



Vitamin B₁₂ supplementation post-gastrectomy: a service closed-loop audit at St. James's Hospital, Dublin

Hugo C. Temperley¹ · Richard Gaule¹ · Cian Murray¹ · James Carey¹ · Niall J. O'Sullivan² · Matthew G. Davey³ · Michelle Fanning⁴ · Jarlath C. Bolger^{1,5} · Narayanasamy Ravi¹ · John V. Reynolds¹ · Claire L. Donohoe¹

Received: 14 June 2022 / Accepted: 3 August 2022
© The Author(s), under exclusive licence to Royal Academy of Medicine in Ireland 2022

Abstract

Background Vitamin B₁₂ (VB12) deficiency is a well-described complication post-gastrectomy. It is caused by the loss of parietal cell mass leading to megaloblastic anaemia. This closed-loop audit assesses patient understanding of and adherence with VB12 supplementation guidelines post-gastrectomy.

Methods A closed-loop audit cycle was performed. After the first cycle, an educational intervention was actioned prior to re-audit. One hundred twenty-five patients who underwent gastrectomy between 2010 and 2020 were available for study (86 total gastrectomies (TG), 39 subtotal gastrectomies (STG)). Twenty-nine patients who had not been adherent with VB12 supplementation/surveillance were eligible for re-audit.

Results 91.9% (79/86) of TG patients reported adherence in regular parenteral VB12 supplementation. Adherence was significantly lower for STG for checking (and/or replacing) their VB12, with only 53.8% (21/39) checking their VB12 levels. 67/125 (53.6%) of the patients stated that they knew it was important to supplement B₁₂ post-gastrectomy. 37.8% (43/113) of participants could explain why this was important, and 14.4% (18/125) had any knowledge of the complications of VB12 deficiency. Following re-audit, 5/8 (57.5%) of TG patients who had not been adherent with VB12 supplementation in the first cycle were now adherent with VB12 supplementation following our educational intervention. 7/17 (41.2%) of the STG group had received VB12 or made arrangements to receive supplemental VB12 if it was indicated.

Conclusion This study demonstrates good adherence in those undergoing TG. Patient understanding correlates with adherence, suggesting that patient education and knowledge reinforcement may be key to adherence with VB12 supplementation. A simple educational intervention can improve adherence with VB12 supplementation in patients undergoing gastrectomy.

Keywords Clinical nutrition · Gastric cancer · General surgery · Surgical oncology · Vitamin B₁₂

All abbreviations are explained at first appearance in text.

Mini abstract: Vitamin B₁₂ (VB12) deficiency is a well-described complication post-gastrectomy. This study demonstrates good adherence in those undergoing TG at our centre. Patient education and knowledge play a key role in VB12 adherence.

✉ Hugo C. Temperley
temperlh@tcd.ie

¹ Department of Surgery, Trinity Centre for Health Sciences, St. James's Hospital and Trinity College Dublin, Dublin 8, Ireland

² Department of Surgery, Tallaght University Hospital, Dublin 24, Ireland

Introduction

Vitamin B₁₂ (VB12) deficiency is a well-described complication post-gastrectomy [1–4]. Transformation of any part of the gastrointestinal (GI) tract can have adverse implications on nutrient absorption, with the loss of parietal cell mass that occurs post-gastrectomy responsible for VB12 deficiency. The main long-term consequence of VB12

³ Discipline of Surgery, National University of Ireland, Galway, Ireland

⁴ Department of Clinical Nutrition, St James's Hospital, Dublin, Ireland

⁵ Department of Surgery, Toronto General Hospital/University Health Network, Toronto, ON, Canada

deficiency is megaloblastic anaemia, which may be complicated by long-term neurological symptoms (paraesthesia, vision loss and ataxia) [5].

