



## Alimentary Tract

## Clinical and nutritional correlates associated with weight changes in achalasia patients and the impact of laparoscopic Heller myotomy



Laura Aurino<sup>a,1</sup>, Marcella Pesce<sup>a,1</sup>, Sara Rurgo<sup>a</sup>, Maria Giovanna Puoti<sup>b</sup>, Barbara Polese<sup>a</sup>, Marianna Capuano<sup>a</sup>, Giuseppe Palomba<sup>a</sup>, Giovanni Aprea<sup>a</sup>, Luisa Seguela<sup>c</sup>, Giuseppe Esposito<sup>c</sup>, Irene Palenca<sup>c</sup>, Eleonora Efficie<sup>a</sup>, Giovanni Sarnelli<sup>a,\*</sup>

<sup>a</sup> Department of Clinical Medicine and Surgery, 'Federico II' University of Naples, Naples, Italy, Via Pansini 5, 80131, Naples, Italy

<sup>b</sup> Department of Pediatric Gastroenterology and Hepatology, Santobono-Pausilipon Children's Hospital, Via Mario Fiore, 6, 80129, Naples, Italy

<sup>c</sup> Department of Physiology and Pharmacology "V. Erspamer", Sapienza University of Rome, Piazzale Aldo Moro 5, 00185 Rome, Italy

## ARTICLE INFO

## Article history:

Received 14 June 2024

Accepted 28 July 2024

Available online 14 August 2024

## Keywords:

Esophageal achalasia

Weight loss

Dysphagia and symptoms' severity

Caloric intake

Body mass index

## ABSTRACT

**Background:** Achalasia is characterized by symptoms of esophageal obstruction, preventing food consumption. However, weight loss is observed only in a subset of patients, and data from literature is conflicting.

**Aims:** Our study aimed at evaluating predictors of weight loss in achalasia patients and at verifying the impact of treatment on nutritional status.

**Methods:** 123 achalasia patients, eligible for laparoscopic Heller myotomy, were studied. Demographic, clinical and nutritional data (calorie intake and macronutrient composition) were recorded at baseline and one-year post-treatment. Significant weight loss/gain was considered for variation of 10% of body weight at baseline and post-treatment, respectively.

**Results:** 57.7% of patients reported weight loss at presentation. These subjects had shorter disease duration, worse symptoms, lower BMI and consumed fewer calories than patients without weight loss. Post-treatment, we observed a considerable improvement in Eckardt score and BMI values. Almost 50% of the population reported significant weight gain, particularly in individuals with weight loss at baseline. Caloric intake also rose significantly, positively affecting BMI categories.

**Conclusion:** We showed that achalasia-induced weight loss is associated with symptoms' severity and disease duration. Conversely, over 50% of treated patients were in the overweight/obese category, highlighting the need for individualized nutritional interventions in achalasia patients.

© 2024 The Author(s). Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l.

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

## 1. Introduction

Idiopathic achalasia is a major esophageal motor disorder of unknown etiology, characterized by altered esophageal peristalsis and impaired relaxation of the lower esophageal sphincter (LES). Achalasia is a rare disorder with an annual incidence of approximately 0.7–1.6/100.000 that seems to increase with age [1,2].

\* Corresponding author at: Department of Clinical Medicine and Surgery, 'Federico II' University of Naples, Naples, Italy; Via Pansini 5, Naples, Italy.

E-mail addresses: [laura.aurino@unina.it](mailto:laura.aurino@unina.it) (L. Aurino), [marcella.pesce@unina.it](mailto:marcella.pesce@unina.it) (M. Pesce), [sararurgo91@gmail.com](mailto:sararurgo91@gmail.com) (S. Rurgo), [giovanna.puoti@hotmail.it](mailto:giovanna.puoti@hotmail.it) (M.G. Puoti), [barbara.polese@gmail.com](mailto:barbara.polese@gmail.com) (B. Polese), [marianna.capuano@unina.it](mailto:marianna.capuano@unina.it) (M. Capuano), [giuseppopalomba3@virgilio.it](mailto:giuseppopalomba3@virgilio.it) (G. Palomba), [aprea@unina.it](mailto:aprea@unina.it) (G. Aprea), [luisa.seguella@uniroma1.it](mailto:luisa.seguella@uniroma1.it) (L. Seguela), [giuseppe.esposito@uniroma1.it](mailto:giuseppe.esposito@uniroma1.it) (G. Esposito), [irene.palenca@uniroma1.it](mailto:irene.palenca@uniroma1.it) (I. Palenca), [eleonora.efficie@hotmail.it](mailto:eleonora.efficie@hotmail.it) (E. Efficie), [sarnelli@unina.it](mailto:sarnelli@unina.it) (G. Sarnelli).

