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Ovomucoid Is Not Superior to Egg White Testing in Predicting Tolerance to Baked Egg

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Abstract

BACKGROUND—Children with egg allergy may tolerate baked egg products. Ovomucoid specific IgE (sIgE) antibody levels have been suggested to predict outcomes of baked egg challenges.

OBJECTIVE—We determined the relationship of ovomucoid and egg white sIgE levels and egg white skin prick test (SPT) wheal size with baked egg challenge outcome.

METHODS—Retrospective review of 1186 patients who underwent ovomucoid sIgE blood testing. Subset analysis was of 169 patients who underwent baked egg food challenges.

RESULTS—Egg white sIgE, ovomucoid sIgE, and egg white SPT were different among those eating regular egg, eating baked egg only, or avoiding all egg ($P < .001$ for all). One hundred forty-two of 169 patients (84.0%) passed baked egg challenges. We were able to establish >90% predictive values for passing baked egg challenge for egg white sIgE, ovomucoid sIgE, and egg white SPT. No patient with egg white SPT wheal <3 mm failed a baked egg challenge. Receiver operating characteristic curve analysis of egg white sIgE, ovomucoid sIgE, and egg white SPT showed areas under the curve of 0.721, 0.645, and 0.624, respectively. No significant difference was observed among these immunologic parameters in their abilities to predict baked egg challenge outcome ($P = .301$).

CONCLUSION—Most children with egg allergy in this study passed baked egg challenges. Ovomucoid sIgE, although a useful clinical predictor of baked egg tolerance, was not superior to egg white SPT or sIgE in predicting outcome of baked egg challenge.

Keywords

Egg allergy; Baked egg; Heated egg; Ovomucoid; Egg white; Food challenge

Hen's egg allergy is a common cause of childhood food allergy, affecting 1% to 2% of children,[1–3] and is the most common food allergy in children with atopic dermatitis.[4,5] Although most children will develop tolerance to egg, children are outgrowing their egg

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allergies at later ages than previously reported.[6] Recent evidence suggests that 70% to 80% of children with egg allergy tolerate baked egg products.[7–10] Tolerance to baked egg may be achieved more rapidly than to regular egg.[11] Chileren with egg allergy who regularly consume baked egg may outgrow their egg allergies earlier than those strictly avoiding egg.[12] Immunologic changes in children incorporating baked egg into their diets include decreased egg protein specific IgE (sIgE) levels and skin prick test (SPT) wheal diameters and increased egg protein specific IgG_4 levels.[10,12]

Egg white contains >20 glycoproteins, with ovomucoid, ovalbumin, ovotransferrin, and lysozyme identified as the main allergens. Although ovalbumin is the most abundant protein in egg white, ovomucoid is the dominant allergen. Exposing proteins to high temperatures through baking reduces allergenicity by destroying conformational epitopes. In addition, allergenicity may be decreased by blocking epitope access through interaction with other food proteins, such as in a wheat matrix in a baked muffin or cupcake.[13] The importance of ovomucoid as an allergen may be related to its stability against heat and digestion with proteinases.[14]

Several studies have reported the importance of ovomucoid sIgE in predicting baked egg tolerance.[10,15–18] Further, Ando et al[15] suggested that ovomucoid sIgE was superior to egg white sIgE in predicting the outcome of heated egg challenge. Taken together, these studies suggest that measurement of sIgE to the heat-stable allergen, ovomucoid, may be an important diagnostic tool in predicting baked egg tolerance. We sought to determine whether ovomucoid sIgE was a superior predictor of tolerance to baked egg.

METHODS

Study design

A retrospective chart review was performed of all patients who underwent blood testing for ovomucoid sIgE at Boston Children's Hospital during an 18-month period from April 2010 through September 2011. Egg white SPT results, total IgE, egg white sIgE levels, clinical history, demographics, and food challenge outcomes were obtained through medical record review. Current egg ingestion practice at the time of ovomucoid sIgE blood test was determined by physician-documented parental report. Current egg ingestion practice was the result of physician recommendation, prior food challenge outcome, or patient-initiated food avoidance or introduction. Patients were excluded from analysis of egg ingestion practices and food challenge outcomes if they had eosinophilic esophagitis (EoE), because the significance of IgE sensitization to foods in EoE is not well understood.[19] The study was approved by the Institutional Review Board of Boston Children's Hospital.

Allergy evaluation

SPT were performed according to previously published methods[20] with the use of the Multi-Test device (Alk-Abello, Round Rock, Texas) and commercially prepared extracts (Greer Laboratories, Lenoir, NC). Control tests for SPT were performed with histamine (positive control) and normal saline (negative control). Wheal diameters were measured 15 minutes after the skin test was placed, in a standard fashion.[20] A SPT wheal diameter at least 3 mm larger than the negative control was considered positive.[21]

Serum samples were analyzed for sIgE with the use of an ImmunoCAP fluorescence enzyme immunoassay (Thermo Scientific, Portage, Mich). The lowest limit of detection of the assay was 0.35 kU/L, and the highest limit of detection was 100 kU/L.

