Chylous ascites has a higher incidence after robotic surgery and is associated with poor recurrence-free survival after rectal cancer surgery

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Abstract

Background: Postoperative chylous ascites is an infrequent condition after colorectal surgery and is easily treatable. However, its effect on the long-term oncological prognosis is not well established. This study aimed to investigate the short-term and long-term impact of chylous ascites treated with neoadjuvant therapy followed by rectal cancer surgery and to evaluate the incidence of chylous ascites after different surgical approaches.

Methods: A total of 898 locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy followed by surgery between January 2010 and December 2018 were included. The clinicopathological data and outcomes of the patients with chylous ascites were compared with those of the patients without chylous ascites. The primary endpoint was recurrence-free survival (RFS). To balance baseline confounders between groups, propensity score matching (PSM) was performed for each patient with a logistic regression model.

Results: Chylous ascites was detected in 3.8% (34/898) of the patients. The incidence of chylous ascites was highest after robotic surgery (6.9%, 6/86), followed by laparoscopic surgery (4.2%, 26/618) and open surgery (1.0%, 2/192, $P = 0.021$). The patients with chylous ascites had a significantly higher number of lymph nodes harvested (15.6 *vs.* 12.8, $P = 0.009$) and a 3-day longer postoperative hospital stay ($P = 0.017$). The 5-year RFS rate was 64.5% in the chylous ascites group, which was significantly lower than the rate in the no chylous ascites group (79.9%; $P = 0.007$). The results remained unchanged after PSM was performed. The chylous ascites group showed a nonsignificant trend towards a higher peritoneal metastasis risk (5.9% *vs.* 1.6%, $P = 0.120$). Univariate analysis and multivariate analysis confirmed chylous ascites (hazard ratio= 3.038, $P < 0.001$) as an independent negative prognostic factor for RFS.

Conclusions: Considering the higher incidence of chylous ascites after laparoscopic and robotic surgery and its adverse prognosis, we recommend sufficient coagulation of the lymphatic tissue near the vessel origins, especially during minimally invasive surgery.

Keywords: Locally advanced rectal cancer; Chylous ascites; Neoadjuvant chemoradiotherapy; Recurrence-free survival

Introduction

Postoperative chylous ascites is an infrequent condition after major abdominal surgery[1] and is caused by the unrecognized interruption of lymphatic channels.[2] Despite its rarity, chylous ascites presents a management problem due to the mechanical, nutritional, and immunological consequences resulting from a constant loss of electrolytes, proteins, lipids, fat-soluble vitamins, immunoglobulins, and lymphocytes.[3] Since postoperative refractory chylous ascites after pancreatoduodenectomy[4] or retroperitoneal lymph node dissection[5] has been reported often in the literature, the degree of chylous leakage after colorectal cancer surgery is milder than that after other surgeries. Chylous ascites has been described with an overall incidence of 11%, especially after pancreatic surgery,[6] which is higher than 1.0% to 7.7% after colorectal surgery.[7,8] Based on our previous experience, conservative management, including dietary modifications, use of total parenteral nutrition (TPN), and administration of somatostatin therapy, was frequently sufficient in almost all cases of postoperative chylous ascites.[9]

Although postoperative chylous ascites after colorectal surgery is easily treatable, its effect on the long-term oncological prognosis is not well established. There is a

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concern that postoperative chylous ascites may cause potential peritoneal dissemination due to the leakage of lymphatic fluid containing cancer cells.[10] However, contradictory results exist between the only two published retrospective studies on this subject.[10,11] Moreover, Baek *et al*[12] proposed that the differences in incidence between the studies are likely to have been influenced by operative technique. The risk of postoperative chylous ascites after different surgical approaches, such as laparoscopic surgery or robotic surgery, still needs to be studied. Due to the inconsistent anatomy of peripheral lymphatic systems around the inferior mesenteric artery, chylous ascites cannot always be avoided in rectal surgery. However, since postoperative chylous ascites is significantly more frequent after surgery for tumors fed by the superior mesenteric artery,[8] only a small number of chylous ascites cases after rectal cancer surgery has been reported in the literature. Neoadjuvant therapy followed by total mesorectal excision (TME) has become the standard of care for patients with locally advanced rectal cancer (LARC).[13] Thus, in the present study, our first aim was to investigate the short-term and long-term impact of chylous ascites after LARC surgery following neoadjuvant therapy in a large-volume center in China. Furthermore, the incidence of chylous ascites after different surgical approaches was compared.

