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Original Article

Nutritional status and quality of life of patients with advanced gastroenteropancreatic neuroendocrine neoplasms in Spain: the NUTRIGETNE (GETNE-S2109) study

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Abstract

Patients with advanced gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) have impaired nutritional and physical performance due to the cancer pathophysiology and its treatment. The NUTRIGETNE study sought to characterize the nutritional status of patients with

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advanced GEP-NENs in Spain. This is a cross-sectional study that included patients with advanced GEP-NENs receiving active oncological treatment. Patients had a complete physical examination, anthropometry, bioelectrical impedance, dynamometry, laboratory analysis, and a comprehensive nutritional risk assessment. Malnutrition was defined according to Global Leadership Initiative on Malnutrition (GLIM) criteria. The study included 399 patients out of the 400 planned (Pearson's $\chi 2$; α 0.05). Median age was 62 years (22-83). Tumors most commonly originated in the small intestine (43.9%) and the pancreas (41.6%), 94.7% were metastatic, and 36.7%, 49.4%, and 12.5% were G1, G2, and G3, respectively. Malnutrition prevalence was 61.9% (25.8% moderate; 36.1% severe), mainly due to low muscle mass (50.9%), which was the most prevalent GLIM phenotypic criteria. Moreover, malnutrition showed a correlation with decreased hand grip strength (mean 23 vs 31.9 kg; $P < .001$) and phase angle (median 5° vs 5.6°; $P < .001$). The prevalence of sarcopenia was 15%. Malnutrition was more frequent in patients with diabetes (74.4% vs 56.7%; $P < .001$), NECs (82.1% vs 60.3%; $P = .062$), and in those treated with chemotherapy (71.2% vs 59.7%; $P = .058$), whereas it did not correlate with tumor origin ($P = .507$), histological grade ($P = .781$), or functionality ($P = .465$). Malnutrition was correlated to body mass index (BMI) ($P = .015$), although it was also diagnosed in a high proportion of patients with no weight loss (63%, 54.1%, and 65.1% of patients with normal BMI, overweight, and obesity, respectively). Cachexia was present in 109 (27.3%) patients. Malnutrition is very prevalent and commonly underdiagnosed in patients with GEP-NENs. It is associated with sarcopenia and a worse QoL, requiring a multifactorial nutritional assessment. Certain factors such as the presence of diabetes may require closer monitoring due to a higher risk of malnutrition.

Key words: nutritional status; malnutrition; sarcopenia; neuroendocrine neoplasms; gastroenteropancreatic.

Implications for Practice

There are few studies exploring the nutritional status of patients with gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) and evidence suggests that the prevalence of malnutrition and sarcopenia in patients with GEP-NENs is high. Malnutrition in these patients often appears concurrently with sarcopenia and diabetes. Body mass index correlated with malnutrition, but still, many patients with normal weight were malnourished. Finally, malnutrition has a correlation with the quality of life (QoL) and symptoms burden of patients with GEP-NENs. Therefore, multidisciplinary management of these patients including continuous and extensive surveillance of the nutritional status by specialized endocrinologists/nutritionists is highly recommended. Further research should explore the use of nutritional interventions to improve the QoL and safety administration of oncologic treatments in patients with GEP-NENs.

Introduction

Neuroendocrine neoplasms (NENs) are malignancies that arise from the neuroendocrine cells localized in endocrine glands or diffuse neuroendocrine cells in the digestive or lung tract.[1-4] The most common primary location of NENs is the gastroenteropancreatic (GEP) tract, which accounts for >60% of all diagnosed cases.[4,5] Some NENs may have hormonal functionality, with the secretion of bioactive substances, peptides, and hormones, which may cause different syndromes such as carcinoid syndrome, development of peptic ulcers, hypoglycemia, hyperglycemia, and diarrhea.[6-10] Patients with NET may develop metabolic disorders such as diabetes mellitus (DM) or obesity, which may have a direct impact on nutritional status.[11] The catabolic metabolism and inflammatory nature of cancer itself may cause weight loss and even cachexia and aggressive anticancer therapeutic approaches may also contribute to a detrimental nutritional status.[12,13] In this context, patients with NENs often have impaired food intake and absorption of nutrients and vitamins.[14]

Previous studies in oncological patients have reported that 64% of all patients show weight reduction in the first 6 months after diagnosis and the prevalence of malnutrition may range between 30% and 70% depending on the cancer type and stage.[15,16] This is of utmost importance because poor nutritional status may impair the efficacy of treatments and the quality of life (QoL) of patients, leading to a worse prognosis. Therefore, nutritional management of oncological patients must be a cornerstone of patient care to optimize clinical outcomes.[17] However, routine nutritional assessment is only performed in ~28% of patients with cancer.[18,19]

Few studies have characterized the nutritional status of patients with GEP-NENs, wherein most studies are observational with a limited sample size. Previous studies reported that ~14%-38% of patients with GEP-NENs are at risk of malnutrition and poor nutritional status negatively influences patient survival.[17,20-24]

The NUTRIGETNE study sought to characterize the nutritional status of a large cohort of patients with advanced GEP-NENs in Spain.

Materials and methods

Study design

NUTRIGETNE (NCT04986085) is an observational, cross-sectional, epidemiologic, multicenter study aimed at describing the nutritional status of patients with advanced GEP-NENs in Spain. The study is led by the Grupo Español de Tumores Neuroendocrinos y Endocrinos (GETNE) and conducted in 17 hospitals in Spain.

The study includes patients with a histologically confirmed diagnosis of GEP-NENs, aged between 18 and 80 years, who were receiving active anticancer treatment following standard clinical practice at an advanced stage at the time of inclusion. The decision to prescribe anticancer treatment was independent of patient inclusion. Allowed treatments included, but were not limited to, somatostatin analogues (SSA), targeted therapies, chemotherapy (CT), radionuclides (PRRT), and locoregional therapies. Pregnant women, patients undergoing palliative treatment or those in the terminal stage or lacking histological confirmation of the disease, were excluded. Written informed consent was obtained from all patients before study enrollment. The trial is approved by a central independent ethics committee, the competent authority in Spain, and the local ethics committees of the participating sites; and is performed in accordance with the Declaration of Helsinki and applicable local and national regulatory requirements and laws.

