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REVIEW ARTICLE

# Impact of malnutrition and nutritional support after gastrectomy in patients with gastric cancer

Min Kyu Kang[1] | Hyuk-Joon Lee[1,2]

[1]Division of Gastrointestinal Surgery, Department of Surgery, Seoul National University Hospital, Seoul, South Korea

[2]Department of Surgery & Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea

**Correspondence**
Hyuk-Joon Lee, Department of Surgery & Cancer Research Institute, Seoul National University Hospital, 101 Daehak-Ro, Jongno-Gu, Seoul 03080, South Korea.
Email: appe98@snu.ac.kr

## Abstract

Malnutrition, characterized by altered body composition and impaired function, is particularly prevalent among gastric cancer patients, affecting up to 60% of them. Malnutrition in these patients can manifest both before and after surgery, due to factors such as gastric outlet obstruction, cancer cachexia, and anatomical changes. Notably, total gastrectomy (TG) presents the most significant nutritional challenges. However, function-preserving gastrectomy, such as pylorus-preserving gastrectomy (PPG) and proximal gastrectomy (PG), have shown promise in improving nutritional outcomes. Effective nutritional risk screening and assessment are vital for identifying patients at risk. Nutritional support not only improves nutritional parameters but also reduces complications, enhances quality of life (QoL) and survival rates. Those unable to maintain more than 50% of the recommended intake for over 7 days are recommended for nutritional support. Common methods of nutritional support include oral nutrition supplements (ONS), enteral nutrition (EN), or parenteral nutrition (PN) depending on the patient's status. Effect of perioperative nutritional support remains controversial. Preoperative interventions including ONS and PN have shown mixed results, with selective benefits in patients with sarcopenia or hypoalbuminaemia, while impact of EN in gastric outlet obstruction patients have been positive. In contrast postoperative support appears to be consistent. Tube feeding after TG has shown improvements, and ONS have been effective in reducing weight loss and improving nutritional biomarkers. PN was also associated with benefits such as weight maintenance and QoL. This review explores the mechanisms, assessment, and clinical impact of malnutrition, emphasizing the importance of nutritional support in gastric cancer patients undergoing gastrectomy.

KEYWORDS
gastrectomy, gastric cancer, malnutrition

## 1 | INTRODUCTION

Malnutrition is a broad term defined as "a state resulting from lack of intake of nutrition that leads to altered body composition and impaired physical and mental function.[1]" According to The European Society for Clinical Nutrition and Metabolism (ESPEN), malnutrition could be diagnosed by either body mass index (BMI) less than 18.5 kg/m$^2$, unintentional weight loss of 10% or 5% over the last 3 months.[2] Gastric cancer remains a significant global burden, ranking 5th in incidence and 4th in mortality worldwide,[3] and the prevalence of malnutrition in gastroesophageal cancer patients can be as high as 60%.[4] In cancer patients, as well as calorie deficient malnutrition, other physiologic manifestations such as sarcopenia and cachexia can exist. Such malnourished patients are exposed to complications, chemotherapy toxicity, diminished quality of life (QoL), and unfavorable survival outcomes.[5] Therefore, an early identification of at-risk patients enables physicians to devise an adequate perioperative support plan. ESPEN recommends routine evaluations of nutritional intake, changes in body weight, and BMI at the point of cancer diagnosis, with further evaluation of symptoms, muscle mass, and physical performance levels if necessary.[6] In this review we will explore the mechanisms, assessment, clinical impact of malnutrition, and nutritional support in gastric cancer patients undergoing gastrectomy.

## 2 | CAUSES AND MECHANISM OF MALNUTRITION

Malnutrition in gastric cancer patients can manifest before or after surgery. Preoperatively, malnutrition is likely a result of impaired oral intake from gastric outlet obstruction and cancer cachexia, which are both consequences of cancer progression. Postoperatively, malnutrition mainly occurs due to reduced oral intake and anatomical changes following gastrectomy. While all of the above can present in both early and advanced stages, preoperative factors are predominantly responsible for weight loss in advanced stages of gastric cancer, while postoperative factors are primary factors of malnutrition in all stage of gastric cancer.

### 2.1 | Preoperative mechanism of malnutrition

In addition to reduction of nutrition consumption due to gastric outlet obstruction, metabolic and inflammatory changes caused by tumors put cancer patients at high risk of malnutrition. In patients with gastrointestinal cancer, 56.2% had weight loss greater than 5% and 31.9% has weight loss greater than 10%.[7] Cachexia has a profound impact in cancer patients, accounting for over 20% of cancer-related deaths.[8,9] Defined as "multifactorial syndrome characterized by an ongoing loss of skeletal muscle that conventional nutritional support cannot fully reverse," cancer cachexia is a spectrum that includes pre-cachexia, cachexia, and refractory cachexia.[9] Main features of cachexia spectrum are illustrated in Figure 1. In cancer cachexia there is preserved non-muscle compartment protein which is a distinguishing feature from cachexia in starvation.[10] This emerges from uncontrolled catabolism, fuelled by pro-inflammatory cytokines and anabolic resistance.[11] Patients experience increased resting energy expenditure, anorexia, loss of adipose tissue, sarcopenia, and diminished protein synthesis.[10]

### 2.2 | Postoperative mechanism of malnutrition

Weight loss after gastrectomy often occurs due to catabolism from surgical stress, and restricted oral intake. The surgical alteration of anatomy diminishes both the reservoir volume and digestive function of the stomach, which contributes to this weight loss. As a result, most significant weight loss occurs in early months after the operation,[12–15] and the rate of weight loss plateaus after 6

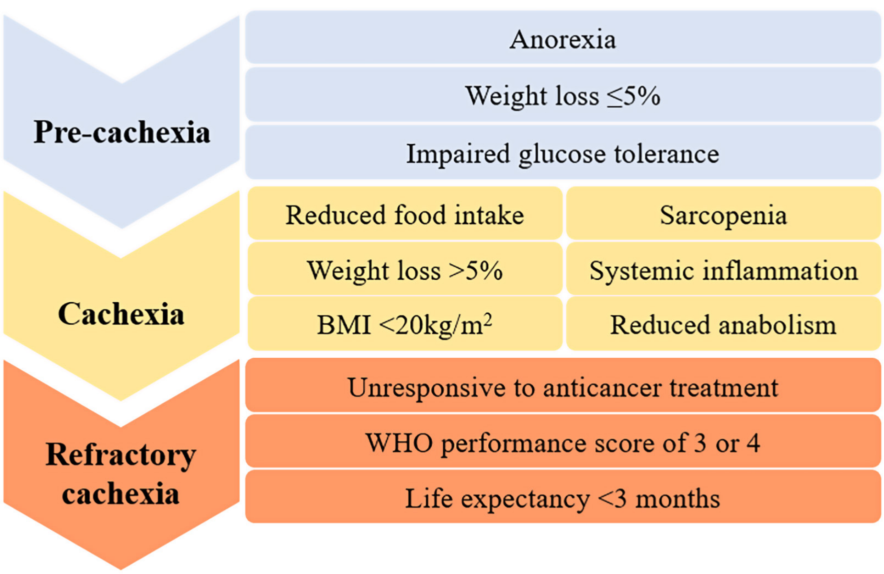


FIGURE 1 Features of cancer cachexia spectrum.

