

Ana o 3 sIgE testing increases the accuracy of cashew allergy diagnosis using a two-step model

Thanh D. Dang, Rachel Peters, Melanie R. Neeland, Tim Brettig, Hayden Green, Vicki McWilliam, Mimi L. K. Tang, Shyamali Dharmage, Anne-Louise Ponsonby, Jennifer Koplin ... [See all authors](#) 

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Abstract

Background

Measurement of cashew-specific IgE (sIgE) is often used to confirm sensitization but does not reliably diagnose clinical allergy. Ana o 3 is the dominant cashew allergen detected in 75–100% of patients with cashew allergy but not currently used in clinical practice.

Objectives

To determine if component-resolved diagnostics using specific IgE to the 2 S albumin from cashew, Ana o 3, improves the accuracy of diagnosing cashew allergy, thereby circumventing the need for an oral food challenge (OFC) in some patients.

Methods

A population-based sample of 5276 children was recruited at age 1 year and followed up at age 6 years. Children with positive cashew skin prick test at age 6 underwent an OFC to clarify allergy status. Forty-seven children (mean age 5.02 ± 0.2) (33 cashew-allergic and 14 cashew-tolerant) had cashew sIgE and Ana o 3 sIgE quantified by ImmunoCAP System FEIA.

Results

A cutoff of >0.32 kUA/L for Ana o 3 sIgE provided 95% specificity and 90% sensitivity and correctly identified 90% of clinical cashew allergy. At the same specificity, the sensitivity

for cashew sIgE (>8.5 kUA/L) was only 26%. Sequential measurement of cashew sIgE followed by Ana o 3 sIgE diagnosed 90% of children with cashew allergy without the need for an OFC.

Conclusion

Ana o 3 sIgE testing provides higher diagnostic accuracy than cashew sIgE. Sequential measurement of cashew sIgE followed by Ana o 3 removed the need for a food challenge from 66% down to 12.8% (5-fold) of children compared with cashew sIgE testing alone.

Abbreviations

AUC

area under curve

ImmunoCAP FEIA

IMMUNOCAP fluorescence enzyme immunoassay

OFC

oral food challenge

PPV

positive predictive value

ROC

receiver operating characteristic

sIgE

specific immunoglobulin E

SPT

skin prick test

Key Message

This study is the first to show that using Ana o 3 specific IgE in a two-step model can predict cashew allergy with more accuracy than the current diagnostic blood test that rely on whole cashew-specific IgE, thereby reducing the need for oral food challenges to clarify clinical allergy status.

1 INTRODUCTION

Cashew nut has become an increasingly important food allergen and is one of the most common causes of food-induced anaphylaxis¹. Diagnosis is straightforward when there is an unequivocal history of clinical reaction to cashew ingestion². However, many patients can have more complicated histories; an oral food challenge (OFC) is required to confirm or exclude a diagnosis of cashew allergy³. Although definitive, the OFC is time-consuming and costly and is associated with a risk of anaphylaxis. Skin prick test (SPT) and cashew-specific

IgE (ImmunoCAP fluorescence enzyme immunoassay) blood test can be used to confirm cashew allergies, but not for the purposes of diagnosis because both have high sensitivity and low specificity for diagnosis of cashew allergy⁴. Furthermore, these tests may be falsely positive due to cross-reactivity to other tree nuts^{5, 6}.

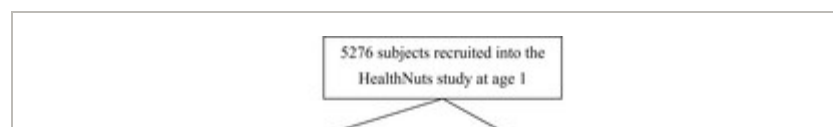
Component resolved diagnostics (CRD) is a new tool that has been shown to support the diagnostic pathway for some food allergens by avoiding OFCs⁷⁻¹⁰. Ana o 3 is the 2S albumin seed storage protein of cashew and, like other proteins in the family, is a highly stable allergen¹¹. Two recent studies in Greece and Germany have found that Ana o 3 was highly predictive of cashew allergy with 93% sensitivity and 95% specificity, but these findings need confirmation in other countries like Australia to confirm the possible regional differences in populations^{12, 13}.

The aim of our study is to determine the use of Ana o 3 in the prediction of cashew allergy and develop models for Ana o 3 testing in the community and clinical using The HealthNuts cohort of clearly defined clinical phenotypes¹⁴.