VB12 is a water-soluble vitamin, and when ingested in its free or nonprotein-bound form, will bind to carrier proteins known as R-binders (transcobalamin I) secreted by salivary glands in the oropharynx, and gastric mucosal cells within the stomach [6]. If VB12 is ingested in its protein-bound form, it must first undergo proteolytic cleavage in the stomach or duodenum where it will bind to an R-binder before entering the duodenum for further cleavage. Upon entry into the second segment of the duodenum, the pancreas will secrete additional protease which will then degrade the R-binders bound to the VB12. It is at this point that VB12 will bind to or complex with intrinsic factor for the remainder of its transition to the ileum of the small intestine for absorption [6]. Post-gastrectomy, the physiological absorption of VB12 is compromised due to a lack of gastric mucosa necessary for the absorptive process, with VB12 deficiency arising as an inevitable and early metabolic consequence.

The Eastern Cooperative Oncology Group (ECOG) outlined that as many as 87% of patients diagnosed with gastric cancer suffer from malnutrition [7]. Nutritional deficiencies in these patients result from disturbance of the natural anatomical and physiological mechanisms responsible for controlling gastric function [7]. VB12 absorption is reduced post-gastrectomy to varying degrees, with greater impairment seen post-total gastrectomy (TG) as compared with subtotal gastrectomy (STG) [8]. Hu et al. explored this concept when they retrospectively reviewed the data of 645 gastrectomies (TG: 176, STG: 469) and found that 100% of TG were VB12 deficient compared with 15.4% of STG [9]. In the absence of adequate replacement, VB12 deficiency will be present in all TG patients and a subset of STG patients [6].

When VB12 deficiency is diagnosed, treatment options include a standardised replacement regimen or close monitoring of VB12 levels and replacement as required. Approximately 4 out of every 5 patients will suffer at least one symptom of VB12 deficiency following gastrectomy [1], including fatigue, cold extremities, paraesthesia, or glossitis [3, 4]. However, it can often be challenging to differentiate symptomatic VB12 deficiency from the expected sequelae of gastric cancer surgery. Fatigue is a common symptom following gastrectomy regardless of VB12 status, and thus, some patients experiencing fatigue may not attribute their symptoms to VB12 deficiency [10, 11].

It is well documented that gastric (and oesophageal) surgical cancer patients are at great risk of malnutrition [12–14]. However, there is inconsistent and lacking data available on patient understanding and knowledge of the role of VB12 in a post-gastrectomy setting. The purpose of our study was to comprehensively audit patient VB12

supplementation adherence and to gain insight into patient understanding of the VB12 supplementation guidelines post-gastrectomy in our tertiary referral centre. We implemented an intervention, in the form of a patient information leaflet, before reauditing these parameters in order to ‘close the loop’. Herein, we present the results of this closed-loop cycle and discuss the impact of simple interventions which may be useful to enhance patient adherence with VB12 supplementation.

Methods

Study population and setting

This audit was registered with our clinical audit department. Thereafter, a closed-loop audit was performed in accordance with local guidelines. In total, 125 patients (86 TG and 39 STG respectively) who attended our centre for gastrectomy between the years of 2010 and 2020 were identified. The inclusion/exclusion flowchart can be seen in Fig. 1.

- Inclusion criteria included patients who underwent gastrectomy between 2010 and 2020.
- Exclusion criteria included patients who were deceased or had active disease undergoing treatment with palliative intent.

