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Effect of Food Allergens on the Duodenal Mucosa Visualized by Probe-Based Confocal Laser Endomicroscopy

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Abstract

Background: Irritable bowel syndrome (IBS) is a chronic condition affecting around 4% of the global population. Despite extensive testing, only half of IBS patients with suspected food allergies receive a definitive diagnosis using current standard tests. Confocal laser endomicroscopy (CLE) provides high-resolution, real-time visualization of the intestinal mucosa and may offer new insights into the relationship between food allergens and IBS. **Methods:** This prospective study evaluated the efficacy of the Food Allergen Sensitivity Test (FAST) using CLE to detect immediate structural and functional changes in the duodenal mucosa of IBS patients following exposure to specific food allergens. Forty patients with IBS, as defined by the ROME IV classification, were recruited. The patients underwent standard upper endoscopy followed by the FAST test using the six most popular food allergens. Participants' IBS symptoms were assessed using the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) questionnaire at baseline, two months, and six months after the test. **Results:** Of the 40 patients recruited, 38 completed the study, and 25 showed a positive reaction to food allergens during the FAST test. Following an allergen-specific exclusion diet for six months, participants experienced significant reductions in IBS-SSS scores, and a significant improvement in their daily life with median scores decreasing from 160 at baseline to 35 at two months and 0 at six months ($p < 0.05$). **Discussion:** This study highlights the potential of CLE in identifying specific food allergens contributing to IBS symptoms. By using the FAST test to guide personalized exclusion diets, patients reported significant improvements in their symptoms, emphasizing the importance of targeted dietary interventions in IBS management. Meanwhile, traditional endoscopy does not allow for the simultaneous treatment of polyps and diverticula, nor the diagnosis of Crohn's disease or ulcerative colitis. **Conclusion:** The FAST test using

CLE is a valuable diagnostic tool for identifying food allergens in IBS patients. Personalized dietary interventions based on FAST test results can lead to significant improvements in clinical outcomes, 65.8% of patients responded positively to the procedure reducing the burden of this chronic condition.

Keywords

Irritable Bowel Syndrome, Confocal Laser Endomicroscopy, Food Allergens, Personalized Dietary Interventions, FAST Test

1. Introduction

Irritable Bowel Syndrome (IBS), or functional colopathy, is a chronic gastrointestinal disorder affecting around 4% of the global population [1]. This syndrome is characterized by chronic abdominal pain or discomfort and a change in bowel habits (constipation, diarrhea, bloating) in the absence of identifiable structural or metabolic abnormalities (e.g., celiac disease, RCH, Crohn's disease) [2]. These symptoms impact the quality of life of these patients, who must therefore incorporate the management of their disease into their daily lives [3]. IBS is subclassified into three subtypes according to the predominant symptom: the IBS-D subtype (diarrheal episodes), the IBS-C subtype (constipation episodes), and finally the IBS-M subtype (diarrhea and constipation) [4]. Dietary factors are among the most represented in terms of causes of this syndrome. Over 60% of IBS patients experience postprandial worsening, which may be linked to food allergies [5] [6]. This reaction may involve non-IgE-mediated mechanisms. Mediated mechanisms [6]. Symptoms related to food allergies can be treated with an exclusion diet, while IBS conditions not related to food lead to symptoms such as bloating, abdominal discomfort, or pain. Current tests are the prick test, IgE assay, or hydrogen breath test, but only about half of IBS patients with IgE-mediated food allergies receive a definitive diagnosis using these methods with these tests [7].

In 2014, Fritscher-Ravens *et al.* [8] described were the first to describe the potential of endomicroscopy in diagnosing food allergies by observing the duodenal mucosal reactions to food allergens in patients with IBS. Confocal laser endomicroscopy (CLE) is a new endoscopic imaging tool that allows visualization of changes in the intestinal mucosa. The use of intravenous fluorescein enables high-resolution real-time in vivo imaging at the micron scale, allowing microscopic evaluation of the mucosal layer during digestive endoscopy [9]-[17].

In 2024 a review was published by Balsiger *et al.* [18] proposing a practical version of the FAST protocol based on an extensive review of the literature and their clinical experience.

Study (Balsiger LM *et al.*) showed substantial to perfect intra-observer agreement and substantial inter-observer agreement for the judgment of acute disruption triggered by feeding of the duodenal epithelial barrier by pCLE, confirming

that this real-time readout is reliable and reproducible.

The present study aims to evaluate, through CLE, the immediate structural and functional changes that occur in the duodenal mucosa in patients with IBS, as well as to identify the patients in whom the exclusion of foods has improved their symptoms.

