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Title	Preoperative risk factors for skeletal muscle mass loss in patients with biliary tract cancer
Author(s)	Sugiura, Ryo; Kuwatani, Masaki; Kawakubo, Kazumichi et al.
Citation	Journal of hepato-biliary-pancreatic sciences, 31(8), 549-558 https://doi.org/10.1002/jhbp.12006
Issue Date	2024-06-06
Doc URL	https://hdl.handle.net/2115/95656
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Type	journal article
File Information	Manuscript-JHBPS-R1.pdf



Preoperative risk factors for skeletal muscle mass loss in patients with biliary tract cancer

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Words count including abstract: 3572

Tables count: 3

Figures count: 4

The study protocol was approved by the Institutional Review Board of Hokkaido University Hospital (approval no: 023-0291) and conducted in accordance with the Declaration of Helsinki revised in 2013. Written informed consent was waived because of the retrospective observational study design, and informed consent was obtained using an optout form.

Abstract

Background: Endoscopic retrograde cholangiography (ERC)-related procedures, usually performed before biliary tract cancer (BTC) surgery, are associated with increased risk for various complications, which can cause sarcopenia. No study has elucidated the relationship between preoperative ERC-related procedures and sarcopenia/skeletal muscle mass loss.

Methods: Patients with BTC who underwent radical surgical resection following ERC-related procedures were included. Skeletal muscle mass was evaluated using the psoas muscle mass index (PMI), which was determined using computed tomography images, and the change in PMI before the initial pre-ERC and surgery (Δ PMI) was calculated. Risk factors for advanced skeletal muscle mass loss, defined as a large Δ PMI, were evaluated.

Results: The study cohort included 90 patients with a median age of 72 (interquartile range, 65–75) years. The median PMI at pre-ERC and surgery were 4.40 and 4.15 cm^2/m^2 , respectively ($P<0.01$). The median Δ PMI was -6.2% (interquartile range, -10.9% – 0.5%). By multivariate analysis, post-ERC pancreatitis and cholangitis before surgery were independent predictive factors for large PMI loss (odds ratio, 4.57 and 3.18, respectively; $P=0.03$ and $P=0.02$, respectively).

Conclusions: Skeletal muscle mass decreases preoperatively in most patients with BTC undergoing ERC. Post-ERC pancreatitis and cholangitis before surgery were independent risk factors for large skeletal muscle mass loss.

Keywords: biliary tract cancer; endoscopic retrograde cholangiography; psoas muscle; sarcopenia; skeletal muscle

Introduction

In patients with biliary tract cancer (BTC), a malignant disease with poor prognosis,¹ surgical resection approaches, such as pancreaticoduodenectomy or major hepatectomy with extrahepatic bile duct resection, are the only potentially curative treatment options.^{2,3} Endoscopic retrograde cholangiography (ERC)-related procedures are widely performed for biliary drainage, histologic diagnosis, and the determination of resectability before curative surgery for BTC; these procedures are frequently performed multiple times for cholangitis, repeat biopsy, and changes of drainage areas due to shifts in surgical approaches.⁴ Importantly, ERC-related procedures are also associated with various complications such as pancreatitis and cholangitis, which can lead to adverse outcomes and prolong the preoperative waiting period.

Sarcopenia is a complex syndrome characterized by a progressive, generalized decrease in skeletal muscle mass and strength.⁵ Sarcopenia is associated with poor physical function and worse outcomes in various diseases.⁶ Several studies focusing on operable BTC found that the diagnosis of sarcopenia before surgery was associated with high rates of postoperative morbidity and tumor recurrence as well as with poor prognosis.⁷⁻⁹ Meanwhile, skeletal muscle mass can decrease during the preoperative waiting period which may be prolonged due to serious complications that occasionally arise in patients undergoing multiple ERC-related procedures before curative surgery. One study demonstrated that advanced skeletal muscle mass loss between diagnosis and surgery was associated with poor prognosis.¹⁰ While studies have demonstrated the association of preoperative diagnosis of sarcopenia

and advanced skeletal muscle mass loss with poor prognosis,^{7–10} no study to date elucidated the actual changes in skeletal muscle mass, considered the details of ERC-related procedures, or focused on the relationship between preoperative ERC-related procedures and skeletal muscle mass loss. In addition, risk factors for preoperative skeletal muscle mass loss are unknown. The present study aimed to identify the risk factors for advanced skeletal muscle mass loss particularly in patients undergoing preoperative ERC-related procedures.