<sup>1</sup> Laura Aurino and Marcella Pesce share first authorship.

<https://doi.org/10.1016/j.dld.2024.07.027>

1590-8658/© 2024 The Author(s). Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Albeit idiopathic, the pathophysiology of the disorder has been well established and is triggered by the loss of the inhibitory innervation of the myenteric plexus of the LES and esophageal body, consequently leading to defective LES relaxation and impaired esophageal peristalsis [2]. The exact etiology underlying the neurodegeneration observed in achalasia patients remains still unclear, although a number of factors have been suggested to play a role; including genetic predisposition, viral infection(s) and autoimmunity [1–7].

The clinical presentation widely varies, encompassing a range of esophageal symptoms suggestive for obstruction, including dysphagia, regurgitation, belching, and heartburn, as well as respiratory manifestations such as nocturnal cough, aspirations, and recurrent pneumonia [2,8]. Patients may report chest pain, regurgita-

tion and significant weight loss at presentation, however, dysphagia undoubtedly represents the hallmark symptom of the disease, reported by 82–100% of patients. The characteristics of the dysphagia are typically described by patients as a progressive difficulty in swallowing both solids and liquids [2].

Despite all patients show esophageal functional obstruction, the subsequent weight loss is reported only in a subset of them. Recent studies indicate, indeed, a variable proportion of weight loss, ranging from 35% to 51% of patients [9,10]. Contrary to what expected not all patients with achalasia report significant weight loss or are underweighted [9,11–15].

At present, the underlying reasons are still unclear [9]. Also, little is known regarding the nutritional status of achalasia patients, the calorie and macronutrient intake, nor the effect of the treatment have been described [13–15]. Some small studies have shown a significant weight gain with shift to obesity post-surgical intervention [11,15].

The aim of the present study was to explore the correlation between symptom severity, demographic characteristics, dietary intakes, and body mass index (BMI) changes in a large population of well-selected patients with achalasia. Secondly, we evaluated the effect of laparoscopic Heller's myotomy (LHM) on the above-described parameters at 12 months after the treatment.

## 2. Materials and methods

### 2.1. Patients' selection and study design

This was an observational study carried out from January 2017 to December 2021 at our Institution. During the study period a total of 153 patients with a clinical and instrumental diagnosis of idiopathic achalasia were prospectively recruited. Thirty out of 153 patients were excluded due to lack of data (Fig. 1).

Diagnosis of achalasia was made based on esophagogastroduodenoscopy, barium esophagogram and high-resolution manometry (and divided into the prevalent subtypes, according to Chicago Classification) [8,16]. All patients included in the study were treated with LHM and were followed-up from the baseline (T0, i.e. the time at the diagnosis) to 12 months post LMH (T12).

In each patient, clinical characteristics, including the age of onset, body weight and BMI, weight loss, time from symptom onset to treatment, achalasia subtype and symptoms severity (Eckardt

Symptom Score – ESS) [17,18] were recorded at T0 and T12, respectively. Technical success was considered as an uneventful LHM with an Eckardt score  $\leq 3$  12 months after surgery as per previous studies [19].

In a subset of patients, the average daily kcal intake and macronutrient percentages were assessed by food frequency quantitative questionnaire [20] and a dedicated software [The WinFood software (version 3.9, Medimatica Srl, Colonella TE, Italy)]. All individuals gave their written informed consent to participate in the protocol and the study was approved by the University Ethics Committee. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008) as reflected in a priori approval by the institution's human research committee.

### 2.2. Statistical analysis

Statistical analysis was performed by dividing the population into two categories of patients, by considering a significant weight loss (at least 10% as compared to body weight values before the onset of symptoms). In the post treatment analysis, a 10% increase of body weight compared to baseline, was instead considered. Categorical variables are presented as number and percentages where indicated. Continuous variables are expressed as mean  $\pm$  standard deviation. Chi-squared and paired *t*-test were used to compare categorical and continuous variables, respectively. Non-normally distributed variables were expressed as median and Interquartile Range (IQR) and were analyzed by using the non-parametric Wilcoxon signed-rank test for paired data (pre-post treatment) or the Mann Whitney test for unpaired data (comparison between patients losing/gaining weight). A *p* value  $<0.05$  was considered statistically significant. Statistical analysis was performed with GraphPad Prism vs. 8.0.1 for Windows (GraphPad Software, San Diego, California USA).

