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Malnourished, gastrointestinal cancer patients undergoing surgery: burden of nutritional risk, use of oral nutritional supplements, and impact on health outcomes

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Running title: Nutritional risk in GI cancer surgery patients

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ABSTRACT

Background and Objectives: Patients with gastrointestinal (GI) malignancies are at high risk for malnutrition because of reduced food intake, poor digestion, and altered absorption. Methods and Study Design: In a retrospective review of medical records for patients admitted to urban hospitals in an Asian nation for GI tumor surgery (gastric, colon, or anorectal cancers), we found that malnutrition was common yet often overlooked. Our review identified records for 349 adult GI-tumor surgery patients. The Nutrition Risk Screening-2002 (NRS-2002) was the most frequently used screening instrument. In further review, we compared outcomes for malnourished GI tumor surgery patients given daily oral nutritional supplements (ONS) to outcomes for patients who were not given ONS. Results: Review of results revealed that only 20% of patients in our sample underwent nutritional screening or assessment on admission. Of those who did, nearly 60% were malnourished. Although due to small sample sizes, no statistically significant differences were observed, malnourished patients who received ONS had fewer complications and shorter lengths of stay by 1-day. Such findings reveal many missed opportunities to improve patient outcomes and to avert excess healthcare costs for treatment of complications, slowed recovery, longer hospital stays, and readmissions. Conclusions: Based on our findings, nutritional training for professionals is necessary to address the serious problems of under-recognition and inadequate treatment of malnutrition in hospitalized patients.

Key Words: gastrointestinal surgery, malnutrition, gastric cancer, colon cancer, anorectal cancer

INTRODUCTION

In patients with gastrointestinal (GI) malignancies, risk for malnutrition is high as result of reduced oral intake, poor digestion, and altered absorption.¹ Patients with head-neck, gastroesophageal, pancreatic, and colorectal cancer are at highest risk of developing malnutrition with prevalence rates between 30 and 60%, depending on tumor location and its treatment.^{2, 3} Specifically, the prevalence of malnutrition was estimated to be 48% for colorectal cancer, and 23% in gastric cancer.1 Similarly, rates of malnutrition were reported as about 50% for patients with GI cancers, with a range depending on the assessment tool used. A recent report using the Patient Generated Subjective Global Assessment (PG-SGA) found 80% of patients hospitalized with gastric cancer were malnourished.⁴ Severe malnutrition is notably common in patients undergoing surgery for GI cancers, in turn raising

risk for 30-day mortality.⁵ For patients with colorectal and gastric cancer, severe malnutrition was associated with an estimated 32% to 40% of early deaths in countries throughout the world.⁵

Early identification and treatment of malnutrition is thus key to achieving optimal management and best possible clinical outcomes for patients with GI cancers. Since 10 to 20% of patients with cancer die from malnutrition rather than the disease itself, the European Society for Clinical Nutrition and Metabolism (ESPEN) recommends nutritional screening and the use of oral nutrition supplements (ONS) at the time of cancer diagnosis and throughout the disease process. In patients with moderate-to-severe upper GI cancer, post-operative nutritional care is effective when implemented in the hospital and continued post-discharge. Recent evidence suggests that pre-operative use of ONS can deliver further benefits for GI cancer patients, as does focus of nutritional care throughout disease course.

Study results have shown the effectiveness of ONS intake to improve nutritional status, reduce hospital readmissions, decrease hospital length of stay, improve response to treatment, and reduce mortality.^{3, 11} In patients with gastric cancer, longer survival was specifically dependent on compliance with ONS intake.¹² Health economic study results showed that ONS use was cost-effective in optimizing post-hospitalization health in cancer survivors, including those with gastrointestinal cancer.¹³⁻¹⁵

This paper analyzes malnutrition screening and utilization of ONS across five hospitals. An understanding of current practice and levels of malnutrition screening and ONS utilization are necessary to understand the current state of nutrition care and identify opportunities for improvement. Our analysis shows that malnutrition screening levels are low and that ONS, a first line interventions for malnutrition, is insufficiently utilized in patients identified as malnourished.