months.[15,16] The patterns of weight loss after gastric cancer surgery can be divided into four categories as shown in Figure 2.[17] Of all types of gastric surgeries, total gastrectomy (TG) poses biggest nutrition-related problems. Patients undergoing TG face reductions of up to 15% in body weight, 8% in protein, and 36% in fat within the first 6 months after surgery.[14] The postoperative weight loss is greatest across all periods after TG when compared to procedures that spare the remnant stomach like subtotal gastrectomy (STG).[15] Larger remnant gastric volume has been associated with smaller reduction in body weight,[18] hemoglobin, and favorable nutritional indexes,[19] but minimally invasive laparoscopic approach has not shown benefits in body weight loss compared to open surgeries.[20,21]

As well as weight-related malnutrition, the absorption of micronutrients is significantly impacted after TG. The shortage of intrinsic factor and subsequently low vitamin $B_{12}$ from loss of parietal cells result in megaloblastic anemia.[22] Additionally, iron deficiency anemia can result after Billroth II or Roux-en-Y reconstruction as ferrous iron ($Fe^{2+}$) is predominantly absorbed in the duodenum.[23] After gastrectomy incidence of anemia can range from 18.7% in the first year to 39.5% by the fifth year, with female gender and TG being notable risk factors.[24]

#### 2.2.1 | Effect of function preserving gastrectomy on nutrition

Given the problems above, there has been increasing efforts to carry out function preserving gastrectomy to spare remnant gastric volume and improve nutritional outcomes when oncologically appropriate. Examples of these are pylorus-preserving gastrectomy (PPG) and proximal gastrectomy (PG). PPG was introduced to preserve the pyloric function, and has benefits such as lower incidence of bile reflux, gallstone formation, and dumping syndrome. Nutritional benefit can be found in the form of smaller postoperative weight reduction compared to distal gastrectomy (DG).[25] A study led by Tsujiura et al. carried out paired analysis of biological markers before and after PPG, and found albumin and total protein remained elevated at 6 months, 1 year, and 2 years after PPG.[26] Other findings include PPG demonstrating smaller reduction in total, visceral, and subcutaneous fat area, and maintained higher levels of albumin and total protein compared to DG.[27]

As an alternative to TG in proximal tumors, PG has gained attraction as gastric reservoir is maintained and gastric acid and intrinsic factor secretion is preserved. Studies have identified advantages of PG in postoperative weight loss,[28–33] hemoglobin,[28,31,33,34] and nutritional markers such as albumin,[28] total protein,[31] and total leukocyte count[28] compared to TG. Some studies have pointed out PG had higher postoperative serum iron and vitamin $B_{12}$ levels than TG,[35] and required less vitamin $B_{12}$ supplementation.[33,36,37] However, other studies have not found significant advantages for PG in BMI, albumin, total protein, and total leukocyte count over TG.[34,35,38]

## 3 | SCREENING AND ASSESMENT OF NUTRITION STATUS

### 3.1 | Nutritional risk screening

It is important to carry out early nutritional status screening as preoperative nutritional status is related with postoperative complications, QoL, and survival. While BMI and body weight loss serves as a quick and straightforward initial screening tool, it has its limitations. Specifically, BMI doesn't distinguish between fat mass and lean body weight.[39] This can be misleading for gastric cancer patients who often present obesity together with sarcopenia.[40] The European Society for Medical Oncology (ESMO) recommends following tools for nutritional risk screening[41]: Nutrition Risk Screening 2002 (NRS-2002),[42] Malnutrition Universal Screening Tool (MUST),[43] Malnutrition Screening Tool (MST),[44] and Short Nutritional Assessment Questionnaire (SNAQ)[45] (Table 1).

### 3.2 | Nutritional assessment

Historically serum albumin has been the key biomarker for assessing nutritional status. However, due to its long half-life and

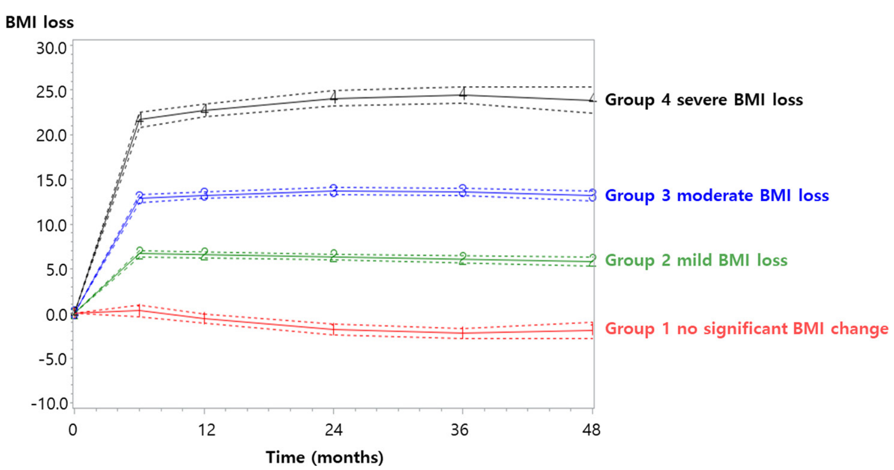


FIGURE 2 Four patterns of weight loss after gastrectomy with 48 months projection of change in BMI.

