Malnutrition by European Society for Clinical Nutrition and Metabolism criteria predicts prognosis in patients with gastrointestinal and hepatobiliary–pancreatic cancer

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[1] **Abbreviations**:

[1] ESPEN, European Society for Clinical Nutrition and Metabolism; EDC, ESPEN diagnostic criteria; GI, gastrointestinal; HBP, hepatobiliary–pancreatic; BMI, body mass index; BIA, bioelectrical impedance analysis; SGA, subjective global assessment; AC, arm circumference; TSF, triceps skinfold thickness; FFMI, fat-free mass index; HR, hazard ratio; CI, confidence interval; UWL, unintentional weight loss

Abstract

Background & Aims: The European Society for Clinical Nutrition and Metabolism (ESPEN) proposed the ESPEN diagnostic criteria (EDC) for malnutrition in 2015. There is no report on the association between the EDC and prognosis in patients with gastrointestinal (GI) and hepatobiliary–pancreatic (HBP) cancer. This study aimed to (1) determine the prevalence of EDC malnutrition, (2) investigate the validity of the EDC as a nutritional and prognostic indicator, and (3) examine which components of the EDC are most related to long-term prognosis in patients with GI and HBP cancers.

Methods: A total of 634 patients with primary GI and HBP cancers who underwent their first resection surgery between July 2014 and March 2018 were retrospectively recruited. According to the EDC, patients were divided into malnourished and non-malnourished groups. Clinical parameters and survival between these two groups were compared. The prognostic effects of the EDC and the EDC components were analyzed using Cox proportional hazard models.

Results: The prevalence of EDC malnutrition was 22%. Anthropometric data and biochemical data were associated with EDC malnutrition. The 5-year survival rate was lower in the malnourished group (72%) than in the non-malnourished group (73%; P = 0.007). The multivariate analysis demonstrated that the malnourished group was an independent risk factor for mortality (hazard ratio = 1.70 in the malnourished group; 95% confidence interval 1.08–2.63; P = 0.024). Among EDC components, body mass index (BMI) of <18.5 kg/m^2 was an independent poor prognostic factor.

Conclusions: EDC malnutrition is associated with poor postoperative long-term prognosis. Among the EDC components, BMI of <18.5 kg/m^2 is most associated with prognosis in patients with preoperative GI and HBP cancers.

Keywords: ESPEN diagnostic criteria, Malnutrition, Body mass index, Fat-free mass index, Gastrointestinal cancer, Prognosis

Introduction

Cancer incidence and mortality are rapidly growing worldwide; in particular, gastrointestinal (GI) and hepatobiliary–pancreatic (HBP) cancers are quite common and have high mortality rates [1]. In recent years, it has been reported that the financial burden of cancer on health insurance and healthcare providers has increased [2]; hence, efforts related to GI and HBP cancer are important in society. Patients with GI and HBP cancer have a high prevalence of malnutrition. The prevalence of malnutrition has been reported to be 83% in patients with pancreatic cancer, 83% in those with gastric cancer, and 60% in those with colorectal cancer [3]. Malnutrition is usually caused by reduced food intake, poor digestion, and poor absorption [4]. Preoperative malnutrition is associated with negative outcomes with regard to postoperative complications, length of stay, and prognosis [5]. Therefore, it is important to diagnose malnutrition appropriately in preoperative patients using relevant methods.

In 2015, the European Society for Clinical Nutrition and Metabolism (ESPEN) proposed the ESPEN diagnostic criteria (EDC) for malnutrition, which aims “to be applied independent of clinical setting and etiology, and to unify international terminology” [6]. To date, several studies have reported on the EDC, including the prevalence of EDC malnutrition [7,8], the association between the EDC and other screening tools [9–12], the association between the EDC and bioelectrical impedance analysis (BIA) [13,14] or sarcopenia [15–17], and the association between EDC malnutrition and mortality [18–24]. However, there is no report on the association between the EDC and prognosis in patients with cancer. In addition, some of the previous studies have limitations, as they were performed without all components of the EDC. Although some of the previous studies examined the prognostic ability of each EDC component, there are no results in patients with GI and HBP cancers.

Therefore, the present study aimed to 1) determine the prevalence of EDC malnutrition,

2) investigate the validity of the EDC as a nutritional and prognostic indicator, and 3) examine which components of the EDC are most related to prognosis in patients with GI and HBP cancers.

Materials and methods

Patients

This was a retrospective, observational study. A total of 723 patients who were admitted to undergo first elective radical resection surgery for primary GI and HBP cancers at the Department of Digestive Surgery and Transplantation in Tokushima University Hospital from July 2014 to March 2018 were recruited. We excluded patients who canceled surgery, had a benign tumor, were at stage 0 or unknown stage, and without data for EDC assessment. This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of Tokushima University Hospital (No. 3157), and all patients agreed to participate in this study.