MATERIALS AND METHODS

Study aims

The underlying study examined the frequency of nutritional assessment for malnutrition diagnoses. The study also examined utilization of ONS, a key intervention for treatment of malnutrition.

Study design

This study was a retrospective analysis of medical records for patients who were admitted between 2017 and 2020 for gastrointestinal tumor surgery (gastric, colon, or anorectal cancers)

to one of five Chinese urban hospitals (Beijing Millennium Monument Hospital affiliated to Capital Medical University, General Hospital of the Chinese People's Liberation Army, Tenth People's Hospital of Shanghai, Peking Union Medical College Hospital, Zhongshan Hospital affiliated to Fudan University).

Records were eligible for inclusion in the analysis if the subjects had hospital stays \geq seven days. Records were excluded if the patient was unable to consume diet orally; had serious intestinal conditions (obstruction, malabsorption, bleeding, perforation); had other severe medical conditions (heart disease, diabetes, hyperlipidemia, electrolyte imbalance, or liver or kidney dysfunction); had serious infections (active tuberculosis, hepatitis B or C, human immunodeficiency virus); or were pregnant or lactating. We also removed subjects with missing values for nutritional assessment. A comparison group included gastrointestinal cancer patients with malnutrition or its risk who did not receive ONS during their hospitalization but otherwise met inclusion criteria. Intervention group patients received ONS during their hospitalization (minimum average daily dosage of 400 kcal/d for \geq five days). The total number of patient records included was 349.

Data collection

Data was extracted from patient medical records and recorded on clinical data forms by participating study physicians. Extracted data included patients' demographic information (age and sex) and type of health insurance (government, commercial, or none). Patients' medical data were cancer diagnosis requiring surgery, other concomitant diseases, current medications, and ongoing treatment for cancer (chemotherapy, radiation therapy, other). We also collected patients' scores for nutrition risk screening or malnutrition assessment, if conducted during hospitalization.

Ethical compliance

This study was reviewed and approved by the Ethics Committees at: Beijing Millennium Monument Hospital (study number 2021-1); General Hospital of the Chinese People's Liberation Army (study number S2021-425-01), Tenth People's Hospital of Shanghai (study number SHSY-IEC-4.1/21-180/01), Peking Union Medical College Hospital (study number S-K1655), and Zhongshan Hospital affiliated to Fudan University (study number B2021-389R). The analysis used medical records, and patient identities were not recorded on the data collection sheets; therefore, a waiver of consent was granted.

Statistical analyses

Descriptive analyses were performed on all patient characteristics. Group comparisons were made to examine differences in nutritional assessment. Between group univariate analysis for the categorical variables were performed using the Chi-square test or the Fisher's exact test. A *p*-value of 0.05 or less was considered statistically significant. All analyses were performed via SAS (SAS Institute Inc., Chicago IL).

RESULTS

Patients hospitalized for GI tumor surgery had a mean age of 61 years, were majority male, and mostly had government health insurance (Table 1). Just one in five (21.5%) hospitalized patients underwent nutritional assessment on admission; of those who did, about 60% were found to be malnourished.

None of the patients who underwent nutritional assessment at admission were later reassessed at discharge, and 17% of those not assessed on admission were assessed at discharge (Table 2). Additionally, no patients with diagnosed malnutrition on admission had a nutritional assessment at discharge (data not shown in tables).

Patients who had their nutritional status screened/ assessed and were considered malnourished were not more likely to receive ONS compared to those who underwent evaluation but were considered adequately nourished (63.6% of malnourished vs 67.9% of not malnourished, p=0.71) (Table 3).

Analysis of the outcomes of patients who received nutrition screening, shows that malnourished patients were more likely to have surgical complications (infectious (18.2% vs 7.1%, p=0.19) and non-infectious (29.6% vs 17.9%, p=0.26)) and a longer hospital stay (26.5 days vs 22.86 days, p=0.15) (Table 4). These differences were not statistically significant, likely due to the limited number of patients who received nutrition screening.

Malnourished patients who received ONS had fewer complications (31.0.% vs. 37.5%, p=0.66) and shorter lengths of stay (25.8 vs 26.8, p=0.77), highlighting the missed opportunity for improving outcomes of malnourished patients (Table 5). However, the differences in outcomes between the groups were not statistically significant, likely due to the small sample size (only 44 patients were diagnosed as malnourished).

