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Review article

Nutritional management of older adults with gastrointestinal cancers: An International Society of Geriatric Oncology (SIOG) review paper

Anna Rachelle Mislang [a,b,1], Samantha Di Donato [a,1], Joleen Hubbard [c], Lalit Krishna [d,e,f], Giuseppe Mottino [g], Federico Bozzetti [h,1], Laura Biganzoli [a,*,1]

[a] Medical Oncology Department, Nuovo Ospedale-Santo Stefano, Instituto Toscano Tumori, 59100 Prato, Italy
[b] Cancer Clinical Trials Unit, Department of Medical Oncology, Royal Adelaide Hospital, 1 Port Road, Thebarton, South Australia 5000, Australia
[c] Mayo Clinic Medical Oncology, 200 First St. SW, Rochester, MN 55905, United States
[d] Duke-NUS Graduate Medical School, Singapore
[e] National Cancer Centre Singapore, Singapore
[f] Centre of Biomedical Ethics at National University Singapore, Singapore
[g] Geriatric Medicine, Nuovo Ospedale-Santo Stefano, 59100 Prato, Italy
[h] Faculty of Medicine, University of Milan, Via Festa del Perdono, 7, 20122 Milan, Italy

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ABSTRACT

Malnutrition is one of the most common physical manifestations of gastrointestinal (GI) cancers and is often under-diagnosed and under-treated. Like cancers, malnutrition occurs more commonly in older adults, with potential negative consequences to quality of life, functional status, tolerance to treatment, and prognosis. Nutritional assessment and management require a proactive and systematic, multi-disciplinary approach. Early assessment, detection, and prompt intervention of cancer–associated malnutrition and cachexia are equally essential to achieve better quality nutritional care for older oncology patients. This article aims to provide an overview of the evidence associated with poor nutrition and outcomes in older adults with GI cancers, and recommends a management approach from a geriatric oncologist's perspective.

Contents

* Corresponding author.
E-mail address: laura.biganzoli@uslcentro.toscana.it (L. Biganzoli).
[1] Equally contributed.

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1. Overview of the Evidence Associated With Poor Nutrition and Outcomes in Older Patients With Gastrointestinal Cancers

Almost 30% of cancer incidence and 32% of cancer deaths worldwide are due to gastrointestinal (GI) malignancies, [1] and both incidence and mortality rise exponentially with age. The aging process is associated with sarcopenia, comorbidities with associated loss of functional reserve of multiple organ systems, and increased vulnerability to frailty [2]. Poor nutritional status is a known poor prognostic factor in patients with malignancies [3,4], causing a significant concern as the risk of cancer and malnutrition are more common in an older population [5]. In general, approximately 10–20% of cancer deaths can be attributed to malnutrition rather than the cancer itself [4,6,7]. The French National Authority for Health defined malnutrition in older adults as one or more of the following: ≥5% weight loss in 1 month or ≥10% in 6 months, and/or Mini-Nutritional Assessment (MNA) score of <17/30, and/or serum albumin <35 g/L, and/or body mass index (BMI) of <21 kg/m^2 [8]. However, a BMI ≥21 does not exclude the diagnosis of malnutrition, such as in the case of sarcopenic obesity [9]. Age >70 years and malnutrition increase the risk of death 2–2.5 times, respectively [4]. However, in older patients, it is often more difficult to delineate age-related versus tumor–related effects on malnutrition. In addition to underrepresentation in clinical trials and lack of management consensus guidelines, very few oncologic papers distinguish young from older adults and the age cut-off values often vary, making their management rather challenging. This article reviews the current evidence supporting the negative impact of poor nutrition on the management outcomes of patients including older adults, with a specific focus on GI cancers. We systematically identified studies published in English over the last decade on the nutritional status of older adults with GI cancers through PubMed and MEDLINE databases, by combining search terms "malnutrition", "sarcopenia", "screening", "GI cancer", and "elderly". Additional articles were identified from citations in the articles that were evaluated. As the terminology relating to malnutrition varies, specific terms and definitions used in this manuscript are defined in Table 1.

1.1. Sarcopenia

The aging process is associated with sarcopenia, a gradual and progressive loss of skeletal muscle mass leading to reduced strength or physical performance [10] that is commonly seen in sedentary older adults. Sarcopenia has an estimated prevalence of 30% among adults >60 years [11] and a decline in muscle mass is expected at a rate of up to 15% per decade at ≥70 years of age [12]. It accelerates the risk for developing adverse outcomes such as functional impairment and disability [13,14], poor quality of life (QoL) and death [10], and its effect could be magnified in the presence of malignancy. Regular aerobic and resistance exercises, along with adequate protein and energy intake have been shown to help counteract the effects of age-related decline in muscle mass, strength, and function in healthy older adults [15]. Specific to cancers, sarcopenia has often led to worse outcomes, including increased risk for developing 5-FU and capecitabine-related ≥ grade 2 toxicities [16,17], the mainstay of treatment for most GI cancers, and a 2-fold increased mortality for patients with colorectal cancer (CRC) with >5% muscle loss post-chemotherapy [18]. Table 2 summarises the negative consequences of sarcopenia in GI cancers.

1.2. Cachexia

Cachexia is provisionally defined as ≥5% involuntary weight loss over 6 months; or BMI <20 and any degree of weight loss ≥ 2%; or sarcopenia and any degree of weight loss >2% [19]. Although, such a definition has gained some popularity among clinicians, it does not account for the different BMI thresholds between younger and older adults [20–22]. Moreover, refractory cachexia, a syndrome commonly defined as irreversible and unresponsive to nutritional interventions [3], may not always be accurate, as the provision of nutritional support becomes more sophisticated and specific. For instance, it is now possible to integrate nutritional supplements with anabolic or anti-catabolic agents [23], to better treat the cachectic status compared to using standard nutritional support.

