Role of Nutritional Status in Predicting the Length of Stay in Cancer: A Systematic Review of the Epidemiological Literature

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Key Words

Length of hospital stay · Malnutrition · Nutritional assessment, screening, status · Oncology

Abstract

Background: Length of stay (LOS) has been used as a surrogate marker for patients' well-being during hospital treatment. We systematically reviewed all pertinent literature on the role of nutritional status in predicting LOS in cancer.

Methods: A systematic search of human studies published in English was conducted using the MEDLINE data base (all articles published as of December 2010). We searched using the terms 'nutritional status' and 'nutritional assessment' and 'nutritional screening' and 'malnutrition' in combination with the following terms: length of stay, length of hospital stay, duration of stay, and duration of hospitalization together with 'cancer' or 'oncology'. **Results:** The MEDLINE search identified a total of 149 articles, of which only 21 met the selection criteria. Of the 21 studies, 10 studies investigated gastrointestinal cancer patients, 4 gynecological cancer, and 7 heterogeneous cancer. Eight studies used subjective global assessment (SGA) or patient-generated SGA (PG-SGA), 9 used serum albumin and/or BMI, and 4 used other methods of nutritional assessment. **Conclusions:** Validated nutritional tools such as SGA/PG-SGA are better predictors of LOS in gastrointestinal cancers requiring surgery than in nonsurgical gastrointestinal cancer patients. Correcting malnutrition may decrease the LOS and perhaps even lower the rate of hospital readmissions in this population.

Introduction

Cancer patients are particularly susceptible to nutritional depletion due to the combined effects of the malignant disease and its treatment [1, 2]. Treatment modalities involving chemotherapy, radiotherapy, and surgery are all known to negatively affect nutritional status. Although the prevalence and magnitude of a diminished nutritional status varies with individual treatment regimens, it is widely accepted that the principal causes related to therapy are the result of commonly experienced side effects such as nausea, vomiting, anorexia, lethargy, diarrhea, esophagitis, and dysphagia [3, 4].

The incidence of malnutrition among patients with cancer has been estimated at between 40 and 80% [5–8]. Nearly 20% of cancer patients are reported to die of malnutrition or its associated complications rather than the malignant disease itself [9]. The prevalence of malnutrition depends on the tumor type, tumor location, stage of the disease, and treatment received and on the type of nutritional assessment method used [5]. These considerations provide a strong rationale for regular nutritional assessment and management for all cancer patients throughout the course of their disease.

An extensive and diverse set of methods are available for assessing nutritional status in cancer patients. Each has its strengths and weaknesses. Among the most commonly employed are: (i) anthropometric measurements, e.g. weight change, arm muscle circumference, and triceps skinfold thickness; (ii) quantitative biochemical assays, e.g.

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serum albumin, transferrin, and nitrogen balance studies; (iii) subjective global assessment (SGA) based on medical history and physical examination; patient-generated SGA (PG-SGA) adapted from the SGA specifically for cancer patients; (iv) the malnutrition screening tool (MST), considered the quickest and most simple tool for nutritional screening by the American Society for Parenteral and Enteral Nutrition (ASPEN); (v) Nutritional Risk Screening 2002 (NRS-2002), designed to detect malnutrition and the risk of developing malnutrition in the hospital setting as recommended by the European Society for Clinical Nutrition and Metabolism (ESPEN) [10], and (vi) the Malnutrition Universal Screening Tool (MUST), developed by the British Association for Parenteral and Enteral Nutrition, devised for application in all adult patients across all health care settings [1]. Many other nutritional parameters, including the Prognostic Nutritional Index, the Nutritional Risk Index, the Nutritional Screening Tool, the Maastricht Index, the Instant Nutrition Assessment, and the Mini Nutritional Assessment, have also been used to attempt to risk stratify patients [3, 11, 12]. The utility of these nutritional screening tools has been evaluated by their ability to predict relevant clinical outcomes, such as complications, treatment response, survival, hospital length of stay (LOS), and higher costs of health care [4, 9, 13].

LOS has been used as a surrogate marker of patients' well-being during hospital treatment [14] and is considered to reflect integration of the severity of illness and the patient's health status affected by genetics, the extent or severity of the trauma or disease, the overall medical or surgical treatment, the quality of care, and the availability of intermediary and long-term care facilities [3]. Reducing the LOS, therefore, has the potential to decrease health care costs, the risk of infections, and other hospital-acquired diseases and to improve patients' quality of life [14]. Malnourished patients often experience a significantly prolonged treatment duration in association with increased morbidities, thereby increasing the LOS [15]. Although the literature provides evidence of an association between nutritional status and LOS in cancer, there are considerable differences among individual studies with respect to the patient population, study design, sample size, and type of nutritional assessment.

