



SAPIENZA
UNIVERSITÀ DI ROMA



GIST AVANZATI:
il valore della gestione
multidisciplinare del paziente

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Responsabile Scientifico
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Ruolo della nutrizione

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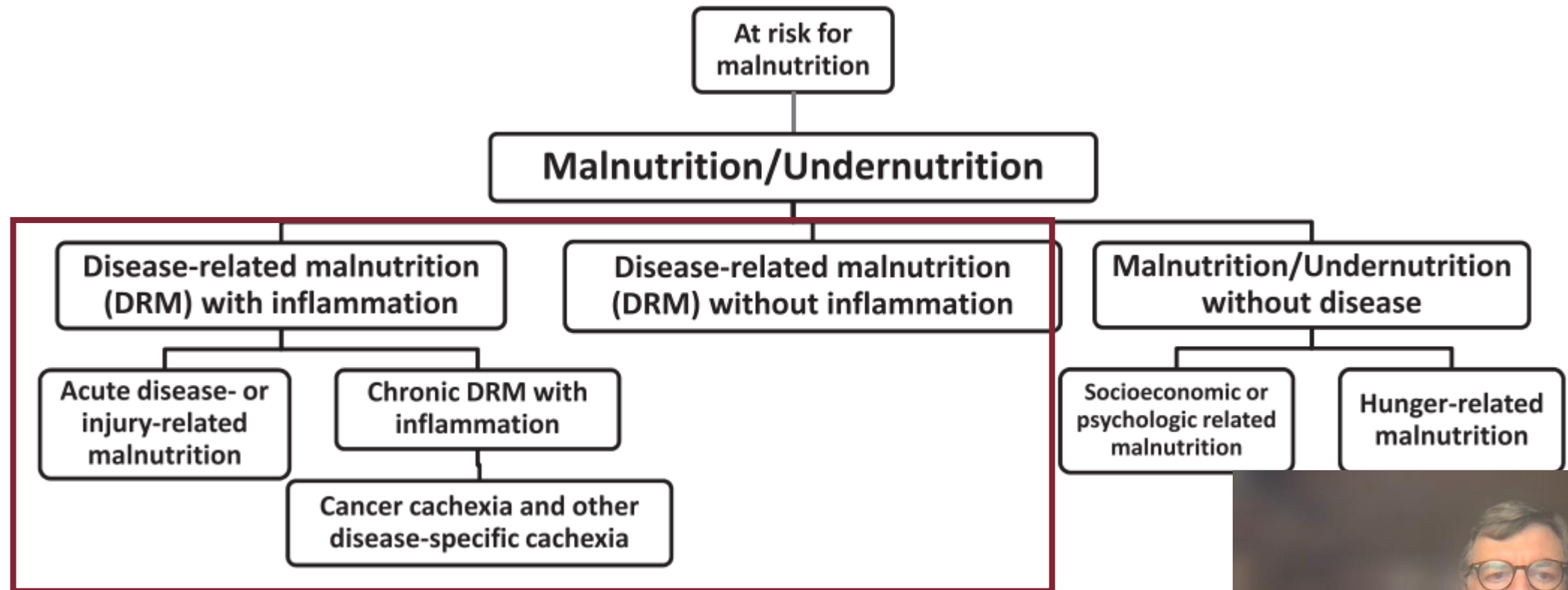
No conflicts of interest to declare regarding this presentation

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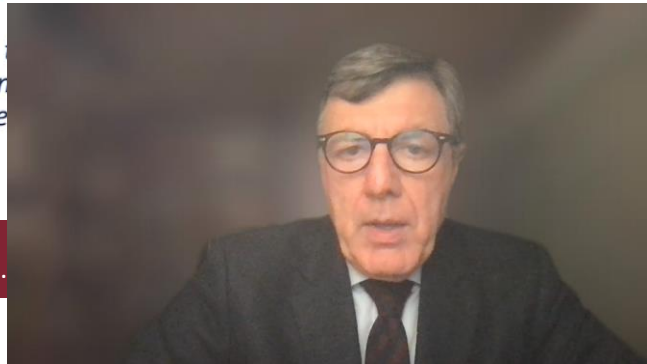
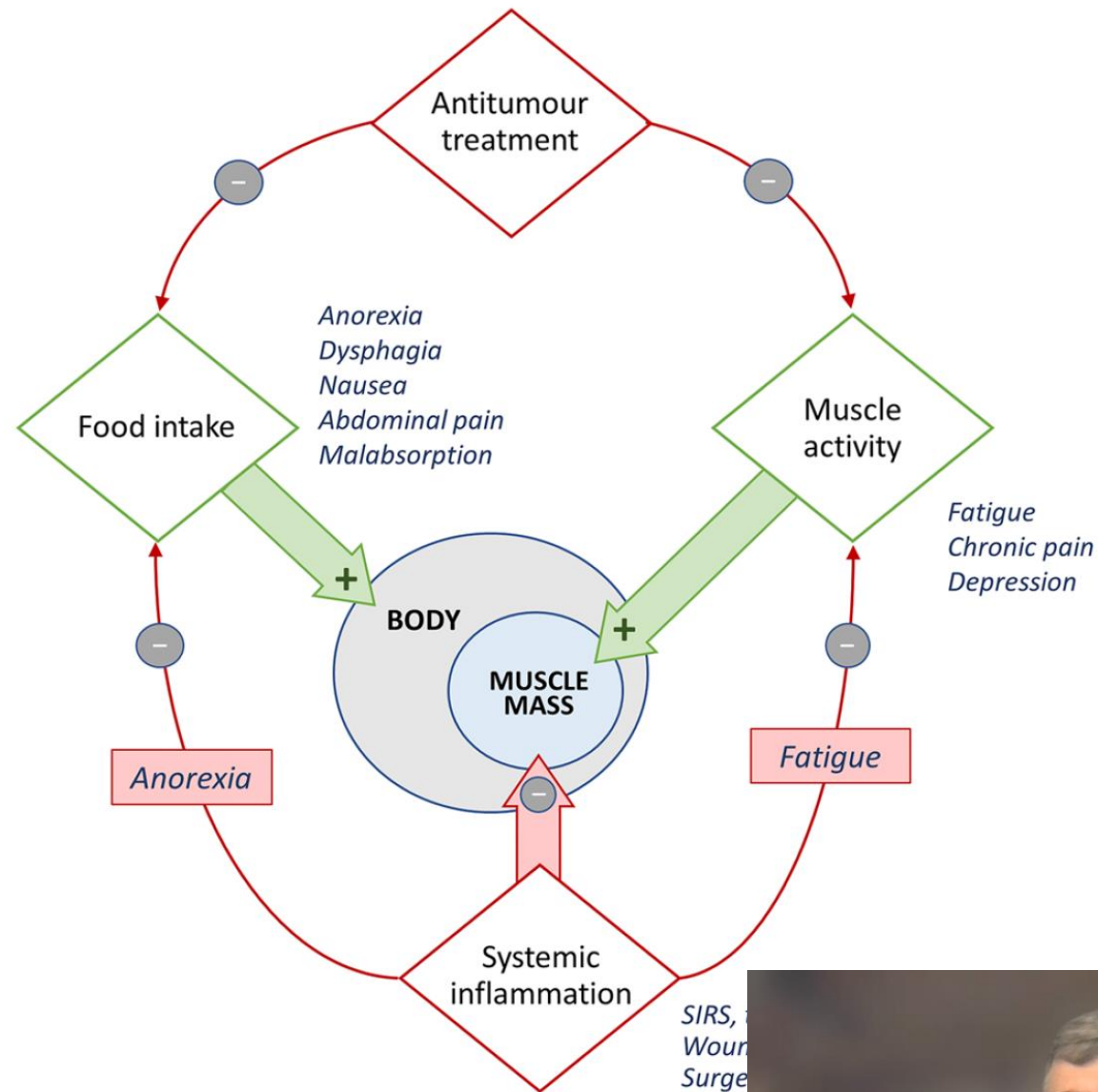


Cancer Related Malnutrition is a specific type of malnutrition



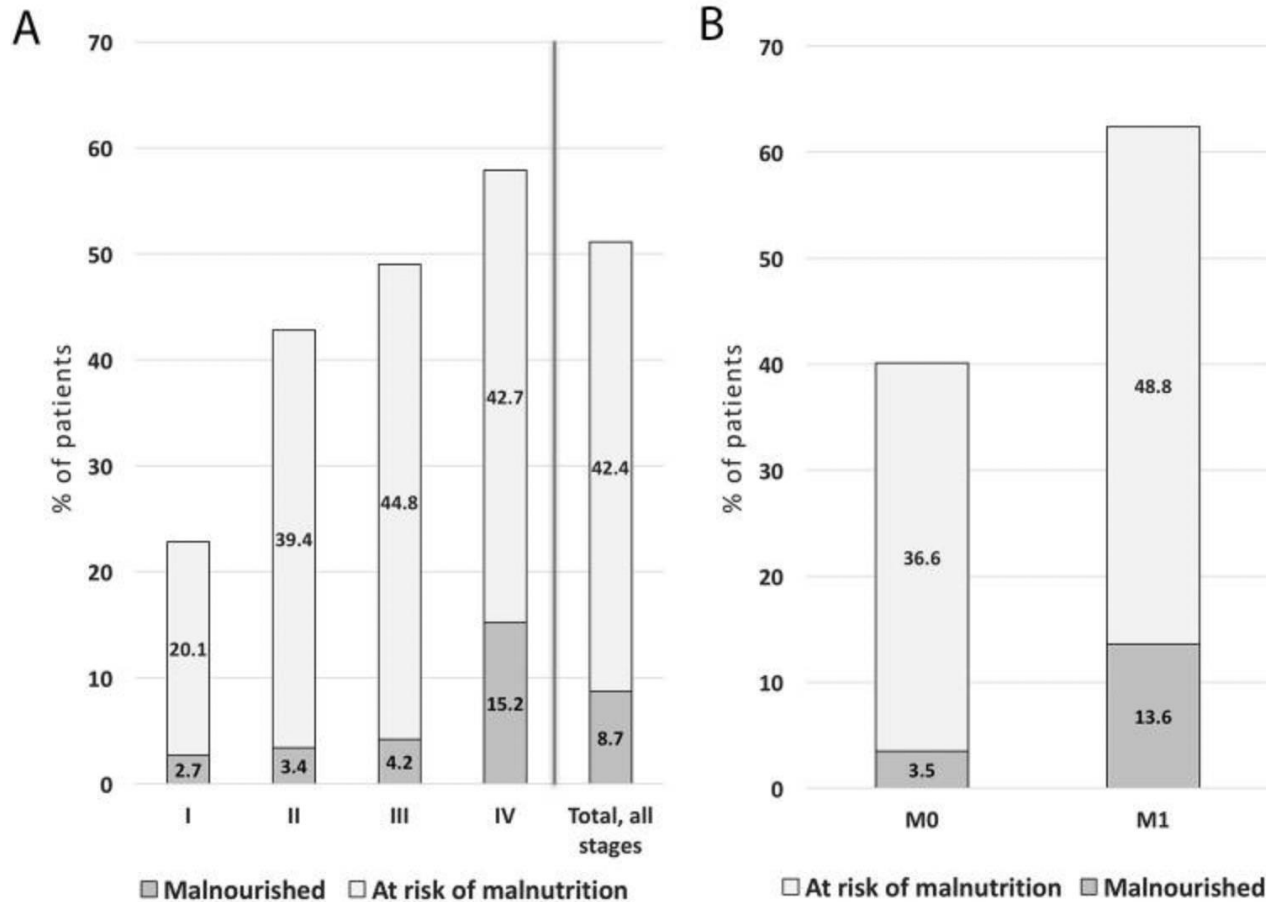


The pathogenesis of cancer-related malnutrition and body composition changes is **multifactorial**





PreMiO study



PreMiO was a prospective, observational study conducted at 22 medical oncology centers across Italy.