**TABLE 1** Nutritional screening and assessment tools.

| | Questionnaire components | Anthropometric measurements | Biochemical markers |
|---|---|---|---|
| *Nutritional Screening Tools* | | | |
| Nutrition Risk Screening 2002 (NRS-2002)[42] | Weight loss, change in food intake, comorbidity and severity, age | BMI | |
| Malnutrition Universal Screening Tool (MUST)[43] | Weight loss, acute disease effect | BMI | |
| Malnutrition Screening Tool (MST)[44] | Weight loss, change in food intake due to appetite loss | | |
| Short Nutritional Assessment Questionnaire (SNAQ)[45] | Weight loss, appetite change, use of oral supplement or tube feeding | | |
| *Nutritional Assessment Tools* | | | |
| Mini nutritional assessment (MNA)[51] | Weight loss, food intake, functional capacity | BMI, calf circumference, mid-arm circumference | |
| Patient-Generated Subjective Global Assessment (PG-SGA)[52] | Weight loss, food intake, symptoms, functional capacity, comorbidity | | |
| Prognostic Nutritional Index (PNI)[53] | | Triceps skin fold | Albumin, transferrin, skin test reactivity |
| COntrol NUTritional Score (CONUT)[54] | | | Albumin, total cholesterol, lymphocyte count |
| Elderly Nutritional Indicators for Geriatric Malnutrition Assessment (ENIGMA)[55] | Functional capacity, nutritional history | | Albumin, hemoglobin, total cholesterol, lymphocyte count |

Abbreviation: BMI, body mass index.

lack of specificity, its utility has been under scrutiny.[46] In contrast, prealbumin is favored because of its shorter half-life and its ability to accurately reflect nutritional status.[47] Multiple studies have highlighted the role of prealbumin in predicting both short-term outcomes[48,49] and long-term survival[50] following gastrectomy. Many assessment tools of nutritional status utilize combination of history and biomarkers. Tools such as Mini nutritional assessment (MNA)[51] and Patient-Generated Subjective Global Assessment (PG-SGA)[52] utilize only questionnaires and anthropometric measurements, whereas Prognostic Nutritional Index (PNI),[53] COntrol NUTritional Score (CONUT),[54] and Elderly Nutritional Indicators for Geriatric Malnutrition Assessment (ENIGMA)[55] include biomarkers (Table 1).

## 3.3 | Sarcopenia assessment

Skeletal muscle loss, or sarcopenia, is a key feature of malnutrition which lead to poor outcome and QoL in cancer patients. Above tools are mostly based on body weight loss and BMI, but these do not always reflect skeletal muscle loss.[56] The European Working Group on Sarcopenia in Older People (EWGSOP) recommends gait speed test as the initial screening for individuals exhibiting low physical performance, using a cut-off point of 0.8 m/s. To diagnose sarcopenia, both diminished muscle strength and muscle mass are essential.[57] The former is measured by the gait speed test, handgrip strength test, and forced expiratory volume test,[58] while the latter can be assessed using computed tomography (CT), magnetic resonance imaging (MRI), dual energy X-ray absorptiometry (DXA), and bioimpedance analysis (BIA).[57] Similarly Global Leadership Initiative on Malnutrition (GLIM) criteria include reduced muscle mass by CT, MRI, DXA, or BIA as a phenotypic criterion for diagnosis of malnutrition.[59]

## 3.4 | Prediction models

Preoperative identification of high-risk patients for malnutrition is crucial, as it allows physicians to strategize preoperative nutritional support.[17] Few studies have introduced nomograms aimed to predict malnutrition or sarcopenia in patients undergoing gastrectomy.[17,60] Recently a study by Park et al. took a novel approach by forecasting BMI loss trajectories after gastrectomy using group-based trajectory monitoring, and developed a predictive nomogram for malnutrition at 6 months after gastrectomy.[17] Their analysis showed majority of BMI reduction occurred within the first 6 months and factors contributing to this loss included age, preoperative BMI, preoperative malnutrition, gender, surgical method, type of reconstruction, and adjuvant chemotherapy. The resulting nomogram demonstrated a C-index of 0.91 in the developmental set, and a bootstrap validation score of 0.91, presenting the model's strong capability to accurately forecast malnutrition after gastrectomy.

## 4 | CLINICAL IMPACT OF MALNUTRITION

### 4.1 | Postoperative complications

The nutritional status is a critical independent risk factor for postoperative complications,[49,61–70] where higher rates of infectious complications,[49,63,65,69] wound complication,[66] and medical complications[67,70] have been reported. Nutritional indicators such as prealbumin,[49] sarcopenia,[61–64,67] weight,[66,69] skeletal muscle index (SMI),[70] and BMI[65,68] have been linked with complications after gastrectomy. Preoperative prealbumin less than 18 mg/dL was identified as a risk factor for infectious complications,[49] and correcting preoperative hypoalbuminaemia can improve survival.[69] Moreover, severe postoperative complications rated as Clavien–Dindo grade ≥ IIIa, are more prevalent in malnourished patients[61,62] with extended hospital stay,[64,66] and the rates of non-surgical complications increased with severity of sarcopenia.[67] However, some studies reported no association between malnutrition and postoperative complications.[71,72] These results are summarized in Table 2.

### 4.2 | Chemotherapy tolerance

In advanced-stage patients, poor nutritional status is related to the effect of chemotherapy and cancer progression. Evidence suggests malnutrition leads to poor tolerance, early cessation of chemotherapy,[73] and increased chemotherapy-related adverse events.[74] Moreover, chemotherapy can further exacerbate weight loss and muscle loss[74,75] in patients. Specifically, body weight loss of more than 15% at 1 month after surgery is a risk factor for discontinuation of S-1 chemotherapy,[76] and delayed use of S-1 for more than 6 months is associated with significant loss of skeletal muscle mass.[77] Furthermore, a 91.7% treatment failure rate is observed in patients with lean body mass loss of more than 5% at 6 months.[78] Around 15% of sarcopenic cancer patients have co-existing obesity, which can obscure the low muscle mass by high weight.[79] This masking effect can mislead the calculation of chemotherapy doses based on body surface area, potentially leading to overdosing and toxicity in sarcopenic obese patients. 5-fluorouracil, a commonly used chemotherapy for gastric cancer, poses a risk of skeletal muscle mass loss especially in patients who receive higher doses relative to their body surface area.[80] Therefore, the use of lean body mass to calculate doses should be considered to individualize the dose and minimize the risk of adverse events.