Data collection

The data, including age, sex, height, weight, cancer site, cancer stage, biochemical results, and dates of operation and death were collected from electronic medical records.

Nutritional assessment

All preoperative nutritional assessments including BIA and anthropometry [arm circumference (AC), triceps skinfold thickness (TSF), and handgrip strength] were performed during the period between admission and surgery by well-trained registered dieticians. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). BIA was performed using Inbody770 (InBody Japan Inc., Tokyo, Japan). BIA was conducted in a standing position and

was not conducted in patients with pacemakers or those who had difficulty standing. Patients fasted for at least 4 h before the measurement. Fat-free mass index (FFMI) was calculated as FFM/height^2 (kg/m^2). AC and TSF at the midpoint of the triceps of the non-dominant arm were measured with an insert tape and adipometer calipers (Abbot Laboratories, Tokyo, Japan). Handgrip strength of both hands was measured in the standing position using a dynamometer (Takei Scientific Instruments Co., Niigata, Japan). The assessments were repeated twice in each hand, and the average of the highest value in each hand was calculated. We calculated ratios with regard to Japanese anthropometric reference data (JARD2001) [25] and presented the values as %AC, %TSF, and %handgrip strength. Biochemical tests were conducted at the Department of Clinical Laboratory in the Tokushima University Hospital. We collected the data (albumin, hemoglobin, total lymphocyte, and C-reactive protein) 1 day before the surgery from electronic medical records. We defined sarcopenia according to handgrip strength and skeletal muscle index. Sarcopenia was diagnosed by low handgrip strength and low skeletal muscle index suggested by the Asian Working Group for Sarcopenia [26]. The cut-off values of low handgrip strength were 26 kg in males and 18 kg in females, and the cut-off values of low skeletal muscle mass index were 7.0 kg/m^2 in males and 5.7 kg/m^2 in females. Cancer cachexia was assessed as described by Fearon et al. [27].

Diagnosis of EDC malnutrition

There are two alternative ways to diagnose malnutrition by EDC: 1) BMI <18.5 kg/m^2 and 2) unintentional weight loss of >10% indefinite of time or >5% over the last three months and BMI <20 kg/m^2 if <70 years of age or <22 kg/m^2 if ≥70 years of age, or FFMI <15 kg/m^2 in females and <17 kg/m^2 in males [6].

Survival outcome

Survival time was calculated from the time of surgery to the last follow-up date (June 30, 2019) or death.

Statistical analysis

Non-normally distributed continuous variables are expressed as median and interquartile range. Continuous variables were compared between malnourished patients and non-malnourished patients using Wilcoxon's rank-sum test. Categorical variables were compared between the two patient groups using the chi-square test. Survival curves were plotted using the Kaplan–Meier method, and differences were evaluated using the log-rank test. Univariate and multivariate Cox proportional hazard regression models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). Baseline variables with $P < 0.1$ in the univariate analysis were included in the multivariate models. All statistical analyses were performed using JMP ver. 13.0 (SAS Institute Inc., Cary, NC, USA). A P-value <0.05 was considered statistically significant. We followed the standard methods to estimate the appropriate sample size for multivariate Cox proportional hazards regression models, with at least 10 outcomes required for each included independent variable. The sample size was calculated using data from our preliminary study, with an expected mortality rate of 10%, we required 400 ($4 \times 10/0.1$) patients (40 incidents) to appropriately perform multivariate Cox proportional hazards regression models with four variables.

Results

Prevalence of EDC malnutrition

Overall, 723 patients were recruited in this study. We excluded 16 patients who canceled surgery, 13 with a benign tumor, 18 with stage 0 or unknown stage, and 42 without data for

EDC assessment. Finally, 634 patients were selected and analyzed (Fig. 1). These patients were evaluated using EDC, and 142 patients (22%) were diagnosed with EDC malnutrition. The details of which EDC components the patients met are shown in Fig. 2. Among the 142 patients, 70 (49%) had BMI <18.5 kg/m^2, 51 (36%) had weight loss and low BMI, and 45 (32%) had weight loss and low FFMI. There were 24 patients (17%) who had unintentional weight loss with both low BMI and FFMI.

Patient characteristics

Table 1 shows patient characteristics and comparison of anthropometric data and nutritional markers for non-malnourished and malnourished groups. Age, sex, cancer site, cancer stage, height, body weight, and BMI were significantly different between the non-malnourished and malnourished groups. Anthropometry data and biochemical data significantly differed between the non-malnourished and malnourished groups. The prevalences of sarcopenia and cachexia were higher in the malnourished group than in the non-malnourished group.