2 METHODS

2.1 Selection of subjects for IgE testing

The methods used in the HealthNuts study have been detailed previously¹⁴. In brief, 11- to 15-month-old infants were recruited from 131 council-run immunization sessions across Melbourne, Australia, and were assessed for their food allergy status. Follow-up methods at 4 and 6 years have been previously described¹⁵, in brief, all participants were followed up via questionnaire (81.3% and 83% participation, respectively, at 4 and 6 years) capturing demographic details, history of food allergy and new food reactions, common allergen exposure information, history of asthma/wheeze, and eczema. Included in the assessment is a SPT to a predetermined panel of 8 foods (milk, egg, peanut, wheat, sesame, cashew, almond, and hazelnut). All those with a detectable cashew SPT weal were offered a cashew OFC unless they had a recent history of IgE-mediated reaction to cashew and cashew SPT (Figure 1). Diagnosis of cashew allergy was defined as a positive food challenge or a clear-cut history of a recent reaction to cashew consistent with established OFC stopping criteria¹⁴, combined with sensitization to cashew extract. The protocol for cashew OFC were consistent with those of the Australian Society of Clinical Immunology and Allergy (ASCIA) using graded, incremental doses administered at 15- to 20-minute intervals with a top dose of 2 teaspoons of crushed cashew. All subjects with sufficient volume of plasma available for sIgE testing from the HealthNuts study were included in this study (Figure 1). If sample was available for the participant at both ages, the most recent sample from wave 3 (6-year time point) was selected for analysis.



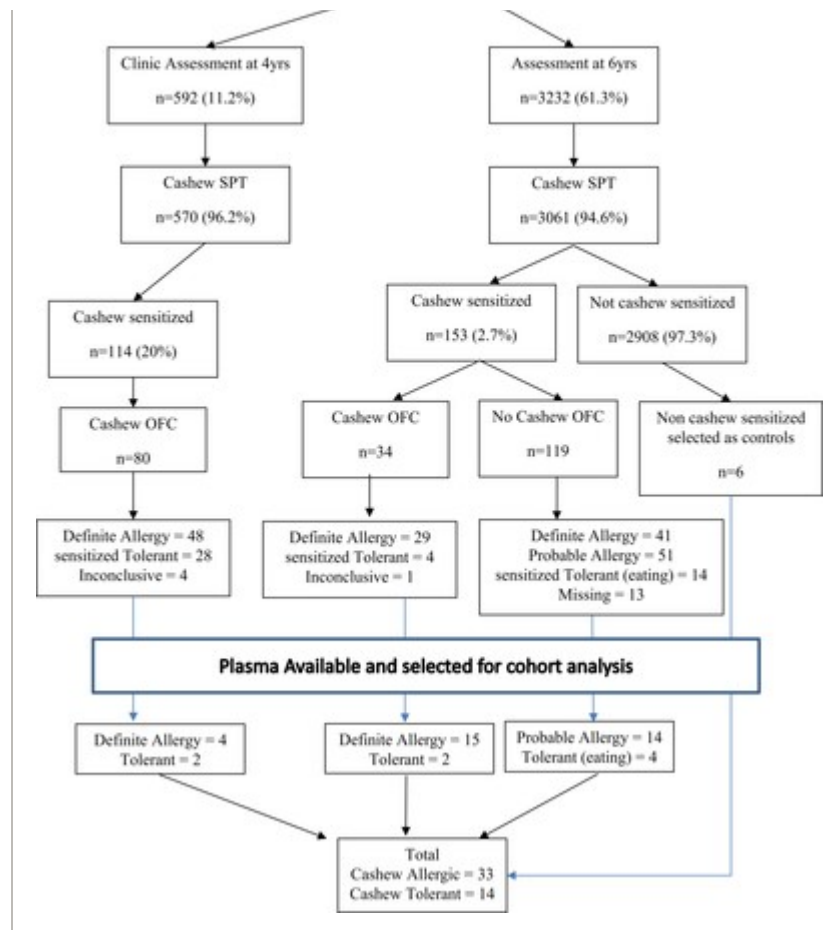


FIGURE 1

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Selection of subjects for Ana o 3 testing

2.2 Definitions

2.2.1 Cashew nut sensitization

SPT ≥ 3 mm (minus negative control) to cashew at clinical assessment

2.2.2 OFC confirmed cashew nut allergy

Any of the following: (1) positive OFC and IgE sensitized (sIgE ≥ 0.35 kUA/l) at 4 or 6 years; (2) history of objective reaction in the past 12 months consistent with HealthNuts OFC stopping criteria following definite exposure to cashew nut and evidence of IgE sensitization at 6 years; or (3) positive OFC at age 4 years and SPT ≥ 8 mm at 6 years of age (n = 19).