## 3. Results

### 3.1. Baseline characteristics and nutritional analysis of patients

The demographics and clinical features of the population are summarized in the Table 1.

Seventy-one out of 123 patients (57.7%) reported weight loss ( $15.4 \pm 7.4$  vs  $2.3 \pm 2.3$  kg; *p*  $< 0.01$ ). Subjects who lost weight

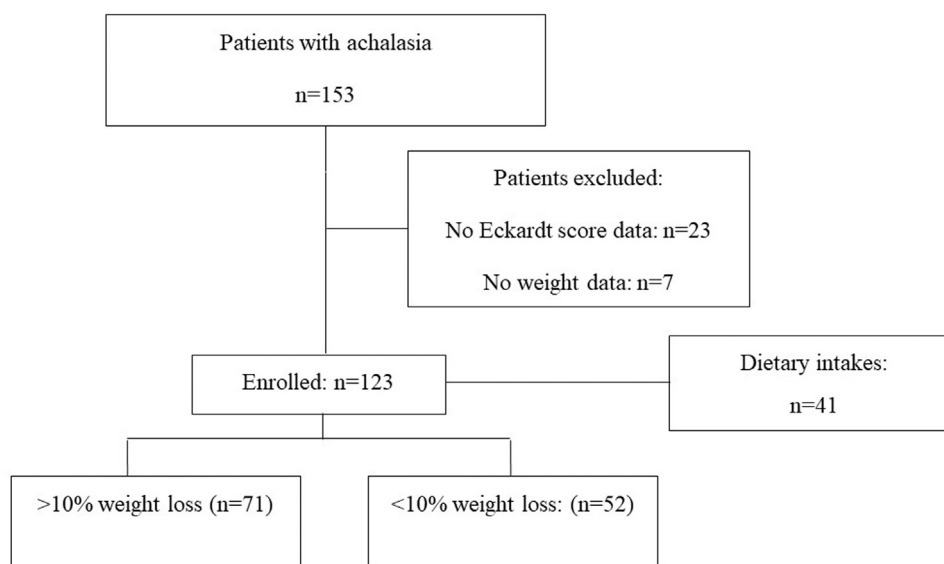


Fig. 1. Representative flow-chart of the studied population.

**Table 1**  
Comparison between patients with and without weight loss.

	All patients n = 123	>10% weight loss n = 71 (57.7)	<10% weight loss n = 52 (42.3)	P-value
Age at onset, years	43±17.9	43.1 ± 18.1	43.3 ± 18.2	NS
Age at diagnosis, years	51±17	49.4 ± 17.2	53±16.8	NS
Male	59 (48%)	35 (28.5%)	24 (19.5%)	NS
Body weight at onset, kg	75.9 ± 15.1	76.7 ± 16.3	74.8 ± 13.4	NS
Body weight at diagnosis, kg	66.1 ± 14.5	61.3 ± 13.3	72.6 ± 13.5	<0.01
BMI at onset, kg/m <sup>2</sup>	26.8 ± 4.8	27.1 ± 4.8	26.5 ± 4.7	NS
BMI at diagnosis, kg/m <sup>2</sup>	23.4 ± 4.6	21.6 ± 3.7	25.7 ± 4.8	<0.01
Symptom duration, years	8 ± 9.6	6.2 ± 8.6	9.7 ± 10.5	<0.05
ESS (median, IQR)	7 (9–5)	7 (10–6)	5 (7.75–4)	<0.01
Type 1 achalasia	16	11 (8.9)	5 (4.1)	NS
Type 2 achalasia	99	55 (44.7)	44 (35.8)	NS
Type 3 achalasia	8	5 (4.1)	3 (2.4)	NS
LES Basal Tone (mmHg)	50.1 ± 18.8	48.8 ± 23.7	52.9 ± 14.1	NS
IRP values (mmHg)	31.3 ± 12.6	33.3 ± 9.1	29.4 ± 13.6	NS

Data are indicated as number/percentage (%) and expressed as (mean±SD). BMI, body mass index; ESS, Eckardt Symptom Score was expressed as median and interquartile range (IQR).

