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ORIGINAL ARTICLE

Prognostic impact of postoperative intra-abdominal infections after elective colorectal cancer resection on survival and local recurrence: a propensity score-matched analysis

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Abstract

Purpose Several authors have reported an association between anastomotic leak and/or intra-abdominal abscess and oncological survival and recurrence. However, no reports have investigated whether combining anastomotic leak/intra-abdominal abscess and positive drainage culture influences long-term oncological outcomes. Therefore, we defined these complications as postoperative intra-abdominal infections. The present study aimed to evaluate the prognostic impact of postoperative intra-abdominal infections on long-term oncological outcomes after curative stage I-III colorectal cancer surgery.

Methods We performed a retrospective analysis of 755 consecutive patients with stage I-III colorectal cancer undergoing curative surgery between 2010 and 2015 by performing a propensity score-matched analysis to reduce selection bias.

Results Of the 755 patients, 62 were matched for postoperative intra-abdominal infections analyses. The median follow-up was 48 months. Compared with the non-infections group, the postoperative intra-abdominal infections group had a significantly shorter local recurrence-free survival ($P = 0.01$ prior to matching, and $P = 0.05$ after matching). No significant difference was found between the groups in terms of overall, cancer-specific free, recurrence-free, or distant recurrence-free survival. However, multivariate analyses identified postoperative intra-abdominal infections as an independent prognostic factor for local recurrence-free survival ($P = 0.04$ prior to matching, and $P = 0.03$ after matching).

Conclusions In this matched-pair analysis comparing stage I-III colorectal cancer patients with and without postoperative intra-abdominal infections, postoperative intra-abdominal infections were associated with poor local recurrence-free survival, but not overall, cancer-specific free, recurrence-free, or distant recurrence-free survival.

Keywords Colorectal cancer · Postoperative intra-abdominal infections · Propensity score-matching · Oncological outcomes · Local recurrence

Introduction

Surgical resection is essential to obtain long-term outcomes for colorectal cancer (CRC), but postoperative complications also have a significant impact on oncological outcomes. Anastomotic leaks (ALs) are one of the most serious complications in patients after CRC resection. Despite continuous improvement in surgical techniques, AL rates vary diversely between 3 and 12% depending on the site of anastomosis [1, 2]. Intra-abdominal abscess (IAA) after CRC surgery may present similarly to AL.

Several publications have reported conflicting results on the long-term oncological survival and recurrence of AL. A recent propensity score analysis by Zimmermann et al. [3] reported no significant differences in overall survival (OS), disease-free survival (DFS), or local recurrence rate (LRR). An analysis of 1181 patients from the Spanish registry found no association between AL and long-term oncological survival and recurrence [4]. On the other hand, a recent meta-analysis by Lu et al. [5] reported that AL impacts cancer-

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specific mortality and the LRR. Mirnezami et al. [6] reported that AL is associated with an increased LRR and reduced long-term cancer-specific survival (CSS) after surgery for CRC. Furthermore, a monocentric matched-pair analysis by Eberhardt et al. [7] concluded that AL and IAA after resection for rectal cancer are associated with increased overall and local recurrence (LR). Although some authors have reported an association between AL and/or IAA and oncological outcomes, the role of AL and/or IAA in long-term oncological survival and recurrence remains uncertain. Moreover, an occult minor leak may be a precursor to IAA or positive drainage culture; therefore, these postoperative complications may be part of the same pathophysiological process. No reports have investigated whether combing AL/IAA and positive drainage culture influences long-term oncological outcomes. Therefore, we defined these complications as postoperative intra-abdominal infections (PIAIs).

The present study aimed to retrospectively evaluate the prognostic impact of PIAIs after curative stage I-III CRC surgery in the overall cohort and between matched groups.

Patients and methods

Between January 2010 and December 2015, 909 consecutive patients underwent elective resection for CRC at Osaka Rosai Hospital, Japan. None of the patients underwent emergency surgery. None of the patients received surgery with inadvertent perforation of the bowel. Patients with carcinoma in situ or palliative resection were excluded from the analysis (n = 154). Palliative surgery was defined as those in which there was a known residual tumor, either distant or local. Thus, the analysis included 755 patients undergoing curative CRC surgery. Subsequently, patients with PIAIs were matched with patients without these conditions via propensity score-matching. This retrospective study was approved by our Institutional Review Board (approval number 31-32).

