Impact of malnutrition on early outcomes after cancer surgery

GlobalSurg Collaborative and NIHR Global Health Unit on Global Surgery

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Impact of malnutrition on early outcomes after cancer surgery: an international, multicentre, prospective cohort study

*GlobalSurg Collaborative and NIHR Global Health Unit on Global Surgery**

Summary

Background Malnutrition represents a key priority for global health policy, yet the impact of nutritional state on cancer surgery worldwide remains poorly described. We aimed to analyse the effect of malnutrition on early postoperative outcomes following elective surgery for colorectal or gastric cancer.

Methods We did an international, multicentre, prospective cohort study of patients undergoing elective surgery for colorectal or gastric cancer between April 1, 2018, and Jan 31, 2019. Patients were excluded if the primary pathology was benign, they presented with cancer recurrence, or if they underwent emergency surgery (within 72 h of hospital admission). Malnutrition was defined with the Global Leadership Initiative on Malnutrition criteria. The primary outcome was death or a major complication within 30 days of surgery. Multilevel logistic regression and a three-way mediation analysis were done to establish the relationship between country income group, nutritional status, and 30-day postoperative outcomes.

Findings This study included 5709 patients (4593 with colorectal cancer and 1116 with gastric cancer) from 381 hospitals in 75 countries. The mean age was 64·8 years (SD 13·5) and 2432 (42·6%) patients were female . Severe malnutrition was present in 1899 (33·3%) of 5709 patients, with a disproportionate burden in upper-middle-income countries (504 [44·4%] of 1135) and low-income and lower-middle-income countries (601 [62·5%] of 962). After adjustment for patient and hospital risk factors, severe malnutrition was associated with an increased risk of 30-day mortality across all country income groups (high income: adjusted odds ratio [aOR] 1·96 [95% CI 1·14–3·37], p=0·015; upper-middle income: 3·05 [1·45–6·42], p=0·003; low income and lower-middle income: 11·57 [5·87–22·80], p<0·0001). Severe malnutrition mediated an estimated 32% of early deaths in low-income and lower-middle-income countries (aOR 1·41 [95% CI 1·22–1·64]) and an estimated 40% of early deaths in upper-middle-income countries (1·18 [1·08–1·30]).

Interpretation Severe malnutrition is common in patients undergoing surgery for gastrointestinal cancers and is a risk factor for 30-day mortality following elective surgery for colorectal or gastric cancer. There is an urgent need to examine whether perioperative nutritional interventions can improve early outcomes following gastrointestinal cancer surgery worldwide.

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See **Comment** page e302

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See **Online** for appendix

Introduction

Cancer surgery is a key global health issue, with the number of new cancer cases worldwide expected to reach 22·2 million in 2030.[1] Surgery is an integral part of cancer treatment, and the *Lancet Oncology* Commission on global cancer surgery estimated that 45 million procedures will be needed worldwide by 2030.[2] Patients with cancer commonly develop malnutrition, which has been linked to elevated all-cause mortality[3] and worse postoperative outcomes.[4] Patients undergoing surgery for cancer often present with loss of bodyweight, sarcopenia, and in some instances cachexia, all of which contribute to poor postoperative outcomes.[5]

A series published in 2020 highlighted that the double burden of malnutrition with the simultaneous presence of undernutrition and overnutrition is increasingly prevalent in low-income and middle-income countries (LMICs).[6] This burden is likely to have been exacerbated by the COVID-19 pandemic causing delays in cancer diagnosis and subsequent presentation of patients with advanced-stage disease.[7] Treating malnutrition in the perioperative period for at least 5 days has been shown to improve outcomes following cancer surgery[8] and reduce hospital inpatient complications,[9,10] and has been identified as an area of high research priority in LMICs.[11]

To the best of our knowledge, there is a scarcity of high-quality data on the burden and impact of malnutrition in patients undergoing surgery for cancer worldwide. Retrospective study designs, small sample sizes, and the use of non-standardised malnutrition classification criteria restrict global comparisons. We aimed to analyse the effect of malnutrition on early

Research in context

Evidence before this study

Before undertaking the present study we searched for published multinational studies assessing the impact of malnutrition on early outcomes after surgery for gastrointestinal cancers, focusing on low-income and middle-income countries (LMICs). We searched PubMed, MEDLINE, Google Scholar, and ClinicalTrials.gov for studies published from inception to Oct 26, 2022, using the search terms "cancer" OR "malignancy" AND "surgery" AND "nutrition" OR "cachexia" AND "developing countries" OR "low income" OR "middle income" OR "low and middle income", without any language restrictions. Identified studies largely focused on single tumour types, were retrospective in nature, did not compare outcomes across multiple income settings, and often measured outcomes with non-standardised criteria. Preoperative nutrition has been identified as a research priority by surgical experts in LMICs.