Nutritional support during chemotherapy also plays a critical role in palliative unresectable gastric cancer patients. While the administration of home parenteral nutrition (PN) has shown improvements in nutritional markers like albumin, prealbumin, cholesterol, high-density lipoprotein, and low-density lipoprotein, it did not demonstrate a positive effect on overall survival (OS).[81] Similarly dietary counseling and support did not significantly impact OS, but it was a prognostic factor for time to treatment failure, defined as the duration from start to discontinuation of chemotherapy.[82]

### 4.3 | Survival

Poor survival outcomes are well documented in malnourished patients undergoing gastrectomy.[68,69,83–91] Several nutritional indicators correlate with poor survival outcomes in gastrectomy patients. Among these are BMI,[68,87,90] PNI,[89] SMI,[70,85,88] skeletal muscle area,[83,84] and malnutrition by GLIM criteria.[91] Low preoperative PNI was not only a predictor of OS, but also cancer-related survival and non-gastric cancer-related death.[89] Interestingly, patients with high BMI had better survival compared to normal or low BMI.[68,90,92] Nutritional status after operation was also important, as in malnourished patients BMI increase at 1 year after surgery was an important factor for long-term survival.[92] Surgery induced sarcopenia described as normal patients who became sarcopenic after surgery, was a risk factor for OS and relapse free survival.[70] Non-gastric cancer-related death rate of patients with low postoperative PNI was significantly lower than that of patients with high postoperative PNI, but this difference was only present in stage I disease.[89] In elderly patients age over 75, sarcopenic patients had worse OS after recurrence than non-sarcopenic patients.[86] Segregating patients by stages saw malnutrition exhibiting lower survival in stage III and IV, but mixed findings in stage I and II.[68,83,87] List of studies are summarized in Table 3.

### 4.4 | Quality of life

Gastrectomy alone can affect the QoL of the patients due to financial difficulties, eating restrictions, and body image concerns,[93–95] but combined with malnutrition the impact is greater.[96] There is very little literature on the effect of malnutrition on QoL in patients undergoing gastrectomy, but it is evident that the level of nutrition is a predictor of QoL.[96–98] Study by Lim et al. compared QoL in gastric cancer patients according to nutritional level by PG-SGA, and showed overall health status, physical functioning, fatigue, pain, loss of appetite, reflux, eating restriction, anxiety, and body image are lower in PG-SGA group C.[96] Additionally, NRS-2002 score was an independent predictor of QoL and score below 3 exhibited higher QoL score.[97] Most gastric cancer patients consumed less nutrition daily than the recommended values, and those with better daily nutritional intake exhibited a higher QoL on global symptoms.[98] In these patients, those with poorer functional examination such as gait speed recorded significantly lower scores on most of the function and symptom scales, but most scales improved within 6 months.[99] The fall in QoL is more evident in elderly patients where physical and role functioning is greatly reduced compared to young patients. In patients with age over 70, physical, role, and social functioning are more compromised compared to younger patients. Although these scores improve over 1 year after surgery, there is significant age-specific difference in

**TABLE 2** Impact of malnutrition in postoperative complications after gastrectomy for gastric cancer.

| Author | Publication year | Country | Study design | Sample size | Complication measured | Nutrition index measured | Key findings | Statistical significance |
|---|---|---|---|---|---|---|---|---|
| Pacelli[72] | 2008 | Italy | Single center, retrospective, cohort | 196 | Major infectious, major non-infectious, minor infectious, minor non-infectious | Weight, albumin, BMI | No association between weight loss, BMI, hypoalbuminemia, and postoperative morbidity | $p > 0.05$ in all groups |
| Bae[49] | 2011 | Korea | Single center, prospective, observational | 183 | Infectious, non-infectious | Prealbumin, albumin, BMI | Overall complication rate is higher in low prealbumin group<br>Preoperative prealbumin <18 mg/dL is a risk factor for infectious complications | 52% vs. 24%, $p = 0.005$<br>OR 2.996 95% CI 1.096–8.188, $p = 0.032$ |
| Chen[68] | 2015 | China | Single center, retrospective, cohort | 1249 | Severe complication (Clavien–Dindo grade ≥ IIIa) | BMI | Severe complication is higher in low BMI group than normal and high BMI group | 7.6% vs. 2.6% vs. 3.3%, $p = 0.006$ |
| Fukuda[65] | 2015 | Japan | Single center, retrospective, observational | 800 | SSI (Clavien–Dindo grade ≥ II) | Weight, BMI, SGA Grade C, albumin | SSI rate is higher in malnourished group than well-nourished group<br>SSI grade ≥ IIIb is higher in malnourished group | 35.5% vs. 14.0%, $p < 0.0001$<br>7.9% vs. 1.1%, $p < 0.0001$ |
| Tegels[71] | 2015 | Netherlands | Single center, retrospective, observational | 149 | Severe complication (Clavien–Dindo grade ≥ IIIa) | Skeletal muscle area by BMI cutoff | No association between sarcopenia and postoperative complication | 26.7% vs. 27.0%, $p = 1.00$ |
| Fukuda[61] | 2016 | Japan | Single center, retrospective, observational | 99 | Severe complication (Clavien–Dindo grade ≥ IIIa) | Sarcopenia according to EWGSOP algorithm | Severe complication rate is higher in sarcopenic group compared to non-sarcopenic group<br>Sarcopenia is a risk factor for severe complications | 28.6% vs. 9.0%, $p = 0.029$<br>OR 4.76 95% CI 1.03–24.30, $p = 0.046$ |
| Wang[64] | 2016 | China | Single center, prospective, cohort | 225 | Postoperative complications (Clavien-Dindo grade ≥ II) | Sarcopenia according to EWGSOP algorithm | Severe complication rate is higher in sarcopenic group compared to non-sarcopenic group<br>Sarcopenia is a risk factor for major complications | 43.8% vs. 14.3%, $p = 0.001$<br>OR 5.021 95% CI 2.229–11.313, $p < 0.001$ |
| Huang[67] | 2017 | China | Single center, prospective, observational | 470 | Operative & medical complications | Handgrip strength, gait speed, skeletal muscle area | Medical complication increases with severity of sarcopenia (non-sarcopenic, pre-sarcopenic, sarcopenic, severely sarcopenic) | 18.7% vs. 23.7% vs. 27.7% vs. 68.8% vs. $p < 0.001$ |

(Continues)