2. Materials and Methods

This is a prospective study promoted by Clinic Trocadero in Paris, France, enrolling patients from 09/2021 to 10/2022. The primary endpoint is to evaluate the structural and functional changes in the duodenal mucosa of IBS patients using CLE and to confirm the safety of the procedure. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from COMMITTEE FOR THE PROTECTION OF PERSONS NORTH WEST III under reference CNRIPH: 21.05.04.55700 with a favorable opinion issued on August 20, 2021 and is registered on ClinicalTrials.gov (NCT05072665) with a registration date of September 1, 2021.

The study recruited 40 patients diagnosed with IBS according to the ROME IV classification. Inclusion criteria for the study are as follows: 1) Patients had to be over 18 years old and diagnosed with IBS according to the ROME IV classification. 2) Patients must have a negative blood test, including IgE levels and anti-transglutaminase IgA (to rule out celiac disease), but present symptoms potentially related to food allergies. 3) Patients must be affiliated with the French Social Security system. In addition, the following conditions had to be excluded: patients under 18 years old, and those under legal protection such as guardianship, pregnant or breastfeeding women, patients with a known allergy to fluorescein, and patients with digestive cancer. All participants were invited to sign the participant consent form.

3. FAST Test Procedure

3.1. Before the Procedure

Initially, patients were seen by a nutritionist. During this consultation, eligible patients were offered the opportunity to undergo the FAST test as part of the routine endoscopy.

Up to 7 days before the procedure, a questionnaire to assess symptom severity (IBS-SSS) was provided to patients who had agreed to participate in the study. The questionnaire responses served as a reference for evaluating symptom progression if a food exclusion diet was to be implemented following the procedure.

Finally, two to three days before the FAST test, patients followed an exclusion diet consuming only hypoallergenic nutritional foods like rice, potatoes, olive oil, and salt.

3.2. During the Procedure

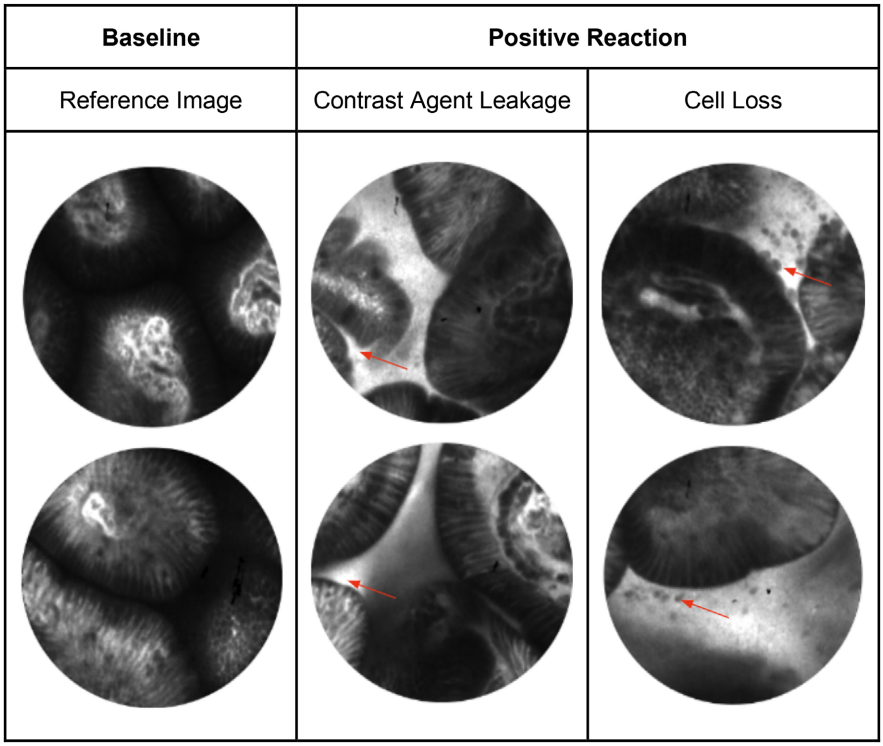
Before starting the FAST test, a standard upper white light endoscopy was per-

formed to observe any signs of structural mucosal anomaly that would suggest a gastrointestinal disease. The patient is positioned on the examination table under general anesthesia, with an anesthesiologist present throughout the procedure. The gastroenterologist uses an endoscope, introduced carefully into the duodenum. If a mucosal anomaly was observed during endoscopy, the FAST test would have been canceled. In cases of mild reflux disease, the test proceeded.

