Taiwan nutritional consensus on the nutrition management for gastric cancer patients receiving gastrectomy

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Received 10 January 2019; received in revised form 17 August 2019; accepted 19 November 2019

Currently, consensus reports on the nutritional management for gastric cancer patients receiving gastric resection are lacking. The Gastroenterological Society of Taiwan therefore organized the Taiwan Gastric Cancer Nutritional Consensus Team to provide an overview of evidence and recommendations on nutritional support for gastric cancer patients undergoing gastrectomy.
Nutritional support; Gastrectomy

This consensus statement on the nutritional support for gastric cancer patients has two major sections: (1) perioperative nutritional support; and (2) long-term postoperative nutritional care. Thirty Taiwan medical experts conducted a consensus conference, by a modified Delphi process, to modify the draft statements.

The key statements included that preoperative nutritional status affects the incidence of operative complications and disease-specific survival in gastric cancer patients undergoing gastrectomy. Following gastrectomy, both early oral and enteral tube feeding can result in a shorter stay than total parenteral nutrition. Compared to late oral feeding, early oral feeding can reduce hospital stay in gastric cancer patients receiving gastrectomy without an increase in complication rate. Routine supplementation with vitamin B12 is indicated for gastric cancer patients undergoing a total gastrectomy. Both high-dose oral vitamin B12 supplementation and intramuscular administration of vitamin B12 are equally effective in the treatment of vitamin B12 deficiency.

Introduction

Although the incidence and mortality of gastric cancer have decreased over the past few decades, gastric cancer remains the 5th most common cancer worldwide, and is the third leading cause of cancer-related deaths in the world. Adequate nutritional support is essential for both gastric cancer patients receiving surgical resection of the tumors and those receiving palliative care. Malnourished patients are at greater risk of adverse clinical outcomes including higher incidence of complications and poor survival in gastric cancer patients undergoing gastrectomy. Therefore, identifying and treating malnutrition is important in the management of gastric cancer.

Clinically, malnutrition is a common problem in patients with gastric cancer. Weight loss is observed in 15% of the patients at initial diagnosis. The condition can be caused by mechanical obstruction of the digestive tract by tumors or anorexia-cachexia syndrome of cancer patients. Nutritional support for gastric cancer patients can be performed by enteral or parenteral route. The enteral route can be further categorized into oral feeding and tube feeding. Although surgical resection of the tumor is the key method in the treatment of gastric cancer in the early stages, there are still lots of controversies concerning the timing and routes of nutritional support in the management of gastric cancer patients following surgery.

Nutritional intolerances and malabsorption may lead to nutritional deficiencies and undesirable clinical consequences in gastric cancer patients following partial or total gastrectomy. The nutritional intolerances of gastric cancer patients receiving gastrectomy are often due to dumping syndrome, gastric stasis and fat maldigestion. Nutritional deficiencies may develop months to years after partial or total gastrectomy. Anemia and metabolic bone disease are the most common manifestations of the nutrient deficiencies in these patients.

Currently, there are no consensus reports on the nutritional support for gastric cancer patients. Although early oral or enteral feeding has been proposed to improve clinical outcomes and to reduce surgical complications in gastric cancer patients following gastrectomy, the postoperative nutritional support for patients undergoing gastrectomy is quite variable between different institutions and surgeons. Therefore, the Gastroenterological Society of Taiwan organized the Taiwan Nutritional Consensus Team for Gastric Cancer to provide an overview of the current evidence on nutritional problems in gastric cancer and the recommendations on nutritional management in gastric cancer patients with gastrectomy.

Scope, setting, and structure for preparation of the consensus statement

The steering committee that established the Taiwan Nutritional Consensus on Nutritional Support for Gastric Cancer was initiated by JT Lin, chaired by WC Chang and BS Sheu. There were also seven other opinion leaders from the Gastroenterological Society of Taiwan (Hsu PI, Chauh CC, Wu MS, Wu CJ. Chui CS, Liou CZ, Lo PZ). The ten members of the steering committee defined the scope of the consensus statement, level of statement evidence, and degree of recommendation.