Oral challenge

Food challenges were performed as open challenges, either under physician supervision at Boston Children's Hospital or at home. Blood and SPT results were obtained within 1 year before the food challenge or, in cases of some failed challenges, the most recent result after challenge failure, medians (interquartile range) 2.28 (−1.56 to 6.13) and 2.30 (−1.41 to 6.02) months, respectively. In the case of a negative number, the blood or SPT result was obtained a given time after a failed challenge. One hundred sixty-seven of 169 patients (98.8%) challenged to baked egg had a history of prior allergic reactions to egg (either baked or regular) documented in the medical record by an allergist and/or egg sensitization, as determined by a positive SPT or elevated serum sIgE. Two patients challenged to baked egg had negative egg protein sIgE and SPT and no prior history of ingestion but had evaluation performed because of personal history of other food allergies.[21] We elected to include patients who were avoiding egg due to atopic dermatitis in our analysis, because testing for food allergies in children with atopic dermatitis is reasonable in specific circumstances.[21]

Patients were considered for baked egg challenge in clinic if egg white SPT wheal was <35 mm and ovomucoid sIgE was <4.00 kU/L, based on previously suggested guidelines.[8] Patients were considered for baked egg challenge at home if egg white SPT wheal was <7 mm and ovomucoid sIgE was <1.00 kU/L.[8,15] Patients with a history of anaphylaxis to baked egg within the past 2 years or unstable asthma were not recommended for food challenges. However, the decision for ordering and determining location (clinic or home) of the food challenge was ultimately at the discretion of the ordering allergist. The physician-supervised baked egg challenge was performed in a standard fashion according to previously published methods.[8,10] Parents were instructed to prepare muffins or cupcakes at home according to a protocol that our clinic provided. The recipe contained two large eggs, including both egg white and yolk. Each muffin or cupcake contained one-third of an egg (approximately 2.2 g of egg protein). The muffins or cupcakes were baked at 350°F in an oven for 30 minutes. A standard graded open food challenge consisted of increasing increments every 15 minutes of one-eighth (275 mg), one-fourth (550 mg), and five-eighths (1375 mg) muffin or cupcake, totaling 2.2 g of egg protein. For home challenges, parents were instructed to introduce baked egg in a manner similar to the clinic challenge protocol.

For physician-supervised challenges, patients were monitored throughout and for 30 to 60 minutes after the completion of the challenge. Challenges were discontinued at the first objective sign of reaction,[21] and treatment was initiated at the discretion of the supervising physician. Home challenges were terminated, and treatment was initiated at the discretion of the parent.

Statistical analysis

Outcome of oral food challenge was used as the "gold standard" by which performance characteristics (sensitivity, specificity, positive predictive value [PPV], and negative predictive value [NPV]) were calculated. The PPV refers to an egg white sIgE, ovomucoid sIgE, or egg white SPT level above which it is a given percentage likely that a patient will react and therefore have a failed food challenge outcome. The NPV refers to a level below which it is a given percentage likely that a patient will not react and therefore have a passed food challenge outcome.[22] Receiver operating characteristic (ROC) curve analysis was used to determine a threshold that would differentiate subjects who were allergic or tolerant to baked egg. The relationship between SPT or sIgE and food challenge outcome was analyzed with logistic regression. Fitted predicted probability curves were plotted with results from the logistic regression.

The strength of association between variables was analyzed with the Spearman correlation coefficient. Continuous variables were analyzed with the Wilcoxon rank sum test.

Dichotomous variables were analyzed with the Pearson's χ^2 or Fisher's exact test, as appropriate. Areas under ROC curves were compared with the use of an algorithm suggested by DeLong et al.[23] A P value <.05 was considered statistically significant.

RESULTS

Features of the ovomucoid database

We conducted a search of all ovomucoid sIgE measurements performed during our study period and identified 1373 individual blood draws, and 1268 had clinical information available in the written medical record (Figure 1). On review of the medical record, we determined the current egg ingestion practices at the time of the ovomucoid sIgE blood test for the 1186 patients with clinical information available and without EoE. The age at the time of ovomucoid sIgE blood test for these 1186 patients was between 0.15 and 23.15 years (median, 4.70 years). Many of these patients had other atopic conditions: 47.8% had asthma, 76.8% had atopic dermatitis, 41.7% had allergic rhinoconjunctivitis (ARC), and 91.6% had other physician-diagnosed food allergies.

On the basis of review of the medical record, we identified patients who underwent oral food challenges to baked egg, the challenge locations (home or clinic), and challenge outcomes (Figure 1).

Correlation of ovomucoid sIgE with egg white sIgE level

We examined the correlation between ovomucoid and egg white sIgE levels for the 1356 blood draws for which ovomucoid and egg white sIgE were performed at the same time (see Figure E1 in this article's Online Repository at www.jaci-inpractice.org). Ovomucoid and egg white sIgE levels were highly correlated (Spearman correlation coefficient = 0.814; P < .001). Although ovomucoid is one of many egg white proteins,[14] 8.3% (n = 113) patients had ovomucoid sIgE levels that exceeded their corresponding egg white sIgE levels, consistent with another report.[24]

Association of blood and skin testing results with egg ingestion practice

Egg white sIgE, ovomucoid sIgE, and egg white SPT were highly associated with egg ingestion practice at the time of ovomucoid sIgE blood test (P < .001 for all) (Figure 2). The higher the levels, the less likely the patient was to be tolerating any form of egg. Total IgE was lower in patients eating regular egg compared with baked egg only (P < .001) and eating regular egg compared with avoiding all egg (P < .001). However, no difference was observed in total IgE between patients eating baked egg only and patients avoiding all egg (P = .189).

