

Risk Factors and Clinical Features in Cashew Nut Oral Food Challenges

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Keywords

Allergy · Cashew nut · Risk factors · Allergic reaction · Oral food challenge

Abstract

Background: Cashew nuts (CN) are capable of causing severe allergic reactions. However, little has been reported about the details of CN oral food challenges (OFC). **Methods:** CN-specific IgE (sIgE) levels were measured for 1 year in 66 patients who underwent an OFC with >3 g CN for diagnosis or confirmation of tolerance acquisition between June 2006 and August 2014. We retrospectively analyzed the OFC and patient background. **Results:** The median (IQR) age of the 66 patients (48 boys/men and 18 girls/women) was 7.0 years (5.7–8.8). Twelve patients (18.2%) had a positive OFC result; 6 of 8 (75%) patients with a history of an immediate reaction to CN failed the OFC. Anaphylaxis was experienced by 5 of these 12 (42%) patients. A history of an immediate reaction to CN and the CN sIgE levels were significantly different for patients with a positive or negative OFC result ($p < 0.01$). Among patients without a previous immediate reaction to CN, the 95% positive predictive value (PPV) for the CN sIgE level for a positive OFC result was 66.1 kU_A/L. **Con-**

clusions: A history of an immediate reaction to CN and high CN sIgE were risk factors for a positive OFC result. The number of positive OFC results was relatively low, but there was a high probability of anaphylaxis. We should consider the indication of OFC carefully for patients with a history of immediate reactions to CN and avoid OFC for patients without such a history whose CN sIgE values are >66.1 kU_A/L (95% PPV).

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Introduction

In preschool children, the prevalence of food allergy is 10% in developed countries and approximately 7% in Asia, including China [1]. A systematic review reported that the prevalence of nut allergy specifically is 0.1–4.3%, primarily owing to allergy to walnuts, cashew nuts, and almonds [2]. The prevalence of cashew nut allergy is 0.06% [3] and it is increasing [4]. In the USA, of all allergies to tree nuts, walnut allergy is the most prevalent, followed by

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cashew nut allergy [5]. In Japan, cashew nuts are an important causative food of all nut allergies, according to an epidemiological investigation of immediate food allergies.

Cashew nuts belong to the Anacardiaceae family, which also includes mangos, pistachios, and ginkgo. The cashew nut is used as an ingredient in Chinese foods and sweets, resulting in a high likelihood of ingestion. Anaphylaxis and serious symptoms can easily occur with cashew nuts [6–8], and cashew nut allergy causes more severe clinical reactions than peanut allergy [9]. Of the 179 children who underwent a double-blind, placebo-controlled oral food challenge (OFC) with cashew nuts in a previous study, 137 (76.5%) had a positive result, and 49 of these children (36%) had an anaphylactic reaction [10]. That study demonstrated the high potency of cashew nut allergens; severe allergic reactions were caused by a minimal amount of cashew nut. Therefore, diagnosing cashew nut allergy is important.

OFC is the gold standard [11–14] for the diagnosis of food allergy and confirmation of tolerance. However, there are few reports summarizing the results of OFC for cashew nuts and the risk factors for a positive cashew nut OFC result. Lange et al. [15] reported the probability curve of cashew nut specific IgE (sIgE) but there is a possibility that the probability curve may change depending on whether or not the patient has a history of immediate reactions to cashew nuts. Therefore, we analyzed the risk factors for symptom induction during a cashew nut OFC and the probability curve of cashew nut sIgE for patients with or without a history of immediate reactions to cashew nuts.

Materials and Methods

Study Population

The study included patients aged 3–22 years who had a sensitization to cashew nuts, which was defined as a positive cashew nut sIgE antibody titer. OFC to cashew nuts was performed at the Department of Pediatrics of Sagami Hospital (Kanagawa, Japan) from June 2006 to August 2014. Inclusion criteria were stable symptoms of atopic dermatitis and bronchial asthma, cashew nut sIgE ≥ 0.35 kU_A/L, cashew nut sIgE measured for 1 year before and 1 year after the OFC, and a sufficient OFC load (>3 g cashew nuts). Exclusion criteria were illness on the day of the OFC and use of antiallergic drugs (e.g., antihistamines) within the last 72 h before the OFC. All patients who met the inclusion criteria underwent OFC, even if the cashew nut sIgE was high or the patients had a prior immediate reaction to cashew nuts. However, if the patients had a prior immediate reaction with a very small amount of cashew nut, we did not perform the cashew nut OFC immediately. In these patients the cashew nut sIgE was reassessed 6–12 months later and the cashew nut OFC was considered if the sIgE had declined.