2.2.3 Non-OFC cashew nut allergy

Any of the following: (1) SPT ≥ 8 mm at age 6 and one of the following, a) history of objective reaction >12 months ago consistent with HealthNuts OFC stopping criteria following definite exposure to the food of interest, or b) parent-report avoiding food due to allergy (n = 14).

2.2.4 Cashew-tolerant

Any of the following (1) negative OFC; (2) SPT 0-2mm; or (3) SPT 3–7 mm and parent-reported ingestion history (eaten >1 time since age 4) (n = 14).

2.3 Cell separation and plasma collection and allergen-specific IgE analysis

Blood was collected into a sodium heparin tube (Sarstedt) after their respective 4 year or 6 year assessment. The blood was centrifugated off at 700 g for 10 minutes within 2 hours after the blood was taken and the plasma was collected and frozen at -80°C until use.

Allergen-sIgE was measured with the ImmunoCAP System FEIA (Phadia AB, Uppsala, Sweden). Plasma samples were analyzed for IgE to whole cashew and Ana o 3 (Phadia AB, Uppsala, Sweden).

2.4 Statistical analysis

Data were analyzed by generating the receiver operating characteristic (ROC) curve, and both the analyses were performed using GraphPad Prism 6.02 software. The sensitivities and specificities were generated for a range of cutoffs for the ROC curve. The p value was reported for the curve, testing the null hypothesis that the area under the curve is equal to 0.50. We also quote estimated positive and negative likelihood ratios, as their interpretation is not dependent on the underlying disease prevalence or the pre-test probability of the individual, which potentially permits the reader to then transfer results to their own patients. A full discussion of the role of the likelihood ratio and interpretation of thresholds is given by Roberts and Lack.¹¹ The SPT, cashew sIgE, and Ana o 3sIgE had a skewed distribution and are reported as median and ranges. The proportions comparing the allergic and tolerant population were tested using the two proportion z-test to determine significance between the two groups. Significance was indicated by a p-value <.05.

2.5 Ethics

Ethics approval was obtained for the HealthNuts study from the Victorian State Government Office for Children (reference no. CDF/07/492), the Victorian State Government Department of Human Services (reference no. 10/07), and the Royal Children's Hospital Human Research Ethics Committee (reference no. 27047 and 32294A).

3 RESULTS

3.1 Clinical features of the study sample

A total of 47 children were selected from the HealthNuts cohort based on plasma availability and included in this study (Figure 1). Thirty-three were cashew allergics, 19 confirmed with an OFC, and 14 were included with a clear clinical reaction in the last 12 months together with a $\text{SPT} \geq 8$ mm. Of the 14 cashew-tolerant children, 4 were confirmed with a cashew OFC, 4 were sensitized tolerant, and 6 were non-sensitized tolerant and were currently ingesting

cashew in their diet. Clinical characteristics of selected cohort are outlined in Table 1 and Table 2. A sensitivity analysis comparing the two cashew-allergic groups show the non-OFC group have higher cashew sIgE and SPT, and no differences in clinical characteristics (Table 2), and were combined for all subsequent analysis. A greater proportion of cashew-allergic children had co-existing food allergies (72.7%) compared to the group of cashew-tolerant children (33.3%), $p < .05$, which was more likely to be a co-existing tree nut allergy (60.6%) compared to (0.67%).

TABLE 1. Demographic and clinical characteristics, stratified by cashew allergy

	Cashew-tolerant (n = 14)	Cashew-allergic (n = 33)
Gender, male n (%)	8 (53.3)	20 (60.6)
Mean Age at OFC, yrs (SD)	4.6 (0.8)	5.2 (1.1)
Mean SPT, mm (SD)		
Cashew SPT	0.87 (0.61)	13.2 (1.26)
Median sIgE, kUA/L (interquartile range)		
Cashew sIgE	0.13 (0.02-0.81)	2.09 (0.8-6.7)
Ana o 3 sIgE	0.03 (0-0.11)	2.45 (0.94-6.64)
Received Cashew OFC, n (%)		
Cashew OFC	3 (20)	19 (58)
Food Allergy Details, n (%)		
No other food allergies	10 (66.67)	9 (27.3)
Co-existing food allergy		
Peanut allergy	2 (13.3)	16 (48.5)
Other tree nut ^a	1 (0.67)	20 (60.6)
Egg allergy	2 (13.3)	9 (27.3)

^a Tree nut allergy: defined as a positive OFC or history of reaction and sensitized (≥ 3 mm). Does not include those with SPT ≥ 8 mm defined as probable allergy in the HealthNuts (n = 19). Individual tree nut allergy details - hazelnut=9, macadamia=2, pecan=2, pistachio=4, walnut=8.