DISCUSSION

Overview of analysis results

In medical records of patients hospitalized for GI cancer surgery in urban Chinese hospitals, just 21% underwent nutritional screening or assessment on admission. Of those, a large proportion (61%) were identified as malnourished. Taken together, such results suggest that malnutrition is common among GI tumor surgery patients, yet likely to be overlooked due to insufficient nutritional screening and assessment in hospitals. Among the 80% of hospitalized GI cancer patients who were not evaluated for nutritional status, there were likely many missed opportunities for individualized nutrition-focused care, including nutritional supplementation and nutrition counseling.

Further, even when nutritional screening or assessment was conducted, and malnutrition detected, the condition was undertreated. Nutritional care, which we measured as prescription and use of daily ONS, was used at similar rates by patients diagnosed with malnutrition and those determined not to be malnourished (64% vs 68%). Further still, we found directional trends for poorer outcomes in malnourished patients who did not receive ONS compared to those who did, i.e., higher rates of infectious complications and 1-day longer lengths of stay. However, neither difference achieved statistical significance, likely because of the small number of patients in these groups.

Yet another concern was that patients diagnosed with malnutrition did not have a follow-up screening at discharge. Awareness and monitoring of nutritional status, particularly for nutritionally vulnerable patients with GI cancer, has been recognized as important. Improvement in nutritional status may predict better recovery from surgery, while worsening nutritional status predicts higher risk for adverse outcomes--hospital readmission or premature death—if nutritional care is not provided. Ensuring that patients diagnosed with malnutrition have follow-up assessment and receive appropriate nutrition care would be an important step toward improving patient outcomes.

Limitations

Our study encounters several of the limitations common to retrospective studies. Firstly, patients were not randomly assigned to ONS and no ONS groups. Findings on the impact of screening and ONS may be confounded due to unobserved factors that may inform whether patients were screened for malnutrition or prescribed ONS. For this reason, we have limited our analysis and discussion to descriptive results on screening practices in these hospitals, association of malnutrition with outcomes, and the provision of ONS to malnourished

patients. We were also unable to examine risk factors for malnutrition due to the low number of patients who received nutrition screening. Although the data analyzed was from multiple hospitals, the number of patients from each hospital was too small to control for differences between hospitals.

Rationale for treating malnutrition and its risk in patients with cancer

Malnutrition is highly prevalent among patients with cancer. The severity of malnutrition generally depends on the tumor type and location, stage of the disease, and treatment.¹⁷ For patients with cancer, study results have shown that malnutrition increased the incidence and severity of treatment-related toxicity, negatively impacted quality of life, and its presence predicted mortality.^{11, 18, 19} Hospitalized cancer patients with malnutrition had greater risk of infections and other complications, longer hospital stays, and poor tolerance and response to treatment—all of which contributed to risk for lessened quality of life and decreased survival.^{17, 20-22} However, shortfalls in identification and treatment of nutritional risk are common. Treatment of patients with cancer often focuses largely on management of the disease, and all-too-frequently, neglects needed management of malnutrition.^{18, 23-25} Other specific areas of concern include identification and treatment of cancer cachexia²⁶ and nutritional care for patients seen in outpatient clinics.

There is evidence from China and elsewhere in the world showing benefits of nutritional and educational interventions on nutritional status among gastric cancer patients.²⁷⁻²⁹ Other studies have shown the effectiveness of ONS intake to improve nutritional status, reduce hospital readmissions, decrease hospital length of stay, improve response to treatment, and reduce mortality.^{3, 11} In patients with gastric cancer, longer survival was dependent on compliance with ONS intake.¹² As well, early evidence shows that ONS is cost-effective in optimizing post-hospitalization health in cancer survivors, including those with gastrointestinal cancer.¹³⁻¹⁵ While potential benefits of nutrition-focused care are substantial, actual benefits are sometimes inconsistent in the medical literature, likely due to differences in patient populations, duration of treatment, patient non-compliance, and weak study design.³⁰ Clearly, further studies must be done to delineate best practices for nutritional care in outpatients visiting cancer clinics.³¹