This study was approved by the ethics committee of the National Hospital Organization, Sagami Hospital (2014/03/18, No. 18). Using the hospital bulletin and documents, we explained the study details and risks of symptoms following provocation to the patients and guardians. Informed consent for the OFC and publication of the data was obtained from all of the participants.

Laboratory Test

Cashew nut and peanut sIgE levels were measured using the ImmunoCAP assay system (Thermo Fisher Scientific, Uppsala, Sweden). Values ≥ 0.35 kU_A/L were considered positive. Cashew nut sIgE levels >100 kU_A/L were conveniently approximated to 101 kU_A/L.

Oral Food Challenge

Cashew nut OFC was performed openly in the outpatient department or during hospitalization. Patients with a history of an immediate reaction and whose cashew nut sIgE titers were higher than class 3 (cashew nut sIgE 3.50 to <17.5 kU_A/L) underwent the OFC during hospitalization.

A pumpkin cake (mixture of pumpkin, *Sorghum bicolor*, sugar, baking soda, and water) and cashew nut powder (Toyo Nuts Foods Co. Ltd., Hyogo, Japan) in predetermined proportions was used for the OFC that occurred during hospitalization. The mixture was heated to 90°C for 1.5 min in a 1,000-W microwave oven. In the outpatient clinic, guardians cooked similar foods for the open OFC.

This study included patients who had a sufficient OFC load (>3 g cashew nuts). The final target amount in cashew nut OFC is 10 g cashew nuts. Patients who do not reach the final target amount in cashew nut OFC usually do another OFC at our hospital.

The cashew nut OFC was conducted using the pumpkin cake in 3 or 2 portions. With 3 portions, one eighth of the total amount was administered initially, three eighths of the total amount was administered 30 min later, and the remaining half was administered 60 min later. With 2 portions, one fourth of the total amount was administered initially, and the remaining three fourths was administered 60 min later.

After the start of the OFC, we observed the patients for at least 2 h. A positive OFC result was determined based on the induced symptoms (Table 1). The OFC ended when a quantity of cashew nut sufficient to cause objective symptoms such as urticaria, coughing, moderate or severe abdominal pain, and vomiting or diarrhea had been consumed. A positive result was defined as symptoms greater than grade 2 or symptoms defined as grade 1 that continued for >30 min. If these symptoms disappeared within 30 min, we continued the OFC and observed whether other symptoms were provoked. If obvious positive symptoms were not observed (uncertain OFC), the patients repeated the cashew nut at home at least 2–3 times to confirm the OFC results, taking the same amount as in the OFC without dividing it. When repeated symptoms were observed, we judged the OFC result as positive. When an adverse reaction was observed, treatment (antihistamines, β_2 -agonists, steroids, or adrenaline) was administered based on European Academy of Allergy and Clinical Immunology food allergy and anaphylaxis guidelines [16]. Anaphylaxis was defined according to the criteria advocated by Simons et al. [17].

Immediate symptoms were defined as obvious objective symptoms (systemic urticaria, continuous coughing, wheezing, moder-

Table 1. Symptom grading for cashew nut allergy

Grade	1 (mild)	2 (moderate)	3 (severe)
Skin	Localized urticaria, exanthema, wheal, pruritus Swollen eye lid or lip	Generalized urticaria, exanthema, wheal, pruritus Swollen face	– –
Gastrointestinal tract	Pruritus of the throat or oral cavity Mild abdominal pain Nausea, emesis, diarrhea	Throat pain Moderate abdominal pain Recurrent emesis, diarrhea	– Cramps Continuous emesis, loss of bowel control
Respiratory tract	Intermittent cough, nasal congestion, sneezing, rhinorrhea –	Repetitive cough Chest tightness, mild wheezing	Persistent cough, hoarseness, “barky” cough Apparent wheezing, dyspnea, cyanosis, saturation <92%, difficulty swallowing or speaking, throat tightness, respiratory arrest
Cardiovascular	–	Pale face, mild hypotension, tachycardia (increase >15 beats/min)	Hypotension, dysrhythmia, severe bradycardia, cardiac arrest
Neurological	Change in activity level, tiredness	Light-headedness, feeling of “impending doom,” somnolence	Confusion, loss of consciousness, incontinence