The objective of this manuscript was to systematically review all of the pertinent literature on the relationship between nutritional status and LOS in cancer with the goal of consolidating and presenting the evidence while attempting to elucidate the most significant clinical implications and directions for future research in this area.

Methods

Data Sources

The MEDLINE data base was used to identify all articles investigating the relationship between nutritional status and LOS in cancer patients (all articles published as of December 2010). We also searched the bibliographies of selected papers to identify relevant articles missed during the primary MEDLINE search.

Study Eligibility Criteria

To be included in the review, an article must have: been published in English, reported data collected in humans with cancer, had nutritional status/assessment/screening as one of the predictor variables, had LOS as one of the outcome measures (primary or secondary), and utilized any of the following study designs (case-control, cohort, cross-sectional, prospective, retrospective, case series, longitudinal, clinical trial, meta-analysis). There were no restrictions in terms of age, ethnicity, or type or stage of cancer.

Search

We searched using the terms 'nutritional status' and 'nutritional assessment' and 'nutritional screening' and 'malnutrition' in combination with the following terms: length of stay, length of hospital stay, duration of stay and duration of hospitalization together with 'cancer' or 'oncology'.

Study Selection

Screening and eligibility assessment of the articles to be included were performed independently by 2 reviewers. Disagreements between reviewers were resolved by consensus.

Data Collection Process

One review author extracted the required data elements from included articles and the second author verified the extracted data. Disagreements were resolved by discussion between the two review authors. Tables 1–3 reflect the template for data collection.

Data Items

The following information was extracted for each included article: first author, year of publication, study place, data collection period, study design, sample size, nutritional assessment method, nutritional groups being compared, LOS comparison across the nutritional groups, conclusion, and variables adjusted for.

Synthesis of Results

The methods for assessing nutritional status were very varied across the selected articles. The only method that has been validated is the SGA/PG-SGA, so we wanted to evaluate results comparing a validated method versus other methods like BMI and serum albumin, which are not validated. As a result, all articles reviewed are summarized in separate tables based on the type of nutritional assessment method used to enable meaningful conclusions to be drawn separately for different nutritional assessment methods as well as to categorize studies into comparable groups in terms of the number of articles in each table. Within each table, studies are arranged chronologically by the year of publication starting with the most recently published study.

Results

Study Selection

The MEDLINE search identified a total of 149 articles based on different combinations of the search terms described above. The titles and abstracts of these 149 articles were reviewed to identify the relevant articles based on the selection criteria described above. Of these 149 articles, 124 were excluded because after reviewing the abstracts it appeared that these papers clearly did not meet the selection criteria. The full texts of the remaining 25 articles were obtained and reviewed. Four more articles failed to meet the selection criteria and were excluded. Finally, 21 articles were selected for the purpose of final inclusion and review in this manuscript. A flowchart describing the results of our literature search is provided in figure 1.

Characteristics of Included Studies

A total of 21 articles published in English were included in this review. For each study included, the data were extracted for the following characteristics: first author, year of publication, study place, data collection period, study design, sample size, nutritional assessment method, nutritional groups being compared, LOS comparison across the nutritional groups, conclusion, and variables adjusted for.

Synthesis of Results

Nutritional Status and LOS – SGA and PG-SGA

Table 1 describes studies exploring the relationship between nutritional status and LOS using SGA or PG-SGA as the primary nutritional assessment method. Of the 8 studies described herein, 6 were prospective [9, 14, 16–19] and 2 were retrospective [5, 20]. The sample size ranged from a minimum of 66 [20] to a maximum of 751 [9]. Populations under study included patients with gastrointestinal cancer, gynecologic cancer, head and neck cancer, multiple myeloma, and lymphoma. The studies divided their population into 3 SGA categories designated A, B, and C representing well-nourished, moderately malnourished, and severely malnourished individuals, respectively. PG-SGA was used as a continuous variable in one study [20]. Notably, SGA was found to be a significant predictor of LOS in all 8 studies such that the mean LOS was significantly higher in the malnourished groups versus the well-nourished groups. Wu et al. [19] found a significant increase in LOS in severely malnourished (SGA C) patients compared to well-nourished (SGA A) or moderately malnourished (SGA B) patients. Another study by Wu et al. [9] suggested that SGA may be a better tool for pre-

Fig. 1. Flowchart depicting the MEDLINE search results.

dicting LOS in surgical gastrointestinal cancer patients compared to all gastrointestinal cancer patients.