Guidelines and processes for nutritional care in patients with cancer

Expert guidelines offer evidence-based recommendations on nutritional care for people with cancer. These include the well-established professional guidelines and recommendations from

Europe (ESPEN),^{6, 7} along with new practical guidelines.⁸ As well, recommendations for cancer nutritional care are available for Australia and North America.^{32, 33} Other guidelines have been developed for nutritional treatment of undernourished patients with cancer cachexia.³⁴

Given the high prevalence and negative impact of malnutrition on patients, validated clinical tools and processes are needed to identify malnourished patients and to initiate nutritional interventions that can improve clinical outcomes and reduce healthcare cost.³⁵ Effective processes to identify and treat malnutrition are needed so improvements in performance are measured and key performance criteria with nutrition care delivery can be established. This requires interventions, beyond nutritional training and education, that focus on implementing evidence-based nutrition care for patients at-risk or malnourished upon hospital admission and throughout their hospital stay as well as at discharge. To this end, the American Academy of Nutrition and Dietetics and Avalere Health, along with other key stakeholders, developed the Malnutrition Quality Improvement Initiative (MQii), which sought to identify and manage malnutrition in older hospitalized adults.35 The MQii initiative highlights the importance of a hospital-based Global Malnutrition Composite Score (GMCS) consisting of four clinical quality measures (screening for malnutrition risk, nutrition assessment, malnutrition diagnosis, and implementation of nutritional care plan) that were validated and used in an electronic format.36 Such measures were designed to improve the quality of hospital-based malnutrition care, focusing on patient outcomes and on reducing healthcare costs, with higher scores indicating better quality of care.³⁶ GMCS was recently included in the Centers for Medicare & Medicaid Services (CMS) Hospital Inpatient Quality Reporting (IQR) Program, thus giving the opportunity to hospitals across United States to internally monitor performance of the GMCS and four component measures over time to facilitate quality improvement for patients who are malnourished or at risk of malnourishment.³⁷ An MOii Toolkit was developed to help hospitals implement the malnutrition initiative.³⁸ While the MQii was initially focused on identifying malnutrition in older hospitalized adults (> 65 years), there is an opportunity to modify this program for patients with cancer.³⁹ Review of 17 society clinical guidelines revealed a lack of consistency in the approach and management of nutritional care for patients with cancer. 40 However, a recent, large multicenter cohort study of hospitalized solid tumor cancer patients concluded that the Global Leadership Initiative on Malnutrition (GLIM) was an effective screening tool for cancer cachexia. 41 Therefore, professional society collaboration on the development of an

MQii-like process for adults hospitalized with cancer offers a unique opportunity to improve the nutritional care for these vulnerable patients.

In addition to identifying and treating malnutrition in hospitalized patients with cancer, focus must also be placed on nutrition interventions in the ambulatory care setting. Almost all patients (90%) with cancer are treated in outpatient clinics or cancer centers. Access to nutrition care is inadequate in ambulatory care with many patients not receiving nutritional screening or intervention. Almost all undetected and untreated, malnutrition impacts the patient's response to treatment and may result in treatment delays, hospitalizations, and decreased quality of life. Almost all undetected and untreated, malnutrition impacts the

Conclusion

Our study results confirmed that people hospitalized for surgical removal of gastrointestinal tumors were at high risk of malnutrition. Nevertheless, only 1 in 5 of these patients in urban Chinese hospitals of our study underwent assessment for malnutrition risk on hospital admission and only a small group of patients received ONS. Directional trends for poorer outcomes in malnourished patients who did not receive ONS compared to those who did, i.e., higher rates of infectious complications and 1-day longer lengths of stay were observed; future research with larger sample sizes to confirm impact of ONS on health and economic outcomes is needed. Such findings represent many missed opportunities to improve patient outcomes and to avert excess healthcare costs for treatment of complications, slowed recovery, longer length of stay, and readmissions.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

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Table 1. The study procedure