^b Tree nut sensitization 3–8 mm: almond=18, hazelnut=30, macadamia=11, pecan=16, pistachio=72, walnut=44.

^c Tree nut sensitization >8 mm: almond=3, hazelnut=15, macadamia=1, pecan=5, pistachio=21, walnut=15.

^d Current eczema, current asthma, current rhinitis=parent-report of doctor diagnosed eczema, asthma, rhinitis.

TABLE 2. Cashew SPT and sIgE stratified by cashew allergy

Allergy Sensitization	Cashew-tolerant (n=14)	Cashew Sensitized Allergic (n=33)	
		Cashew-allergic (n=19)	Probable Cashew-allergic (n=15)
Cashew SPT < 8 mm, n (%)	14 (100%)	3 (16%)	0 (0%)
Mean Cashew SPT, mm ($\pm$ SD)	0.87 ($\pm$ 0.61)	11.7 ($\pm$ 0.85)	15.6 ($\pm$ 1.89)
Cashew sIgE <8.5 kUA/l, n (%)	14 (100%)	15 (79%)	10 (67%)
Mean Cashew sIgE kUA/l, ($\pm$ SD)	0.90 ($\pm$ 0.56)	7.64 ($\pm$ 3.06)	15.0 ($\pm$ 5.86)
Median Cashew sIgE (kUA/l)	0.03 [0.02-0.96]	2.09 [0.24-44.4]	5.07 [0.1-79.4]
Ana o 3 sIgE <0.32 kUA/l, n (%)	14 (100%)	2 (11%)	2 (13%)
Mean Ana o 3 sIgE, kUA/l,($\pm$ SD)	0.11 ($\pm$ 0.06)	6.8 ($\pm$ 2.66)	14.3 ($\pm$ 5.32)
Median Ana o 3 sIgE (kUA/l)	1.88 [0.01-0.96]	2.45 [0-42.93]	6.72 [0.1-72.69]

A cutoff <0.1 kuA/l is classified as a negative result and is considered non-sensitized.

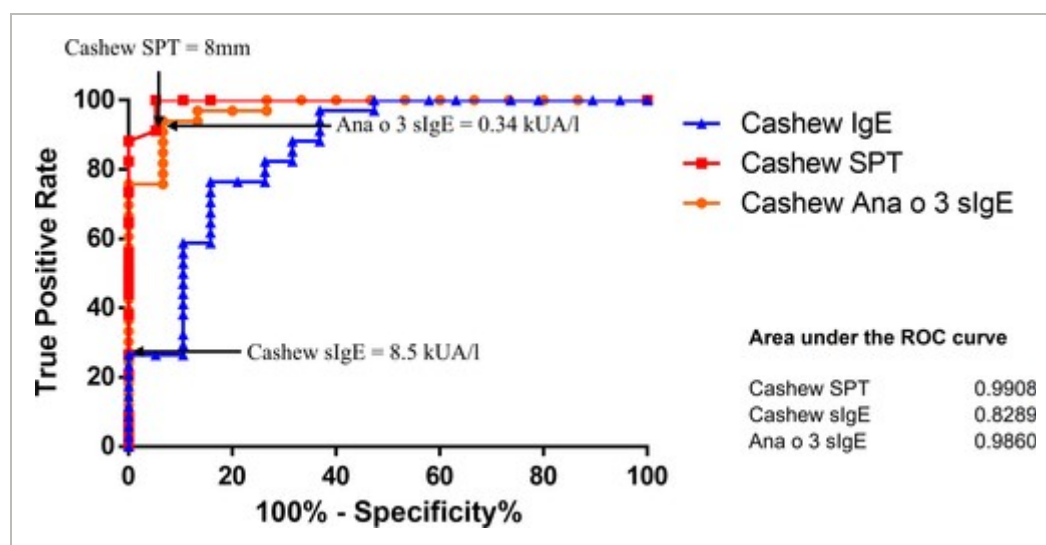


FIGURE 2

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ROC curves showing true positive rates (sensitivity) plotted against the false-positive rate (specificity) for different cutoff points of the quantified components of Ana o 3 (orange circles squares) and whole cashew extract (blue triangles). The points highlighted for Ana o 3 sIgE, cashew sIgE, cashew SPT indicate putative levels for determining 95% specificity (0.34kUA/l, 8.5kUA/l, and 8mm, respectively) for cashew allergy. The area under curve is 0.986, 0.991, and 0.823 for Ana o 3 sIgE, cashew SPT, and cashew sIgE, respectively