Methods

The electronic database at our institution was searched. A total of 1067 patients diagnosed with clinical (c) T3, T4 or cTxN+ rectal cancer who underwent neoadjuvant therapy followed by curative-intent surgery between January 2010 and December 2018 were identified. Patients who met the following criteria were excluded: (1) stage IV disease; (2) missing data regarding tumor recurrence; and (3) synchronous malignancy. Finally, a total of 898 patients were included in the current study. Pathological data regarding tumor regression grading[14] were reevaluated by a pathologist in the case of missing data.

As previously reported,[15] neoadjuvant radiotherapy was delivered to the whole pelvis at a dose of 45 Gy in 25 fractions (1.8 Gy/fraction), followed by a primary tumor boost of 5.4 Gy. Concurrent chemotherapy was administered with radiation using capecitabine plus oxaliplatin (XELOX) or 5-fluorouracil/folinic acid plus oxaliplatin (FOLFOX) regimens. Standard TME was performed for patients with mid- and low rectal cancers, and partial mesorectal excision with a distal margin of at least 5 cm was performed for high rectal cancers. D3 lymph node dissection, which is defined as the dissection of all regional lymph nodes with a high ligation technique for the inferior mesenteric artery, was routinely performed in our institution.[16] The patients routinely started on a liquid diet on the day of the surgery. A postoperative follow-up strategy was reported in our previous study.[16]

Chylous ascites was diagnosed as white milky fluid in the drainage tube that contained high levels of triglycerides (triglycerides $>$ 110 mg/dL or positive for chylomicrons). For all patients with milky drainage fluid, the drainage fluid was routinely tested for the concentration of triglycerides (since 2012) or the presence or absence of chylomicrons (from 2010 to 2012). For the diagnosis of chylomicrons, the ascites samples were mixed with an equal volume of ether (1:1) solution and then thoroughly mixed. Finally, the middle layer was subjected to microscopic examination to detect the presence of chylomicrons.

The primary endpoint was recurrence-free survival (RFS), which was defined as the time interval from surgical resection to recurrence, metastasis or last follow-up if recurrence did not occur. Overall survival (OS) was defined as the time from surgery to either death or last follow-up.

Statistical analysis

All statistical analyses were performed using R (version 3.5.1) and STATA (version 15.0; StataCorp, College Station, TX, USA). Patients were divided into a chylous ascites group and a no chylous ascites group. Discrete variables were compared between groups using Fisher exact test and χ^2 test, as appropriate. Continuous outcomes were compared using parametric (Student's *t* test, analysis of variance) and nonparametric (Mann-Whitney *U*, Kruskal-Wallis) tests, as appropriate. RFS and OS were summarized with the Kaplan-Meier method and compared with a log-rank test. To balance baseline confounders between groups, propensity score matching (PSM) was performed for each patient with a logistic regression model. The covariates included in the model were age, tumor distance to the anal verge, preoperative serum carcino-embryonic antigen (CEA) levels, preoperative serum carbohydrate antigen 199 (CA199) levels, ypT stage, ypN stage, neural invasion, lymphovascular invasion, and surgical approach. One-to-five matching without replacement was performed using a 0.02 caliper width. Cox proportional hazards models were used to perform univariate and multivariate analyses for RFS. Significant variables ($P < 0.010$) by univariate analysis were entered into the multivariate model to identify independent prognostic factors for RFS. *P* values <0.050 were considered to indicate statistical significance.