Nutritional Status and LOS – BMI or Serum Albumin or Both

Table 2 describes studies exploring the relationship between nutritional status and LOS using either BMI, serum albumin, or both as the nutritional assessment method(s). Of the 9 studies described herein, 6 were retrospective [13, 21–25] while 3 were prospective [12, 26, 27]. The sample size ranged from a minimum of 84 [13] to a maximum of 2,258 [27]. Study populations included patients with gastrointestinal cancer, gynecologic cancer, leukemia, or lymphoma and patients undergoing various cancer surgeries. Three studies used BMI only [12, 26, 27], 1 used serum albumin only [13], and 5 used a combination of both [21–25]. In the 3 studies using BMI as the nutritional assessment method, no relationship between BMI and LOS was demonstrated. The study using serum albumin found a statistically significant longer LOS in the hypoalbuminemic group versus the nonhypoalbuminemic group. In the remaining 5 studies using a combination of BMI and serum albumin, BMI was not significantly associated with LOS, while albumin levels were in 4 of the 5 studies [21–23, 25].

Nutritional Status and LOS – Other Measures

Table 3 includes studies examining the relationship between nutritional status and LOS using other nutritional assessment measures such as NRS-2002, MUST, and MST [1, 10]. One study used the recommendations of the French health authority to define malnutrition using age, BMI, and weight loss [28], while another one used the Prognostic Nutritional Index based on serum albumin, transferrin, triceps skinfolds, and skin sensitivity tests [29]. Of the 4 studies described herein [1, 10, 28, 29], all were prospective. The sample size ranged from a minimum of 67 [29] to a maximum of 1,545 [28]. The populations studied involved patients with the following cancers: breast, head and neck region, colorectal region, colon, lung, digestive system, genitourinary, endocrine glands, soft tissues, respiratory system, thoracic region, bones and joints, eye and lachrymal region, hematological, and hematopoietic system. All 4 studies found a higher LOS associated with malnourished status.

Discussion

The present study aimed to review the literature on the relationship between nutritional status and LOS in cancer. A total of 21 articles were selected for the purpose of final inclusion and review in this manuscript. Of the 21 studies, 10 studies investigated gastrointestinal cancer patients, 4 investigated gynecological cancer patients, and 7 investigated heterogeneous or multiple cancer patients. Among the 10 studies looking at the association between nutritional status and LOS in gastrointestinal cancer patients, only 4 studies showed that a better nutritional status was associated with a shorter LOS. The remaining 6 studies showed that nutritional status did not have any significant impact on LOS. Among the 4 studies exploring the relationship between nutritional status and LOS in gynecological cancers, 2 studies showed that a better nutritional status was associated with a shorter LOS. The tools used in these studies were PG-SGA [14] and the Prognostic Nutrition Index [29], respectively. In the remaining 2 studies, BMI was not found to be associated with LOS while serum albumin levels were. Among the 7 studies exploring the relationship between nutritional status and LOS in heterogeneous samples of cancer patients, 6 studies showed that malnourished status was significantly associated with a longer LOS. One of these studies mentioned that, though SGA was predictive of LOS, the study was underpowered to undertake multivariate analysis to overcome the is-

ssues related to bias and confounding [16]. One study, however, showed no association between nutritional status and LOS [21].

SGA is the only MST recommended by the ASPEN board of directors [16]. SGA is a simple, easy-to-apply and cost-effective method that has been validated for diverse groups of patients. SGA is one of the better available assessment methods, not only because it is patient centered and incorporates the clinical history and physical examination but also because it does not require laboratory testing or medical imaging exams [18, 19]. Reliable SGA grading, however, depends on the collection of a correct history and physical observation and requires a skilled dietician to carry out the assessment [18]. Nutrition assessment tools such as the scored PG-SGA enable quick assessment of the nutritional status, identification of nutrition impact symptoms, and implementation of appropriate nutrition support. An advantage of the PG-SGA as a nutrition assessment tool is that the score can be used as an outcome measure in nutrition intervention studies as it may be more sensitive to changes in nutritional status than the global SGA rating [20]. Also, by performing serial measurements, the change in the PG-SGA score may be used to demonstrate subtle changes in nutritional status. The high sensitivity and specificity of the PG-SGA score indicates that it strongly predicts nutritional status as defined by SGA. Unlike SGA, which places patients into categories, the continuous scoring system of the PG-SGA allows prioritization of patients requiring more urgent treatment and thus may facilitate a more effective use of resources [5]. In this review, 8 studies used SGA/PG-SGA as a validated nutritional assessment tool and in all 8 studies SGA/PG-SGA was found to be a significant predictor of LOS such that the mean LOS was significantly higher in the malnourished groups versus the well-nourished groups.