Added value of this study

To the best of our knowledge, the present study is the first to provide comprehensive data across multiple income settings on the impact of malnutrition on early outcomes in patients undergoing surgery for colorectal or gastric cancer. We prospectively collected data from 381 hospitals in 75 countries using standardised and validated methods. Severe malnutrition was common across all income groups. After case-mix adjustment, patients with severe malnutrition had higher rates of postoperative surgical-site infection and 30-day mortality than patients with no or moderate malnutrition. A third of the excess early mortality in LMICs following surgery was mediated by the presence of severe malnutrition.

Implications of all the available evidence

Malnutrition is disproportionately higher in LMICs than in high-income countries. Malnutrition contributes to significantly worse postoperative surgical-site infection and early mortality rates, with patients in LMICs experiencing additional morbidity and mortality risks. An urgent assessment of perioperative nutritional interventions led by in-country investigators is needed to evaluate the ability of these interventions to reduce early morbidity and mortality following surgery for cancer.

postoperative outcomes in patients undergoing elective surgery for colorectal or gastric cancer.

Methods

Study design and participants

We did an international, multicentre, prospective cohort study of patients undergoing elective surgery for colorectal or gastric cancer. Predefined data items were collected according to a previously published protocol.[12] Investigators included consecutive patients undergoing surgery for breast, colorectal, and gastric cancer within 4-week time intervals between April 1, 2018, and Jan 31, 2019. Local investigators could select any 4-week interval within this period. Only patients with colorectal or gastric cancer were included in the present analysis because of the known high burden of malnutrition in patients with gastrointestinal cancer.[3]

Patients aged 18 years or older undergoing any procedure (laparoscopic, open, or robotic) requiring a skin incision under general or neuraxial anaesthesia were eligible for inclusion in this study. Patients undergoing purely diagnostic or staging procedures were excluded, as were patients undergoing surgical procedures for benign disease or cancer recurrence. Patients who underwent emergency surgery, defined as occurring within 72 h of hospital admission, were also excluded, as preoperative oral nutrition given for less than 3 days is often ineffective.[13]

Although the UK National Health Service (NHS) Research Ethics Committee considered this study exempt from formal research registration (South East Scotland Research Ethics Service, reference NR/161AB6), individual centres obtained their own audit or institutional approval as appropriate. In participating hospitals in some countries, informed patient consent was taken orally or in writing, where required, whereas in other countries the requirement for patient consent was waived by local research ethics committees. This study was done in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[14]

Data collection and validation

A summary of key patient and disease variables collected is provided in the appendix (p 1). Briefly, variables were selected to be objective, standardised, easily transcribed, and internationally relevant to maximise completeness and accuracy. Demographic variables such as age, sex, smoking, and comorbidities were identified on the basis of patient notes. Complications and death were confirmed through patient records at the 30-day follow-up, including any hospital notes or death certificates issued, or both. Nutritional status was defined with the Global Leadership Initiative on Malnutrition (GLIM) criteria,[15] based on either BMI or percentage bodyweight loss within the preceding 6 months. Patients were defined as having severe malnutrition if they presented with a BMI less than 18·5 kg/m² or more than 10% unintentional bodyweight loss in 6 months.

Local investigators uploaded patient records to a secure online website through the Research Electronic Data Capture (REDCap) system.[16] The lead investigator at each site checked the accuracy of all cases before submitting data. To ensure data quality, real-time assessment was done upon entry into the database and disparities were highlighted to local collaborators for immediate review. The submitted data were then checked centrally, and when missing data were identified the local lead investigator was contacted and asked to complete the record. Online data visualisation tools aided this process. Records that remained incomplete were included in the patient flowchart but excluded from the analysis. Data were validated in three parts across a representative sample of centres according to a prespecified protocol. Case ascertainment and the accuracy of the collected data have previously been shown to be high.[17]

Outcomes

The primary outcomes were postoperative mortality and a major complication within 30 days of surgery, as defined by Clavien–Dindo grade III, IV, or V.[18] Death was included in the definition of major complication and therefore was not a competing risk. Secondary outcome measures were defined in the protocol[12] and included any 30-day complication (defined by Clavien-Dindo grade I–V), anastomotic leak, and surgical-site infection. Patients were assessed at 30 days to examine postoperative outcomes, with follow-up done in person, by telephone, or by review of medical records. In the event where 30-day follow-up records were unavailable, outcome status at the point of discharge from the hospital was recorded.

Statistical analysis

Scarce data meant that an a-priori sample size accounting for patient clustering was not possible. Variation across different international health settings was assessed by stratifying countries by World Bank country group classifications. Differences between country income groups were tested with the Pearson χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables.

Multilevel logistic regression models were constructed to account for case mix (differing patient, disease, and operative characteristics), with population stratification by hospital and country of residence incorporated as random intercepts with constrained gradients. An interaction term between country income group and nutritional state was included within each model to account for the potential co-linear relationship between malnutrition and World Bank tertile.[19]

Models were constructed with the following principles: confounders identified in previous studies were accounted for; demographic variables such as age and sex were included in model exploration; population stratification by hospital and country of residence was incorporated as random effects; all first-order interactions were checked and included in final models if found to be influential (reaching statistical significance, defined as $p<0\cdot05$, or resulting in a ≥10% change in the odds ratio of the explanatory variable of interest); and final model selection was done with a criterion-based approach by minimising the Akaike information criterion (AIC) and discrimination was determined with the C-statistic (area under the receiver operator curve). Effect estimates are presented as adjusted odds ratios (aORs) and 95% CIs. The variables included in the final models were World Bank income group, cancer type, age, sex, and disease stage.