The FAST test and CLE results were performed and interpreted, they were carried out by a gastroenterologist with several years of clinical experience in functional intestinal disorders, specifically trained in the CLE technique by professionals from the company MaunaKea Technologies, which developed this process. This training included supervised practical sessions as well as standardized reading criteria, allowing for reproducible interpretation in accordance with current recommendations. In case of doubt or discordance, a peer review was carried out to strengthen the reliability of the analysis

After injection of 2.5 ml 10% fluorescein (SERB Laboratory, Paris, France) intravenously to the patient, before any injection of allergen, an initial capture with the mucosal endomicroscopy system was performed at a minimum of 4 sites (about 20 seconds each) to check the integrity of the mucosa (*i.e.*, the absence of contrast agent leakage into the lumen) and establish a comparative baseline *i.e.* reference sequences. During the acquisition of reference sequences and all subsequent acquisitions, mucosal areas presenting bleeding and other visible signs of inflammation would not be imaged to avoid false positives Allergens were selected in order of frequency from most important to least frequent, according to multicenter studies [19] [20] on allergen sensitization once the reference images were acquired, the standardized suspensions of food anllergens were sprayed onto the duodenal mucosa using a catheter inserted into the working channel of the endoscope in the specified order: 3 g of wheat flour, 1.5 g of milk powder, 1.5 g of dehydrated egg white, 3 g of peanut powder, 3 g of soy flour and 1.5 g of dry yeast. Each allergen was diluted in 30 mL 0.9% sodium chloride solution with one food allergen suspension administered at a time. The center received pre-prepared dry food allergens and diluted them right before endoscopy. The first suspension of food allergen was applied to the duodenal mucosa, starting with the most distal part of the duodenum. Two minutes after applying the food allergen, observation with the CLE system began by applying the GastroFlex™ UHD probe (Mauna Kea Technologies, Paris, France) to the duodenal mucosa where the suspension of food allergen was projected. Indeed, the first allergens tested (wheat, milk, eggs) are among the most frequently involved in food hypersensitivity reactions, particularly in patients with functional intestinal disorders such as irritable bowel syndrome, all our allergens were from the same sources across all patients to ensure consistency in exposure. All allergens used were derived from organic products, with no known additives or contaminants, to minimize confounding factors. Prioritizing these allergens made it possible to quickly identify a possible reaction and interrupt the study, as planned in the protocol, in order to limit patient expo-

sure. Observation lasted up to 3 minutes per observed site and can reach 8 min. If no reaction was observed, the same procedure was repeated using a new suspension of food allergen applied a few centimeters further along the gastrointestinal tract. Distilled water was used to rinse the mucosa after each allergen application. If a reaction was observed the test would end. Reactions are presented in "Figure 1" below. The FAST test could be conducted using up to 6 different food allergens as long as the total duration after fluorescein injection did not exceed 30 minutes.



Reference Image: Before exposure to food allergens, the study investigator records a reference endomicroscopy video for comparison after food allergen exposure and checks the integrity of the duodenal mucosa without exposure to food allergens. This image shows the absence of leakage, cell loss, or disruption of the intestinal barrier with a mostly dark lumen compared to the clear villi. **Contrast Agent Leakage:** The spaces formed by exposure to food allergens allow the contrast agent to infiltrate the lumen, giving a white/bright light in contrast to the darkening villi (red arrows). **Cell Loss:** The intestinal epithelium, which represents a thin layer of the villi, breaks down due to pronounced and continuous cell loss (red arrows).

Figure 1. CLE criteria to identify a positive reaction.

In our study, the analysis was performed by practitioners specifically trained in reading and interpreting the CLE test, following standardized protocols to ensure optimal reproducibility. We recognize, however, that this skill is not yet widely disseminated, which may currently limit the accessibility of the test in some centers. This highlights the importance of developing specific training and promoting standardization of CLE interpretation to enable a wider and more reliable use of this method in clinical practice.

3.3. Device Under Study: Cellvizio® System

Probe-based Confocal Laser Endomicroscopy (pCLE) is a technology that allows for real-time, in vivo, high-resolution microscopic imaging of living tissues during endoscopy procedures. The image acquisition is performed using the Cellvizio® system with optical fiber probes called Confocal Miniprobes™ (Mauna Kea Technologies, Paris, France). In this study, the Confocal Miniprobe™ GastroFlex™ UHD, was used during endoscopy procedures. pCLE imaging is based on a 488 nm laser used in conjunction with the administration of fluorescein, a fluorophore whose safety has been demonstrated.

4. Follow-Up and Evaluation

A first visit with a nutritionist took place within two weeks following the procedure for patients who had a positive reaction to the FAST test. During this visit, an elimination diet of the food allergen would be prescribed for 6 months based on the specific food intolerance identified.