All recorded clinical and pathological data were revalidated according to medical and pathology records. Patient demographic data on age, sex, body mass index, diabetes mellitus, the American Society of Anesthesiologists physical status classification, primary tumor site, neoadjuvant chemotherapy, surgical approach, diverting stoma, PIAIs, histological grade, pathological (p) T stage, pN stage, pTNM stage (according to the Union for International Cancer Control [UICC] 8th version) [8], adjuvant chemotherapy, and recurrence were collected. No missing data were present for the examined variables.

PIAIs were defined as postoperative organ/space infections with at least one of AL, IAA, or positive drainage culture. AL was defined as clinically apparent leakage such as fecal liquid discharge and purulent drainage obtained from drain placed into the organ/space and confirmed using computed tomography (CT) imaging, contrast enema, and/or colonoscopy. IAA was defined as a postoperative intra-abdominal fluid collection confirmed by CT imaging with fever, leukocytosis, or increased C-reactive protein (CRP) levels that required treatment with fasting, antibiotics, or drainage. Drain culture was obtained from drain placed into the organ/space for purposes of clinical diagnosis or treatment, and positive drainage culture was defined as drain culture positive without intra-abdominal fluid collection confirmed by CT imaging.

Adjuvant chemotherapy was recommended for all patients with UICC stage III CRC. The follow-up protocol was the same for both groups. Following curative CRC resection, the surveillance schedule was based on guidelines issued by the Japanese Society for Cancer of the Colon and Rectum [9]. The postoperative follow-up involved physical examination at every follow-up, measurement of serum CEA every 3 months, chest and abdominal CT every 6 months, and colonoscopies at 1, 3, and 5 years after resection. Recurrent disease was diagnosed based on clinical, laboratory, diagnostic imaging, and pathological findings. If patients had recurrence, then the date when the recurrence was first noted and its location and extent were recorded.

Oncological outcomes

Oncological outcomes were OS, CSS, recurrence-free survival (RFS), local recurrence-free survival (LRFS), and distant recurrence-free survival (DRFS). OS was defined as the time from the date of surgery to the day of death from any cause. CSS was defined as the time from the date of surgery to the day of death from CRC. RFS, LRFS, and DRFS were defined as the time from the date of surgery and the identification of either radiological or histological recurrence or death from any cause.

Statistical analysis using propensity score-matching

Prior to propensity score-matching, baseline patient characteristics were compared through bivariate analyses to assess any imbalance of covariates. Propensity score-matching was then applied to minimize the possibility of selection bias and to adjust for significant differences in the baseline characteristics of patients (Fig. 1). The first step of the matching process was to complete a multivariate logistic regression analysis to obtain propensity scores. Covariates selected for analysis in regression models were sex, primary tumor site, neoadjuvant chemotherapy, and surgical approach for PIAIs analyses. Covariates with $P < 0.05$ were chosen to adjust for significant differences. The next step was the 1:1 matching process, using a caliper set at 0.2. After propensity score-matching, baseline characteristics, including covariates not entered into the propensity score model, were compared between groups using bivariate analyses.