**Table 2**  
Effect of Laparoscopic Heller Myotomy on weight gain.

	All patients n = 123	>10% weight gain n = 58 (47.2)	<10% weight gain n = 65 (52.8)	P-value
Body weight, kg	73±15	72±15	74±15	NS
Weight gain, kg	7 ± 6	11±6	3 ± 2	<0.01
BMI, kg/m <sup>2</sup>	26±5	25.6 ± 4	26±5	NS
ESS (median, IQR)	2 (2–0)	1.5 (2–0)	2 (3–0)	NS
Type 1 achalasia	16	8 (6.5)	8 (6.5)	NS
Type 2 achalasia	99	48 (39)	51 (41.5)	NS
Type 3 achalasia	8	2 (1.6)	6 (4.8)	NS
LES Basal tone (mmHg)	19.2 ± 9.1	18.9 ± 8.9	20.4 ± 7.1	NS
IRP values (mmHg)	11.9 ± 4.6	12.4 ± 3.1	11.7 ± 3.2	NS

Data are indicated as number/percentage (%) and expressed as (mean±SD). BMI, body mass index; ESS, Eckardt Symptom Score was expressed as median and interquartile range (IQR).

had a shorter disease duration, more severe symptoms and lower baseline body weight and BMI at diagnosis, than patients without weight loss. No significant differences emerged for all other analyzed variables, nor did manometrically characterized achalasia subtype differ between the two groups.

Nutritional evaluation was available in 41 patients to evaluate calorie and macronutrient intake. The analysis revealed that, patients who lost weight consumed significantly fewer calories than subjects without weight loss (946 ± 196 vs 1327 ± 347 kcal;  $p < 0.01$ ), with no significant difference in the percentage of carbohydrate, fat, and protein consumption (40.5 ± 8.5 vs 45.6 ± 8.1, 42.5 ± 9.5 vs. 37.8 ± 10.6 and 16.9 ± 3.1 vs. 16.6 ± 3.2, respectively; all  $p = ns$ ).

### 3.2. Impact of LHM treatment on body weight, clinical, and nutritional parameters

LHM was a technical success in 100% of patients. At the 12-month follow-up, a significant improvement in the Eckardt score was observed compared to baseline [2 (2–0) vs. 7 (9–5);  $p < 0.01$ ], with an average body weight gain of 7 kgs and a significant increase in BMI (23.4 ± 4.6 vs. 26±5 kg/m<sup>2</sup>,  $p < 0.01$ ). Fifty-eight out of 123 patients (47.2%) reported a weight gain of at least 10% compared to pre-treatment values, with a significant increase of 8 kg compared to patients without a similar body weight increase. No differences emerged for the other analyzed variables (data are presented in Table 2). Most interestingly, post-treatment body weight gain was likely dependent on baseline weight, being higher in patients who reported >10% weight loss at baseline (8.6 ± 7.1 vs.

4.4 ± 4 kg;  $p < 0.01$ ), while ESS were similar [1.5 (2–0) vs. 2 (3–0);  $p=ns$ ].