A second visit occurred at 2 months follow-up. During this visit, the patient filled out the IBS-SSS questionnaire to assess the severity of symptoms.

A third visit took place at 6 months follow-up, either in person or by phone, with the completion of the same questionnaire. The patients adhered to the doctor's instructions throughout the follow-up.

Adherence to the exclusion diet was assessed through regular follow-up visits with Dr. Dalu, during which patients reported their clinical progress and any difficulties in following the recommendations. Although food diaries were not systematically used in this pilot study, patients were encouraged to record foods consumed and symptoms experienced to facilitate discussion at follow-up visits.

Irritable Bowel Syndrome Severity Scoring System Questionnaire

IBS-SSS Questionnaire was used to assess symptom severity in participants with IBS for participants, was introduced by Francis *et al.* in 1997 [21], at baseline, 2-months, and 6-months after the FAST procedure.

In our study, a reaction was considered positive when specific, reproducible mucosal changes were observed following allergen exposure during confocal laser endomicroscopy (CLE). These changes included fluorescein leakage into the intestinal lumen, widening of intercellular spaces, visible activation of immune cells, and disruption of epithelial architecture. These criteria were predefined and applied consistently across all patients.

To ensure the reliability of our observations, a reaction was considered positive only if at least two distinct mucosal sites exhibited characteristic changes following allergen application.

Washout Procedures and Observation Window: To prevent cross-contamination between allergen applications, the confocal endomicroscopy probe was thoroughly rinsed with sterile saline after each exposure allergen. The mucosal surface was also flushed with sterile saline to remove any residual allergen. Mucosal responses were monitored within a 2-minute window following each allergen appli-

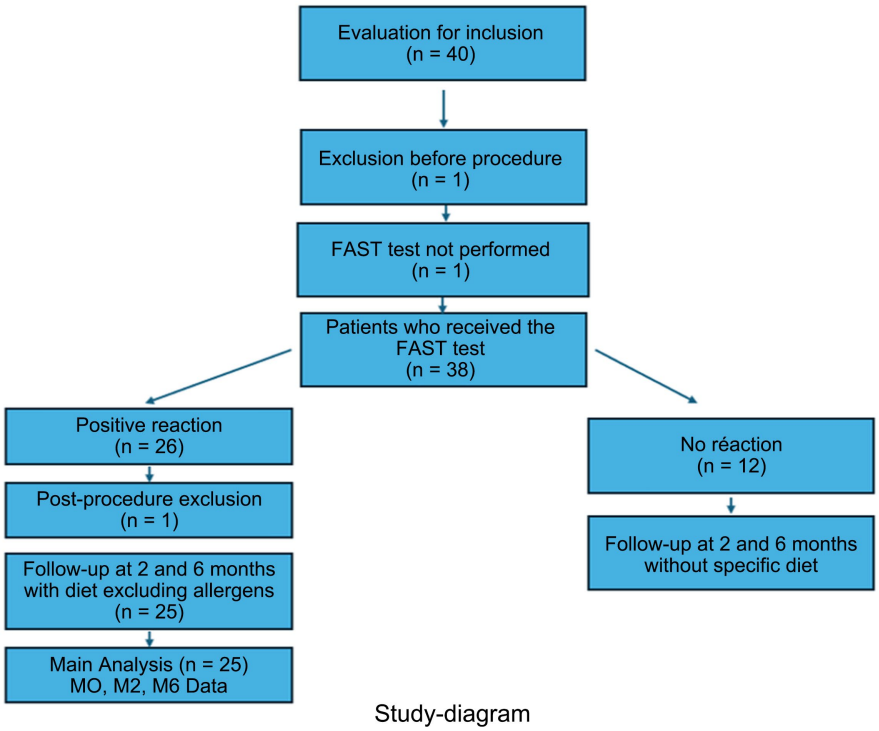
cation. This timeframe was selected based on prior studies involving confocal laser endomicroscopy in food allergy diagnostics, which have demonstrated that mucosal changes typically occur within the first few minutes of exposure. The 2-minute window allowed for the detection of immediate, reproducible, and specific reactions while minimizing interference from delayed or nonspecific responses.

After the examination, patients remain on an outpatient basis for a few hours under observation. The doctor visits them to reassure them, re-explain the procedure and how it went.