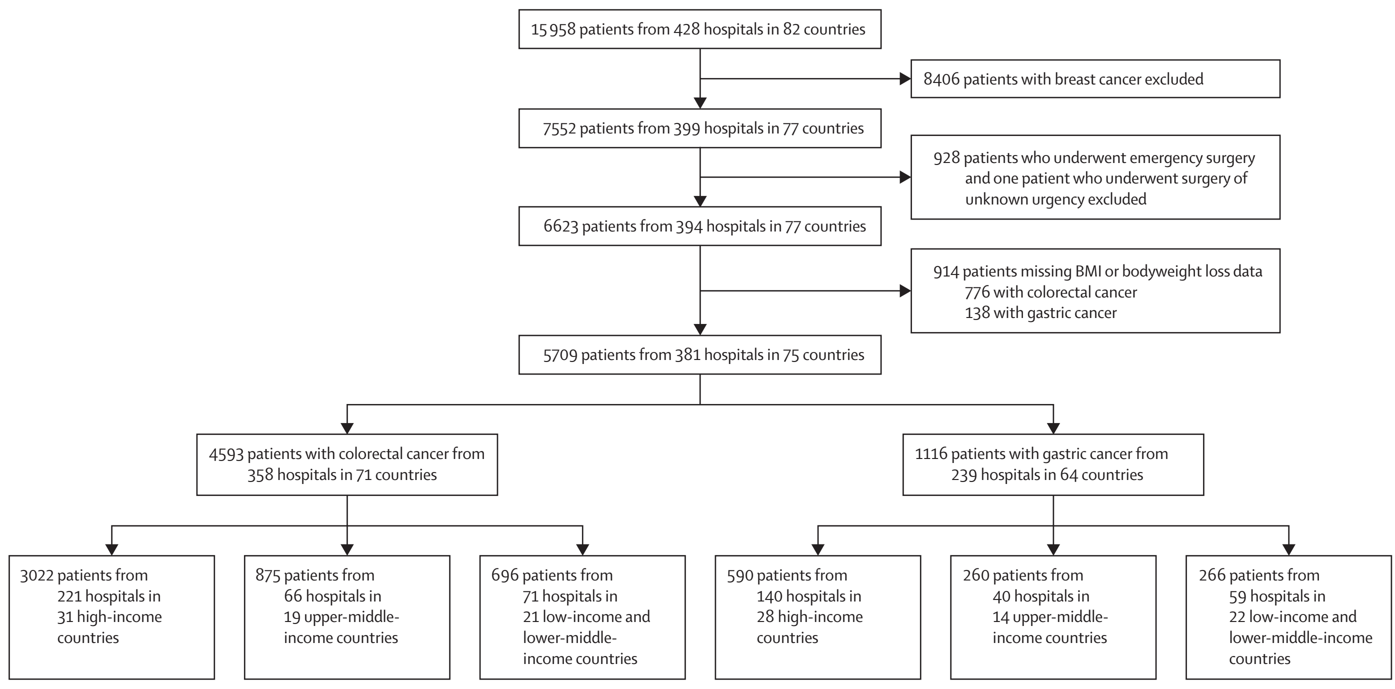

Figure 1: **Patient flowchart**

	Patients with no or moderate malnutrition	Patients with severe malnutrition	All patients
World Bank income group			
High income	2818 (74·0%)	794 (41·8%)	3612 (63·3%)
Upper-middle income	631 (16·6%)	504 (26·4%)	1135 (19·9%)
Low income or lower-middle income	361 (9·4%)	601 (31·6%)	962 (16·8%)
Cancer type			
Colorectal (colon or rectum)	3237 (85·0%)	1356 (71·4%)	4593 (80·5%)
Gastric (stomach)	573 (15·0%)	543 (28·6%)	1116 (19·5%)
Age, years			
Mean (SD)	65·8 (12·8)	62·6 (14·7)	64·8 (13·5)
Sex			
Female	1601 (42·0%)	831 (43·7%)	2432 (42·6%)
Male	2206 (57·9%)	1067 (56·2%)	3273 (57·3%)
Missing	3 (0·1%)	1 (0·1%)	4 (0·1%)
ASA score			
I	499 (13·1%)	312 (16·4%)	811 (14·1%)
II	2020 (53·0%)	968 (51·0%)	2988 (52·3%)
III	1161 (30·5%)	536 (28·2%)	1697 (29·7%)
IV	94 (2·5%)	53 (2·8%)	147 (2·6%)
V	1 (0·0%)	6 (0·3%)	7 (0·1%)
Missing	35 (0·9%)	24 (1·3%)	59 (0·9%)
ECOG performance status			
0	2178 (57·2%)	738 (38·9%)	2916 (51·1%)
1	1026 (26·9%)	675 (35·5%)	1701 (29·8%)
2	407 (10·7%)	290 (15·3%)	697 (12·2%)
3 or 4	122 (3·2%)	164 (8·6%)	286 (5·0%)
Missing	77 (2·0%)	32 (1·7%)	109 (1·9%)
Cancer stage			
I	1378 (36·2%)	385 (20·3%)	1763 (30·9%)
II	819 (21·5%)	393 (20·7%)	1212 (21·2%)
III	1279 (33·6%)	811 (42·7%)	2090 (36·6%)
IV	316 (8·3%)	288 (15·2%)	604 (10·6%)
Missing	18 (0·4%)	22 (1·1%)	40 (0·7%)
Smoking status			
Never smoked	2265 (59·4%)	1113 (58·6%)	3378 (59·2%)
Stopped >6 weeks ago	851 (22·3%)	365 (19·2%)	1216 (21·3%)
Current smoker	459 (11·9%)	317 (16·7%)	776 (13·6%)
Missing	235 (6·2%)	104 (5·5%)	339 (5·9%)
(Continued from previous column)			
Diabetes			
No	3071 (80·6%)	1501 (79·0%)	4572 (80·1%)
Non-insulin dependent	545 (14·3%)	271 (14·3%)	816 (14·3%)
Insulin	153 (4·0%)	83 (4·4%)	236 (4·1%)
Missing	41 (1·1%)	44 (2·3%)	85 (1·5%)
HIV status			
Negative	3799 (99·7%)	1897 (99·9%)	5696 (99·8%)
Positive	10 (0·3%)	2 (0·1%)	12 (0·2%)
Missing	1 (0·0%)	0 (0·0%)	1 (0·0%)
BMI			
Normal bodyweight (18·5–24·9 kg/m²)	1558 (40·9%)	954 (50·2%)	2512 (44·0%)
Underweight (<18·5 kg/m²)	0 (0·0%)	307 (16·2%)	307 (5·4%)
Overweight or obese (>24·9 kg/m²)	2252 (59·1%)	638 (33·6%)	2890 (50·6%)
>10% bodyweight loss			
No	3810 (100·0%)	69 (3·6%)	3879 (67·9%)
Yes	0 (0·0%)	1830 (96·4%)	1830 (32·1%)

(Table continues in next column)

Data are n (%) or mean (SD). ASA=American Society of Anesthesiologists. ECOG=Eastern Cooperative Oncology Group.