TABLE 2 (Continued)

| Author | Publication year | Country | Study design | Sample size | Complication measured | Nutrition index measured | Key findings | Statistical significance |
|---|---|---|---|---|---|---|---|---|
| Zheng[69] | 2017 | China | Single center, prospective, observational | 1976 | Surgical & systemic complications | Weight, BMI, SGA Grade C, albumin | Overall complication rate is higher in malnutrition group than well-nourished group | 21.4% vs. 15.5%, $p = 0.005$ |
| O'Brien[62] | 2018 | Ireland | Single center, retrospective, cohort | 56 | Severe complication (Clavien–Dindo grade ≥ IIIa) | Skeletal muscle area | Sarcopenia is a risk factor for severe complications | OR 3.508 95% CI 1.048–11.739, $p = 0.042$ |
| Tamura[63] | 2019 | Japan | Single center, retrospective, observational | 153 | Postoperative complications (Clavien–Dindo grade ≥ II) | Muscle mass index | Sarcopenia is a risk factor for postoperative infectious complications | OR 4.358 95% CI 1.224–15.721, $p = 0.024$ |
| Lee[66] | 2021 | USA | National, retrospective, cohort | 2088 | Bleeding, infection, wound complications, respiratory failure, shock | Calorie deficiency, sarcopenia, cachexia, weight | Malnutrition is a risk factor for wound complication, postoperative infection, respiratory failure | OR 3.00 95% CI 1.59–5.66, $p < 0.001$<br>OR 2.20 95% CI 1.45–3.34, $p < 0.001$<br>OR 1.93 95% CI 1.29–2.89, $p = 0.002$ |
| Lee[70] | 2021 | Korea | Single center, retrospective, cohort | 1801 | Severe complication (Clavien–Dindo grade ≥ III) | SMI | Pulmonary complication is higher in sarcopenic group than non-sarcopenic group | 2.2% vs. 5.1%, $p < 0.01$ |

Abbreviations: BMI, body mass index; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Old People; OR, odds ratio; SGA, subjective global assessment; SMI, skeletal muscle index; SSI, surgical site infection.

**TABLE 3** Impact of malnutrition on survival after gastrectomy for gastric cancer.

| Author | Publication year | Country | Study design | Sample size | Comparison groups | 5-year OS | HR (95% CI) | Additional findings |
|---|---|---|---|---|---|---|---|---|
| Chen[68] | 2015 | China | Single center, retrospective, cohort | 1249 | Low vs. normal vs. high BMI | 39.2% vs. 50.8% vs. 60.7%, $p<0.001$ | Low: 1.405 (1.102–1.727), $p=0.005$<br>High: 0.764 (0.588–0.993), $p=0.044$ | BMI did not affect OS in stage I and II disease |
| Ejaz[90] | 2015 | USA | Multicenter, retrospective, observational | 775 | Underweight vs. normal, vs. overweight vs. obese BMI | 13.4% vs. 36.0% vs. 47.3 vs. 42.7, $p<0.001$ | Underweight: 1.50 (0.93–2.41), $p=0.10$<br>Overweight: 0.91 (0.66–1.27), $p=0.58$<br>Obese: 1.13 (0.79–1.61), $p=0.51$ | Underweight with low preoperative albumin level has worse OS compared to underweight with normal albumin |
| Lee[92] | 2016 | Korea | Single center, retrospective, observational | 1090 | Low vs. normal vs. high BMI 1 year after operation | 69.1% vs. 74.2% vs. 84.7%, $p<0.001$ | Low: 1.01 (0.72–1.40), $p=0.974$<br>High: 0.64 (0.41–1.02), $p=0.058$ | Postoperative >10% weight loss results worse survival compared to <10% weight loss |
| Migita[87] | 2016 | Japan | Single center, retrospective, observational | 638 | Low vs. normal vs. high BMI | 66.6% vs. 81.3% vs. 79.9%, $p=0.0001$ | Low: 1.797 (1.097–2.943), $p=0.020$<br>High: 1.396 (0.884–2.204), $p=0.153$ | OS is lower in stage I underweight group than in stage I normal and overweight group<br>OS is lower in stage II and III underweight group than in stage II and III normal group |
| Zhuang[83] | 2016 | China | Single center, prospective, cohort | 937 | Sarcopenic vs. non-sarcopenic | 42.6% vs. 69.4%, $p<0.001$ | 1.653 (1.332–2.052), $p<0.001$ | Sarcopenia is risk factor for OS in patients with stage II and III, but not in stage I |
| Zheng[69] | 2017 | China | Single center, prospective, cohort | 1976 | Malnourished vs. non-malnourished | *3-year OS*<br>59.1% vs. 75.0%, $p<0.001$ | 1.211 (1.01–1.452), $p=0.039$ | Preoperative correction of hypoalbuminaemia improve 3-year OS in stage II and III |
| Kuwada[84] | 2018 | Japan | Single center, retrospective, observational | 491 | Sarcopenic vs. non-sarcopenic | 56% vs. 72%, $p=0.0002$ | 1.46 (1.01–2.09), $p=0.0454$ | Sarcopenia with comorbidity is a risk factor for non-gastric cancer related death |
| Nishigori[85] | 2018 | Japan | Single center, retrospective, cohort | 177 | Sarcopenic vs. non-sarcopenic | 48% vs. 68%, $p=0.013$ | 2.00 (1.24–3.24), $p=0.005$ | Different sarcopenia cutoffs reported in the literature present differences in OS |
| Yamamoto[86] | 2019 | Japan | Single center, retrospective, cohort | 90 | Elderly sarcopenic vs. non-sarcopenic | *3-year OS*<br>Non-sarcopenic>sarcopenic, $p<0.0001$ | 2.92 (1.14–7.75), $p=0.025$ | Sarcopenic elderly patients have worse OS after recurrence than non-sarcopenic elderly patients |
| Lee[70] | 2021 | Korea | Single center, retrospective, cohort | 1801 | Preoperative normal vs. pre-sarcopenic vs. sarcopenic<br>Postoperative normal vs. pre-sarcopenic vs. sarcopenic | 93.7% vs. 90.3% vs. 86.0%, $p<0.001$<br>94.7% vs. 90.8% vs 85.7%, $p<0.001$ | Pre-sarcopenic: 1.21 (0.85–1.73), $p=0.29$<br>Sarcopenic: 1.16 (0.80–1.67), $p=0.43$<br>Pre-sarcopenic: 1.36 (0.92–1.99), $p=0.12$<br>Sarcopenic: 1.42 (0.97–2.08), $p=0.07$ | SMI loss is an independent risk factor for OS in entire cohort and in men<br>Surgery induced sarcopenia is an independent risk factor for OS and RFS in entire cohort and in men |
| Sakurai[88] | 2021 | Japan | Single center, retrospective, cohort | 1054 | Sarcopenic vs. non-sarcopenic | 62.9% vs. 79.3%, $p<0.001$ | 1.96 (1.42–2.68), $p<0.001$ | SMI is not an independent predictor of OS and CSS in female patients |