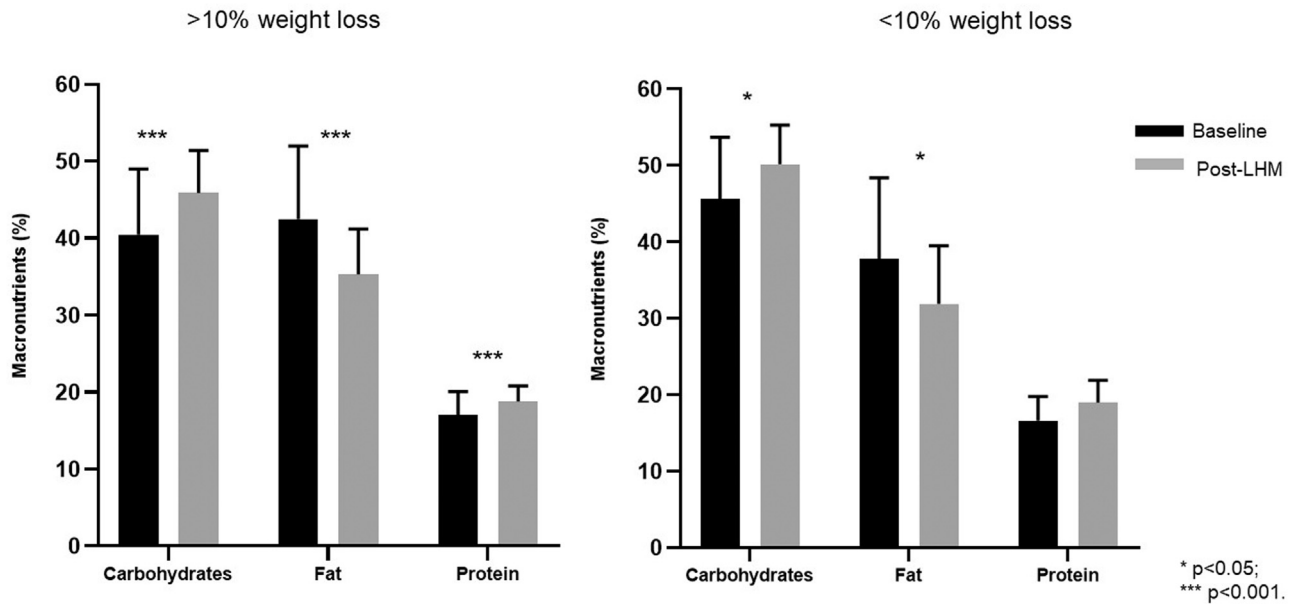
In general, there was a notable rise in calorie intake following the LHM, showing an increase of 273 Kcal compared to baseline values (1029.7 ± 281.7 vs 1302±226.7,  $p < 0.01$ ). This was accompanied by a concurrent increase in the percentage of carbohydrate and protein consumption, along with a reduction in lipid intake (41.6 ± 8.6 vs 46.9 ± 5.7, 16.9 ± 3.1 vs 18.6 ± 2.2, and 41.5 ± 9.8 vs 34.5 ± 6.3; all  $p < 0.01$ ).

Further analysis, by dividing the subjects into the two groups based on >10% weight loss at baseline and those without such weight loss, revealed that the caloric intake increased significantly in both groups post-treatment (946±196 vs 1234±180 kcal and 1327±347 vs 1545±216 kcal; all  $p < 0.01$ ). Notably, the group with >10% weight loss at baseline exhibited the highest increase in caloric intake. In these subjects, there was a significant decrease in fat consumption and a significant increase in carbohydrates and protein (see Fig. 2).

### 3.3. Influence of LHM on BMI categories and changes

LHM resulted in an overall increase in body weight, leading to a significant shift in patients across different BMI categories. Fig. 3 illustrates that, after 12 months of treatment, there was a noteworthy decrease in the number of underweight individuals, accompanied by an increase in overweight and obese subjects, while the percentage of normal weight individuals remained relatively constant.

Further insights are provided in Table 3, detailing the transition of patients from each BMI category before treatment to post-

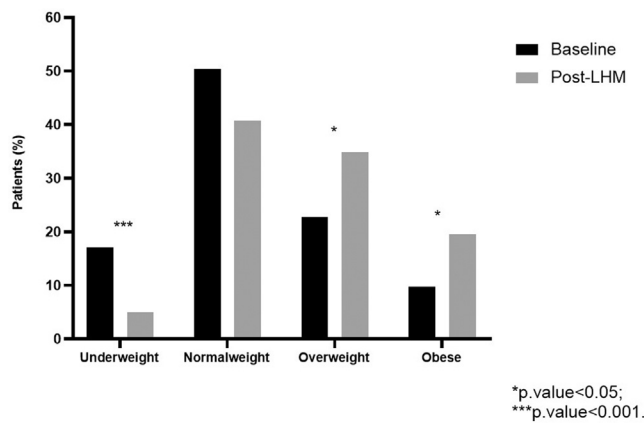


**Fig. 2.** Macronutrients consumption before and after laparoscopic Heller Myotomy. Macronutrients consumption at baseline and 12-month after LHM in patients presenting with severe weight loss (>10% weight loss, left) and in patients who did not present with significant weight loss (<10% weight loss, right). \*\*\**p* < 0.001; \**p* < 0.05. Abbreviations: Post-LHM, post Laparoscopic Heller Myotomy.