Study assessments and endpoints

The study consists of a single visit wherein the patients signed an informed consent form, and their demographic, oncological, and relevant medical records were collected.

A nutritionist, specialized nurse, or specialist doctor performed a complete physical examination including anthropometry, bioelectrical impedance (BIA), dynamometry, and laboratory analysis. Muscle strength is assessed by handgrip strength using hand dynamometers that are locally available at the sites. Hormonal levels are monitored in patients with functional tumors.

Nutritional risk assessment is performed using the PREvención con DIeta MEDiterranea (PREDIMED) test, Malnutrition Universal Screening Tool (MUST) test, and Subjective Global Assessment (SGA) test.[25-27] The Global Leadership Initiative on Malnutrition (GLIM) criteria is used to diagnose and stratify malnutrition. Patients were required to have at least one etiologic (inflammation, reduced food intake) and one phenotypic (weight loss, low body mass index [BMI], reduced muscle mass) criterion to be considered malnourished.[28-30] See Supplementary Materials.

Sarcopenia was defined, according to EWGSOP criteria, as low muscle mass in BIA coincident with low muscle performance as assessed by handgrip strength.[31]

Cachexia is defined based on the criteria of Fearon et al., including patients with severe weight loss (>5%); or the combination of a mild weight loss (2%-5%) and low basal BMI (<20 kg/m^2); or low skeletal muscle index (male < 7.26 kg/m^2; female < 5.45 kg/m^2) and weight loss > 2%.[32]

Caloric-protein nutritional requirements are calculated according to the ESPEN guidelines.[17]

The symptomatic burden is assessed through the collection of adverse events (AEs) reported by patients during hospital visits. AEs are coded and graded according to the National Cancer Institute Common Terminology Criteria for AEs.

Patient self-reported QoL is assessed using the European Organisation for Research and Treatment of Cancer QLQ-C30 questionnaire and the specific module for NETs, QLQ-GINET21,[33,34] which were administered at the time of visit, before any other study-specific assessment was performed.

Statistical analysis

The sample size was estimated based on the prevalence of malnutrition, which was expected to be ~30% according to previous studies.[14,18,20-23] Following a Monte Carlo simulation, the sample size required to reach a 3% confidence interval (CI) precision was 400 patients.

To prevent selection bias, patients were consecutively included when visiting the corresponding health centers for outpatient visits or hospitalization.

The efficacy and safety are assessed in all patients who underwent nutritional assessment. Data are analyzed using standard statistical methods. Continuous variables are summarized as *n*, median, mean, standard deviation, range, or 95% CIs as applicable. Categorical data are represented as frequency counts and percentages of subjects within each category. Age- and sex-dependent endpoints are analyzed in subgroups based on these characteristics.

A matching analysis is conducted post hoc to examine the interdependent relationships of the variables in the database to understand which patient profiles were associated with malnutrition.[35] See Supplementary Information for more detail on matching analysis.

All statistical tests are considered 2-tailed, and results with P <.05 are considered statistically significant. All statistical analyses are performed using the R software (Supplementary Information).

Results

Patient characteristics

From July 2021 to July 2023, 434 patients were screened and 408 (94%) were included. Nine patients were not evaluated by a nutritionist, resulting in 399 (91.9%) evaluable patients for the analysis (Supplementary Figure S1). The median age was 62 (range: 22-83) years, most were males (57.1%) and had grade 1 or 2 (86.2%) tumors. Metastasis was present in 96.2% of the patients and a quarter (24.6%) were functional (Table 1). Metabolic high-risk vascular comorbidities were present in 210 (52.6%) patients, with hypertension (40.9%) being the most common, followed by DM (30.3%) and dyslipidemia (24.3%).

Risk of malnutrition

The risk of malnutrition was assessed using the MUST and SGA scores correlated with malnutrition according to the GLIM criteria (Supplementary Table S1). The MUST had a sensitivity of 88.1% and 92.9% in the intermediate and high-risk groups, respectively. The SGA had a sensitivity of 90.8% and 95.7% in the intermediate and high-risk groups, respectively. The PREDIMED score was similar in patients with and without malnutrition, with a median score of 8 (range: 0-13) and 9 (range: 0-14), respectively.

Malnutrition diagnosis

According to the GLIM criteria, the prevalence of malnutrition was 61.9%, with 103 (25.8%) and 144 (36.1%) patients experiencing moderate and severe malnutrition, respectively (Figure 1A). Reduced food intake was reported in 84 (21.1%) patients. The most common phenotypic criteria was the low muscle mass, being moderate in 110 (27.6%) patients and severe in 93 (23.3%). Weight loss occurred in 82 (20.6%) patients and was severe in 41 (10.3%). The BMI was below the normal range in 65 (16.3%) patients and severely decreased in 27 (6.8%).

Malnutrition was correlated with BMI (P =.015). However, malnutrition was still diagnosed in 116 (63%) patients with normal BMI, 80 (54.1%) patients overweight, and 28 (65.1%) obese (Figure 1B). Cachexia was observed in 109 (27.3%) patients.

Malnutrition risk factors

DM was diagnosed in 121 (30.3%) patients who show a higher concomitant prevalence of malnutrition according to the GLIM criteria (74.4% vs 56.7%; P <.001) (Figure 1C). Nausea and vomiting symptoms determined through physical examination during the medical visit also correlated with a higher prevalence of malnutrition (82.9% vs 60.3%; P =.019) (Figure 1D). Low muscle mass indicators also correlated with malnutrition (Figure 1E-H).

Tumor characteristics did not correlate with malnutrition (Figure 2). However, the prevalence of malnutrition increased in patients with NEC (82.1% vs 60.3%; P =.062) and those receiving CT (71.3% vs 59.7%; P =.058) despite not reaching statistical significance (Figure 2).