***Table:* Patient characteristics stratified by nutritional status**

The relationship between country income group and 30-day mortality was examined in a three-way decomposition of total effects into direct, indirect, and interactive effects. The mediator examined was nutritional status, defined as the presence or absence of severe malnutrition, with an exposure–mediator interaction term specified if informative. The model accounted for country income group and patient-level covariates, with uncertainty determined with bootstrap resampling (5000 draws) and 95% CIs constructed by use of percentiles.

A sensitivity analysis based on multiple imputation with chained equations was done to account for missing values for all statistical models, under the missing at random assumption. Ten sets, each with ten iterations, were imputed with available patient-level explanatory variables according to the methodology described by Sterne and colleagues.[20] The outcome variable was included as a predictor but excluded from imputation, with Rubin's rules used to combine results.

All analyses were done with the R Foundation Statistical Program (version 4.1.1), with the finalfit, tidyverse, regmedint, and lme4 functions.

This study was prospectively registered with ClinicalTrials.gov (NCT03471494).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

Results

5709 patients (4593 with colorectal cancer and 1116 with gastric cancer) from 381 hospitals in 75 countries were included (figure 1). Of all patients, 3612 (63·3%) were from high-income countries, 1135 (19·9%) were from upper-middle-income countries, and 962 (16·8%) were from low-income and lower-middle-income countries. Patient characteristics grouped by nutritional status are shown in the table, and patient characteristics grouped by country income group are shown in the appendix (p 3). Missingness of primary outcomes (30-day mortality and major complications) was similar across variables of interest (appendix p 5).

Severe malnutrition was common across all income groups. Overall, 1899 (33·3%) patients were severely malnourished at the time of their elective surgery, with a higher burden of severe malnutrition found in upper-middle-income (504 [44·4%] of 1135) and low-income and lower-middle-income (601 [62·5%] of 962) settings compared to high-income settings (794 [22·0%] of 3612). Severe malnutriton was more likely in patients from upper-middle-income (aOR 2·83 [95% CI 2·46–3·26]; p<0·0001) and low-income and lower-middle-income countries (aOR 5·91 [5·08–6·89]; p<0·0001; figure 2) than in patients from high-income countries. A further descriptive model is included in the appendix (p 8).