FIRST VISIT

(N=1,952)

- >50% had malnutrition
- 9% were obese
- 43% were



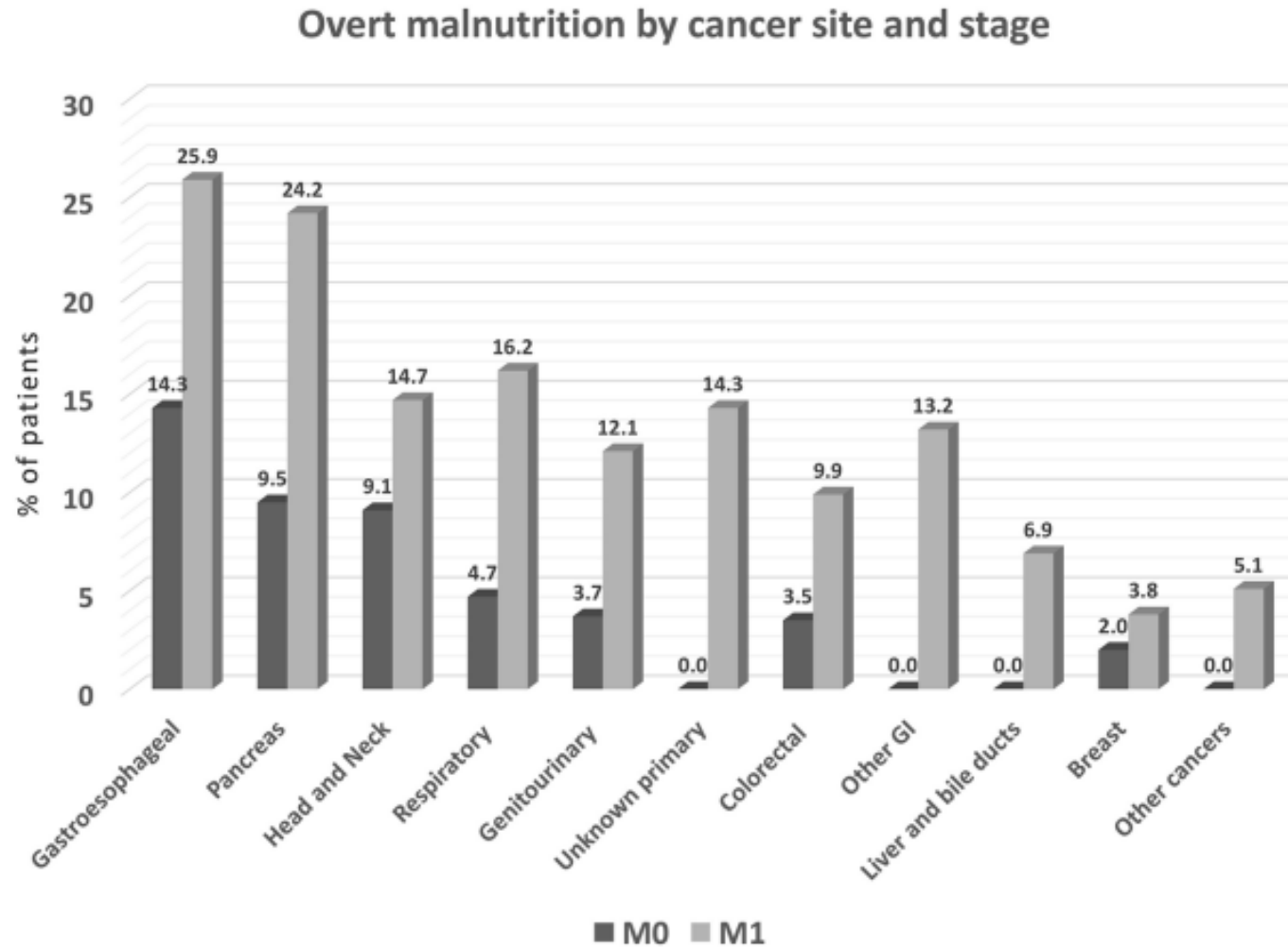
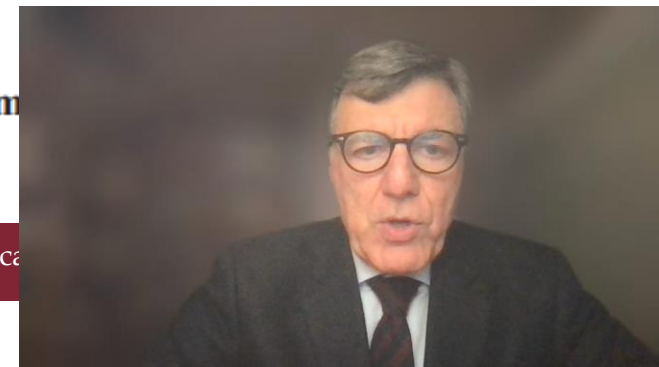
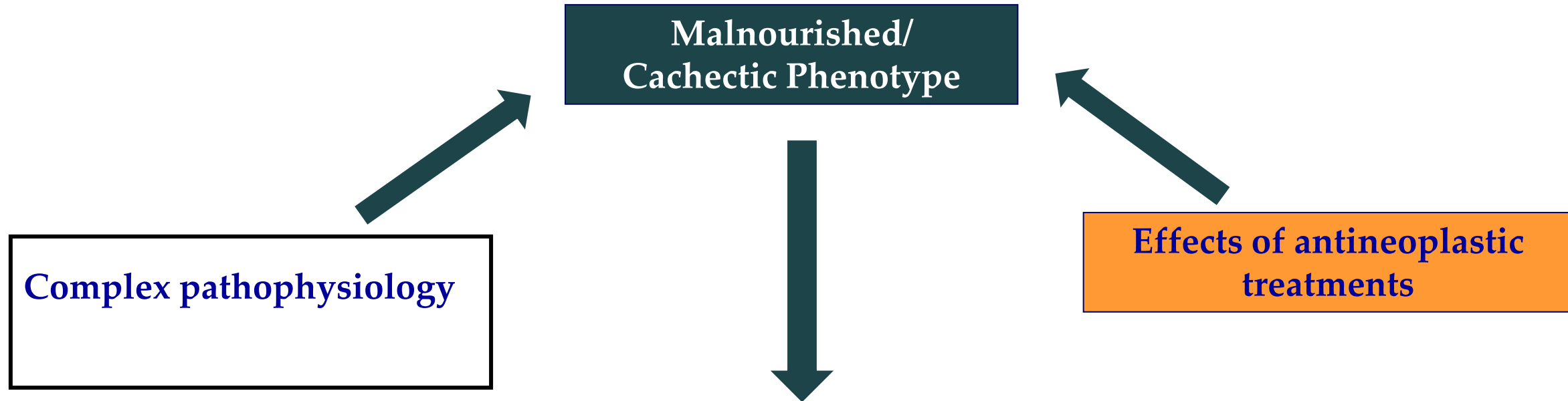


Figure 3: Prevalence of overt malnutrition by cancer site (% of patients with specified tumor type), with malnutrition defined as MNA score <17 (N=1925). M0 = stage I-III, M1 = stage IV. P<0.001 among cancer site groups.





Cancer-related weight loss/ malnutrition/sarcopenia/cachexia



Outcome
(tolerance to treatments, morbidity, quality of life)

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Association Between the Nutritional Risk and the Survival Rate in Newly Diagnosed GIST Patients

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AIMS:

- incidence of malnutrition in **newly diagnosed GIST patients**
- the proportion of participants in need of nutritional intervention
- the relationship between nutritional status and overall survival (OS)

TABLE 1 | General and tumor characteristics of study participants ($n = 1268$).

Variables	N (Percentage)
Age (years)	59.9 ± 4.2 *
Sex (male)	665 (52.44%)
Weight loss	
No WL (0–1.9% of body weight)	801 (63.17%)
Mild WL (2–2.9% in 1-month or 2–5.9% in 6 months)	208 (16.40%)
Moderate WL (3–4.9% in 1-month or 6–9.9% in 6 months)	117 (9.23%)
Severe WL (5–9.9% in 1-month or 10–19.9% in 6 months)	88 (6.94%)
Very severe WL (>10% in 1-month or >20% in 6 months)	54 (4.26%)
Tumor location	
Stomach	887 (69.95%)
Duodenum	54 (4.26%)
Intestine	235 (18.53%)
Colon	30 (2.37%)
Mesentery	62 (4.89%)
Tumor size (cm)	
<5.0	383 (30.21%)
5.0~10.0	
>10.0	

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Methods:

- retrospective study n=1268 GIST patients treated in hospital from January 2014 to January 2018
- Nutritional Risk Screening 2002 (NRS2002) and Patient-Generated Subjective Global Assessment (PG-SGA) were used to assess the nutritional status of all patients.

NRS2002 SCORE:

≥ 3 the patient is at nutritional risk and a nutritional program should be drawn up.
 < 3 weekly reassessment of the patient.

NUTRITIONAL TRIAGE BASED ON THE SCORE OF THE SCORED PG-SGA:

0-1 No need for intervention at this stage. Routine periodic reevaluation during treatment.

2-3 Patient and family education by dietitian, nurse or other specialist with pharmacological intervention based on symptomatology investigation and laboratory values as appropriate.

4-8 A dietitian is needed, assisted by a nurse or physician depending on the symptomatology.

≥ 9 Indicates immediate need for better symptom control and/or intervention options for nutrient intake.