The severity score was based on the organ system that was most affected by the symptoms. Hypotension was defined as: systolic blood pressure <70 mm Hg (age 1 month to 1 year), <70 mm Hg + (2 × age) (age 1–10 years), and <90 mm Hg (age >11 years). Mild hypotension was defined as systolic blood pressure <80 mm Hg (age 1 month to 1 year), <80 mm Hg + (2 × age) (age 1–10 years), and <100 mm Hg (age >11 years). This definition was modified using the anaphylactic symptom grading of the European Academy of Allergology and Clinical Immunology guidelines.

ate to severe abdominal pain, vomiting, and diarrhea). Immediate symptoms refer to allergic reactions that occur within 2 h after the causal food intake.

Statistical Analysis

Analyses were performed using the Mann-Whitney *U* test for continuous variables and Fisher’s exact test for dichotomous variables. We conducted comparisons for patients with positive and negative OFC results. Results are expressed as medians and 25th to 75th percentiles. The statistically optimal cut-off levels of sIgE to cashew nut were determined using receiver operating characteristic curves. After plotting the receiver operating characteristic curves, the area under the curve, sensitivity, specificity, positive predictive value (PPV), and negative predictive value were calculated.

To identify the potential factors that could predict a positive cashew nut OFC result, multivariable logistic regression analysis was performed in a stepwise manner. A history of immediate reactions to cashew nuts and cashew nut sIgE antibody titer were adjusted for onset age. We created probability curves using regression analysis after logarithmic transformation of the cashew sIgE titer. We studied the association between cashew nut and peanut sIgE using Spearman’s rank correlation coefficient. Data were analyzed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). *p* < 0.05 were considered statistically significant.

Results

Baseline Subject Characteristics

Of the 88 patients who underwent the cashew nut OFC, 12 subjects with insufficient clinical data and 10 subjects who underwent an OFC with <3 g cashew nut were excluded (Fig. 1). Therefore, the analyses included 66 children (48 boys/men and 18 girls/women; Table 2) with a median (IQR) age of 7.0 years (5.7–8.8). The most common reason for cashew nut elimination was a positive cashew nut sIgE without ingestion of cashew nuts (80.3%), followed by a history of immediate reactions to cashew nuts (12.1%) and a history of an immediate reaction to peanuts and other nuts (7.6%) (online suppl. Fig. 1; see www.karger.com/doi/10.1159/000486120 for all online suppl. material).

Twenty-one patients had a history of immediate reactions to peanuts (31.8%), and 14 patients had a history of immediate reactions to any nut except cashew nuts (21.2%). Fifty patients had atopic dermatitis (75.8%), and

