Peeling the Peanut: Characterizing Peanut Allergy With the New Food Allergy Severity Score

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Peanut allergy is a major cause of severe food reactions worldwide. Together with tree nuts, it remains the most prevalent cause of fatal food anaphylaxis, according to reports from the US and the UK [1-3]. Many studies have identified predictors of severity of peanut allergy to improve risk stratification. These predictors include age at onset of allergy, atopic comorbidities, and food extract–specific IgE levels [4-6]. It is also known that sensitization to specific molecular peanut allergens, such as seed storage proteins, entails a higher risk of anaphylaxis [5,7]. Sensitization profiles and clinical presentations may differ according to diet and environmental exposure. In Mediterranean countries, frequent sensitization to peach lipid transfer protein (LTP) and cross-reactivity between food LTPs (including peanut LTP) is widely reported [6,8]. On the other hand, sensitization to Bet v 1 homologues (PR-10) have been identified mostly in Northern Europe and are associated with sensitization to birch tree pollen and milder symptoms, such as oral allergy syndrome [9]. This variability in the clinical presentation of food allergy highlights the need for a common language to characterize the severity of reactions worldwide and to better investigate clinical predictors.

The new ordinal food allergy severity score (oFASS) is a recently validated tool that makes it possible to standardize the assessment of severity and may contribute to a better identification of predictors [10]. A mild oFASS-3 score involves only the oral cavity. A moderate oFASS-3 score includes 1 or more of the following organs/systems: skin, nose, eyes, digestive system, and uterus, as well as the oral cavity. Lastly, a more severe oFASS-3 score includes the previous organs/systems and involvement of 1 or more of the following: larynx, bronchi, cardiovascular system, and nervous system. This scoring system has more detailed variations, especially oFASS-5, which further stratifies the moderate and severe degrees into 2 additional steps, resulting in an increasing severity scale ranging from 1 to 5. The aim of this study was

to characterize peanut allergy in a Portuguese cohort using this newly developed severity stratification score.

A cross-sectional study was conducted at the allergy clinic of a tertiary hospital from 2015 to 2022. To be included, the patients had to fulfill the following IgE-mediated peanut allergy criteria: positive specific IgE to peanut extract (≥0.35 kU_A/L); and reported symptoms to peanut and anaphylaxis classified according to the EAACI guidelines [11]. Demographic, clinical, and laboratory variables were correlated with the oFASS-3 and oFASS-5 scores of the patient's worst reaction to search for individual predictors of peanut allergy severity. The statistical analysis was conducted using STATA 16.1. *P* values of <.05 for correlations were considered statistically significant. The Mann-Whitney test was used for associations between dichotomous and categorical or continuous variables. Correlations between continuous and categorical data were assessed using the Spearman rank coefficient.

Overall, 80 patients with peanut allergy were evaluated (39 males [48.8%]; median [IQR] age, 23 [13-30] years). Despite correlating significantly with each other (*P*<.001), the highest correlation coefficients were recorded for oFAAS-5, both with oFASS-3 (r=0.911) and with peanut anaphylaxis (r=0.824). Thus, oFASS-5 was used to characterize peanut allergy (Table). Most patients had an oFASS-5 of 3 (31.2%), with an overall median of 2 (1-3), ie, potential involvement of the oral cavity, as well as the skin, nose/eyes, uterus, and digestive system. No patients had reactions with an oFASS-5 of 5 (most severe reaction, with confirmed involvement of either the cardiovascular system or neurologic system and possible involvement of other organs/systems). Despite the absence of sex differences, earlier allergy onset (r=–0.410, *P*<.001) and younger age at the time of the most severe reactions to peanut (r=–0.317, *P*=.005) were associated with higher oFASS-5 scores. Atopic background–related variables (allergic rhinoconjunctivitis, asthma, and atopic dermatitis) and reaction cofactors (exercise, alcohol, and NSAIDs) did not correlate significantly with oFAAS-5. Concomitant anaphylaxis to tree nuts was significantly associated with higher oFASS-5 in reactions to peanut (*P*<.001). The levels of peanut or tree nut sIgE extracts did not correlate with oFASS-5. Correlations were also observed for blood eosinophil count and total IgE levels, although these were not significant. However, sensitization to the peanut seed storage protein Ara h 2 was associated with higher oFASS-5 (P=.008), while Bet v 1 (a homologue of the

Table. Clinical Characteristics of Associations Between Peanut-Allergic Patients and oFASS-5.