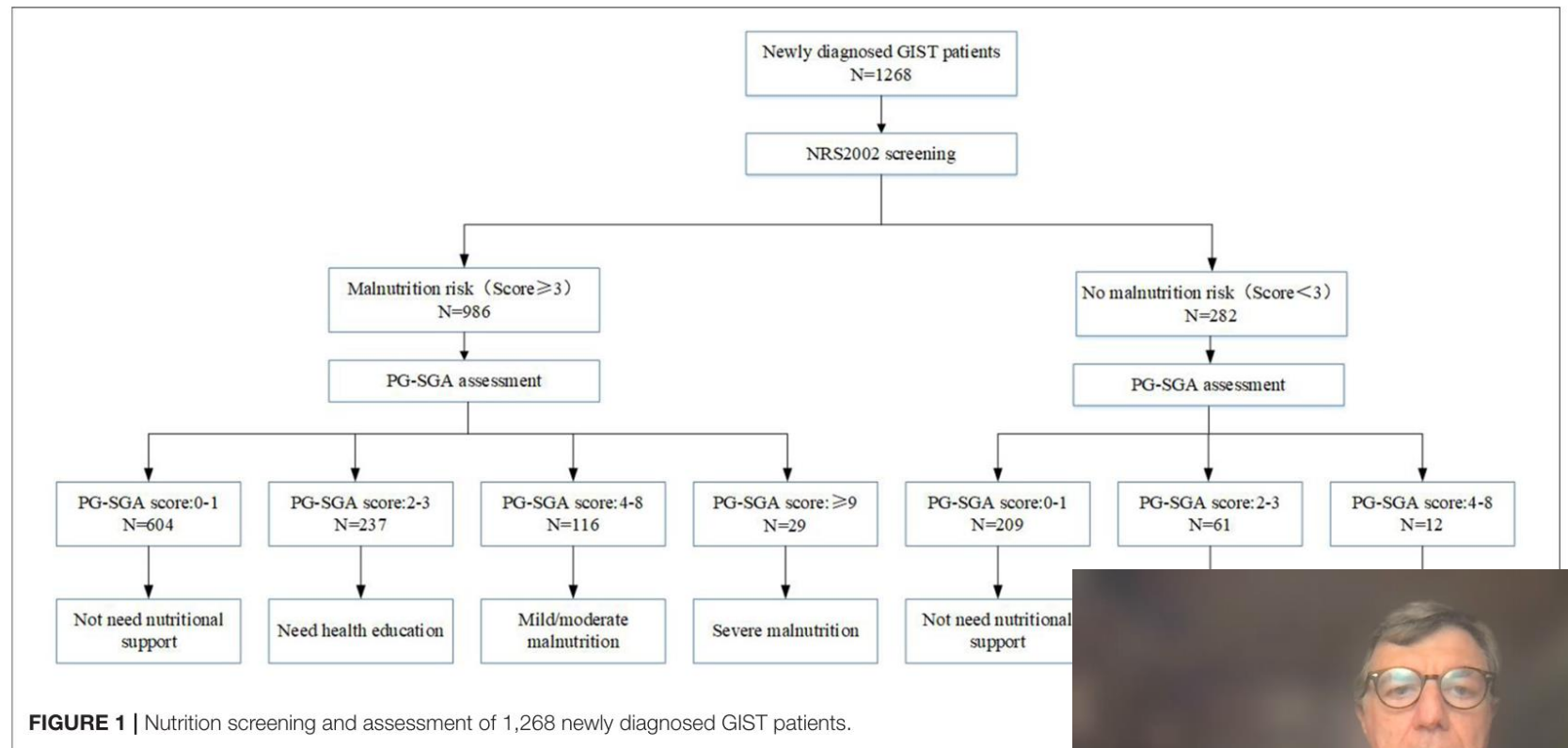


TABLE 3 | The relationship between risk classification and incidence of nutritional risk in newly diagnosed GIST patients (N = 1,268) [n(%)].

Group	N	PG-SGA				Malnutrition incidence
		0~1(%)	2~3(%)	4~8(%)	≥9(%)	
High risk	279	91 (32.62)	99 (35.48)	65 (12.54)	24 (8.60)	188 (67.38)
Moderate risk	543	323 (59.48)	159 (29.28)	56 (10.31)	5 (0.92)	220 (40.52)*
Low risk	309	269 (87.06)	33 (10.68)	7 (2.27)	0 (0)	40 (12.94)*
Very low risk	137	130 (94.89)	7 (5.11)	0 (0)	0 (0)	7 (5.11)*

*Compared with high risk group, two-sided chi-square test, all p < 0.05.

According to 2008 version NIH stromal tumor risk classification standard the comparison between groups showed that the risk of malnutrition in the high-risk group was significantly higher than that in the other three groups (p<0.05)

TABLE 4 | Location of gastrointestinal stromal tumors and incidence of nutritional risk (N = 1,268) [n(%)].

Group	N	PG-SGA				Malnutrition incidence
		0~1(%)	2~3(%)	4~8(%)	≥9(%)	
Stomach	887	605 (68.21)	180 (20.29)	88 (9.92)	14 (1.58)	282 (46.61)*
Duodenum	54	29 (53.70)	19 (35.19)	5 (9.26)	1 (1.85)	25 (46.30)*
Intestine	235	139 (59.15)	73 (31.06)	17 (7.23)	6 (2.55)	96 (40.85)*
Colon	30	20 (66.67)	6 (20.00)	3 (10.00)	1 (3.33)	
Mesentery	62	20 (32.26)	20 (32.26)	15 (24.19)	7 (11.29)	

*Compared with mesentery group, two-sided chi-square test, all p < 0.05.

The comparison among groups showed that the risk of malnutrition in patients with mesentery significantly higher (p<0.05)



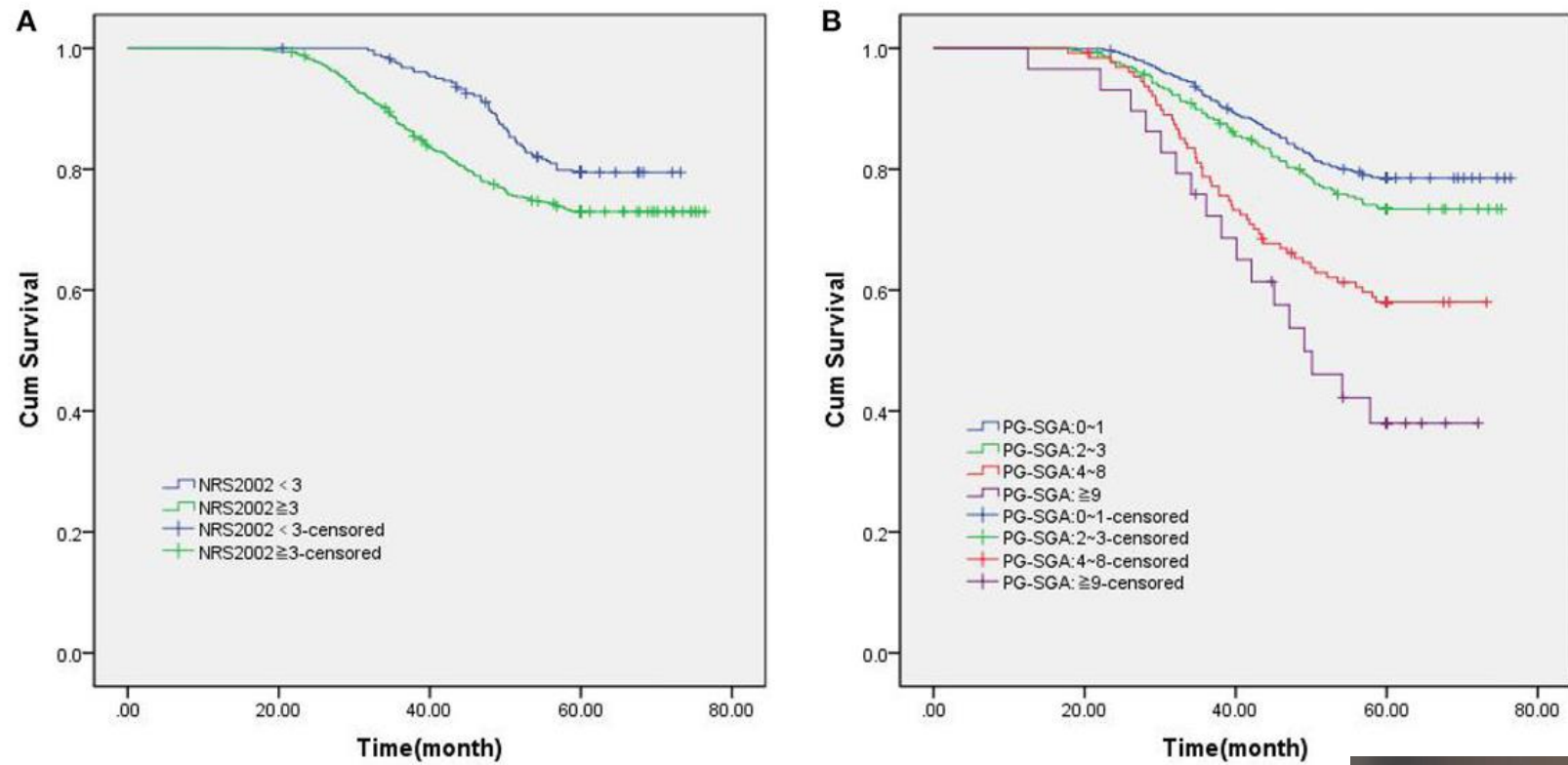


FIGURE 2 | Kaplan-Meier survival curves in patients with newly diagnosed GIST patients. **(A)** Overall survival based on NRS2002 scores. **(B)** Overall survival based on PG-SGA scores.



Association Between the Nutritional Risk and the Survival Rate in Newly Diagnosed GIST Patients

Ping'an Ding¹, Honghai Guo¹, Peigang Yang¹, Chenyu Sun², Yuan Tian¹, Yang Liu¹, Yong Li¹ and Qun Zhao^{1*}

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CONCLUSIONS:

- ❑ About 12.38% of GIST patients had malnutrition at the time of diagnosis, and more than 1/10 of GIST patients needed urgent nutritional intervention and management.
- ❑ More attention should be paid to the nutritional status of GIST patients, especially those with high risk of malnutrition, such as elderly patients and tumors located in the mesent

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n=413

Relationship Between Nutritional Status and Clinical Outcome in Patients With Gastrointestinal Stromal Tumor After Surgical Resection

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Methods:

- ❑ Retrospective study n=413 GIST patients who underwent surgical resection in the Fourth Hospital of Hebei Medical University from January 2016 to January 2020.
- ❑ Nutritional risk screening 2002 (NRS2002) and Patient-Generated Subjective Global Assessment (PG-SGA) to assess the nutritional status of all patients at admission and discharge, and the correlation between nutritional risk and clinical outcomes was analyzed.

TABLE 1 | Patient baseline demographic and clinical characteristics at admission.

Variables	N (Percentage)
Age (years)	59.7 ± 10.3 *
Sex (male)	201 (48.32%)
Tumor location	
Stomach	253 (61.26%)
Duodenum	25 (6.05%)
Intestine	76 (18.40%)
Colon	29 (7.02%)
Mesentery	30 (7.26%)
Tumor size (cm)	5.3 ± 4.8*
Nuclear mitotic figure (50HPF)	
<5	149 (36.08%)
6~10	236 (57.14%)
>10	28 (6.78%)
c-kit exons	
Positive	268 (64.89%)
Negative	145 (35.11%)
PDGFRA exons	
Positive	
Negative	

*Mean ± SD.