Methods

Study design

This retrospective observational study was conducted in Hokkaido University Hospital in Sapporo, Japan. The electronic medical records were searched to identify consecutive patients with BTC who underwent both the initial preoperative ERC-related procedures and radical surgical resection in the study institution between January 2011 and May 2023. The inclusion criteria were as follows: 1) histopathologic diagnosis of BTC, 2) available computed tomography (CT) images both before and after the initial preoperative ERC-related procedures during the preoperative period, and 3) available consent of the patient or their family for study enrollment using the optout form. The exclusion criteria were as follows: 1) patients who underwent percutaneous/transmural biliary drainage before the initial ERC, 2) those who underwent endoscopic papillectomy, 3) those who underwent preoperative chemotherapy, 4) those whose radical surgical resection was cancelled during operation, 5) those with

distant metastases diagnosed based on the surgically resected specimens, and 4) refusal to enroll in the study by the patient or their families.

The study protocol was approved by the Institutional Review Board of Hokkaido University Hospital (approval no: 023-0291) and conducted in accordance with the Declaration of Helsinki revised in 2013. Written informed consent was waived because of the retrospective observational study design, and informed consent was obtained using an optout form.

Determination of skeletal muscle mass loss

In the present study, the changes in skeletal muscle mass were determined using the psoas muscle mass index (PMI). The PMI was calculated by dividing the sum of the cross-sectional area of the right and left psoas muscles at the L3 level by height squared (cm^2/m^2) based on measurements obtained by the manual tracing of target areas on computed tomography (CT) images (Fig. 1), as previously reported.¹¹

In the present study, both pre- and post-ERC PMIs were evaluated. Pre-ERC PMI was defined as the PMI determined using CT images obtained before the first preoperative ERC, and post-ERC PMI was defined as the PMI determined using the last preoperative CT images obtained after the final ERC.

Preoperative endoscopic procedures

ERC was performed with the patients under conscious sedation with fentanyl and midazolam, and the standard station approach was used with a therapeutic duodenoscope (TJF-240, JF-260V, or TJF-260V;

Olympus Medical Systems, Tokyo, Japan). Transpapillary bile duct cannulation was mainly performed using the wire-guided cannulation method, and the double-guidewire technique or precut papillotomy was performed in cases where this method failed. Briefly, the bile duct was filled with the contrast medium after cannulation. Following ERC, biopsy forceps were used to perform multiple transpapillary biopsies from the primary and other lesions. In cases where biliary drainage was required, a nasobiliary tube/stent was inserted across the biliary strictures after the biopsy. In cases where the biliary stricture was in the hepatic hilum, a single drainage tube/stent was placed only in the future remnant liver lobe for initial biliary drainage. The diameters of nasobiliary drainage tubes and biliary stents were mainly 6 Fr and 7 Fr, respectively. In cases where cytology without biliary drainage was intended, a nasobiliary tube was placed in the target lesion (bile duct or gallbladder) and the tube was removed at a later date after the conclusion of multiple cytologic examinations. Endoscopic sphincterotomy (ES) was not performed as a routine procedure, and it was performed at the discretion of the endoscopist. A prophylactic pancreatic stent was inserted for preventing post-ERC pancreatitis in high-risk patients as previously reported.¹²

Management during the preoperative waiting period

Patients with nasobiliary tubes were administered bile replacement by oral intake. Patients with jaundice were on a regular diet without dietary restrictions. Patients with cholangitis were fasted once and restarted on oral intake after the observation of a declining trend in fever, levels of inflammatory

markers, and serum hepatobiliary enzyme levels. In cases where cholangitis did not improve, endoscopic reintervention was performed using biliary tube/stent exchange. Patients with pancreatitis were fasted until the disappearance of abdominal pain and the observation of a decreasing trend in serum pancreatic enzyme levels.

Definitions

Δ PMI was calculated as follows: Δ PMI (%) = ((PMI based on post-ERC CT images – PMI based on pre-ERC CT images) / PMI based on pre-ERC CT images) $\times$ 100. No study to date has reported reference Δ PMI values for patients with BTC. Therefore, a large PMI loss was defined based on the median Δ PMI of the present study cohort (–6.2%). For reference, the annual changes in PMI were –1.3%, –3.5%, and –6.1% in patients with Child–Pugh grade A, B, and C liver cirrhosis, respectively.¹³ Sarcopenia was defined as a PMI of <3.74 cm²/m² for males and <2.29 cm²/m² for females, according to a previous study in healthy adults in Hokkaido, Japan.¹¹

The neutrophil–lymphocyte ratio was used as an inflammation-based prognostic factor. The presence and severity of pancreatitis, bleeding, liver abscess, and perforation related to the ERC-related procedures were defined according to the American Society for Gastrointestinal Endoscopy guidelines.¹⁴ Acute cholangitis and cholecystitis were defined according to the 2018 Tokyo guidelines.¹⁵ Distant and regional lymph node metastases were defined according to the classification of biliary tract cancers established by the Japanese Society of Hepato-Biliary-Pancreatic Surgery.¹⁶

Postoperative complications were defined by the Clavien-Dindo classification system.¹⁷

Outcome measures

The primary outcome was risk factors for large PMI loss regarding baseline characteristics, ERC details, clinical course during the preoperative waiting period, and postoperative pathologic results. Secondary outcomes were the amount of PMI, Δ PMI, and change in the frequency of sarcopenia. Postoperative complication and overall survival were also analyzed.