Search and review of literature and initiate draft statements

The literature concerning the nutritional support for patients receiving gastrectomy was searched using MEDLINE, the Cochrane Center Register of Controlled Trials, Embase, and the ISI Web of Knowledge. There were also manual searches of the bibliographies of key articles and abstracts from the proceedings of the major gastroenterology conferences over the past 20 years (July 1997 to June 2017). The keywords used in the searches were the following: gastric cancer, gastrectomy, nutritional support, enteral nutrition, parental nutrition, oral feeding, complication and nutritional deficiency. The steering committee summarized the findings in two sections of the consensus statements: (1) perioperative nutritional support, and (2) long-term postoperative nutritional care. Based on a review of the literature, the draft statements of this consensus were established by the section leaders. For each
process to achieve agreement of statement and recommendation grade

An expert group on the nutrition support of gastric cancer was established by The Gastroenterological Society of Taiwan. Group members were chosen based on their expertise and contribution to the literatures. In total, the expert group included the 10 members of the steering committee and another 20 experts of cancer nutritional support. The draft statements were sent to all experts before the consensus meeting on February 11–12, 2017, in Tainan. During this 2-day consensus meeting, each draft statement with supporting evidence was presented sequentially. Based on a modified Delphi process with two separate iterations, all participants voted anonymously for the first round of statements, and then modified the statements after discussion. There was a second round of voting until a consensus was reached (agreement by at least 80% of the expert members). Statements were rejected if the agreement was <80%. The experts also discussed the level of evidence suggested by the steering committee and graded the recommendations by voting for each statement. The recommendation grade ranged from A to D (A: accept completely; B: accept with some reservation; C: accept with major reservation; D: reject) as in our previous consensus statement [9]. Each grade was defined by the most votes. The conference was performed by the grants from the Gastroenterology Society of Taiwan. Before voting, all experts provided written disclosures of financial conflicts of interest in the prior 3 years.

Consensus statements

A summary of the statements, evidence levels, agreements and grades of recommendation of the consensus is shown in Table 1.

Section I. Perioperative nutritional support.

Statement 1. Preoperative malnutrition is associated with increased complication and poor survival in gastric cancer patients receiving gastrectomy (Evidence level: 2b, Agreement: 100%, Recommendation: A).

A retrospective cohort study by Oh et al. demonstrated that malnutrition was a predictor of postoperative wound complications in gastric cancer patient undergoing gastrectomy. Among the patients with wound complications in that study, 62/66 (94%) belonged to the malnourished group (Nutrition Risk index [NRI] < 97.5), and 4/66 (6%) patients to the non-malnourished group (NRI ≥ 97.5). Further analysis revealed that the NRI was the only factor predicting wound complications. Another retrospective cohort study by Kanda et al. showed that in gastric cancer patients receiving curative gastrectomy, the malnourished group (Prognostic Nutrition Index [PNI] < 47) had a higher rate of post-operative complications and experienced significantly shorter overall survival and disease-free survival than the non-malnourished group (PNI ≥ 47). Sakurai et al. also disclosed that the preoperative PNI was an independent predictive factor for both overall survival and disease-specific survival in gastric cancer patients undergoing surgery. Another cohort study by Fukuda et al. investigated the prevalence of malnutrition among 800 gastric cancer patients undergoing gastrectomy and the impacts of optimal preoperative nutritional support on preventing surgical site infections. Optimal nutritional support was examined in terms of both duration and calorie intake. Overall, 152 patients (19.0%) were classified as malnourished. The incidence of surgical site infections was significantly higher in malnourished patients than in well-nourished patients (35.5 vs. 14.0%). The incidence of surgical site infections in the well-nutritional supported group receiving adequate energy support for at least 10 days was significantly lower (17.0 vs. 45.4%) than in the poorly supported group, which received inadequate or no energy support or adequate energy support for <10 days. Multivariate analysis showed that well-managed nutritional support was an independent factor associated with fewer surgical site infections with odds ratio of 0.14 (95% confidence interval: 0.05–0.37). Thus, preoperative malnutrition is associated with increased complication and poor survival in gastric cancer patients receiving gastrectomy.