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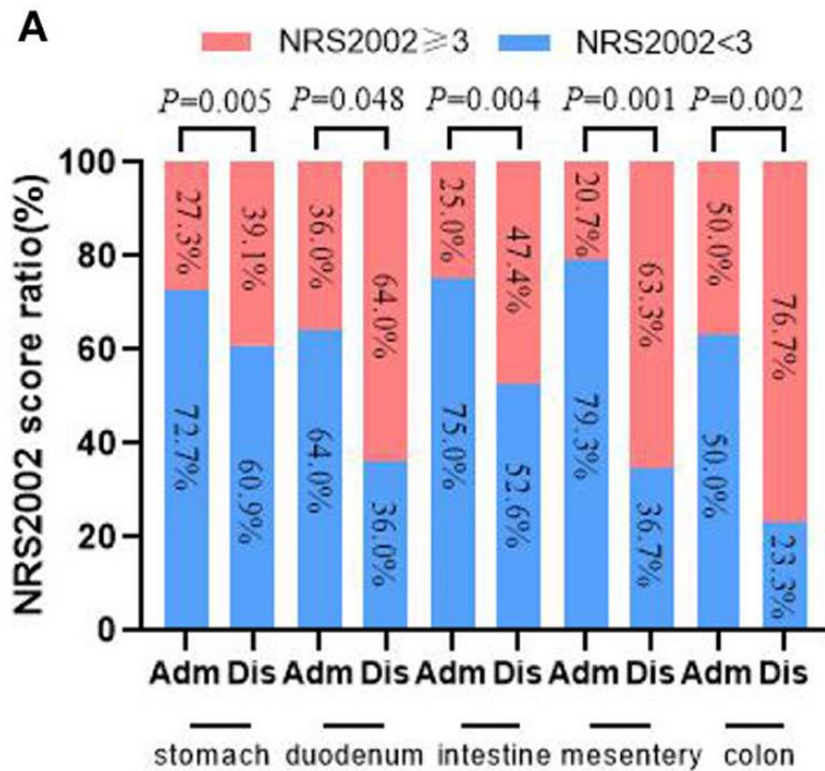


Figure A. Changes of NRS2002 screening in 413 GIST patients at admission and discharge.

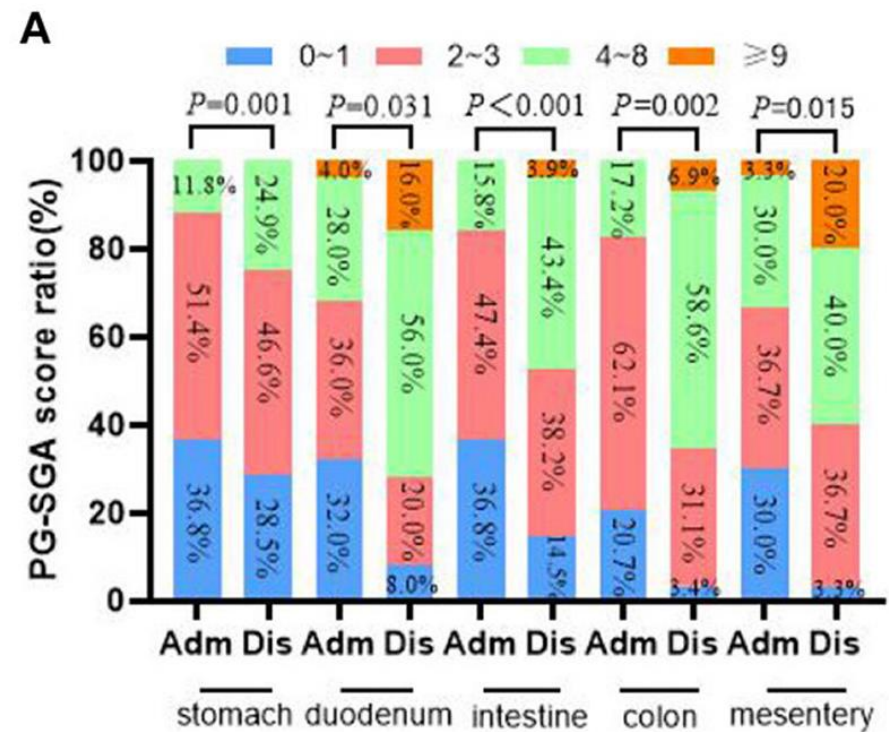


Figure A. Changes of PG-SGA nutritional assessment in 413 GIST patients at admission and discharge.

The proportion of nutritional risk (27.60%) and malnutrition (15.73%) in GIST is high, **but the nutritional status is further deteriorated at discharge**, and the malnutrition rates are 46.73 and 37.29%, respectively.

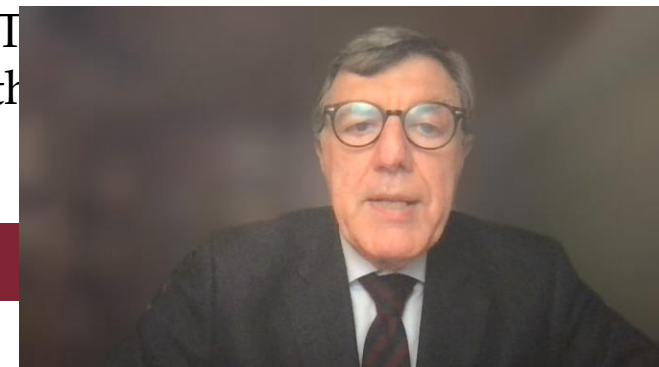




TABLE 3 | Comparison of postoperative complications based on PG-SGA score [n (%)].

Variable	PG-SGA<4		P	Total 1	PG-SGA ≥4		P	Total 2	P*	P**
	Support (A) (N = 15)	No support (B) (N = 333)			Support (C) (N = 49)	No support (D) (N = 16)				
Total	3 (20.00)	60 (18.02)	1.000 ^b	63 (18.10)	10 (20.41)	9 (56.25)	0.006	19 (29.23)	<0.001	0.039
Wound infection	1 (6.67)	3 (0.90)	0.417 ^b	4 (1.15)	1 (2.04)	1 (6.25)	0.990 ^b	2 (3.08)	0.446 ^b	0.530 ^b
Anastomotic leakage	0 (0)	4 (1.20)	–	4 (1.15)	1 (2.04)	0 (0)	–	1 (1.54)	–	1.000 ^b
Lymphatic leakage	0 (0)	0 (0)	–	0 (0)	0 (0)	1 (6.25)	–	1 (1.54)	–	–
Abdominal infection	0 (0)	1 (0.30)	–	1 (0.29)	0 (0)	1 (6.25)	–	1 (1.54)	0.166	1.000 ^b
Abdominal bleeding	0 (0)	3 (0.90)	–	3 (0.86)	0 (0)	1 (6.25)	–	1 (1.54)	0.446 ^b	1.000 ^b
Anastomotic bleeding	0 (0)	2 (0.60)	–	2 (0.57)	0 (0)	0 (0)	–	0 (0)	–	–
intestinal obstruction	0 (0)	3 (0.90)	–	3 (0.86)	0 (0)	1 (6.25)	–	1 (1.54)	0.446 ^b	1.000 ^b
Respiratory complications	2 (13.33)	42 (12.61)	1.000 ^b	44 (12.64)	7 (14.29)	4 (25.00)	0.543 ^b	11 (16.92)	0.293 ^b	<0.001
Cardiovascular complications	0 (0)	2 (0.60)	–	2 (0.57)	1 (2.04)	0 (0)	–	1 (1.54)	–	0.965 ^b

Note: *B vs. D; **Total 1 vs. Total 2; ^bContinuity correction; PG-SGA, patient-Generated Subjective Global Assessment.

The incidence of surgical-related complications in patients with malnutrition (29.23%) was significantly higher than that in patients without malnutrition.

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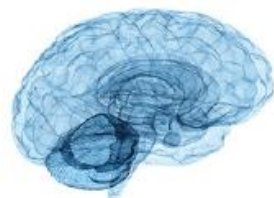


Sarcopenia is the common phenotype of different conditions

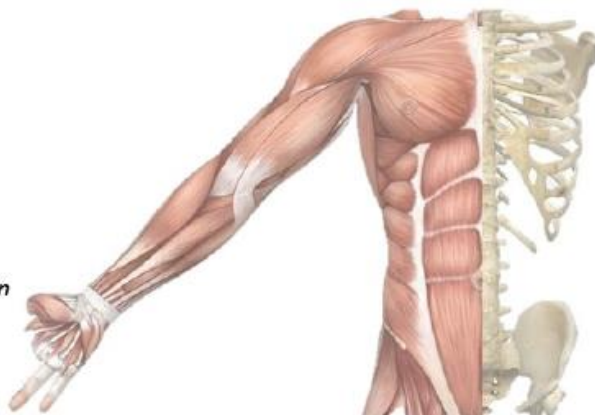
Sarcopenia related factors



Age-related
Sex Hormones
Apoptosis
Mitochondrial Dysfunction



Neuro-degenerative diseases
Motoneuron loss



Physical inactivity
Immobility
Poor cardiovascular health
Poor metabolic and muscular health



Endocrine
Corticosteroids
GH and IGF-1
Thyroid
Insulin Resistance



Cancer cachexia



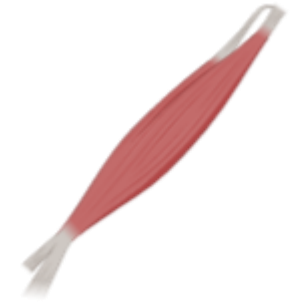
Starvation
Malabsorption of nutrients
Poor nutrition
Taste disturbances



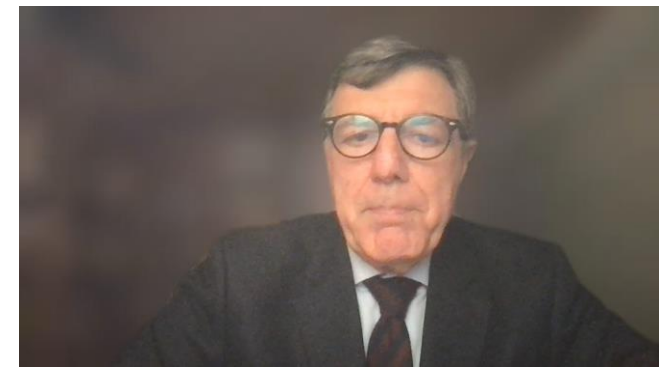
TABLE 2 Total prevalence of sarcopenia in different tumors

Tumors	Studies, n	Patients, n	Mean age	Prevalence of sarcopenia, n (%)	95% CI
Breast cancer	13	4858	53.7	32 (3)	30.9–33.6
CC	10	1693	63.7	54 (0)	51.7–56.4
Colorectal cancer	47	33,221	60.6	28 (3)	27.8–28.7
Endometrial cancer	1	176	70.0	34 (7)	27.6–41.7
Esophageal cancer	32	4086	64.0	52 (9)	51.3–54.4
Gastric cancer	34	9438	64.0	32 (8)	31.9–33.8
HCC	23	5189	66.8	28 (4)	27.1– 29.6
HNSCC	24	6649	59.2	39 (9)	38.8–41.1
Lung cancer	16	3187	66.1	44 (2)	42.5–45.9
Melanoma	2	115	53.0	29 (6)	21.2–37.9
Ovarian cancer	9	1543	64.3	46 (5)	44.0–49.0
Pancreatic cancer	27	4462	65.2	40 (4)	39.0–41.8
Prostate cancer	6	1273	69.4	61 (0)	58.3–63.6
Renal cell cancer	17	3064	59.5	44(4)	42.6–46.1
Sarcoma	2	252	62.6	51 (2)	45.0– 57.4
Thyroid cancer	3	257	63.0	51 (0)	44.9–57.1
Urothelial cancer	12	1800	70.5	50 (7)	48.4–53.0
UCC	2	551	56.6	48 (8)	44.6–53.0
Total	280	81,814	61.9	35 (3)	34.9–35.6

Abbreviations: CC, cholangiocarcinoma; HCC, hepatocellular cancer; HNSCC, head and neck squamous cell cancer; UCC, uterine cervical cancer.