**Table 3**  
Number of patients within respective BMI categories changing from baseline to 12 months post-Laparoscopic Heller Myotomy Treatment.

Post-LHM BMI category	Pre-LHM BMI category				Total
	Underweight	Normalweight	Overweight	Obese	
Underweight	6 (4.9)	0	0	0	6
Normalweight	15 (12.2)	35 (28.5)	0	–	50
Overweight	0	25 (20.3)	18 (14.6)	–	43
Obese	0	2 (1.6)	10 (8.1)	12 (9.8)	24
Total	21	62	28	12	123

Data are indicated as number/percentage (%). BMI, body mass index; LHM, Laparoscopic Heller Myotomy Treatment.



**Fig. 3.** Classification of patients into BMI categories at baseline and following laparoscopic Heller Myotomy. At 1 year- follow up a significant decrease in underweight patients was observed. In parallel, we recorded an increase in both overweight and obese individuals, with a percentage exceeding half of the population in the BMI category>25. \*\*\**p* < 0.001; \**p* < 0.05. Abbreviations: Post-LHM, post Laparoscopic Heller Myotomy.

treatment. Among underweight patients, fifteen moved to a normal weight category. In the normal BMI range, twenty-five individuals transitioned to overweight, with two progressing to the obese category. Ten out of the twenty-eight overweight patients became obese post-treatment, while all obese patients (*n* = 12) maintained their obese status post-LHM.

#### 4. Discussion

The impact of achalasia on the nutritional status of patients is controversial [9,13–15,20]. Although esophageal food impaction is present in most patients and may theoretically affect the ability to consume regular meals, not all achalasia patients experience dramatic weight loss or are underweight at presentation [9,13,20–23]. It might be reasonable to assume that patients with more severe achalasia would experience greater weight loss. However, data from previous studies yielded conflicting results, likely because no studies analyzed the characteristics of achalasia patients or demographic variables and their impact on nutritional status. The findings presented in our study provide valuable insights into the demographic, clinical, and nutritional characteristics of patients with achalasia, both before and after treatment.

Our findings showed that only 57.7% of untreated patients reported significant weight loss, indicating the multifactorial nature of weight changes in achalasia. Those who experienced weight loss had a shorter disease duration, more severe symptoms, and lower body weight at diagnosis. Interestingly, no significant differences were observed in manometrically-characterized achalasia subtypes, suggesting that other factors beyond subtype classification contribute to weight changes in this population. In a 2018 study, it was reported that only 51% of patients with achalasia lose weight, and the Authors observed that weight loss was more frequent in patients with type 2 achalasia than the other subtype [9]. In contrast, we detected no differences in weight loss among the various types of achalasia. This observation warrants careful consideration, espe-

cially considering that type 2 achalasia is the predominant subtype, and that our study encompasses a larger population than the earlier research [9]. Most importantly, we employed more precise and standardized criteria for weight loss (<10%), and this may account for some differences compared to other studies in which a specific cut-off for weight loss was lacking [24].

Our findings align with data from the literature, indicating that patients who reported weight loss had a significantly shorter duration of symptoms than patients with stable weight [9].

We believe that patients who lose weight require medical advice before patients with stable weight, as unintentional weight loss can be a sign of a serious illness [25]. According to Patel et al., who demonstrated that weight loss appears to be independent of gender and age at diagnosis [9], our study confirmed that factors such as age at onset, age at diagnosis, body weight, and BMI at onset were not significantly associated with weight loss.

Based on our findings, it is reasonable that weight loss can be attributed to a decrease in dietary calorie intake. This aligns with the observations of Ghoshal et al., who noted that untreated achalasia patients reported lower calorie, protein, and calcium intake compared to healthy subjects [20]. In our study, the nutritional assessment confirmed the link between weight loss and diminished caloric intake. Patients experiencing weight loss consumed considerably fewer calories compared to those without weight loss. Importantly, this decrease in calorie intake did not correspond to variations in the proportion of carbohydrate, fat, and protein consumption. This emphasizes the need to consider overall caloric intake, rather than specific macronutrient percentages, when evaluating nutritional status in untreated achalasia patients.