While serum albumin was found to be a predictor of LOS in 5 out of the 6 studies reviewed, and has long been associated with poor outcomes, this is more likely due to inflammatory metabolism and a decreased synthesis of negative acute-phase proteins than to nutritional status [30, 31]. Although serum albumin is often used to assess nutritional status because it is easy and inexpensive, it is really more of an indicator of the severity of the illness rather than changes in nutritional status [32]. It is not recommended as a sole indicator of nutritional status because of the effect of the inflammatory process on its synthesis as well as the fact that it can be affected by many acute interventions and hydration status. Another example of the limitations of serum albumin as an indicator of

Table 1. Relationship between nutritional status (assessed using SGA and PG-SGA) and LOS

First author, year (study place)	Data collection period	Study design	Sample size	Nutritional assessment method	Groups being compared
Laky, 2010 (Australia) [14]	March 2004 to December 2006	Prospective	157 patients with presumed or proven primary gynecological cancer	PG-SGA	PG-SGA A: well nourished (n = 118) (reference group) PG-SGA B and C: moderately malnourished or suspected of being malnourished and severely malnourished (n = 39)
Wu, 2010 (China) [19]	August 2004 to August 2006	Prospective	505 gastrointestinal cancers: gastric (n = 258), colorectal (n = 247)	SGA	SGA-A: well nourished (n = 275) SGA-B: mildly to moderately malnourished (n = 214) SGA-C: severely malnourished (n = 14)
Wu, 2009 (China) [9]	August 2004 to August 2006	Prospective	751 adult patients diagnosed with gastrointestinal cancer (including stomach, colon, or rectal cancer)	SGA	SGA-A: well nourished (n = 389) SGA-B: mildly to moderately malnourished (n = 332) SGA-C: severely malnourished (n = 30)
Wakahara, 2007 (Japan) [18]	July 2004 to April 2005	Prospective	262 patients with digestive diseases, 110 patients with cancer	SGA	SGA A: normal nutrition (n = 138) SGA B: moderate malnutrition (n = 81) SGA C: severe malnutrition (n = 43)
Horsley, 2005 (Australia) [20]	NA	Retrospective consecutive case series	66 cancers patients. Type: multiple myeloma (n = 27), non-Hodgkin's lymphoma (n = 13), B-cell lymphoma (n = 5), chronic lymphocytic leukemia (n = 4), acute myeloid lymphoma (n = 2), Ewing's sarcoma (n = 2), others (n = 13)	PG-SGA	According to the SGA, patients could be categorized as follows: SGA A: well nourished (n = 48) SGA B: moderately malnourished (n = 15) SGA C: severely malnourished (n = 3) The PG-SGA score was used as a continuous variable
Shirodkar, 2005 (India) [16]	February 1999 and November 1999	Prospective observational study, consecutive patients	266 cancer patients. Type: head and neck region (n = 112), gastrointestinal tract (n = 53), breast (n = 30), thorax (n = 28), genitourinary tract (n = 27), bone and soft tissue (n = 16)	SGA and BMI	Preoperative malnutrition groups based on BMI levels: Nil-mild: <18.5 (n = 110) Moderate: 18.5–20.0 (n = 53) Severe: >20.0 (n = 103) Based on SGA scores: SGA A: none or minimal malnutrition (n = 152) SGA B: moderate malnutrition (n = 98) SGA C: severe malnutrition (n = 16)
Bauer, 2002 (Australia) [5]	3-month period	Retrospective convenience sample	71 cancer patients. Type: lymphoma (49%), breast (13%), prostate, esophagus, lung, sarcoma and myeloma (4%)	SGA	SGA A: well nourished (n = 17) SGA B: moderately or suspected of being malnourished (n = 42) SGA C: severely malnourished (n = 12)
Ulander, 1998 (Sweden) [17]	November 1992 to June 1994	Prospective consecutive case series	75 colorectal cancer patients	SGA Preoperative weight loss Weight loss during hospitalization	SGA A: well nourished (n = 71) SGA B or C: malnourished (n = 4)