Results

Demographic data

Chylous ascites was detected in 34 of the 898 patients (3.8%) who underwent rectal cancer surgery after neoadjuvant therapy. The median time until the development of chylous ascites was 4 (range, 1–11; average, 4.8 ± 2.6) days after surgery. Conservative therapy aimed at promoting decreased lymph production was routinely employed in our institution. The management algorithm integrates the supply of a low-fat diet, use of TPN, and administration of somatostatin therapy. It is worth noting that somatostatin therapy was attempted early in the course of treatment. The daily drainage amount was measured and recorded for 20 out of the 34 patients with chylous ascites. The average maximum drainage volume was 262 ± 167 mL/day, while the average drainage volume was 215 ± 174 mL, 164 ± 148 mL, and 112 ± 91 mL on the first, second, and third days after developing chylous ascites, respectively. On the day the drainage tube

was removed, the average drainage volume had decreased to 102 ± 144 mL. The patients with chylous ascites were discharged a median of 7 (range, 2–45; average, 7.2 ± 7.1) days after the development of chylous ascites. The longest and shortest hospital stays for chylous ascites patients were 56 days and 6 days, respectively. None of our patients with postoperative chylous ascites required surgical treatment. The median time for the removal of the abdominal drainage tube was 5 (2–45) days.

The baseline and pathological data are summarized in Table 1. Patients in the chylous ascites group were younger than those in the no chylous ascites group (52.4 *vs*. 56.4 years, $P = 0.043$). Minimally invasive surgery, including laparoscopic surgery and robotic surgery, was performed relatively more often in the chylous ascites group than in the no chylous ascites group. In particular, the incidence of chylous ascites was highest after robotic surgery (6.9%, 6/86), followed by laparoscopic surgery (4.2%, 26/618) and open surgery (1.0%, 2/192, $P = 0.021$). In addition, there was a nonsignificant trend towards a higher rate of neural invasion in the chylous ascites group than in the no chylous ascites group (11.8% *vs*. 4.1%, $P = 0.055$). The patients with chylous ascites had a significantly higher number of lymph nodes harvested (15.6 *vs*. 12.8, $P = 0.009$). The remaining baseline characteristics and pathological data did not differ between groups. After PSM, 34 patients in the chylous ascites group and 174 patients in the no chylous ascites group were matched.

Comparison of short-term outcomes

The short-term outcomes are shown in Table 2. The rate of conversion to laparotomy was similar between groups. The postoperative hospital stay was 3 days longer in the chylous ascites group than in the no chylous ascites group (unmatched patients: 11.9 *vs*. 8.9 days, $P = 0.017$; propensity-score matched patients: 11.9 *vs*. 8.5 days, $P = 0.002$). Other postoperative complications, including wound infection, anastomotic leakage, intra-abdominal infection, anastomotic bleeding, early postoperative small bowel obstruction, and pneumonia, did not differ between groups.

Comparison of long-term outcomes

The median follow-up period was 49 (interquartile range, 29–67) months. The 5-year cumulative RFS rate was 64.5% in the chylous ascites group, which was significantly lower than the rate in the no chylous ascites group (79.9%; $P = 0.007$) [Figure 1A]. There was a nonsignificant trend towards a lower 5-year OS rate in the chylous ascites group than in the no chylous ascites group (70.7% *vs*. 83.3%, $P = 0.066$) [Figure 1B]. The results remained unchanged after PSM was performed [Figure 1C and 1D].

The recurrence rates were not different in the subgroup analysis regardless of recurrence or metastasis site, including local recurrence, liver metastases, lung metastases, bone metastases, brain metastases, and peritoneal metastases [Table 3]. However, the chylous ascites group showed a nonsignificant trend towards a higher peritoneal metastasis risk (5.9% *vs*. 1.6%, $P = 0.120$).

Prognostic factors related to RFS

In the univariate analysis, pT stage (hazard ratio [HR] = 1.567, $P < 0.001$), pN stage (HR = 2.123, $P < 0.001$), tumor distance to anal verge (HR = 0.932, $P = 0.032$), preoperative serum CEA levels (HR = 1.011, $P < 0.001$), preoperative serum CA199 levels (HR = 1.003, $P < 0.001$), tumor regression grade (HR = 1.625, $P < 0.001$), neural invasion (HR = 3.066, $P < 0.001$), lymphovascular invasion (HR = 1.869, $P = 0.068$), histopathology (HR = 1.608, $P = 0.046$), distal margin (HR = 5.368, $P = 0.094$), surgical approach (laparoscopic surgery *vs*. open: HR = 0.669, $P = 0.017$; robotic surgery *vs*. open: HR = 0.428, $P = 0.026$), surgical procedure (HR = 0.058, $P = 0.031$), chylous ascites (HR = 2.127, $P = 0.016$), and chemoradiotherapy (CRT) surgery interval (HR = 0.930, $P = 0.058$) were associated with RFS in LARC patients treated with CRT and surgery [Table 4]. Of these factors, chylous ascites (HR = 3.038, $P < 0.001$) remained one of the independent negative prognostic factors for RFS in multivariate analysis [Table 4]. The other independent prognostic factors included pT stage, pN stage, tumor distance to anal verge, preoperative serum CEA levels, and neural invasion.

