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CLINICAL NUTRITION RESEARCH

Nutritional Care of Gastric Cancer Patients with Clinical Outcomes and Complications: A Review

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The incidence and mortality of gastric cancer have been steadily decreased over the past few decades. However, gastric cancer is still one of the leading causes of cancer deaths across many regions of the world, particularly in Asian countries. In previous studies, nutrition has been considered one of significant risk factors in gastric cancer patients. Especially, malnourished patients are at greater risk of adverse clinical outcomes (e.g., longer hospital stay) and higher incidence of complications (e.g., wound/infectious complications) compared to well-nourished patients. Malnutrition is commonly found in advanced gastric cancer patients due to poor absorption of essential nutrients after surgery. Therefore, nutritional support protocols, such as early oral and enternal feeding, have been proposed in many studies, to improve unfavorable clinical outcomes and to reduce complications due to delayed application of oral nutritional support or parental feeding. Also, the supplied with enternal immune-enriched diet had more benefits in improving clinical outcomes and fewer complications compared to a group supplied with control formula. Using nutritional screening tools, such as nutritional risk index (NRI) and nutritional risk screening (NRS 2002), malnourished patients showed higher incidence of complications and lower survival rates than non-malnourished patients. However, a long-term nutritional intervention, such as nutritional counseling, was not effective in the patients. Therefore, early assessment of nutritional status in patients using a proper nutritional screening tool is suggested to prevent malnutrition and adverse health outcomes. Further studies with numerous ethnic groups may provide stronger scientific evidences in association between nutritional care and recovery from surgery in patients with gastric cancer.

Key Words: Gastric cancer, Nutrition, Clinical outcome, Complication, Review

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Introduction

Over the past few decades, the prevention of gastric cancer has been considered as one of the most important aspects of cancer control strategy due to high incidence and low survival rates [1,2]. As reported by the GLOBOCAN in 2012 [3], gastric cancer is the third leading cause of cancer deaths (8.8% of total cancer deaths) worldwide. The incidence was 952 per 100,000 population in both sexes, and age-standardized incidence rate was about twice as high in male as it was in female (621 and 320 per 100,000, respectively). The mortality rate of gastric cancer is highest in Eastern Asia (mainly in China) (24% and 9.8% in male and female, respectively), whereas the rate is lowest in North America (2.8% and 1.5%, respectively). Also, 5-year survival rate among gastric cancer patients is still low across many regions worldwide [4,5]. In Korea, the incidence of gastric cancer accounted for 13.8% in both sexes, which was the second highest of all cancer sites in 2012 (e.g., 18.5% and 9.0% in male and female, respectively) [6].

Insufficient nutrient absorption may cause severe weight loss, particularly in patients with advanced cancer stage after surgery [7]. These patients are at a high risk of malnourished status and may increase the risk of complications due to poor absorption of essential nutrients (e.g., vitamin B_{12}). Malnutrition, defined as alteration in nutritional status, can negatively influence the capacity of defensive system in our body and may cause adverse clinical manifestations [8]. Adverse clinical outcomes are commonly seen in malnourished patients, such as increased length of hospital stay and high incidence of complications, morbidity, and/or mortality [9-11]. Therefore, effective nutritional intervention and/or assessment may play a significant role in early detection and screening of malnourished patients to promote recovery of cancer-associated treatment and to improve further prognosis [12]. The purpose of this review is to evaluate the effects of nutritional care on clinical outcomes and complication of gastric cancer by systemic review of relevant literatures.

Methods

A literature search was conducted through PubMed for articles published between January 1st, 1995 and December 31st, 2015. The keywords were searched for the following terms: '(gastric OR gastric cancer) AND (gastrectomy OR gastric cancer surgery) AND (diet OR nutrition).' A total of 1,509 studies were shown searching with the key words (Figure 1). After screening the title and abstract of articles, articles which contain other than gastric cancer and/or gastrectomy were excluded (n = 805). Of the full-text articles (n = 704), additional articles were excluded due to following reasons: 1) studies not relevant to gastric cancer patients with nutritional care (e.g., oral, enternal/parental feeding, and nutritional intervention and screening tool) (n = 582), 2) results not relevant to clinical outcomes (e.g., hospital stay, morbidity, and mortality, etc.) and/or complications (n = 39), 3) studies evaluated only experimental group (n = 3), 4) studies evaluated other than humans (n = 8), 5) languages other than English (n = 20), and 6) review and meta-analysis (n = 34). Three articles were additionally included by following references of other articles. Through this selection of eligible studies, final 21 studies were identified for this review. Considering geological regions, there were 17 studies identified from Asian countries (e.g., China, Japan, Korea, and Singapore) and 4 studies from Europe (e.g., Spain, U.K., Poland, and Italy).