Statistical analysis

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan),¹⁸ which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). Data were presented as medians with interquartile range for nonparametric variables and as percentages for categorical variables. The Wilcoxon signed-rank sum test was performed between two groups. Categorical variables were compared using the Fisher's exact test. Risk factors for a large PMI loss were analyzed using logistic regression analysis. Parameters with a *P* value of <0.10 in the univariate analysis were included in the multivariate analysis. Receiver operating characteristic curve analysis was used to determine the cutoff values for continuous variables, including serum total bilirubin, serum hemoglobin A1c, preoperative waiting period, and fasting period for the assessment of their association with a large PMI loss. Survival duration from the day of radical

surgical resection until death was estimated using the Kaplan–Meier method, and the differences between the two groups were evaluated using the log-rank test. Patients who died of other causes with no evidence of recurrence were censored. Potential prognostic factors of survival were analyzed using the Cox proportional hazards model, and variables with a *P* value of <0.05 in the univariate analysis were included in the multivariate analysis. A *P* value of <0.05 was considered statistically significant.

Results

Baseline cohort characteristics

Among a total of 121 patients with BTC identified during the study period, 90 patients who fulfilled the inclusion and exclusion criteria were included in the final analysis (Fig. 2). Briefly, the study cohort included 63 men and 27 women with a median age of 72 (65–75) years. Table 1 shows the baseline patient characteristics. The final diagnoses were cholangiocarcinoma, ampullary cancer, and gallbladder cancer in 70, 12, and 8 patients, respectively. There were no significant differences in baseline characteristics between the patients with and without large PMI loss (*P* > 0.05).

Table 2 shows the summary of ERC-related procedures and the clinical course of the patients. 73 patients (81.1%) required nasobiliary tube/stent placement before surgery for biliary drainage, whereas 17 patients (18.9%) underwent only biopsy or temporary placement of a nasobiliary/nasogallbladder tube. For initial preoperative biliary drainage without temporary tube placement, endoscopic biliary stenting was performed in 43 patients, including stenting placed across the papilla in 31 patients and

above the papilla in 12 patients, whereas endoscopic nasobiliary drainage was performed in 30 patients. The diameters of stent were 7- and 8.5-Fr in 37 and 6 patients, respectively, and those of nasobiliary tube were 6- and 5-Fr in 25 and 5 patients, respectively. ES was performed in 30 patients (33.3%), and a prophylactic pancreatic stent was inserted in 12 patients (13.3%). A median of 2 (1–3) ERC-related procedures were performed in the overall cohort. ERC-related adverse events occurred in 33 patients (36.7%). The most frequent adverse event was pancreatitis ($n = 20$, 22.2%), which was mild, moderate, and severe in 9, 9, and 2 patients, respectively. Pancreatitis occurred in 10.0% and 28.3% of patients with and without ES, respectively. Although not statistically significant, pancreatitis tended to occur more frequently in patients without ES ($P = 0.06$). Pancreatitis occurred in 33.3% and 20.5% of patients with and without prophylactic pancreatic stent, and prophylactic pancreatic stent were not associated with pancreatitis ($P = 0.45$). During the preoperative period, cholangitis occurred in 37 patients (41.1%) and percutaneous transhepatic portal vein embolization was performed in 21 patients (23.3%). There were significant differences between the patients with and without large PMI loss in all adverse event rate, post-ERC pancreatitis rate, and cholangitis before surgery ($P < 0.05$). Patients with large PMI loss had a significantly longer fasting period than those without large PMI loss ($P < 0.01$).

The median duration between the initial preoperative ERC and surgery was 49 (35–62) days. The histopathologic evaluation of surgical resection specimens identified regional lymph node metastases in 35 patients (38.9%).

Preoperative change in PMI

The median duration between the pre-ERC CT and ERC was 6 (2–13) days, whereas the median duration between the post-ERC CT and radical surgical resection was 7 (3–14) days. The median pre- and post-ERC PMIs were 4.40 (3.57–5.26) and 4.15 (3.35–5.00) cm²/m², respectively (Fig. 3). The median Δ PMI was -6.2% (-10.9% – 0.5%), with a significant PMI decline from the first ERC to surgery ($P < 0.01$). The frequencies of sarcopenia based on the pre-ERC and post-ERC CT images were 7.8% ($n = 7$) and 18.9% ($n = 17$), respectively, with a significant increase from the first ERC to surgery ($P = 0.04$).