Several validated questionnaires including the NRI, PNI, Nutritional Risk Screening 2002 (NRS 2002), and Short Nutritional Assessment Questionnaire (SNAQ) are available for the assessment of nutrition status in gastric cancer. The low NRI and high NRS 2002 score are associated with an increased rate of postoperative complications. A high SNAQ score is associated with an increased mortality compared to a low SNAQ score. The PNI is predictive of decreased survival rate after gastrectomy. A recent randomized controlled trial showed that preoperative enteral nutrition improved the postoperative nutritional status and immune function of gastric cancer patients receiving radical gastrectomy. The low nutritional supply group received 500 mL/day of a standard oral nutritional supplement for 2 weeks before gastrectomy and for 4 weeks postoperatively. Among the severely malnourished patients, the perioperative oral nutritional supplement group had a lower incidence of overall complications than control group. This randomized controlled trial suggests that adequate nutritional support can improve the clinical outcomes of malnourished patients who undergo gastrectomy. The oral nutritional supplement group received 500 mL/day of a standard oral nutritional supplement for 2 weeks before gastrectomy and for 4 weeks postoperatively. Among the severely malnourished patients, the perioperative oral nutritional supplement group had a lower incidence of overall complications than control group. This randomized controlled trial suggests that adequate nutritional support can improve the clinical outcomes of malnourished gastric cancer patients receiving gastrectomy. In the guidelines of the European Society for Parenteral and Enteral Nutrition (ESPEN), preoperative nutritional support is recommended for gastric cancer patients with insufficient dietary intake defined as an oral food intake <500 Kcal/day or ≤75% of the requirement for more than 1–2 weeks.

In gastric cancer patients with insufficient dietary intake and intact gastrointestinal tract, enteral nutrition is...
preferred to parenteral nutrition for preoperative nutrition support, and may be performed through a nasogastric or a nasoenteric tube. However, preoperative nutrition support can be conducted by a parenteral route in gastric cancer patients with obstruction of the upper gastrointestinal tract or a nonfunctional gastrointestinal tract.

Statement 2. Preoperative clear oral carbohydrate fluid loading may shorten the length of hospital stay, compared with overnight fasting, in gastric cancer patients receiving gastrectomy (Evidence level: 2b, Agreement: 86.7%, Grade of recommendation: B).

The enhanced recovery after surgery (ERAS) protocol involves the integrated application of various medical interventions to enhance recovery after surgery. Preoperative carbohydrate loading is one of the main elements of ERAS protocol and has been demonstrated to reduce insulin resistance after surgery. According to the ERAS protocol, patients are allowed a normal diet until the day before surgery. A preoperative carbohydrate loading (800 mL of a 12.5% carbohydrate drink the night before operation and 400 mL of a 12.5% carbohydrate drink in the morning of the operation day 2–3 h prior to the induction of anesthesia) is recommended to reduce insulin resistance induced by surgery and to sustain normal bowel function.

A prospective randomized controlled trial by Kim et al. showed that preoperative clear oral carbohydrate fluid loading shortened the length of hospital stay, compared with overnight fasting, in gastric cancer patients receiving gastrectomy. Another retrospective cohort study also demonstrated that preoperative clear oral carbohydrate fluid loading resulted in a shorter hospital stay than overnight fasting in gastric cancer patients receiving gastrectomy. In addition, the former also had fewer complications than the latter.

Statement 3. Following gastrectomy for gastric cancer, early enteral tube feeding may shorten hospital stay and decrease medical cost compared to total parenteral nutrition (Evidence level: 2b, Agreement: 86.7%, Grade of recommendation: B).

After surgical treatment, small intestinal functions resume between 6 and 12 h after surgery, indicating that enteral nutrition could be started at that time. A systematic review and meta-analysis including 30 randomized controlled trials revealed that early use of enteral nutrition in gastrointestinal malignancy patients after surgery could significantly reduce the postoperative complications and shorten the length of hospital stay compared to parenteral nutrition.

Enteral nutrition can be categorized into oral feeding and tube feeding. A retrospective cohort study by Chen et al. showed that nasojejunal tube feeding was safe and well tolerated. It could shorten the hospital stay as well as reduce costs in gastric cancer patients receiving total gastrectomy compared with total parenteral nutrition.

Table 1. The statements, evidence levels, agreements and grades of recommendation of the Taiwan Nutritional Consensus on the Nutrition Management for Gastric Cancer Patients Receiving Gastrectomy.