Sarcopenia is a frequent condition in oncology with a prevalence of 35.3%.





Negative clinical impact of sarcopenia

- Respiratory failure
- Asthenia, fatigue
- Impaired physical function
- Increased risk of falls/fractures
- Impaired QoL
- **Reduced survival**
- **Reduced tolerance to treatments**





ELSEVIER

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjournal.com

Applied nutritional investigation

Association between preoperative skeletal muscle mass depletion and poor relapse-free survival in patients with gastrointestinal stromal tumors after complete resection

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METHODS:

- ❑ retrospective study n=445 patients with primary resectable GISTs who had undergone surgical treatment between January 2013 and January 2021.
- ❑ The lumbar skeletal muscle index (SMI) was assessed using abdominal computed tomography images taken within 7 d preoperatively

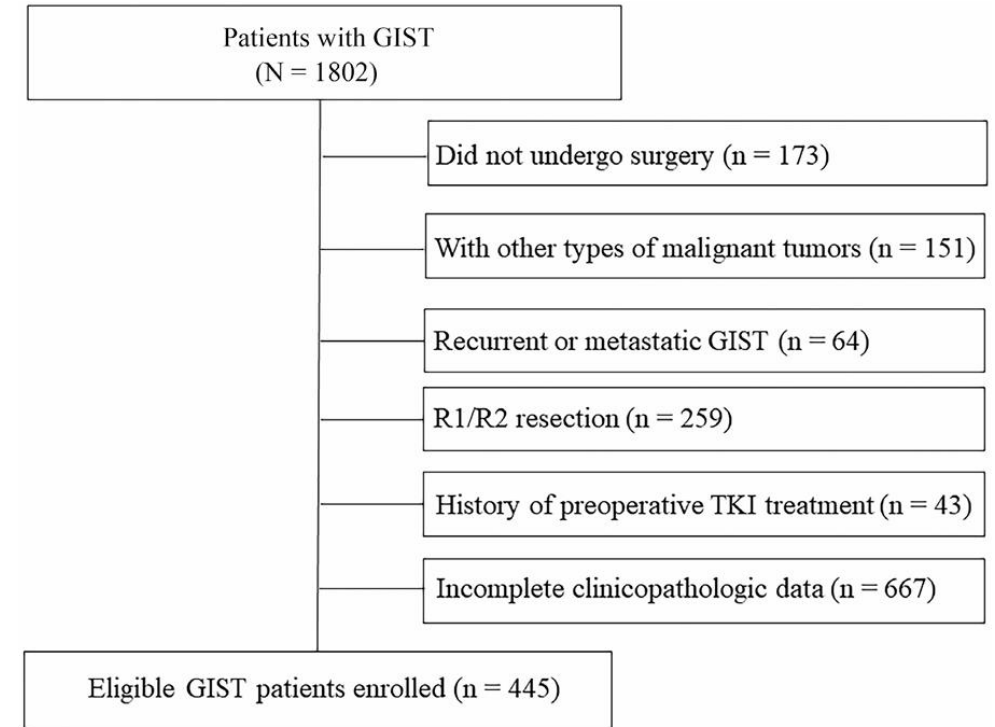


Fig. 1. Flow chart depicting the patient selection process. GIST, gastrointestinal stromal tumor; TKI, tyrosine kinase inhibitor.

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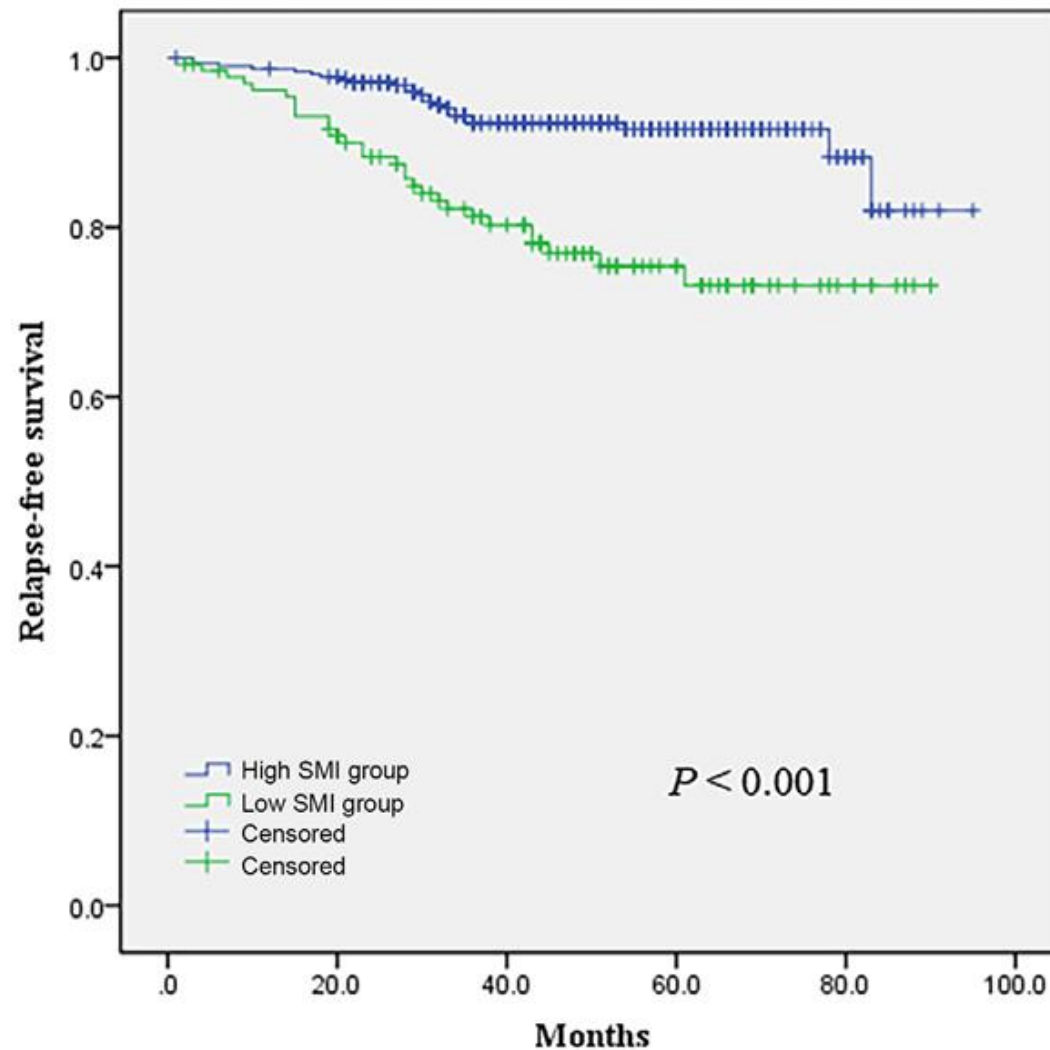


Fig. 2. Comparison of relapse-free survival between low and high SMI groups of all patients. SMI, skeletal muscle index.

RESULTS:

- During a median follow-up of 45 mo (range, 2–95 mo), 53 patients (11.9%) relapsed and 33 (7.4%) died.
- Patients with SMM depletion had a poorer RFS than those without SMM depletion ($P < 0.001$).



Preoperative SMM depletion was an independent poor prognostic factor for RFS after surgery in patients with primary GISTs







This study aimed to investigate the correlation between sarcopenia and adverse events (AEs) of postoperative imatinib therapy through computed tomography (CT) quantitative body composition for intermediate- and high-risk gastrointestinal stromal tumors (GISTs).

Original Article

The correlation of sarcopenia and adverse events of imatinib therapy postoperatively in gastrointestinal stromal tumor through computed tomography quantitative body composition

Xinyi Shao ^{a,1}, Hao Wu ^{a,1}, Chen Huang ^a, Hanyu Yin ^a, Pengfei Wang ^b, Xiaoli Wu ^{a,1}  



- retrospective study: n= 208 patients with intermediate- and high-risk GIST treated surgically and treated with imatinib afterward at the First Affiliated Hospital of Wenzhou Medical University between October 2011 and October 2021.
- Images of preoperative CT scans within 1 month were used to determine the body composition of the patients.
- On the basis of the L3 skeletal muscle index, patients were classified into sarcopenia and nonsarcopenia groups.

RESULTS

- The proportion of AEs related to imatinib in the sarcopenia group was higher, and this disparity had a significant statistical significance ($P = .013$).
- Sarcopenia was significantly associated with hemoglobin reduction compared with nonsarcopenia ($P = .015$).
- There was a significant difference between the sarcopenia group and the nonsarcopenia group in the ratio of severe AEs (grades 3-4).
- Hemoglobin content (odds ratio [OR], 0.981; 95% CI, 0.963-1.000; $P = .045$), sex (OR, 0.416; 95% CI, 0.19 (OR, 5.631; 95% CI, 2.262-14.014; $P < .001$) were the influential factors of imatinib severe AEs in patient risk GIST within 1 year after imatinib treatment.