Outcomes of oral food challenges

Baseline clinical characteristics and immunologic parameters were analyzed relative to baked egg challenge location (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Compared with patients challenged at home, patients challenged in clinic were older (P < .001) and more likely to have diagnoses of asthma (P = .009) and ARC (P = .013). No difference was observed in sex, diagnoses of atopic dermatitis or other food allergies, or symptoms at first reported egg reaction. Patients challenged in clinic had larger egg white SPT wheals (P < .001) and higher total IgE (P = .034) than patients challenged at home. No differences were observed among egg white or ovomucoid sIgE.

One hundred forty-two of 169 patients (84.0%) passed baked egg challenges. Baseline clinical characteristics were analyzed relative to baked egg challenge outcome (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). No difference was observed in age at the time of challenge, sex, or symptoms at first reported egg reaction. Eighty-one of 86 patients (94.2%) avoiding egg due to atopic dermatitis had atopic dermatitis as the only initial symptom. The remaining five patients also reported immediate cutaneous reactions with egg exposure. Seventy of 81 patients (86.4%) had egg exclusion recommended in the setting of atopic dermatitis, without clear atopic dermatitis flaring after egg ingestion. Eleven of 81 patients (13.6%) had atopic dermatitis flaring presumed secondary to egg ingestion. Among the 81 patients avoiding egg due to atopic dermatitis, no significant difference was observed in baked egg challenge outcomes according to presence or absence of atopic dermatitis flaring presumed secondary to egg ingestion ($P = .371$).

Patients with a diagnosis of asthma were more likely to fail a baked egg challenge ($P = .047$). Of patients who failed baked egg challenges, 3 of 5 (60.0%) who met criteria for anaphylaxis had a diagnosis of asthma and 15 of 22 (68.2%) who did not meet criteria for anaphylaxis had a diagnosis of asthma ($P = .999$). None of the two patients treated with epinephrine had a diagnosis of asthma. Diagnoses of other atopic conditions were not associated with food challenge outcomes. Symptoms or treatments administered during baked egg challenge failures did not differ significantly by challenge location (see Table E3 in this article's Online Repository at www.jaci-inpractice.org). Most of the allergic reactions during baked egg challenge failures resolved without treatment (66.7% of challenge failures, n = 18). Five patients (18.5% of challenge failures, 3.0% of challenges overall) met criteria for anaphylaxis.[25] Two patients (7.4% of challenge failures, 1.2% of challenges overall) were treated with intramuscular epinephrine. The details of reactions fulfilling criteria for anaphylaxis and/or requiring epinephrine are described subsequently.

One patient had anaphylaxis with cutaneous and gastrointestinal symptoms that self-resolved. Three patients had anaphylaxis with gastrointestinal and upper airway symptoms; one did not require treatment and two were treated with oral diphenhydramine. A fifth patient with anaphylaxis had upper and lower airway symptoms of tongue pruritus, hoarse voice, and wheezing and was also treated with epinephrine. The second patient treated with epinephrine developed upper airway symptoms of sneezing, conjunctivitis, repeated throat clearing, and sensation of throat tightness. These two patients treated with intramuscular epinephrine were also given oral diphenhydramine and oral prednisolone with resolution of symptoms, were electively transferred to the emergency department for monitoring, and discharged home after 4 hours of observation without symptom recurrence.

Ability of blood and skin testing results to predict outcome of baked egg challenge

Egg white sIgE, ovomucoid sIgE, and egg white SPT levels were significantly lower in subjects who passed baked egg challenges, compared with subjects who failed (Table I). Total IgE level was not predictive of baked egg challenge outcome.

Although egg white and ovomucoid sIgEs were significantly associated with baked egg challenge outcome ($P < .001$ and $P = .003$, respectively), patients with egg white and ovomucoid sIgEs <0.35 kU/L failed baked egg challenges. Two patients with both egg white and ovomucoid sIgE <0.35 kU/L failed baked egg challenges; however, both had positive egg white SPTs. No other patients with egg white sIgE <0.35 kU/L failed baked egg challenges. In addition to the two patients with ovomucoid sIgE <0.35 kU/L described above, seven more patients with ovomucoid sIgE <0.35 kU/L failed baked egg challenges. However, these seven patients had elevated egg white sIgE and positive egg white SPTs. Egg white SPT wheal was also significantly associated with baked egg challenge outcome ($P = .035$), and no patient with egg white SPT wheal <3 mm failed a baked egg challenge.