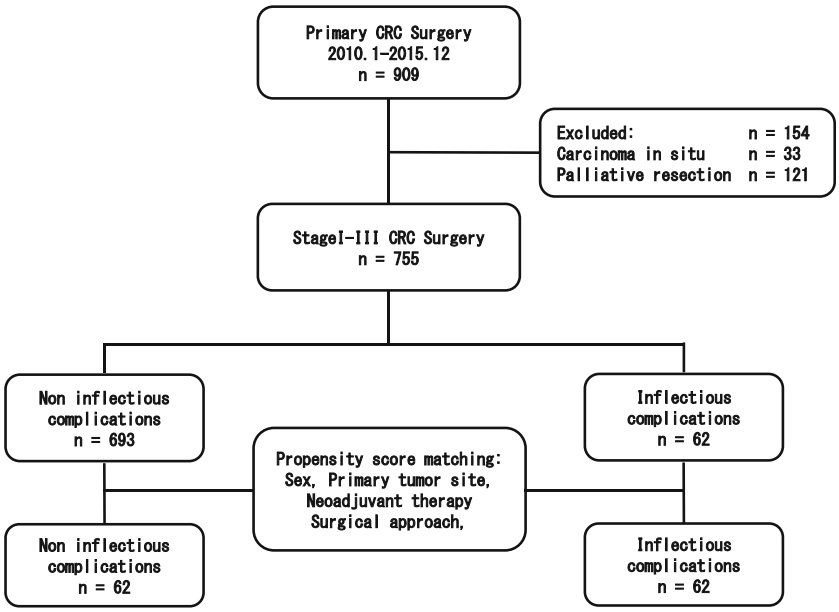

Fig. 1 Flow diagram describing the patient-matching process

The χ^2 and Mann–Whitney U tests were used for comparisons of categorical variables. For long-term outcomes, Kaplan-Meier curves were plotted and patients with and without PIAIs compared using the log-rank analysis. Univariate and multivariate analyses for OS, CSS, RFS, LRFS, and DRFS were conducted using the Cox proportional hazards model, with hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). Initially, a significance level of 0.10 ($P < 0.10$) in the univariate analysis was taken for inclusion in the multivariate analysis. Significant variables to $P < 0.10$ were used to create a multivariate analysis model. In the final model, variables significant at $P < 0.05$ were considered significant in the multivariate analysis. All statistical analyses were performed using JMP Pro Version 13 (SAS Institute, Inc., Cary, NC, USA).

Results

Baseline patient characteristics

An overview of our study is shown in Fig. 1. Of the 909 consecutive patients who underwent elective CRC surgery, 154 patients were excluded. Thus, the total sample size included 755 patients who underwent curative CRC surgery. Table 1 provides the baseline patient characteristics. Sixty-two patients (8.2%) were classified as presenting with evidence of PIAIs. Significant group-dependent differences were observed in terms of sex, neoadjuvant chemotherapy, primary tumor site, and surgical approach. After matching for PIAIs, 62 matched pairs were selected. The baseline characteristics of the patients were conserved among the two matched groups. The recurrence rate did not significantly differ between the matched groups or in the overall cohort.

The PIAIs profiles and treatments are given in Table 2. With regard to PIAI profiles, 47 (75.8%) were AL, 12 (19.4%) IAA, and 3 (4.8%) positive drainage culture. The majority (46.8%) were treated conservatively. The number of patients with fasting only, or fasting and antibiotics was 4 (13.8%) and 25 (86.2%), respectively. The other patients underwent reoperation with drainage and/or the formation of ileostomy or colostomy (38.7%), and 14.5% of patients received interventional drainage. The modality for PIAIs diagnosis was computed tomography (CT) only in 47 patients (75.8%), CT and colonoscopy in 7 (11.3%), CT and enema in 5 (8.1%), and drain culture in 3 (4.8%). Supplementary Table 1 presents the relationship between PIAIs and recurrence. Median PIAIs diagnosis interval after surgery was 6 (range, 1–18) days, and the median serum WBC and CRP values at PIAIs diagnosis were 10,050 (range, 1500–37,200) μL and 14.95 (range, 4.57–35.93) mg/dL. Median duration of treatment for PIAIs was 24 (range, 5–74) days. No significant difference was found between the groups.

Effects of PIAI on oncological outcomes

In our study ($n = 755$), without adjusting for background, 71 patients (9.4%) died from CRC, with 143 (18.9%) all-cause deaths during follow-up. The number of patients with overall recurrence, distant recurrence, and LR was 128 (16.9%), 118 (15.6%), and 27 (3.6%), respectively. Compared with the non-PIAIs group, the patients with PIAIs had significantly shorter LRFS ($P = 0.01$; Fig. 3a). However, no significant difference was found between the groups in terms of OS, CSS, RFS, and DRFS (Fig. 2a and Fig. 3A).