Sarcopenia

The handgrip strength is below normal in 86 (21.6%) patients. Sarcopenia prevalence in our population is 15% (Figure 3A). Low handgrip strength also correlates with malnutrition (mean handgrip strength 32.3 vs 25.8 kg; P <.001).

Table 1. Baseline patient characteristics.

Characteristic	Total (*N* = 399)
Median age (range); years	62 (22–83)
Sex; *n* (%)	
Male	228 (57.1)
Female	171 (42.9)
Race; *n* (%)	
Caucasian	380 (95.2)
Hispanic	13 (3.3)
African	6 (1.5)
ECOG-PS; *n* (%)	
Score 0	213 (53.4)
Score 1	125 (31.3)
Score ≥ 2	20 (5)
Unknown	41 (10)
Tumor grade WHO; *n* (%)[a]	
Grade 1	147 (36.8)
Grade 2	197 (49.4)
Grade 3	50 (12.5)
Unknown	5 (1.3)
Differentiation; *n* (%)	
NET	361 (90.5)
NEC	28 (7)
Unknown	10 (2.5)
Functionality; *n* (%)	
Yes	98 (24.6)
No	295 (73.9)
Unknown	6 (1.5)
Primary tumor location, *n* (%)	
Small intestine	177 (44.4)
Pancreas	167 (41.9)
Colorectal	18 (4.5)
Gastric	10 (2.5)
Other/unknown	25 (6.3)
Metastasis at inclusion, *n* (%)	
0	15 (3.8)
1	227 (56.9)
≥2	157 (39.3)
Most common sites of metastasis; *n* (%)	
Liver	332 (83.2)
Lymph nodes	86 (21.6)
Peritoneum	55 (13.8)
Lung	28 (7.0)
Previous lines; *n* (%)	
1	217 (54.4)
2	92 (23.1)
≥2	90 (22.6)
Type of previous lines, *n* (%)	
SSA	342 (85.7)
PRRT	109 (27.3)
TKI	108 (27.1)
Chemotherapy	80 (20.1)
Clinical trial	42 (10.5)
TACE or locoregional therapy	11 (2.8)
Immunotherapy	7 (1.8)
Others	6 (1.5)

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group Performance Status; NEC, neuroendocrine carcinoma; NET, neuroendocrine tumor; PRRT, peptide receptor radionuclides; SSA, somatostatin analogs; TKIs, tyrosine kinase inhibitors; WHO, World Health Organization.

The prevalence of sarcopenia is higher in patients with carcinomas (35.7% vs 13.4%; *P* <.001) and in those previously treated with PRRT (23.1% vs 12.9%; *P* =.018) or everolimus (24% vs 13.7%; *P* =.028) (Figure 3B and C).

Laboratory parameters

The C-reactive protein (CRP) level at baseline is >3 mg/dL in 123 (53.5%) patients, and up to 61% in patients with malnutrition. CRP indirectly correlates with hemoglobin, hematocrit, albumin, prealbumin, and cholesterol; however, these associations are lost in patients with malnutrition (Figure 4). CRP levels are significantly increased (mean 12.2 vs 5.8 mg/L; *P* =.029) and albumin levels are significantly decreased (mean 42.7 vs 44 g/L; *P* =.004) in patients with malnutrition. Vitamin D is severely reduced in 66 (27.1%) out of 242 assessed patients. Severe vitamin D deficiency is most frequent among patients with sarcopenia which had a prevalence of 30.7%. Interestingly, vitamin levels show no significant alterations or correlation with other laboratory parameters altered by malnutrition (Figure 4 and Supplementary Table S2).

Quality of life

The global QLQ-C30 score (mean 83.5 vs 77.5 arbitrary units [AU]; *P* <.001) and global health status (mean 71 vs 59.2 AU; *P* <.001) are significantly worse in patients with malnutrition according to the GLIM criteria (Figure 5). The physical (mean 89.4 vs 80 AU; *P* <.001), role (mean 86.5 vs 76.7 AU; *P* <.001), and social (mean 82.1 vs 73.3 AU; *P* =.002) functioning scores are significantly worse in patients with malnutrition (Figure 5; see Supplementary Table S3 for definition of question numbers). Patients with malnourishment report a significant increase in symptoms of fatigue (mean 25.1 vs 35.4 AU; *P* <.001), nausea and vomiting (mean 4.3 vs 7.5 AU; *P* =.027), appetite loss (mean 8.3 vs 21.7 AU; *P* <.001), and constipation (mean 10.4 vs 16.7 AU; *P* =.026). Night sweats (21% vs 32.5%; *P* =.018), difficulties eating (11.9% vs 25.8%; *P* <.001), and weight loss (24.3% vs 43.5%; *P* <.001) are also more common among patients with malnutrition. A greater number of patients with malnutrition report to have limitations to travel (38% vs 53.4%; *P* <.001) (see Supplementary Figure S2 for detailed graphics on each statistically significant QoL item).

Similarly, sarcopenia is significantly associated with QLQ-C30 score (mean 81.1 vs 74.9 AU; *P* =.007), global health status (mean 65.8 vs 52.3 AU; *P* <.001), physical (mean 86.2 vs 71.9 AU; *P* <.001), and role functioning (mean 82.5 vs 73 AU; *P* =.019) (Figure 5). Fatigue (mean 29.3 vs 40.8 AU; *P* =.003) and appetite loss (mean 14.3 vs 28.5 AU; *P* <.001) are significantly increased in patients with sarcopenia. Patients with