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RESEARCH

Open Access

Effect of skeletal muscle loss during neoadjuvant imatinib therapy on clinical outcomes in patients with locally advanced GIST



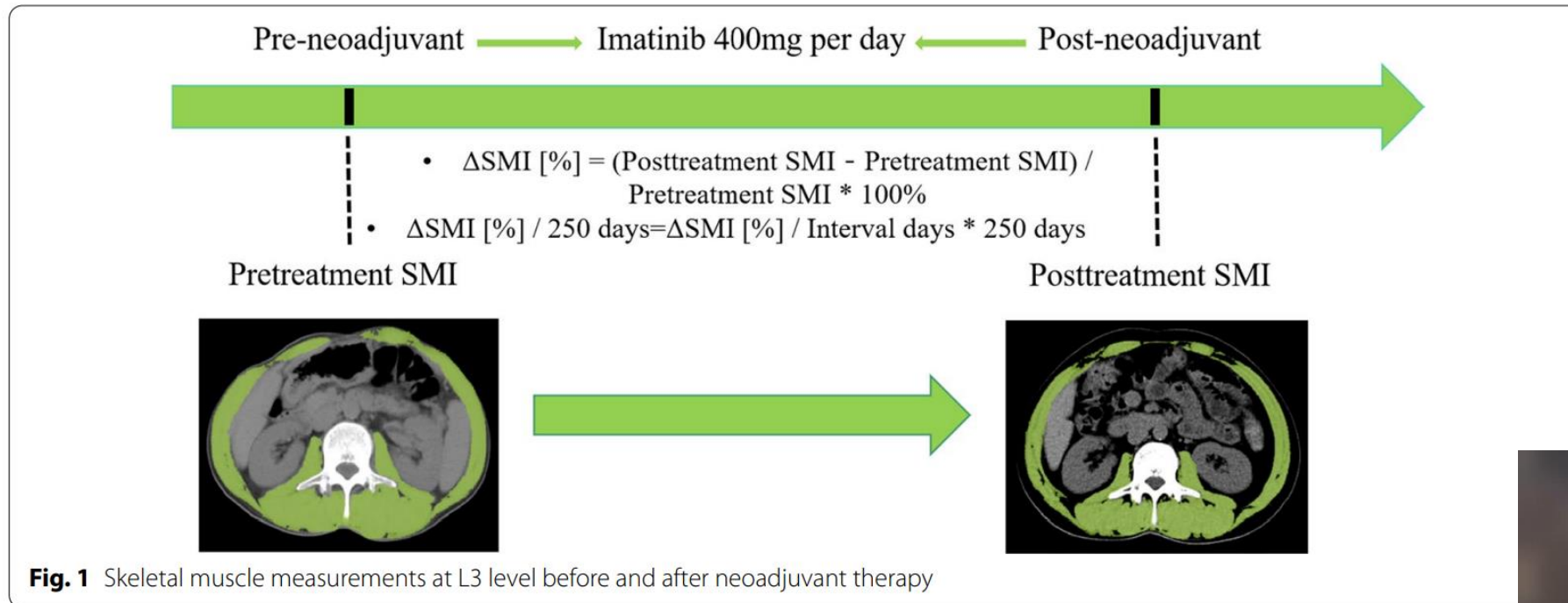
Ping'an Ding^{1,2†}, Honghai Guo^{1,2†}, Xiaoxiao He^{3†}, Chenyu Sun^{4†}, Scott Lowe⁵, Rachel Bentley⁵, Qin Zhou⁶, Peigang Yang^{1,2}, Yuan Tian^{1,2}, Yang Liu^{1,2}, Li Yang^{3*} and Qun Zhao^{1,2*}



to investigate the impact of changes in skeletal muscle before and after neoadjuvant therapy with imatinib on clinical outcomes in locally advanced GIST(LA-GIST)



retrospective study: n= 57 patients with LA-GIST who underwent neoadjuvant imatinib therapy in the Fourth Hospital of Hebei Medical University from January 2013 to March 2019



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Table 2 Correlation between skeletal muscle status and postoperative complications (N = 57)

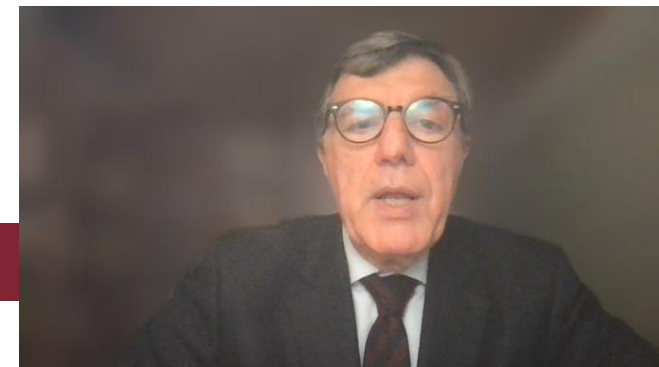
Variable	Pre-neoadjuvant		p	Post-neoadjuvant		p	ΔSMI (%) / 250 days		p
	Sarcopenia (n = 20)	No-sarcopenia (n = 37)		Sarcopenia (n = 30)	No-sarcopenia (n = 27)		SML (n = 25)	No-SML (n = 32)	
Clavien-Dindo classification			0.517 ^b			0.517 ^b			0.154 ^b
I~II	7 (35.00%)	12 (32.43%)		12 (40.00%)	7 (25.93%)		11 (44.00%)	8 (25.00%)	
III	2 (15.00%)	2 (5.41%)		2 (6.67%)	2 (7.41%)		4 (16.00%)	0 (0)	
Total ^a	9 (45.00%)	14 (37.84%)	0.599	14 (46.67%)	9 (33.33%)	0.306	15 (60.00%)	8 (25.00%)	0.008
Wound infection	2 (10.00%)	1 (2.70%)	0.279	2 (6.67%)	1 (3.70%)	0.617	3 (12.00%)	0 (0)	0.079 ^b
Anastomotic leakage	3 (15.00%)	2 (5.41%)	0.332	4 (13.33%)	1 (3.70%)	0.199	4 (16.00%)	1 (3.13%)	0.157
Lymphatic leakage	1 (5.00%)	2 (5.41%)	0.948	2 (6.67%)	1 (3.70%)	0.617	3 (12.00%)	0 (0)	0.079 ^b
Abdominal infection	2 (10.00%)	2 (5.41%)	0.607	3 (10.00%)	1 (3.70%)	0.353	3 (12.00%)	1 (3.13%)	0.309
Abdominal bleeding	1 (5.00%)	3 (8.12%)	0.661	2 (6.67%)	2 (7.41%)	0.913	3 (12.00%)	1 (3.13%)	0.309
Anastomotic bleeding	1 (5.00%)	2 (5.41%)	0.948	2 (6.67%)	1 (3.70%)	0.617	3 (12.00%)	0 (0)	0.079 ^b
Intestinal obstruction	2 (10.00%)	1 (2.70%)	0.239	2 (6.67%)	1 (3.70%)	0.617	3 (12.00%)	0 (0)	0.079 ^b
Respiratory complications	5 (25.00%)	3 (8.12%)	0.114	6 (20.00%)	2 (7.41%)	0.172	5 (20.00%)	3 (9.38%)	0.016
Cardiovascular complications	3 (15.00%)	2 (5.41%)	0.332	4 (13.33%)	1 (3.70%)	0.199	3 (12.00%)	2 (6.25%)	0.645

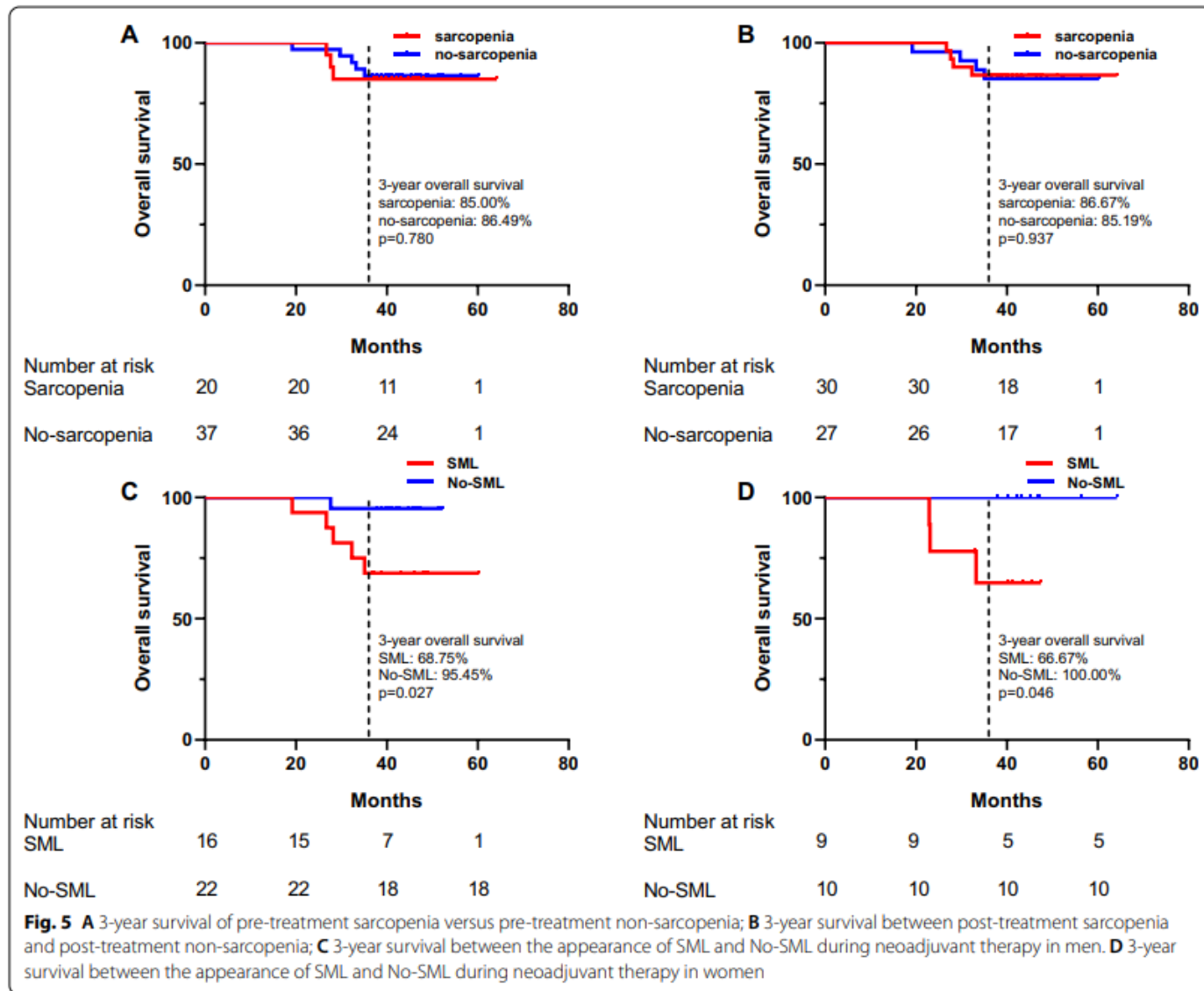
SMI skeletal muscle index, SML Significant muscle loss

^a Since multiple complications may occur simultaneously in the same patient, the sum of each sub-item is not equal to that of the parent

^b Calculated by Fisher's exact test

Patients with Skeletal Mass Loss during neoadjuvant therapy had a higher incidence of postoperative complications (60.00% vs. 25.00%, p=0.008)