Table 1. Patient characteristics

	All n = 634	Non-malnourished n = 492	Malnourished n = 142	P-value
Age (years)	70 (64–77)	69 (63–76)	72 (67–79)	**<0.001**
Sex				
Male	405 (64%)	331 (67%)	74 (52%)	**<0.001**
Female	229 (36%)	161 (33%)	68 (48%)	
Cancer site				

Colorectal	270 (43%)	202 (41%)	68 (48%)	**0.001**
Stomach	193 (30%)	160 (33%)	33 (23%)	
Liver	87 (14%)	75 (15%)	12 (8%)	
Bile duct	45 (7%)	33 (7%)	12 (8%)	
Pancreas	39 (6%)	22 (4%)	17 (12%)	
Stage				
I	219 (35%)	196 (40%)	23 (16%)	**<0.001**
II	199 (31%)	143 (29%)	56 (39%)	
III	148 (23%)	103 (21%)	45 (32%)	
IV	68 (11%)	50 (10%)	18 (13%)	
Height (cm)	160.0 (152.0–167.0)	161.0 (154.0–167.4)	156.0 (149.0–165.0)	**<0.001**
Body weight (kg)	57.2 (49.6–65.4)	60.7 (53.9–67.5)	47.2 (40.9–52.0)	**<0.001**
BMI (kg/m^2)	22.4 (20.6–24.6)	23.3 (21.8–25.3)	18.8 (17.4–20.8)	**<0.001**
%Arm circumference (%)	102 (94–109)	104 (98–110)	91 (84–97)	**<0.001**
%Triceps skinfold thickness (%)	66 (44–91)	71 (56–98)	43 (29–61)	**<0.001**
%Handgrip strength (%)	81 (69–93)	83 (73–94)	75 (60–86)	**<0.001**
Skeletal muscle index (kg/m^2)	6.7 (5.8–7.4)	7.0 (6.1–7.6)	5.7 (5.1–6.5)	**<0.001**
Body fat mass (kg)	14.7 (10.7–18.5)	15.8 (12.6–20.1)	10.3 (6.9–13.1)	**<0.001**

ECW/TBW	0.390 (0.384–0.397)	0.389 (0.384–0.395)	0.395 (0.390–0.401)	**<0.001**
Phase angle (°)	4.7 (4.2–5.3)	4.9 (4.4–5.4)	4.2 (3.7–4.6)	**<0.001**
Albumin (g/dL)	3.8 (3.4–4.1)	3.9 (3.5–4.1)	3.6 (3.2–3.9)	**<0.001**
Hemoglobin (g/dL)	12.7 (11.1–13.9)	12.9 (11.3–14.1)	11.9 (10.7–13.3)	**<0.001**
Total lymphocyte count (/mm^3)	1435 (1086–1773)	1443 (1092–1792)	1392 (1060–1707)	0.231
C-reactive protein level (mg/dL)	0.10 (0.05–0.31)	0.10 (0.05–0.24)	0.13 (0.05–0.53)	**0.023**
Sarcopenia (n, %)	76 (15%)	43 (11%)	33 (33%)	**<0.001**
Cachexia (n, %)	218 (37%)	100 (22%)	118 (86%)	**<0.001**

BMI, body mass index; ECW/TBW, extracellular water/total body water

Survival outcome

The 5-year survival curves differed significantly between the non-malnourished and malnourished groups (Fig. 3). Overall survival was significantly lower in the malnourished group than in the non-malnourished group (72% vs. 73%, P = 0.007). Table 2 shows the univariate and multivariate HRs and 95% CIs. In the univariate analysis, cancer site, cancer stage, and EDC malnutrition were significant risk factors for mortality, whereas age and sex were not a significant risk factor. In the multivariate analysis, EDC malnutrition was identified as an independent risk factor for mortality. Table 3 shows the results of a detailed analysis for the association of each EDC component with mortality. In the multivariate analysis, data were adjusted for sex, cancer site, and cancer stage. Among EDC malnourished patients, only BMI <18.5 kg/m^2 was a significant risk factor for mortality in both univariate and multivariate analyses.

We performed a subgroup analysis of Kaplan–Meier survival by cancer type and cancer stage. Fig. 4 shows the 5-year survival curves for each cancer type. In colorectal cancer (A), overall survival was significantly lower in the malnourished group than in the non-malnourished group (77% vs. 85%, P = 0.037). As shown in Fig. 5, in stage I (A) and IV (D), overall survival was significantly lower in the malnourished group than in the non-malnourished group (86% vs. 95%, P = 0.023 and 16% vs. 28%, P = 0.027).