5. Statistical Analysis

A sample size calculation was not performed due to the limited data available in the literature at the time the protocol was submitted to the ethics committee. Results of continuous variables will be expressed as means and standard deviations, or as medians and interquartile ranges. Continuous variables will be compared using Student's t-test or the Mann-Whitney U test in the R software to determine the significance of the change in symptom severity scores before the procedure, at 2 months, and at 6 months after dietary exclusion. In case of non-normal data distribution, the Wilcoxon signed-rank test will be used. The significance level is set at 0.05. As a result, the statistical power to detect differences may be limited. Moreover, without a priori estimation of the required sample size, the generalizability of the findings is reduced, as the observed results may be influenced by chance variation or insufficient representation of the broader population.

6. Results



Study-diagram

Participant Demographics and Clinical Characteristics

Initially, 40 patients were recruited for the study, with ages ranging from 25 to 59 years (mean age: 43.6 years). However, two patients were excluded during follow-up; one patient was unable to complete the FAST test due to spontaneous extravasation of fluorescein, which was a study exclusion criterion. A fibroscopic examination was nevertheless performed and the patient was able to leave the clinic without any adverse effects or secondary complications. There were no adverse effects from the use of fluroscein during the study or at any time during its use for other indications, particularly in EBO or mucosectomy scar control or for polyp characterization or for other indications. leaving 38 participants with subtypes IBS-D, IBS-C and IBS-M. Of these, 26 initially exhibited a positive reaction to food allergens during the FAST procedure and were put on a dietary exclusion regimen. After further evaluation, one patient did not meet all inclusion criteria and was excluded, leading to 25 patients being included in the final analysis(schema). This group had a mean age of 45.3 years, ranging from 29 to 59 years. The demographic and clinical characteristics are summarized in "Table 1" with 30.8% males compared to only 25% males in the recruited cohort. The BMI was slightly lower in the analyzed patients (24.58 vs. 25.73). Comorbidities we noticed that Hypothyroidism was more frequent among analyzed patients (56% vs. 37.5%). Diabetes was somewhat less common in the analyzed group (16% vs. 22.5%).

Table 1. General and analyzed populations.

Characteristics	Recruited Patients (n = 40)	Analyzed Patients (n = 25)
Sex (M/F)	10/30	8/17
Proportion of Males (%)	25%	30.8%
Age (Mean)	43.6	45.3
BMI (Mean)	25.73	24.58
Hypothyroidism (%)	37.5	56%
Diabetes (%)	22.5%	16%
Transit Disorders (%)	22.5%	28%
Other Conditions (%)	17.5%	0%

Transit disorders were slightly more prevalent in the analyzed population (28% vs. 22.5%). The 12 patients who tested negative underwent the same follow-up at 2 and 6 months, including completion of questionnaires. These patients had a variety of personal or family histories such as digestive polyps, gastroesophageal reflux disease (GERD), chronic inflammatory bowel disease (IBD) including Crohn's disease, functional colopathy and esophagitis, which could partly explain

their digestive disorders. Management was adapted according to this history, ranging from carrying out additional tests to the exclusion of certain allergens (such as gluten or milk). This approach resulted in a significant reduction in digestive symptoms and a significant improvement in their quality of life for the majority of them.

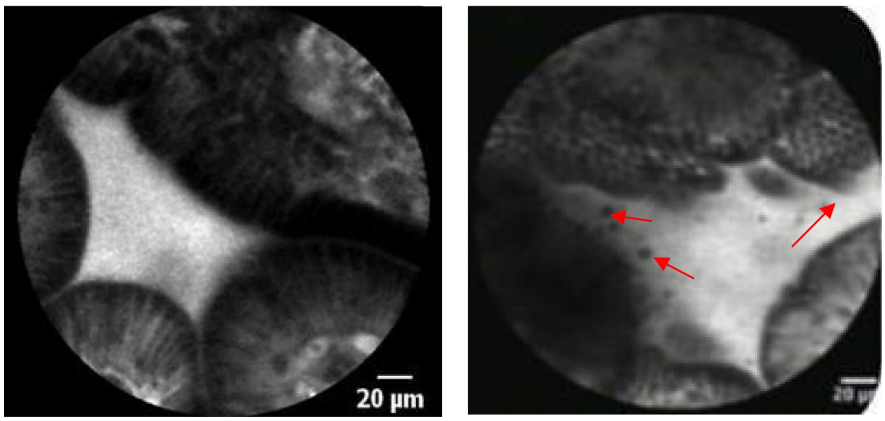
Allergen Specific Responses and Outcomes

The analyzed population showed varied responses to different allergens. The most frequently observed positive reactions were to wheat (44%) and milk (32%), followed by eggs (12%). Reactions to peanut (8%) and soy (4%) were less common, while yeast did not elicit any positive reactions (0%).

