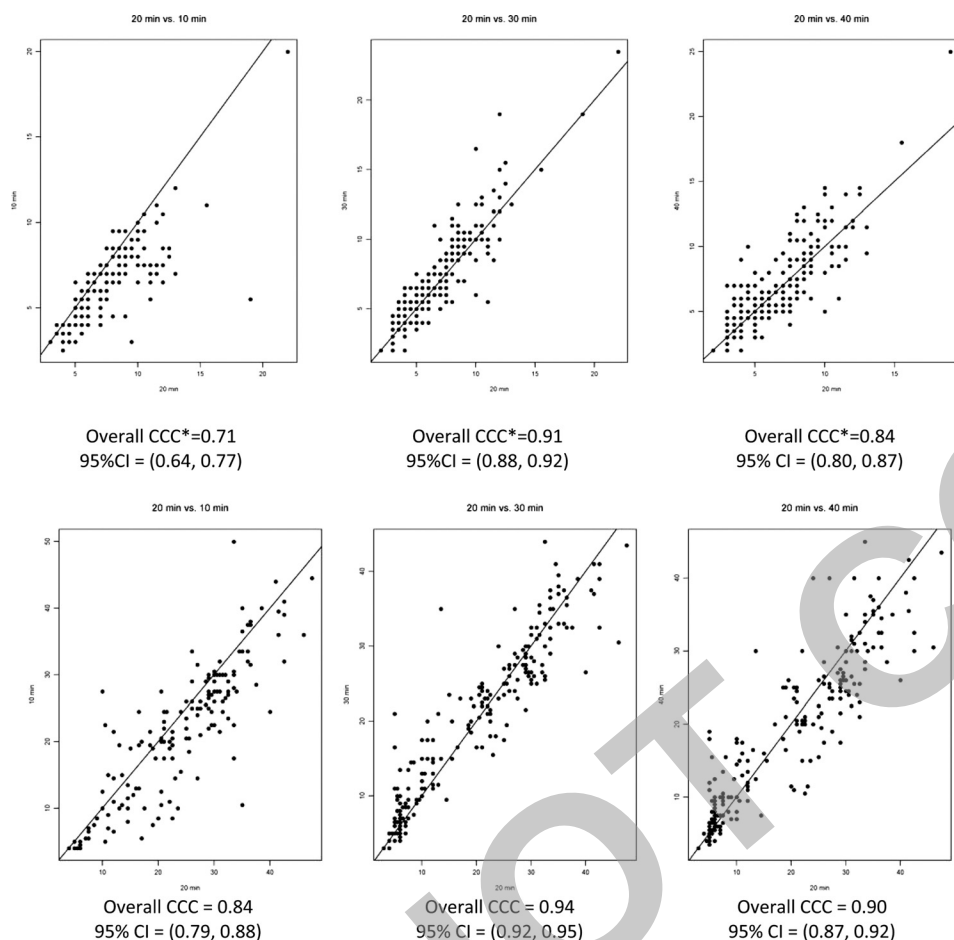


Figure 1. Concordance correlation coefficient for wheal measurements comparing 20 minutes versus 10 minutes, 20 minutes versus 30 minutes, and 20 minutes versus 40 minutes.

40 minutes after placement. Mean wheal and flare diameters were calculated (sum of the longest diameter and the perpendicular diameter divided by two). In patients with a positive control (≥ 3 mm greater than the negative control), a mean wheal that was at least 3 mm greater than the negative control was interpreted as a positive SPT to that allergen. Skin tests were placed, read, and measured by the same investigator.

Statistical Analysis

To assess agreement among multiple time points, the concordance correlation coefficient (CCC) and 95% confidence interval (CI) were calculated between the paired measurements for the wheal measurements and the flare measurements. Three comparisons were evaluated: 20 minutes versus 10 minutes, 20 minutes versus 30 minutes, and 20 minutes versus 40 minutes after skin test placement (Figs. 1 and 2). The CCC was interpreted as follows: (<0.50 , poor agreement; $0.50-0.75$, moderate agreement; $0.75-0.90$, good agreement; >0.90 , excellent agreement).

To evaluate the changes in the wheal and flare sizes over time, the average differences between the measurements at each time point were assessed. Repeated measures analysis of variance (RMANOVA) models were fit to the wheal and

flare sizes, and then the model-adjusted pair-wise comparisons between the time points were evaluated.

RESULTS

Comparison paired wheal measurements at 20 minutes versus 10 minutes yielded moderate agreement (CCC, 0.71; CI, 0.64, 0.77; $p < 0.001$), at 20 minutes versus 30 minutes there was excellent agreement (CCC, 0.91; CI, 0.88, 0.92; $p < 0.001$), and at 20 minutes versus 40 minutes there was good agreement (CCC, 0.84; CI, 0.80, 0.87; $p < 0.001$; Fig. 1).

Comparison paired flare measurements at 20 minutes versus 10 minutes yielded good agreement (CCC, 0.84; CI, 0.79, 0.88; $p < 0.001$), at 20 minutes versus 30 minutes there was excellent agreement (CCC, 0.94; CI, 0.92, 0.95; $p < 0.001$), and at 20 minutes versus 40 minutes there was good agreement (CCC, 0.90; CI, 0.87, 0.92; $p < 0.001$; Fig. 2).