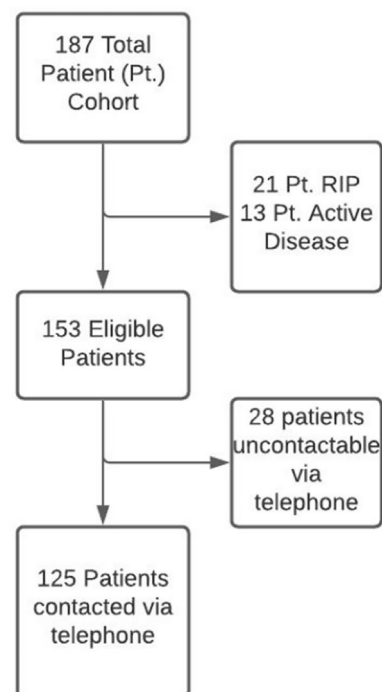


Fig. 1 Inclusion/exclusion flowchart. Pt: patient, RIP: dead at time of audit

Patients meeting inclusion criteria after exclusion were identified from a prospective database held for audit and research purposes. Approval for the study was exempted by the local research ethics committee, as it was principally an audit for assessment of service delivery. A data protection impact analysis was undertaken, and the study was completed in compliance with General Data Protection Regulation (GDPR) legislation. Patient data were collected by reviewing electronic hospital records and through telephone surveys. Patients were asked standardised questions regarding their adherence to VB12 supplementation/surveillance regimens as organised by their primary care provider. We also assessed patient knowledge of VB12 in general and why it was important for them to be replacing VB12. The specific questions that the patients were asked as part of our survey were drawn up by three consultant upper-gastrointestinal (UGI) surgeons (Table 1). These data were collected between January and June 2021. To ensure that we followed a recognised standard and recommendation, we aligned our survey with consensus-based guidelines from the National Comprehensive Cancer Network [15], which publishes on postoperative nutritional gastrectomy surveillance strategy.

All data was inserted into an Excel spreadsheet (Microsoft, Redmond, WA, USA) for statistical analysis. A pre-determined call format was implemented in the form of a survey; if the patient answered, a verbal consent script was read and consent gained. Next, we ascertained the patient's knowledge of the importance of VB12 supplementation through a survey, using the consensus-based guidelines as above (Table 1). The data collected was broadly broken down into (1) patient characteristics, (2) whether or not they were supplementing or surveillance VB12, and (3) patient knowledge and education.

At our tertiary cancer centre, the standard protocol for VB12 post-gastrectomy involves verbally communicating with patients the importance of VB12, providing VB12 information in nutritional counselling (verbally and written information), including information on the discharge

summary to the general practitioner (GP), and checking adherence at post-operative visits. All patients are seen at least once in the first 2 months post-surgery by a registered dietician to discuss nutritional issues post-gastrectomy including VB12 replacement and monitoring. This routine advice on discharge and post-operative visits involves educating patients on the need for routine replacement with intramuscular injections of VB12 in all TG and discussing patient choice to have B12 levels monitored and replaced as required by the GP or replaced routinely by the GP.

Follow-up measurements

This was followed by an educational intervention—we developed a patient information leaflet entitled “Vitamin B12 Supplementation—Information for Patients Following a Total or Subtotal Gastrectomy” which was sent to 29 patients (8 TG, 21 STG) who had not been adherent with VB12 supplementation/surveillance, in November 2021. This leaflet was written up, using evidence-based research [12, 16, 17], by the multidisciplinary team including registered dietitians and surgeons. Patients were contacted 4 weeks later to assess if they had made arrangements to be treated or tested. The same call format was followed. All patients confirmed they had received the leaflet. These data are displayed in Table 3.

Statistical analyses

Basic descriptive statistics (i.e. Fisher's exact and unpaired-samples *t* tests) were used as appropriate to determine the adherence to recommendations as well as the association between knowledge and adherence of patients included in this study [18, 19]. All tests of significance were two-tailed with $p < 0.050$ indicating statistical significance. Descriptive statistics were performed using the Statistical Package for Social Sciences (SPSS) version 26 (International Business Machines Corporation, Armonk, NY).

Table 1 Questionnaire

	Questions asked over the phone
1	Do you remember being told when you left hospital that your vitamin B ₁₂ levels should be checked/replaced if found to be low by GP?
2	If yes, who was it who told them? e.g. intern, dietician
3	Did you know it was important to check vitamin B ₁₂ /replace after gastrectomy?
4	Do you know why it is important to replace vitamin B ₁₂ ?
5	Do you know what can happen if you're vitamin B ₁₂ deficient?
6	Did their GP contact them after their surgery to talk about/check vitamin B ₁₂ levels?
7	Do you get vitamin B ₁₂ injections from your GP?
8	If yes, how often do you get them?
9	Do you have any queries or are you unsure of anything?