<table>
<thead>
<tr>
<th>No.</th>
<th>Statements</th>
<th>Evidence level</th>
<th>Agreement</th>
<th>Recommendation grade</th>
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<tbody>
<tr>
<td>1</td>
<td>Preoperative malnutrition is associated with increased complication and poor survival in gastric cancer patients receiving gastrectomy.</td>
<td>2b</td>
<td>100%</td>
<td>A</td>
</tr>
<tr>
<td>2</td>
<td>Preoperative clear oral carbohydrate fluid loading may shorten the length of hospital stay, compared with overnight fasting, in gastric cancer patients receiving gastrectomy.</td>
<td>2b</td>
<td>86.7%</td>
<td>B</td>
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<tr>
<td>3</td>
<td>Following gastrectomy for gastric cancer, early enteral tube feeding may shorten hospital stay and decrease medical cost compared to total parenteral nutrition.</td>
<td>2b</td>
<td>86.7%</td>
<td>B</td>
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<tr>
<td>4</td>
<td>Following gastrectomy for gastric cancer, patients receiving early oral feeding have a shorter hospital stay without increasing complications than those receiving parenteral nutrition.</td>
<td>1b</td>
<td>100%</td>
<td>A</td>
</tr>
<tr>
<td>5</td>
<td>In gastric cancer patients following gastrectomy, early oral feeding decreases the length of hospital stay compared to late oral feeding.</td>
<td>1a</td>
<td>97%</td>
<td>A/B</td>
</tr>
<tr>
<td>6</td>
<td>Supplementation with vitamin B&lt;sub&gt;12&lt;/sub&gt; is indicated for gastric cancer patients receiving total gastrectomy.</td>
<td>2b</td>
<td>100%</td>
<td>A</td>
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<tr>
<td>7</td>
<td>Both high-dose oral and intramuscular vitamin B&lt;sub&gt;12&lt;/sub&gt; supplements are effective for the treatment of vitamin B&lt;sub&gt;12&lt;/sub&gt; deficiency in gastric cancer patients receiving total gastrectomy (Evidence level: 2b, Agreement: 90%, Grade of recommendation: B).</td>
<td>2b</td>
<td>100%</td>
<td>A</td>
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<tr>
<td>8</td>
<td>Iron deficiency anemia following gastric cancer surgery should be monitored, especially in female patients.</td>
<td>2b</td>
<td>100%</td>
<td>A</td>
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</table>
Another randomized control trial by Sand et al. also showed that total parenteral nutrition was more than four times as expensive as enteral tube feeding in gastric cancer patients undergoing curative total gastrectomy.\(^{28}\) Furthermore, there was a tendency to an increased risk of diarrhea in the patients receiving total parenteral nutrition.\(^{28}\) In conclusion, compared to total parenteral nutrition, early enteral tube feeding may shorten hospital stay and decrease medical cost in gastric cancer patients following gastrectomy.

Statement 4. Following gastrectomy for gastric cancer, patients receiving early oral feeding have a shorter hospital stay without increasing complications than those receiving parenteral nutrition (Evidence level: 1b, Agreement: 100%, Grade of recommendation: A).

"Early oral feeding (EOF)" is one of the most important postoperative elements in the ERAS.\(^{23}\) Several studies demonstrated that EOF was feasible and safe even starting on the day of surgery irrespective of the extent of the gastric resection and the type of surgery.\(^{21,23–31}\) A recent randomized control trial by Li et al. documented that EOF decreased hospital stay, shortened anal exhaust time, and significantly reduced hospital costs in gastric cancer patients receiving gastrectomy compared with peripheral parenteral nutrition.\(^{32}\) Another randomized controlled trial revealed that EOF beginning on postoperative day 3 resulted in less hospital cost and shorter hospital stay than total parenteral nutrition in gastric cancer patients undergoing total gastrectomy.\(^{33}\) To sum up, gastric cancer patients receiving EOF following gastrectomy have a shorter hospital stay than those receiving parenteral nutrition.

Statement 5. In gastric cancer patients following gastrectomy, early oral feeding decreases the length of hospital stay compared to late oral feeding (Evidence level: 1a, Agreement: 97%, Grade of recommendation: A: 50%, B: 50%).