Table 2. Univariate and multivariate Cox proportional hazard models

					Univariate			Multivariate		
	At risk (n)	Number with events (n)	Person years	Number with events/100 person years	HR	95% CI	P-value	HR	95% CI	P-value
Age (years)					1.01	0.99–1.03	0.231			
Sex										
Female	229	27	557.9	4.8	Reference			Reference		
Male	405	70	948.0	7.4	1.52	0.99–2.41	0.058	1.53	0.98–2.47	0.065
Cancer site										
Colorectal	270	26	692.5	3.8	Reference			Reference		
Stomach	193	22	451.0	4.9	1.31	0.74–2.32	0.350	2.00	1.11–3.59	**0.023**
Liver	87	21	200.4	10.5	2.82	1.59–5.01	**<0.001**	2.37	1.32–4.26	**0.005**
Bile duct	45	12	95.6	12.6	3.34	1.68–6.63	**0.002**	3.04	1.52–6.08	**0.004**
Pancreas	39	16	66.3	24.1	6.49	3.48–12.13	**<0.001**	3.71	1.89–7.27	**<0.001**
Stage										
I	219	9	530.8	1.7	Reference			Reference		
II	199	23	493.3	4.7	2.73	1.31–6.23	**0.007**	2.51	1.17–5.87	**0.018**
III	148	30	353.8	8.5	5.02	2.48–11.23	**<0.001**	4.60	2.18–10.62	**<0.001**
IV	68	35	128.0	27.3	16.11	8.09–35.70	**<0.001**	12.76	6.04–29.55	**<0.001**
EDC										
Non-malnourished	492	66	1193.1	5.5	Reference			Reference		
Malnourished	142	31	312.8	9.9	1.79	1.16–2.72	**0.010**	1.70	1.08–2.63	**0.024**

EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria; HR, hazard ratio; CI, confidence interval

Table 3. Univariate and multivariate Cox proportional hazard models according to the EDC and the EDC components

					Univariate			Multivariate*		
	At risk (n)	Number with events (n)	Person years	Number with events/100 person years	HR	95% CI	P-value	HR	95% CI	P-value
EDC	142	31	312.8	9.9	1.79	1.16–2.72	**0.010**	1.70	1.08–2.63	**0.024**
BMI <18.5 kg/m^2	70	20	139.8	14.3	2.57	1.53–4.12	**<0.001**	2.28	1.32–3.75	**0.004**
UWL + age-related BMI	51	8	121.3	6.6	1.01	0.45–1.95	0.987	0.93	0.41–1.82	0.844
UWL + sex-related FFMI	45	8	106.2	7.5	1.19	0.53–2.29	0.652	1.30	0.57–2.57	0.506
UWL + age-related BMI + sex-related FFMI	24	5	54.6	9.2	1.42	0.50–3.16	0.465	1.37	0.47–3.10	0.524

EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria; BMI, body mass index; UWL, unintentional weight loss; FFMI, fat-free mass index; HR, hazard ratio; CI, confidence interval

*: In the multivariate analysis, sex, cancer site, and cancer stage were adjusted.

Discussion

The present study investigated the prevalence of EDC malnutrition and the validity of the EDC as a nutritional and prognostic indicator in patients with GI and HBP cancers. Biochemical data that was not included in EDC was associated with EDC malnutrition. The prevalences of sarcopenia and cachexia were higher in EDC malnourished patients than in non-malnourished patients. EDC malnutrition was a poor prognostic factor independent of sex, cancer site, and cancer stage. Among EDC components, we found that BMI <18.5 kg/m^2 was an independent poor prognostic factor.

In this study, the prevalence of EDC malnutrition was 22% in patients with preoperative GI and HBP cancers, which is similar to the prevalence of 20% previously reported in patients with GI cancer [9].

The EDC were associated with biochemical data such as albumin levels and anthropometry data such as %AC, %TSF, and %handgrip strength, which are not included in EDC components. In addition, the proportions of sarcopenia and cachexia were higher in the malnourished group than in the non-malnourished group (33% vs. 11% and 86% vs. 22%, respectively). The ESPEN consensus group mentioned the terminology of malnutrition and provided a conceptual tree of nutritional disorders [6]. They showed that cachexia and sarcopenia are related to malnutrition and are at least partly covered by the general term of malnutrition. Our results may support their conceptual model of nutritional disorders.