Results

In gastric cancer patients, the effectiveness of nutritional

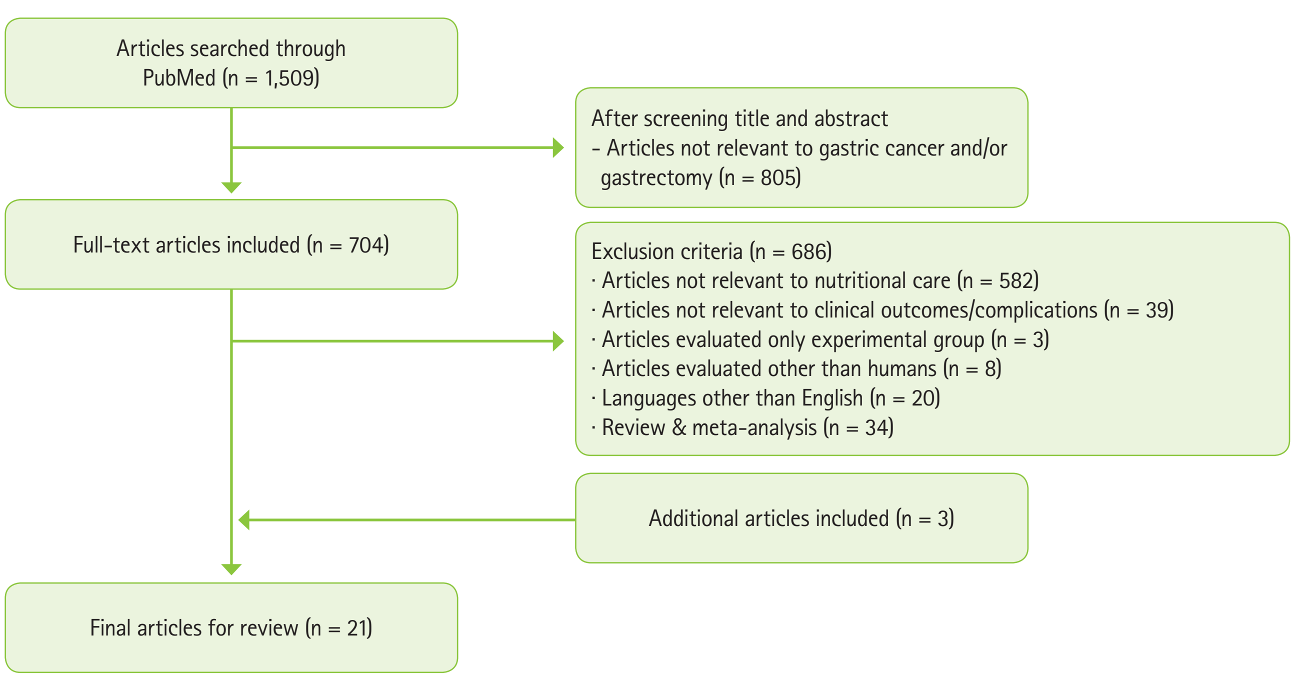

Figure 1. Selection process for eligible studies.

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feeding (e.g., oral and enternal/parental feeding), intervention (e.g., nutritional counseling), and screening tools (e.g., nutritional risk index [NRI] and nutritional risk screening [NRS 2002]) were evaluated to find association with gastric cancer. Each method of nutritional care was compared between experimental and control groups in several types of studies to find differences in clinical outcomes and complications.

The effects of preoperative oral feeding

The effects of immunonutrition in patients before surgery were evaluated by comparing early postoperative days (POD) (Table 1). Well-nourished patients given with 1,000 mL/day of preoperative oral supplementation in the form of an immune-enriched enteral feed (Impact®, Ajinomoto Pharmaceutical Company, Tokyo, Japan) added to normal diet for 5 consecutive days before surgery showed no significant differences in postoperative outcomes compared to a group with regular diet [13]. In other study, patients given with preoperative oral immunonutrition (e.g., oral immune-enhanced formulas supplemented with arginine, ribonucleic acid [RNA] and omega-3 fatty acids) for 7 consecutive days before surgery had significantly shorter duration of systemic inflammatory response syndrome (SIRS) (0.77 [± 0.90]/1.34 [± 1.45] days as experimental vs. control group, p = 0.04), and fewer infectious complications (N = 2 [7%]/8 [28%], p = 0.039), such as infection of incisional wound and effusion (N = 1 [3%]/2 [7%]), respiratory tract infection (N = 1 [3%]/2 [7%]), abdominal cavity empyema and effusion (N = 0 [0%]/3 [10%]), and catheter infections (N = 0 [0%]/1 [3%]) compared to a group with standard formulas [14].

The effects of postoperative oral feeding

The effects of early and late oral feeding (EOF/LOF) in surgical patients were compared on postoperative days (Table 1). Patients with EOF had shorter duration of hospital stay (days) (18.5 [± 5.9]/21.7 [± 8.8], p = 0.02 [15]; 6.28 [± 1.26]/7.69 [± 1.53], p = 0.048 [16]; 8.03 [± 1.43]/9.97 [± 2.07], p < 0.001 [17]; 7.2 [± 1.7]/8.5 [± 2.9], p < 0.044 [18]; 7.4 [± 1.9]/8.9 [± 4.0], p = 0.004 [19]; 7/8, p < 0.001 [20]) and time until flatus (days) (2.06 [± 1.47]/3.56 [± 1.04], p = 0.044 [16]; 1.96 [± 0.58]/2.97 [± 0.66], p < 0.001 [17]; 1.9 [± 1.2]/2.9 [± 0.8], p = 0.036 [18]), less number of hospital re-admission rate (N = 1 [4%]/3 [12%], p = 0.047 [18]), and surgical complications (N = 27 [15%]/40 [24%], p = 0.027; abdominal fluid collection [N = 8/20, p = 0.008]) and general complications (N = 15 [8%]/38 [23%], p < 0.001; pneumonia [N = 9/24, p < 0.003] and respiratory failure [N = 6/17, p = 0.009]) [20] compared to a group with LOF. Oral enternal nutrition for surgical patients was also effective in reducing hospital stay (23.1 [± 7.2]/27.6 [± 4.7] days, p = 0.034) [21].