A randomized controlled trial by Hirao et al. showed that early gastric cancer patients with EOF after distal gastrectomy had a shorter postoperative hospital stay and a higher oral energy intake on early phase, compared with those with late oral feeding (LOF).\(^{34}\) The incidence of complications did not show significant differences between patients receiving EOF and LOF. A meta-analysis including six randomized controlled trials and 454 patients showed that no significant differences were observed for the postoperative complication, readmission rate and incidence of anastomotic leakage between the gastric cancer patient groups receiving EOF and LOF after gastrectomy.\(^{35}\) However, EOF was associated with significant shorter duration of the hospital stay and time to first flatus. In conclusion, EOF decreases the length of hospital stay in gastric cancer patients following gastrectomy, compared to LOF.

The incidence of dumping syndrome following total or subtotal gastrectomy ranges from 1% to 75%.\(^{35,36}\) Early dumping syndrome attributed to loss of the gastric reservoir and accelerated gastric emptying of hyperosmolar contents into the proximal small intestine occurs about 15–30 min after ingestion of a meal.\(^{37}\) The common symptoms include epigastric fullness, vomiting, abdominal cramps and diarrhea. Late dumping syndrome presenting with sweating, anxiety, hunger and weakness occurs about two to 3 h after meals. Reactive hypoglycemia is contributed to the symptoms of later dumping syndrome. The general management of early or late dumping syndrome includes eating six or more small meals a day, limiting fluid consumption after meals and avoiding high-sugar food.

Section II. Long-term postoperative nutritional care.

Statement 1. Supplementation with vitamin B\(_{12}\) is indicated for gastric cancer patients receiving total gastrectomy (Evidence level: 2b, Agreement: 100%, Grade of recommendation: A).

Nutrient deficiencies and undesirable clinical consequences due to alterations in digestion and impaired nutrition absorption may develop following total or subtotal gastrectomy. Common nutritional problems following gastrectomy include vitamin B\(_{12}\), folate, iron, calcium and vitamin D deficiencies. The nutrient deficiencies are attributed to malabsorption, rapid gastrointestinal transit time, bacterial overgrowth and insufficient oral intake.\(^{38–40}\) Cohort studies showed no significant differences in weight loss after gastric resection between total gastrectomy and subtotal gastrectomy.\(^{41}\) In addition, similar post-prandial discomforts including epigastric fullness, early satiety and symptoms of the dumping syndrome are present in gastric cancer patients following either total or subtotal gastrectomy.\(^{38}\) Nutrient deficiencies develop months to years following gastrectomy and can result in deleterious clinical consequences. Anemia and metabolic bone disease are the most common manifestations of the nutrient deficiencies in gastric cancer patients receiving gastrectomy.\(^{36,38–40}\)

Anemia and neurological disorder due to vitamin B\(_{12}\) deficiency are common long-term complications after gastrectomy in gastric cancer patients without adequate nutritional supplementation. Intrinsic factor, which is mainly secreted by parietal cell, is necessary to absorb enteral vitamin B\(_{12}\).\(^{40}\) Reduction in intrinsic factor and reduced gastric acidity may contribute to the deficiency of vitamin B\(_{12}\) in patients receiving total or subtotal gastrectomy. A retrospective study including 645 patients showed that cumulative rates of vitamin B\(_{12}\) deficiency were 100% for total gastrectomy and 15.7% for subtotal gastrectomy 4 years after surgery \(P < 0.001\). The median time to vitamin B\(_{12}\) deficiency was 15 months after total gastrectomy.\(^{41}\) Symptoms of vitamin B\(_{12}\) deficiency include lassitude, dizziness, fatigability, chills, numbness in extremities, and neurological disorders.\(^{41}\) However, clinical features can be non-specific or absent in some patients.\(^{43}\) Therefore, routine supplementation with vitamin B\(_{12}\) is indicated for gastric cancer patients receiving total gastrectomy, and periodic serum monitoring and supplementation of vitamin B\(_{12}\) is warranted for gastric cancer patients receiving subtotal gastrectomy (Table 2).