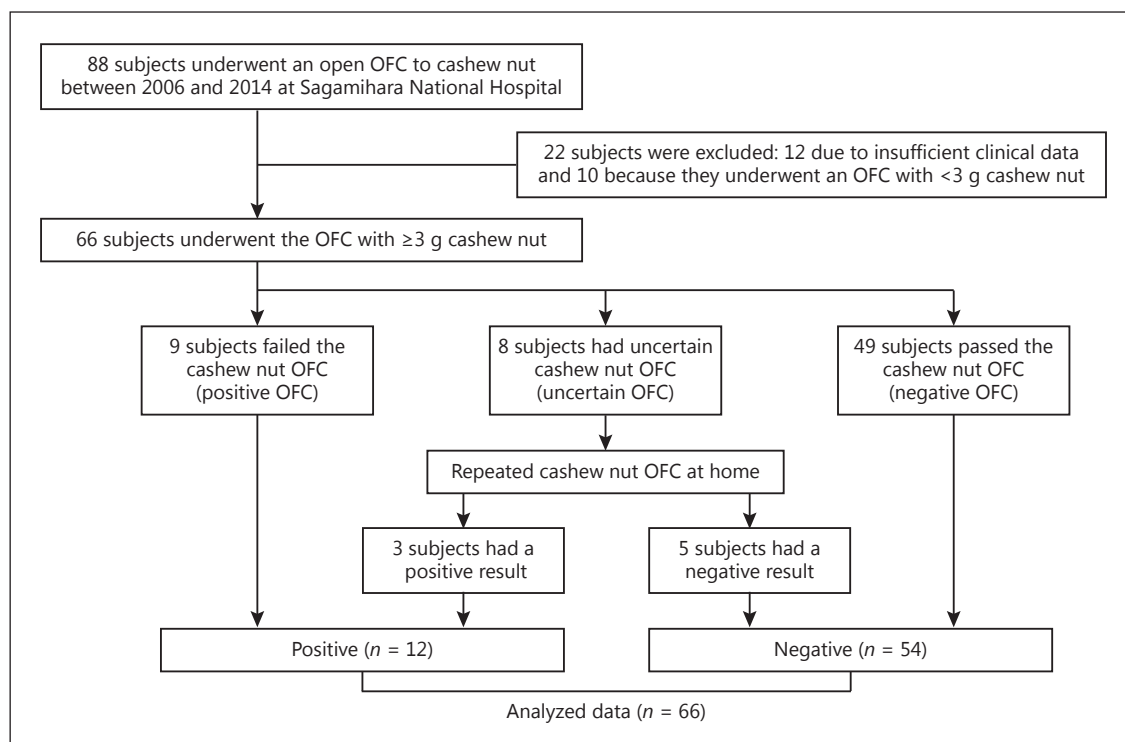


Fig. 1. Flowchart showing enrolled patients to assess the usefulness of OFC for cashew nut allergy. OFC, oral food challenge.

30 patients had bronchial asthma (45.5%). The median cashew nut sIgE level was 2.8 kU_A/L (1.5–4.8). The median time between the laboratory test and the cashew nut OFC was 4.1 months (1.8–6.7).

Results of the Cashew Nut OFC

Among the 66 patients, 9 (13.7%) had a positive result, 49 (74.2%) had a negative result, and 8 (12.1%) had an uncertain result in the cashew nut OFC. Finally, 12 patients (18.2%) were considered to have positive results, and 54 patients (81.2%) were considered to have negative results. In the majority of patients ($n = 10$; 83.3%) symptoms appear in <30 min. Gastrointestinal symptoms were the most common initial symptoms in 11 of the patients with a positive result (91.7%); they were also the most common symptoms overall, occurring in 11 of the patients (91.7%) with a positive result, followed by skin symptoms ($n = 7$; 58.3%) and respiratory symptoms ($n = 6$; 50%) (Table 3).

Anaphylaxis appeared in 5 of the 12 cashew nut-reactive patients (online suppl. Table 1). These patients did not have a history of an immediate reaction to cashew nuts and peanuts, and respiratory symptoms were ob-

served in all of these patients. The majority of the reactions were treated with antihistamines and/or steroids. One subject (8.3%) received 1 dose of adrenaline because of persistent severe abdominal pain (Table 3).

Comparison between Patients with Positive and Negative OFC Results

We compared patients with positive and negative results (Table 2). Patients with positive results had significantly higher rates of a history of immediate reactions to cashew nuts (50.0 vs. 3.7%, $p = 0.001$) and anaphylaxis due to cashew nuts (16.7 vs. 3.7%, $p = 0.026$), as well as a significantly higher cashew nut sIgE level (5.2 [3.5–12.7] vs. 2.5 kU_A/L [1.1–3.7], $p = 0.003$) (Table 2). No significant differences in age, sex, history of immediate reactions to peanuts or any nuts except cashew nuts, history of immediate reactions to other foods, rate of complications with allergic diseases, and total IgE values between the patients based on the OFC results. Two of the 8 patients who had a history of immediate reactions to cashew nuts had a negative result; one of these patients experienced anaphylaxis due to cashew nuts. Among these 2 patients, the cashew nut sIgE level slightly decreased from

Table 2. Analysis of factors associated with a positive result in the cashew nut OFC

	Total sample (n = 66)	Positive OFC (n = 12)	Negative OFC (n = 54)	p value
Male/female ratio	48/18	9/3	39/15	0.845 ^a
Age, years	7.0 (5.7–8.8)	7.8 (6.6–9.8)	7.0 (5.4–8.6)	0.157 ^b
Past history of FA				
History of an immediate reaction to cashew nut	8 (12.1)	6 (50.0)	2 (3.7)	0.001 ^a
Anaphylaxis due to cashew nut	3 (4.5)	2 (16.7)	1 (1.9)	0.026 ^a
Immediate reaction to peanut	21 (31.8)	4 (33.3)	17 (31.5)	0.901 ^a
Immediate reaction to any nut without cashew nut	14 (21.2)	3 (25.0)	11 (20.1)	0.723 ^a
Immediate reaction to any food	54 (81.8)	12 (100)	42 (77.8)	0.071 ^a
Comorbid disease				
Atopic dermatitis	50 (75.8)	8 (66.7)	42 (77.8)	0.417 ^a
Bronchial asthma	30 (45.5)	6 (50.0)	24 (44.4)	0.727 ^a
Allergic rhinitis	25 (37.9)	7 (58.3)	18 (33.3)	0.106 ^a
Allergic conjunctivitis	16 (22.5)	3 (25.0)	13 (24.1)	0.946 ^a
Total IgE, IU/mL	1,425.0 (752.5–2,475.0)	1,022.0 (628.0–3,317.5)	1,440.0 (894.8–2,475.0)	0.710 ^b
Peanut sIgE, kU _A /L	12.2 (2.3–41)	11.5 (5.9–51.5)	14.4 (3.6–42.2)	0.936 ^b
Cashew nut sIgE, kU _A /L	2.8 (1.5–4.8)	5.2 (3.5–12.7)	2.5 (1.1–3.7)	0.003 ^b