Cachexia is commonly associated with inadequate nutrient intake leading to a general state of deterioration and deconditioning, decreased or absent physical activity, and altered metabolism due to a pathological systemic inflammatory response [24]. This condition can occur even in the absence of apparent weight loss, or prior to losing fat mass, and can be exacerbated by cancer therapy [25]. It may also be obscured by obesity, resulting in under-diagnosis and excess mortality [25]. The cancer itself and its related treatments often cause taste and smell alterations, appetite loss, swallowing and absorption disorders, and enhanced catabolism [19], leading to higher nutritional risk. In the absence of appropriate intervention, loss of substantial muscle mass is almost inevitable and will eventually lead to progressive cachexia. Management is therefore multidimensional, and involves early initiation of nutritional care or support, resistance exercises to prevent muscle atrophy, endurance exercises to counteract fatigue, and treatment of inflammation-related hypermetabolic state [19] where possible.

1.3. Gastrointestinal Cancers

Nutritional risk, although common in older adults with cancer, is notably higher in patients with GI malignancies, particularly in the presence of GI symptoms [26] such as, anorexia, early satiety, nausea, vomiting, dysphagia, odynophagia, diarrhea, constipation, malabsorption, and pain. In some patients, unintentional weight loss, mostly from GI symptoms, is present long before the diagnosis of malignancy is made. Weight loss at presentation has been associated with reduced ability to tolerate anti-cancer therapy, increased severe dose-limiting toxicities, lesser response rates, worse QoL, decline in performance status, and shorter survival outcomes among patients with locally advanced or metastatic GI cancers [27]. The prevalence varies depending on the definition used in the literature and the GI cancer type – 28–54% in hepatocellular, 39–71% in colorectal, and 56% in pancreatic cancers [28].

Table 1
Terminology.
(Adapted from [3,19].)

	Etiology	Intervention
Anorexia	Limited food intake from altered CNS appetite signals related to disease or its treatment, or from structural or functional limitations to food intake (i.e. mucositis, obstruction, altered intestinal transit, etc.)	Pharmacologic agents
Starvation	Loss of body fat & non-fat mass caused by poor protein-energy or nutrient intake	Adequate nutritional support
Sarcopenia	Reduction or loss of skeletal muscle mass and strength with aging, which may lead to functional impairment	Physical exercise High protein and energy diet
Cancer cachexia	Involuntary multifactorial wasting of protein or energy stores and skeletal muscle mass, with or without loss of fat mass.	Physical exercise High protein and energy diet
	Release of pro-inflammatory cytokines results in significant weight loss, altered body composition, and decline in physical function	Anti-inflammatory agents Anti-cancer treatment

CNS = central nervous system.

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Table 2
Consequences of malnutrition in studies including older patients with GI cancers.

Disease Author, year (reference)	Study design	Primary endpoint	Study population, n Age in years	Treatment regimen given	Results	
					Sarcopenic rate	Outcome
Esophageal or esophagogastric cancer						
Anadavadivelan et al., 2016 [96]	Retrospective dataset from a prospectively collected data Multicentre	Association between sarcopenia and/or sarcopenic obesity and DLT after cycle 1 CT	n = 72 Age: 67 ± 7 Resectable disease	Neoadjuvant Cisplatin + 5-FU	43% Sarcopenic obesity: 14%	Increased DLT with sarcopenic obese (OR 5.54; $p = 0.04$)
Tamandl et al., 2016 [97]	Retrospective data from hospital information system Single centre	Impact of sarcopenia on survival post-surgery	n = 200 Median age: 63.9	Surgery	65%	Worse OS • Sarcopenia: HR 1.87, $p = 0.011$ • ≤40 HU muscle attenuation: HR 1.91, $p = 0.019$ • FMi: HR 3.47, $p = 0.016$
Tan et al., 2015 [34]	Retrospective data from MDT Single centre	Predictors of DLT	n = 89 Age: 65.8 ± 8.1 Potentially curative, locally advanced disease	Neoadjuvant CT: ECX or CF	49%	Sarcopenia • more common in older patients (68.6 ± 7 years vs. 63.1 ± 8.3 years) • higher DLT (54.5% vs. 28.9%; $p = 0.015$) • lower median OS (569 vs. 1013 days); $p = 0.04$ • no difference in OS in patients with DLT independent of sarcopenia
Gastric cancer						
Aahlin et al., 2017 [98]	Retrospective analysis of patient files Two centres	Skeletal muscle index and outcomes	n = 137 Median age: 70	Periop CT (EOX or ECX regimen) + surgery	45%	Reduction in lean tissue mass during neoadjuvant CT ($p = 0.001$) Poor OS in patients with low preop skeletal muscle index (HR 1.91, $p = 0.019$)
Palmela et al., 2017 [99]	Retrospective data from electronic records Single centre	Prevalence of sarcopenia and association with CT toxicity and long-term outcomes	n = 48 Age: 68 ± 10	Neoadjuvant CT	23% Sarcopenic obesity: 10%	Age > 65: lower muscle attenuation DLT: 46% Sarcopenia: • Increased CT termination (OR 4.23, $p = 0.05$) Sarcopenic obesity: • Lower OS (6 vs. 25 months, $p = 0$)
Qiu et al., 2015 [35]	Prospective data from NRS Single centre	Prevalence and prognostic value of nutrition risk (all stages) and nutritional support (stage IV only)	n = 830 ≥70: 401 (48%)	CT	50.7 (NRS ≥3)	• Longer median OS for NRS <3: 31.9 vs. 25.7 months, $p < 0.001$ • NRS shift with nutritional support: 30.3% • Improved median survival with NRS shift: 14.3 vs. 9.6 months; $p = 0.001$
Seo et al., 2016 [100]	Retrospective study of medical records Single centre	Association of nutritional status indices with CT-induced adverse events	n = 234 >65: 38 (26%)	Adjuvant CT	59%	• LBM and low albumin increased risk for grade 3 or 4 hematological toxicities • Age was an independent risk factor for grade 3 or 4 non-hematological toxicities
Hepatocellular cancer						
Harimoto et al., 2016 [101]	Retrospective data from clinical records Single centre	Outcomes of sarcopenia in ≥70 years post-hepatic resection	n = 296 ≥70: 139 (47%)	Hepatectomy	37.8% Age ≥ 70: 41%	Significantly poorer OS in patients ≥70 with sarcopenia • sarcopenia • Child-Pugh B • Multiple tumors • Poor differentiation Significantly poorer DFS in patients ≥70 with sarcopenia • Sarcopenia • Stage III or IV Blood transfusion
Voron et al., 2015 [102]	Retrospective analysis of prospectively maintained computer database Single centre	Prognostic factors on liver surgery	n = 109 Age: 61.6 ± 13.3 ≥60: 38 (64%)	Liver surgery	54%	Sarcopenia: • more common in older patients ($p = 0.013$) • 71.2 vs. 40% disease recurrence ($p = 0.002$) • 34 vs. 14% deaths at 21.23 months median follow-up • shorter median PFS (10.1 vs. 34.23 months, $p < 0.001$) • shorter median OS (52.3 vs. 70.3 months, $p = 0.015$) • poorer OS (HR = 3.19, $p = 0.013$)