Discussion

Less attention has been devoted to chylous ascites after colorectal surgery than after other types of surgery because it is frequently milder and more easily managed. In the present study, the average maximum drainage volume was only 262 ± 167 mL/day. Furthermore, most previous studies reported successful management of chyle leakage with conservative management,[12] while surgical repair of the lymph fistula was rarely needed.[17] Although data on the standard treatment regimens for chylous ascites are largely unavailable, a management algorithm with a step-up approach has been frequently employed.[8] This step-up approach includes dietary control with a low-fat diet as the initial treatment; somatostatin analogs are introduced only when patients are unresponsive to the initial therapy.[8] In the present study, none of our patients with postoperative chylous ascites required surgical intervention. It is worth noting that somatostatin therapy was attempted early in the course of treatment for postoperative chylous ascites in our institution, since somatostatin is effective in diminishing the intestinal absorption of fats and attenuating lymph flow in the major lymphatic channels.[18] After a series of treatments, the mean duration of hospital stay was 11.9 days for patients with chylous ascites in our cohort, which align with the previously reported range of 9.2 to 14 days.[10,11] The patients with chylous ascites were discharged a median of 7 days after the development of chylous ascites, showing that the natural healing time of chylous ascites was approximately 1 week.

For the 898 patients in our cohort, the incidence rate was 3.8% for chylous ascites after rectal surgery following neoadjuvant therapy, which aligns with the reported range

Table 1: Comparison of demographic data of locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy followed by surgery with or without chylous ascites ($n = 898$).