The distribution of unadjusted mortality and complications stratified by nutritional status across income group are shown in the appendix (pp 9–10). Severely malnourished patients had higher postoperative mortality than patients with no or moderate malnutrition across all income groups (high income: 25 [3·2%] of 784 *vs* 38 [1·4%] of 2804; upper-middle income: 19 [3·8%] of 497 *vs* eight [1·3%] of 624; low income and lower-middle income: 45 [7·6%] of 591 *vs* ten [2·8%] of 358; appendix p 11). The proportion of patients who developed postoperative complications or surgical-site infection was higher in those with severe malnutrition than in those with no or moderate malnutrition, particularly in low-income and lower-middle-income countries. This association was similar across both colorectal and gastric cancer (appendix p 12). The distribution of unadjusted major complications (defined as Clavien–Dindo grade III or IV) across all postoperative outcomes is shown in the appendix (p 13).

Outcomes were adjusted in three-level models accounting for patient and disease factors nested within hospitals and country of treatment (figure 3; appendix pp 15–29). Severe malnutrition was associated with an increased risk of 30-day mortality across all income groups (high income: aOR 1·96 [95% CI 1·14–3·37], p=0·015; upper-middle income: 3·05 [1·45–6·42], p=0·003; low income and lower-middle income: 11·57 [5·87–22·80], p<0·0001). In low-income and lower-middle-income countries, patients with no or moderate malnutrition also had an increased risk of mortality at 30 days (aOR 4·47 [95% CI 1·81–11·03], p=0·001). A loss of more than 10% of a patient's bodyweight in the 6 months preceding their operation was associated with an increased risk of 30-day mortality (aOR 2·02 [95% CI 1·36–2·99], p=0·00053), as was being underweight (BMI <18·5 kg/m²) at the point of undergoing surgery (aOR 2·59 [95% CI 1·50–4·47], p=0·001; appendix p 30). Patients who were overweight appeared to have a lower risk of 30-day mortality, but this association was not significant (aOR 0·80 [95% CI 0·54–1·18], p=0·26; appendix p 30).

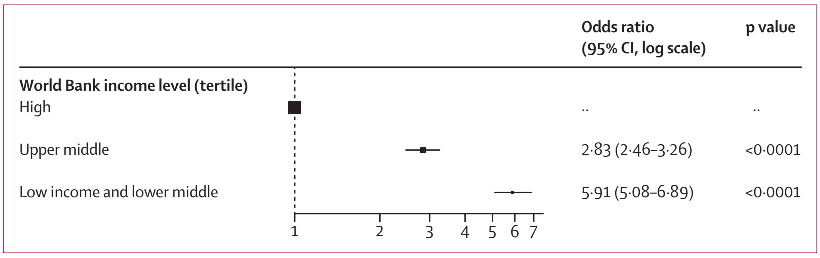

Figure 2: **Multivariable regression model for factors associated with presence of severe malnutrition**

The proportion of patients sustaining a major complication, any complication, or an anastomotic leak in adjusted analyses was similar across country income groups, except for potential evidence of fewer major complications in the absence of severe malnutrition in the upper-middle-income group (figure 4A–C). However, surgical-site infection was more likely to occur in patients with severe malnutrition in the upper-middle-income country group (aOR 2·30 [95% CI 1·46–3·62]; p=0·00035) and across all nutritional states in low-income and lower-middle-income country groups (no or moderate malnutrition: aOR 2·77 [95% CI 1·70–4·51]; p<0·0001; severe malnutriton: 3·00 [1·90–4·74]; p<0·0001; figure 4D). Similar associations were seen across colorectal and gastric cancer individually and in sensitivity analyses accounting for missing data (appendix pp 15–42).

The associations between country income group and 30-day mortality (figure 5A) and surgical-site infection (figure 5B) were examined in a three-way decomposition mediation model of nutritional status. A notable proportion of the excess mortality was mediated by severe malnutrition in upper-middle-income countries (aOR 1·18 [95% CI 1·08–1·30], 40%) and low-income and lower-middle-income countries (1·41 [1·22–1·64], 32%). Excess surgical-site infections were also mediated by severe malnutrition in upper-middle-income (aOR 1·04 [95% CI 1·01–1·07], 7%) and low-income and lower-middle-income (1·08 [1·02–1·15], 11%) countries. All effects persisted in a sensitivity analysis accounting for missing data (appendix pp 43–45).

Discussion

In this prospective study of patients undergoing cancer surgery from 381 hospitals in 75 countries, severe malnutrition was present across all income levels, with a disproportionate burden observed outside high-income settings. Severe malnutrition was associated with an increased risk of surgical-site infection and 30-day mortality, mediating around a third of early deaths following surgery for cancer. We noted additional morbidity and mortality even after adjustment for case mix, indicating that severe malnutrition imposed additional risks across all income groups, and particularly within LMICs.

Provision of safe and equitable surgical care is increasingly recognised as an essential part of cancer care, while improving nutrition forms part of the UN Sustainable Development Goal 2.[21] As delays in presentation are associated with poorer survival secondary to cancer cachexia,[22] early cancer detection programmes and improved access to surgical care are likely to reduce preoperative malnutrition rates in LMICs. However, patients often present with malnutrition despite good access to cancer care services.[22] Although malnutrition is associated with poorer outcomes, it represents a potentially modifiable risk factor to reduce the effects of cancer cachexia within the early postoperative period.[23] Meta-analyses of randomised controlled trials done in both high-income countries[24] and LMICs[8] have shown that simple perioperative oral nutritional supplementation can reduce early morbidity and mortality, potentially representing a low-cost and sustainable intervention in LMICs to improve surgical outcomes.