The effects of enternal and parental feeding

The effects of enternal and parental feeding were compared by assessing early postoperative outcomes (Table 2). Patients with early enternal nutrition (EEN) showed significantly shorter hospital stay (16.2 [± 3.6]/19.7 [± 4.5] days, p < 0.001) and time until flatus (2.2 [± 0.3]/3.7 [± 0.5] days, p < 0.001 [22]), whereas no significant differences were found between EEN and total parental nutrition (TPN) [23]. Compared to traditional perioperative treatment (TP) (e.g., nasoenteral feeding tube and postoperative intravenous infusion), hospital stay (7.73 [± 2.13]/9.77 [± 1.76] days, p = 0.002), time until flatus (78.8 [± 9.3]/85.3 [± 8.4] hours, p = 0.011), and duration of fever (80.2 [± 6.0]/88.1 [± 8.1] hours, p = 0.012) were also shorter in patients with EEN [24].

The effects of enternal immune-enriched diet (ID) and control formula were compared postoperatively (Table 2). Surgical patients given with ID (e.g., formula supplemented with arginine, omega-3 fatty acids and RNA) had significantly shorter hospital stay (13/15 days, p = 0.02) and fewer postoperative complications, such as suture failure (N = 0 [0%]/5 [16.6%], p = 0.03), and wound-healing (N = 0 [0%]/8 [26.7%], p = 0.005), infectious (N = 2 [6.7%]/9 [30%], p = 0.01) and global complications (N = 4 [13.3%]/13 [43.3%], p = 0.01) compared to a group given with isocaloric-isonitrogenous formula [25]. These findings were also similar to other study in hospital stay (e.g., shortened hospital stay (12.7 [± 2.3]/15.9 [± 3.4] days, p = 0.029) and duration of SIRS (1.1 [± 0.89]/2.2 [± 1.02] days, p = 0.036), and fewer infectious complications (N = 4 [7.4%]/11 [20%], p = 0.041), such as wound (N = 1 [1.8%]/3 [5.4%]), respiratory tract (N = 2 [3.7%]/5 [9%]), and urinary tract infection (N = 1 [1.8%]/2 [3.6%]), sepsis (N = 0 [0%]/1 [1.8%]), and anastomotic leakage (N = 2 [3.7%]/4 [7.3%], p = 0.045) [26]. However, both nutritional intervention groups did not show significant differences in mortality.

The differences between PN and other feeding types were compared postoperatively (Table 2). Surgical patients given with PN showed significantly less weight loss (-3.8/-5.2 kg, p = 0.008) [27] and fewer total complications (N = 1/6, p = 0.033) [28] compared to a group with intravenous fluids (IVF) and soybean oil.

Table 1. The effects of oral feeding on clinical outcomes and complications in gastric cancer patients

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Preoperative							
Fujitani et al. (2012) Japan [13]	RCT (Feb. 2006 -Dec. 2009)	127/115 (ID/CT) ID (Impact® added to normal diet for 5 days before surgery)	ID (64, median) (range: 26-78) CT (65, median) (range: 30-79)	Gastric adeno-carcinoma (T1-T4)	1) Hospital stay (days) - ID (18 [9-85]) - CT (17 [10-88]) - p = 0.395 2) Re-operation - ID (0 [0]) - CT (0 [0]) 3) Mortality - ID (0 [0]) - CT (0 [0])	1) Any complication - abdominal abscess - pancreatic fistula - anastomotic leakage - wound infection or dehiscence - drain infection - pneumonia - venous catheter infection - pleural effusion - postoperative bleeding - Ileus 2) SIRS	1) 37 (30.8)/29 (26.1); p = 0.468 - 11 (9.2)/7 (6.3); p = 0.469 - 8 (6.7)/7 (6.3); p = 1.000 - 3 (2.5)/3 (2.7); p = 1.000 - 13 (10.8)/8 (7.2); p = 0.369 - 3 (2.5)/1 (0.9); p = 0.623 - 5 (4.2)/0 (0); p = 0.061 - 2 (1.7)/1 (0.9); p = 1.000 - 1 (0.8)/1 (0.9); p = 1.000 - 3 (2.5)/0 (0); p = 0.248 - 2 (1.7)/1 (0.9); p = 1.000 2) 46 (38.3)/34 (30.6); p = 0.268
Okamoto et al. (2009) Japan [14]	RCT (Apr. 2005-July. 2007)	30/30 (ID/CT) ID (formulas supple-mented with arginine, RNA, & ω-3 fatty acids for 7 days before surgery)	ID (66.9 ± 11.5) CT (70.9 ± 13.2)	Gastric carci-noma (I-IV)	1) Hospital stay (days) - ID (23.8 ± 16.6) - CT (25 ± 10.6) - p = 0.22	1) Infectious complications - infection of incisional wound/effusion - respiratory tract infection - abdominal cavity empyema/effusion - catheter infection 2) Non-infectious complications - cardiac dysfunction - intestinal obstruction - edematous of anastomosis - bleeding 3) SIRS (days)	1) 2 (7)/8 (28); p = 0.039 - 1 (3)/2 (7) - 1 (3)/2 (7) - 0/3 (10) - 0/1 (3) 2) 4 (13)/4 (13); p = 1.000 - 0/1 (3) - 1 (3)/0 - 2 (7)/3 (10) - 1 (3)/0 3) 0.77 (± 0.90)/1.34 (± 1.45); p = 0.04
Postoperative							
Hirao et al. (2005) Japan [15]	RCT (Nov. 1999-Nov. 2002)	53/50 (EOF/CR)	EOF (62 ± 10) (range: 35-82) CR (61 ± 13) (range: 29-85)	Gastric carci-noma (Ia, Ib)	1) Hospital stay (days) - EOF (18.5 ± 5.9) - CR (21.7 ± 8.8) - p = 0.02 2) Weight loss (kg) - EOF (-3.7 ± 1.6) - CR (-4.4 ± 2.2) - p = 0.07	1) Vomiting and postprandial pain 2) Fever 3) Anastomotic leakage 4) Intra-abdominal abscess 5) Ileus 6) Intra-abdominal bleeding 7) Pneumonia 8) Lymphorrhea 9) Anorexia 10) Constipation	1) 8 (15)/8 (16); ns 2) 7 (13)/4 (8); ns 3) 0/1; ns 4) 1/1; ns 5) 0/1 (2); ns 6) 1 (2)/0; ns 7) 0/1 (2); ns 8) 1/0; ns 9) 1/0; ns 10) 0/1 (2); ns