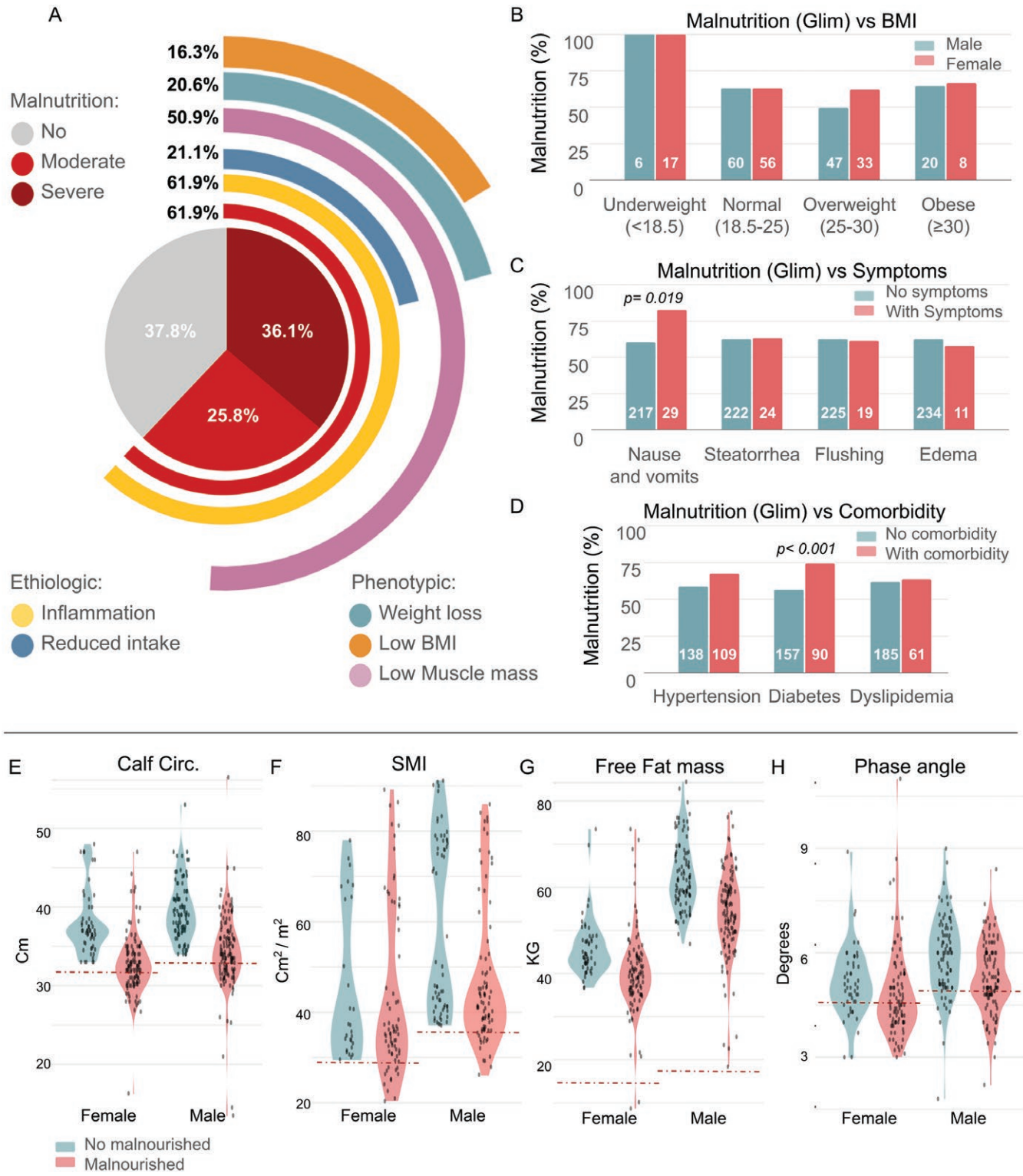

Figure 1. Malnutrition prevalence and nutrition profile. (A) Prevalence of malnutrition according to Glim criteria. Prevalence of malnutrition in patients subgroups clustered by BMI (B), presence of symptoms (C), comorbidities (D), calf circumference (E), SMI (F), free fat mass (g), and phase angle (h). Abbreviations: BMI, body mass index; Circ, circumference; SMI, skeletal muscle mass.

sarcopenia also feel more frequent difficulties eating (17.5% vs 38.2%; P =.002) and travel limitations (44% vs 64.8%; P <.001) (Figure 5 and Supplementary Figure S3).

Symptomatic burden

In total, 77 (19.3%) patients report at least one AE. The most common AEs are fatigue (8.8%), diarrhea (5.5%), and anemia (3.8%), which occur more frequently in patients with malnutrition (Supplementary Figure S4).

Coincidence analysis

Our study collects 382 variables. To facilitate the understanding of the complex relationships that may occur, we employed a matching approach. Malnutrition is linked to most variables

