Comparison of Severity Scorings in Oral Food Challenges With Cow's Milk

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To the Editor:

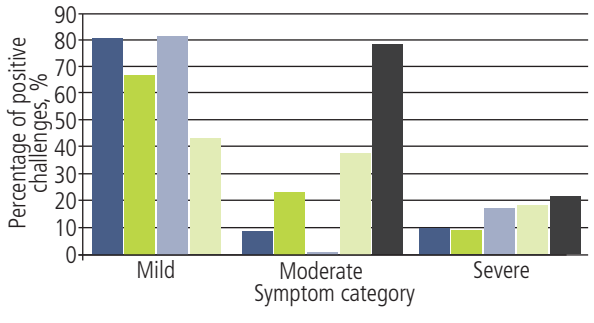
Cow's milk allergy (CMA) is the most common food allergy in early childhood. Its diagnosis is based on clinical history, sensitization, and oral food challenge (OFC). Different scoring systems have been developed to objectively assess OFC symptoms and their severity. However, the large number of scoring systems reflects the difficulty of fully standardizing assessment of symptoms [1]. We compared 2 widely used methods for assessing symptoms, namely, that of Hourihane et al [2] and that of Sampson [3] and investigated their differences in open OFCs with cow's milk. Furthermore, we compared these scores with the Food Allergy Severity Score (FASS) [4], the only validated scoring system developed to date.

We challenged 135 Finnish children (median [IQR] age, 1.8 [1.3-3.7] years) with cow's milk at the Helsinki University Skin and Allergy Hospital, as previously described [5], and evaluated the reactions according to the PRACTALL consensus criteria [6]. Symptom severity was assessed retrospectively by author ON with the severity scoring system of Hourihane et al (HSS) [2], that of Sampson (SSS) [3], a modified HSS (mHSS) [7], and a modified SSS (mSSS) (sFile S1). Additionally, FASS was applied for all the reactions using R studio and the code provided by the developers of FASS [4]. All symptoms evaluated according to the PRACTALL criteria and their respective severity scorings appear in sTable S2. ON acquired a second opinion from author KP in cases of uncertainty. The level of agreement between the scoring systems was determined by a linearly weighted Cohen κ using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp.). The Sampson grades were classified as mild (grades 1 and 2), moderate (grade 3), and severe (grades 4 and 5). Tables and graphs were prepared using Microsoft Excel (version 2211).

Positive results were recorded in 103 of the 135 challenges (76%). Six of the positive reactions were excluded from further analysis because of inconclusive symptoms. The Figure shows the severity of the reactions according to the SSS, HSS, mSSS, mHSS, and FASS (ordinal format, 3 grades [oFASS-3]) [4].

Agreement on the severity of the reaction between SSS and HSS was weak (weighted Cohen κ, 0.496). Unlike SSS, HSS was affected by the cumulative reactive dose. Abdominal pain was recognized only by HSS, while inspiratory stridor was not identified by SSS. SSS identified many symptoms not recognized by HSS, namely, flushing, oral allergy syndrome (OAS), lip swelling, nausea, diarrhea, loss of bowel control, dysphagia, upper airway symptoms (sneezing, rhinorrhea, nasal congestion), cardiovascular symptoms (tachycardia, hypotension, severe bradycardia, dysrhythmia, cardiac arrest), dyspnea, cyanosis, feeling of impending doom, light headedness, and change in activity level. Symptoms not recognized by either scoring system included persistent cough, itching and rubbing of eyes and nose, and decrease in arterial blood saturation.

Some symptoms were scored differently. Vomiting was graded as moderate by HSS, but as mild (1 episode of vomiting) or moderate (>1 episode) by SSS. Angioedema was moderate with HSS but mild with SSS, whereas generalized



		SSS		
		Mild (1-2)	Moderate (3)	Severe (4-5)
HSS	Mild (1-5)	58*	7	0
	Moderate (6-13)	20	2*	1
	Severe (14-23)	0	0	9*

Figure. Bar chart representing the severity of oral food challenge reaction assessed based on the 5 different scoring systems (n=97). The severity of reactions graded similarly by both SSS and HSS is marked with an asterisk. The scores leading to the corresponding severity grades are shown in parenthesis. SSS indicates Sampson severity score [3]; HSS, Hourihane severity score [2]; mSSS, modified Sampson severity score (sTable S1); mHSS, modified Hourihane severity score [7]; oFASS-3, Food Allergy Severity Score, ordinal format, 3 grades [4].

urticaria was either mild or moderate by HSS, depending on the cumulative reactive dose, but was graded as mild with SSS.