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Table 1. Continued

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Postoperative							
Hong et al. (2014) China [16]	RCT (Oct. 2011-Mar. 2013)	40/44 (EOF/LOF)	EOF (55.4 ± 11.2) LOF (52.1 ± 10.3)	pTNM (I-IV)	1) Hospital stay (days) - EOF (6.28 ± 1.26) - LOF (7.69 ± 1.53) - p = 0.048 2) Time until flatus (days) - EOF (2.06 ± 1.47) - LOF (3.56 ± 1.04) - p = 0.044 3) Re-operation - EOF (0 [0]) - LOF (1 [2.27]) - p =0.337	1) Anastomotic leak 2) Fever 3) Pulmonary infection 4) Wound infection 5) Wound bleeding 6) Wound dehiscence	1) 0/0 2) 1 (2.50)/1 (2.27); p = 0.946 3) 0 (0)/1 (2.27); p = 0.337 4) 1 (2.50)/1 (2.27); p = 0.946 5) 0/0 6) 0/0
Hur et al. (2009) Korea [17]	Pilot (Sep. 2007-Jan. 2008)	35/31 (EOF/LOF)	EOF (55.2 ± 15.4) (range: 21-85)	Gastric adeno-carcinoma (AJCC: I-IV)	1) Hospital stay (days) - EOF (8.03 ± 1.43) - LOF (9.97 ± 2.07) - p < 0.001 2) Time until flatus (days) - EOF (1.96 ± 0.58) - LOF (2.97 ± 0.66) - p < 0.001	1) Morbidity - infective complication - GI morbidity - other morbidity	1) 8 (22.9)/10 (32.3); p = 0.392 - 4 (11.4)/6 (19.4); p = 0.496 - 2 (5.7)/3 (9.7); p = 0.659 - 2 (5.7)/1 (3.8); p = 1.000
Hur et al. (2011) Korea [18]	RCT (Jul. 2008-Feb. 2009)	28/26 (EOF/LOF)	20-75	Gastric adeno-carcinoma	1) Hospital stay (days) - EOF (7.2 ± 1.7) - LOF (8.5 ± 2.9) - p = 0.044 2) Time until flatus (days) - EOF (1.9 ± 1.2) - LOF (2.9 ± 0.8) - p = 0.036 3) Re-operation - EOF (0 [0]) - LOF (2 [8]) - p = 0.227 4) Re-admission - EOF (1 [4]) - LOF (3 [12]) - p = 0.047	1) Morbidity	1) 7 (25)/8 (31); p = 0.636