GP general practitioner

Table 2 Performance of the system to replace or monitor B12 after gastrectomy

	Overall	TG	STG
Sex (M:F)	81:44	55:31	26:13
Age	Mean: 71.34 Range: 31–91	Mean: 72.2 Range: 31–91	Mean: 69.0 Range: 40–87
Operation date (mean)	2015	2015	2015
Time from operation date to phone call	Mean: 4.7 years	/	/
Replacing/checking VB12	100/125 (80%)	79/86 (91.9%)—replacing	21/39 (53.8%)—checking and/or replacing
Interval (months)	3.29	3.04 months (replace)	4.7 month (replace / check)
Was there a DC summary?	94/125 (75.2%)	63/86 (73.2%)	31/39 (79.5%)
Was there advice related to VB12 on the DC summary?	58/94 (61.7%)	40/63 (63.5%)	18/31 (58.1%)
Where was it found in the DC summary?	‘Advice to GP’ section—42/58 (72.4%)	‘Advice to GP’ section—27/40 (67.5%)	‘advice to GP’ section – 15/18 (83.3%)
When leaving the hospital, were they informed that VB12 levels should be checked/replaced if low by the GP?	Yes: 80/125 (64.0%) No: 34/125 (27.2%) Unsure: 11/125 (8.8%)	Yes: 59/86 (68.6%) No: 18/86 (20.9%) Unsure: 9/86 (10.5%)	Yes: 21/39 (53.8%) No: 16/39 (41.0%) Unsure: 2/39 (5.2%)
Did they know it was important to check VB12/replace after a gastrectomy?	67/125 (53.6%)	51/86 (59.3%)	16/39 (41.0%)
Did the GP contact them after their surgery to talk about/check VB12 levels?	48/125 (38.4%)	39/86 (45.3%)	9/39 (23.1%)
Do they know why it is important that they are replacing VB12?	43/113 (37.8%)	34/74 (45.9%)	13/39 (33.3%)
Do they know what can happen if they do not get their VB12?	18/125 (14.4%)	14/86 (16.3%)	4/39 (10.0%)

STG sub-total gastrectomy, TG total gastrectomy, M male, F female, GP general practitioner, VB12 vitamin B₁₂, DC discharge

Results

Study cohort

In total, 187 patients were eligible for inclusion in the current analysis and were assessed. During screening, a further 34 patients were excluded (13 were undergoing treatment with palliative intent for recurrent disease and 21 had died prior to study start). Of these, 81.7% (125/153)

of the patients answered and consented for inclusion. The mean age was 71.34 years (STG: 69.0 (40–87), TG 72.2 (31–91)). In regard to sex, both STG and TG groups were male majority. For STG, 26 were male and 13 female, while for TG, 55 were male and 31 female. The mean time of surgery to our original phone call was 4.7 years (3 months–10 years). Patient characteristics are outlined in Tables 2 and 3.

Table 3 Re-audit of patients who were not adherent to VB12 supplementation/monitoring after educational intervention

	Re-audit (overall)	Re-audit (TG)	Re-audit (STG)
Surgery (TG:STG)	8:17	8	17
Sex (M:F)	16:9	6:2	11:6
Age	69.3 (40–91)	73.3 (57–91)	66.6 (40–78)
Did you find the leaflet helpful?	23/25 (92%)	8/8 (100%)	13/17 (76.5%)
Now aware of importance of B12?	14/25 (56%)	7/8 (87.5%)	8/17 (47.1%)
Have you received or made arrangements to receive supplemental VB12?	14/25 (56%)	5/8 (57.5%)	7/17 (41.2%)
Have you made arrangements to monitor VB12 levels?	4/25	2/8 (25%)	2/17 (11.7%)
Reasons for not making arrangements	3—no symptoms 2—check levels instead 2—oral B12 1—COVID	1—no symptoms	2—no symptoms 2—check levels instead 2—oral B12 1—COVID