(Continues)

**TABLE 3** (Continued)

| Author | Publication year | Country | Study design | Sample size | Comparison groups | 5-year OS | HR (95% CI) | Additional findings |
|---|---|---|---|---|---|---|---|---|
| Matsui[91] | 2022 | Japan | Single center, retrospective, cohort | 512 | Normal vs. moderate vs. severe malnutrition | Normal>moderate>severe, $p<0.001$ | Moderate: 1.689 (1.107–2.576), $p=0.015$<br>Severe: 1.918 (1.275–2.884), $p=0.002$ | Long term OS, CSS, OCS, and DFS are lower in moderate and severe malnutrition compared to normal group |

Abbreviations: BMI, body mass index; CI, confidence interval; CSS, cancer-specific survival; DFS, disease-free survival; HR, hazard ratio; OCS, other-cause survival; OS, overall survival; RFS, relapse-free survival; SMI, skeletal muscle index.

physical functioning even at 1 year after surgery.[100] For most patients, functions and symptoms generally revert to pre-surgery levels around 6 months after surgery. However, as many as 35% of patients may never return their QoL levels to pre-surgery levels.[101]

## 5 | NUTRITIONAL SUPPORT IN GASTRIC CANCER PATIENTS

Managing nutrition in cancer patients can be challenging, especially if the patient is in a cachectic state. This requires a multidisciplinary approach and a comprehensive assessment of the patient's status. Nutritional support is provided through dietary counseling, medications, enteral nutrition (EN), oral nutrition supplements (ONS), or PN based on the patient's status. EN involves nutrient delivery via gastric or jejunal feeding tube in the form of solution. ONS provide additional nutrition in the form of powder or solution for patients who cannot meet their energy requirements with food alone. PN involves intravenous delivery of nutrients, and there are two types. Total parenteral nutrition (TPN) provides the sole nutritional support for patients who are unable to obtain nutrients by any other method, while supplemental parenteral nutrition (SPN) supplements existing nutritional intake.

### 5.1 | Preoperative nutritional support

In any case of malnutrition, those who cannot maintain more than 50% of the recommended intake for over 7 days are recommended for nutritional support of some form.[102] Studies that have investigated the perioperative effect of ONS have mostly failed to produce meaningful results in weight, nutrition biomarkers, and complication rates,[103–105] but was selectively beneficial in preventing complications in PG-SGA grade C patients.[106] A pilot study for preoperative exercise programme combined with ONS in sarcopenic patients showed improvement in handgrip strength, gait speed, and SMI, with some patients becoming non-sarcopenic after the intervention.[107] These findings may have resulted from ONS tolerance issues, as 50.8% of patients found it difficult to consume the full prescribed amount even at 1 month after the operation.[106]

Similar results were seen in preoperative PN as it failed to produce benefits in short-term clinical outcomes[108] and nutrition indexes,[109] but was selectively beneficial in reducing complication rates in sarcopenic patients with hypoalbuminaemia.[110] One study demonstrated duration of preoperative nutritional support is important, as the severity of infectious complications decreased with increasing duration of preoperative support, but this study did not control the duration, route, or the calorie intake.[65]

Patients with gastric outlet obstruction often have very poor nutritional status, and one of the methods of nutritional support is through EN tube feeding. Two studies have demonstrated the advantages of preoperative tube EN in this group of patients by increasing weight and nutritional biomarkers.[111,112] The effects of preoperative nutritional support are summarized in Table 4.

**TABLE 4** Effect of preoperative nutritional support in gastric cancer patients.

| Studies | Publication year | Country | Study design | Sample size | Time of intervention | Nutritional intervention details | Comparison group details | Key findings |
|---|---|---|---|---|---|---|---|---|
| *Oral nutrition supplements* | | | | | | | | |
| Fujitani[103] | 2012 | Japan | Single center, RCT | 244 | Preoperative, for 5 days before operation | Impact® (Ajinomoto Pharmaceutical Company, Tokyo, Japan) & standard diet | Standard diet | ONS failed to demonstrate advantage in complication rates (30.8% vs 26.1%, $p > 0.05$) |
| Ida[105] | 2017 | Japan | Multicenter, RCT | 124 | Perioperative, for 7 days before and 21 days after operation | ProSure® (Abbott Japan, Tokyo, Japan) 600 kcal with 2.2 g eicosapentaenoic acid & standard diet | Standard diet | ONS failed to prevent weight loss compared to standard diet at 1 month (8.7% vs. 8.5%, $p = 0.818$) and 3 months after operation (13.5% vs 13.0%, $p = 0.529$) |
| Kong[106] | 2018 | Korea | Single center, RCT | 127 | Perioperative, for 2 weeks before operation and for 2 weeks from POD5 | Ensure® powder (Abbott Laboratories, Lake Bluff, IL) 500 kcal & standard diet | Standard diet | ONS failed to demonstrate advantage in weight, total protein, albumin, prealbumin, and hemoglobin ($p > 0.05$)<br>ONS prevents complications in PG-SGA grade C patients (22.7% vs. 57.1%, $p = 0.036$) |
| He[104] | 2022 | China | Single center, RCT | 67 | Preoperative, for 7 days before operation | Preoperative ONS | Preoperative dietary advice only | ONS failed to demonstrate advantage in postoperative albumin, prealbumin, total protein, total lymphocyte count |
| *Parenteral nutrition* | | | | | | | | |
| Bozzetti[109] | 2000 | Italy | Single center, RCT | 90 | Perioperative TPN, for 10 days before and 9 days after operation | Freamine III (Baxter, Kendall McGaw Laboratories Inc, Irvine, CA) & Intralipid 20% (Kabi Pharmacia AB, Stockholm, Sweden) | No preoperative support. Postoperative IV fluid only | Complication rate is lower in TPN group compared to control group (37% vs. 57%, $p = 0.03$)<br>Weight, albumin, prealbumin, transferrin was not different after perioperative TPN ($p > 0.05$) |
| Xu[108] | 2021 | China | Single center, retrospective, observational | 368 | Preoperative, SPN for 3 to 7 days before operation | Preoperative SPN 10 kcal/kg/day | Standard diet | No improvement of short-term clinical outcome after short preoperative SPN ($p > 0.05$) |
| Huang[110] | 2022 | China | Single center, retrospective, observational | 428 | Preoperative, SPN for 3 to 7 days before operation | Preoperative SPN | Standard diet | Short preoperative SPN is beneficial in reducing postoperative surgical complications in sarcopenic patients with albumin levels <35 g/L ($p = 0.025$) |
| *Enteral nutrition for obstructive gastric cancer* | | | | | | | | |
| Chen[111] | 2017 | China | Single center, RCT | 68 | Preoperative, EN for 14 days vs preoperative TPN for 7 days | Nutrison (Nutricia) 1500-2000 mL/day via nasojejunal tube | TPN | From admission (53.97 kg vs. 52.33 kg, $p = 0.405$) to preoperative day (56.35 kg vs. 52.81 kg, $p = 0.046$) weight increased in EN group but not in TPN group<br>Albumin, prealbumin, and transferrin in EN group increased but not in TPN group |