In order to standardize the follow-up and to evaluate the effect of achalasia treatment on clinical and nutritional parameters, we chose to evaluate the effect of LHM after 12 months. In highly selected patients, LHM emerged as a highly successful intervention, with a 100% technical success rate. The 12-month follow-up revealed a substantial improvement in the Eckardt score, reflecting the effectiveness of the treatment in alleviating symptoms. Weight-related outcomes were notable, with an average body weight gain of 7 kgs and a significant increase in BMI as compared to pre-treatment values. Furthermore, almost 50% of patients reported a weight gain of at least 10%, demonstrating the positive impact of LHM on reversing weight loss trends.

Analysis of BMI categories demonstrated a significant decrease in underweight patients, accompanied by an increase in overweight and obese individuals after LHM. Notably, 12.2% of underweight patients transitioned to a normal BMI category, highlighting the persistent challenges in achieving substantial weight gain in this subgroup. Meanwhile, the majority of overweight and obese patients maintained or increased their status, reinforcing the need for individualized nutritional interventions post-treatment.

Further emphasizing the positive nutritional impact of the treatment, we recorded an overall, significant increase in caloric intake. However, the nutritional analysis revealed distinct patterns in macronutrient composition changes based on weight loss status. Patients who lost weight exhibited a decrease in fat intake and an increase in carbohydrate and protein, suggesting a comprehensive shift in dietary habits. Conversely, patients without significant weight loss showed a significant decrease in fat and an increase in carbohydrate, but not protein intake, suggesting the contribution of different adaptive eating behaviors to weight changes.

Our study is not without limitations. Firstly, the nutritional analysis was available for only a subset of patients, as several patients failed to perform the questionnaire either at baseline or post-treatment and were therefore excluded from the final analysis for lack of data. Secondly, albeit all patients were required to perform a timed barium esophagogram (TBE) before and after surgery, most patients have performed single barium swallows given the

limited use of this method. However, LHM success was not solely based on clinical response as assessed by the standardized ESS. Indeed, all patients were followed up also with HRM and manometry data confirmed an  $IRP \leq 15$  in all patients' groups following treatment. Finally, post-surgical incidence of reflux was not evaluated in our population nor the need of proton pump inhibitors therapy. Future research should focus on more detailed assessments, including anthropometry, body composition, and biochemical parameters, to provide a comprehensive understanding of nutritional changes in this population. Despite these limitations, our study provides valuable insights into the understanding of achalasia and its intricate relationship with nutritional status. The positive effects of LHM on weight gain and nutritional improvements highlight the importance of considering nutritional interventions as part of the overall management strategy for achalasia patients. Attention must be paid to underweight patients who report worse symptom severity to minimize surgical complications due to inadequate nutritional status. Likewise, individualized nutritional interventions are warranted post-treatment, especially in the subsets of normal weight and overweight patients who are at high risk of obesity.

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## Institutional review board statement

The study was performed according to the 1975 Declaration of Helsinki principles and approval was obtained from the Institutional Review Board and Ethics Committee and each patient through specific informed consent.

## Informed consent statement

Informed consent was obtained from all subjects involved in the study.

## Conflict of interest

The Authors declare that there is no conflict of interest.

## Author contribution

**Laura Aurino:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Software, Validation, Visualization, Writing – original draft. **Marcella Pesce:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Software, Validation, Visualization, Writing – original draft. **Sara Rurgo:** Investigation, Writing – review & editing. **Maria Giovanna Puoti:** Investigation, Writing – review & editing. **Barbara Polese:** Investigation, Writing – review & editing. **Marianna Capuano:** Investigation, Writing – review & editing. **Giuseppe Palomba:** Investigation, Writing – review & editing. **Giovanni Aprea:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Software, Validation, Visualization, Writing – original draft. **Luisa Seguella:** Investigation, Writing – review & editing. **Giuseppe Esposito:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Software, Validation, Visualization, Writing – original draft. **Irene Palenca:** Investigation, Writing – review & editing. **Eleonora Efficie:** Investigation, Writing – review & editing. **Giovanni Sarnelli:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Software, Validation, Visualization, Writing – original draft.