STG sub-total gastrectomy, TG total gastrectomy, M male, F female, B12 vitamin B12

Initial audit

Overall (TG and STG)

Overall, 75.2% (94/125) of the patients had discharge summaries available on the electronic hospital record, and 61.7% (58/94) of these contained advice about VB12. The most common location where this advice was found was in the ‘advice to GP’ section—72.4% (42/58).

80/125 (64.0%) of the patients reported that they were ‘informed’ verbally on discharge that their VB12 levels should be replaced or checked/replaced if low by their GP. Overall, 48/125 (38.4%) were contacted by their GP after their surgery to talk about checking or replacing VB12 levels (TG: 39/86 (45.3%), STG: 9/39 (23.1%)). 67/125 (53.6%) of the patients stated that they knew the importance of VB12 supplementation post-gastrectomy, while only 37.8% (47/125) of the participants could explain why this was important and 14.4% (18/125) had any knowledge of the complications of VB12 deficiency.

Patients who understood the requirement for B12 replacement were significantly more likely to be adherent than those who did not (92.5% (62/67) versus 41.4% (24/58), $p < 0.001$). We found a non-statistically significant association between adherence to the VB12 recommendations and the time between date surgery and the phone call. The median duration of follow-up in the adherent group did not differ significantly from that of the non-adherent group (4.36 versus 4.73 years, log-rank test, $p = 0.23$).

TG versus STG

In total, 91.9% (79/86) of our TG patients reported adherence in regular parenteral VB12 supplementation. Adherence was significantly lower for STG for checking and/or replacing their VB12 at 53.8% (21/39, $p < 0.001$).

The advice section in the discharge summary was not completed more frequently in TG versus STG (63.5% versus 58.1%, Fisher’s exact test, $p = 0.824$), nor was the recall of verbal advice at time of discharge reported as different (TG: 68.6% (59/86) versus STG, 21/39 (53.8%), $p = 0.157$). Similarly, it appears that knowledge of the need to replace B12 was equivalent: TG 59.3% versus STG 41.0%, $p = 0.081$. The only difference observed was that GPs were more likely to contact patients post-TG regarding the need for replacement versus post-STG: TG: 39/86 (45.3%), STG: 9/39 (23.1%), $p = 0.049$. These figures are demonstrated in Table 2.

Re-audit (closed-loop) data

Overall

Thirty-one patients were eligible to be recontacted for reaudit. Two of these patients died before being contacted,

and therefore, twenty-nine patients were sent the patient information leaflet and contacted at 4 weeks (TG: 27.6% (8/29) and STG: 72.4% (21/29), 86.2% (25/29)). Of the 25 contactable, 92% (23/25) reported that they found the leaflet helpful and 8% (2/25) stated they had not read the leaflet. Fifty-six percent (14/25) reported they were now aware of the importance of VB12 supplementation/surveillance, and of these, 12/14 had received or made arrangements to receive VB12 (100% of the TG group and 41.2% of the STG group). In total, 56% (14/25) had received or made arrangements to receive supplemental VB12 and a further 16% (4/25) had made arrangements to have their VB12 levels checked. Of those who had not made arrangements for supplementation/surveillance, the reasons stated for non-adherence were as follows: an absence of symptoms, 12% (3/25); regular oral VB12 supplementation, 8% (2/25); and risk of COVID-19 in the community, 4% (1/25). This closed-loop data is displayed in Table 3.