Values are reported as numbers (%) or medians (IQR) unless otherwise stated. OFC, oral food challenge; FA, food allergy; sIgE, specific IgE. ^a Fisher's exact test. ^b Mann-Whitney *U* test.

Table 3. Symptoms and administered treatments during the cashew OFC for patients with a positive result

	Positive cashew nut OFC (n = 12)
Symptoms	
Gastrointestinal	11 (91.7)
Skin	7 (58.3)
Respiratory	6 (50.0)
Nerve	3 (25.0)
Cardiovascular	1 (8.3)
Anaphylaxis	5 (41.7)
Treatments	
Antihistamines	7 (58.3)
Steroids	5 (41.7)
β ₂ -Inhalation	4 (25.0)
Adrenaline	1 (8.3)

Data are presented as numbers (%). OFC, oral food challenge.

3.69 to 3.37 kU_A/L after approximately 1 year for the patient who experienced anaphylaxis due to cashew nuts. In the other patient, 3 years had passed after the immediate reaction to cashew nut. Six (75%) out of 8 patients with a history of an immediate reaction reacted to the OFC.

The area under the curve for a positive cashew nut OFC result was 0.77. The optimal cashew nut sIgE cut-off level was 5.04 kU_A/L, which had a sensitivity, specificity, negative predictive value, and PPV of 87.04, 66.67, 95.90, and 36.4%, respectively.

Factors Predictive of a Positive Cashew Nut OFC Result

To identify the potential factors that may predict a positive cashew nut OFC result, multiple logistic regression analysis was performed in a stepwise manner (Table 4). History of immediate reactions to cashew nuts and cashew nut sIgE antibody titer were adjusted for onset age. In the multivariable logistic regression analysis, a history of immediate reactions to cashew nuts (OR 38.58; 95% CI 4.89–304.08, *p* = 0.001), cashew nut sIgE (OR per 10-fold increase: 16.17; 95% CI 2.42–107.95, *p* = 0.004) predicted a positive cashew nut OFC result.

Probability Curve

We made 2 kinds of probability curves: one for all patients and another for 58 patients without a history of an immediate reaction to cashew nuts (Fig. 2). The 95, 90, 80, 50, 10, and 5% PPV for the cashew nut sIgE level for a positive reaction to the cashew nut OFC was 149.5, 80.1, 40.7, 12.8, 2.0, and 1.1 kU_A/L, respectively (online suppl.