## References

- [1] Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. *Lancet* 2014;383(9911):83–93.
- [2] Savarino E, Bhatia S, Roman S, Sifrim D, et al. Achalasia. *Nat Rev Dis Primers* 2022;8(1):28.
- [3] Gockel I, Becker J, Wouters MM, et al. Common variants in the HLA-DQ region confer susceptibility to idiopathic achalasia. *Nat Genet* 2014;46(8):901–4.
- [4] Sarnelli G, Grosso M, Palumbo I, et al. Allele-specific transcriptional activity of the variable number of tandem repeats of the inducible nitric oxide synthase gene is associated with idiopathic achalasia. *United European Gastroenterol J* 2017;5(2):200–7.
- [5] Sarnelli G. Impact of genetic polymorphisms on the pathogenesis of achalasia: an age-dependent paradigm? *Neurogastroenterol Motil* 2009;21(6):575–8.
- [6] Reddy CA, Allen-Brady K, Uchida AM, et al. Achalasia is strongly associated with eosinophilic esophagitis and other allergic disorders. *Clin Gastroenterol Hepatol* 2024;22(1) 34–41.e2.
- [7] Cassarano S, Pesce M, Cargioli M, et al. Clinical correlation and disease phenotype in patients with esophageal achalasia and comorbid autoimmune diseases. *Dis Esophagus* 2021;34(1) doaa072.
- [8] Zaninotto G, Bennett C, Boeckxstaens G, et al. The 2018 ISDE achalasia guidelines. *Dis Esophagus* 2018;31(9):10.
- [9] Patel DA, Naik R, Slaughter JC, et al. Weight loss in achalasia is determined by its phenotype. *Dis Esophagus* 2018;31(9):10.
- [10] Fisichella PM, Raz D, Palazzo F, et al. Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. *World J Surg* 2008;32(9):1974–9.
- [11] Hew S, Motomura D, Bechara R. Changes in weight following peroral endoscopic myotomy: results from a North American center. *Endosc Int Open* 2021;9(10):E1491–6.
- [12] Cohen DL, Avivi E, Bermont A, et al. Correlation between lower esophageal sphincter metrics on high-resolution manometry and the clinical presentation of patients with newly diagnosed achalasia. *Diagnostics (Basel)* 2023;13(6):1136.
- [13] Milito P, Aquilino K, Lazzari V, et al. The malnutrition universal screening tool can predict malnutrition in patients with esophageal achalasia. *Eur J Gastroenterol Hepatol* 2020;32(9):1135–40.
- [14] Newberry C, Vajravelu RK, Pickett-Blakely O, et al. Achalasia patients are at nutritional risk regardless of presenting weight category. *Dig Dis Sci* 2018;63(5):1243–9.
- [15] Perez-Ortiz AC, Narváez-Chávez S, Furuzawa-Carballeda, et al. Long-term risk of adult overweight and obesity among achalasia patients who underwent Heller Myotomy. *Neurogastroenterol Motil* 2020;32(10):e13921.
- [16] Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: chicago classification version 4.0©. *Neurogastroenterol Motil* 2021;33(1):e14058.
- [17] Taft TH, Carlson DA, Triggs J, et al. Evaluating the reliability and construct validity of the Eckardt symptom score as a measure of achalasia severity. *Neurogastroenterol Motil* 2018;30(6):e13287.
- [18] Slone S, Kumar A, Jacobs J, et al. Accuracy of Achalasia Quality of Life and Eckardt scores for assessment of clinical improvement post treatment for achalasia. *Dis Esophagus* 2021;34(2) doaa080.
- [19] Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. *Gastroenterology* 1992;103(6):1732–8.
- [20] Ghoshal UC, Thakur PK, Misra A. Frequency and factors associated with malnutrition among patients with achalasia and effect of pneumatic dilation. *JGH Open* 2019;3(6):468–73.
- [21] Patel DA, Kim HP, Zifodya, et al. Idiopathic (primary) achalasia: a review. *Orphanet J Rare Dis* 2015;10:89.
- [22] Pandolfino JE, Carlson DA, McGarva J, et al. Validation of the achalasia patient-reported outcomes questionnaire. *Aliment Pharmacol Ther* 2022;56(10):1434–43.
- [23] Pesce M, Pagliaro M, Sarnelli G, et al. Modern achalasia: diagnosis, classification, and treatment. *J Neurogastroenterol Motil* 2023;29(4):419–27.
- [24] Skeie E, Tangvik RE, Nymo LS, et al. Weight loss and BMI criteria in GLIM's definition of malnutrition is associated with postoperative complications following abdominal resections – Results from a national quality registry. *Clin Nutr* 2020;39(5):1593–9.
- [25] Perera LAM, Chopra A, Shaw AL. Approach to patients with unintentional weight loss. *Med Clin North Am* 2021;105(1):175–86.