In our cohort, 20 of the 81 reactions scored as mild by SSS were scored as moderate by HSS. This was due to vomiting in 10 cases, generalized urticaria elicited by a small dose in 6 cases, and abdominal pain in 4 cases (instead graded as OAS in 2, nausea in 1, and nasal congestion in 1 with SSS). Seven cases of rhinorrhea were moderate according to SSS but mild with HSS, as local skin reactions were used for grading. One case of dyspnea scored as severe by SSS was moderate with HSS owing to abdominal pain. Eight cases of persistent cough were not recognized by either scoring system. Instead, they were graded based on vomiting in 2, local skin reactions in 3, and generalized urticaria in 1 case. The remaining 2 cases were scored according to rhinorrhea with SSS and local skin reactions with HSS.

The differences between SSS and HSS were especially pronounced in gastrointestinal symptoms. Vomiting was graded differently, and OAS was not recognized by HSS. In addition, HSS always graded abdominal pain as moderate, whereas SSS neglected it altogether. Relatively common symptoms such as persistent cough and ocular itching were neglected by both scorings. HSS, which was originally developed for peanut challenge, does not recognize upper airway symptoms, dysrhythmias, or changes in activity level. In addition, identification of severe respiratory symptoms and laryngeal symptoms depends largely on individual interpretation in HSS.

Our mSSS (sFile S1) added mild and severe abdominal pain as recognized symptoms (grades 2 and 3, respectively) and graded intermittent and constant sneezing and rhinorrhea as mild (grade 2) and moderate (grade 3) symptoms [8]. Ocular itching was added as a mild symptom [9]. Persistent cough and inspiratory stridor were added as severe grade 4 symptoms. Agreement between SSS and mSSS was moderate (weighted Cohen κ, 0.663). The results of the comparison between HSS and mHSS are shown in sFile S3. Their mutual agreement was weak (weighted Cohen κ, 0.570).

FASS recognizes symptoms according to the PRATCALL consensus criteria [6]. It uses the organs and systems affected rather than symptoms alone when grading the severity of a reaction. Grade 1 (OAS) is considered mild, grades 2 and 3 moderate (respectively, 1 and at least 2 of skin, nose/eye, digestive tract, and uterus affected), and grades 4 (larynx or bronchi) and 5 (cardiovascular or nervous system) as severe. Mild and moderate reactions assessed by SSS or HSS were moderate in FASS, apart from 12 cases considered severe. These included 1 case of weakness, 1 case of dyspnea (severe in SSS), and 10 cases of frequent coughing not recognized by either scoring system. All cases assessed as severe by either SSS or HSS were also severe in FASS.

Using oFASS-3 [4], no reaction was mild, since there were no patients with only oral or pharyngeal itching. Of these reactions, 76 (78%) were moderate and 21 (22%) severe (Figure). Using oFASS-5 [4], 54 of the moderate reactions (71%) were grade 2 and 22 (29%) were grade 3. Of the severe reactions, 17 (81%) were grade 4 and 4 (19%) were grade 5.

Unlike SSS and HSS, FASS recognized both itching and rubbing of the eyes and nose and frequent coughing. Compared to SSS, FASS recognized abdominal pain and inspiratory stridor. It did not recognize nasal congestion, dyspnea, respiratory arrest, dysphagia, loss of bowel control, or feeling of impending doom. In addition, dysrhythmia, severe bradycardia, and cyanosis were not specified. The weighted Cohen κ was 0.150. Unlike HSS, FASS recognized flushing, lip edema, OAS, nausea, upper respiratory symptoms (rhinorrhea, sneezing), changes in activity level, weakness, tachycardia, hypotension, and diarrhea. It also better specified laryngeal symptoms, collapse, and severe respiratory symptoms. The weighted Cohen κ was 0.155. These κ values are probably explained by the absence of patients with OAS as their only symptom, recognition of frequent coughing as a symptom, and the use of organs and systems to grade severity instead of symptoms alone. When oFASS-5 was compared with SSS grades 1 to 5, the κ value increased to 0.261, thus further supporting the role of different views on OAS and coughing as explanations for the small κ values.

Our results for the severity of reactions in 97 positive oral cow's milk challenges show that different severity scoring systems generate different grades. Clinicians worldwide use varied scoring systems, further increasing heterogeneity. Even identical scoring systems show substantial interobserver variability for symptom assessment, with the κ for mutual agreement being 0.31 to 0.46 [10]. Attempts to predict the severity of reactions using different markers, such as specific IgE, would benefit from a unified severity scoring system. Currently, only 1 severity scoring system has been properly validated [4]. As such, there is much anticipation for the DEFASE project undertaken by the World Allergy Organization to further our understanding of the severity of food allergies [1].

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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