(Continues)

**TABLE 4** (Continued)

| Studies | Publication year | Country | Study design | Sample size | Time of intervention | Nutritional intervention details | Comparison group details | Key findings |
|---|---|---|---|---|---|---|---|---|
| Izumi[112] | 2022 | Japan | Single center, retrospective, observational | 50 | Preoperative, by median 10 days before operation | Omega-3 fatty acid enriched EN via nasojejunal tube | Not applicable | Prealbumin increased after preoperative EN (10.5%, IQR 0.63–38.2, $p<0.0001$)<br>EN administration period is longer in the prealbumin elevated group than that in non-elevated group (13 days vs. 7 days, $p=0.007$) |

Abbreviations: EN, enteral nutrition; IQR, interquartile range; IV, intravenous; ONS, oral nutrition supplements; POD, postoperative day; RCT, randomized controlled trial; SPN, supplemental parenteral nutrition; TPN, total parenteral nutrition.

### 5.2 | Postoperative nutritional support

The beneficial effects of tube feeding were apparent after TG, as postoperative levels of albumin, prealbumin, and hemoglobin was higher following TG. However, these effects were not as evident after DG.[113] A novel study investigated the effectiveness of nocturnal home EN after TG. This strategy was effective in reducing postoperative weight loss and improving prealbumin levels at 3 and 6 months after surgery.[114]

Postoperative ONS have demonstrated some advantages in reducing weight loss after surgery, with benefits observed a few months after operation.[115–119] Specifically, significant weight loss reduction was more apparent following TG compared to DG.[115–117] In terms of nutritional biomarkers, postoperative ONS resulted in elevated levels of albumin, total protein, and cholesterol.[120] The amount of ONS consumed after surgery is crucial for maintaining weight. Consumption exceeding 200 mL of ONS was effective in preventing weight loss at both 3 months[118] and 12 months after the operation.[119] However, studies report mixed findings regarding long-term effects. While one study showed the difference in weight loss between patients on ONS and standard diet diminished within 1 year after operation,[119] another study demonstrated significant differences in weight reduction 1 year after operation.[117]

There are little studies on the effect of PN after gastrectomy. Administering TPN following surgery resulted in reduced immediate weight loss, and patients were able to maintain their weight more effectively after discharge.[121] Additionally, postoperative SPN was found to enhance psychological status, QoL, immune function, and nutritional biomarkers such as albumin, prealbumin, and hemoglobin.[122] The initiation time of SPN influenced the rate of nosocomial infections. Starting SPN early on postoperative day 3 was associated with a lower infection rate compared to commencing SPN late on postoperative day 8.[123]

Other modalities of support include gastrointestinal hormone therapy and dietary counseling. Studies focusing on ghrelin, a hormone produced in the stomach that stimulates appetite, have shown significant findings. After a gastrectomy, ghrelin levels typically decrease, leading to reduced appetite.[124] Research indicates that administering ghrelin injections for 10 days after surgery can minimize weight loss compared to a placebo group.[125] Following gastrectomy, changes in the gastric capacity and function necessitate adjustments in patients eating patterns. Nutritional support team (NST) can provide dietary education, monitor patient progress, and create personalized dietary plans. Publications have documented positive effects of NST involvement, including improvements in postoperative weight retention,[126,127] dietary intake,[128] and skeletal muscle retention.[127] The impact of these postoperative nutritional support strategies is detailed in Table 5.

### 5.3 | Nutritional support for postoperative complication

Some studies on postoperative EN have concentrated on patients unable to consume food by mouth due to complications. In cases

**TABLE 5** Effect of postoperative nutritional support in gastric cancer patients.

| Studies | Publication year | Country | Study design | Sample size | Time of intervention | Nutritional intervention details | Comparison group details | Key findings |
|---|---|---|---|---|---|---|---|---|
| *Enteral nutrition* | | | | | | | | |
| Komatsu[114] | 2022 | Japan | Single center, prospective, cohort. | 46 | From POD1 to 3 months post operation | Night continuous EN Elental® (EA Pharma Co, Tokyo, Japan) via jejunostomy tube | Standard diet | Night EN reduce weight loss at 3 months (4.0% vs 15.2%, $p<0.0001$) and 6 months (7.7% vs. 17.7%, $p<0.0001$)<br>Prealbumin is higher in night EN at 3 months ($p<0.0001$) and 6 months ($p=0.0037$) than control group |
| Li[113] | 2023 | China | Single center, retrospective, cohort | 715 | After operation | EN via jejunostomy tube | Patients without jejunostomy tube | Albumin, prealbumin, and hemoglobin is higher in intervention group 1 month after TG ($p<0.05$) |
| *Oral nutrition supplements* | | | | | | | | |
| Imamura[116] | 2016 | Japan | Multicenter, RCT | 112 | For 6–8 weeks after starting standard diet | Elental® (Ajinomoto Pharmaceuticals, Tokyo, Japan) 300 kcal/day & standard diet | Standard diet | ONS reduce postoperative weight loss at 6–8 weeks compared to standard diet (4.86% vs 6.60%, $p=0.047$)<br>ONS reduce postoperative weight loss after TG (5.03% vs. 9.13%, $p=0.012$) |
| Hatao[115] | 2017 | Japan/ Taiwan | Multicenter, RCT | 113 | From starting standard diet to 12 weeks after discharge | Anom® (Otsuka, Japan) 400 kcal/day & standard diet | Standard diet | Weight is better maintained in ONS group 3 months after TG compared to control group (88.5% vs. 85.6%, $p=0.03$) |
| Kobayashi[118] | 2017 | Japan | Multicenter, prospective, cohort | 82 | Started within POD7 for 3 months | Racol® NF (Otsuka Pharmaceutical Factory, Japan) & standard diet | Standard diet | Adherence to ONS therapy result in smaller weight loss 3 months after gastrectomy (6.1% vs. 10.4%, $p<0.001$) |
| Kong[120] | 2017 | Korea | Multicenter, RCT | 174 | From discharge for 8 weeks | Encover® (EN Otsuka Pharmaceutical, Hanamaki City, Japan) & standard diet | Standard diet | ONS failed to reduce weight loss at 8 weeks after discharge (6.23% vs. 6.67%, $p=0.599$)<br>Total protein, cholesterol, and albumin was higher in EN group after discharge ($p<0.05$) |
| Kimura[117] | 2019 | Japan | Multicenter, RCT | 106 | For 6–8 weeks after operation | Elental® (EA Pharma Co., Tokyo, Japan) 300 kcal/ day & standard diet | Standard diet | ONS result lower body weight loss at 1 year after TG (9.66% vs. 15.11%, $p=0.015$) |