Table 1. Continued

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Postoperative							
Jeong et al. (2014) Korea [19]	Case-control (Sep. 2010- Mar. 2011)	74/96 (EOF/LOF)	EOF (59.9 ± 11.6) LOF (61.2 ± 11.9)	EGC/AGC (AJCC: T1a, T1b, T2, T3, T4a)	1) Hospital stay (days) - EOF (7.4 ± 1.9) - LOF (8.9 ± 4.0) - p = 0.004 2) Time until flatus (days) - EOF (2.7 ± 1.3) - LOF (2.6 ± 1.0) - p = 0.524 3) Re-operation - EOF (1 [1.4]) - LOF (2 [2.1]) - p = 0.820 4) Morbidity - EOF (9 [12.2]) - LOF (12 [12.5]) - p = 0.947 5) Mortality - EOF (0 [0]) - LOF (0 [0])	1) Morbidity 2) Local complications 3) Systemic complications	1) 9 (12.2)/12 (12.5); p = 0.947 2) 8 (10.8)/10 (10.4); p = 0.933 3) 2 (2.7)/3 (3.1); p = 0.767
Kamei et al. (2005) Japan [21]	RCT (Jan. 2001- Dec. 2002)	27/21 (OEN/TPN)	OEN (62 ± 10) TPN (65 ± 11)	Gastric carci-noma (tumor site: lower, middle, upper, entire, remnant)	1) Hospital stay (days) - OEN (23.1 ± 7.2) - TPN (27.6 ± 4.7) - p = 0.0345	1) Esophagojejunal leak 2) Leakage of duodenal stump 3) Ileus 4) Pancreatitis 5) Wound infection 6) Deep venous thrombosis 7) Abdominal cramps 8) Diarrhea 9) Nausea	1) 0/2 (9.5); p = 0.105 2) 1 (3.7)/0; p = 0.383 3) 1 (3.7)/1 (4.7); p = 0.859 4) 1 (3.7)/0; p = 0.383 5) 2 (7.4)/1 (4.7); p = 0.714 6) 0/1 (4.7); p = 0.261 7) 2 (7.4)/1 (4.7); p = 0.714 8) 7 (25.9)/4 (19.0); p = 0.583 9) 4 (14.8)/2 (9.5); p = 0.591

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Table 1. Continued

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Postoperative							
Sierzega et al. (2015) Poland [20]	RCT (2006-2012)	185/168 (EOF/LOF)	EOF (63, median) LOF (64, median) (range: 26-84)	AJCC (T1-T4)	1) Hospital stay (days, median) - EOF [7] - LOF [8] - p < 0.001 2) Re-operation - EOF [11] - LOF [11] - p = 0.815 3) Mortality - EOF [5] - LOF [6] - p = 0.639	1) Surgical complications - wound infection - abdominal fluid collection - anastomotic leakage - pancreatic fistula - abscess - peritonitis - ileus - abdominal bleeding - duodenal stump leakage - other 2) General complications - pneumonia - respiratory failure - heart failure - renal failure - urinary tract infection - sepsis - liver failure - other	1) 27 (15)/40 (24); p = 0.027 - 12/12; p = 0.806 - 8/20; p = 0.008 - 7/2; p = 0.122 - 6/11; p = 0.147 - 3/8; p = 0.089 - 3/1; p = 0.362 - 3/1; p = 0.362 - 1/1; p = 0.945 - 1/4; p = 0.143 - 3/4; p = 0.609 2) 15 (8)/38 (23); p < 0.001 - 9/24; p = 0.003 - 6/17; p = 0.009 - 6/11; p = 0.147 - 2/4; p = 0.345 - 1/4; p = 0.143 - 1/5; p = 0.077 - 0/2; p = 0.136 - 3/4; p = 0.609

RCT: randomized controlled trial, ID: immunonutrition diet, CR: conventional fixed regimen, EOF: early oral feeding, LOF: late oral feeding, RNA: ribonucleic acid, SIRS: systematic inflammatory response syndrome, OEN: oral enternal nutrition, TPN: total parental nutrition, pTNM: pathological tumor-node-metastasis, EGC: early gastric cancer, AGC: advanced gastric cancer, AJCC: American Joint Committee on Cancer Classification, ns: not significant, CT: control group, GI: Gastrointestinal.

Table 2. The effects of enternal and parental feeding on clinical outcomes and complications in gastric cancer patients

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Early enternal nutrition (EEN) vs. Parental nutrition (PN) & Traditional perioperative treatment (TP)							
Kim et al. (2012) Korea [23]	RCT (Mar. 2006-July. 2007)	17/16 (EEN/TPN)	EEN (60) TPN (64.5) [median]	AGC	1) Hospital stay (days) - EN [12] - TPN [13] - p = 0.289	1) Infectious complication 2) Nausea & vomiting 3) Abdominal distension	1) 0/0 2) 2 (11.7)/0; p = 0.485 3) 1 (5.9)/0; p = 1.000
Li et al. (2015) China [22]	RCT (Jan. 2006-Dec. 2013)	34/34 (EEN/PN)	67.7 ± 7.2 (range: 60-86)	I, II, IIIa, IIIb	1) Hospital stay (days) - EN (16.2 ± 3.6) - PN (19.7 ± 4.5) - p < 0.001 2) Time until flatus (days) - EN (2.2 ± 0.3) - PN (3.7 ± 0.5) - p < 0.001	1) Incidence of complications	1) 29 (10.6)/38 (14.0); ns
Li et al. (2015) China [24]	RCT (Jul. 2010-May. 2014)	150/150 (EEN/TP)	EEN (59.2 ± 9.7) TP (60.4 ± 9.2) TP (nasoenteral feeding tube & postoperative intravenous infusion)	-	1) Hospital stay (days) - EEN (7.73 ± 2.13) - TP (9.77 ± 1.76) - p = 0.002 2) Time until flatus (hr) - EEN (78.8 ± 9.3) - TP (85.3 ± 8.4) - p = 0.011	1) Incidence of complications 2) Fever duration (hr)	1) 21 (14.0)/26 (17.3); p = 0.232 2) 80.2 ± 6.0/88.1 ± 8.1; p = 0.012
Enternal immunonutrition (ID) vs. Isocaloric–isonitrogenous formula (IF)							
Farreras et al. (2005) Spain [25]	RCT (Jan. 1999-Sep. 2000)	30/30 (ID/IF)	ID (66.7 ± 8.3) IF (69.2 ± 13.8)	Gastric adeno-carcinoma	1) Hospital stay (days) - ID [13] - IF [15] - p = 0.02 2) Mortality - ID (1 [3.3]) - IF (2 [6.7]) - ns	1) Wound-healing complications 2) Suture failure 3) Infectious complications 4) Global complications 5) Dehiscence 6) Evisceration 7) Surgical wound infection 8) Intraabdominal abscess 9) Sepsis 10) Pneumonia 11) Urinary tract infection	1) 0 (0)/8 (26.7); p = 0.005 2) 0 (0)/5 (16.6); p = 0.03 3) 2 (6.7)/9 (30); p = 0.01 4) 4 (13.3)/13 (43.3); p = 0.01 5) 0/2 (6.7); ns 6) 0/1 (3.3); ns 7) 1 (3.3)/4 (13.3); ns 8) 0/1 (3.3); ns 9) 0/0 10) 0/2 (6.7); ns 11) 1 (3.3)/2 (6.7); ns