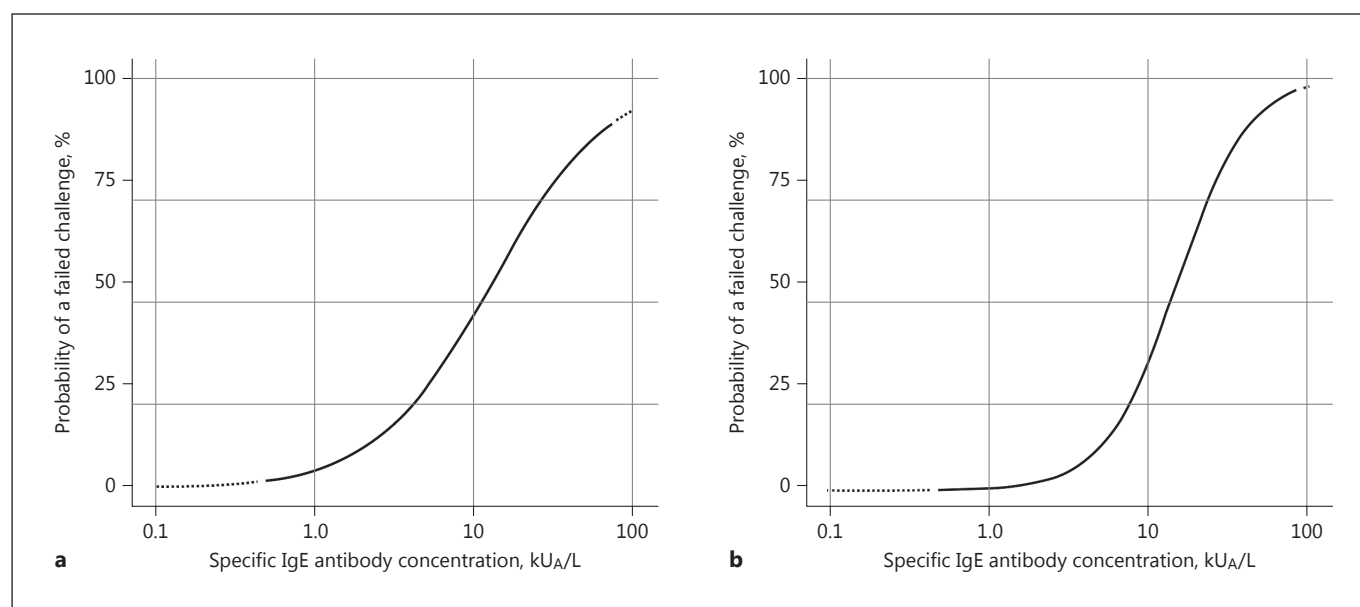


Fig. 2. Predicted probability from logistic regression for positive cashew nut OFC outcomes. Probability curves for all patients ($n = 66$; **a**) and patients without a history of immediate reactions to cashew nuts ($n = 58$; **b**). The predictive value is indicated by the dotted line. OFC, oral food challenge.

Table 4. Factors predictive of a positive cashew nut OFC result

	Crude OR (95% CI)	<i>p</i> value	OR adjusted for age (95% CI)	<i>p</i> value
History of an immediate reaction to cashew nuts	26.00 (4.26–158.82)	<0.001	38.58 (4.89–304.08)	0.001
Cashew nut sIgE (per 10-fold increase)	15.73 (2.31–104.39)	0.004	16.17 (2.42–107.95)	0.004

OFC, oral food challenge; sIgE, specific IgE; OR, odds ratio; CI, confidence interval.

Table 2). The maximum value of cashew nut sIgE in our study was 74.5 kU_A/L, so we expressed the 95 and 90% PPV as predicted values. In the patients without history of an immediate reaction to cashew nuts, the 95, 90, 80, 50, 10 and 5% PPV was 66.1, 45.1, 29.8, 14.6, 4.8, and 3.2 kU_A/L, respectively. In the patients with history of an immediate reaction to cashew nuts, we were not able to create probability curves because of the comparatively lower number of cases.

Antigenic Cross-Reactivity of Cashew Nut and Peanut sIgE

We showed the association between cashew nut and peanut sIgE levels. Cashew nut sIgE levels were not associated with peanut sIgE levels ($r = 0.019$, $p = 0.905$; online suppl. Fig. 2).

Discussion

In this study, we described the risk factors and clinical features of positive cashew nut OFC result. Furthermore, we investigated probability curves for patients with or without a history of immediate reactions to cashew nut.

Based on the results of the present study, the risk factors for a positive cashew nut OFC result are a history of immediate reactions to cashew nuts and a high cashew nut sIgE antibody titer anaphylaxis due to cashew nuts. Peanut sIgE level did not correlate with cashew nut sIgE.

We did not perform skin prick testing because of the lack of reagents for cashew nuts in Japan at the time of this study, although a wheal diameter (with cashew nuts) ≥ 8 mm predicted a positive food challenge result with >95% accuracy in a previous study [18]. The previously

reported significant risk factors for a failed OFC for tree nuts, meats, seeds, shellfish, and grains are wheal size, a history of other food allergies, and a younger age [19]. The lack of significant differences in terms of a history of other food allergies and age between positive and negative OFC results in the present study might be explained by the difference in sample size (366 vs. 66 cases) and differences in subjects. Therefore, cashew nut OFC in patients with these risk factors should be performed with caution.

