

RESEARCH NOTE

A prospective analysis of allergy skin-prick test wheal size association with symptom severity

Lucia S. Ryll BS¹ | Matthew L. Rohlfing MD² | Samuel J. Rubin MDMPH² |
Jennifer Lauver RN² | Michael P. Platt MDMSc^{1,2} | Christopher D. Brook MD^{1,2}

¹ Boston University School of Medicine, Boston, Massachusetts, USA

² Department of Otolaryngology–Head and Neck Surgery, Boston Medical Center, Boston, Massachusetts, USA

Correspondence

Christopher D. Brook MD, Boston Medical Center, 800 Harrison Ave, BCD 5th floor, Boston, MA 02118, USA.

Email: Chris.Brook@bmc.org

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KEYWORDS

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INTRODUCTION

Allergic rhinitis (AR) affects 10% to 30% of people in the United States, and its prevalence worldwide is rising.^{1,2} AR has significant economic impact, accounting for 2.5% of clinical visits in the United States. In addition to respiratory tract symptoms, AR is associated with anxiety, depression, fatigue, and irritability. Given these impacts, it is crucial that allergy tests are evaluated to ensure proper interpretation and treatment planning.

Percutaneous skin-prick testing (SPT) has been widely validated and has comparable sensitivity and specificity to immunoglobulin E (IgE) blood testing³; however, SPT has variable interpretation.

A common misconception among patients and clinicians is the assumption that wheal size correlates with allergic symptom severity. Several studies have demonstrated a correlation between wheal size and serum IgE levels, but neither have been shown to be predictive of symptom severity or quality of life.^{4–6} Using SPT wheal size to approximate a patient's allergic severity can lead to inaccurate avoidance counseling and misguided clinical decision making. For patients experiencing severe symptoms requiring allergen immunotherapy, clinicians may underestimate the possibility of anaphylaxis to allergens that produced a smaller wheal. This study aims to determine whether there is a correlation between wheal size

and allergy symptoms as measured by multiple patient-reported outcome measures. The authors hypothesize that previously published retrospective analyses will be confirmed in this novel, prospective investigation.

METHODS

Study population

This study was approved by the Institutional Review Board at Boston Medical Center (BMC). Adult patients who presented to the Otolaryngology–Head and Neck Surgery Clinic at BMC between January 1, 2017 and November 1, 2020 for in vivo percutaneous SPT were offered enrollment. Patients were excluded if they did not understand English or Spanish, were pregnant, or were <18 years old.

Study design

Subjects received percutaneous in vivo testing using the Multi-Test II PC application device (Lincoln Diagnostics, Decatur, IL, USA) on the volar forearm. Extracts were obtained from ALK-Abello (Hørsholm, Denmark) and subjects were tested with a variety of common allergens,

TABLE 1 Descriptive analysis of allergy skin-prick testing results

Outcome measure	Mean	95% CI of mean	Median	Range
Average wheal size for positive allergens (mm)	8.4	7.9–8.9	8.0	4.01–6.7
Number of positive skin-prick tests	6.3	5.4–7.1	5	1–21
Maximum wheal size (mm)	12.8	11.6–14.0	12	4–35

Abbreviation: CI, confidence interval.

TABLE 2 Linear regression analysis of allergy skin-prick testing variables and various patients reported outcome measures

Allergy skin-prick testing outcomes	Rhinitis Control Assessment Test		Mini Rhinoconjunctivitis Quality of Life Questionnaire				Voice Handicap Index		22-item Sino-Nasal Outcome Test	
	Regression coefficient (R^2)		Regression coefficient (R^2)		Regression coefficient (R^2)		Regression coefficient (R^2)		Regression coefficient (R^2)	
	p		p		p		p		p	
Average wheal size for positive allergens	0.021	0.233	0.009	0.305	0.005	0.462	0.005	0.528		
Number of positive skin-prick tests	<0.001	0.921	0.002	0.616	0.002	0.616	0.03	0.104		
Maximum wheal size	0.018	0.143	0.004	0.498	0.009	0.3	0.013	0.296		

with histamine as a positive control and glycerin as a negative control. Patient-reported outcome measures recorded included Voice Handicap Index (VHI), Rhinitis Control Assessment Test (RCAT), mini Rhinoconjunctivitis Quality of Life Questionnaire (mRQLQ), and the 22-item Sino-Nasal Outcome Test (SNOT-22).

Data analysis

Positive testing was defined as a wheal size of ≥ 3 mm. Mean positive wheal size, number of positive responses, and maximum wheal size were determined. Linear regression analysis was performed with SPSS, version 23.0 (IBM, Armonk, NY, USA). Statistical significance was considered $p < 0.05$.

RESULTS

A total of 118 subjects had positive skin-prick allergy testing. The most common allergens were to dust mites *Dermatophagoides farinae* ($n = 78$, 66.1%) and *Dermatophagoides pteronyssinus* ($n = 70$, 59.3%). The mean number of positive allergens per patient was 6.3. Mean $\pm$ standard deviation (SD) wheal size was 8.4 ± 2.7 mm (Table 1).

Linear regression analysis revealed no significant correlations between wheal size variables and patient questionnaires (Table 2).

DISCUSSION

The SPT is an accurate and reliable method for identification of patients with allergic sensitization.⁷ However, this novel prospective study shows that SPT wheal size cannot be used to predict symptom severity or quality of life in patients with environmental allergies.

Similar to these findings, Tatar et al.⁴ found no correlation between SPT wheal size and symptom scores in 150 patients with AR. Radcliffe et al.⁵ retrospectively analyzed 91 patients with seasonal rhinoconjunctivitis and found that neither SPT wheal size nor SPT conjunctival provocation tests could predict symptom severity or mRQLQ scores.

In contrast, Souille et al.⁸ assessed 59 asthmatic children with skin prick test, serum IgE (RAST), and bronchial provocation test and found a moderate concordance (<68%) between the three tests. Similarly, Bryant et al.⁹ found a significant correlation between the degree of bronchial and cutaneous allergic reactivity in 153 asthmatic patients. These findings suggest that SPT may be more predictive of bronchial reactivity to inhalant allergies; however, more recent studies in asthmatic patients have shown that SPT does not correlate with asthma symptom severity or control.¹⁰

Although SPT positivity is correlated with presence of elevated serum IgE levels, neither correlates with symptom severity.³ Radcliffe et al.⁵ proposed that skin testing may not be representative of symptom response because the skin is not the primary organ involved in aeroallergen

diseases. Still, studies evaluating insect venom-allergic patients, where the skin is the initial involved organ, also show that neither SPT wheal size nor serum IgE levels were predictive of allergic severity.⁶ These findings indicate that severity of an allergic reaction is likely not solely dependent on the early phase response involving IgE antibody production and mast cell degranulation causing wheal formation. In patients with chronic AR, repetitive exposure to airborne allergens may induce a prolonged late-phase reaction with resident mast and T cells localized to the upper airway, which may influence the severity of the clinical response independent of mast cells involved in early phase degranulation during SPT.

Allergic disease has significant quality of life and economic impacts, and its prevalence is increasing. Therefore, it is crucial to evaluate diagnostic tools to ensure proper interpretation and disease management. Although SPT has been widely validated as an accurate and cost-effective test,⁷ our study and others have shown its accuracy is limited to the identification of allergic sensitization only and cannot be used as a surrogate for allergic symptom severity.^{4–6}

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CONFLICT OF INTEREST

Nothing to report.

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