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Table 2. Continued

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Enternal immunonutrition (ID) vs. Isocaloric–isonitrogenous formula (IF)							
Marano et al. (2013) Italy [26]	RCT (2006-2011)	54/55 (ID/IF)	ID (66.6) IF (65.1) (range: 55-78)	Gastric adeno-carci-noma (T1-T4)	1) Hospital stay (days) - ID (12.7 ± 2.3) - IF (15.9 ± 3.4) - p = 0.029 2) Mortality - ID (1 [1.8]) - IF (1 [1.8]) - p = 0.325	1) Infectious complications - wound infection - respiratory tract infection - urinary tract infection - sepsis 2) Anastomotic leakage 3) SIRS (days)	1) 4 (7.4)/11 (20); p = 0.041 - 1 (1.8)/3 (5.4) - 2 (3.7)/5 (9) - 1 (1.8)/2 (3.6) - 0/1 (1.8) 2) 2 (3.7)/4 (7.3); p = 0.045 3) 1.1 ± 0.89/2.2 ± 1.02; p = 0.036
Parental nutrition (PN) vs. Intravenous fluids (IVF) & Soybean oil							
Ryan et al. (2007) UK [27]	Retrospective (Feb. 1998-Oct. 2006)	38/52 (TPN/IVF)	65 ± 12 (range: 26-85)	Gastric adeno-carcinoma, GIST, lymphoma	1) Hospital stay (days) - TPN (21.8 ± 20) - IVF (17.6 ± 8.6) - p = 0.184 2) Weight loss - TPN (-3.8 kg) - IVF (-5.2 kg) - p = 0.008	1) Any complication 2) Wound infection 3) Multiple organ failure 4) Respiratory failure 5) Mortality 6) Pneumonia 7) Sepsis	1) 43.2/27.5; p = 0.189 2) 2.7/5.9; p = 0.636 3) 2.7/0; p = 0.42 4) 8.1/2.0; p = 0.305 5) 8.1/0; p = 0.071 6) 8.1/7.8; p = 1.000 7) 16.2/5.9; p = 0.158
Wei et al. (2014) China [28]	RCT (May. 2007-May. 2008)	26/20 (PN/CT)	PN (50.5, median) (range: 29-75) CT (59, median) (range: 36-74)	TNM I-II		1) Total complications - incisional wound infection - abdominal infection - urinary infection - pulmonary infection	1) 1/6; p = 0.033 - 1/3; p = 0.303 - 0/1; p = 0.435 - 0/1; p = 0.435 - 0/1; p = 0.435

RCT: randomized controlled trial, SIRS: systematic inflammatory response syndrome, GIST: gastrointestinal stromal tumor, AGC: advanced gastric cancer, TNM: tumor-node-metastasis, CT: control group, ns: not significant, TPN: total parental nutrition.

The effects of nutritional intervention/assessment and screening

The effects of nutritional intervention in surgical patients were evaluated for postoperative outcomes (Table 3). Following nutritional counseling (NC) for 6 to 24 months in surgical patients, no significant changes were shown in weight loss [29]. Similarly, in elderly patients aged over 80 years with nutritional assessment for over 1-year period, there were no significant differences in weight loss, but the overall survival was significantly lower than those aged younger than 80 years (48.8%/72.9%, $p = 0.032$) [30]. Also, surgical patients who participated in clinical pathway with multidisciplinary program (e.g., nutritional support) had shorter hospital stay (11.29/14.04 days [mean], $p = 0.023$) compared to pre-pathway group with conventional treatment [31].

Nutritional status in patients was measured with nutritional screening tools for postoperative outcomes (Table 3). Using NRI, malnourished patients (NRI < 97.5) showed greater incidence of wound complications than non-malnourished patients (NRI ≥ 97.5) (N = 62 [10.9%]/4 [3.8%], $p = 0.027$) [32]. Also, using NRS 2002, patients at high risk of malnutrition (NRS ≥ 3) with advanced gastric cancer stage showed significantly lower survival rates than those at low risk (NRS < 3) (median: 25.7 vs. 31.9 vs. months, $p < 0.001$) [33].