Regarding the characteristics of the subjects with positive OFC results, there are 2 primary findings. First, 12 patients (18.2%) had a positive OFC result, and anaphylaxis occurred in 5 of the 12 patients (41.7%) with positive cashew nut OFC results. Although there were not many positive cashew nut OFC results, anaphylaxis was observed frequently. The ratio of anaphylaxis in this study was approximately equal to that in the study of van der Valk et al. [10]. That study from The Netherlands found that the median levels of sIgE (5.48 kU_A/L) to cashew nut and Ana o 3 (13.80 kU_A/L) in the anaphylaxis group were similar to those of the mild group (6.00 and 9.69 kU_A/L, respectively) [20]. Therefore, the symptom severity of cashew nut allergy may not be related to cashew nut sIgE or cashew nut components values. Cashew nut allergy can cause serious symptoms such as anaphylaxis [7–9] and life-threatening symptoms in some cases [21], which is consistent with our results. Therefore, if positive symptoms are detected during a cashew nut OFC, severe symptoms should be closely monitored. Second, gastrointestinal symptoms were the most common symptoms, occurring in 11 of the patients (91.7%) with positive OFC results. The study by van der Valk et al. [10] described that patients who performed a cashew nut OFC most frequently had gastrointestinal symptoms. Andorf et al. [22] reported that gastrointestinal symptoms occurred more often in patients with a high level of Ana o 3. Cashew nut allergy reportedly causes more gastrointestinal symptoms than peanut allergy [23]. Following specific OFC, gastrointestinal symptoms occurred in 17.6% of children for hazelnut and 45.7% of children for peanut [24]. In the present study, a number of oral symptoms were observed for 8 of the 11 patients who experienced gastrointestinal symptoms.

In present study, three fourths of the patients with a history of immediate reactions to cashew nuts failed the OFC. So, we considered the indication of OFC for such patients prior to OFC. In a previous study, 95% PPV for positive symptoms was identified for a walnut sIgE of 18.5 kU_A/L [25]. Among the patients without a history of immediate reactions to cashew nuts, the 95% PPV was 66.1

kU_A/L. We should avoid OFC for patients without an immediate reaction to cashew nuts with a cashew nut sIgE value ≥ 66.1 kU_A/L (95% PPV). We should perform OFC in patients with this characteristic whose cashew nut sIgE value is 90–95% PPV. Furthermore, we may exclude cashew nut allergy without OFC for patients whose cashew nut sIgE value is < 3.2 kU_A/L (5% PPV) without a previous reaction to cashew nuts.

This study has several limitations. First, it was an open OFC, not a double-blind, placebo-controlled OFC. However, we considered a positive OFC result to be the obvious onset of objective symptoms. Also, if obvious objective symptoms were not observed, a repeated intake at home was used to study the validity of the results. Therefore, the influence of the open challenge method was considered to be low. Second, we did not investigate the allergen components of cashew nuts. Sensitization to Ana o 3 is predictive of cashew nut allergy [26]. Studies from Lange et al. [15] have shown a probability curve for a positive cashew nut OFC result by Ana o 3. But Ana o 3 can only be measured for research in Japan; therefore examining cashew nut sIgE is useful. Third, the sample size was small. However, few people perform cashew nut OFC even though they are allergic to cashew nuts. There are 3 main reasons for this. First, patients do not feel the need to complete a cashew nut OFC as they think that they should just avoid eating cashew nuts. Second, egg, milk and wheat OFCs are usually performed earlier than cashew nut OFC because they are often eaten in daily life. Third, many people think cashew nut allergy induces severe symptoms, so they avoid cashew nut OFC. A larger number of subjects will be needed in future studies.