3.2 Accuracy of diagnosing cashew allergy using SPT and cashew sIgE

Using previously defined threshold for diagnosing cashew allergy (SPT wheal ≥ 8 mm)¹⁶, we assessed the utility of cashew SPTs and ImmunoCAP cashew sIgE measurements to diagnose cashew allergy in our cohort. 87.9% (n = 29) had a SPT results of 8 mm or greater and could be given a diagnosis of cashew allergy; however, 12% (n = 4) with SPT results of 3 to 7 mm would require an OFC to confirm the presence of allergy (Figure 3A). At a threshold of 8.5 kUA/l for cashew sIgE, where 95% specificity was reached, only 26% with cashew allergy (n = 9) could be given a diagnosis of cashew allergy, leaving 31 children with levels between 0.10 and 8.5 kUA/L and would require a OFC to confirm the presence of allergy (Figure 3A).

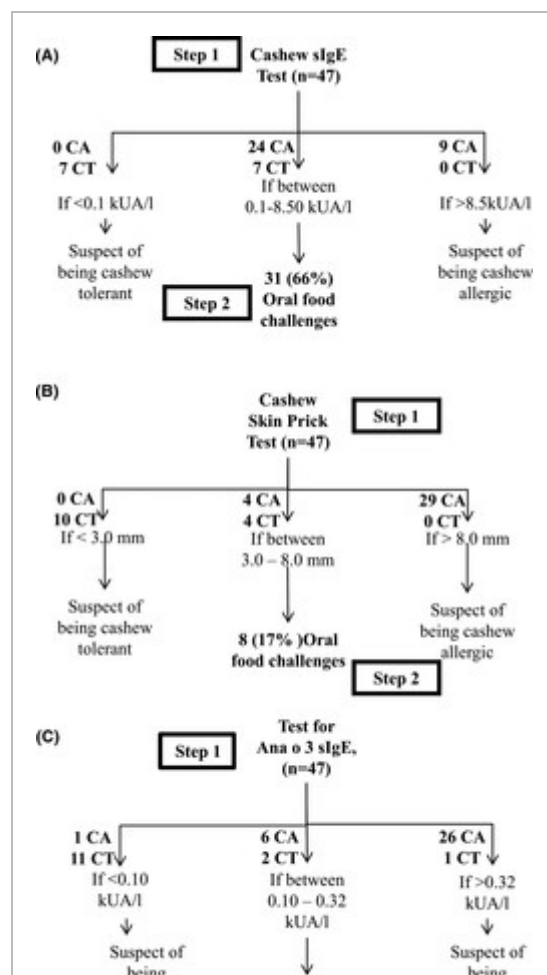




FIGURE 3

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(A–C) Comparison of various methods of diagnosing cashew allergy with Cashew sIgE (A), Cashew SPT (B), or Ana o 3 sIgE (C) followed by an oral food challenge. Patients from this study were examined using identified cutoffs for cashew sIgE and SPT to determine the stringency of each test. CA stands for cashew-allergic and CT stands for cashew-tolerant

3.3 Ana o 3 ImmunoCAP testing

To describe the accuracy of Ana o 3 sIgE testing, we report a number of Ana o 3 sIgE and cashew sIgE thresholds along with the sensitivities and specificities (Table 3). Ana o 3 sIgE level of >0.320 kUA/L provides 93.3% specificity and 90% sensitivity (95% CI, 73% to 95%), compared to cashew sIgE level of 8.54 kUA/L which provides a 95% specificity and a significantly lower sensitivity of 26% (95% CI, 13% to 44%; $p < .001$; Table 3).

TABLE 3. Sensitivity and specificity of various cutoffs for Ana o 3 and cashew sIgE

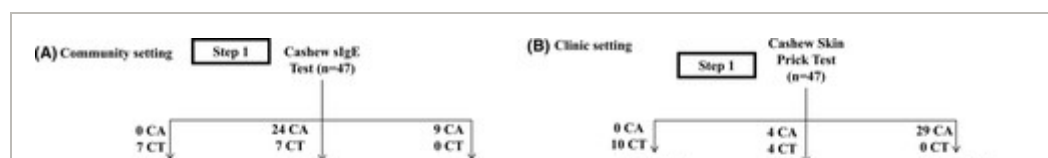
Ana o 3-specific IgE						Cashew-specific IgE				
Cutoff (kUA/l)	Sensitivity %	95% CI	Specificity %	95% CI	PLR ^a	Cutoff (KUA/l)	Sensitivity %	95% CI	Spe %	
Cashew allergics (n=19) versus Cashew sensitized tolerant (n=14)										
>0.1046	95	76.39% to 99.74%	66.67	43.75% to 83.72%	2.85	>0.1250	100	83.89% to 100.0%	42.	
>0.2135	95	76.39% to 99.74%	88.89	67.20% to 98.03%	8.55	>0.3500	85	63.96% to 94.76%	63.	
>0.3399	90	69.90% to 98.22%	94.44	74.24% to 99.72%	16.2	>1.055	65	43.29% to 81.88%	84.	
>0.6982	80	58.40% to 91.93%	94.44	74.24% to 99.72%	14.4	>1.670	55	34.21% to 74.18%	84.	
>0.9071	75	53.13% to 88.81%	94.44	74.24% to 99.72%	13.5	>6.695	25	11.19% to 46.87%	89.	