Table 1 Baseline characteristics between non-PIAIs and PIAIs

	Overall ($n = 755$)					Propensity score-matched pairs ($n = 124$)				
	Non-PIAIs group ($n = 693$)		PIAIs group ($n = 62$)		P	Non-PIAIs group ($n = 62$)		PIAIs group ($n = 62$)		P
	N	%	N	%		N	%	N	%	
Sex					0.0123					1.0000
Male	392	56.6	45	72.6		45	72.6	45	72.6	
Female	301	43.4	17	27.4		17	27.4	17	27.4	
Age, year					0.2157					1.0000
< 70	301	43.4	32	51.6		32	51.6	32	51.6	
≧ 70	392	56.6	30	48.4		30	48.4	30	48.4	
BMI category, kg/m^2					0.1304					0.6695
< 20	194	28.0	18	29.0		19	30.6	23	37.1	
20–24	368	53.1	39	62.9		35	56.5	29	46.7	
25–29	110	15.9	4	6.5		4	6.5	6	9.7	
≧ 30	21	3.0	1	1.6		4	6.5	4	6.5	
DM					0.5934					0.4877
Absent	567	81.8	49	79.0		52	83.9	49	79.0	
Present	126	18.2	13	21.0		10	16.1	13	21.0	
ASA					0.2896					0.1690
1	125	18.1	8	12.9		10	16.1	8	12.9	
2	459	66.2	47	75.8		38	61.3	47	75.8	
3	109	15.7	7	11.3		14	22.6	7	11.3	
Primary site					0.0002					1.0000
Colon	439	63.4	24	38.7		24	38.7	24	38.7	
Rectum	254	36.7	38	61.3		38	61.3	38	61.3	
Neoadjuvant chemotherapy					0.0017					1.0000
Absent	666	96.1	53	85.5		53	85.5	53	85.5	
Present	27	3.90	9	14.50		9	14.5	9	14.5	
Surgical approach					0.0002					1.0000
Open	467	67.4	27	43.5		35	56.5	35	56.5	
Laparoscopic	226	32.6	35	56.5		27	43.5	27	43.5	
Conversion	20	2.9	2	3.2		1	1.6	2	3.2	
Diverting stoma					0.1691					0.3061
Absent	649	93.7	55	88.7		51	82.3	55	88.7	
Present	44	6.3	7	11.3		11	17.7	7	11.3	
Histological grade					0.7088					0.7520
Pap/Well/Moderate	646	93.2	57	91.9		56	90.3	57	91.9	
Muc/Poor/sig	47	6.8	5	8.1		6	9.7	5	8.1	
pT stage					0.9979					0.7455
T1	106	15.3	9	14.5		7	11.3	9	14.5	
T2	119	17.2	11	17.7		14	22.6	11	17.7	
T3	337	48.6	30	48.4		26	41.9	30	48.4	
T4	131	18.9	12	19.4		15	24.2	12	19.4	
pN stage					0.9265					0.6781
N0	409	59.0	38	61.3		37	59.7	41	66.1	
N1	190	27.4	16	25.8		18	29.0	15	24.2	
N2	93	13.4	8	12.9		7	11.3	6	9.7	
N3	1	0.2	0	0.0		0	0.0	0	0.0	
UICC stage					0.8578					0.5023
I	190	27.4	16	25.8		18	29.0	16	25.8	
II	222	32.0	22	35.5		16	25.8	22	35.5	
III	281	40.6	24	38.7		28	45.2	24	38.7	
Adjuvant chemotherapy					0.1928					0.6814
Absent	498	78.3	74	70.5		45	72.6	47	75.8	
Present	195	21.7	31	29.5		17	27.4	15	24.2	
Recurrence					0.8558					0.8031
Absent	575	83.0	52	83.9		53	85.5	52	83.9	
Present	118	17.0	10	16.1		9	14.5	10	16.1	

BMI, body mass index; *DM*, diabetes mellitus; *ASA*, American Society of Anaesthesiologists; *UICC*, Union for International Cancer Control; *PIAIs*, postoperative intra-abdominal infections; *HR*, hazard ratio; *CI*, confidence interval

Matched patients with PIAIs had poorer LRFS than the non-PIAIs group ($P = 0.05$; Fig. 3b). In terms of OS, CSS, RFS, and DRFS, no significant difference was found between the matched groups or the overall cohort (Fig. 2b and Fig. 3b).

Prognostic factors for survival after colorectal surgery

Table 3 presents the univariate and multivariate regression analyses for PIAIs in the overall cohort ($n = 755$) and the matched cohort ($n = 124$).

Overall survival

Supplementary Table 2 presents the univariate and multivariate analyses of OS. Univariate analysis identified eight variables significantly associated with poor OS, including PIAIs. Multivariate analysis showed that seven of these variables were independently associated with poor OS. After matching, univariate analysis revealed seven variables that are significant predictors of OS. In multivariate analysis, three of these variables were independent factors. PIAIs had no significant influence (Table 3).

Cancer-specific survival

Supplementary Table 3 presents the univariate and multivariate analyses of CSS. Univariate analysis identified five variables significantly associated with poor CSS. Multivariate analysis showed that these variables were independently associated with poor CSS. After matching, univariate analysis revealed four variables that are significant predictors of CSS. In multivariate analysis, one of these variables was an independent factor. PIAIs had no significant influence (Table 3).