Characteristics	Unmatched patients			Propensity-matched patients		
	No chylous ascites ($n = 864$)	Chylous ascites ($n = 34$)	*P* value	No chylous ascites ($n = 174$)	Chylous ascites ($n = 34$)	*P* value
Gender*			0.460			0.430
Male	568 (65.7)	25 (73.5)		113 (64.9)	25 (73.5)	
Female	296 (34.3)	9 (26.5)		61 (35.1)	9 (26.5)	
Age (years)†	56.4 ± 11.2	52.4 ± 13.0	0.043	53.1 ± 11.6	52.4 ± 13.0	0.770
Tumor distance to anal verge (cm)†	6.5 ± 4.0	7.5 ± 2.6	0.150	7.0 ± 7.5	7.5 ± 2.6	0.740
Preoperative serum CEA levels (ng/mL)‡	2.5 (0.2–336.8)	2.7 (0.5–46.1)	0.230	2.5 (0.2–271.4)	2.7 (0.5–46.1)	0.460
Preoperative serum CA199 levels (U/mL)‡	11.0 (0.6–1000.0)	11.5 (0.6–421.8)	0.580	11.0 (0.6–1000.0)	11.5 (0.6–421.8)	0.750
ypT stage*			0.370			0.810
ypT0	188 (21.8)	8 (23.5)		45 (25.9)	8 (23.5)	
ypT1	61 (7.1)	2 (5.9)		11 (6.3)	2 (5.9)	
ypT2	212 (24.5)	12 (35.3)		45 (25.9)	12 (35.3)	
ypT3	372 (43.1)	10 (29.4)		64 (36.8)	10 (29.4)	
ypT4	31 (3.6)	2 (5.9)		9 (5.2)	2 (5.9)	
ypN stage*			0.950			0.930
ypN0	643 (74.4)	27 (79.4)		140 (80.5)	27 (79.4)	
ypN1	178 (20.6)	6 (17.6)		26 (14.9)	6 (17.6)	
ypN2	43 (5.0)	1 (2.9)		8 (4.6)	1 (2.9)	
ypTNM stage*			0.300			0.650
0	177 (20.5)	8 (23.5)		45 (25.9)	8 (23.5)	
I	222 (25.7)	13 (38.2)		50 (28.7)	13 (38.2)	
II	244 (28.2)	6 (17.6)		45 (25.9)	6 (17.6)	
III	221 (25.6)	7 (20.6)		34 (19.5)	7 (20.6)	
Complete pathologic response*			0.670			1.000
No	687 (79.5)	26 (76.5)		129 (74.1)	26 (76.5)	
Yes	177 (20.5)	8 (23.5)		45 (25.9)	8 (23.5)	
Tumor regression grade*			0.880			0.810
0	185 (21.4)	8 (23.5)		43 (24.7)	8 (23.5)	
1	288 (33.3)	9 (26.5)		60 (34.5)	9 (26.5)	
2	328 (38.0)	14 (41.2)		62 (35.6)	14 (41.2)	
3	55 (6.4)	2 (5.9)		9 (5.2)	2 (5.9)	
Data missing	8 (0.9)	1 (2.9)		0	1 (2.9)	
Surgical access*			0.021			0.290
Open	190 (22.0)	2 (5.9)		22 (12.6)	2 (5.9)	
Laparoscopic surgery	592 (68.5)	26 (76.5)		107 (61.5)	26 (76.5)	
Robotic surgery	82 (9.5)	6 (17.6)		45 (25.9)	6 (17.6)	
Neural invasion*			0.055			1.000
No	829 (95.9)	30 (88.2)		155 (89.1)	30 (88.2)	
Yes	35 (4.1)	4 (11.8)		19 (10.9)	4 (11.8)	
Lymphovascular invasion*			0.110			0.730
No	836 (96.8)	31 (91.2)		161 (92.5)	31 (91.2)	
Yes	28 (3.2)	3 (8.8)		13 (7.5)	3 (8.8)	
Histopathology*			1.000			1.000
Adenocarcinoma	795 (92.0)	32 (94.1)		165 (94.8)	32 (94.1)	
Mucinous or signet ring adenocarcinoma	69 (8.0)	2 (5.9)		9 (5.2)	2 (5.9)	
Distal margin*			1.000			–
Negative	862 (99.8)	34 (100.0)		174 (100.0)	34 (100.0)	
Positive	2 (0.2)	0		0	0	
Pathologic circumferential margin*			1.000			1.000
Negative	856 (99.1)	34 (100.0)		171 (98.3)	34 (100.0)	
Positive	8 (0.9)	0		3 (1.7)	0	
Number of lymph nodes harvested†	12.8 ± 6.1	15.6 ± 8.0	0.009	13.0 ± 5.9	15.6 ± 8.0	0.027

*The data are expressed as the number (percentage). †The data are expressed as the mean ± standard deviation. ‡The data are expressed as the median (range). CEA: Carcino-embryonic antigen; CA199: Carbohydrate antigen 199.

Table 2: Comparison of short-term outcomes of locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy followed by surgery with or without chylous ascites (n = 898).

Variable	Unmatched patients			Propensity-matched patients		
	No chylous ascites (n = 864)	Chylous ascites (n = 34)	P value	No chylous ascites (n = 174)	Chylous ascites (n = 34)	P value
Conversion to laparotomy*	6 (0.7)	0	1.000	0	0	–
Wound infection*	35 (4.1)	1 (2.9)	1.000	6 (3.4)	1 (2.9)	1.000
Anastomotic leakage*	34 (3.9)	1 (2.9)	1.000	10 (5.7)	1 (2.9)	1.000
Intra-abdominal infection*	80 (9.3)	1 (2.9)	0.350	17 (9.8)	1 (2.9)	0.320
Anastomotic bleeding*	1 (0.1)	0	1.000	0	0	–
Early postoperative small bowel obstruction*	33 (3.8)	2 (5.9)	0.390	6 (3.4)	2 (5.9)	0.620
Pneumonia*	51 (5.9)	2 (5.9)	1.000	10 (5.7)	2 (5.9)	1.000
Postoperative hospital stay (days)†	8.9 ± 7.1	11.9 ± 8.4)	0.017	8.5 ± 5.0)	11.9 ± 8.4	0.002

*The data are expressed as the number (percentage). †The data are expressed as the mean ± standard deviation.