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Table 2 (*continued*)

Disease Author, year (reference)	Study design	Primary endpoint	Study population, n Age in years	Treatment regimen given	Results	
					Sarcopenic rate	Outcome
Colorectal cancer						
Aaldriks et al., 2013 [38]	Prospective analysis of patient records Multicentre	GA to predict tolerance & feasibility of treatment with adjuvant or palliative CT	n = 143 Median age: 75 (70–92) 70–79: 88% ≥80: 12%	Adjuvant CT: 38% Palliative CT: 62%	28%	Toxicities: 78% MNA <23.5 • Adjuvant CT: 20% • Palliative CT: 33% Mortality (15 months median follow-up) among patients receiving palliative CT • 2.76-fold risk in MNA <23.5 ($p < 0.001$) • 2.72-fold risk in GFI frail
Ali et al., 2016 [103]	Prospective data from physician's notes Multicentre	Toxicity associated with LBM during first 4 cycles DLT if ≥Gr 3 or ≥Gr 2 for neuropathy	n = 138 Age: 61.5 ± 10.3 Stage IV	FOLFOX or FOLFIRINOX ± cetuximab	40%	Dose ≥3.55 mg oxaliplatin/kg ↑ risk for DLT 25% of DLT was due to neuropathy
Barret et al., 2014 [33]	Prospective, cross-sectional study based on patient records Multicentre	Effect of sarcopenia on CT toxicity	n = 51 Age: 65 (22–84) Stage IV	FP ± oxaliplatin or irinotecan or irinotecan alone	71%	Sarcopenia was significantly associated with grade 3 or 4 toxicities (OR 13.55; $p = 0.043$)
Jung et al., 2015 [104]	Analysis of prospectively maintained cancer registry Single centre	Effect of decreased muscle mass on toxicity & survival	n = 299 ≥60: 127 (55%) Stage III	Adjuvant oxaliplatin, 5-FU, leucovorin	Obesity BMI ≥ 25: 19%	1 SD decrement in PI was associated with increased in all grade 3–4 toxicities (OR 1.56) and overall mortality (OR 1.85) Higher mortality with: • age ≥60 (HR 2.94; $p = 0.028$) • BMI ≥25 (HR 4.35; $p = 0.011$)
Miyamoto et al., 2015 [18]	Retrospective data from patient records Single centre	Prognostic value of skeletal muscle mass pre-CT and rate of skeletal muscle change in cross-sectional area post-CT	n = 182 ≥70: 54 (30%) Unresectable disease	1st line CT ± targeted therapy	20%	Median follow-up, months PFS: 8.1 OS: 23.2 Skeletal muscle loss >5% post-CT was significantly associated with poorer PFS and OS
Prado et al., 2007 [16]	Prospective data from patient records Single centre	Predictor of toxicities after cycle 1	n = 62 Age: 60.3 ± 9.9 High risk stage II or stage III	Adjuvant 5-FU and leucovorin	–	20 mg 5FU/kg LBM is a significant predictor of overall toxicity (OR 16.75; $p = 0.013$)
Pancreatic cancer						
Wu et al., 2014 [105]	Retrospective chart review Single centre	Impact of postoperative complications to TTA of adjuvant therapy	n = 1144 Median age: 68 >68: 48.6%	Adjuvant CT	–	Overall complication rate: 49% • >68 years: 53% TTA: 60 days Overall adjuvant therapy rate: 54.2% • >68 years: 39.7% Median OS: 18.1 months • ≤68 vs. >68 years: 20 vs. 15 months ($p < 0.001$)