Risk factors for large PMI loss

Large PMI loss was defined as a Δ PMI of $<-6.2\%$, which was the median Δ PMI in the present study cohort. In univariate analysis of the patient characteristics, ERC-related procedures, clinical course, and postoperative pathologic results, post-ERC pancreatitis, cholangitis before surgery, and fasting period were identified significant risk factors for large PMI loss ($P < 0.05$) (Table 4). In addition, regional lymph node metastasis was a potential predictive factor for large PMI loss ($P < 0.10$). By multivariate analysis, post-ERC pancreatitis and cholangitis before surgery were independent predictive factors for large PMI loss (odds ratio, 4.57 and 3.18, respectively; $P = 0.03$ and $P = 0.02$, respectively).

Postoperative short-term outcomes

Complications of Clavien-Dindo classification $\geq$ III occurred in 40.0% and 57.8% of patients with and without large PMI loss, respectively (not significant) (Supplemental Table 1). There was not significantly different in the distribution of postoperative complications between patients with and without large PMI loss ($P = 0.51$). The postoperative hospital stays were not significantly different between the two groups (median 32 vs. 38 days, $P = 0.27$).

Survival rate

During the study period, 41 patients died due to the primary disease. The median survival in the overall cohort was 5.2 years (Fig. 4a). Although the median survival was not significantly different between the patients with and without large PMI loss ($P = 0.22$), prognosis tended to be worse with large PMI loss (Fig. 4b). By univariate analysis, a neutrophil–lymphocyte ratio of >3.0 before initial ERC, cholangitis before surgery, presence of sarcopenia at surgery, and presence of regional lymph node metastasis were significant poor prognostic factors ($P < 0.05$) (Supplemental Table 2). By multivariate analysis, a neutrophil–lymphocyte ratio of >3.0 before initial ERC and presence of regional lymph node metastasis were independent poor prognostic factors of survival (hazard ratio, 1.95 and 2.09, respectively; $P = 0.04$ and $P = 0.04$, respectively).

The analysis of 83 patients who did not have sarcopenia at the time of preoperative ERC based on the pre-ERC PMI revealed that 10 patients had sarcopenia at surgery whereas the remaining 73 patients did not have sarcopenia at surgery. The medians of pre-ERC PMI in patients with and without developing sarcopenia were 3.95 (2.77–4.34) and 4.57 (3.87–5.42) cm²/m², respectively, and patients with sarcopenia had significantly lower pre-ERC PMI than those without sarcopenia ($P = 0.01$) (Supplemental Table 3). Developing sarcopenia was more frequently observed in patients with regional lymph node metastasis ($P = 0.01$). The median survival time was significantly different between those with and without sarcopenia at surgery (1.6 and 6.9 years, respectively; $P < 0.01$) (Fig. 4c).

Discussion

Several studies have shown that sarcopenia at various timepoints before surgery is associated with high rates of postoperative morbidity and tumor recurrence as well as with poor prognosis in patients with BTC.^{7–9} ERC-related procedures are performed, often multiple times, before surgery for BTC and are associated with increased risk of complications, which can lead to serious outcomes and prolong the preoperative waiting period. Therefore, we hypothesized that sarcopenia/skeletal muscle mass loss would develop after ERC-related procedures. One study in patients with perihilar cholangiocarcinoma reported that a large PMI loss between the time of diagnosis and the time of surgery was associated with poor prognosis.¹⁰ However, the study compared patients with PMIs

above and below the median Δ PMI and did not disclose the actual Δ PMI. Furthermore, changes in the frequency of sarcopenia in all patients, details of ERC-related procedures, and the clinical course of the patients were not discussed. In the present study, we evaluated the details of Δ PMI and the change in the frequency of sarcopenia from ERC to surgery and found a decrease in PMI in most patients and an increase in the frequency of sarcopenia between ERC and surgery.

Our analyses revealed that advanced PMI loss ($\leq -6.2\%$) was more frequently observed in patients with post-ERC pancreatitis. Most patients with acute pancreatitis, including those with post-ERC pancreatitis, have mild or moderately severe forms, which are self-limited conditions that recover within days to a week based on subjective symptoms and inflammatory parameters. However, in early-stage acute pancreatitis, even mild or moderate disease is associated with energy breakdown and a negative nitrogen balance,¹⁹ resulting in decreased skeletal muscle mass. Importantly, initiating oral/enteral feeding immediately following the relief of pain and the decline in elevated serum pancreatic enzyme levels was a general nutritional strategy in the study institution during the study period. Recent guidelines recommend early oral or enteral feeding as soon as clinically tolerable to reduce the length of hospital stay and the medical cost in patients with mild pancreatitis and to prevent organ failure and death in those with severe pancreatitis.²⁰ Therefore, immediate oral intake may reduce PMI loss due to acute pancreatitis in patients with BTC undergoing preoperative ERC-related procedures.

In our study, the incidence of pancreatitis in the overall cohort was relatively high and although not statistically significant, pancreatitis tended to occur more frequently in patients without ES. A multicenter randomized controlled trial previously showed that ES before endoscopic transpapillary biliary drainage with plastic tube/stent placement could have the preventive effect on the occurrence of post-ERC pancreatitis.²¹ Therefore, ES should be considered in preoperative ERC for BTC.