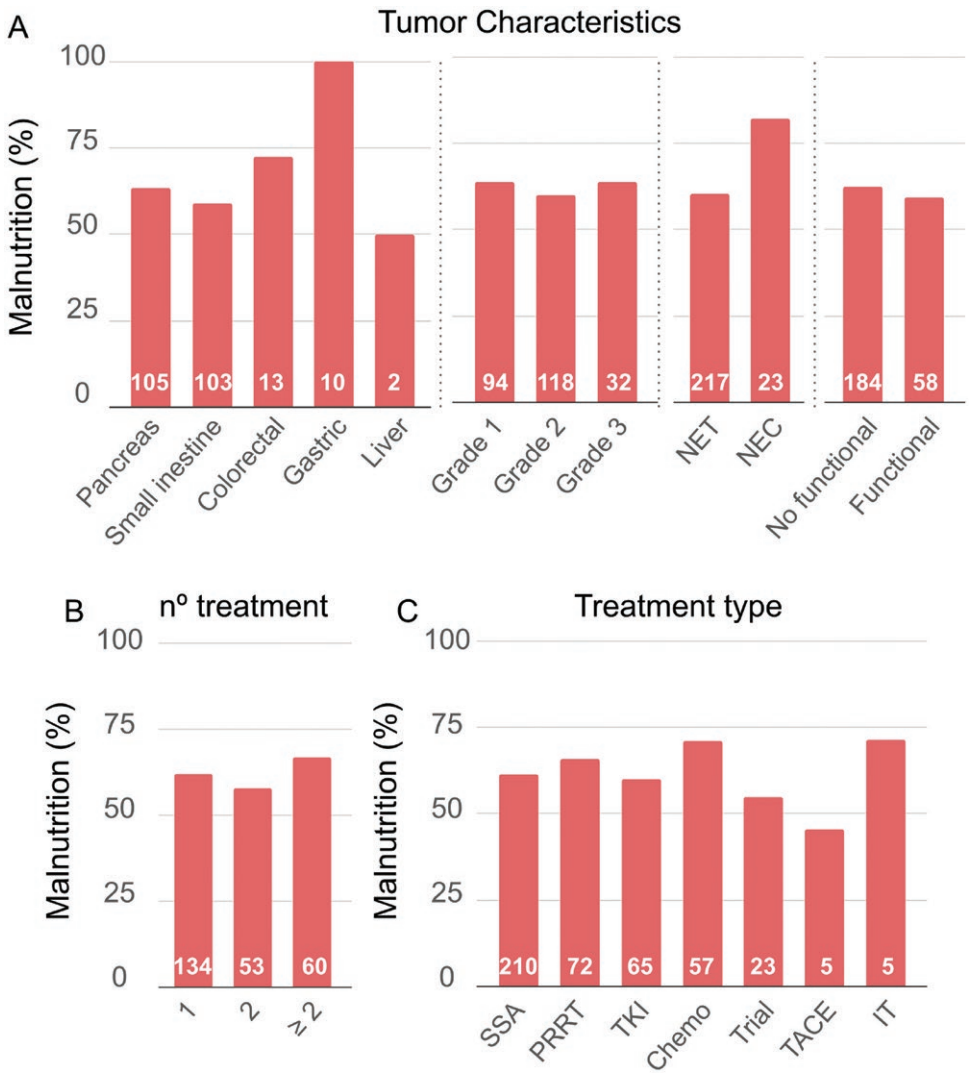

Figure 2. Malnutrition prevalence by cancer type. (A) Malnutrition according to cancer characteristics including tumor primary origin, grade (WHO), histology, and functionality. (B) Malnutrition according to the number of previous treatments. (C) Malnutrition according to the type of previous treatments. Abbreviations: Chemo, chemotherapy; IT, immunotherapy; NEC, neuroendocrine carcinoma; NET, neuroendocrine tumors; PRRT, peptine receptor radiotherapy; SSA, somatostatin analogs; TACE, transarterial chemoembolization; TKI, tyrosine kinase inhibitors.

correlated with it at a single level or directly used for its diagnosis (Figure 6).

Sarcopenia is one of the most closely related variables. Among patient-reported QoL outcomes, loss of appetite or the ability to walk has a high coincidence level with malnutrition and interacts with the Eastern Cooperative Oncology Group (ECOG) performance status score, global QoL, low FFMI, and reduced calf circumference. CRP levels interact with malnutrition, DM, and variables related to muscle status such as handgrip strength, sarcopenia, and SMI.

Discussion

These are the final results of the NUTRIGETNE study, which constitutes the largest cohort of patients with GEP-NENs with a comprehensive nutritional and functional assessment. The results are considered representative of the real-world population of patients with GEP-NENs in Spain, showing that the prevalence of malnutrition is very high and is concurrent with low muscle mass and sarcopenia in a substantial number of cases. The prevalence rates of malnutrition, sarcopenia, and cachexia were 61.9%, 15%, and 27.3%, respectively. Smaller retrospective studies have reported malnutrition rates of ~30% which is less than half.[14,18,20-23] This difference may be explained by the fact that our population comprises a higher number of patients in advanced stages. For instance, 96.2% of the patients in our cohort have stage IV disease and almost half received 2 or more systemic treatments. The prevalence of malnutrition increased to 42.3% in patients receiving systemic treatment in previous reports.[18] Moreover, the use of different screening tools and the lack of standardization in nutritional assessment across studies could have an impact on the estimation of malnutrition prevalence. Classically used indicators of nutritional status such as BMI, MUST, or SGA show a low correlation with malnutrition. Patients with NEN have a low muscle mass, which is not always reflected in a low BMI. Therefore, it is recommended that a broader nutritional assessment should be performed.

Interestingly, malnutrition prevalence is not influenced by tumor characteristics. Patients with carcinomas or those