Probability curves for passing baked egg challenges based on egg white sIgE, ovomucoid sIgE, and egg white SPT were generated (Figure 3, *A*–*C*). ROC curve analysis for egg white sIgE, ovomucoid sIgE, and egg white SPT revealed areas under the curve (AUCs) of 0.721, 0.645, and 0.624, respectively (Figure 3, *D*). No significant difference was observed among the AUCs ($P = .301$).

We identified >90% predictive values for passing baked egg challenges (>90% NPV) for egg white sIgE of 6.00 kU/L, ovomucoid sIgE of 0.35 kU/L, and egg white SPT wheal of 11 mm (Table II). Predictive values >90% for failing baked egg challenges (>90% PPV) could not be established. However, >95% specificity, proposed by some as a positive decision point above which challenge should not be considered,[15] was established for egg white sIgE of 9.65 kU/L, ovomucoid sIgE of 3.38 kU/L, and egg white SPT wheal of 25 mm.

DISCUSSION

We found that measurement of ovomucoid sIgE may aid in predicting outcomes of baked egg challenge, but it is not superior to measurement of egg white sIgE and SPT and should not replace these other valuable diagnostic tests. To our knowledge, this retrospective study of 169 baked egg challenges is the largest reported to date and one of the few studies to evaluate the utility of ovomucoid sIgE in predicting outcomes of baked egg challenges. We reported for the first time on outcomes of home baked egg challenges in addition to clinic challenges. We found that most patients with egg allergy tolerated baked egg products, consistent with prior observations.[7–10] This study is the first to report observational data on immunologic parameters of a large number of patients consuming egg in various forms.

Ingestion of baked egg products is well tolerated and safe in most patients with egg allergy.[7–10] Presently, predictors of outcomes of baked egg challenge are limited, and oral food challenge remains the only means of conclusively establishing baked egg tolerance.

We attempted to identify clinical predictors of baked egg tolerance. In our study, a diagnosis of asthma was associated with failed outcome of baked egg challenge. This association has not been reported previously. Despite this finding, only one patient failed a baked egg challenge due to lower airway symptoms (wheezing), which resolved with intramuscular epinephrine, and this patient did not have a previous diagnosis of asthma. No patient required treatment with inhaled bronchodilators during a failed baked egg challenge.

We attempted to identify immunologic predictors of baked egg tolerance. On the basis of retrospective observations, egg white sIgE, ovomucoid sIgE, and egg white SPT were highly associated with current egg ingestion practice. Specifically, the higher the levels, the less likely the patient was to tolerate any form of egg. Although total IgE level was also associated with current egg ingestion practice at time of laboratory evaluation, this association was not as robust and did not persist when evaluated more specifically by food challenge outcome.

To more specifically identify immunologic predictors of baked egg tolerance, we performed a subset analysis of patients who underwent baked egg challenges. Patients with lower egg white sIgE, ovomucoid sIgE, and egg white SPT levels were more likely to pass baked egg challenges, compared with patients with higher levels. We were able to establish >90% predictive values for passing baked egg challenges for egg white sIgE of 6.00 kU/L, ovomucoid sIgE of 0.35 kU/L, and egg white SPT wheal of 11 mm. Patients with undetectable egg white and ovomucoid sIgEs failed baked egg challenges, as noted in other studies.[10,15,17] No patient with a negative egg white SPT failed a baked egg challenge. Other groups have reported no patient failing baked egg challenges with egg white SPT wheal <10

mm[8] and <4 mm.[7] Thus, a negative egg white SPT is highly predictive of passing a baked egg challenge, even when analyzed across several studies in different patient populations.

Several groups have shown ovomucoid sIgE levels predict baked egg tolerance,[10,15–18] and Ando et al[15] suggested that ovomucoid sIgE was superior to egg white sIgE. We found that, although predictive of challenge outcome, ovomucoid sIgE was not superior to egg white sIgE or SPT.

Other groups have analyzed the utility of various immunologic parameters in predicting outcomes of baked egg challenge. Des Roches et al[9] performed baked egg challenges (cake) in 60 subjects and found egg white SPT predicted challenge outcome; they did not evaluate sIgE levels. Lemon-Mule et al[10] performed baked egg challenges (muffins and waffles) in 117 subjects and found egg white sIgE, ovomucoid sIgE, and egg white SPT all predicted outcome of baked egg challenge. Caubet et al[17] performed additional analysis on 107 baked egg challenges from the study by Lemon-Mule et al[10] and confirmed these findings. They also performed ROC curve analysis and found that ovomucoid sIgE did not perform better that egg white sIgE in predicting outcome of baked egg challenge, which is consistent with our results. Lieberman et al[7] performed baked egg challenges (muffins) in 100 subjects and found egg white SPT and sIgE predicted challenge outcome; they did not evaluate ovomucoid sIgE. Ando et al[15] performed challenges to extensively heated egg in 108 subjects and found both egg white and ovomucoid sIgE predicted challenge outcome; they did not evaluate egg white SPT levels. However, comparisons between the study by Ando et al[15] and ours should be drawn with caution, because they challenged subjects to liquid egg white heated at 195°F for 60 minutes, without the addition of wheat. Our protocol involved cooking egg at 350°F with wheat flour in a muffin or cupcake. Cooking egg together with wheat flour induces ovomucoid polymerization, leading to aggregation and insolubility of ovomucoid.[26] Thus, concentrations and conformations of egg proteins may vary depending on the baked egg protocol used, leading to differences in food challenge outcomes and predictive values of immunologic parameters.