The presence of cholangitis before surgery was an independent risk factor for advanced PMI loss. Cholangitis results from biliary infection and increased intraductal pressure due to contrast medium or various endoscopic procedures performed immediately after ERC or from tube/stent dysfunction, such as occlusion or dislocation, in the long term. Increased intraductal pressure results in increased endotoxemia, bacterial translocation, and the induction of various cytokines.²² Several proinflammatory cytokines have been implicated in the pathogenesis of sepsis secondary to cholangitis.^{23,24} Even in patients whose symptoms improve relatively early with ERC-related procedures, the substantial systemic inflammatory response during cholangitis results in skeletal muscle mass loss. Biliary drainage can reduce the cytokine levels, which are elevated during acute cholangitis.²⁵ Therefore, biliary drainage should be performed as early as possible in cases of suspicious preoperative cholangitis in patients with BTC.

Cholangitis before surgery has previously been reported to occur in 30.3–37.2% and 18.1–44.4% of patients with malignant hilar and distal biliary obstruction, respectively.^{26–29} The incidences of cholangitis before surgery in these studies were similar to ours. Meanwhile, our result would be

caused by the long preoperative waiting period in this study. Multiple stents and large-bore stent are associated with longer stent patency than single stent or thick stent as previously reported.³⁰ Therefore, the choice of multiple or large-bore stents might reduce cholangitis before surgery, especially with distal biliary obstruction. Tube/stent dysfunction-related cholangitis theoretically increases with the longer preoperative waiting time;^{4,29} therefore, the patients requiring biliary drainage should undergo radical surgery as early as possible.

A previous study focusing patients with perihilar cholangiocarcinoma who underwent major hepatectomy showed that a large PMI loss was associated with poor prognosis,¹⁰ although our study did not show it statistically. Our study included patients with various types of BTC as well as a variety of surgical methods. Furthermore, the number of patients in our study was relatively small compared with those of many previous reports, which included about several hundred patients.⁷⁻¹⁰ Future prospective studies are needed to accurately assess the association between large PMI loss and surgical outcomes (complication and survival rate).

The present study has several limitations. First, this was a retrospective study with a relatively small sample size. Second, the cohort included patients with various BTC types. Third, we evaluated PMI only based on CT images and did not include the direct measurements of muscle strength, such as walking speed and grip strength. Fourth, the relationship between serum albumin level prior to ERC-related procedure and other factors associated with nutritional status or PMI was not investigated. Fifth, an accurate assessment of rehabilitation and nutritional therapy after ERC-related

procedures was not available. These factors would be expected to impact skeletal muscle mass loss; therefore, future prospective studies are necessary for the accurate evaluation of risk factors, including rehabilitation and nutritional therapy, for loss of PMI and actual muscle strength in the preoperative period in patients with BTC.

In conclusion, in the present retrospective observational study, we observed a decline in skeletal muscle mass during the period between preoperative ERC and radical surgical resection in most patients with BTC, while revealing post-ERC pancreatitis and cholangitis before surgery as risk factors for advanced skeletal muscle mass loss.

Acknowledgement: We express our deepest appreciation to the gastroenterological endoscopists and surgeons at the study institution.

Disclosure Statement: The authors declare no conflicts of interest associated with this manuscript.

Funding: No funding was received for this article.

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Tables

Table 1. Baseline characteristics of study participants

	With large PMI loss (n = 45)	Without large PMI loss (n = 45)	<i>P</i> value
Age, median (IQR), year	72 (65–75)	72 (66–76)	0.76
Male sex, n (%)	33 (73.3)	30 (66.7)	0.65
Body mass index, median (IQR), kg/m ²	23.4 (21.6–25.5)	23.5 (21.5–24.6)	0.65
Final diagnosis, n (%)			0.08
Cholangiocarcinoma	37 (82.2)	33 (73.3)	
Ampullary cancer	7 (15.6)	5 (11.1)	
Gallbladder cancer	1 (2.2)	7 (15.6)	
Serum T-BIL before initial ERC, median (IQR), mg/dL			
	1.3 (0.8–9.4)	1.1 (0.8–3.0)	0.26
Serum hemoglobin A1c, median (IQR), %	5.7 (5.4–6.7)	5.7 (5.2–6.5)	0.76
Neutrophil–lymphocyte ratio before initial ERC, median (IQR)			
	2.5 (1.7–4.4)	2.7 (2.0–3.7)	0.75
Presence of sarcopenia prior to initial ERC, n (%)			
	4 (8.9)	3 (6.7)	1

ERC, endoscopic retrograde cholangiography; IQR, interquartile range; PMI, psoas muscle mass index; T-BIL, total bilirubin

Table 2. Details of ERC-related procedure, clinical course, and postoperative pathology