Repeated measures analysis of variance models indicated that the average size of the wheal measurements at 20 minutes is not significantly different from 10 minutes ($p = 0.33$), 30 minutes ($p = 0.42$), or 40 minutes ($p = 0.93$) based on a statistically significant value of $p = 0.05$. Similarly, the average size of the flare measurements at 20 minutes is not significantly differ-

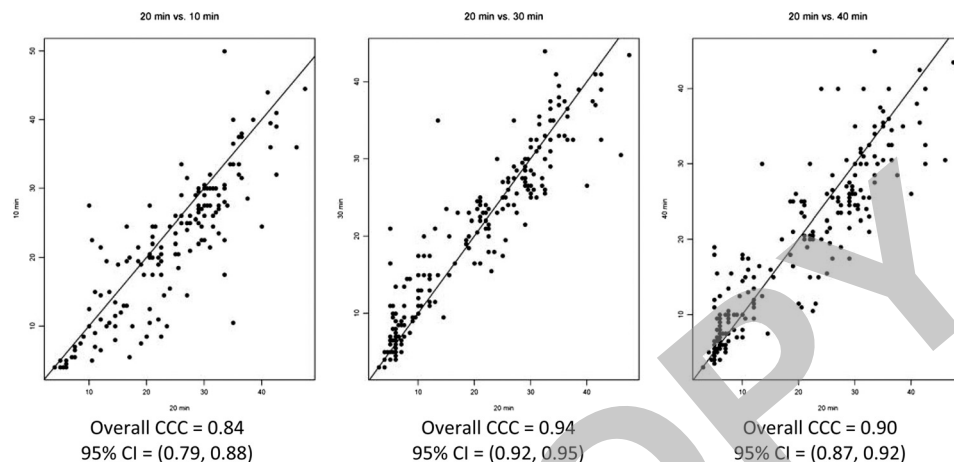


Figure 2. Concordance correlation coefficient for flare measurements comparing 20 minutes versus 10 minutes, 20 minutes versus 30 minutes, and 20 minutes versus 40 minutes.

Table 1 Model-adjusted mean changes between time points: RMANOVA

Outcome	Time (min)	Model-Adjusted Mean Size (SE)	Comparison	Average Difference (SE)	Paired <i>t</i> -Test <i>p</i> Value
Wheal	10	6.3 (0.3)	20–10	0.25 (0.3)	0.33
	20	6.5 (0.3)	20–30	−0.18 (0.2)	0.42
	30	6.7 (0.3)	20–40	0.02 (0.2)	0.93
	40	6.5 (0.3)			
Flare	10	23.3 (1.3)	20–10	−1.77 (1.0)	0.07
	20	21.5 (1.2)	20–30	0.15 (0.9)	0.87
	30	21.3 (1.2)	20–40	1.54 (0.9)	0.08
	40	19.9 (1.2)			

RMANOVA = Repeated measures Analysis of Variance.

ent from 10 minutes ($p = 0.07$), 30 minutes ($p = 0.87$), or 40 minutes ($p = 0.08$; Table 1).

DISCUSSION

This study was designed to compare the immediate hypersensitivity reaction to SPT at 20 minutes after placement with the reaction at 10, 30, and 40 minutes to assess the congruence of the readings. Reading the SPT at 30 minutes resulted in excellent agreement with the SPT read at 20 minutes for both flare and wheal readings. At 40 minutes the reading was in good agreement with the SPT findings at 20 minutes for both wheal and flare reactions. The 10-minute reading indicated moderate agreement for wheal and good agreement for flare reaction. This indicates that if an emergency or clinical duties do not permit the operator to read the SPT at 20 minutes, the test can still be read at 30 minutes with excellent agreement, but that correlation between time points decreases if the SPT is read earlier at 10 minutes or later at 40 minutes.

Furthermore, the results from the RMANOVA are in agreement with the conclusions from the CCC analysis and indicate that there were no statistically significant differences between readings at the 20-minute time point and the additional three time points. This study

shows that clinical SPTs can be placed and read up to 40 minutes later, but it is more reliable to read the SPTs between 20 and 30 minutes.

It is our hope that these data will reduce pressure on the clinician during busy times in the clinic to read skin tests at the exact time designated by the practice parameter,⁶ which is 15–20 minutes. Even outside this time interval skin tests can be read with reliable outcomes and assessed to help determine appropriate care of the allergic patient.

REFERENCES

- Petersson G, Dreborg S, and Ingestad R. Clinical history, skin prick test and RAST in the diagnosis of birch and timothy pollinosis. *Allergy* 41:398–407, 1986.
- Adinoff AD, Rosloniec DM, McCall LL, and Nelson HS. A comparison of six epicutaneous devices in the performance of immediate hypersensitivity skin testing. *J Allergy Clin Immunol* 84:168–174, 1989.
- Nelson HS. Variables in allergy skin testing. *Immunol Allergy Clin North Am* 2:281–290, 2001.
- Oppenheimer MD, and Nelson HS. Skin testing: A survey of allergists. *Ann Allergy Asthma Immunol* 96:19–23, 2006.
- Dolen WK. Skin testing techniques. *Immunol Allergy Clin North Am* 21:273–279, 2001.
- Bernstein IL, and Storms WW. Practice parameters for allergy diagnostic testing. *Ann Allergy* 75:543–625, 1995.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.