^a PLR is the positive likelihood ratio calculated by (sensitivity/(1-specificity)) and indicates the likelihood of having peanut allergy.

Compared with both SPTs and cashew sIgE measurements, measurement of Ana o 3 sIgE correctly identified more patients with true cashew allergy when cutoffs for 93% specificity or a 95% PPV were applied. The mean Ana o 3 sIgE level for the 33 patients with cashew allergy was 6.86 (standard deviation 11.9) kUA/L compared with 0.193 (0.281) kUA/L in the cashew-sensitized subjects who did not have cashew allergy and 0.0246 (0.0377) in the non-sensitized, non-cashew-allergic patients ($p = .001$) (Table 2). The area under the curve for the cashew sIgE ROC curve is 0.83 (95% CI, 0.79–0.99) compared with an area under the curve of 0.98 (95% CI, 0.88–1.00) for Ana o 3, indicating that Ana o 3 performs significantly better than cashew sIgE ($p < .027$, Figure 2). We found the performance of Ana o 3 sIgE and cashew SPT are comparable (Table S1), with the AUC for cashew SPT was 0.99 (95% CI, 0.89–1.00).

3.4 Diagnosing cashew allergy using a combination of previous methods and Ana o 3

We next investigated whether Ana o 3 could be used to sequentially to diagnose cashew allergy in patients who had SPT and sIgE below the cutoffs of 8 mm and 8.5 kUA/L, respectively. Figure 3 represents the number of OFCs that would be required if the current thresholds for cashew sIgE measurements, SPTs, and Ana o 3 sIgE measurements were used to diagnose cashew allergy in the absence of any other tests. Of the 47 children included in this study, OFCs would be required to confirm the allergy status on 31 (66%) based on cashew sIgE, 8 (17%) based on cashew SPT, and 8 (17%) based on Ana o 3 measurements. Figure 4 shows the number of OFCs required when incorporating the two methods of SPT or cashew sIgE as the first-line tests, together with Ana o 3 sIgE measurement as a second line of testing to help improve the accuracy of distinguishing patients with cashew allergy from those with cashew tolerance. In the first model, we report the results representative of a primary healthcare scenario involving only a blood test to diagnose cashew allergy. Of the 31 patients with cashew sIgE levels between 0.1 and 8.5 kUA/L successfully identified an additional 21 patients as cashew-allergic, and 3 children as cashew-tolerant with Ana o 3 sIgE testing (Figure 4A). Hence, incorporating Ana o 3 testing in combination with cashew sIgE testing would reduce the number of OFCs needed by from 65.96% down to 12.76% (a fold change of 5.2). In the second model, Ana o 3 testing patients with cashew SPT between 3 and 8mm identified a further 6 patients allergic to cashew, reducing the number of OFCs required by 17.02% down to 4.26% (a fold change of 4) (Figure 4B).