	With large PMI loss (n = 45)	Without large PMI loss (n = 45)	<i>P</i> value
Biliary drainage without temporally tube placement, n (%)	37 (82.2)	36 (80.0)	1
Initial biliary drainage method, n (%)			0.35
Endoscopic biliary stenting	24 (64.9)	19 (52.8)	
Endoscopic nasobiliary drainage	13 (35.1)	17 (47.2)	
Number of ERC-related procedure, times (IQR)	2 (1–3)	1 (1–2)	0.33
Adverse event due to ERC-related procedure, n (%)			
	23 (51.1)	10 (22.2)	< 0.01
Pancreatitis	15 (33.3)	5 (11.1)	0.02
Cholangitis	9 (20.0)	4 (8.9)	0.23
Cholecystitis	1 (2.2)	1 (2.2)	1
Bleeding	1 (2.2)	1 (2.2)	1
Bile duct collapse	1 (2.2)	0	1
Pancreatic leak	1 (2.2)	0	1
Liver abscess	0	1 (2.2)	1
Cholangitis before surgery, n (%)	25 (55.6)	12 (26.7)	< 0.01
Percutaneous transhepatic portal vein embolization, n (%)			
	10 (22.2)	12 (26.7)	0.81
Fasting period, days (IQR)	3 (2–6)	2 (1–3)	< 0.01
Preoperative waiting period, days (IQR)	50 (32–65)	48 (36–57)	0.98
Regional lymph node metastasis, (%)	22 (55.6)	13 (26.7)	0.08

ERC, endoscopic retrograde cholangiography; IQR, interquartile range; PMI, psoas muscle mass index;

Table 3. Univariate and multivariate analyses of risk factors for large PMI loss

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Age, >75 vs. ≤75 years	1 (1–1)	0.62		
Sex, male vs. female	1.37 (0.57–3.40)	0.49		
Cholangiocarcinoma vs. other	1.68 (0.61–4.62)	0.31		
Serum T-BIL level, >4.7 vs. ≤4.7 mg/dL	2.00 (0.77–5.21)	0.16		
Hemoglobin A1c, >6.6 vs. ≤6.6 %	1.68 (0.61–4.62)	0.31		
Neutrophil–lymphocyte ratio, >3.0 vs. ≤3.0	1 (0.43–2.32)	1		
Biliary drainage, presence vs. absence	1.16 (0.40–3.33)	0.79		
Initial biliary drainage, ENBD vs. other	0.82 (0.34–1.97)	0.66		
Pancreatitis, presence vs. absence	4.00 (1.31–12.2)	<0.01	4.57 (1.15–18.2)	0.03
Cholangitis until surgery, presence vs. absence	3.44 (1.42–8.32)	<0.01	3.18 (1.17–8.66)	0.02
PTPE, presence vs. absence	0.77 (0.30–2.06)	0.62		
Preoperative waiting period, >53 vs. ≤53 days	1.32 (0.57–3.10)	0.52		
Fasting period, >3 vs. ≤3 days	2.80 (1.12–7.00)	0.03	0.93 (0.28–3.09)	0.91
N factor, presence vs. absence	2.35 (0.99–5.62)	0.05	1.96 (0.75–5.14)	0.17

CI, confidence interval; ENBD, endoscopic nasobiliary drainage; ERC, endoscopic retrograde cholangiography; OR, odds ratio; PMI, psoas muscle mass index; PTPE, percutaneous transhepatic portal vein embolization; N, regional lymph node metastasis; T-BIL, total bilirubin

Figure legends

Figure 1. Measurement of psoas muscle mass index. The sum of the cross-sectional area of the right and left psoas muscles at the L3 level is calculated by manual tracing of computed tomography (CT) images, which is then divided by the height squared (cm^2/m^2).

Left, CT image obtained before endoscopic retrograde cholangiography (ERC); Right, CT image obtained after ERC