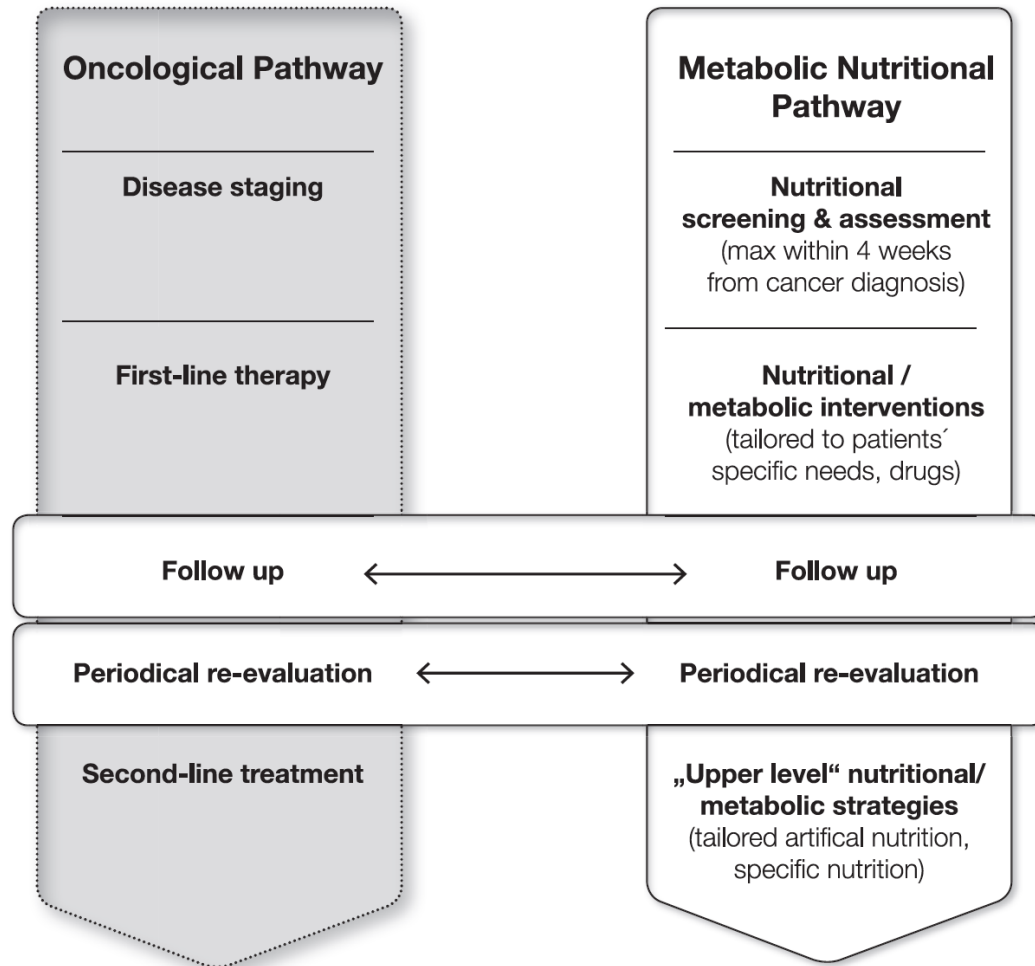




The development of Skeletal Mass Loss during neoadjuvant therapy in LA-GIST patients, rather than pre- and post treatment sarcopenia, is a major prognostic factor for the long-term prognosis and is also associated with recent postoperative complication rates and pathological regression.



The parallel pathway....



....and its components

- Medical history
- Nutrition history
- General examination
- Anthropometric measurements (BW, BMI, %WL)
- Screening/assessment of anorexia (FAACT,etc)
- QoL
- Muscle function (e.g. HGS)
- Body composition (e.g. BIA, DEXA, CT)
- Estimation of nutritional needs
- **Elaboration of nutritional plan**
- **Planning of metabolic-nutritional follow-up**



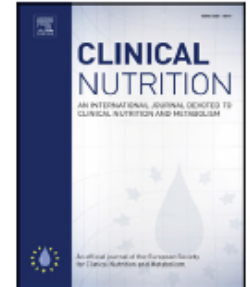


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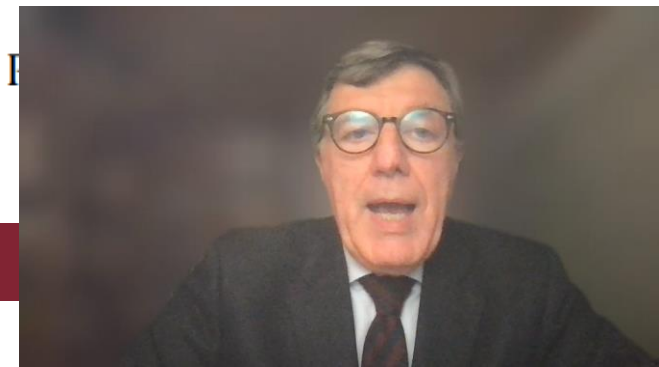
ESPEN Guideline

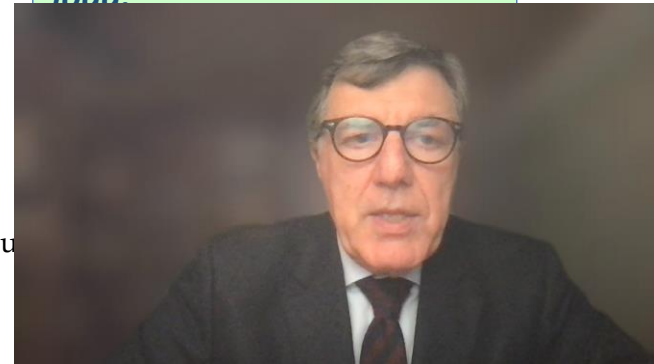
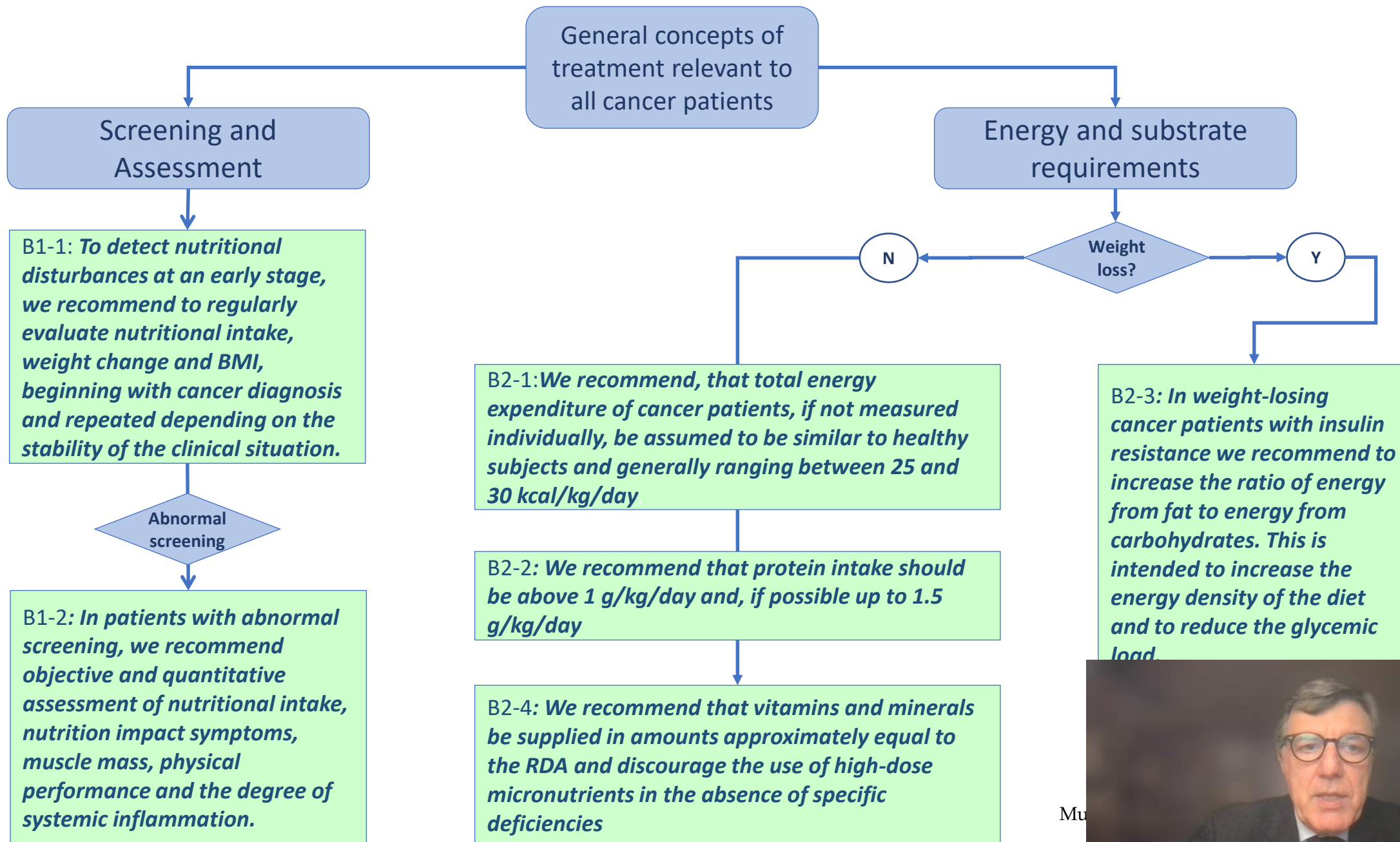
ESPEN practical guideline: Clinical Nutrition in cancer

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Nutritional care in cancer is a continuum decisional flow- chart: from oral nutrition to medical nutrition