RR/HR (95% CI) or LOS comparison	Conclusion	Variables adjusted for
OR for prolonged LOS >5 days Univariate: 6.89 (2.48–19.2), $p < 0.001$ Multivariate: 5.28 (0.98–28.5), $p = 0.05$	Malnutrition, low quality of life scores and being diagnosed with advanced ovarian cancer are the major determinants of prolonged LOS in gynecological cancer patients.	Age and surgical approach
Mean $\pm$ SD = 20.8 $\pm$ 8.6 days, 21.1 $\pm$ 7.8 days, and 29.1 $\pm$ 15.1 days for SGA A, SGA B, and SGA C, respectively, $p \leq 0.001$	The SGA could help predict certain health outcomes such as LOS and in-hospital medical expenditures.	None
Univariate: Mean $\pm$ SD = 17.1 $\pm$ 9.7 days, 17.3 $\pm$ 9.0 days, and 21.1 $\pm$ 14.6 days, respectively, for SGA A, SGA B, and SGA C, $p = 0.086$ Multivariate: For all gastrointestinal cancer patients: SGA A (reference group)/SGA C, $p = 0.09$; SGA B (reference group)/SGA C, $p = 0.07$ For surgical gastrointestinal cancer patients: SGA A (reference group)/SGA C, $p = 0.02$; SGA B (reference group)/SGA C, $p = 0.01$	The SGA is a reliable assessment tool and helps to predict the hospital stay and medical expenditures of Chinese surgical gastrointestinal cancer patients.	Age, sex, education background, weight loss, BMI, mid-upper arm muscle circumference, triceps skinfold thickness, albumin, TNM staging, tumor site, treatment
Mean $\pm$ SD = 24 $\pm$ 31, 40 $\pm$ 49, and 57 $\pm$ 74, respectively, for SGA A, SGA B, and SGA C, $p < 0.01$ SGA used as a continuous variable: $r = 0.296$, $p < 0.01$	The SGA is a simple and reliable predictor for hospital stay in patients with digestive diseases.	None
PG-SGA score used as a categorical variable: Mean $\pm$ SD posttransplant LOS in days = 16.9 $\pm$ 6.3 and 23.9 $\pm$ 9.9 for well-nourished (PG-SGA A) and malnourished (PG-SGA B and C) groups, respectively, $p = 0.002$ PG-SGA score used as a continuous variable: $r = 0.308$, $p = 0.013$	Malnutrition prior to peripheral blood stem cell transplantation is associated with an increased LOS.	None
Preoperative malnutrition groups based on BMI levels: Median postoperative days = 6, 7, and 6 for nil-mild, moderate, and severe malnutrition groups, respectively, $p = 0.19$ Based on SGA scores: Median postoperative days = 5, 7, and 10 for A, B and C SGA groups, respectively, $p < 0.001$	The SGA is a simple and inexpensive way to identify clinically relevant malnutrition in Indian patients undergoing cancer surgery.	None
LOS in days for all 3 comparison groups: Median (range) = 7.0 (1–24), 14.0 (1–40), and 9.5 (1–30) for SGA A, SGA B, and SGA C, respectively, $p = 0.063$ LOS in days by grouping SGA B and SGA C together: Median (range) = 7.0 (1–24) and 13.0 (1–40) for SGA A and SGA B+C, respectively, $p = 0.024$	Prior nutritional status was significantly associated with LOS.	Age, diagnosis, percentage weight loss, BMI
Three patient groups based on LOS: <8 days ($n = 19$), 8–14 days ($n = 45$), >14 days ($n = 11$) Energy intake in kcal/day: mean $\pm$ SD (range) = 755 $\pm$ 242 (0–1,200) for <8 days, 801 $\pm$ 180 (0–1,133) for 8–14 days, and 823 $\pm$ 249 (380–1,345) for >14 days, NS Preoperative weight loss in %: mean $\pm$ SD (range) = 3.1 $\pm$ 5.2 (0–15.1) for <8 days, 3.5 $\pm$ 4.5 (0–16.0) for 8–14 days, and 1.1 $\pm$ 1.5 (0–4.6) for >14 days, NS Postoperative weight loss during hospitalization in %: mean $\pm$ SD (range) = 3.3 $\pm$ 2.2 (–2.1 to 6.4) for <8 days, 4.9 $\pm$ 4.6, (–9.1 to 17.0) for 8–14 days, and 6.5 $\pm$ 5.9 (–7.4 to 15.1) for >14 days, $p < 0.05$	Preoperative nutritional status, nutrition-associated complications, and LOS did not change the nutritional support and intake.	None

Table 2. Relationship between nutritional status (assessed using BMI or serum albumin or both) and LOS