In our study, 2 of 27 challenge failures (7.4%) or 2 of 169 challenges overall (1.2%) required treatment with epinephrine. Reports of failed baked egg challenges in the literature which required epinephrine range from 0% to 22.2%.[7,8,10,11] No patient in our study had protracted or biphasic reactions or required hospitalization for prolonged monitoring. Most challenge failures were because of gastrointestinal symptoms, similar to other reports.[7,11]

We chose to investigate baked egg in forms and amounts typically ingested in the Western diet. Among subjects who failed food challenges at home, variability in the degree of baking and perception of allergic symptoms are possibilities. It may have been beneficial to perform a physician-supervised food challenge to confirm the home reactions, but this was beyond the scope of our study.

Despite these limitations, our study is important because it is one of the few to analyze the utility of ovomucoid sIgE and the largest evaluating predictors of baked egg challenge outcomes. We identified >90% NPVs for baked egg challenge outcomes for egg white and ovomucoid sIgE and egg white SPT. On the basis of our findings, we propose using the following cutoffs to identify patients who would pass a baked egg challenge (approximately 90% rate of passing): ovomucoid sIgE of 0.35 kU/L, egg white sIgE of 6.00 kU/ L, and egg white SPT wheal of 11 mm. Egg white SPT wheal <3 mm could identify patients who may be candidates for home introduction of baked egg (100% rate of passing baked egg challenge). Although we were not able to identify >90% PPVs for baked egg challenge outcomes, we were able to determine cutoffs at which >95% specificity could be established (suggesting levels at which food challenges could be excluded because of a high probability

of having a true food allergy): ovomucoid sIgE of 3.38 kU/L, egg white sIgE of 9.65 kU/L, and egg white SPT wheal of 25 mm.

In summary, we defined novel decision points based on serum sIgE and SPT that may be useful in predicting outcomes of baked egg challenges. Compared with egg white sIgE and SPT, ovomucoid sIgE was a useful but not superior predictor of baked egg challenge outcome.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations used

ARC	Allergic rhinoconjunctivitis
AUC	Area under the curve
EoE	Eosinophilic esophagitis
NPV	Negative predictive value
PPV	Positive predictive value
ROC	Receiver operating characteristic
sIgE	Specific IgE
SPT	Skin prick test

References

1. Caubet JC, Wang J. Current understanding of egg allergy. Pediatr Clin North Am. 2011; 58:427–43. xi. [PubMed: 21453811]
2. Sicherer SH, Sampson HA. Food allergy. J Allergy Clin Immunol. 2006; 117:S470–5. [PubMed: 16455349]
3. Eggesbo M, Botten G, Halvorsen R, Magnus P. The prevalence of allergy to egg: a population-based study in young children. Allergy. 2001; 56:403–11. [PubMed: 11350303]
4. Eigenmann PA, Sicherer SH, Borkowski TA, Cohen BA, Sampson HA. Prevalence of IgE-mediated food allergy among children with atopic dermatitis. Pediatrics. 1998; 101:E8. [PubMed: 9481027]
5. Sampson HA, McCaskill CC. Food hypersensitivity and atopic dermatitis: evaluation of 113 patients. J Pediatr. 1985; 107:669–75. [PubMed: 4056964]
6. Savage JH, Matsui EC, Skripak JM, Wood RA. The natural history of egg allergy. J Allergy Clin Immunol. 2007; 120:1413–7. [PubMed: 18073126]
7. Lieberman JA, Huang FR, Sampson HA, Nowak-Wegrzyn A. Outcomes of 100 consecutive open, baked-egg oral food challenges in the allergy office. J Allergy Clin Immunol. 2012; 129:1682–1684.e2. [PubMed: 22657409]
8. Cortot CF, Sheehan WJ, Permaul P, Friedlander JL, Baxi SN, Gaffin JM, et al. Role of specific IgE and skin-prick testing in predicting food challenge results to baked egg. Allergy Asthma Proc. 2012; 33:275–81. [PubMed: 22584194]
9. Des Roches A, Nguyen M, Paradis L, Primeau MN, Singer S. Tolerance to cooked egg in an egg allergic population. Allergy. 2006; 61:900–1. [PubMed: 16792596]