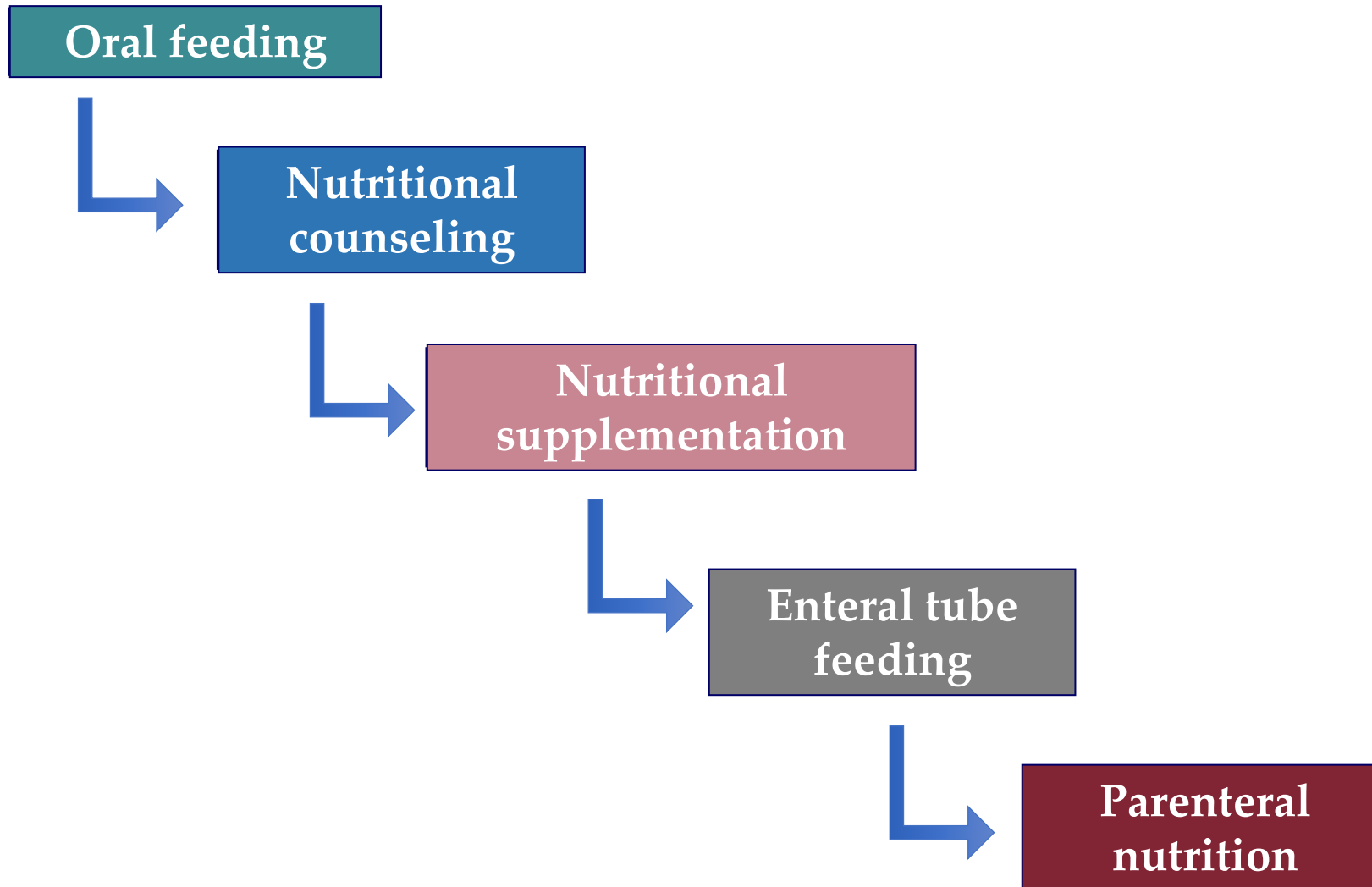


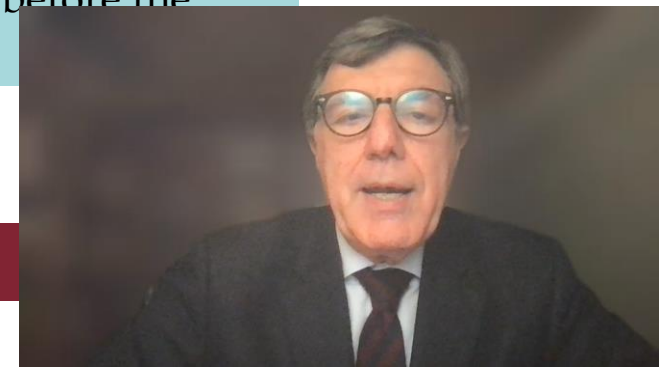


TABLE 2 | Patient-generated subjective global assessment classification and nutritional therapy situation ($N = 1,268$).

Nutrition support	Total (%)	PG-SGA			
		0~1(%)	2~3(%)	4~8(%)	≥ 9 (%)
No	1058 (83.43)	779 (95.82)	239 (80.20)	38 (29.69)	2 (6.90)
Yes					
PN	30 (2.37)	0 (0)	5 (1.68)	14 (10.94)	11 (37.93)
EN	153 (12.07)	34 (4.18)	52 (17.45)	57 (44.53)	10 (34.48)
EN and PN	27 (2.13)	0 (0)	2 (0.67)	19 (14.84)	6 (20.69)

PN, parenteral nutrition; EN, enteral nutrition; PG-SGA, patient-generated subjective global assessment.

This study found that only 117 (74.52%) of the 157 patients who needed nutritional intervention (PG-SGA score ≥ 4) received nutritional support one week before the treatment.



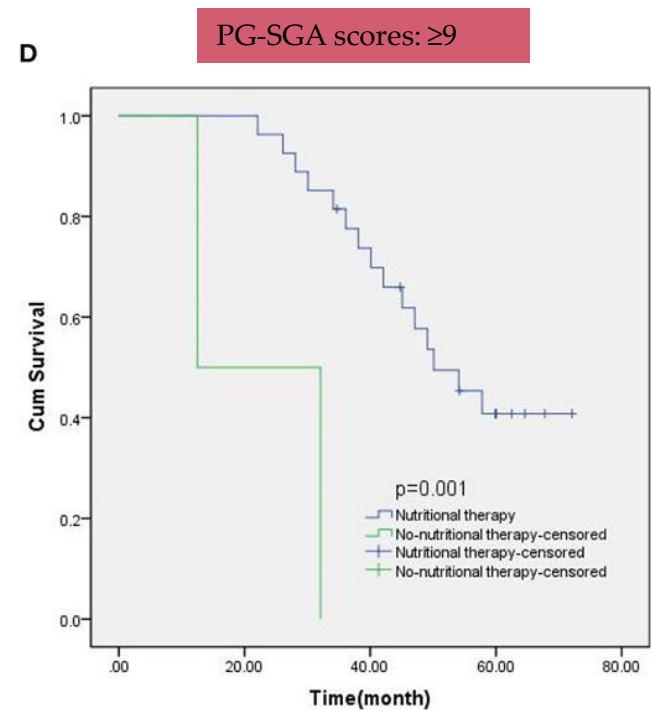
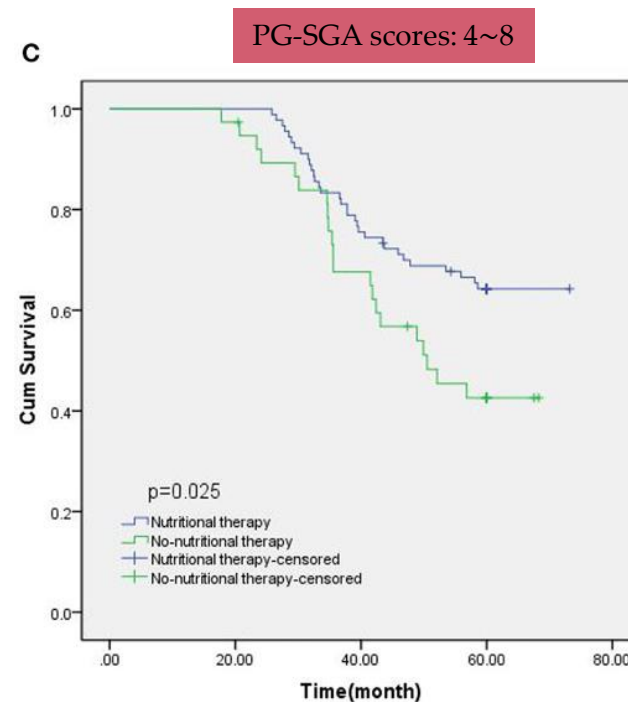
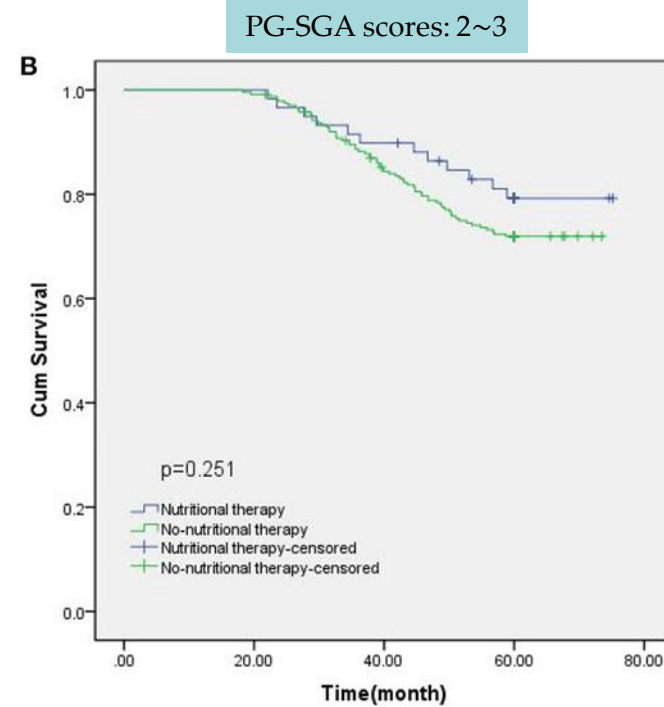
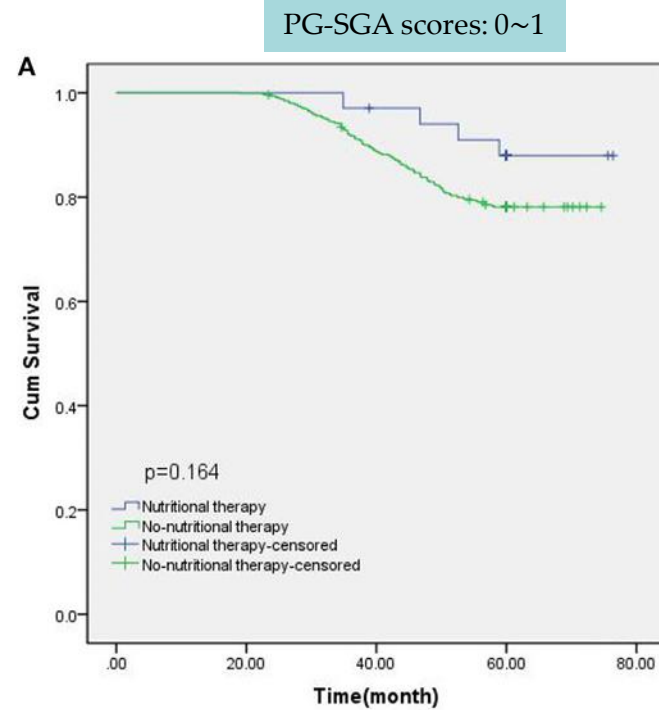


FIGURE 3 | The prognosis of GIST patients with different PG-SGA scores in nutritional therapy and without any intervention.

In patients with PG-SGA score of 4 ~ 8, especially those with PG SGA score ≥ 9 , nutritional therapy significantly improved the prognosis of patients, and the survival time was better than that of patients without nutritional intervention ($p=0.025$; $p=0.001$)





Take-home messages

- La malnutrizione in corso di neoplasia ha una patogenesi multifattoriale
- La prevalenza di rischio nutrizionale e di malnutrizione per difetto è elevata nei pazienti con GIST ed è maggiore nei GIST a localizzazione mesenterica e nei tumori classificati come ad alto rischio
- La presenza di malnutrizione nei GIST è un fattore prognostico negativo
- La perdita di massa muscolare prima dell'intervento chirurgico per GIST è un fattore prognostico negativo
- La perdita di massa muscolare durante il trattamento neo-adiuvante con Imatinib è un fattore predittivo di aumentata tossicità e di prognosi peggiore
- La terapia nutrizionale nei pazienti GIST con malnutrizione aumenta significativamente la sopravvivenza