Discussion and conclusion

Regular monitoring and supplementation of VB12 levels are important post-gastrectomy. This study demonstrates good adherence in those undergoing TG. Patient understanding correlates with adherence, suggesting that patient education and knowledge reinforcement may be key to adherence with VB12 supplementation. Improved verbal communication and education in regard to the importance of taking VB12 post-gastrectomy, as an inpatient and when followed up in the clinic, are vital in post-gastrectomy patients. Written information leaflets for patients undergoing gastrectomies are of benefit. Gastrectomy services should continue to improve the inclusion of VB12 advice on discharge summaries.

The ‘*Nutrition and Survivorship Clinic*’ from our tertiary cancer centre, in Oesophageal and Gastric Cancer, has demonstrated a high prevalence of iron deficiency, iron deficiency anaemia and vitamin D deficiency at 1-year post-surgery [12]. Although there is a large amount of data available on morbidity, mortality and major complications post-gastrectomy, there is inconsistent and often conflicting data focusing on postoperative nutrition and patient adherence with their new nutritional regime [14, 20–22]. This can in turn affect the overall survival and quality-of-life outcomes of the patient. The evidence, however, is clear that post-TG/STG or post-oesophagectomy patients may have a severely compromised nutritional status [14, 23–27]. This can be worsened by the addition of more complex regimens of chemotherapy and radiotherapy, as for many patients, a multimodal therapy is warranted to improve oncologic outcomes.

Adherence amongst this cohort of patients is a key issue. According to Nutrition Risk Screening (NRS 2002), when oral nutrition support was provided to patients after gastric cancer surgery, the patients' average daily intake during the first 3 months was about a half of the recommended requirements. As the patient survival rate and life expectancy increase, the nutritional sequelae and the need to monitor become ever more important. The consensus-based guidelines from the National Comprehensive Cancer Network [28] suggest monitoring VB12 levels, as well as bone health (Ca⁺⁺ and vitamin D), in surgically treated patients (especially after TG), and treat as indicated.

Our findings show the importance of education in ensuring adherence to VB12 supplementation and surveillance, with the highest levels of adherence seen in those who understood the importance of VB12. This highlights the need for continued patient education following gastric surgery using different approaches, spread over time. Furthermore, the requirement for B12 supplementation in patients following a STG is variable and not universal as it is post-TG. The adherence to supplementation, or level checking and supplementation as required, was lower in those who had undergone STG in this study, despite similar nutritional counselling, and remained lower despite a targeted educational intervention compared to TG. One reason may be less clear guidance to primary care providers on the potential requirement for supplementation—in this cohort, GPs were less likely to contact patients after STG regarding supplementation. This warrants attention during patient and provider counselling and further study to understand the difference between cohorts. Our centre attempts to improve adherence by re-iterating and educating on the importance of adherence rates during follow-up clinic visits, to patients and, where possible, to family members or supporters of patients.

Although, to our knowledge, there are no randomised trials to guide a postoperative surveillance strategy in gastrectomy patients, we believe that a large-scale retrospective study from multiple centres would be adequate. This was recently performed in post-oesophagectomy patients. Murphy et al. [12] established a personalised multidisciplinary survivorship clinic at their centre; mean body weight loss at 6 months was $8.5 \pm 6.6\%$ and at 12 months, $8.8 \pm 7.3\%$; and found micronutrient deficiency was present in 79.4% of the patients preoperatively and 80.6% after 1 year, most commonly iron deficiency (preoperative: 43.2% and postoperative: 45.9%). Veeralakshmanan et al. [13] analysed 63 patients post-oesophagectomy and/or TG/STG gastrectomy for malignant tumours. The proportion of patients with deficiency in ferritin, folate, VB12 and vitamin D was 42.86%, 9.52%, 6.35%, and 36.67% respectively. Heneghan et al. [14] performed a retrospective review on 66 oesophageal or gastric oncologic patients and

found that malabsorption was evident in 73% of patients. With such large numbers of patients nutrient deficient following gastric and oesophageal cancer surgery, there is no doubt that further work is needed in nutrition and patient education to ensure best patient outcomes.