(Continues)

TABLE 5 (Continued)

| Studies | Publication year | Country | Study design | Sample size | Time of intervention | Nutritional intervention details | Comparison group details | Key findings |
|---|---|---|---|---|---|---|---|---|
| Miyazaki[119] | 2021 | Japan | Multicenter, RCT | 880 | From 3 days after starting standard diet for 12 weeks | Racol® NF (Otsuka Pharmaceuticals Factory, Tokyo, Japan) 400 kcal/day & standard diet | Standard diet | Weight loss at 3 months is lower in ONS group than control group (7.1% vs. 8.5%, $p=0.0011$)<br>Weight loss difference is not significant at 1 year after operation (9.3% vs. 9.8%, $p=0.37$) |
| *Parenteral nutrition* | | | | | | | | |
| Ryan[121] | 2007 | Ireland | Single center, retrospective, observational | 90 | From POD1 until starting standard diet | TPN | IV fluid only | Immediate postoperative weight loss (4.6% vs. 6.6%, $p=0.023$) and weight loss at follow-up (4.9% vs. 10.5%, $p=0.014$) is better in TPN group |
| Jin[122] | 2018 | China | Single center, RCT | 80 | From POD1 for 4–8 days | 1 L SPN (Olimel peri 2.5%®, Baxter, Germany) & vitamin (Cernevit®, Baxter, Germany) & trace elements (Inzolen® Köhler Pharma, Germany) | 1 L isotonic fluid (E153, Berlin-Chemie AG, Berlin, Germany) | Albumin, prealbumin, and hemoglobin is higher in intervention group ($p<0.05$) |
| Gao[123] | 2022 | China | Multicenter, RCT | 229 | Early vs. late SPN for minimum of 5 days until 80% energy target met by EN | EN from POD1 & early SPN from POD3 | EN from POD 1 & late SPN from POD 8 | Early SPN received more energy between POD 3 and 7 compared to the late SPN group (26.5 kcal/kg/day vs. 15.1 kcal/kg/day, $p=0.001$)<br>Early SPN had fewer nosocomial infections compared to late SPN group (8.7% vs. 18.4%, $p=0.04$) |
| *Gastrointestinal hormone* | | | | | | | | |
| Adachi[125] | 2010 | Japan | Single center, RCT | 20 | After starting standard diet | IV infusion of synthetic human ghrelin (3 μg/kg) twice daily for 10 days | Placebo (IV saline) twice daily for 10 days | Intervention group had smaller weight loss ($p=0.044$), improved appetite ($p=0.032$), and food intake ($p=0.030$) than the placebo group |

TABLE 5 (Continued)

| Studies | Publication year | Country | Study design | Sample size | Time of intervention | Nutritional intervention details | Comparison group details | Key findings |
|---|---|---|---|---|---|---|---|---|
| *Dietary counseling* | | | | | | | | |
| Kim[128] | 2014 | Korea | Single center, RCT | 48 | On the day of discharge (T1) and 1 (T2), 2 (T3) and 6 (T4) weeks after discharge | Two 1-hour face to face sessions (T1&T2) & two 20-minute telephone counseling sessions (T3&T4) | Inpatient group education, individual education, discharge education | Intervention did not improve weight, BMI, or muscle mass ($p > 0.05$), but improved functional status and dietary intake ($p < 0.05$) |
| Chen[126] | 2022 | China | Single center, retrospective, observational | 146 | Inpatient period | NST-driven individualized nutrition support plan | Conventional nutrition support | NST reduced proportion of underweight BMI patients at 1 month after operation ($p < 0.05$) |
| Takata[127] | 2023 | Japan | Single center, retrospective, observational | 93 | Before operation, before discharge, at postoperative 1, 3, 6, and 12 months | Education on post gastrectomy syndrome, dietary advice, ONS when necessary, body composition measurement | Nutrition counseling before discharge | Weight loss is lower in intervention group at 1 (−6.2% vs. −7.9%, $p = 0.005$), 6 (−7.8% vs. −12.3%, $p = 0.001$), and 12 months (−7.9% vs. −13.2%, $p < 0.05$)<br>Skeletal muscle loss was lower at 12 months (−5.3% vs. −12.8%, $p = 0.002$) |

Abbreviations: BMI, body mass index; EN, enteral nutrition; IV, intravenous; NST, nutritional support team; ONS, oral nutrition supplements; POD, postoperative day; RCT, randomized controlled trial; SPN, supplemental parenteral nutrition; TG, total gastrectomy; TPN, total parenteral nutrition.

of oesophagojejunal fistula following TG, complete closure was achieved on days 8, 14, and 25 for three patients after initiating EN tube feeding.[129] In patients with anastomosis leakage receiving EN tube feeding, it was observed that the white blood cell count and C-reactive protein levels were higher in the PN group on days 7, 10, and 15 following the diagnosis of anastomosis leakage. This resulted in a longer duration of intravenous antibiotic administration. However, there was no significant difference in the time taken to commence an oral diet or the length of postoperative hospital stay.[130]

## 6 | CONCLUSION

Malnutrition significantly impacts gastric cancer patients, presenting in forms like cachexia and sarcopenia. Various tools and models have been developed to screen and assess the nutritional status, providing physicians with a framework for early identification of at-risk patients and ensuring timely interventions. It is important to provide adequate perioperative nutritional support, specifically tailored for those identified as malnourished, to avoid complication, improve QoL, and potentially improve survival. Future studies should focus on developing evidence for optimal nutritional interventions, and exploring the long-term impact of combined nutritional and rehabilitative support in this patient population.

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### ORCID

*Min Kyu Kang* https://orcid.org/0000-0001-5816-5877

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