Several prospective and retrospective studies have linked nutritional impairments in GI cancers with negative outcomes as shown in Table 2. Nutritional status screening of 1453 patients with cancer (median age 64, range 55–71, 64% had GI cancers), in the outpatient setting using the Nutritional Risk Score (NRS-2002) of ≥3 as "at-risk", reported a 22% high nutritional-risk rate among patients with GI cancer, particularly in the presence of worsening performance status, fatigue and anorexia symptoms [29]. In a cross-sectional study of 313 patients (mean age 63 years) with GI cancers, the malnutrition rate was 52%, where 25% was severe and underestimated by the treating physicians [30]. Among patients aged ≥70 years (30%), 39% had moderate and 18% had severe malnutrition [30]. Factors associated with severe malnutrition include performance status, ≥3 prior lines of treatment, pancreatic, and gastric cancers [30]. Malnutrition has also led to increased incidence of perioperative complications (i.e. infections, delayed wound healing, wound dehiscence, etc.), poorer tolerance or augmented toxicities to treatment, altered QoL, higher hospital costs, and mortality [31]. In a cohort study associating sarcopenia with postoperative morbidity and mortality after CRC surgery ($n = 310$), 51.3% of patients were aged >70 years; age was an independent predictor of mortality, and sarcopenia was associated with a higher 30-day or in-hospital mortality (8.8% vs. 0.7%) [32]. A combination of instruments assessing function, nutrition, frailty, and sarcopenia can accurately predict post-operative sepsis [32]. In a multicentre study including 51 metastatic CRC patients (median age 65 years), sarcopenia was associated with grade 3–4 chemotherapy toxicities (odds ratio, OR 13.55, $p = 0.043$) [33]. Similarly, sarcopenia was a significant predictor of dose limiting toxicity in patients with esophago-gastric cancer ($n = 89$, median age 65.8 years) receiving neoadjuvant chemotherapy (OR 2.95; 95% confidence interval, CI 1.23–7.09; $p = 0.015$) [34], while NRS-2002 ≥3 was an independent adverse prognostic factor in 830 patients with gastric cancer (48% aged ≥70 years), where the median survival for NRS-2002 <3 was 31.9 months vs. 25.7 months for NRS-2002 ≥3 ($p < 0.001$) [35].

Older patients on chemotherapy who are "at risk" of malnutrition according to the MNA have a 2-fold increase in 1-year mortality [36]. Likewise, a higher 1-year mortality (OR 2.77) was noted in malnourished older (≥70 years) patients treated with first-line chemotherapy [37]. In a prospective study of 143 patients aged ≥70 years with CRC, poor MNA score not only increased the risk of mortality in

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Table 3
Nutritional screening tools.

Tool	Variables		Abnormal score		Intervention
Malnutrition Screening Tool [47]	1. Have you or the patient lost weight recently without trying?		≥2		Dietician referral for full assessment and intervention Monitor weight Rescreen patients
	No	0			
	Unsure	2			
	Yes, how much (kg)				
	1–5	1			
	6–10	2			
	10–14	3			
	≥15	4			
	Unsure	2			
	2. Have you or the patient been eating poorly because of decreased appetite?				
	No	0			
	Yes	1			
Mini-Nutritional Assessment-Short Form Revised [48]	A. Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?		12–14 8–11 0–7	Normal At risk Malnourished	
	Severe decrease	0			
	Moderate decrease	1			
	No decrease	2			
	B. Weight loss during the last 3 months				
	>3 kg (6.6 lb)	0			
	Does not know	1			
	1–3 kg (2.2–6.6 lb)	2			
	None	3			
	C. Mobility				
	Bed or chair bound	0			
	Out of bed or chair	1			
	Goes out	2			
	D. Has suffered psychological stress or acute disease in the past 3 months?				
	Yes	0			
	No	2			
	E. Neuropsychological problems				
	Severe dementia or depression	0			
	Mild dementia	1			
	None	2			
	F.				
	1. Body mass index (BMI), weight in kg/height in m^2				
	Less than 19	0			
	19–less than 21	1			
	21–less than 23	2			
	23 or greater	3			
	2. Calf circumference (CC) in cm				
	<31	0			
	≥31	3			
Nutritional Risk Screening (NRS 2002) [49]	Part 1. Initial screening				
	Yes or no	BMI < 20.5 Weight loss in 3 months Reduced dietary intake in the last week Severely ill	If the answer is **yes** to any questions If the answer is **no** to all the questions		Proceed to Part 2 Re-screen patient at weekly intervals If the patient is at risk, e.g. scheduled for a major operation, consider a preventative nutritional care plan
	Part 2. Final screening				
	Impaired nutritional status		Add total score:		
	0 Absent	Normal	≥3		At risk: initiate nutritional care plan
	1 Mild	Weight loss (WL) >5% in 3 months or food intake (FI) <50–75% of normal requirement in preceding week			
	2 Moderate	WL >5% in 2 months or BMI 18.5–20.5 + impaired general condition or FI 25–60% of normal requirement in preceding week			
	3 Severe	WL >5% in 1 month (>15% in 3 months) or BMI <18.5 + impaired general condition or FI 0–25% of normal requirement in preceding week			
	Severity of disease				
	0 Absent	Normal	<3		Re-screen patient at weekly intervals If the patient is at risk, e.g. scheduled for a major operation, consider a preventative nutritional care plan
	1 Mild	Hip fracture; acute complications of chronic disease; cirrhosis; COPD; diabetes; hemodialysis; oncology			
	2 Moderate	Major abdominal surgery; stroke; severe pneumonia; hematologic malignancy			
	3 Severe	Head injury; bone marrow transplant; ICU (APACHE > 10)			
	Age if ≥70 years: add 1 to total score				

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Table 3 (*continued*)