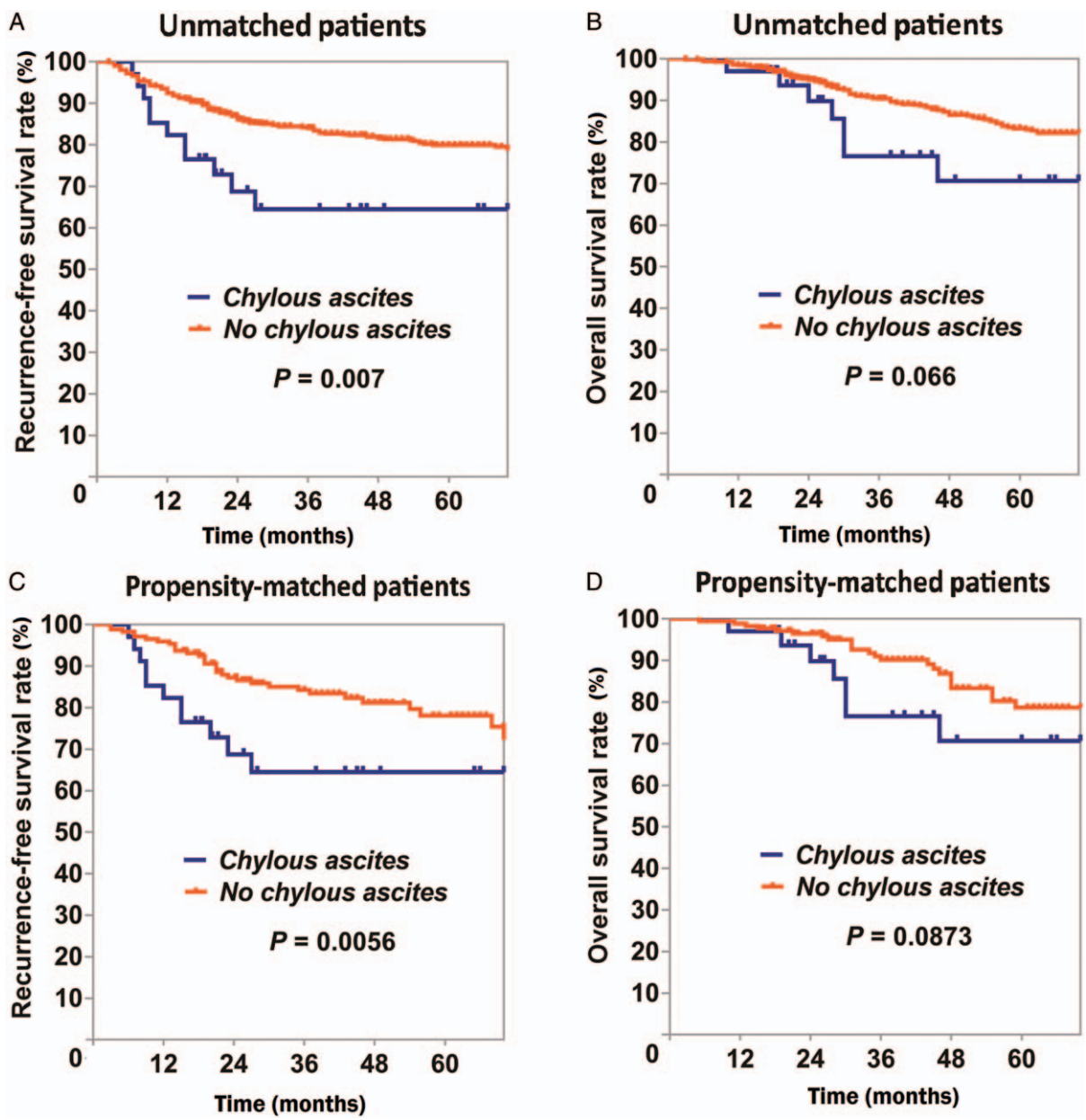

Figure 1: Comparison of survival between the chylous ascites group and the no chylous ascites group. (A) RFS of unmatched patients, (B) RFS of propensity-matched patients, (C) OS of unmatched patients, and (D) OS of propensity-matched patients. OS: Overall survival; RFS: Recurrence-free survival.