10. Lemon-Mule H, Sampson HA, Sicherer SH, Shreffler WG, Noone S, Nowak-Wegrzyn A. Immunologic changes in children with egg allergy ingesting extensively heated egg. J Allergy Clin Immunol. 2008; 122:977–983.e1. [PubMed: 18851876]
11. Clark A, Islam S, King Y, Deighton J, Szun S, Anagnostou K, et al. A longitudinal study of resolution of allergy to well-cooked and uncooked egg. Clin Exp Allergy. 2011; 41:706–12. [PubMed: 21488997]
12. Leonard SA, Sampson HA, Sicherer SH, Noone S, Moshier EL, Godbold J, et al. Dietary baked egg accelerates resolution of egg allergy in children. J Allergy Clin Immunol. 2012; 130:473–480.e1. [PubMed: 22846751]
13. Nowak-Wegrzyn A, Fiocchi A. Rare, medium, or well done? The effect of heating and food matrix on food protein allergenicity. Curr Opin Allergy Clin Immunol. 2009; 9:234–7. [PubMed: 19444093]
14. Caubet JC, Kondo Y, Urisu A, Nowak-Wegrzyn A. Molecular diagnosis of egg allergy. Curr Opin Allergy Clin Immunol. 2011; 11:210–5. [PubMed: 21467927]
15. Ando H, Moverare R, Kondo Y, Tsuge I, Tanaka A, Borres MP, et al. Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. J Allergy Clin Immunol. 2008; 122:583–8. [PubMed: 18692888]
16. Urisu A, Ando H, Morita Y, Wada E, Yasaki T, Yamada K, et al. Allergenic activity of heated and ovomucoid-depleted egg white. J Allergy Clin Immunol. 1997; 100:171–6. [PubMed: 9275136]
17. Caubet JC, Bencharitiwong R, Moshier E, Godbold JH, Sampson HA, Nowak-Wegrzyn A. Significance of ovomucoid- and ovalbumin-specific IgE/IgG(4) ratios in egg allergy. J Allergy Clin Immunol. 2012; 129:739–47. [PubMed: 22277199]
18. Alessandri C, Zennaro D, Scala E, Ferrara R, Bernardi ML, Santoro M, et al. Ovomucoid (Gal d 1) specific IgE detected by microarray system predict tolerability to boiled hen's egg and an increased risk to progress to multiple environmental allergen sensitisation. Clin Exp Allergy. 2012; 42:441–50. [PubMed: 22168465]
19. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol. 2011; 128:3–20.e6. quiz 1–2. [PubMed: 21477849]
20. Bernstein IL, Li JT, Bernstein DI, Hamilton R, Spector SL, Tan R, et al. Allergy diagnostic testing: an updated practice parameter. Ann Allergy Asthma Immunol. 2008; 100:S1–148.
21. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: report of the NIAID-sponsored expert panel. J Allergy Clin Immunol. 2010; 126:S1–58. [PubMed: 21134576]
22. Sampson HA, Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. J Allergy Clin Immunol. 1997; 100:444–51. [PubMed: 9338535]
23. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988; 44:837–45. [PubMed: 3203132]
24. Haneda Y, Kando N, Yasui M, Kobayashi T, Maeda T, Hino A, et al. Ovomucoids IgE is a better marker than egg white-specific IgE to diagnose boiled egg allergy. J Allergy Clin Immunol. 2012; 129:1681–2. [PubMed: 22552111]
25. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: summary report–second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med. 2006; 47:373–80. [PubMed: 16546624]
26. Kato Y, Watanabe H, Matsuda T. Ovomucoid rendered insoluble by heating with wheat gluten but not with milk casein. Biosci Biotechnol Biochem. 2000; 64:198–201. [PubMed: 10766508]

What is already known about this topic?

Children with egg allergy may tolerate baked egg products. Ovomucoid specific IgE antibody levels have been suggested to predict outcomes of baked egg challenges.

What does this article add to our knowledge?

Measurement of specific IgE to ovomucoid may aid, together with egg white specific IgE and skin prick test, in predicting outcomes of baked egg challenges. No single measure appears superior.

How does this study impact current management guidelines?

Specific IgE to ovomucoid, a heat-stable allergen, is a useful but not superior immunologic marker for predicting baked egg tolerance. Egg white specific IgE and skin prick testing remain important predictors of baked egg tolerance.

