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Prediction of peanut-challenge outcome with biomarkers

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Background: Food challenges are currently the gold standard to diagnose/monitor food allergies, but are time-consuming and potentially harmful, suggesting the need for the development of a reliable serum biomarker-based tool.

Method: The VIPES/OLFUS data encompass 110 pediatric patients who underwent 3 peanut-challenges: at inclusion, year-1 and year-2 of Viaskin® treatment, totaling 310 challenges. Concentrations of serum biomarkers related to peanut allergy (including peanut-specific IgE [p-sIgE], peanut-specific IgG4 [p-sIgG4] and Ara h 2 p-sIgE [a2-sIgE]) and clinical variables were collected before each challenge. The peanut-challenge outcome was to be modeled as a binary endpoint defined by 3 reactive threshold doses: 300mg, 1000mg, 2000mg. Univariate analysis evaluated all possible predictors by 2-sided non-parametric statistical tests comparing children below and above each threshold dose. Multivariate analysis used a multiple random resampling methodology. Data were randomly split 200 times in training/test sets. The training set allowed identification of the most useful variables and building models. The test set evaluated the solution "learned" on the training set, predicting the endpoint on the patients of the test set and comparing it to the real outcome.

Results: For the 300mg cut-off, 13 variables differed significantly, p-sIgG4/a2-sIgE and p-sIgG4/p-sIgE were the most discriminating (both p-values<0.001). For the 1000mg cut-off, 14 variables differed significantly, including age, p-sIgG4/p-sIgE and p-sIgG4/a2-sIgE were the most discriminating (both <0.001). For the 2000mg cut-off, 13 variables differed significantly, and p-sIgG4/a2-sIgE and p-sIgG4/p-sIgE were the most discriminating (both <0.001).
Best performances were obtained with linear models. Signatures of 2-4 variables gave the highest AUCs. The 300mg endpoint was modeled with 2 variables (AUC=0.73±0.058), the 1000mg endpoint with 4 variables (AUC=0.80±0.062) and the 2000mg endpoint with 3 variables (AUC=0.84±0.075). The ratios p-sIgG4/a2-sIgE and p-sIgG4/p-sIgE are important determinants in all 3 models.

Conclusion: Modeling peanut-challenges based on a limited subset of serum biomarkers is feasible. The combination of the 3 models could be considered to reduce the use of peanut-challenges, especially challenges which would have been very likely to be negative, in both clinical studies and routine.