This distribution highlights that wheat and milk represent the predominant allergens in this cohort, whereas legume-derived allergens (soy, peanut) and yeast played a comparatively minor role in Table 2 and Figure 2 shows the image of wheat allergen with and without reaction.

Table 2. Allergen detection times.

Allergen	% Positive	Detection Time (Mean)
Wheat	44%	6 min 16 sec
Milk	32%	5 min 18 sec
Eggs	12%	5 min 10 sec
Soy	4%	8 min 02 sec
Peanut	8%	Not Determined
Yeast	0%	0 sec



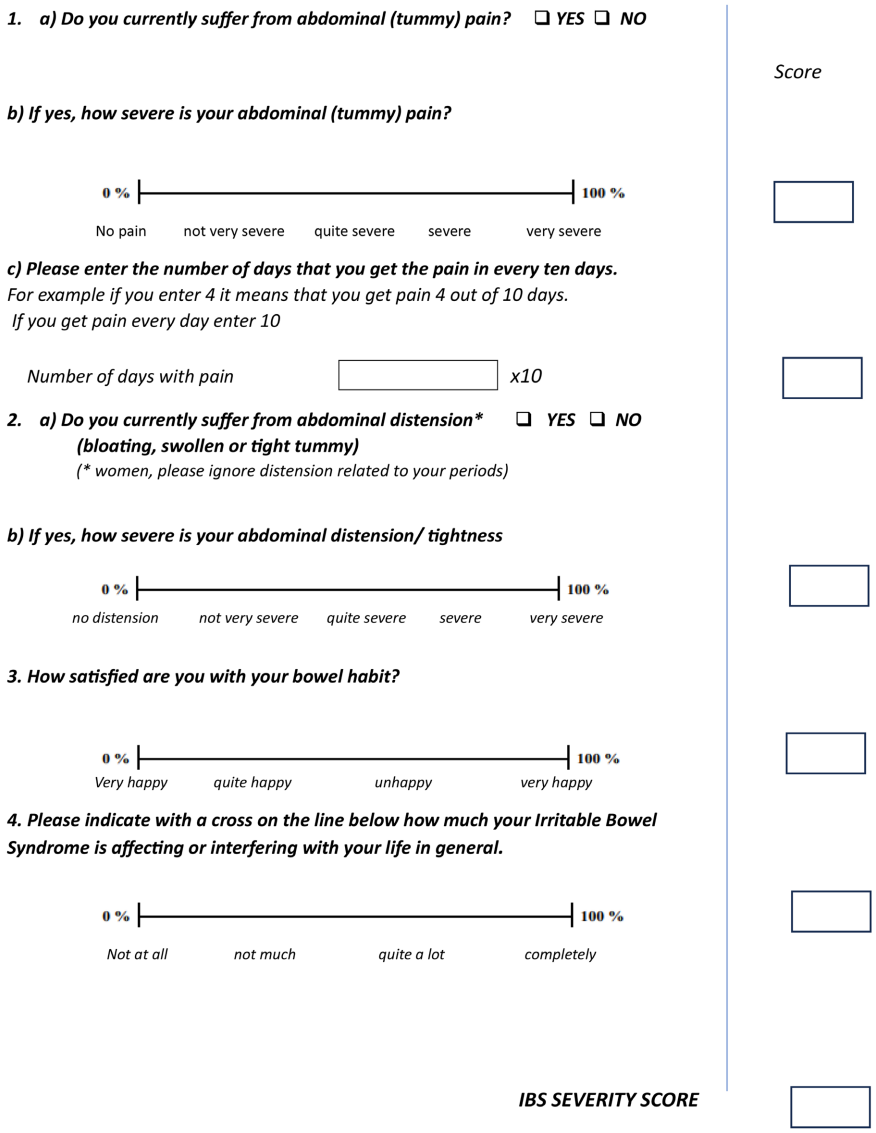
Note: Left image: No reaction to the allergen (wheat). Right image: Contrast agent leakage and cell loss can be observed after the mucosa was exposed to the allergen (wheat), red arrows highlighting cell loss and bright background typical of contrast agent leakage; Note: In case of uncertainty regarding the reaction to an allergen during the procedure, the investigator took additional time to ensure whether the reaction is positive or negative. This is why the duration exceeded 5 minutes on mean.

Figure 2. Images of wheat allergen with and without reaction.

Clinical Outcomes

Out of the 25 patients who reacted to the FAST procedure and had a change of diet, 23 had an improvement of their symptoms according to their Francis score.