The rates of severe malnutrition reported in our study were higher than previous estimates across LMICs for patients undergoing surgery for cancer.[25] For patients with severe malnutrition undergoing surgery, 30-day mortality was elevated across all income groups. We also found higher unadjusted postoperative complication rates in patients with severe malnutrition across all

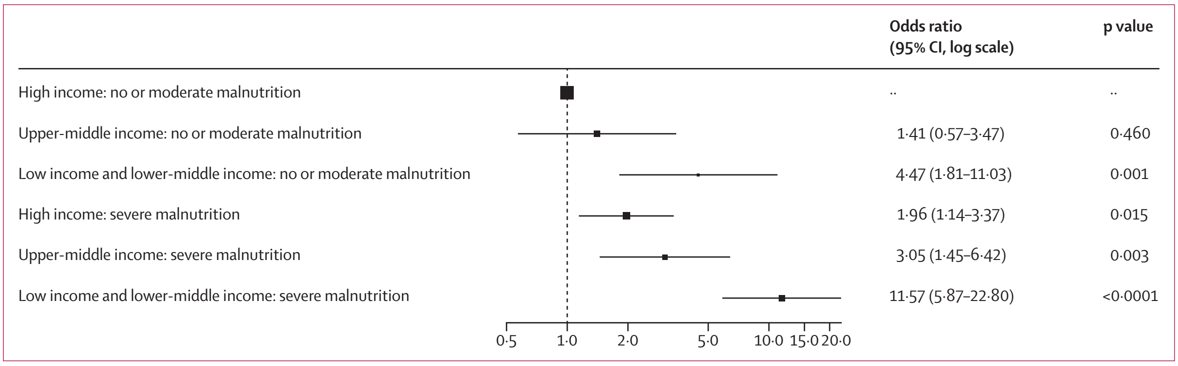

Figure 3: **Multilevel logistic regression-adjusted 30-day mortality by World Bank country income group and nutritional status (interaction term)**
Model adjusted for World Bank income group, cancer type, age, sex, and disease stage, with population stratification by hospital and country of residence.