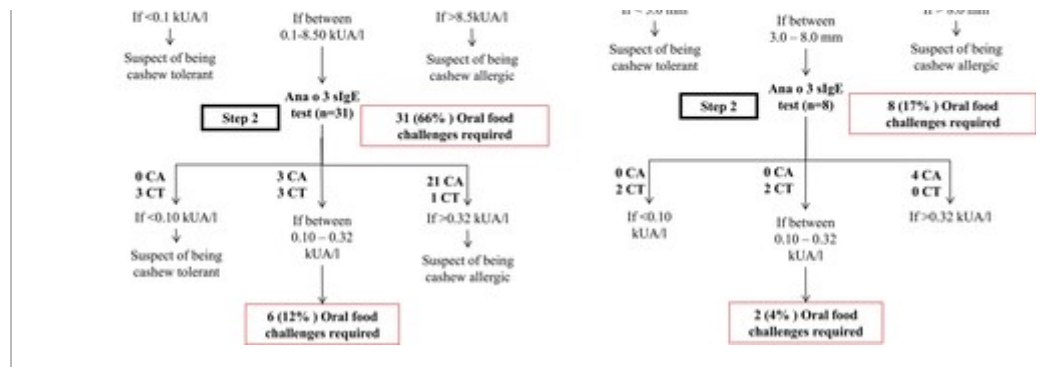


FIGURE 4

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(A-B) Comparison of clinical scenarios for diagnosing cashew allergy using a 2-step model in a community setting (A), or an allergy clinic setting (B). Cashew sIgE or Cashew SPT was assessed as the first-line test followed by Ana o 3 sIgE to help improve the diagnosis of cashew allergy when either cashew sIgE or cashew SPT tests results fall the respective cutoffs of either 0.35-8.5 kUA/l or 3-8mm. CA and CT denote the number of cashew-allergic and cashew-tolerant children respectively that fall into the designated ranges

4 DISCUSSION

This study reports the utility of Ana o 3-specific IgE testing in a cohort of with clearly defined clinical outcomes and developed testing models to correctly diagnose cashew allergy and reduce the number of OFCs. We found that Ana o 3 sIgE testing was more accurate in determining cashew allergy compared to cashew sIgE alone against the OFC. In addition, every allergic patient in our cohort was sensitized to Ana o 3, which means, on the other hand, that an undetectable level of specific IgE to Ana o 3 might be a good predictor of a negative challenge outcome.

The use of CRD for the improvement of food allergy diagnostics has been demonstrated for many foods, particularly with S2 albumin proteins such as Ara h 2 for peanut^{7, 17}. Our findings are similar to others which have reported Ana o 3 sIgE levels^{12, 13, 18}, indicating that Ana o 3 is consistently good for differentiating between allergic and tolerant pediatric patients. These studies including German, Japanese, Greek, and now Australian populations, consistently showing that Ana o 3 sIgE levels between 0.3 and 0.4 kUA/l are highly sensitive and specific for cashew allergy ($\geq 90\%$, and $\geq 95\%$, respectively).

Although the performance of cashew SPT was comparable to Ana o 3 sIgE testing, SPT is usually performed in a specialist setting, with the patient waiting times are at present significant exceeding 12 months in many centers in Australia¹⁴. By comparison, blood testing for Ana o 3 and whole cashew sIgE can be easily accessed in the community by primary and secondary healthcare professionals with access to diagnostic laboratories. Using our cohort, testing with cashew sIgE followed by Ana o 3 sIgE could substantially reduce the number of OFCs required to diagnose cashew allergy from 66% to 12%. Given that the cutoff of ≤ 0.1 kUA/l for Ana o 3 can identify 78.5% of cashew-tolerant children while

only having a 3% false-negative rate, this would support the gradual introduction of cashew into the diet if the child has not already eaten the food. While the use of Ana o 3 in the diagnosis of cashew allergy in the community has significant advantages, in an allergy clinic setting, cashew SPT still provides a rapid and accurate method for determining cashew allergy, and Ana o 3 sIgE could be used as a subsequent test to reduce the number of patients requiring an OFC.

The strengths of this study include the cohort of clearly phenotyped cashew-allergic and cashew-tolerant children through a SPT and an OFC. True population negative controls provided better evaluation of the performance of these tests as a screening tool for cashew allergy. This is the first study to present models on cashew SPT in combination with Ana o 3 sIgE and whole cashew sIgE on all subjects. The weakness of the current study is that not all children underwent OFC as the gold standard in food allergy diagnostics. However, clinically relevant cashew allergy was determined very carefully focusing on clear objective reactions to cashew in the patients' history. Few studies have been presented on the pattern of concomitant food allergies in tree nut-allergic patients ¹⁹ and our pediatric cohort.

In conclusion, our findings suggest that Ana o 3 sIgE testing used sequentially with cashew sIgE offers improved diagnostic accuracy for cashew allergy compared with whole cashew extract SPT or sIgE testing alone. This approach would be especially advantageous in settings where access to an allergy specialist, and hence, OFC is not readily available. The combined Ana o 3 and whole cashew sIgE testing approach substantially reduces the need for an OFC, which is expected to alleviate strain and demand on clinical allergy services.

Conflict of interest

M. L. K. Tang is on the Nestle Medical Advisory Board Oceania; is a past member of the Danone Nutricia Global Scientific Advisory Board and Medical Advisory Board ANZ; has received lecture fees from Danone Nutricia, Abbott Australasia, and Nestle; is employed by and holds stock options for Prota Therapeutics; had performed consultancy services for Deerfield Consultancy, GLC Consultancy, and Bayer; and has a patent through MCRI. V. McWilliam reports personal fees from speaker honorariums for Aspen Global, Abbott Australasia, and Nestle Health Sciences and personal fees from an Advisory Panel Consultancy for Nutricia outside the submitted work. The rest of the authors declare that they have no relevant conflicts of interest.