Table 2 PIAIs profile and treatment

	Patients with PIAIs ($n = 62$)
PIAIs profile, *n* (%)	
Anastomotic leakage	47 (75.8)
Intra-abdominal abscess	12 (19.4)
Positive drainage culture	3 (4.8)
Modality of PIAIs diagnosis, *n* (%)	
CT only	47 (75.8)
CT and colonoscopy	7 (11.3)
CT and enema	5 (8.1)
Drainage culture	3 (4.8)
Type of treatment for PIAIs, *n* (%)	
Conservative treatment	29 (46.8)
Fasting only	4/29 (13.8)
Fasting and antibiotics	25/29 (86.2)
Reoperation	24 (38.7)
Drainage	9 (14.5)

PIAIs, postoperative intra-abdominal infections; *CT*, computed tomography

Recurrence-free survival

Supplementary Table 4 presents the univariate and multivariate analyses of RFS. Univariate analysis identified seven variables significantly associated with poor RFS. Multivariate analysis showed that six of these variables were independently associated with poor RFS. After matching, univariate analysis revealed seven variables that are significant predictors of RFS. In multivariate analysis, five of these variables were independent factors. PIAIs had no significant influence (Table 3).

Local recurrence-free survival

Supplementary Table 5 presents the univariate and multivariate analyses of LRFS. Univariate analysis identified eight variables significantly associated with poor LRFS, including PIAIs. Multivariate analysis identified all of these variables as being independently associated with poor LRFS. PIAIs had significant influence (HR 1.65, 95% CI 0.97–2.63; $P = 0.04$; Table 3). After matching, univariate analysis revealed eight variables that are significant predictors of LRFS, including PIAIs. In multivariate analysis, four of these variables were independent factors. PIAIs had significant influence (HR 2.29, 95% CI 1.04–4.32; $P = 0.03$; Table 3).

Distant recurrence-free survival

Supplementary Table 6 presents the univariate and multivariate analyses of DRFS. Univariate analysis identified seven variables significantly associated with poor DRFS. Multivariate analysis showed that six of these variables were independently associated with poor DRFS. After matching, univariate analysis revealed seven variables that are significant predictors of DRFS. In multivariate analysis, five of these variables were independent factors. PIAIs had no significant influence (Table 3).

Discussion

Our present study highlights the prognostic impact of PIAIs on oncological outcomes after curative surgery for stage I-III CRC. Our results demonstrate that PIAIs were an independent predictor of LRFS in the entire patient cohort or matched cohort, but other oncological outcomes were not associated with PIAIs. Our retrospective study, with a propensity score-matched analysis, reduces the possibility of selection bias and provides new insight into the negative implications of PIAIs in patients with stage I-III CRC.