Folate deficiency may also develop after total or subtotal gastrectomy. Red blood cell (RBC) folate is a better indicator of low folate stores than serum folate, which is affected by recent folate intake. RBC folate should be applied when diagnosing a folate deficiency. A daily dose of...
Table 2 Post-operative supplements of vitamin B₁₂, iron, calcium and vitamin D in patients receiving total gastrectomy and subtotal gastrectomy.

<table>
<thead>
<tr>
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<th>Total gastrectomy</th>
<th>Subtotal gastrectomy</th>
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<tbody>
<tr>
<td>Vitamin B₁₂</td>
<td></td>
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<tr>
<td>1. Prophylactic oral, intramuscular or subcutaneous supplement of vitamin B₁₂ (e.g., intramuscular injection of 1000 µg in alternate months).</td>
<td>1. Periodical (e.g., every 6 months) monitor for serum vitamin B₁₂ level and supplement of vitamin B₁₂ as needed.</td>
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<tr>
<td>2. In case of mild deficiency, oral vitamin B₁₂ (500 –1000 mcg/day) is warranted. If severe deficiency exists, give intramuscular or subcutaneous vitamin B₁₂ 1000–2000 mcg/month.</td>
<td>2. Periodical (e.g., every 6 months) monitor for serum ferritin and hemoglobin levels.</td>
<td></td>
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<tr>
<td>3. Periodical (e.g., every 6 months) monitor for serum ferritin and hemoglobin levels.</td>
<td>4. In case of iron deficiency, oral supplement (e.g., 150 to 300 elemental iron/day for about 4–6 months) is needed.</td>
<td></td>
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<tr>
<td>Iron</td>
<td></td>
<td></td>
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<tr>
<td>1. Periodical (e.g., every 6 months) monitor for serum ferritin and hemoglobin levels.</td>
<td>2. In case of iron deficiency, oral supplement (e.g., 150 to 300 elemental iron/day for about 4–6 months) is needed.</td>
<td></td>
</tr>
<tr>
<td>Calcium and vitamin D</td>
<td>1. Periodical (e.g., every 1 year) monitor for 25-hydroxy vitamin D and bone mineral density.</td>
<td>2. Prophylactic supplement with daily multivitamin tablets (e.g., multivitamin tablet containing 250 mg calcium and 400 IU vitamin D) may be considered.</td>
</tr>
<tr>
<td></td>
<td>1. Periodical (e.g., every 1 year) monitor for 25-hydroxy vitamin D and bone mineral density.</td>
<td>2. Prophylactic supplement with daily multivitamin tablets (e.g., multivitamin tablet containing 250 mg calcium and 400 IU vitamin D) may be considered.</td>
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5 mg folate is recommended in patients with folate deficiency.⁴³

Statement 2. Both high-dose oral and intramuscular vitamin B₁₂ supplements are effective for the treatment of vitamin B₁₂ deficiency in gastric cancer patients receiving total gastrectomy (Evidence level: 2b, Agreement: 100%, Grade of recommendation: B).

Interestingly, enteral vitamin B₁₂ supplement increases serum vitamin B₁₂ concentration rapidly. Symptoms resolution was comparable in patients who received enteral and parenteral supplementation. It is possible that the body adapts after total gastrectomy and may produce intrinsic factor in the duodenum and jejunum.⁴² A prospective study showed that oral vitamin B₁₂ replacement (1.5 mg once daily meccobalamine) was as effective as intramuscular vitamin B₁₂ injections (1 mg cyanocobalamin weekly for 5 weeks and monthly thereafter) for reversing serum vitamin B₁₂ level and improving neurological symptoms in gastric cancer patients with vitamin B₁₂ deficiency after total gastrectomy.⁴⁴ A systematic review of limited randomized controlled trials regarding oral vitamin B₁₂ versus intramuscular vitamin B₁₂ for vitamin B₁₂ deficiency suggested that oral vitamin B₁₂ may be as effective as intramuscular administration in obtaining short-term haematological and neurological responses in vitamin B₁₂-deficient patients.⁴⁵

Statement 3. Iron deficiency anemia following gastric cancer surgery should be monitored, especially in female patients (Evidence level: 2b, Agreement: 100%, Grade of recommendation: A).