Table 3: Comparison of recurrence data of locally advanced rectal cancer patients treated with neoadjuvant chemoradiotherapy followed by surgery with or without chylous ascites ($n = 898$).

Characteristics	Unmatched patients			Propensity-matched patients		
	No chylous ascites ($n = 864$)	Chylous ascites ($n = 34$)	*P* value	No chylous ascites ($n = 174$)	Chylous ascites ($n = 34$)	*P* value
Local recurrence	38 (4.4)	2 (5.9)	0.66	6 (3.4)	2 (5.9)	0.62
Liver metastases	35 (4.1)	3 (8.8)	0.17	8 (4.6)	3 (8.8)	0.39
Lung metastases	85 (9.8)	2 (5.9)	0.76	20 (11.5)	2 (5.9)	0.54
Bone metastases	22 (2.5)	0	1.00	1 (0.6)	0	1.00
Brain metastases	6 (0.7)	0	1.00	1 (0.6)	0	1.00
Peritoneal metastases	14 (1.6)	2 (5.9)	0.12	4 (2.3)	2 (5.9)	0.25

Data are expressed as *n* (%).

Table 4: Univariate and multivariate analysis for the prognostic factors of recurrence-free survival.

Variable	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Gender (female *vs*. male)	0.971	0.706–1.335	0.857			
Age (>60 years *vs*. ≤60 years)	0.990	0.977–1.003	0.120			
pT stage (per stage)	1.567	1.350–1.820	<0.001	1.304	1.066–1.595	0.010
pN stage (per stage)	2.123	1.723–2.615	<0.001	1.598	1.250–2.042	<0.001
Tumor distance to anal verge (per cm)	0.932	0.875–0.994	0.032	0.916	0.847–0.992	0.031
Preoperative serum CEA levels (>5 *vs*. ≤5 ng/mL)	1.011	1.008–1.014	<0.001	1.010	1.005–1.015	<0.001
Preoperative serum CA199 levels (>37 *vs*. ≤37 U/mL)	1.003	1.002–1.004	<0.001	0.999	0.998–1.001	0.268
Tumor regression grade (per grade)	1.625	1.360–1.942	<0.001	1.138	0.880–1.472	0.325
Neural invasion (yes *vs*. no)	3.066	1.828–5.142	<0.001	1.788	1.003–3.189	0.049
Lymphovascular invasion (yes *vs*. no)	1.869	0.955 –3.659	0.068	0.811	0.388–1.696	0.578
Histopathology (mucinous or signet ring adenocarcinoma *vs*. adenocarcinoma)	1.608	1.009–2.565	0.046	0.995	0.602–1.645	0.985
Distal margin (positive *vs*. negative)	5.368	0.749–38.466	0.094	3.748	0.507–27.676	0.195
Pathologic circumferential margin (positive *vs*. negative)	1.512	0.375–6.096	0.561			
Number of lymph nodes harvested (per one)	1.019	0.995–1.044	0.113			
Surgical access (open)	1.000		0.017	1.000		0.209
Laparoscopic surgery *vs*. open	0.669	0.480–0.932	0.017	0.769	0.538–1.100	0.151

CEA: Carcino-embryonic antigen; CI: Confidence interval; CA199: Carbohydrate antigen 199.

after colorectal cancer surgery. Interestingly, the incidence of chylous ascites was highest after robotic surgery (6.9%), followed by laparoscopic surgery (4.2%) and open surgery (1.0%). It is known that patients who undergo robotic surgery for colorectal cancer have a significantly shorter time to oral tolerance than patients who undergo conventional laparoscopic surgery.[19] Similarly, the duration of bowel recovery (ie, days until the first bowel movement) is shorter for laparoscopic rectal excision than for open surgery for rectal cancer.[20] Since the occurrence of chylous leakage is associated with the formation of chyli after the intake of high-fat nutrients, the association between differences regarding high-fat intake and the incidence of chylous ascites among these three surgical techniques is worth studying. However, although all patients in this cohort routinely started a liquid diet on the day of surgery, the data regarding diet tolerance were not available. This is a limitation of our study, and these data will be included in the future studies. Furthermore, due to a lack of force feedback from the robotic system, surgeons are more likely to incompletely and insufficiently seal the inferior mesenteric arterial sheath that is rich in lymphatics. Interestingly, a short operative time (odds ratio, 0.994), reflecting incomplete coagulation, was an independent risk factor for chylous ascites in a previous study.[11] To the best of our knowledge, our study is the first to analyze differences in the incidence of chylous ascites among these three surgical approaches. Regarding the other risk factors for chylous ascites, our present data suggested an association between chylous ascites and a higher number of lymph nodes harvested, which is consistent with a previous report.[11] One explanation may be that abundant lymphatic channels with a rich collection of lymph nodes are more likely to be injured during the skeletonization of vascular structures.