Francis score:



A statistically significant reduction in the IBS-SSS score was observed in the study population, indicating a significant improvement in symptoms post dietary intervention. Scores decreased substantially from the initial visit to the follow-ups at 2 months and 6 months. The specific details and statistical significance of these changes are captured in Table 3.

The reduction in IBS-SSS scores from baseline to 2 months and 6 months post-intervention was both statistically significant, supporting the effectiveness of the FAST test and subsequent dietary modifications in managing symptoms associated with allergen sensitivities.

Table 3. IBS-SSS score changes over time.

Time Point	Francis Score (Median)	Statistical Significance (p-value)
Baseline	160	-
2 Months Follow-up	35	0.002093
6 Months Follow-up	0	0.000043

The Wilcoxon signed-rank test was used to evaluate the significativity of the reduction in IBS-SSS scores as normality could not be proven. The Wilcoxon signed-rank test showed a significant difference between baseline and two month, with an estimated location shift of 79 (95% CI [45.50; 192], p = 0.00209); and from baseline to 6 months post-intervention, with an estimated location shift of 152.94 (95% CI [105; 220], p = 0.0001). These findings support the effectiveness of the FAST test as a useful tool for identifying specific food allergens. By excluding these allergens from their diets, patients with IBS experienced marked improvements in their symptoms, shown by study [22]. This positive outcome underscores the utility of the FAST test in enhancing dietary management for individuals with IBS.

The findings confirm that the FAST procedure is a valuable diagnostic tool for identifying specific food allergens contributing to gastrointestinal symptoms in patients. The dietary exclusion based on FAST results leads to significant improvements in clinical outcomes, demonstrating its utility in dietary management for individuals with hypersensitivity to specific foods.

7. Discussion

This prospective pilot study has demonstrated a significant improvement in the clinical symptoms of IBS patients through the targeted exclusion of specific food allergens identified using the FAST test. This study not only reinforces the link between food allergens and IBS symptoms but also highlights the potential for personalized dietary interventions in managing this complex condition.

We fully acknowledge that the lack of a control group is a significant weakness, particularly in the context of irritable bowel syndrome (IBS), where the placebo response rate can indeed be high. This methodological constraint was related to available resources and the exploratory nature of our work, which primarily aimed to generate hypotheses.

Furthermore, the small sample size (n = 25) and the single geographic location of the participants (a single clinic in France) limit the external validity of the results and their generalizability to other populations. We nevertheless emphasize that this pilot study constitutes a necessary first step in evaluating the potential role of food allergens in IBS and paves the way for larger, randomized, controlled studies that will confirm these preliminary findings.

Implications of Findings

The findings from this study suggest that the traditional approach to managing

IBS, which often includes generalized dietary guidelines and symptomatic treatment, may be enhanced by incorporating targeted diagnostic tests like the FAST test. By identifying specific food allergens that exacerbate symptoms, healthcare providers can tailor dietary interventions that are more effective and personalized. This approach could lead to better patient outcomes, as evidenced by the significant reductions in the Francis scores from baseline to 6 months.

Comparison with Existing Literature

The effectiveness of the FAST test aligns with the growing body of literature that supports the use of exclusion diets in the management of IBS. Studies such as those by Fritscher-Ravens *et al.* [8] and Rath *et al.* [23] have previously demonstrated the utility of endomicroscopy in identifying mucosal reactions to food allergens. Rath *et al.* previously showed that CLE had a sensitivity and specificity of 96% and 67%, respectively, to identify food allergy through visualization of barrier dysfunction in a cohort of 60 patients. Fritscher-Ravens *et al.* in their study were able to highlight the quality criteria of food allergy such as: Epithelial breaks forming gaps and intervillous space lightening due to secretion of fluorescein into the lumen. Also, 19 of the 22 patients that had a food allergen-induced reaction confirmed by CLE were able to have IBS symptoms improvement after a food exclusion diet.

Strengths of the Study

One of the major strengths of this study is its innovative use of confocal laser endomicroscopy to directly observe the effects of food allergens on the duodenal mucosa. This method provides a clear and immediate understanding of how specific foods affect patients, allowing for rapid and accurate identification of allergens that may not be detected through traditional testing methods such as skin prick tests or IgE assays.

Limitations and Future Research

[18]CLE shows mucosal reactions; possible symptomatic benefit, but needs validation. Despite its promising results, this study has some limitations that should be addressed in future research. The sample size was relatively small, and the study was conducted in a single center, which may limit the generalizability of the findings. Besides, in the future research the 6 allergens samples used in the study, should come from the same brand and sources to minimize variability and reduce potential bias in allergen reactivity. Moreover, we should think about a new strategy to test the effect of the 6 allergens during the CLE test in order to continue the examination even if a positive reaction is observed with the first food allergen. Additionally, the follow-up period was limited to 6 months; longer follow-up periods may be needed to understand the long-term efficacy. This study also lacks a control group, which could have been useful in evaluating the placebo effect of dietary change. Further studies should aim to replicate these findings in larger, multicenter trials with diverse populations.