Our study had several limitations. Firstly, the sample size was relatively small, as we are assessing a single centre's performance over a limited time frame. Secondly, in our study, not all patients had discharge summaries available on the electronic health record, so we cannot be certain that they or their GP were aware of the requirement for VB12 supplementation. Lastly, a significant proportion of patients in both the original questionnaire (18.3%) and at re-audit (13.8%) were not contactable. Nonetheless, they were, however, contacted by telephone twice and, if not successfully contacted, they were contacted on a third occasion 1 week later in a further attempt to complete the questionnaire.

We believe our paper could be utilised as an example by other hospitals to create evidence-based protocols for VB12 supplementation post-gastrectomy, auditing against their respective protocols and implementing simple measures to improve adherence and patient understanding. It emphasises the importance of using multiple means of communication over time. The patient leaflet designed for the re-audit is now used as protocol for micronutrient screening and supplementation in post-operative gastrectomy patients, and we recommend its use in other cancer tertiary centres. As a result of this closed-loop audit, from 1st January 2022, routine screening of micronutrients in all patients at 1-year post-oesophagectomy and gastrectomy will commence. As per the protocol for surveillance post-UGI surgery, patients will attend in person at the 12-month post-surgery time point and virtually at the 15-month time point as routine. We were able to improve adherence and patient understanding using simple measures, demonstrating that patient adherence can be improved through greater awareness of VB12.

Author contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Hugo C. Temperley, Richard Gaule, Cian Murray, James Carey, Matthew G. Davy and Niall J. O'Sullivan. The first draft of the manuscript was written by Hugo Temperley. Michelle Fanning, Jarlath C. Bolger, Narayanasamy Ravi, John V. Reynolds and Claire L. Donohoe commented on previous versions of the manuscript. All authors read and approved the final manuscript. Claire L. Donohoe was the senior author on the paper.

Data availability The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

Consent of publication Informed consent to be included in the study, or the equivalent, was obtained from all patients.

Conflict of interest The authors declare no competing interests.