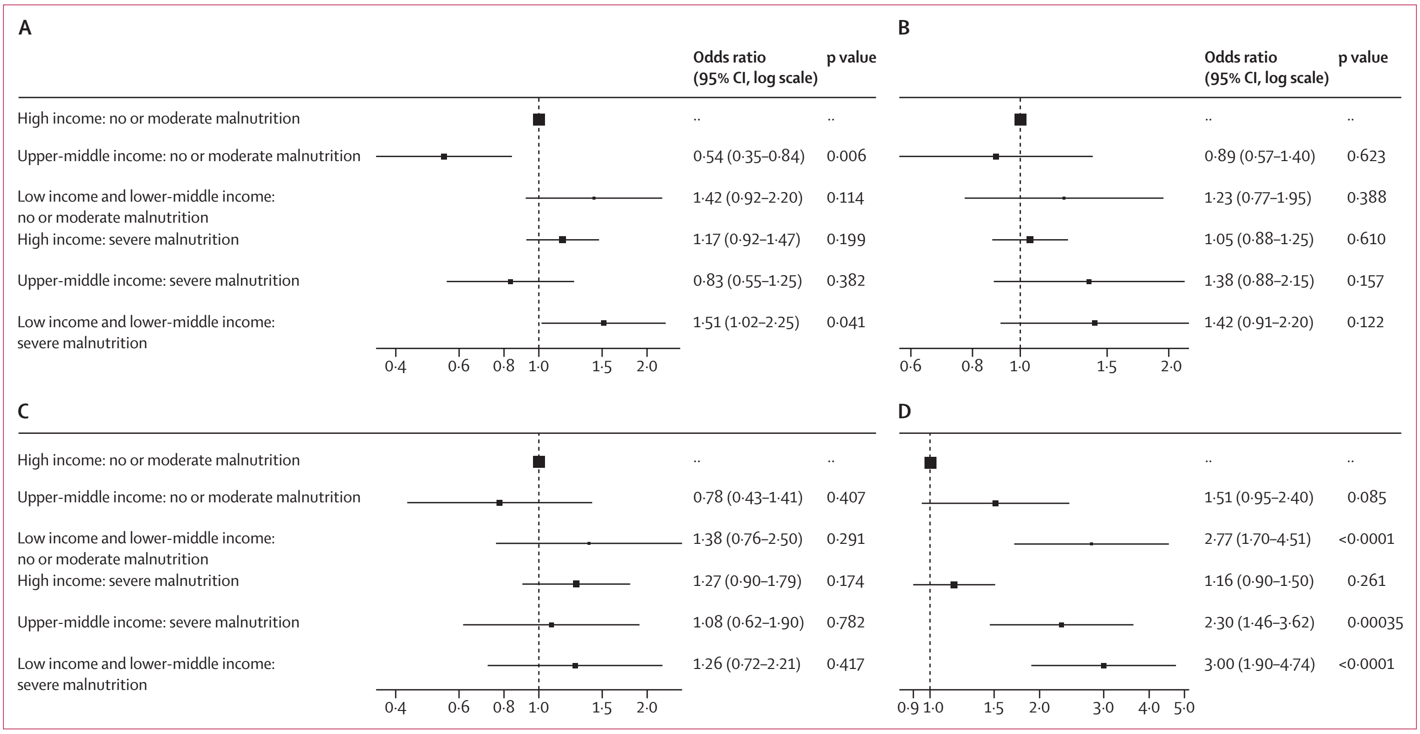

Figure 4: **Multilevel logistic regression-adjusted outcomes by World Bank country income group and nutritional status.**
(A) Major postoperative complication. (B) All postoperative complications. (C) Anastomotic leak. (D) Surgical-site infection. All models were adjusted for World Bank income group, cancer type, age, sex, and disease stage.

income groups. These differences disappeared after case-mix adjustment in high-income countries but remained in LMICs. Increased postoperative complication rates have been previously reported in malnourished patients undergoing surgery within LMICs,[26] but the use of non-standardised outcome definitions has restricted interpretation of these findings.

Malnutrition reduces the physiological capacity to compensate for traumatic events, including major surgery,[26] with the negative impact of malnutrition on the anabolic process of wound healing and postoperative recovery well described.[27] Excess mortality in malnourished patients is likely to occur secondary to the inability to recover from the associated physiological stress associated with postoperative complications.[27] This finding highlights the importance of recognising nutritionally vulnerable patients early to allow additional support and escalation of care if appropriate.

Various nutritional assessment tools have been proposed to identify patients at increased risk of surgical complications, but these are often time consuming to complete.[15] Despite high levels of awareness about the importance of nutritional assessment, few health-care providers routinely screen patients for malnutrition,[28] emphasising the need for simple and efficient assessment tools. In 2019, GLIM convened major clinical nutrition societies to reach a global consensus on the identification of criteria for the diagnosis of malnutrition in clinical settings.[15]

Our study provides evidence that GLIM criteria can be applied to a global patient cohort, and that this definition of malnutrition is associated with 30-day mortality and surgical-site infection following surgery for cancer. Furthermore, more than 10% bodyweight loss in 6 months and low BMI (<18·5 kg/m²), both diagnostic of cancer cachexia, were associated with 30-day mortality following cancer surgery in our cohort. This finding suggests that these criteria have potential as a simple preoperative screening tool to identify nutritionally vulnerable patients; however, further comparison with existing nutritional assessment tools in LMICs, such as the Malnutrition Universal Screening Tool and Subjective Global Assessment, is required to clarify the relative prognostic efficiency of GLIM criteria during routine use in the clinical setting.

A major strength of this study is its prospective design and use of standardised criteria to assess nutritional status and postoperative outcomes across multiple income settings. Data quality was ensured though collaborator-facing web applications and real-time data entry quality assurance, with independent validation verifying data accuracy and case ascertainment. Assessment of nutritional status and outcomes was standardised, and training was provided through an online platform. The quantification of surgical cancer care in resource-limited settings has been hindered by an insufficient amount of high-quality data. This study therefore contributes to closing this knowledge gap and allows meaningful comparisons from multiple income settings following case-mix adjustment.