Additionally, research into the mechanisms by which specific food allergens affect the mucosa and contribute to IBS symptoms could provide deeper insights into the pathophysiology of IBS and potentially lead to the development of new

therapeutic strategies.

Allergen Detection Times and Associated Hypothyroid Prevalence:

Allergen	% Positive	Detection Time (Mean)	Hypothyroidism Prevalence
Wheat	44%	6 min 16 sec	45.5%
Milk	32%	5 min 18 sec	50%

The prevalence of hypothyroidism was high in both allergen groups, reaching 50% in patients sensitized to milk and 45.5% in those sensitized to wheat. These figures are markedly higher than the expected prevalence of hypothyroidism in the general population, suggesting a possible association between food sensitization (particularly to wheat and milk) and thyroid dysfunction.

Potential immunological link: The coexistence of food sensitization and hypothyroidism may be explained by shared autoimmune mechanisms. For wheat, evidence exists regarding celiac disease and its strong association with autoimmune thyroiditis (Hashimoto's disease). In the case of milk, certain proteins (e.g., casein, beta-lactoglobulin) could induce cross-reactivity or stimulate immune responses that favor thyroid dysregulation.

Pathophysiological hypothesis: Repeated activation of the immune system by food allergens may contribute to a chronic inflammatory state, thereby increasing the risk of developing or exacerbating autoimmune thyroid disorders.

Clinical implications: Particular attention should be given to thyroid monitoring in patients presenting with food sensitization to wheat and milk. A multidisciplinary approach involving both allergologists and endocrinologists could improve the management of these patients.

The doctor-patient relationship relies largely on trust and subjective feedback from the patient regarding symptoms, such as digestion or fatigue. After identifying a food allergen, the patient eliminates the food concerned and generally reports a disappearance of bloating and postprandial fatigue. However, this improvement may be influenced by several confounding factors, including the choice of a more balanced and less processed diet, independent of the specific avoidance of the allergen. This potential bias must be taken into account when interpreting the results. Nevertheless, this shift towards a healthier diet is in itself an expected benefit in terms of public health.

8. Conclusions

In conclusion, this study underscores the importance of personalized medicine approaches in the management of IBS, particularly using dietary modifications based on specific diagnostic tests like the FAST test. The significant improvements in symptoms following allergen-specific dietary interventions suggest that this could become an essential component of IBS management for patients suffering

from IBS, potentially reducing the burden of this chronic condition.

Allergen-specific dietary interventions based on pCLE detection of changes in the duodenal mucosa make a marked difference in identifying exactly which allergen is problematic. This point highlights the critical role of pCLE in enhancing the precision of allergen identification, ensuring more effective and targeted dietary modifications.

Declarations

- Ethics approval and consent to participate: This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from COMMITTEE FOR THE PROTECTION OF PERSONS NORTH WEST III under reference CNRIPH: 21.05.04.55700 with a favorable opinion issued on August 20, 2021 and is registered on ClinicalTrials.gov (NCT05072665) with a registration date of September 1, 2021 Written informed consent was obtained from all participants prior to their inclusion in the study.
- Consent for publication: All participants agreed to the analysis of the data in an anonymous way and the publication of the results, the agreement was obligated with the signature of the consent
- Availability of data and materials: All data generated or analyzed during this study are included in this published article

Authors' Contributions

- Study conception and design: Dr JM Canard, Dr A. Dalu and Mrs B. Benkessou
- Data collection: CRA Trocadero Clinic
- Analysis and interpretation of results: Dr Canard, Dr Dalu and clinical research team; Manuscript writing: Dr Canard, Bouchra Benkessou and CRA Trocadero Clinic
- All authors, Dr JM Canard, Dr A Dalu and Mrs B Benkessou have read and approved the final version.

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Trial Registration

NCT05072665 with a registration date of September 1, 2021.

Conflicts of Interest

The authors declare that they have no known competing financial interests or per-

sonal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

FAST: Food Allergen Sensitivity Test
CLE: Confocal laser endomicroscopy
IBS-D: Irritable Bowel Syndrome diarrhea
IBS-C: Irritable Bowel Syndrome constipation
IBS-M: Irritable Bowel Syndrome-diarrhea and constipation
IBS-SSS: Irritable Bowel Syndrome Severity Scoring System