Iron deficiency anemia is a common disorder in gastric cancer patients following total or subtotal gastrectomy.⁴⁶,⁴⁷ Malabsorption of dietary iron possibly results from a reduction of gastric acid secretion and bypassing of the duodenum. Reduced gastric acidity impairs the conversion of nonheme iron into the more absorbable ferrous form.⁴⁸ The reconstruction after gastrectomy may decrease iron absorption due to bypass the duodenum and proximal jejunum, the major sites of iron absorption. A retrospective cohort study including 161 patients to evaluate anemia after curative gastrectomy in early gastric cancer patients showed that the incidence of iron deficiency anemia, defined as anemia (hemoglobin <12 g/dL in women and <13 g/dL in men) with serum ferritin <20 µg/dL, increased during the follow up and became the major cause of anemia at 48 months after surgery.⁴⁹ The incidence of iron deficiency was significantly higher in female patients than in male gastric cancer patients after gastrectomy.⁴⁶ To sum up, iron deficiency anemia following gastric cancer surgery should be monitored, especially in female patients.

Besides vitamin B₁₂ and iron deficiency anemia, the prevalence of metabolic bone disease including osteoporosis, osteopenia is also high in gastrectomy patients. A low bone mineral density (BMD) has been reported in 27%–44% of patients with gastrectomy.⁴⁹ Klein et al. reported that vertebral bony fractures were three times as common in men who had received a subtotal gastrectomy with B-II anastomosis when compared with controls.⁴⁹ Post-gastrectomy osteoporosis is multifactorial. It has been attributed to decreased intake of calcium, vitamin D and
altered absorption.\textsuperscript{51} Therefore, taking calcium-rich foods such as milk, cheese, sardines and dark leafy greens is encouraged for patients who have undergone a gastrectomy. Currently, no universal guidelines for the supplementation of calcium or vitamin D in patients with gastrectomy are available. Nonetheless, prophylactic supplementation with daily multivitamin tablets containing 250 mg calcium and 400 IU vitamin D may be considered (Table 2).\textsuperscript{52} Additionally, periodic monitoring of BMD every one to two years for gastric cancer patients receiving total or subtotal gastrectomy is warranted.\textsuperscript{52} Prompt initiation of anti-resorptive agents (calcium, vitamin D and bisphosphonates) and bone forming agents (recombinant hormone PTH) should be considered in severe cases.

A recent cohort study investigated serum zinc and copper levels in gastric cancer patients receiving gastrectomy and relationship between the copper/zinc ratio and the complication of anastomotic leak after surgery.\textsuperscript{53} The data showed that copper/zinc ratio was significantly higher at stage IV than in the earlier stages. Preoperative copper/zinc ratio in gastric cancer patients with post-operative anastomotic leak was significantly higher than that in gastric cancer patients without it. Therefore; pre-operative and post-operative monitoring and correction for serum levels of zinc and copper levels are suggested.

**Summary**

Fig. 1 shows the algorithm of nutritional management for gastric cancer patients receiving a gastrectomy. Preoperative nutritional assessment with nutritional support patients with malnutrition is indicated for gastric cancer patients undergoing gastrectomy. Preoperative clear oral carbohydrate fluid loading can lead to a shorter length of hospital stay than overnight fasting in gastric cancer patients who have undergone a gastrectomy. Following surgery for gastric cancer, both early oral and enteral tube feeding can result in a shorter hospital length than total parenteral nutrition. Compared to late oral feeding, early oral feeding can reduce hospital stay in gastric cancer patients receiving gastrectomy without an increase in the complication rate. Periodic nutritional assessment and intervention is important to prevent nutrient deficiencies in gastric cancer patients following surgery. Routine supplementation with vitamin B\textsubscript{12} is indicated for gastric cancer patients receiving total gastrectomy, and periodic serum monitoring and supplementation of vitamin B\textsubscript{12} is warranted for gastric cancer patients receiving subtotal gastrectomy. Iron deficiency anemia is a common disorder in gastric cancer patients following total or subtotal gastrectomy. It should be monitored following gastric cancer surgery, especially in female patients.

**Declaration of Competing Interest**

The authors have no conflicts of interest relevant to this article.

**Acknowledgements**

This work was supported by the grant from the Gastroenterology Society of Taiwan and the Abbott Taiwan.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2019.11.014.

**References**