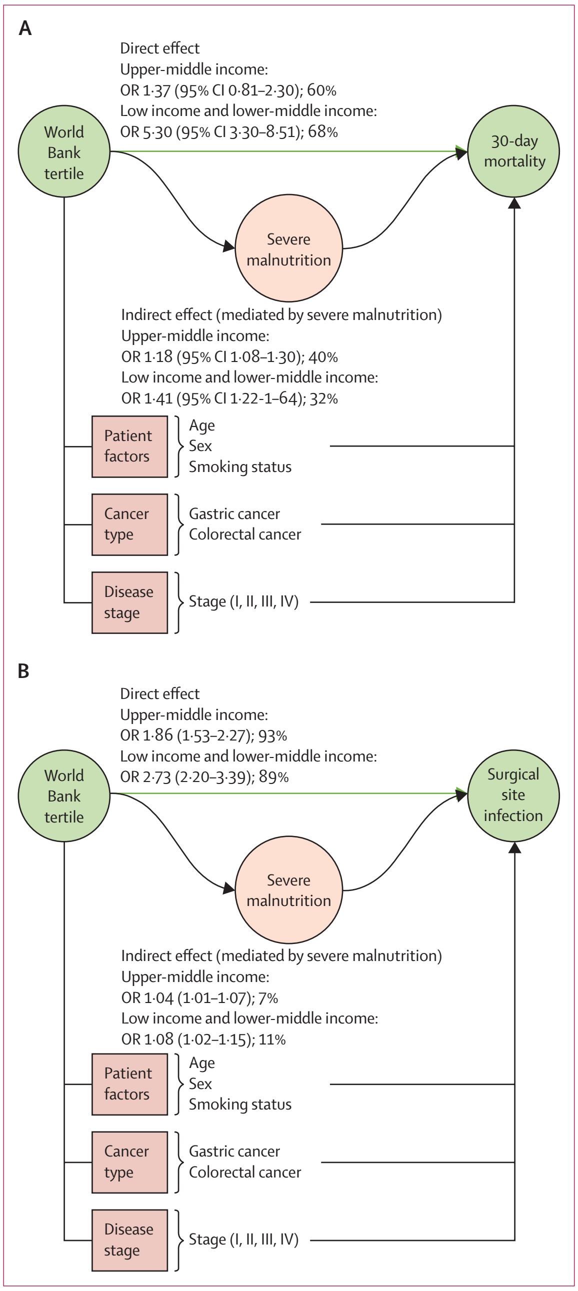

Figure 5: **Three-way decomposition mediation model of the association between country income group and 30-day mortality (A) and surgical-site infection (B), mediated by nutritional state**
Model adjusted for patient, cancer, and disease covariates. Uncertainty determined with bootstrap resampling (5000 draws) and 95% CIs constructed with percentiles. OR=odds ratio.

Our study has important limitations. We were only able to identify the presence of patients with severe malnutrition before surgery, using percentage bodyweight loss and a-priori categorised BMI, to ensure a high percentage of data completeness. Therefore, the comparison group contained both well-nourished patients and those with moderate malnutrition. As a result, our analysis is likely to have underestimated the true effect of severe malnutrition on postoperative outcomes. Meanwhile, we were unable to determine the mediation or additive effects of chronic malnutrition, which might be reflected by a low BMI at presentation. Bodyweight loss alone was a strong predictor of 30-day mortality, but further work is required to investigate the importance of chronic malnutrition to early postoperative outcomes following cancer surgery. Furthermore, for this analysis we used the phenotypic GLIM criteria and were unable to further stratify patients according to aetiological criteria, reduced food intake, and inflammatory markers.

We recognise that extending the follow-up period to 90 days would have allowed better capture of postoperative complications, since the impact of nutritional status was likely to persist beyond 30 days. However, the shorter 30-day follow-up period was chosen for pragmatic reasons to facilitate data completeness, particularly across resource-limited settings.

This prospective study did not include other globally prevalent cancers associated with malnutrition, such as gynaecological and oral cancer.[3] To maximise case ascertainment and ensure data quality, a pragmatic decision was made to collect data on cancer types commonly treated across our collaborative network. Our results might therefore only be generalisable to patients presenting with colorectal or gastric cancer; additional studies are required to determine the impact of nutritional status on early postoperative outcomes globally for different cancers. We plan to explore this further in future work exploring early outcomes after surgery for breast cancer.

Additionally, we were not able to measure all relevant patient, disease, and hospital variables, and therefore residual confounding exists. In particular, differences in operative approach (minimally invasive versus open) were difficult to accommodate in analyses because many hospitals in LMICs cannot offer these minimally invasive procedures. Further studies assessing the benefits of these approaches will probably identify important opportunities for intervention. It will also be of interest to ascertain how surgical outcomes are influenced by the experience and expertise of surgeons; however, this analysis was beyond the scope of our study.

Finally, the combined impact of patient comorbidity on early postoperative outcomes following cancer surgery in this cohort remains uncertain. Preoperative comorbidity is known to correlate with poorer nutritional state, with potential confounding possible despite model adjustment for important patient and disease factors. However, the factors included in our model are likely to be co-linear with overall measures of patient comorbidity; furthermore, our results remained consistent across sensitivity analyses.

Severe malnutrition is common and associated with an increase in 30-day mortality and surgical-site infection rates following elective cancer surgery worldwide. This finding suggests that perioperative nutrition remains a promising and untapped target for future studies to determine which perioperative interventions can reduce mortality rates and prevent severe complications. If effective interventions are found, the identification and treatment of malnutrition perioperatively might represent a potential low-cost, sustainable intervention in LMICs to reduce postoperative mortality and complications. If research gaps are addressed, preoperative oral nutrition is likely to form part of future global surgical guidelines as a simple measure that can improve outcomes after surgery for cancer. An international pilot randomised controlled trial investigating the feasibility and effectiveness of a perioperative oral nutritional intervention delivered the week before elective cancer surgery is underway (NCT04448041).

In conclusion, severe malnutrition represents a high global burden in cancer surgery and is an independent risk factor for 30-day mortality and surgical-site infection following elective surgery for colorectal or gastric cancer worldwide. Perioperative nutritional interventions might improve outcomes after cancer surgery and are a promising area of future research, which should particularly focus on suitable oral interventions across all income settings.

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Declaration of interests

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Data sharing

The dataset can be explored through an online visualisation tool. Hospital-level data can be shared by submitting an application via email to the corresponding author. For analyses of patient-level identifiable data within our trusted research environment, please email the corresponding author.

For the **online visualisation tool** see http://cancer.globalsurg.org

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