Variables[a]	oFASS-5 (n=80)					Overall	*P* Value	Spearman coefficient[b]
	1 n=23, 28.8%	2 n=22, 27.5%	3 n=25, 31.2%	4 n=10, 12.5%	5 n=0, 0%			
Demographic data								
Median age at onset of food allergy (n=80)	16	15	8	8		12	<.001[c]	–0.410
Median age at most severe reaction (n=80)	28	24	22	16		23	.005[c]	–0.317
Male sex, No. (%) (n=80)	10 (43.5)	12 (54.6)	11 (44.0)	6 (60.0)		39 (48.8)	.651	
Clinical background								
Asthma, No. (%) (n=75)	13 (59.1)	11 (55.0)	14 (56.0)	5 (11.6)		43 (57.3)	.996	
Allergic rhinoconjunctivitis, No. (%) (n=78)	18 (78.3)	16 (76.2)	18 (72.0)	7 (77.8)		59 (75.6)	.750	
Atopic dermatitis, No. (%) (n=74)	6 (27.3)	8 (38.1)	10 (43.5)	2 (25.0)		26 (35.1)	.566	
Cofactors, No. (%) (n=66)	4 (22.2)	4 (20.0)	6 (31.6)	3 (33.3)		17 (25.8)	.393	
Anaphylaxis to peanut, No. (%) (n=80)	0 (0)	2 (9.1)	22 (88.0)	10 (100.0)		34 (42.5)	<.001[c]	0.824
Reactions to tree nuts, No. (%) (n=75)	16 (72.7)	15 (75.0)	12 (52.2)	4 (40.0)		47 (62.7)	.035c	
Anaphylaxis to tree nuts, No. (%) (n=46)	0 (0)	0 (0)	6 (50.0)	3 (100.0)		9 (19.6)	<.001[c]	
Laboratory data								
Median total IgE, IU/mL (n=44)	203	358	238	615		342	.204	0.176
Blood eosinophil count/µL (n=34)	180	300	390	300		250	.081	0.303
Median sIgE to peanut, kU_A/L (n=80)	1.64	2.24	1.94	3.60		1.94	.151	0.176
Ara h 2 positivity, No. (%) (n=37)	0 (0)	2 (15.4)	3 (30.0)	4 (57.1)		9 (25.7)	.008[c]	
Ara h 9 positivity, No. (%) (n=12)	0 (0)	3 (100.0)	3 (75.0)	3 (75.0)		9 (75.0)	.787	
Pru p 3 positivity, No. (%) (n=63)	15 (68.2)	9 (20.4)	14 (31.8)	6 (13.6)		44 (69.8)	.680	
Bet v 1 positivity, No. (%) (n=22)	3 (60.0)	2 (22.2)	0 (0)	0 (0)		5 (22.7)	.014[c]	

[a]Number of patients collected in parentheses reflects available data; anaphylaxis to peanut/tree nuts classified according to EAACI criteria [11].
[b]Used when statistically applicable.
[c]Statistically significant.

peanut PR-10 Ara h 8) was associated with a lower oFASS-5 (P=.014). Despite the high prevalence of sensitization to LTP (69.8% of 63 measurements), neither Pru p 3 nor Ara h 9 was associated with a higher peanut oFASS-5 score.

The newly validated oFASS score proved useful for stratifying the severity of peanut allergy in our cohort. We found that it was easy to apply, correlated significantly with peanut anaphylaxis, and provided numerical information that was not available in traditional dichotomic descriptions (eg, anaphylaxis vs nonanaphylaxis; with skin symptoms vs without).

oFASS-based characterization identified previously well-known predictors, such as sensitization to seed storage proteins (Ara h 2) for severe reactions and PR-10 (Bet v 1) for mild reactions. Interestingly, despite frequent sensitization to LTPs in our cohort, neither Pru p 3 nor the peanut LTP Ara h 9 correlated with oFASS-5, suggesting that severity of LTP allergy is highly variable and may depend on the type of food involved. In our study, oFASS identified the predictors of anaphylaxis to peanut to be lower age of peanut allergy onset and concomitant anaphylaxis to tree nuts, in accordance with findings of the recent EuroPrevall study [5].

Our study was limited by its retrospective design, meaning that some data were missing, particularly regarding the limited available peanut molecular profile; a larger and more diverse sample could have strengthened the power of our statistical analysis [12]. However, there is still room to explore the full potential of this tool in peanut allergy, and future studies should include more peanut molecular proteins, such as the PR-10 Ara h 8 and other seed storage proteins, such as Ara h 1 [13], in order to build detailed sensitization and cross-reactivity profiles. Such an approach has the potential to improve dietary recommendations and influence decisions regarding food immunotherapy. In addition, regional differences in the sensitization patterns of peanut allergy (eg, Mediterranean vs Northern Europe) could be better compared with a widespread and multicenter use of the oFASS score, enabling more accurate models for predicting severity and leading to a more in-depth understanding of regional impacts.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentations

The data reported here were presented as a Poster at the 2022 FAAM Congress.

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