The prognosis of patients with cancer differs depending on the cancer site and stage [28]. In particular, the mortality rate is higher for pancreatic cancer than for other cancers. Our results showed that EDC malnutrition was an independent prognostic factor (HR 1.70) even after factor adjustment. There are several reports on the EDC and prognosis in general old women, general hospitalized patients, geriatric hospitalized type 2 diabetic patients, and chronic obstructive pulmonary disease patients [18–24]. Our results showed that EDC could be used in patients with preoperative GI and HBP cancers. In our subgroup analysis by cancer type, we found a significant difference in the survival rate between the malnourished group and the non-malnourished group only in colorectal cancer. In other cancers, the survival curve of the malnourished group was lower than that of non-malnourished group, although the differences were not significant. In subgroup analysis by cancer stage, a significant difference in the survival rate between the malnourished group and the non-malnourished group was observed only in stage I and IV. These results may be due to the small sample size of each cancer type and cancer stage. Further studies are needed to increase the number of

cases to allow additional subgroup analysis. We also investigated the validity of the EDC components as prognostic predictors. In our study, BMI of <18.5 kg/m^2 was an independent poor prognostic factor. Several reports showed that low BMI and low skeletal muscle mass were associated with poor prognosis in patients with GI and HBP cancers [29–31]. However, the only predictor of poor prognosis was BMI <18.5 kg/m^2 in our results. This may be related to cut-off values for FFMI and BMI. BMI and body composition are known to differ by race [32,33] and the FFMI cut-off value of the EDC have been calculated using healthy Caucasian data [6,34]. Therefore, we should carefully consider the cut-off values of BMI and FFMI in the Asian population. In September 2018, the Global Leadership Initiative on Malnutrition (GLIM), which is composed of representatives from four major academic societies on nutrition from around the world, including ESPEN, developed and reported new universal criteria in diagnosing malnutrition [35]. The GLIM criteria proposed other cut-off values of BMI and FFMI in the Asian population [35]. Recently, Japanese researchers suggested that the optimal cut-off BMI values for the Asian population to grade malnutrition severity were 17.0 kg/m^2 for patients aged <70 years and 17.8 kg/m^2 for those aged ≥70 years [36]. Further studies are needed to secure consensus reference data in the Asian population. In several studies, which compared EDC and GLIM criteria [37–43], GLIM criteria showed higher prevalence of malnutrition than EDC and low agreement of these two criteria. In contrast, the two sets of criteria showed a 100% concordance for patients with severe malnutrition in patients with inflammatory bowel disease [42]. There is a report that EDC may be more sensitive in predicting the incidence of sarcopenia than the GLIM criteria [43]. From these reports, EDC may be useful for detecting more severe malnutrition. Sanchez-Rodriguez et al. and Kootaka et al. reported that malnutrition according to EDC and GLIM criteria were associated with higher mortality risk [37,39]. Although there are several reports on the

validity of EDC and GLIM criteria [11,13,15–24,37,39,40,42,43], further studies are required to diagnose malnutrition.

The strength of the present study is that this is the first study on the association between the EDC and prognosis in patients with cancer. The present study has some limitations. First, as this was a single institutional study, the results cannot be applied to all facilities. Second, we could not perform pre-screening before diagnosing EDC malnutrition because the data for screening could not be gathered owing to the retrospective nature of the study. Third, we could not adjust multivariate analyses for medications used, other medical interventions, and other lifestyle factors, such as physical activity.

Conclusion

EDC are associated with both nutritional status and postoperative prognosis. EDC malnutrition was a poor prognostic factor independent of sex, cancer site, and cancer stage in patients with GI and HBP cancers. Among EDC components, BMI <18.5 kg/m^2 was an independent poor prognostic factor. Further studies are needed to consider the race-specific cut-off values of the BMI and FFMI, especially in the Asian population.

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Author contributions

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Conflict of Interest

None.

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Figure Legends

Fig. 1. Flowchart of patients analyzed in this study

GI, gastrointestinal; HBP, hepatobiliary–pancreatic; EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria

Fig. 2. Details of malnourished patients according to the EDC

Low BMI means BMI >18.5 kg/m^2 to <20 kg/m^2 if <70 years of age or <22 kg/m^2 if ≥70 years of age.

Low FFMI means FFMI <15 kg/m^2 in females or <17 kg/m^2 in males.

BMI, body mass index; FFMI, fat-free mass index; EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria

Fig. 3. Kaplan–Meier survival curves according to EDC malnutrition

Overall survival was calculated from the time of surgery to the last follow-up date or death. The dotted line represents the non-malnourished group, and the solid line represents the malnourished group.

EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria

Fig. 4. Kaplan–Meier survival curves according to EDC malnutrition subgrouped by cancer site: colorectal (A), stomach (B), liver (C), bile duct (D), and pancreatic (E) cancer. Overall survival was calculated from the time of surgery to the last follow-up date or death. The dotted line represents the non-malnourished group, and the solid line represents the malnourished group.

EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria

Fig. 5. Kaplan–Meier survival curves according to EDC malnutrition subgrouped by cancer stage: Stage I (A), II (B), III (C), and IV (D). Overall survival was calculated from the time of surgery to the last follow-up date or death. The dotted line represents the non-malnourished group, and the solid line represents the malnourished group.

EDC, European Society for Clinical Nutrition and Metabolism diagnostic criteria

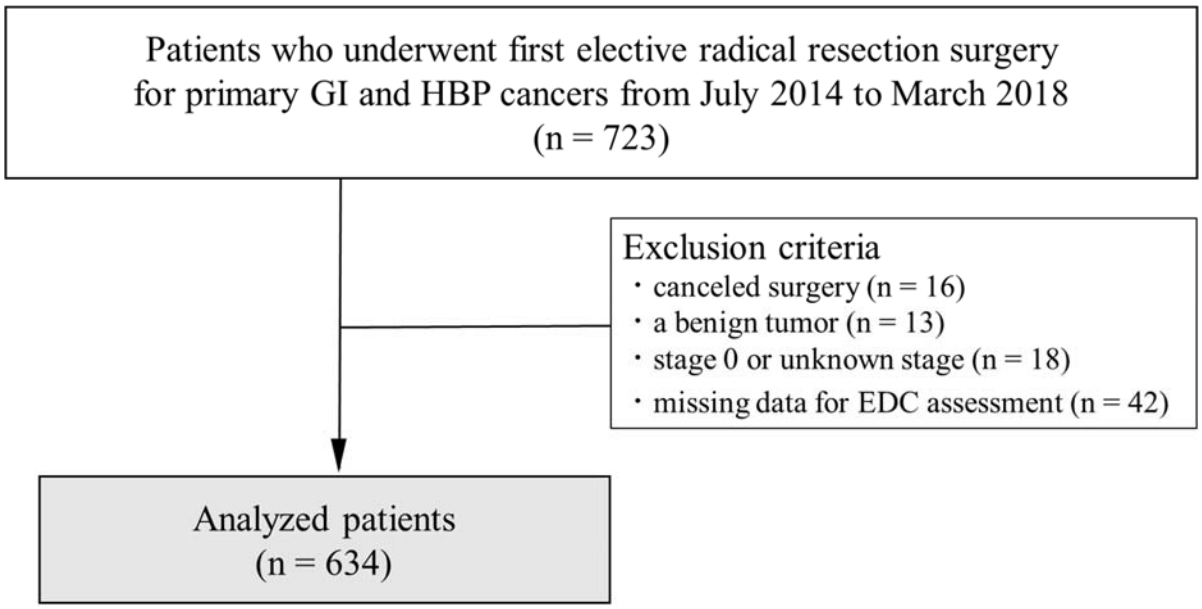
Patients who underwent first elective radical resection surgery
for primary GI and HBP cancers from July 2014 to March 2018
(n = 723)
Exclusion criteria
・canceled surgery (n = 16)
・a benign tumor (n = 13)
・stage 0 or unknown stage (n = 18)
・missing data for EDC assessment (n = 42)
Analyzed patients
(n = 634)

Fig. 1.

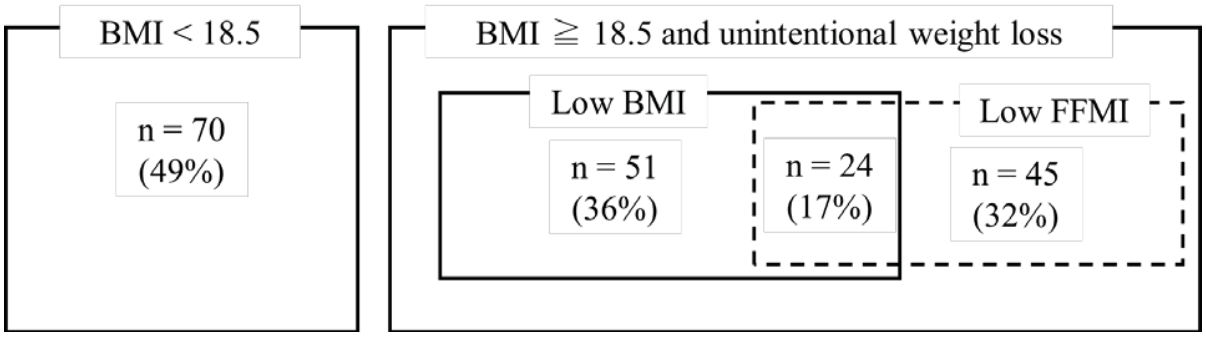
BMI < 18.5
n = 70
(49%)
BMI ≧ 18.5 and unintentional weight loss
Low BMI
n = 51
(36%)
n = 24
(17%)
Low FFMI
n = 45
(32%)

Fig. 2.