First author, year (study place)	Data collection period	Study design	Sample size	Nutritional assessment method	Groups being compared
Beghetto, 2009 (Brazil) [21]	2002 and 2004	Retro-spective	Total patients: n = 434 Only cancer patients: n = 169	BMI Albumin SGA Weight loss Serum lymphocyte count	BMI ≥ 18.5 (n = 46) (reference group) and < 18.5 (n = 386) Albumin > 3.5 g/dl (reference group) and < 3.5 g/dl (n = 99) SGA A (well nourished) (n = 212) (reference group), SGA B (moderately malnourished or suspicious for malnutrition) (n = 83), and SGA C (severely malnourished) (n = 139) Weight loss $< 5\%$ (reference group) and $> 5\%$ (n = 216) Serum lymphocyte count $> 1,500$ U/ μ l (reference group) and $\leq 1,500$ U/ μ l (n = 249)
Hendry, 2009 (Northern Europe) [26]	March 2002 to December 2005	Pro-spective	1,035 open colorectal surgery patients	BMI	BMI < 20 and ≥ 20
Leung, 2009 (USA) [24]	2002–2007	Retro-spective	183 patients undergoing colorectal resection for neoplasms	BMI and decrease in serum albumin	BMI < 30 and ≥ 30 Albumin change $< 70\%$ (n = 87) and $\geq 70\%$ (n = 96)
Skipworth, 2009 (UK) [12]	January 2001 to March 2004	Pro-spective	93 patients with esophago-gastric carcinoma. Type: esophagic (n = 40), gastric (n = 53)	BMI and weight loss	Four groups: No weight loss and BMI > 25 (n = 34) No weight loss and BMI < 25 (n = 14) Weight loss and BMI > 25 (n = 20) Weight loss and BMI < 25 (n = 25)
Mullen, 2008 (USA) [27]	2001–2004	Pro-spective	2,258 patients undergoing major intra-abdominal cancer surgery	BMI	Underweight: BMI ≤ 18.5 (n = 55) Normal weight: BMI = 18.5–25.5 (n = 819) Overweight: BMI = 25.1–30.0 (n = 811) Obese I: BMI = 30.1–35 (n = 357) Obese II: BMI = 35.1–40 (n = 137) Obese III: BMI = 40 (n = 79)
Diaz-Montez, 2007 (USA) [23]	January 1, 1994, to June 30, 2004	Retro-spective	95 ovarian cancer surgery patients	BMI and serum albumin	BMI levels < 30 , ≥ 30 , and unknown Albumin levels < 3.5 g/dl (reference group) and ≥ 3.5 g/dl
Lohsiriwat, 2007 (Thailand) [13]	January 2004 to December 2005	Retro-spective	84 patients with adenocarcinoma of the right-sided colon	Serum albumin	Nonhypoalbuminemic: albumin ≥ 3.5 g/dl (n = 36) Hypoalbuminemic: albumin < 3.5 g/dl (n = 48)
De Luis, 2006 (Spain) [22]	January 1999 to December 2003	Retro-spective	1,088 patients: leukemia and lymphoma (11.5%), solid cancer (37.4%)	BMI Albumin Mid-arm muscle area Mid-arm muscle circumference Weight loss	Weight loss, mid-arm muscle circumference, and mid-arm muscle area. BMI and albumin were used as continuous variables.
Massad, 1993 (USA) [25]	January 1, 1990, to December 31, 1990	Retro-spective	155 gynecologic oncology patients Primary site: ovarian (n = 54), endometrial (n = 46), cervical (n = 33), vulvar (n = 10), fallopian (n = 4), peritoneal (n = 2)	BMI and serum albumin	BMI and serum albumin levels were used as continuous variables.