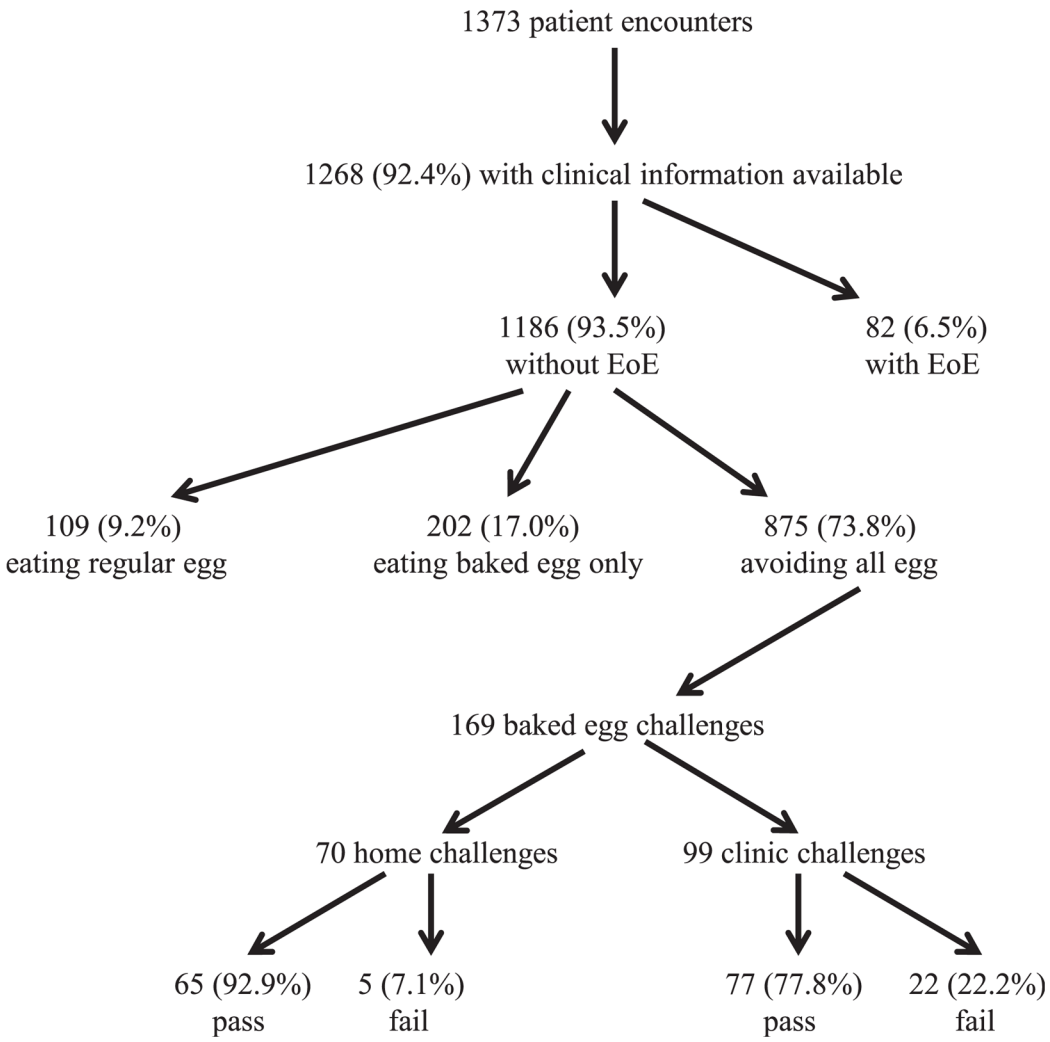

FIGURE 1.
Structure of ovomucoid database. Flow diagram of study design.

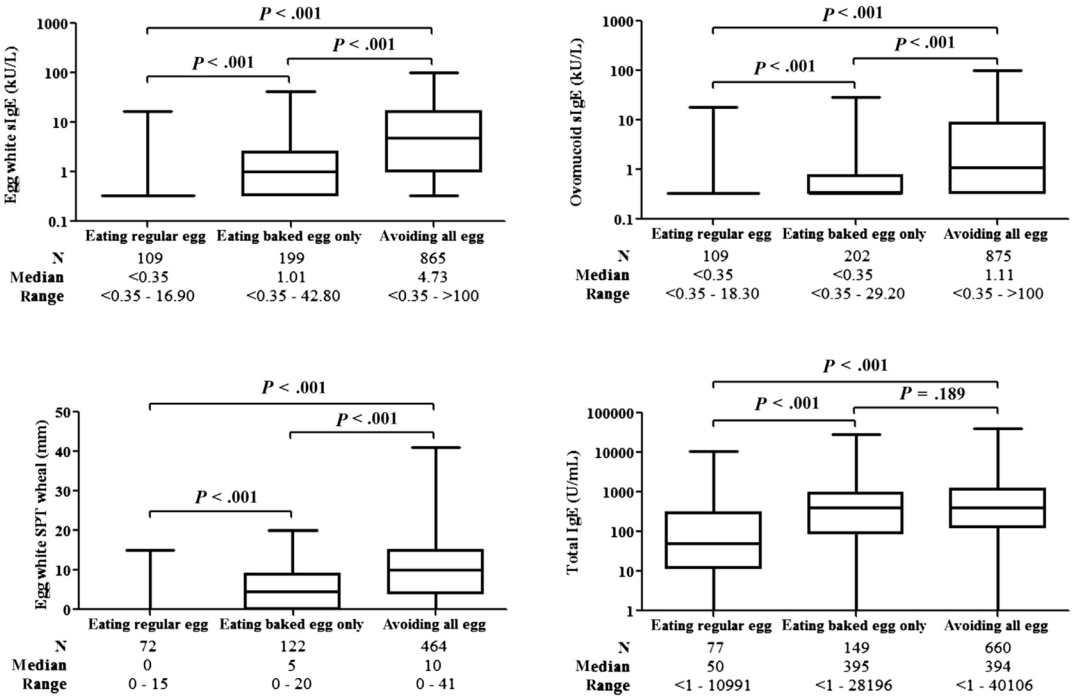

FIGURE 2.

Immunologic parameters based on current egg ingestion status. SPT results were obtained within 1 month of blood test.