Demographics	_
Age in years, mean (± SD)	61.8 (± 11.5)
Sex, N (% of total)	
Male	242 (69.3%)
Female	107 (30.7%)
Medical	
Primary Diagnosis, N (% of total)	
Gastric Cancer	200 (57.3%)
Colon Cancer,	88 (25.2%)
Anorectal Cancer	61 (17.5%)
Comorbidity, N (% of total)*	
Eye, Ear, Nose, Throat	4 (1.2%)
Central Nervous System	8 (2.4%)
Cardiovascular	90 (26.6%)
Endocrine-Metabolic	32 (9.6%)
Gastrointestinal	96 (28.7%)
Allergies	2 (0.6%)
Renal	17 (5.2%)
Malignancies	77 (23.0%)
Hepatic	31 (9.4%)
Other	64 (19.3%)
Nutritional status	
Nutrition assessment at admission, N (% of total)	
Yes	75 (21.5%)
No	274 (78.5%)
Diagnosed with malnutrition of those who had nutrition assessment at admission, N (% of	
Yes	44 (61.1%)
No	28 (38.9%)
Missing	3
Nutrition assessment at discharge (N, % of total)	
Yes	46 (13.2%)
No	303 (86.8%)

N, number; SD, standard deviation

Table 2. Nutritional status assessment at admission and discharge

	Nutrition status assessed at discharge		
Nutritional status assessed at admission	Yes	No	
Yes, N (% admission assessment	0 (0%)	75 (100%)	$\chi^2 = 14.5$, p<0.001
group)			
No, N (% admission assessment	46 (16.8%)	228 (83.2%)	
group)			

 $[\]chi^2,$ Chi-squared; N, number of observations; T, Student's t-test; SD, standard deviation.

Table 3. Use of ONS when diagnosed with malnutrition in patients receiving nutrition screening $(N_{\text{screening}} = 75)^{\dagger}$

Nutrition status assessed at discharge			
Nutritional status assessed at admission	Yes	No	
Yes, N (% screening group)	0 (0%)	75 (100%)	$\chi^2 = 14.5$, p<0.001
No, N (% screening group)	46 (16.8%)	228 (83.2%)	

 $[\]chi^2,$ Chi-squared; N, number of observations; T, Student's t-test; SD, standard deviation. $^\dagger Limited$ to patients who had a nutritional assessment

[†]Patients could have multiple comorbid conditions. Percentages will not sum to 100.

Table 4. Complication rates in surgical patients by malnutrition diagnosis in patients receiving nutrition screening $(N_{\text{screening}} = 75)^{\dagger}$

	Malnourished	Not malnourished	χ^2 or T
Any complication, N (% nutrition risk group)	15 (34.1%)	6 (21.4%))	1.33 (<i>p</i> =0.25)
Infectious complication, N (% nutrition risk group)	8 (18.2%)	2 (7.1%)	3.72 (<i>p</i> =0.19)
Noninfectious complication, N (% of ONS group)	13 (29.6%)	5 (17.9%)	1.25 (<i>p</i> =0.26)
Length of stay, Mean days (Standard deviation)	26.5 (11.1)	22.86 (8.2)	1.47 (<i>p</i> =0.15)

 $[\]chi^2,$ Chi-squared; N, number of observations; T, Student's t-test; SD, standard deviation. $^\dagger Limited$ to patients who had a nutritional assessment

Table 5. Outcomes of patients with diagnosed malnutrition by ONS utilization in patients receiving nutrition screening $(N_{\text{screening}} = 75)^{\dagger}$

	Received ONS		χ ² or T
	Yes	No	
Any complication, N (% nutrition risk group)	9 (31.0%)	6 (37.5%)	$\chi^2 = 0.19 \ (p = 0.66)$
Infectious complication, N (% nutrition risk group)	4 (13.8%)	4 (25.0%)	$\chi^2 = 0.89 \ (p = 0.35)$
Noninfectious complication, N (% of ONS group)	8 (27.6%)	5 (31.3%)	$\chi^2 = 0.89 \ (p = 0.35)$ $\chi^2 = 0.07 \ (p = 0.80)$
Length of Stay, Mean days (SD)	25.8 (10.6)	26.8 (12.6)	$t=-0.3 \ (p=0.77)$

 $[\]chi^2,$ Chi-squared; N, number of observations; T, Student's t-test; SD, standard deviation. $^\dagger Limited$ to patients who had a nutritional assessment