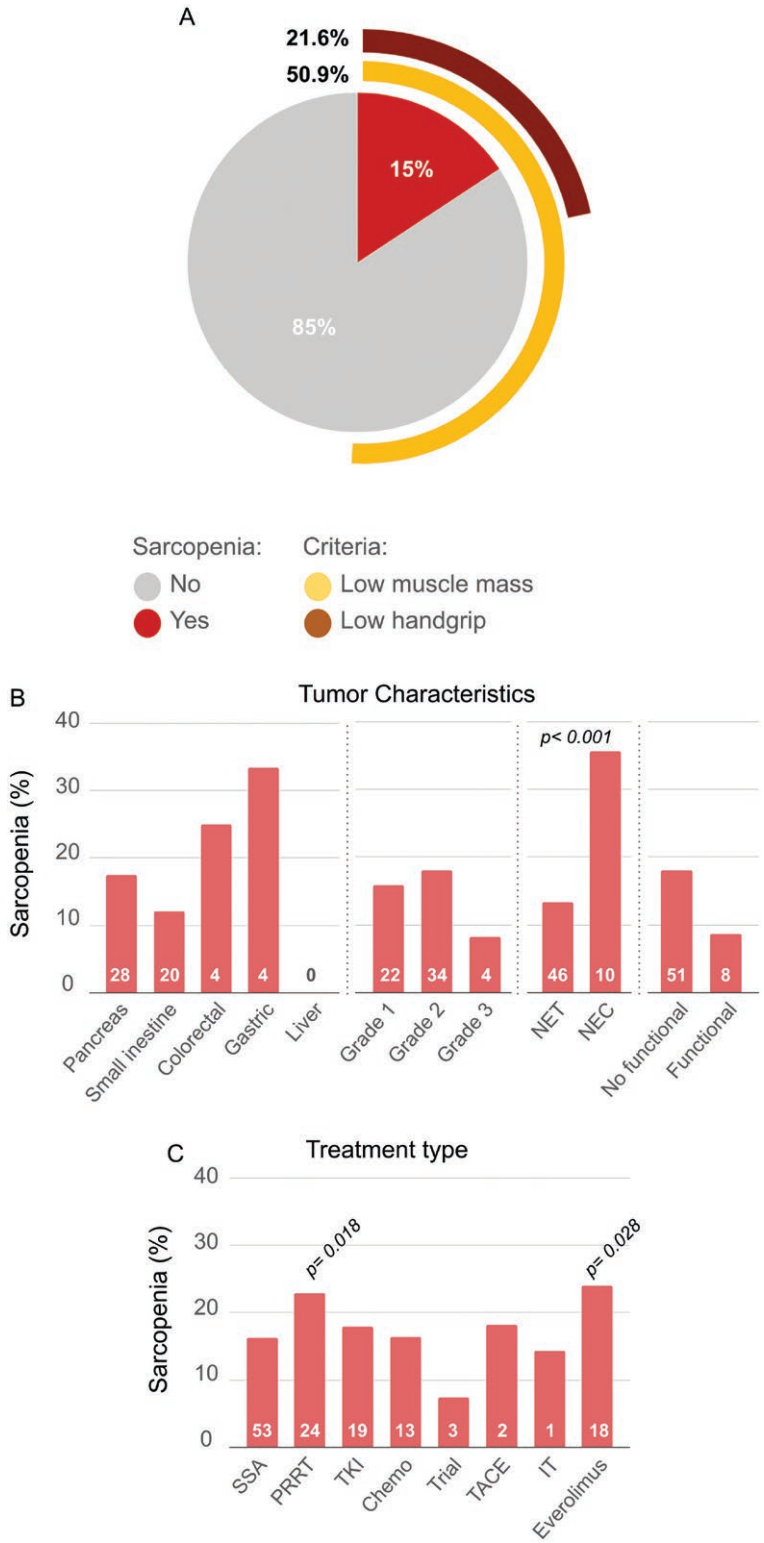

Figure 3. Sarcopenia prevalence. (A) Prevalence of sarcopenia and criteria determining sarcopenia. (B) Sarcopenia according to cancer characteristics including tumor primary origin, grade (WHO), histology, and functionality. (C) Sarcopenia according to the type of previous treatments. Abbreviations: Chemo, chemotherapy; IT, immunotherapy; NEC, neuroendocrine carcinoma; NET neuroendocrine tumors; PRRT, peptine receptor radiotherapy; SSA, somatostatin analogs; TACE, transarterial chemoembolization; TKI, tyrosine kinase inhibitors.

receiving CT show a tendency toward worse nutritional status, in line with previous reports.[14,18,20-23] Tumor grade, location, and functionality do not correlate with malnutrition. A deleterious effect of SSAs on nutritional status is not observed despite previous evidence suggesting that it may cause malabsorption, diarrhea, or bloating.[36]

DM is prevalent in patients with GEP-NENs, specially in specific types such as glucagonoma or pancreatic NETs