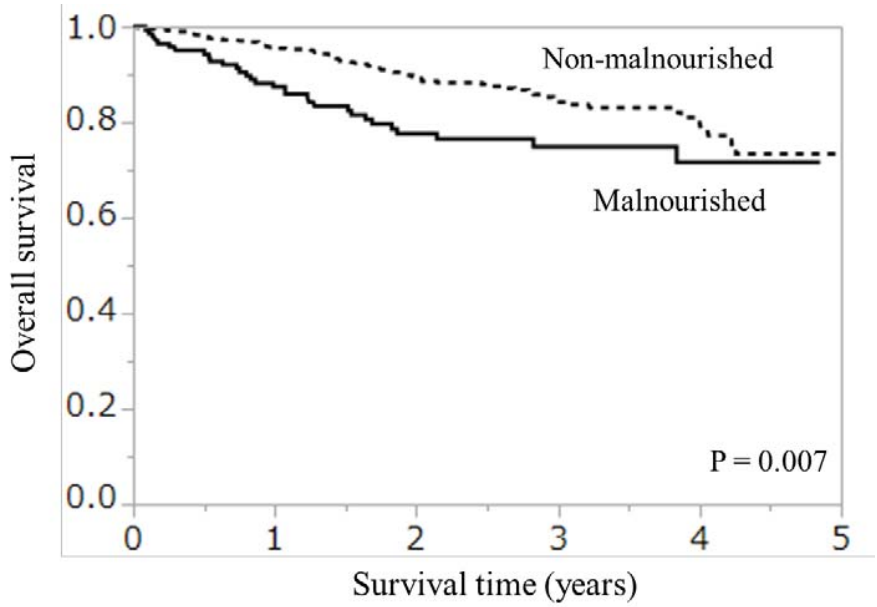
1.0
0.8
0.6
0.4
0.2
0.0
Overall survival
Non-malnourished
Malnourished
P = 0.007
0
1
2
3
4
5
Survival time (years)

Fig. 3.

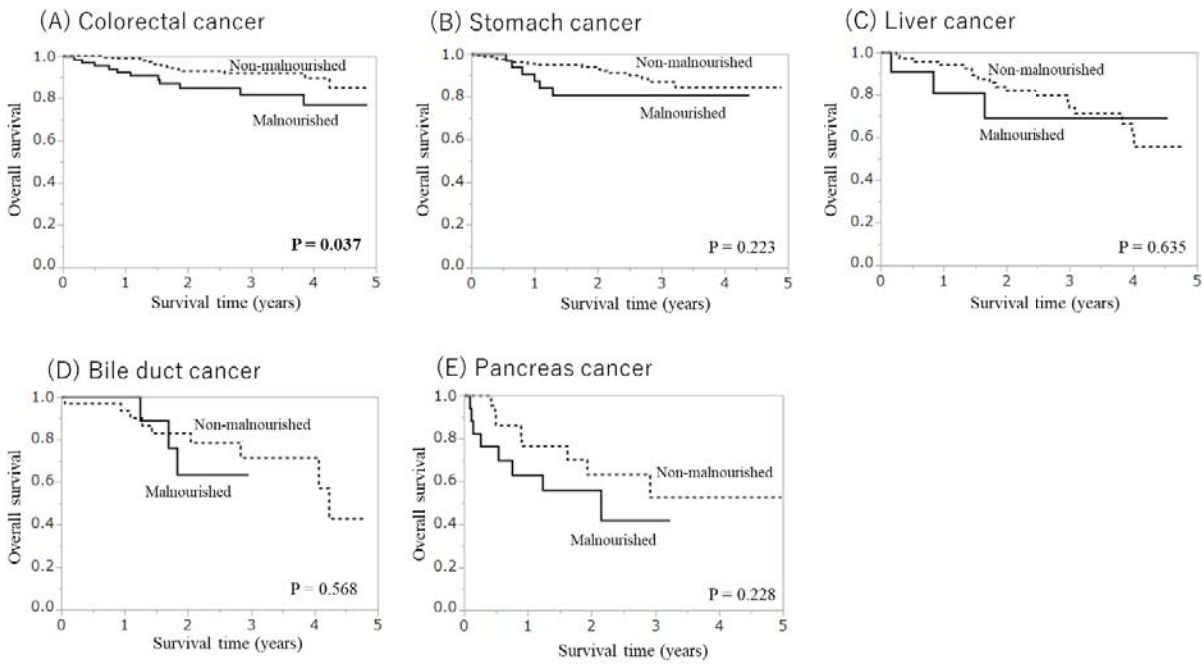
(A) Colorectal cancer
Non-malnourished
Malnourished
P = 0.037
Overall survival
Survival time (years)
(B) Stomach cancer
Non-malnourished
Malnourished
P = 0.223
Overall survival
Survival time (years)
(C) Liver cancer
Non-malnourished
Malnourished
P = 0.635
Overall survival
Survival time (years)
(D) Bile duct cancer
Non-malnourished
Malnourished
P = 0.568
Overall survival
Survival time (years)
(E) Pancreas cancer
Non-malnourished
Malnourished
P = 0.228
Overall survival
Survival time (years)