Considering the possibility of cancer cell spillage through the leaked lymphatic fluid, the impact of chylous ascites on oncologic outcome needs evaluation. Similar 3-year disease-free survival rates were observed between patients with and without chylous ascites after colorectal cancer surgery in a South Korean population.[11] However, the

definition of chylous ascites was solely based on clinical signs, regardless of triglyceride levels, so another 3.0% of patients with milky drainage fluid were not considered to have chylous ascites because of the low drainage volume. In addition, stage IV patients were included in the comparison, which might be a confounding factor in the analysis of newly diagnosed recurrence. In the present large retrospective study, postoperative chylous ascites after nonmetastatic rectal cancer surgery was associated with a poor 5-year RFS before and after PSM and was further confirmed to be an independent negative prognostic factor for RFS in multivariate analysis. This result is consistent with reports from another study by Matsuda *et al*[10] The 3-year disease-free survival in that study was significantly lower in the chylous ascites group after laparoscopic colorectal surgery (chylous ascites *vs*. no chylous ascites: 76.2% *vs*. 93.4%). Moreover, a significant difference in the recurrence rate was observed (chylous ascites *vs*. no chylous ascites: 22.2% *vs*. 3.9%). However, only nine patients with chylous ascites were included in the survival analysis; thus, further subgroup analysis based on the site of metastasis was not possible. Theoretically, the leakage of lymphatic fluid containing tumor cells could result in potential peritoneal dissemination. In the present study, we observed a nonsignificant trend towards a higher peritoneal metastasis risk in the chylous ascites group (5.9% *vs*. 1.6%). Another explanation is that a prolonged length of hospital stay due to chylous ascites might result in a delay in the start of adjuvant chemotherapy.[21] However, the postoperative hospital stay was only 3 days longer in the chylous ascites group than in the no chylous ascites group in our cohort. This 3-day delay might have little effect on prognosis. Of note, in a previous small sample study, peritoneal recurrence developed only in patients with pT3 tumors after laparoscopic surgery, whereas all patients with peritoneal recurrence after open surgery had pT4 tumors. It is worth noting that one patient in the laparoscopic group was revealed to have peritoneal metastasis 6 months after surgery and developed chylous ascites as a postoperative complication.[22] Thus, considering the high incidence of chylous ascites after laparoscopic and robotic surgery and its adverse prognosis, meticulous clipping or sufficient coagulation of the lymphatic tissue near the vessel origins is necessary during minimally invasive surgery.

The limitations of this work include its retrospective nature and the relatively small number of postoperative chylous ascites cases due to the low incidence of this condition. In addition, the criteria defining chylous ascites differed, although slightly, among previous studies,[8,10,23] which might have caused bias in the comparisons of our results with previous studies. Thus, a prospective study with standard diagnostic criteria for chylous ascites is necessary.

In conclusion, using a large cohort, we observed an overall incidence rate of 3.8% for chylous ascites after rectal surgery following neoadjuvant therapy. The incidence of chylous ascites was highest after robotic surgery (6.9%), followed by laparoscopic surgery (4.2%) and open surgery (1.0%). Furthermore, postoperative chylous ascites was associated with poor long-term oncologic outcomes and may possibly be associated with peritoneal recurrence. We recommend sufficient coagulation of the inferior mesenteric arterial sheath that is rich in lymphatics to prevent chylous ascites, especially during minimally invasive surgery.

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Conflicts of interest

None.

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