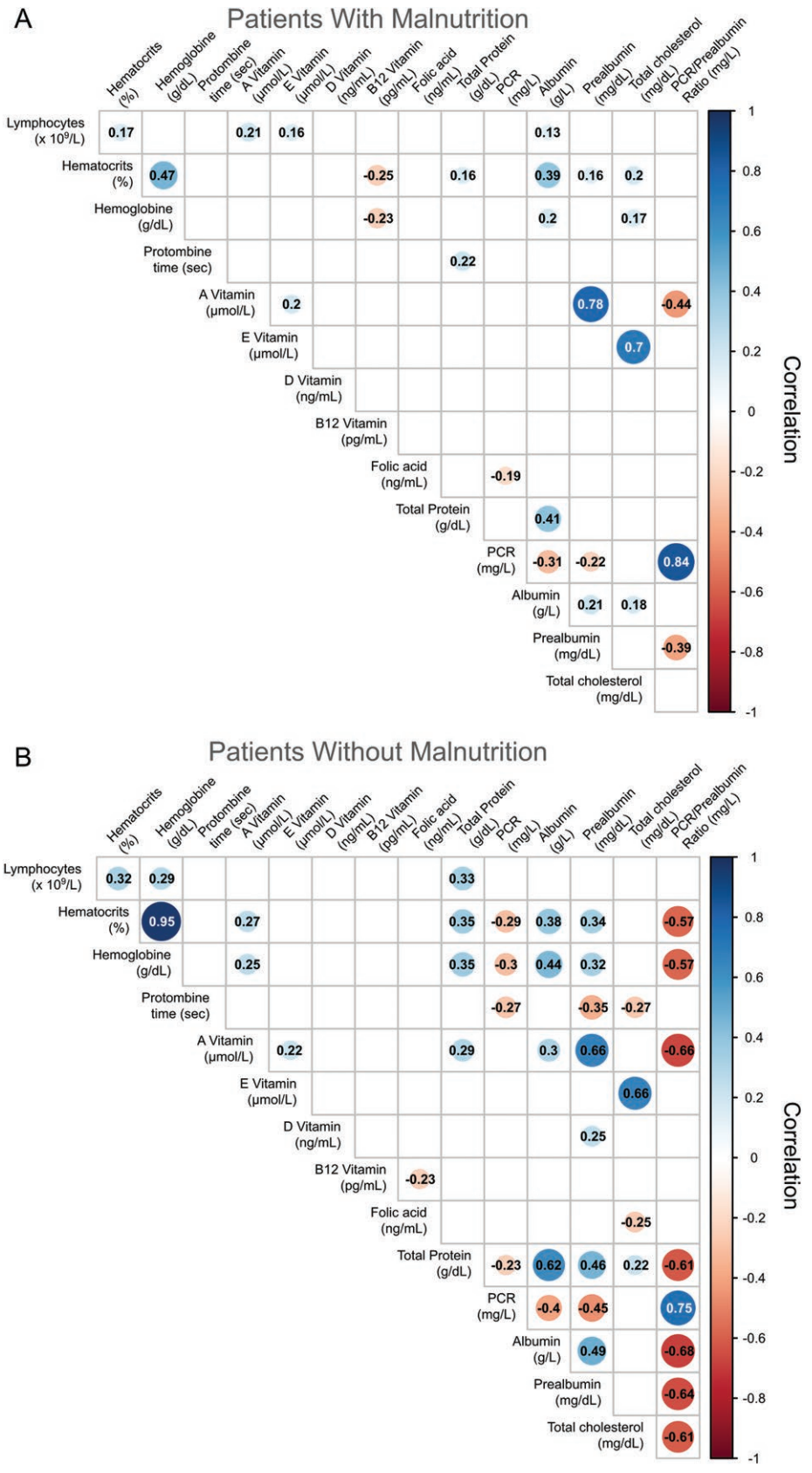

Figure 4. Correlation between laboratory parameters. Correlation between laboratory parameters in patients with malnutrition (A) and patients without malnutrition (B). Showing significant correlations. The values in the squares and color indicate the correlation level.

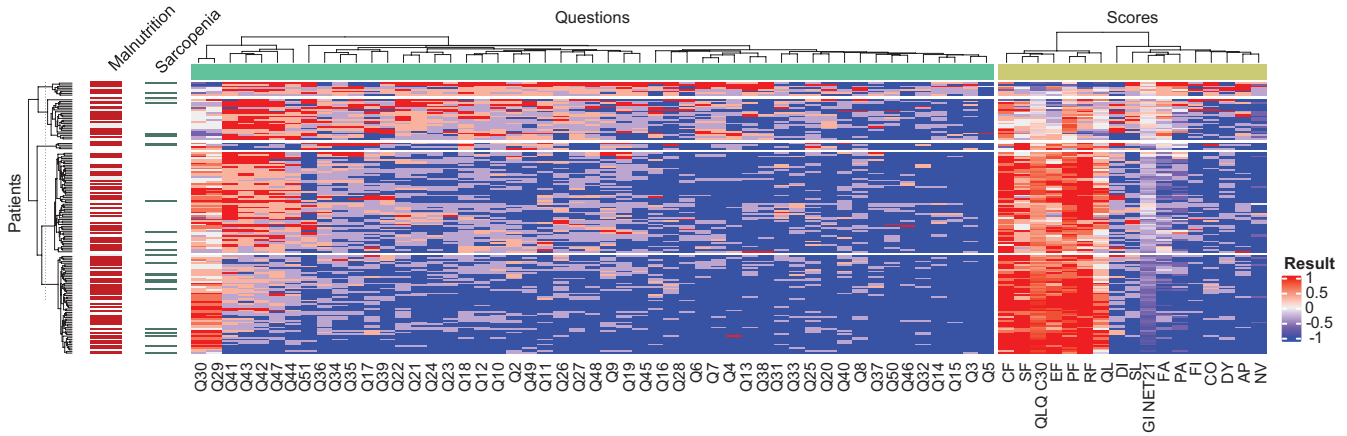

Figure 5. Quality of life (QoL). Malnutrition is shown in the first column in red. Values for each QoL item are standardized. Abbreviations: AP, appetite loss; CF, cognitive functioning; CO, constipation; DI, diarrhoea; DY, dyspnoea; EF, emotional functioning; FA, fatigue; FI, financial difficulties; NV, nausea and vomiting; PA, pain; PF, physical functioning; QL, global health status; RF, role functioning; SF, social functioning; SL, insomnia. See Supplementary Information for detail on each specific question/item.Supplementary Information