Tool	Variables	Abnormal score	Intervention
Malnutrition Universal Screening Tool (MUST) [50]	**5 steps to measure:** 1. BMI *(BMI kg/m²)* — *Score* >20 (>30 obese) — 0 18.5–20 — 1 <18.5 — 2 2. Unplanned weight loss in past 3–6 months *(%)* — *Score* <5 — 0 5–10 — 1 >10 — 2 3. Effect of acute disease Acutely ill, presence or probability of no nutritional intake for >5 days — *Score* 2	4. Add scores to calculate overall risk of malnutrition Overall score — Risk of malnutrition 0 — Low 1 — Medium ≥2 — High	5. Management **Routine clinical care** Repeat screening In-patient: weekly Care homes: monthly Community: annually **Observe** Document dietary intake for 3 days *If adequate*: no concerns, repeat screening: In-patient: weekly Care homes: monthly Community: every 2–3 months *If inadequate*: clinical concern – follow local policy, set goals, improve and increase overall nutritional intake, monitor and review care plan regularly **Treat*** Refer to dietician, nutritional support team, or implement local policy Set goals, improve and increase nutritional intake Monitor and review care plan: In-patient: weekly Care homes: monthly Community: monthly

*Unless no benefit is expected from nutritional support, e.g. imminent death
All risk categories:
- Treat underlying condition and provide help and advice on food choices, eating, drinking when necessary
- Record malnutrition risk category
- Record need for special diets and follow local policy

Re-assess subjects identified at risk as they move through care settings

patients receiving palliative chemotherapy (HR 2.76, 95% CI 1.60–4.77; $p < 0.001$) but also predicted for less tolerance to chemotherapy ($p = 0.008$) [38]. Cachexia was associated with poorer survival and performance status in pancreatic cancer, independent of tumor size and metastatic load [39]. Interestingly, sarcopenia alone was not predictive of decreased survival in a systematic review of pancreatic cancer [40]. A recent systematic review and meta-analysis (37 studies, 56% with GI cancers) of the prognostic value of low skeletal muscle index obtained from CT screening on any solid tumors at various stages demonstrated that sarcopenia was associated with worse cancer-specific and disease-free survival [41].

2. Management Approach From a Geriatric Oncologist's Perspective

Weight loss of as little as 5% of body weight has been linked to lower survival and treatment response in patients with cancer [42]. For patients with colon, gastric, and pancreatic cancers, survival improvement without weight loss was 51%, 33%, and 14%, respectively relative to survival with weight loss [42]. In addition, poor performance status has been directly correlated with weight loss, suggesting that muscle loss may impact the level of activity [42]. Therefore, it is recommended to evaluate the nutritional status of all patients undergoing oncological treatment [31] from the time of cancer diagnosis and repeated as clinically indicated for inadequate nutritional intake, weight loss, and low BMI, and to assess for treatable nutrition impact symptoms and metabolic derangements if found to be "at risk" [43]. Evaluation could be as simple as serial measurement of body weight, or by using nutritional screening tools, which are quick and easily completed by any health staff, or with a more exhaustive nutritional assessment, performed by trained personnel. Such evaluation may be particularly more relevant to perform in older patients with cancer, as nutritional impairments are more prevalent, yet easily overlooked without proper assessment [44,45]. As the process of aging occurs at a heterogeneous pace, the International Society of Geriatric Oncology (SIOG) recommends that all older patients with cancer, especially those considered for anticancer treatment, undergo a comprehensive geriatric assessment (CGA) [46], which includes the evaluation of comorbidity, function, nutrition, psychosocial status, and presence of geriatric syndromes, as these provide multidimensional information on the patients' over-all health status that may be predictive of mortality and treatment tolerance.

2.1. Nutritional Assessment Tools in Older Adults With GI Cancers

Much information can be gleaned from a full nutritional assessment, but as with any comprehensive assessment tool, it is time-consuming and requires specialized nutritional expertise, hence it may be impractical to use in all patients in a busy oncology clinic. Screening tools are more useful in this setting and only malnourished patients and those at risk of malnutrition on screening are referred for a full nutritional assessment and intervention. Validated nutritional screening tools, such as the Malnutrition Screening Tool (MST) [47], the Mini-Nutritional Assessment Short Form Revised (MNA-SF) [48], the Nutrition Risk Screening (NRS-2002) [49], and the Malnutrition Universal Screening Tool (MUST) [50] may be used in older oncology patients, though these screening tools have not been evaluated specifically for older adults with GI malignancies. Table 3 summarises the variables assessed, cut-off values and proposed interventions in these screening tools. There remains no gold standard for nutritional screening and which cut-off values to use to initiate further assessment, as none of these tools were designed specifically for diagnostic, prognostic, or interventional

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purposes. Despite the lack of expert consensus on which tool to use, particularly in older patients with cancer, it is clear that screening with any of the validated tools mentioned, at the very least, should be performed at the time of diagnosis, on admission to hospitals or care homes, during clinic follow-ups, and at regular intervals depending on clinical status [51]. Selection of the most appropriate screening tool is based on setting, familiarity, and practicality [52].

A more specific assessment, such as the MNA, should follow an abnormal screening test to detect which patients might benefit from appropriately designed interventions [43]. The MNA is a well-established and validated nutritional assessment tool in older adults, consisting of 18 items grouped in 4 headings: anthropometric measurements (BMI, weight loss, arm and calf circumferences), general assessment (lifestyle, medication, mobility, and presence of depression or dementia), short dietary assessment (number of meals, food, and fluid intake, and feeding autonomy), and subjective assessment (self-perception of health and nutrition) [53]. The maximum score is 30, with threshold values of ≥24 for well-nourished, 17–23.5 for at-risk, and <17 for malnourished. The sensitivity, specificity, and positive predictive values according to the clinical status were 96%, 98%, and 97%, respectively [54]. It has been correlated with cancer cachexia features [55] and was one of the independent predictors for chemotherapy toxicity [56] and early death [37,57,58].