Discussion

This review evaluated the effects of oral and EN/PN feeding, and nutritional intervention/assessment and screening on clinical outcomes and complications in gastric cancer patients. In surgical patients with oral feeding, some improvements were shown in shortened duration of hospital stay and flatus, and some of wound and infectious complications. Particularly, decreased hospital stay in patients is significant for prevention of increasing further complications and reduction in burden of hospital stay costs. This result may also indicate fast and enhanced recovery by nutritional care. These findings were also found in other cancer types, such as surgical patients with colorectal (e.g., shortened hospital stay and fewer total complications) [34], gastrointestinal (e.g., fewer total complications) [35], and laryngeal cancer (e.g., shortened hospital stay) [36]. This may suggest that early oral route after surgery is well-tolerable and feasible in cancer patients, and is also effective on clinical outcomes, but not in morbidity and mortality. Tube feeding in cancer patients was also suggested in several studies, especially greater benefits of EN over PN [37,38]. In gastric cancer patients, no significant differences were found between EEN and PN, but in other cancer types, faster recovery of intestinal gut oxygenation and shorter duration of intensive care unit (ICU) were shown in surgical patients with upper gastrointestinal [39] and oesophageal cancer [40], respectively. Moreover, enternal ID, formula supplemented with arginine, omega-3 fatty acids, and RNA, was also effective in modulating cell-mediated immunologic [41,42] and inflammatory response [43], and reducing wound and infectious complications [44], and multiple organ failure [45] in previous studies.

A long-term nutritional intervention (e.g., nutritional advice) did not significantly affect postoperative outcomes in gastric cancer patients (e.g., weight gain and overall survival). For a short-term nutritional advice, it was not also effective in weight gain after surgery [46] or reducing incidence of treatment-related side effects and/or improving micronutrient deficiency among patients receiving radio- and/or chemotherapy [47]. However, there are limited numbers of studies investigating on long-term postoperative nutritional intervention in gastric cancer patients, which were based on individual nutritional advice supplying with ordinary oral food intake or supplements. Therefore, future studies may require additional ways of improving quality of long-term intervention in those patients.

Nutritional screening tools to evaluate nutritional status in gastric cancer patients were effective in measuring postoperative outcomes. NRI, developed by the Veterans Affairs Total Parenteral Nutrition Cooperative Study Group in 1991 [48], showed some benefits to measure the occurrence of non-infectious postoperative complications [49] and mortality [50] in malnourished patients after surgery of digestive systems. Another nutritional screening tool, NRS (2002), introduced by the European Society for Clinical Nutrition and Metabolism (ESPEN) [51], is also considered to provide benefits in evaluating nutritional status in hospitalized patients, particularly elderly [52]. Among several nutritional screening tools, NRS (2002) is well-correlated with nutritional parameters (e.g., body weight and BMI), and considered one of favorable nutritional indicators to measure malnourished status in patients [53]. In particular, malnutrition is commonly seen in advanced gastric cancer patients due to severe weight loss from poor nutrition absorption from removal of stomach [54,55]. These findings were also consistent in a large cohort study in patients with advanced cancer stage in Korea, and showed longer hospital stay and higher readmission rate [56]. In other cancer types, malnourished patients who underwent upper gastrointestinal

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Table 3. The effects of nutritional intervention/assessment and screening on clinical outcomes and complications in gastric cancer patients

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Nutritional status measurement (indicator)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Nutritional intervention & assessment								
Lee et al. (2002) Korea [29]	RCT (Oct. 1999-Dec. 2000)	22/18 (NC/NNC)	NC (54.1 [± 11.4]) NNC (57.6 [± 12.0])	EGC (T1N0/T1N1)	NC (6-24 months, postoperatively)	1) Weight loss (kg) - NC (-8.6) - NNC (-6.6) - ns	-	-
Nakanoko et al. (2015) Japan [30]	Retrospective (1998-2008)	430/41 (< 80/≥ 80yrs)	< 80yrs (62, median) ≥ 80yrs (82.1, median)	Gastric adeno-carcinoma (I-IV, T1-T4)	WL[NA] (> 1 yr period, postoperatively; < 80yrs[-6.0 ± 7.4] ≥ 80yrs[-6.8 ± 5.3])	1) Overall survival - < 80 yrs (72.9) - ≥ 80 yrs (48.8) - p = 0.032 2) 5-year cumulative survival - < 80 yrs (78.2) - ≥ 80 yrs (81.8) - p = 0.963	1) Surgery related (%) - pancreatic-related abscess - anastomotic leakage - bleeding - others 2) Non-surgery related (%) - pneumonia - cardiovascular dysfunction - delirium - others 3) Total complications	1) ns - 11 (2.6)/0 - 7 (1.5)/0 - 2 (0.4)/0 - 12 (2.8)/1 (2.4) 2) ns - 1 (0.2)/0 - 0/1 (2.4) - 10 (2.3)/1 (2.4) - 8 (1.9)/2 (4.9) 3) 55 (12.8)/4 (9.8); ns
So et al. (2008) Singapore [31]	Cohort (Jan. 2000-Apr. 2005)	61/54 (PG/PPG)	PG (66.3) PPG (63.7)	AJCC (0-4)	Clinical pathway PG (multidisciplinary program: preoperative education & counseling, pain control, physiotherapy, nutritional support, surgical care)	1) Hospital stay (days, mean) - PG (11.29) - PPG (14.04) - p = 0.023 2) Re-admission rate (30-day) - PG (11 [18]) - PPG (7 [13.0]) - p = 0.455 3) Mortality - PG (0 [0]) - PPG (3 [5.6]) - p = 0.062	1) Complication rate	1) p = 0.960 - PG (24 [39.3]) - PPG (21 [38.9])