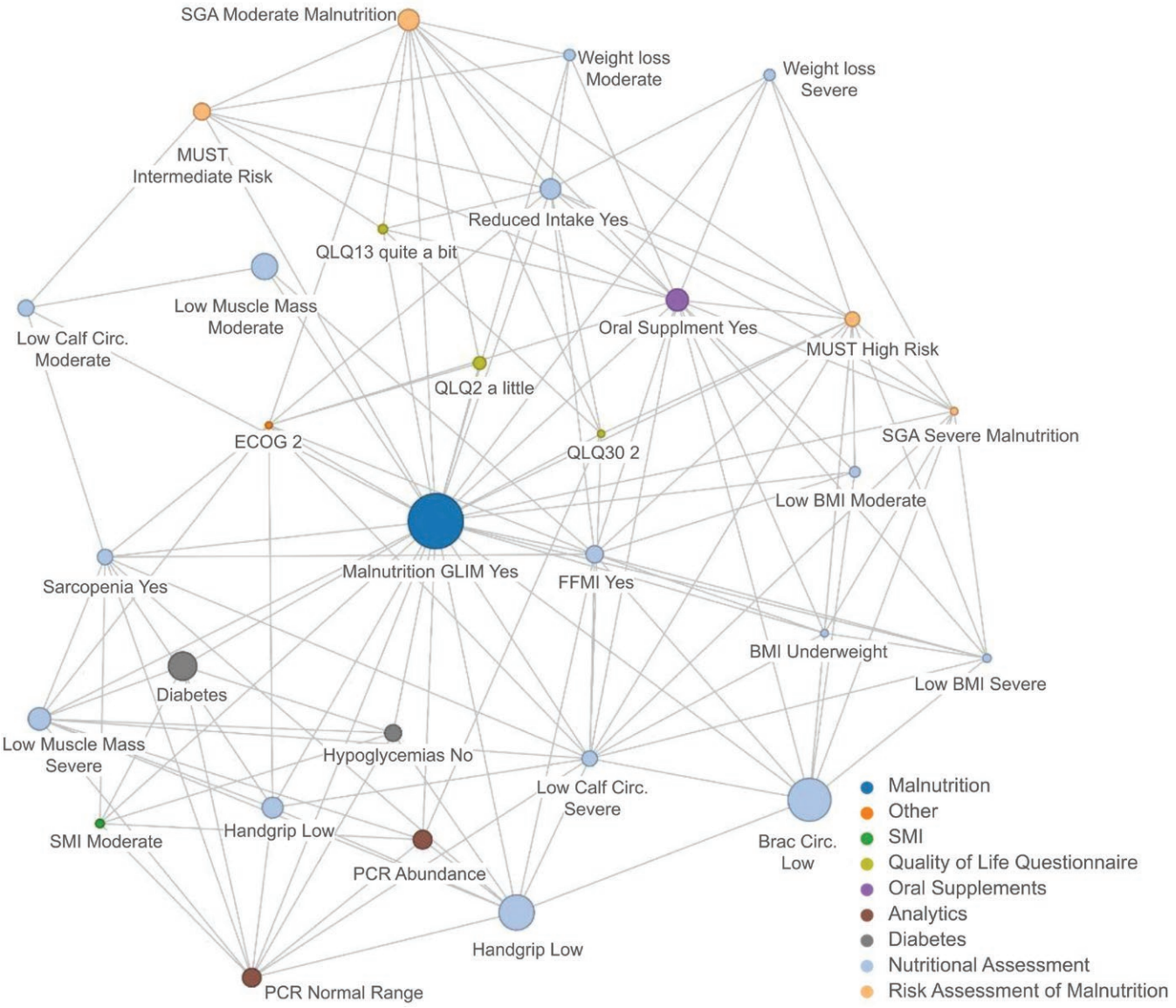

Figure 6. Coincidence analysis of malnutrition. The graph shows the variables that are correlated with malnutrition according to GLIM criteria [YES]. The width of the dots represents the number of patients contained in the group. Lines show crosstalk between variables. The distance is proportional to the level of coincide between both variables. All lines shown are statistically significant coincidences and the graph only shows the variables that have at least one significant association with malnutrition. Color is used to classify variables in different main groups.

that undergo surgical resection. Additionally, the use of SSA or mTOR inhibitors may impair glucose metabolism.[37] In the present study, one third of patients were diagnosed with DM. The presence of concomitant DM seems to be linked to worse nutritional status and prognosis in patients with GEP-NENs.[38] Thus, DM control should be pursued to optimize nutritional status and survival. Early reports have shown that patients with GEP-NENs and DM who received metformin had better survival outcomes, although the evidence for this is still controversial and entirely retrospective.[39]

The muscle status should be carefully monitored according to our results. Sarcopenia is particularly prevalent in patients with carcinomas and those treated with PRRT, yet far from the 87.2% rate determined by CT scan in previous studies.[40] Most patients received PRRT as the first- or second-line treatment after progression to SSA. The use of everolimus seems to predispose to sarcopenia, similar to previous reports describing that mTOR inhibitors significantly decrease skeletal muscle mass (SMI).[41] Phase angle, a surrogate of muscle mass and independent prognostic factor, and vitamin D were significantly lower in GEP-NENs than in healthy subjects and might be used for monitoring.[42-44]

At the biochemical level, CRP elevation, reduction in hematocrit, and alterations in cholesterol and albumin levels seem to be related to SMI and nutritional status. Some studies reported similar effects in other gastrointestinal cancer types.[45-48] A threshold of 3.0 mg/dL for CRP has been proposed as a reasonable indicator of inflammation leading to reduced food intake and has been proposed to be included in the GLIM criteria.[49]

According to our data, special attention should be taken to symptoms of nausea and vomiting, loss of appetite, or inability to go for a walk as potential indicators of malnutrition. Previous reports also showed that malnutrition increases the number of complications.[20,21,23,32,50-53]

The management of gastrointestinal side effects or symptoms must be prioritized in these patients to improve the overall nutritional status. Previous reports already concluded that interventions with proton pump inhibitors or tryptophan hydroxylase inhibitors reduced symptomatology and improved patient outcomes.[54,55]

This study had some limitations. No control group was established. Due to the cross-sectional design, the prognosis could not be related to nutritional status. The variability of disease presentations and treatments reported led to some subgroups having a small representation. The study plans a prospective follow-up to determine the prognosis of these patients. Physical examinations were performed using local equipment, which lacked the homogenization of measurements between hospitals. Nutritional ultrasound was not performed because it was not available at some centers and aimed to avoid interobserver variability, taking into account that bioimpedance is more reproducible.

Conclusion

In conclusion, this is the largest study showing that malnutrition is very prevalent and probably underdiagnosed in patients with GEP-NENs due to its multifactorial origin. Malnutrition occurs concomitantly with sarcopenia in many cases and was correlated with poorer QoL and symptoms. Monitoring malnutrition is specially recommended for patients with DM, who have an increased prevalence. The implementation of routine nutritional assessment will help to better understand the mechanisms underlying malnutrition in patients with GEP-NENs and establish strategies for interventions to reduce the malnutrition burden and potentially enhance the QoL and treatment outcomes.

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Author contributions

Maribel del Olmo-García and María Argente Pla were responsible for the study design, conceptualization, data curation, coordination, interpretation of study results, and manuscript original drafting. All coauthors contributed substantially to patient accrual, investigation, methodology, validation, visualization, and review of the manuscript.

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Conflict of interest

M.d.O.-G. declares advisory role for Ipsen, Novartis, AAA, and Pfizer; received economic support for congresses Ipsen, Advanz, and AAA; and act as speaker on behalf of Ipsen, Advanz, AAA, and Novartis.

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Data Availability

The data are available from the corresponding author upon reasonable request (equivalent purposes to those for which the patients grant their consent to use the data). Data will be provided anonymously, with no identifiable data.

Supplementary material

Supplementary material is available at *The Oncologist* online.

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