RR/HR (95% CI) or LOS comparison	Conclusion	Variables adjusted for
Results for n = 434, OR for prolonged LOS > 15 days: BMI: univariate: 1.47 (0.80–2.69), p = 0.21; multivariate NS Albumin: univariate: 2.77 (1.71–4.47), p < 0.01; multivariate, 2.4 (1.5–4.0), significant SGA: univariate: for SGA B: –1.31 (0.79–2.18), p = 0.30; for SGA C: –1.86 (1.20–2.86), p < 0.01; multivariate: NS Weight loss: univariate: 1.88 (1.29–2.76), p < 0.01; multivariate: 1.6 (1.1–3.4), significant Serum lymphocyte count: univariate: 1.65 (1.13–2.43), p = 0.01; multivariate: NS	The methods adopted for assessment of the nutritional status appeared to be weak predictors of death, infection, and hospital stay. Except for low serum albumin, isolated use of these methods adds little information in identifying the effect of nutritional status on clinically relevant outcomes.	Age, gender, nonsurgical admission, cancer, C-statistic
Univariate: the total hospital stay in days expressed as the median (interquartile range) was 6 (4–8) in the case of each group, i.e. <20 and ≥20, p = 0.820; multivariate: NS	BMI was not found to be significantly associated with LOS.	Age, American Society of Anesthesiologists (ASA) grade, sex, type of surgery and lesion
BMI: median LOS = 8 days in each group (<30 and ≥30), p = 0.289 Albumin change: median LOS in days = 8 and 7, respectively, for <70% and ≥70%, p = 0.489	Postoperative complications were the only variables predictive of prolonged LOS after colorectal resection.	Coronary artery disease, diabetes mellitus, chronic heart failure, chronic obstructive pulmonary disease
Median in days (range) = 15 (11.5–17), 10.5 (9.5–15), 12 (10–15.5), and 13.5 (11–19.5), respectively, for groups A, B, C, and D, NS	Preoperative weight loss and low BMI did not significantly influence the complication rate, perioperative mortality rate, LOS, or short-term prognosis.	None
Mean LOS in days = 13.5, 11.2, 11.7, 10.6, 11.7, and 10.3, respectively, for the underweight, normal weight, overweight, obese I, obese II, and obese III categories, p = 0.95	The differences in LOS across BMI classes were not statistically significant.	None
BMI levels: Univariate: among patients admitted for <48 h, 23 and 13% of patients, respectively, had BMI <30, ≥30, and unknown, while among those admitted for ≥48 h, 42, 9, and 3 patients, respectively, had BMI <30, ≥30, and unknown, p = 0.05. Multivariate: NS Albumin levels: Univariate: mean (range) = 3.74 (2.1–4.9) and 3.37 (1.4–4.6), respectively, for those admitted for <48 and ≥48 h, p = 0.03. Multivariate: 0.23 (0.07–0.77), p = 0.02	Extensive fluid resuscitation during surgery, poor nutritional status, and age ≥63 years are associated with a prolonged postoperative SICU stay.	Race, stage, bowel resection, ventilator dependence, pulmonary artery catheter, Charlson comorbidity index, American Society of Anesthesiologists score, CA-125, alkaline phosphatase, ascites, operation room time, hematocrit, estimated blood loss, tumor size
Univariate: mean ± SD = 6.8 ± 2.6 days and 9.6 ± 4.7 days for nonhypoalbuminemic and hypoalbuminemic groups, respectively, p = 0.001. Multivariate: NS	Serum albumin was significantly prognostic for a greater LOS upon univariate analysis but not upon multivariate analysis.	None
LOS was divided into 4 quartiles: Q1 (<15 days), Q2 (16–23 days), Q3 (24–35 days), and Q4 (>35 days) All results are expressed as means ± SD: Weight loss in kg: 4.4 ± 8.3, 4.4 ± 10.6, 3.8 ± 10.4, and 4.7 ± 8.9, respectively, for Q1, Q2, Q3, and Q4, NS Mid-arm muscle circumference in cm: 21.8 ± 3.2, 22.4 ± 3.4, 22.8 ± 3.4, and 22.5 ± 3.3, respectively, for Q1, Q2, Q3, and Q4, NS Mid-arm muscle area in cm ² : 26.1 ± 4.5, 26.7 ± 4.2, 26.9 ± 4.4, and 26.7 ± 4.3, respectively, for Q1, Q2, Q3, and Q4, NS BMI: 23.2 ± 4.8, 24.3 ± 4.6, 24.14 ± 4.5, and 24.1 ± 4.7, respectively, for Q1, Q2, Q3, and Q4, NS Albumin in g/dl: 2.8 ± 0.7, 2.9 ± 0.8, 2.6 ± 0.7, and 2.5 ± 0.6, respectively, for Q1, Q2, Q3, and Q4, p < 0.05. Correlation between albumin and LOS: r = –0.2; p < 0.05	The serum albumin levels are a good marker of LOS; a decrease in admission levels produces an increase in LOS.	Age, sex
BMI: NS Albumin: p < 0.001	Hemoglobin and serum albumin were inversely correlated with LOS, while BMI was not. Interventions that optimize hemoglobin and albumin preoperatively may result in decreased LOS.	Age, race, attending physician, funded versus charity care, pre-operative medications or medical conditions, preoperative hemoglobin, vulvar or fallopian tube primary, estimated surgical blood loss, prior platinum-based chemotherapy, prior radiotherapy remote from surgery, other primary sites

Table 3. Relationship between nutritional status (assessed using others measures) and LOS

First author, year (study place)	Data collection period	Study design	Sample size	Nutritional assessment method
Guo, 2010 (China) [10]	January 2004 to December 2007	Prospective	314 gastric carcinoma patients	NRS-2002
Pressoir, 2010 (France) [28]	October 2007 to January 2008	Prospective, observational multicenter study	1,545 hospitalized cancer patients. Type: breast (n = 375), head and neck (n = 179), colorectal (n = 156), hematological (n = 156), gynecological (n = 137), upper digestive (n = 103), lung (n = 90), others (n = 349)	Recommendations of the French health authority using age, BMI, and weight loss
Amaral, 2008 (Portugal) [1]	March 2005 to June 2005	Prospective	130 cancers patients. Type: head and neck (n = 27), peritoneal and gastrointestinal (n = 25), breast (n = 23) genitourinary system (n = 17) lymph ganglia (n = 10), endocrine glands (n = 6), soft tissues (n = 5), respiratory system and thoracic organs (n = 5), bones and joints (n = 4), hematopoietic system and endothelial reticulum (n = 2), eye and lachrymal gland (n = 1), others (n = 1)	NRS-2002, MUST, and MST
Santos, 2000 (Australia) [29]	1996	Prospective, consecutive case series	67 gynecologic oncology patients. Primary tumor site: cervix (n = 32), uterus (n = 16) ovary (n = 11), vulva (n = 1)	Prognostic Nutritional Index based on serum albumin, transferrin, triceps skinfold, and skin sensitivity tests

nutritional status is the fact that it is often found to be within normal limits in individuals with severe anorexia nervosa, when even an untrained eye can detect malnutrition in this population.