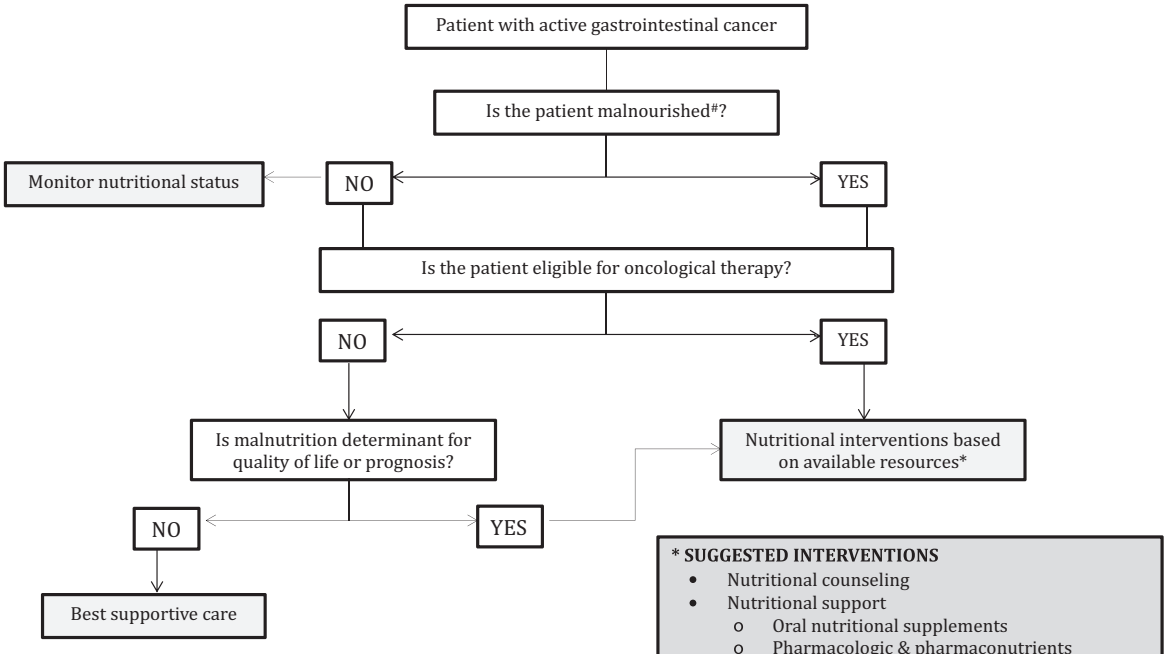
More recently, other assessment tools have been studied using scoring systems. Martin et al. developed a cancer weight loss grading system incorporating %weight loss and BMI that predicted nearly a 5-fold difference in median survival between grades 0 (least risk) and 4 (highest risk), independent of cancer site, stage, and performance status [59]. The Patient- and Nutrition-Derived Outcome Risk Assessment Score (PANDORA) is a simple risk scoring system that includes age, BMI, mobility, nutrient intake, main patient group, cancer, and fluid status, and has been validated to predict 30-day hospital mortality [60]. Specific to older patients, a nomogram was developed based on CGA factors in older patients with cancer, showing that advanced stage, anemia, depression, and poor ECOG performance status were independently predictive of moderate to high-risk of malnutrition [61]. However, use of the scoring system is yet to be validated in clinical practice. The lack of a gold standard for both screening and full nutritional assessment tools highlights the dearth of research focusing on validated tools to measure malnutrition.

2.2. Role of Nutritional, Pharmacologic & Physical Intervention in Older Adults With GI Cancers

An oncologist is expected to know about patient-, disease-, and treatment-related factors, and therefore has the critical responsibility of identifying patients who will potentially benefit from nutritional support and strategies, including knowing when to refer to dieticians and integrate the nutritional plan within the oncologic regimen [62]. Although it is clear that a specific intervention is needed to counteract and manage the deleterious effects of malnutrition, the efficacy and choice of interventional strategies remain contentious, and evidence for nutritional management specific to older patients with GI cancers is lacking. In addition to aging heterogeneity, the patient's nutritional needs vary according to disease site, cancer stage, disease burden, and comorbidities that may limit treatment generalization. Algorithms for managing nutritional needs of older patients with cancer with GI cancers are illustrated in Figs. 1 and 2, which may be used as a guide for the treating oncologist.

2.2.1. Nutritional Intervention

Nutritional counselling, which includes dietary history, diagnosis, and therapy, is recommended to malnourished patients with GI cancers requiring chemotherapy [63], and is usually performed by trained



#Malnutrition is defined as weight loss ≥5% within 1 month or 10% within 6 months, and/or mini nutritional assessment (MNA) <17, and/or serum albumin <35 g/L and/or body mass index (BMI) ≤21 in patients ≥70 years (Ref. 8)

Fig. 1. Nutritional management algorithm for older patients with gastrointestinal cancers.