Table 3. Continued

Author (year, country)	Study type	Population (N)	Age (years, mean ± S.D)	Cancer type (stage)	Nutritional status measurement (indicator)	Clinical outcomes (mean ± S.D, N [%])	Complications	Result (experimental vs. control group [N (%)])
Nutritional screening tool (malnourished vs. non-malnourished)								
Oh et al. (2012) Korea [32]	Retrospective (Jan. 2008- Jun. 2008)	Total (669) NRI < 97.5 (N = 566) NRI ≥ 97.5 (N = 103)	All (56.77 ± 11.4) NRI < 97.5 (57.15 ± 11.7) NRI ≥ 97.5 (54.70 ± 9.6)	Gastric adeno-carcinoma (EGC/AGC)	NRI < 97.5 (malnourished) NRI ≥ 97.5 (non-malnourished)	1) Hospital stay (days) - NRI < 97.5 (12.76 ± 4.02) - NRI ≥ 97.5 (12.01 ± 2.45) - p = 0.160	1) Comorbid diseases - hypertension - diabetes mellitus - pulmonary tuberculosis - cardiovascular diseases - hepatitis - others 2) Wound complication	1) p = 0.365 - 130 (23)/29 (28.1) - 66 (11.7)/20 (19.4) - 22 (3.9)/7 (6.8) - 13 (2.3)/3 (2.9) - 40 (7.1)/5 (4.8) - 18 (3)/1 (1) 2) 62 (10.9)/4 (3.8); p = 0.027
Qiu et al. (2014) China [33]	RCT (2012-2013)	Total (830) NRS < 3 (279M/139F) NRS ≥ 3 (269M/152F)	≤ 59 > 59	Gastric adeno-carcinoma (TNM I-IV)	NRS < 3 (low malnourished risk group) NRS ≥ 3 (high malnourished risk group)	1) Survival (median) - NRS < 3 (31.9 months) - NRS ≥ 3 (25.7 months) - p < 0.001	-	-

NC: nutritional counseling group, NNC: non-nutritional counseling group, PPG: pre-pathway group, PG: pathway group, EGC: early gastric cancer, AGC: advanced gastric cancer, AJCC: American Joint Committee on Cancer, TNM: tumor-node-metastasis, NRI: nutritional risk index, NRS: nutritional risk screening, NA: nutritional assessment, WL: weight loss, ns: not significant, M: male, F: female, RCT: randomized controlled trial.

and colorectal cancer surgery with delayed and inadequate postoperative nutritional practices also had higher incidence of adverse clinical outcomes (e.g., hospital stay) compared to well-nourished patients [57]. In a meta-analysis, malnourished cancer patients or those at high risk of malnutrition with oral nutritional intervention did not improve survival rates [58]. Therefore, these studies suggested that early identification of nutritional status in cancer patients using appropriate nutritional screening tools can provide benefits in prevention of adverse clinical outcomes and improve further prognosis [59,60].

It has been well-known that nutritional care in gastric cancer patients is critical to improve cancer prognosis. A significance of this review is that it summarized numerous ways of nutritional interventions and assessments to find the differences in a wide range of geological regions and ethnic groups for the last 20 years. In recent years, the importance of nutritional care has been significantly increased due to relatively poor survival rates and prognosis of gastric cancer patients related with high malnutrition status. Therefore, recent studies have focused on clinical outcomes and complications relying on their nutritional status with measurement of various nutritional parameters.

However, there are some limitations found in this review. For example, due to inconsistent findings in small numbers of studies investigating the association between nutritional care and gastric cancer related to clinical outcomes and complications, the results may remain inconclusive. Although broad range of gastric cancers were investigated (e.g., upper gastrointestinal cancer), the findings are still insufficient and inconsistent. Therefore, early intensive nutritional care is suggested to provide more benefits for those patients to reduce possible complications, morbidity, and mortality. In addition, most studies were performed in Asian countries, but this can be explained due to relatively higher incidence and mortality

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rate of gastric cancer compared to other regions worldwide. In future studies, it may be required to investigate various ethnic groups in a large population to improve the quality of scientific evidences in association between nutritional care and gastric cancer.

Conclusion

In gastric cancer patients, early nutritional feeding and effective nutritional intervention with a proper nutritional screening tool are suggested to promote clinical outcomes and reduce complications. Also, early identification of nutritional status in patients may prevent malnutrition and provide benefits in increasing their survival rates. Furthermore, additional analyses on ethnic groups or populations may enhance scientific evidences in association between nutritional care and gastric cancer.

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