Fig. 4.

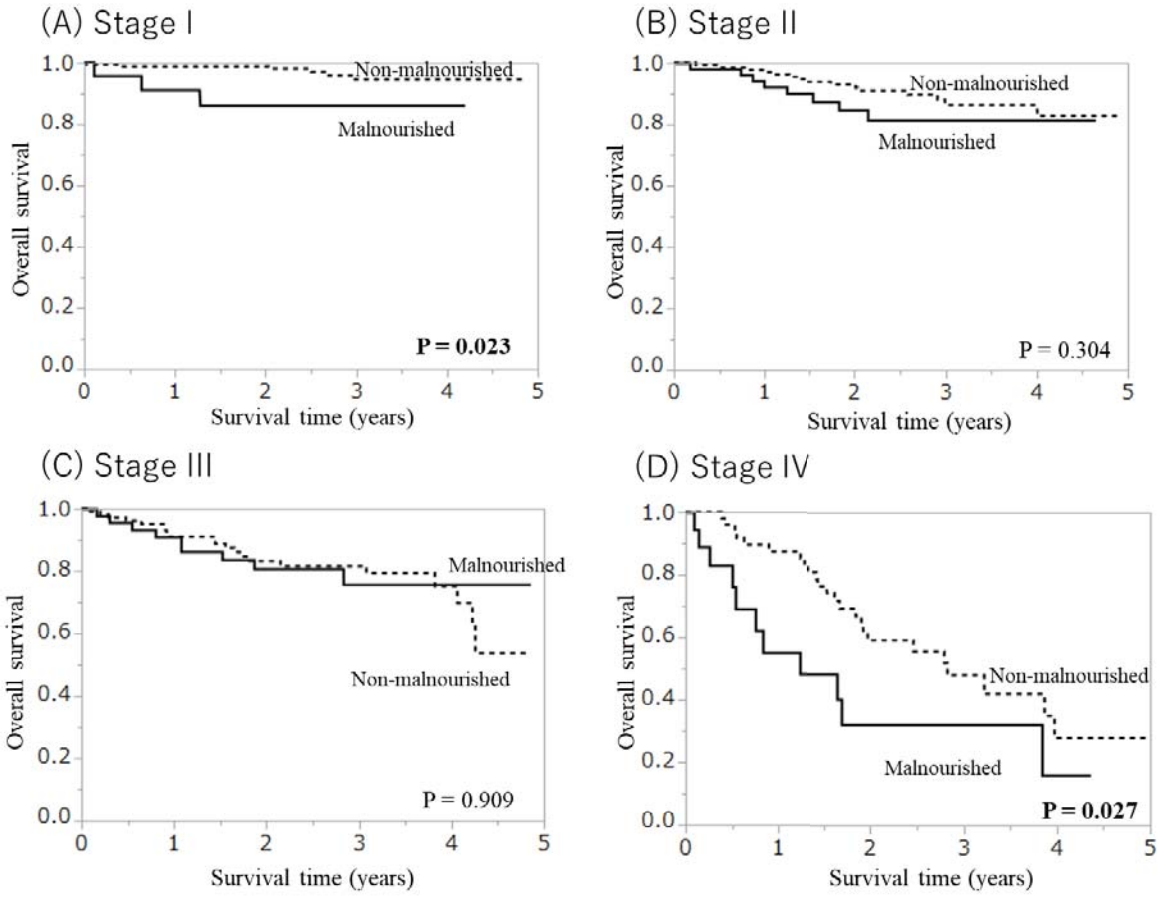
(A) Stage I
Non-malnourished
Malnourished
P = 0.023
Overall survival
Survival time (years)
(B) Stage II
Non-malnourished
Malnourished
P = 0.304
Overall survival
Survival time (years)
(C) Stage III
Malnourished
Non-malnourished
P = 0.909
Overall survival
Survival time (years)
(D) Stage IV
Non-malnourished
Malnourished
P = 0.027
Overall survival
Survival time (years)

Fig. 5.