In conclusion, risk factors for a positive OFC result were a high cashew nut sIgE titer, a history of immediate reactions, and anaphylaxis due to cashew nuts. Although the positive rate of cashew nut OFC was low, anaphylaxis during OFC was common. We should consider the indication of OFC carefully for patients with a history of immediate reactions to cashew nuts because the positive rate of cashew nut OFC was high. In patients without an immediate reaction to cashew nuts, the possibility of cashew nut allergy is low with a cashew nut sIgE value $< 5\%$ PPV and we may exclude cashew nut allergy. In patients with this characteristic, we should perform OFC in cases with a cashew nut sIgE PPV value of 5–95% and avoid OFC in cases with a PPV $> 95\%$.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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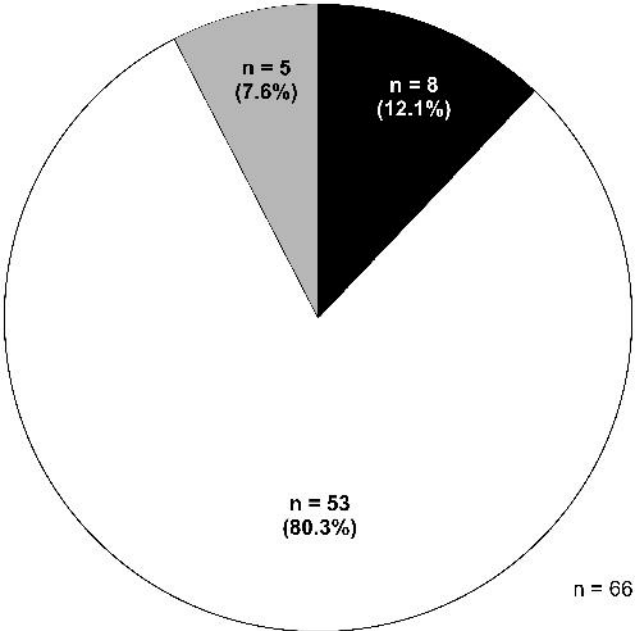
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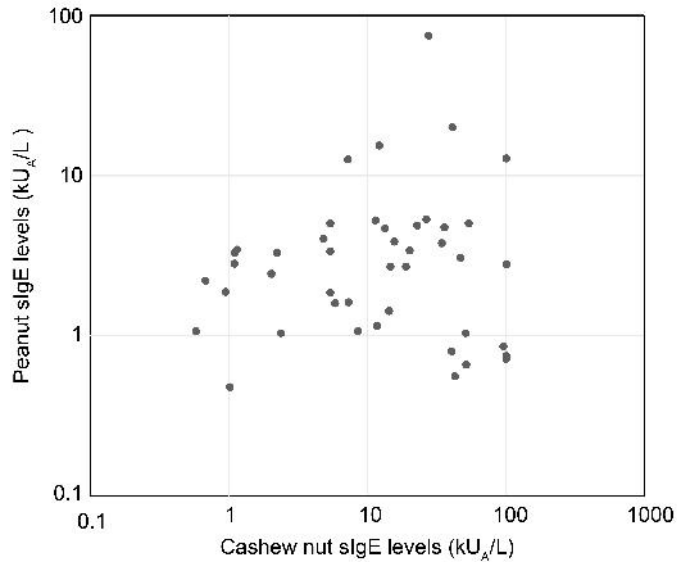
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Fig. S1. Reasons for elimination of cashew nut.

Fig. S2. Relationships between peanut and cashew nut sIgE levels. sIgE, specific IgE.



- History of immediate reaction
- Sensitization to positive cashew nut sIgE
- Others



1 **Supplemental Table 1.** Anaphylaxis for patients who experienced a positive cashew OFC result

	1	2	3	4	5	
Sex	M	F	M	M	M	
Age (years)	13	6	5	10	9	
Past history of FA	History of an immediate reaction to cashew nut	-	-	-	-	
	Immediate reaction to peanut	+	-	-	-	
	Immediate reaction to any nut except cashew nut	-	-	Walnut	Mixed nuts	
	Threshold dose at OFC to cashew nut	2.5	4	1.25	6.25	10
	Cashew nut-sIgE (kUA/L)	2.44	7.45	22.7	12.6	5.26
	Clinical signs	Urticaria Wheezing Abdominal pain	Urticaria Wheezing	Urticaria Dyspnea Vomit	Urticaria Wheezing Abdominal pain Activity low	Abdominal pain Tachycardia Pale
	Treatment	AH β2 Steroids Ad	AH β2 Steroids	AH β2 Steroids	AH β2	AH Steroids

2 OFC, oral food challenge; FA, food allergy; Ad, adrenaline; β2, β2-inhalation; AH, antihistamine; sIgE, specific IgE

1 **Supplementary Table 2.** Clinical efficacy of cashew nut sIgE for predicting positive OFC

Group	5% PPV	10% PPV	50% PPV	80% PPV	90% PPV	95% PPV
All patients [cashew nut sIgE (kU _A /L)]	1.1	2.0	12.8	40.7	80.1	149.5
Patients without history of an immediate reaction to cashew nut [cashew nut sIgE (kU _A /L)]	3.2	4.8	14.6	29.8	45.1	66.1

2 PPV, positive predictive value; sIgE, specific IgE