BMI was not found to be a good indicator of LOS. The BMI reflects patients' weight and height, and then assumptions are made about body composition based on the BMI. It does not take into account a decline in oral intake or clinically significant weight changes with a corresponding loss of body cell mass, which may have occurred prior to hospitalization. Clinically significant weight loss has previously been found to be associated with morbidity and mortality. Moreover, individuals with BMIs <18.5 are not always malnourished or undernourished, whereas individuals with a normal BMI can be malnourished. It is also likely that there is a wide variation in body composition and nutritional status in the overweight and obese populations. Interestingly, in this review tools like the NRS and

MUST, which take into account weight loss and declines in intake in addition to the BMI, did correlate with LOS.

Like most other systematic reviews, this review also suffers from potential publication bias. In general, this bias exists when studies reporting positive associations are more likely to get published. It remains possible that some unpublished studies containing valuable data might have gone undetected. Since we restricted this systematic review to include studies published in English only, it is possible that language bias might have affected our conclusions. Despite these limitations, we believe that the extensive available literature reviewed here demonstrates a strong association between nutritional status and LOS in cancer.

We propose some new avenues for further research in this area. The role of timely nutritional assessment and intervention in oncology cannot be overemphasized. Despite this, there is no consensus on how to manage patients based on any nutritional metric reviewed. This re-

Groups being compared	RR/HR (95% CI) or LOS comparison	Conclusion	Variables adjusted for
Nutritional risk used as a categorized variable Preoperative NRS-2002 <3 and preoperative NRS-2002 ≥3 Nutritional risk used as a continuous variable	Mean ± SD = 13.60 ± 7.24 days and 19.06 ± 11.79 days, respectively, for NRS-2002 <3 and NRS-2002 ≥3, p = 0.000. r = 0.177, p = 0.002	Preoperative nutrition score (NRS-2002) ≥3 predicted more postoperative complications and longer LOS.	None
Malnutrition absent (69.1%) and present (30.9%) Among those with malnutrition: moderate (18.6%), severe (12.2%) Note: LOS was available only for 879 patients	Median LOS in days = 19.3 ± 19.4 and 13.3 ± 19.4, respectively, for those without and with malnutrition, p < 0.0001	In French comprehensive cancer centers, 1 out of 3 cancer patients are malnourished and this was associated with a longer LOS.	None
Based on NRS-2002: NRS-2002 <3 (well nourished) (reference group) and NRS-2002 ≥3 (undernourished) Based on MUST: MUST <1 (low risk of malnutrition) (reference group) and MUST ≥1 (high risk of malnutrition) Based on MST: MST <2 (low risk of malnutrition) (reference group) and MST ≥2 (high risk of malnutrition)	Univariate: mean LOS in days (mean ± SD) = 7.5 ± 4.4 and 12.5 ± 11.9, respectively, for NRS-2002 <3 (well nourished) and NRS-2002 ≥3 (undernourished), p = 0.016. OR for an LOS of ≥7 days Multivariate: NRS: Crude OR: 2.13 (0.89–5.17), NS Adjusted OR: 2.47 (1.05–5.80), p = 0.003 MUST: Crude OR: 3.19 (1.43–7.16), p < 0.001 Adjusted OR: 3.24 (1.50–7.00), p = 0.038 MST: Crude OR: 2.16 (0.75–6.42), NS Adjusted OR: 2.31 (0.84–6.36), NS	MUST had the highest agreement with NRS-2002 in hospitalized cancer patients and better identified patients at risk for a longer LOS.	Sex, age
Prognostic Nutritional Index used as a categorized variable <40, nourished (n = 31); ≥40, malnourished (n = 36). Prognostic Nutritional Index used as a continuous variable	Prognostic Nutritional Index used as a categorized variable LOS in days described as the median (interquartile range) = 6 (4–7) and 8 (6–15.5), respectively, for nourished and malnourished groups, p = 0.004. Prognostic Nutritional Index used as a continuous variable: r = 0.32, p = 0.009	Malnutrition is common in gynecologic oncology patients and contributes to longer hospital stays.	None

view provides a strong rationale for devising such standards of practice and testing their value in controlled clinical studies. This would apply for all clinical manifestations of malnutrition broadly, as well as specific situations where a causative relationship is apparent. Another useful research area to pursue would be the investigation of the relationship between nutritional assessment and intervention and LOS across different countries to gain a better understanding of how the nutritional assessment and intervention practices differ across several nations.

Conclusions

Based on this review, it appears that nutritional status measured using a validated tool such as SGA/PG-SGA is a better predictor of LOS in gastrointestinal cancers requiring surgery compared with nonsurgical gastrointestinal cancer patients. Since surgery is associated with morbidity

like infections and wound complications, which can increase LOS, it may be prudent to provide nutrition support during the perioperative period in these individuals. It makes sense to implement the ASPEN guidelines for oncology patients, which include nutritional screening, assessment, and intervention as appropriate. Correcting malnutrition may decrease the LOS and perhaps even lowers the rate of hospital readmissions in this population.

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