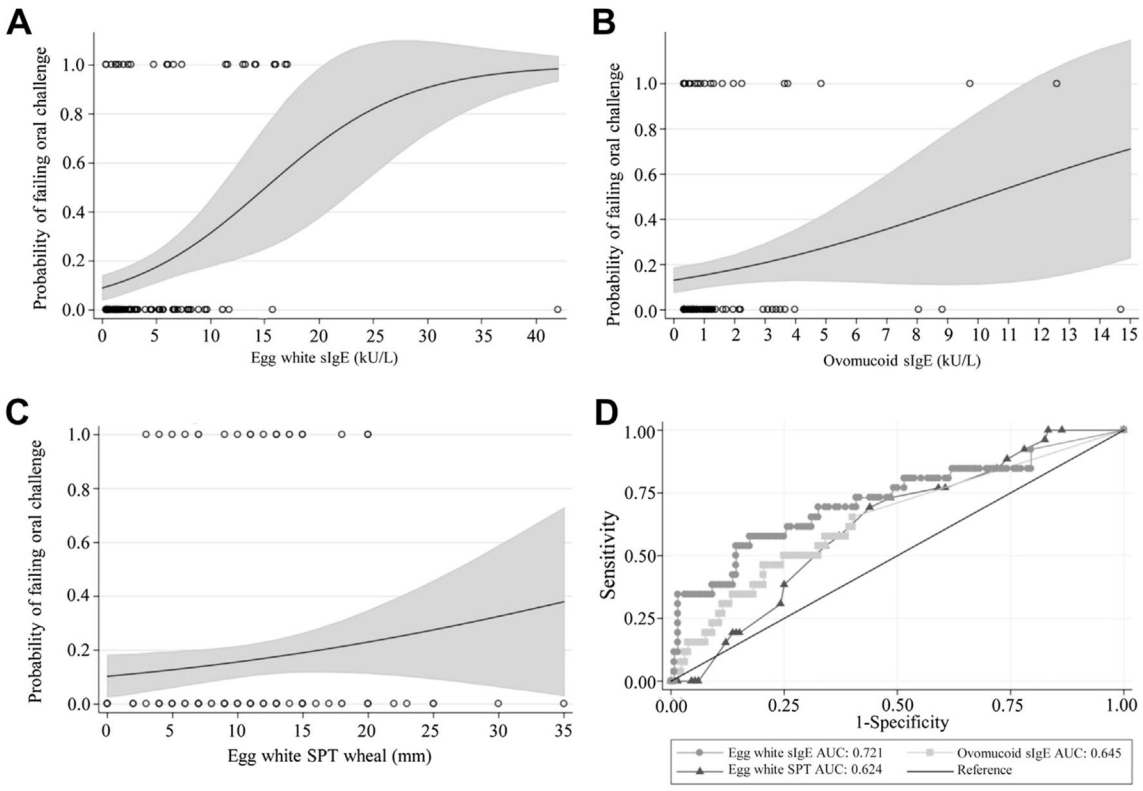

FIGURE 3.

Predicted probabilities of baked egg challenge outcome. **A–C**, Estimated probability curves for failing oral baked egg challenge at a given egg white sIgE (n = 161), ovomucoid sIgE (n = 162), or egg white SPT (n = 147) level derived from logistic regression. Blood and SPT results were obtained within 1 year before challenge date. Open circles represent individual subjects. Shaded regions indicate 95% confidence limits. **D**, ROC curves show the performance of egg white sIgE, ovomucoid sIgE, and egg white SPT in relation to baked egg challenge outcome. No significant difference was observed among the AUCs ($P = .301$).

TABLE I

Immunologic parameters of patients challenged to baked egg

	Pass (n = 142), median (range)	Fail (n = 27), median (range)	*P* value
Skin prick testing			
Egg white wheal (mm), median (range)	9 (0 to 35)	13 (3 to 20)	.035*
No. of patients with measurements available	122	25	
Blood testing			
Egg white sIgE (kU/L), median (range)	1.31 (<0.35 to 42.00)	6.00 (<0.35 to 17.10)	<.001*
No. of patients with measurements available	135	26	
Ovomucoid sIgE (kU/L), median (range)	<0.35 (<0.35 to 14.70)	0.76 (<0.35 to 12.60)	.003*
No. of patients with measurements available	136	26	
Total IgE (U/mL), median (range)	218 (2 to 4779)	319 (19 to 2387)	.357
No. of patients with measurements available	135	26	

*
P values <.05.

TABLE II

Performance characteristics of immunologic parameters at various cutoff values

	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Egg white sIgE (kU/L)	0.35	92.6	19.1	18.0	93.1
	2.39	66.7	67.4	28.1	91.3
	6.00	51.9	85.8	41.2	90.3
	9.65	37.0	95.0	58.8	88.7
Ovomucoid sIgE (kU/L)	0.35	66.7	61.3	24.7	90.6
	3.38	18.5	95.1	41.7	86.0
	4.85	11.1	97.9	50.0	85.3
	9.74	7.41	99.3	66.7	84.9
Egg white SPT wheal (mm)	3	100	16.5	19.0	100
	4	96.2	17.3	18.5	95.8
	11	69.2	55.6	23.4	90.2
	25	0	95.5	0	83.0

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