

SUPPLEMENTARY MATERIAL**Gastrointestinal symptoms, under the tip of the iceberg in lipid transfer protein food allergy**Supplementary data**Material and methods***Patient selection*

Our sample included 512 Pru p 3-allergic patients, aged between 18 and 75 years (mean age: 41 years), referred to our centre from June 2013 to May 2022 due to suspected symptoms consistent with food allergy (FA) and/or other allergies. Patients were recruited consecutively based on peach LTP sIgE (Pru p 3) measured by ImmunoCAP® (ThermoFisher Scientific, Uppsala, Sweden) and presenting clinical symptoms compatible with LTP food allergy [1]. sIgE to Pru p 3 ≥ 0.10 kU/L was considered positive. Total IgE (tIgE) was determined using ImmunoCAP® (Thermofisher Scientific).

The clinical information provided by the patients was cross-checked with electronic records from the Allergy Department. To diminish variability in the diagnosis, all patients were evaluated by two doctors following the same protocol, which was agreed in the national Asthma, Adverse and Allergic Reactions Network (ARADyAL).

Demographic data, respiratory and food allergy symptoms and food allergy reaction features, including severity score by Brown's scale¹, total IgE (tIgE), peach, Pru p 3, Mal d 3, Jug r 3, Ara h 9, Cor a 8 and Tri a 14 sIgE (ImmunoCAP®, ThermoFisher Scientific, Uppsala, Sweden) were analysed. We also performed skin prick test with peach LTP (ALK-Abelló®, Madrid, Spain) and pollens (including grass, wall pellitory, mugwort, olive tree, cypress and plane tree pollen) (Diater®, Madrid, Spain).

Patients were grouped into two clinical phenotypes, according to the presence of gastrointestinal symptoms related to LTP-containing food intake, identified by clinical history: (1) Gastrointestinal group (GI-YES) included patients with a history of gastrointestinal symptoms (abdominal pain, cramping, bloating, nausea, vomiting, diarrhea, constipation or early satiety) related to LTP-containing food intake; and (2) Non-GI group (GI-NO), comprising patients in which GI symptoms had never been associated.

Systemic reactions severity score was graded according to Brown's scale, which categorizes systemic reactions into three grades.

Informed consent was obtained from all participating subjects. The study was approved by the local ethics committee of the Hospital Clinic (Barcelona, Spain).

Statistical analysis

Quantitative variables were expressed as means \pm standard deviation and range, and qualitative variables by absolute frequencies and percentages. Quantitative variables were analyzed by Student's t test and/or Mann-Whitney U test, as appropriate. Associations between explanatory and outcome variables were estimated by calculating the odds ratio (OR) and 95% confidence interval (CI) for quantitative variables and by applying the χ^2 or Fisher's exact test to the qualitative variables. A P value below 0.05 was considered significant. The statistical software used was SPSS v.24.

References:

1. Skypala IJ, Asero R, Barber D, Cecchi L, Diaz Perales A, Hoffmann-Sommergruber K, et al; European Academy of Allergy; Clinical Immunology (EAACI) Task Force: Non-specific Lipid Transfer Protein Allergy Across Europe. Non-specific lipid-transfer proteins: Allergen structure and function, cross-reactivity, sensitization, and epidemiology. *Clin Transl Allergy*. 2021;11(3):e12010. doi: 10.1002/ct2.12010. PMID: 34025983.