Figure 2. Study flow chart

Figure 3. Changes in psoas muscle mass index (PMI) between pre-ERC and post-ERC

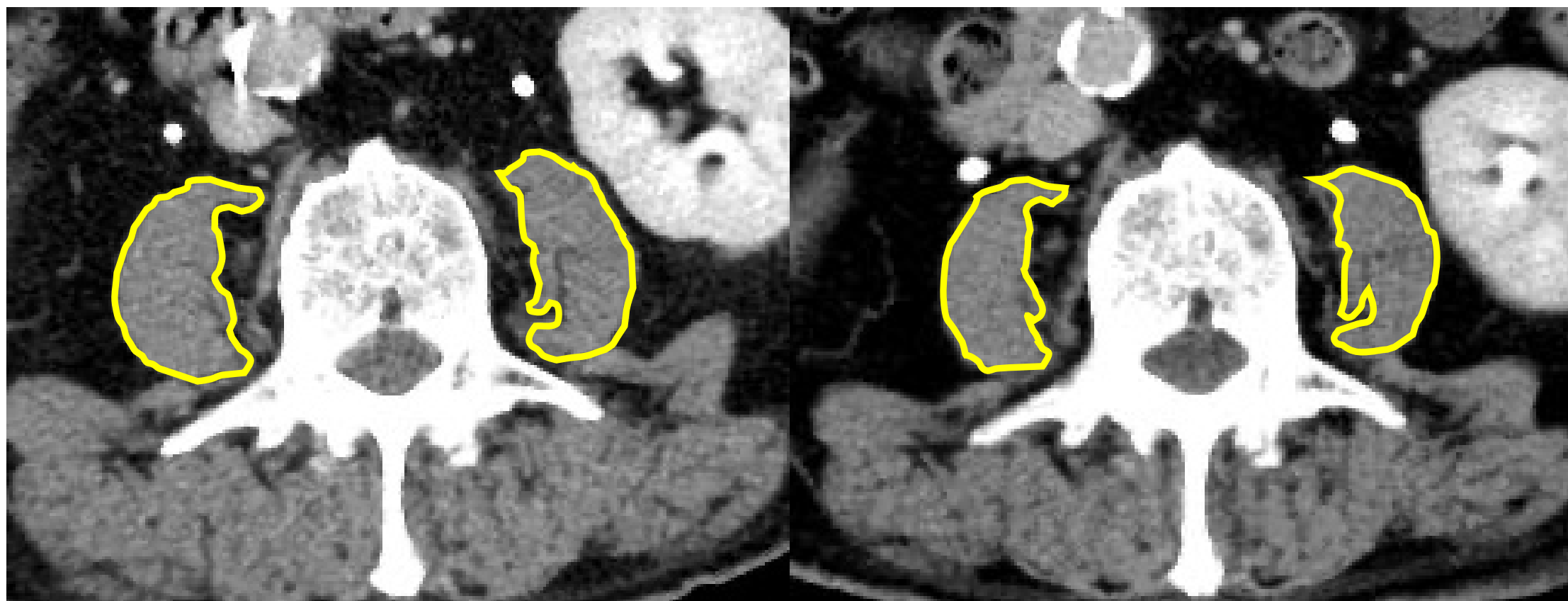
PMI values decreased significantly from pre-ERC to post-ERC ($P < 0.01$).

Figure 4.

A. Rate of survival rate in the overall cohort.

B. Rates of survival in patients categorized according to the presence of large PMI loss. The rate of survival was not significantly different between the patients with and without large PMI loss ($P = 0.22$).

C. Rates of survival in patients with and without sarcopenia at surgery. The rate of survival was significantly different between the two groups ($P < 0.01$).



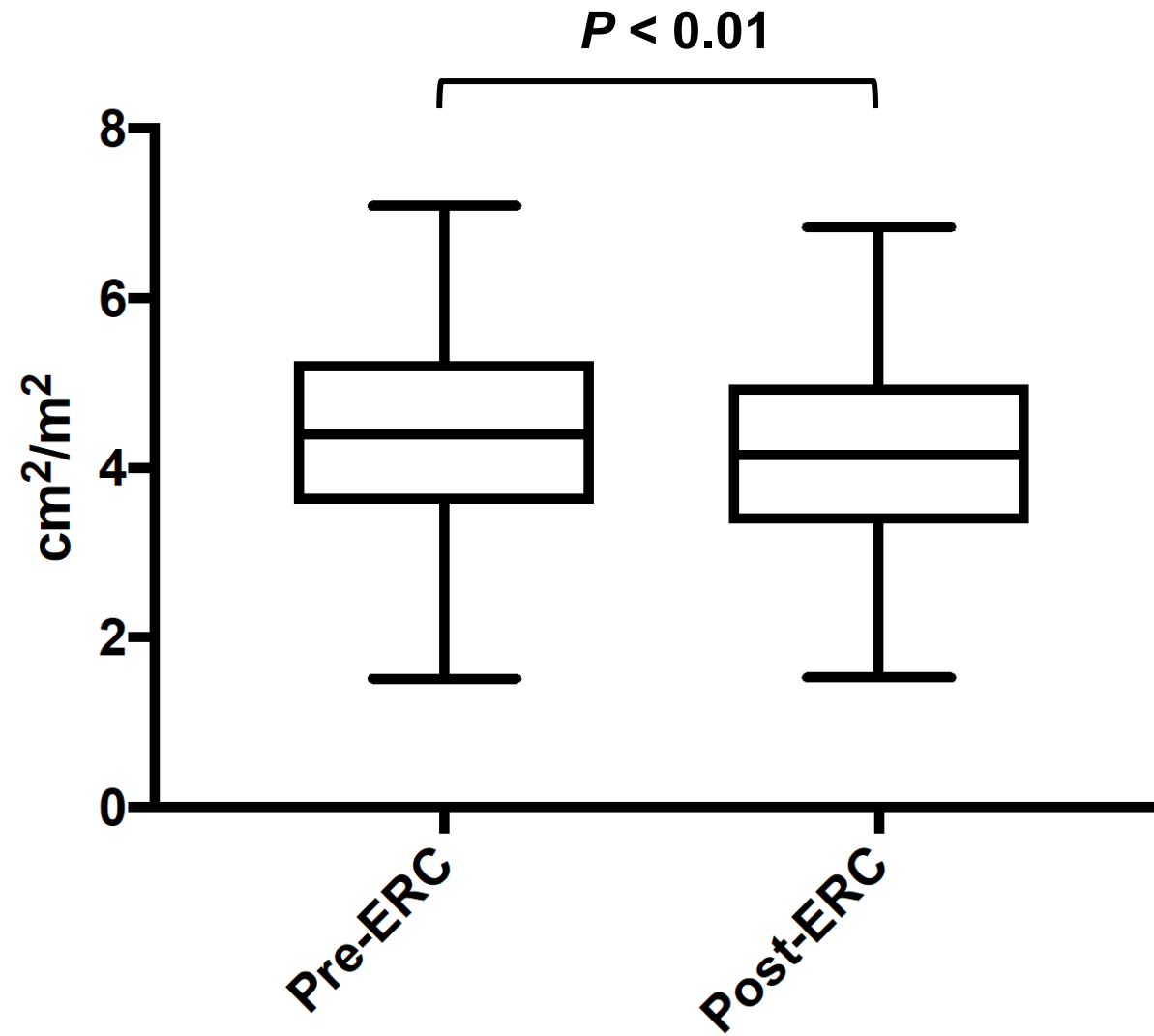
Search of the database
between January 2011 and May 2023