References

- Jun JH, Yoo JE, Lee JA et al (2016) Anemia after gastrectomy in long-term survivors of gastric cancer: a retrospective cohort study. *Int J Surg* 28:162–168
- Lee SM, Oh J, Chun MR, Lee SY (2019) Methylmalonic acid and homocysteine as indicators of vitamin B12 deficiency in patients with gastric cancer after gastrectomy. *Nutrients* 11(2)
- Adachi S, Kawamoto T, Otsuka M et al (2000) Enteral vitamin B12 supplements reverse postgastrectomy B12 deficiency. *Ann Surg* 232(2):199–201
- Kim HI, Hyung WJ, Song KJ et al (2011) Oral vitamin B12 replacement: an effective treatment for vitamin B12 deficiency after total gastrectomy in gastric cancer patients. *Ann Surg Oncol* 18(13):3711–3717
- O'Leary F, Samman S (2010) Vitamin B12 in health and disease. *Nutrients* 2(3):299–306
- Ankar A, Kumar A (2022) Vitamin B12 deficiency. In: *StatPearls*. Treasure Island (FL)
- Dewys WD, Begg C, Lavin PT et al (1980) Prognostic effect of weight loss prior to chemotherapy in cancer patients. *Am J Med* 69:491–497
- Cueto J, Urdaneta LF, Belin RP, Doberneck RC (1965) Vitamin B12 and iron deficiency after partial gastrectomy. *Arch Surg* 91(6):995–997. <https://doi.org/10.1001/archsurg.1965.01320180129026>
- Hu Y, Kim HI, Hyung WJ et al (2013) Vitamin B(12) deficiency after gastrectomy for gastric cancer: an analysis of clinical patterns and risk factors. *Ann Surg* 258(6):970–975
- Park KB, Park JY, Lee SS et al (2020) Chronological changes in quality of life and body composition after gastrectomy for locally advanced gastric cancer. *Ann Surg Treat Res* 98(5):262–269
- Stone P, Richards M, Hardy J (1998) Fatigue in patients with cancer. *Eur J Cancer* 34(11):1670–1676
- Murphy CF, Fanning M, Raftery N et al (2021) Early experience with a nutrition and survivorship clinic in esophageal cancer. *Dis Esophagus* 34(2):doaa061. <https://doi.org/10.1093/dote/doaa061>
- Veeralakshmanan P, Tham JC, Wright A et al (2020) Nutritional deficiency post esophageal and gastric cancer surgery: a quality improvement study. *Ann Med Surg (Lond)* 29(56):19–22. <https://doi.org/10.1016/j.amsu.2020.05.032>. PMID:32566222;PMCID:PMC7296330
- Heneghan HM, Zaborowski A, Fanning M et al (2015) Prospective study of malabsorption and malnutrition after esophageal and gastric cancer surgery. *Ann Surg* 262(5):803–807;discussion 807–808
- Watson DI, Thompson SK, Devitt PG et al (2020) Five year follow-up of a randomized controlled trial of laparoscopic repair of very large hiatus hernia with sutures versus absorbable versus nonabsorbable mesh. *Ann Surg* 272(2):241–247
- Moretti D, Goede JS, Zeder C et al (2015) Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood* 126(17):1981–1989. <https://doi.org/10.1182/blood-2015-05-642223>. (Epub 2015 Aug 19 PMID: 26289639)
- Muñoz M, Gómez-Ramírez S, Besser M et al (2017) Current misconceptions in diagnosis and management of iron deficiency. *Blood Transfus* 15(5):422–437. <https://doi.org/10.2450/2017.0113-17>. PMID:28880842;PMCID:PMC5589705
- Kim HY (2017) Statistical notes for clinical researchers: chi-squared test and Fisher's exact test. *Restor Dent Endod* 42(2):152–155. <https://doi.org/10.5395/rde.2017.42.2.152>. Epub 2017 Mar 30. PMID: 28503482; PMCID: PMC5426219.
- Wadhwa RR, Marappa-Ganeshan R (2022) T test. 2022 Jan 19. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing. PMID: 31971709
- Wan GY, Yuan H, Xue H (2021) Assessment of compliance with oral nutritional supplementation and exploration of barriers and facilitators for patients after gastrectomy: a mixed-methods study. *J Adv Nurs* 77(6):2845–2859
- Mulazzani GEG, Corti F, Della Valle S, Di Bartolomeo M (2021) Nutritional support indications in gastroesophageal cancer patients: from perioperative to palliative systemic therapy. A Comprehensive Review of the Last Decade. *Nutrients* 13(8)
- Imamura H, Nishikawa K, Kishi K et al (2016) Effects of an oral elemental nutritional supplement on post-gastrectomy body weight loss in gastric cancer patients: a randomized controlled clinical trial. *Ann Surg Oncol* 23(9):2928–2935
- Veeralakshmanan P, Tham JC, Wright A et al (2020) Nutritional deficiency post esophageal and gastric cancer surgery: a quality improvement study. *Ann Med Surg (Lond)* 56:19–22
- Baker M, Halliday V, Williams RN, Bowrey DJ (2016) A systematic review of the nutritional consequences of esophagectomy. *Clin Nutr* 35(5):987–994
- Huddy JR, Macharg FM, Lawn AM, Preston SR (2013) Exocrine pancreatic insufficiency following esophagectomy. *Dis Esophagus* 26(6):594–597
- Gemmill EH, Humes DJ, Catton JA (2015) Systematic review of enhanced recovery after gastro-oesophageal cancer surgery. *Ann R Coll Surg Engl* 97(3):173–179
- Martin L, Lagergren J, Lindblad M et al (2007) Malnutrition after oesophageal cancer surgery in Sweden. *Br J Surg* 94(12):1496–1500
- National Comprehensive Cancer Network (NCCN) (2022) NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/physician_gls. (Accessed on 21 Feb 2022)

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.