Author Contribution

Thanh D Dang: Conceptualization (equal); Data curation (equal); Formal analysis (lead); Methodology (lead); Supervision (equal); Writing – original draft (lead); Writing – review & editing (equal). **Rachel Louise Peters:** Conceptualization (equal); Formal analysis (equal); Methodology (equal); Writing – original draft (equal); Writing – review & editing (equal). **Melanie Neeland:** Methodology (equal); Writing – review & editing (equal). **Tim Brettig:**

Methodology (equal); Writing – review & editing (equal). **Hayden Green:** Data curation (equal); Methodology (equal). **Vicki McWilliam:** Conceptualization (equal); Methodology (equal); Writing – review & editing (equal). **Mimi Tang:** Methodology (equal); Writing – review & editing (equal). **Shyamali C Dharmage:** Methodology (equal); Writing – review & editing (equal). **Anne-Louise Ponsonby:** Methodology (equal); Writing – review & editing (equal). **Jennifer Julia Koplin:** Conceptualization (equal); Funding acquisition (equal); Investigation (equal); Writing – review & editing (equal). **Kirsten Perrett:** Conceptualization (equal); Funding acquisition (equal); Investigation (equal); Supervision (equal); Writing – review & editing (equal).

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Supplementary table 1. Performance of Ana o 3 sIgE and Cashew SPT thresholds

<u>Ana o 3-specific IgE</u>						<u>Cashew SPT</u>					
Cashew allergics (n=19) versus Cashew sensitized tolerant (n=14)											
<u>Cut-off (kUA/l)</u>	<u>Sensitivity %</u>	<u>95% CI</u>	<u>Specificity %</u>	<u>95% CI</u>	<u>PLR*</u>	<u>Cut-off (mm)</u>	<u>Sensitivity %</u>	<u>95% CI</u>	<u>Specificity %</u>	<u>95% CI</u>	<u>PLR*</u>
> 0.1046	95	76.39% to 99.74%	66.67	43.75% to 83.72%	2.85	> 3	85.7	57.19% to 98.22%	100.0	82.35% to 100.0%	-
> 0.2135	95	76.39% to 99.74%	88.89	67.20% to 98.03%	8.55	> 6	92.9	66.13% to 99.82%	100.0	82.35% to 100.0%	-
> 0.3399	90	69.90% to 98.22%	94.44	74.24% to 99.72%	16.2	> 7	92.9	66.13% to 99.82%	89.47	66.86% to 98.70%	8.821
> 0.6982	80	58.40% to 91.93%	94.44	74.24% to 99.72%	14.4	> 8	100	76.84% to 100.0%	84.21	60.42% to 96.62%	6.333
> 0.9071	75	53.13% to 88.81%	94.44	74.24% to 99.72%	13.5	> 9	100	76.84% to 100.0%	78.95	54.43% to 93.95%	4.750
> 0.9947	75	53.13% to 88.81%	100	82.41% to 100.0%	17.6	> 10	100	76.84% to 100.0%	68.42	43.45% to 87.42%	3.167
> 1.134	70	48.10% to 85.45%	100	82.41% to 100.0%	14.2	> 11	100	76.84% to 100.0%	52.63	28.86% to 75.55%	2.111
All cashew allergics (n=33) versus Cashew sensitized tolerant (n=14)											
> 0.09909	100.0	89.42% to 100.0%	73.33	44.90% to 92.21%	3.750	> 3	100.0	89.42% to 100.0%	85.71	57.19% to 98.22%	7.000
> 0.2135	93.94	79.77% to 99.26%	93.33	68.05% to 99.83%	14.09	> 6	100.0	89.42% to 100.0%	92.86	66.13% to 99.82%	14.00
> 0.3272	90.91	75.67% to 98.08%	93.33	68.05% to 99.83%	13.64	> 7	93.94	79.77% to 99.26%	92.86	66.13% to 99.82%	13.15
> 0.6180	84.85	68.10% to 94.89%	93.33	68.05% to 99.83%	12.73	> 8	90.91	75.67% to 98.08%	100.0	76.84% to 100.0%	-
> 0.9947	75.76	57.74% to 88.91%	100.0	78.20% to 100.0%	-	> 9.000	84.85	68.10% to 94.89%	100.0	76.84% to 100.0%	-
						> 10	66.67	48.17% to 82.04%	100.0	76.84% to 100.0%	-

* PLR is the positive likelihood ratio calculated by (sensitivity/(1-specificity)) and indicates the likelihood of having peanut allergy