Assessed for eligibility (n = 121)

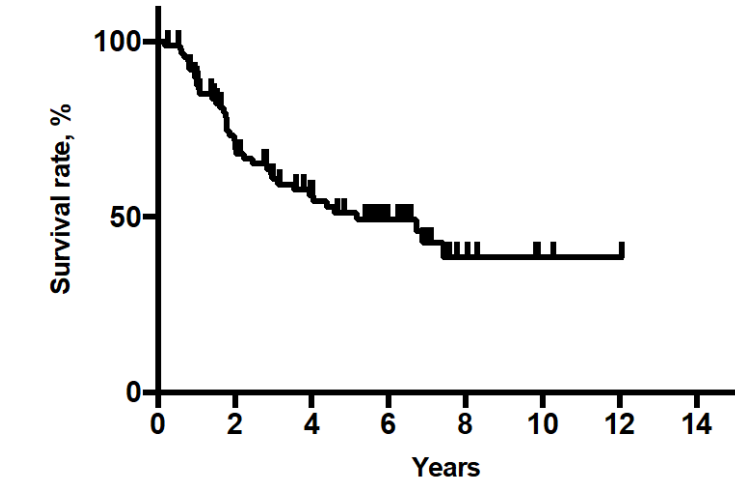
Preoperative CT scans not performed twice (n = 12)
Distant metastases (n = 8)
Surgery canceled during the operation (n = 7)
Preoperative chemotherapy (n = 2)
Post-percutaneous biliary drainage (n = 1)
Post-endoscopic papillectomy (n = 1)

Analyzed (n = 90)

Psoas muscle mass index



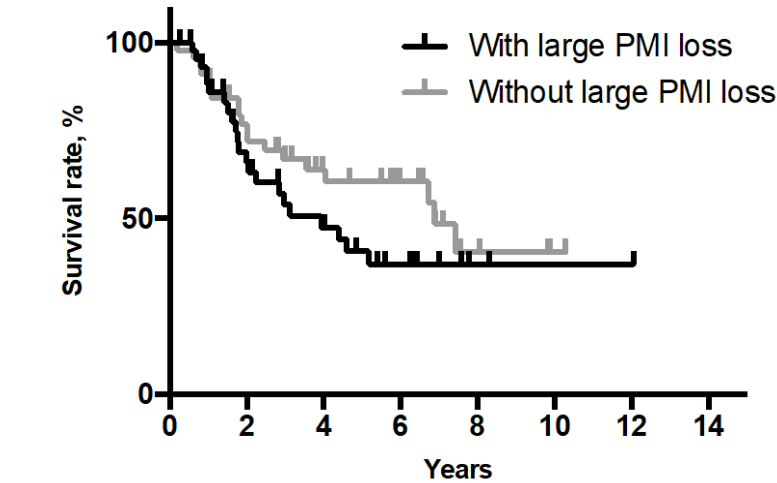
(a)



Number at risk

90	54	34	20	6	2	1
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(b)



Number at risk

With large PMI loss						
45	31	19	12	4	1	0
Without large PMI loss						
45	23	15	8	2	1	1

(c)



Number at risk

With sarcopenia						
73	46	29	20	6	2	1
Without sarcopenia						
10	3	3	0	0	0	0