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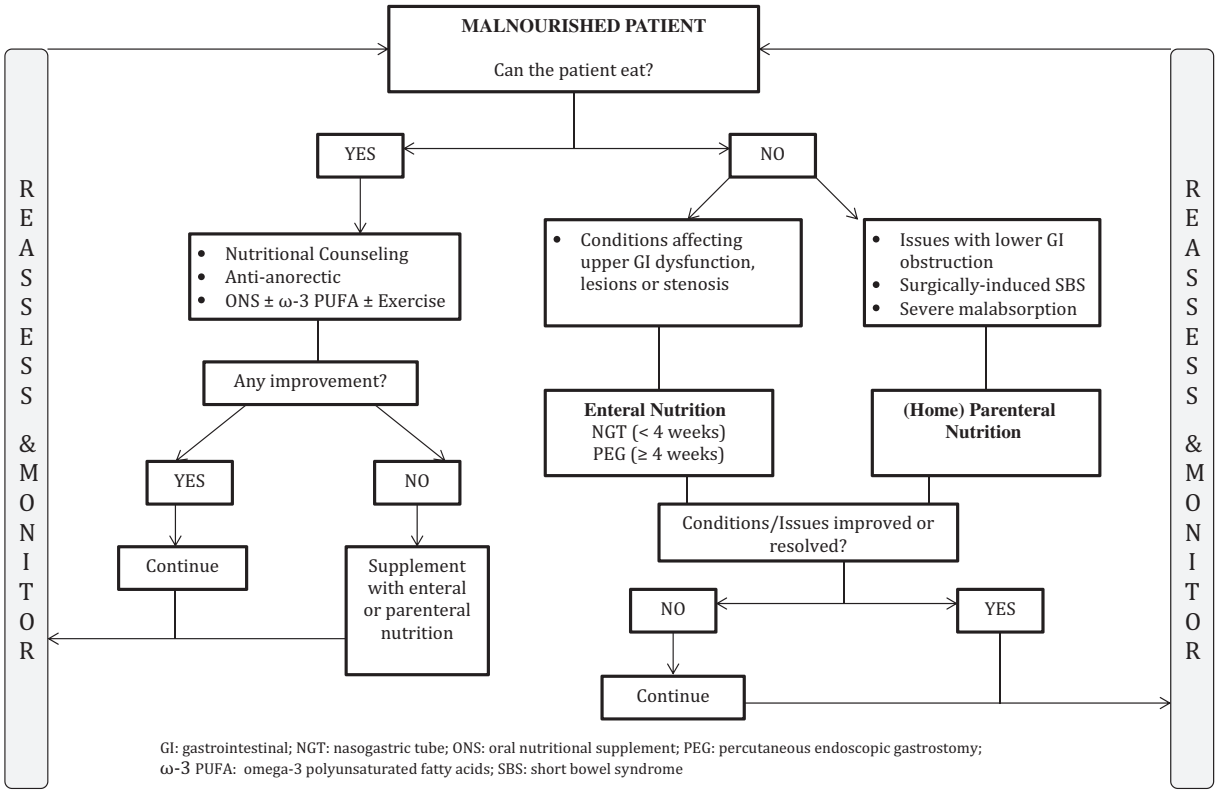

Fig. 2. Strategies for nutritional approach in a malnourished GI cancer patient.

dieticians [43]. Individualized dietary counselling of patients receiving chemotherapy and/or radiotherapy for esophageal or gastric cancers has been associated with improved weight maintenance, energy- and protein-intake without any significant effects on QoL, treatment-related toxicities, or prevalence of micronutrient deficiencies [64]. In contrast, a proportional improvement of QoL with adequate nutritional status was observed among patients with CRC receiving radiotherapy [65]. Notably, dietary counselling is an individualized, time-consuming process, which often fails when used in already severely anorectic patients, although it appears effective in patients with digestive problems caused by radiation or chemotherapy [66]. The effect of dietary interventions on QoL, based on two systematic reviews and meta-analyses [67,68], remains inconclusive, particularly among patients receiving chemotherapy. Moreover, no trials have shown any benefit on mortality [68–70] and similar results were found in older populations with cancers [71]. As some nutritional interventions may not always be feasible, particularly in institutions not equipped with specific "nutritional units" to accommodate a large number of patients needing intervention, it is critical to personalize and tailor interventions to each institution's available resources (Fig. 1).

Although the best way to maintain or increase energy- and protein-intake is with normal food, it is often difficult and nutritional supplements are often required. Specific to GI cancers, where problems with dysgeusia, early satiety, nausea, vomiting, or compromised gastric or intestinal transit are more prevalent, the utility of an oral approach may be limited. If oral intake is deemed inadequate or impossible, either due to the disease or treatment, then supportive feeding, via enteral or parenteral feeding, may be considered (Fig. 2), taking into account the goal of treatment (curative vs. palliative), disease trajectory, estimated life expectancy, and with anticipated benefits weighed against the potential risks, burdens, and costs. Enteral feeding (oral supplements ± intensive counselling or tube feeding) may be as efficient as parenteral feeding, particularly if intestinal functions are preserved [72], and provides the added benefit of maintaining the gut barrier, fewer infectious complications, and lower costs [43]. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on enteral nutrition in the older population recommend the use of gastrostomy for long-term (≥4 weeks) nutritional support over nasogastric tubes due to fewer treatment failures, better nutritional status, and convenience to the patient [73]. However, there is no significant difference in the clinical benefit between nasogastric and gastrostomy feeding [74] in terms of infection rate and survival outcomes in a systematic review of studies conducted in patients with head and neck cancers [75]. The ESPEN recommends that nutritional therapy should be started if malnutrition already exists or if it is anticipated that the patient will not be able to eat for >7 days [43].

If enteral nutrition is not feasible, contraindicated, or not tolerable in malnourished cancer patients, then short-term parenteral nutrition may be considered, particularly in patients with acute GI complications from surgery, chemotherapy and/or radiotherapy (e.g. severe radiation enteritis or severe malabsorption) [76]. This decision must be balanced against a realistic outlook for recovery [77] and prognosis. Of note, the risk of developing refeeding syndrome increases with the degree of nutritional depletion and must be monitored and managed pre-emptively [78].

Patients with rapidly progressive disease with poor performance status and limited life expectancy are less likely to benefit from aggressive nutritional interventions. However, trial of oral or less invasive nutritional support may be offered to provide symptomatic or comfort care [43]. Long-term (home) parenteral nutrition (HPN) may be considered in patients with subacute or chronic radiation enteropathy, or as a palliative nutritional support in hypophagic or (sub)obstructed patients with acceptable performance status, or in patients who are expected to die sooner from starvation rather than cancer [76]. Among 414 cachectic (sub)obstructed, incurable patients (41% were ≥65 years and 56% had GI cancers), HPN has been associated with a longer 3- and 6-month

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survival (than is expected with total macronutrient deprivation) and varies considerably with Karnofsky performance status and Glasgow prognostic score [79]. Complications from long-term enteral (tube obstruction or displacement, diarrhea, or constipation) or parenteral (infections, thrombosis, or obstruction) nutrition are similar regardless of age [80], although a higher risk for central catheter vascular erosion ($p = 0.009$) [81] was seen in older compared to younger patients.

2.2.2. Pharmacologic Intervention

Supportive drugs, such as antiemetics to relieve nausea, analgesics to relieve pain associated with swallowing or other GI activity, motility agents to treat constipation or diarrhea, prokinetics to improve intestinal transit, and pharmaconutrients such as $\omega-3$ fatty acids to improve appetite and body weight, may be used to target the main pathogenic mechanisms of cancer cachexia [43]. Corticosteroids may increase appetite, control pain, alleviate nausea or vomiting, and improve QoL [82] but may only be used for a restricted period of time (1–3 weeks), due to early loss of efficacy [83], and the side-effects with long-term use may be more problematic in the elderly where sarcopenia, insulin resistance, infections, or delirium are more prevalent. Thus, corticosteroids may be more useful in the palliative setting among patients with limited life expectancy [84]. There is insufficient evidence to recommend any particular corticosteroid drug over another, or recommend a dosing regimen [84]. Progestins (megestrol acetate and medroxyprogesterone acetate) increase appetite, caloric intake and body weight but not fat-free mass, with minimal effect on QoL [82] and higher rates of edema, thromboembolism, and deaths [82]. $\omega-3$ fatty acids (fish oil) improve appetite, oral intake, lean body mass and body weight in patients with advanced cancer and at risk of malnutrition [3]. A non-significant delay in time to tumor progression was noted when supplemental 2 g/day of fish oil was given to patients with advanced CRC in the first 9 weeks of chemotherapy [85]. Less chemotherapy-induced stomatitis and diarrhea, and more hepatoprotective effects were noted with $\omega-3$-rich enteral nutrition support than with the $\omega-3$-poor formulation, among 61 patients (mean age 64.5 ± 8.4 years) who received neoadjuvant chemotherapy for esophageal cancer. Branched-chain amino acids, especially leucine, promote muscle protein synthesis in older adults, provided that renal function is not severely impaired [15]. There are insufficient consistent clinical data to recommend use of cannabinoids to improve appetite [86,87] or the use of NSAIDs to increase body weight [88], amino acids to improve fat-free mass [89], or androgenic steroids to boost muscle mass [90].

2.2.3. Physical Intervention

There is a strong association between physical activities and preservation of body composition among highly active older adults [91]. Physical activities in patients with cancer have been associated with improved aerobic fitness, muscle strength, health-related QoL, and psychological benefits [92,93]. However, most of these studies were conducted in women with early stage breast cancers who clearly have different demands compared to patients with GI cancers. Combinations of resistance exercises and aerobic muscle training may provide significant benefit in physical performance [94], at least among patients who are not limited by extreme fatigue. The ESPEN recommends all older people to undertake daily physical activities (resistance training, aerobic exercise) for as long as possible [15]. However, data specific to older patients with GI cancer are lacking. Physical activity may ameliorate the age-related decrease in energy expenditure, and individualized physical interventions to reduce inactivity and avoidance of a sedentary lifestyle are essential [43].

3. Palliative and Ethical Considerations

As with any older patients with malignancy, nutritional treatment goals must be individualized within the context of the disease trajectory or prognosis, overall health status or life expectancy, and patient preferences. Timely palliative care and social work referrals may be necessary to provide a holistic psycho-emotional assessment and support to address the impact of sarcopenia or cancer cachexia. Discussion with patients (and caregivers) regarding artificial nutritional and hydration must be done as early as possible, particularly in the setting of a pre-terminal stage when such interventions are futile. Nevertheless, a short trial with a pre-specified endpoint may be considered in select cases of prognostic uncertainty, with the understanding that the intervention will be discontinued if the patient derives no benefit or deteriorates with the intervention [95]. The decision to initiate, continue or withhold, or withdraw nutritional interventions in imminently dying patients is often challenging, and a rather controversial topic riddled with social, cultural, economic, and emotional implications, and is beyond the scope of this paper.

4. Conclusion

Nutritional risks are common in GI malignancies and in older patients with cancer. Inadequate nutrient intake often leads to deterioration of general state and deconditioning. Malnutrition in older patients with cancer is associated with poorer health outcomes, worse prognosis, and less tolerance to treatment. Screening for nutritional risks is essential upon diagnosis followed by further assessment if found at risk or abnormal, with regular monitoring thereafter. Interventions, including physical activities, dietary counselling, supplemental nutrition, and enteral or parenteral feedings should be considered in order to improve function, nutritional status, and possibly QoL. Management relies on a multidisciplinary effort between the oncologists, other health care professionals, and caregivers. In the absence of a well-defined consensus for managing the nutritional needs of older patients with GI cancers, personalized treatment with the use of good clinical judgement is crucial.

Author Contributions

Concept and design: A.R. Mislang, S. Di Donato, G. Mottino, L. Biganzoli, F. Bozzetti
Manuscript writing and approval: A.R. Mislang, S. Di Donato, J. Hubbard, L. Krisna, G. Mottino, L. Biganzoli, F. Bozzetti

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