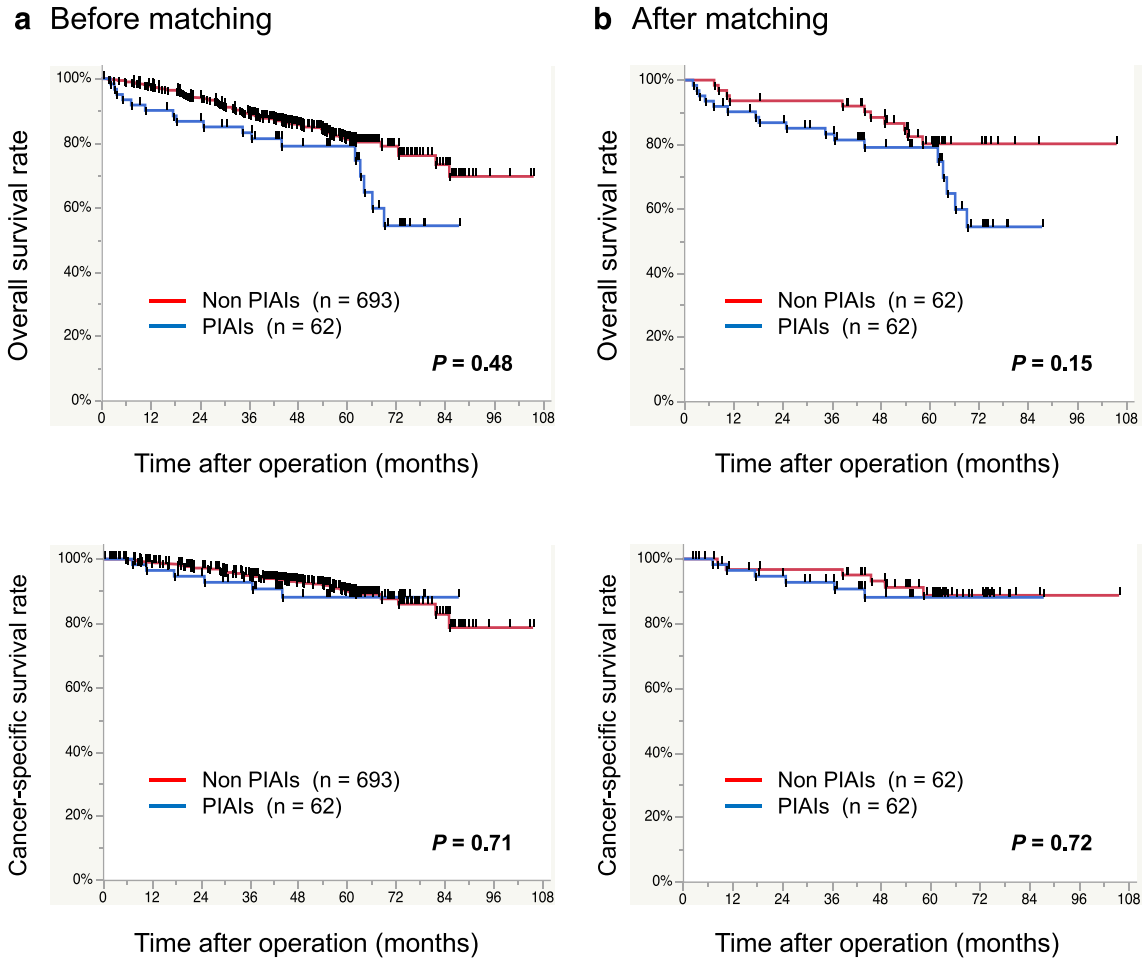

Fig. 2 Kaplan-Meier curves for overall survival and cancer-specific survival according to PIAIs. **a** Before and **b** after matching

Reviewing the current literature, notably, several publications have reported conflicting results on the long-term oncological survival and recurrence of AL and/or IAA. In the present study, we demonstrated that PIAIs were an independent predictor of LRFS in the entire patient cohort or matched cohort, but other oncological outcomes (OS, CSS, RFS, or DRFS) were not associated with PIAIs. Several studies and meta-analysis found similar results to our study. A case-control study by Eberhardt et al. [7] concluded that AL and IAA are associated with increased overall recurrence and LR in patients who underwent surgery for rectal cancer. A prospective, multicenter, randomized study by Docherty et al. [10] showed that AL was a significant independent prognostic factor influencing LRR. Another large series of 1834 patients obtained from a large multicenter UK database by Branagan et al. [11] showed a 25.1% LRR in patients with rectal anastomoses complicated by AL compared with a 10.4% recurrence rate without AL. After rectal anastomosis, an AL was associated with a significant increase in LR. Furthermore, previous meta-analysis reported that AL after restorative rectal cancer surgery is associated with higher LR and reduced long-term survival, but AL does not increase distant recurrence [5, 6]. A recent systematic review and meta-analysis demonstrated that AL after CRC resection is associated with increased LR and poor long-term outcomes, including OS, CSS, and DFS [12]. Contrary to that, a case-control study performed a matched-pair analysis by Eberhardt et al. [7] showed that AL and IAA did not affect survival and recurrence at 5 years survival or recurrence in patients undergoing colon cancer surgery. A registry study with the Swedish Rectal Cancer Registry by Jörgren et al. [13] demonstrated that AL is not a proven risk factor for LR, distant metastasis, or overall recurrence and has no impact on 5-year OS or 5-year CSS. Espín et al. [4] conducted a multicenter observation study using the Spanish Rectal Cancer Project database, reporting that AL is not associated with LR, overall recurrence, OS, or CSS undergoing low anterior resection. Moreover, Zimmermann et al. [3] reported no significant differences in OS, DFS, and LRR. Summarizing the current literature, these results were as heterogenous as they were different in study design types.

One of the strengths of our study is that a propensity score-matched analysis was applied to minimize the possibility of selection bias and to adjust for significant differences in the baseline characteristics of the patient cohort. Another strength

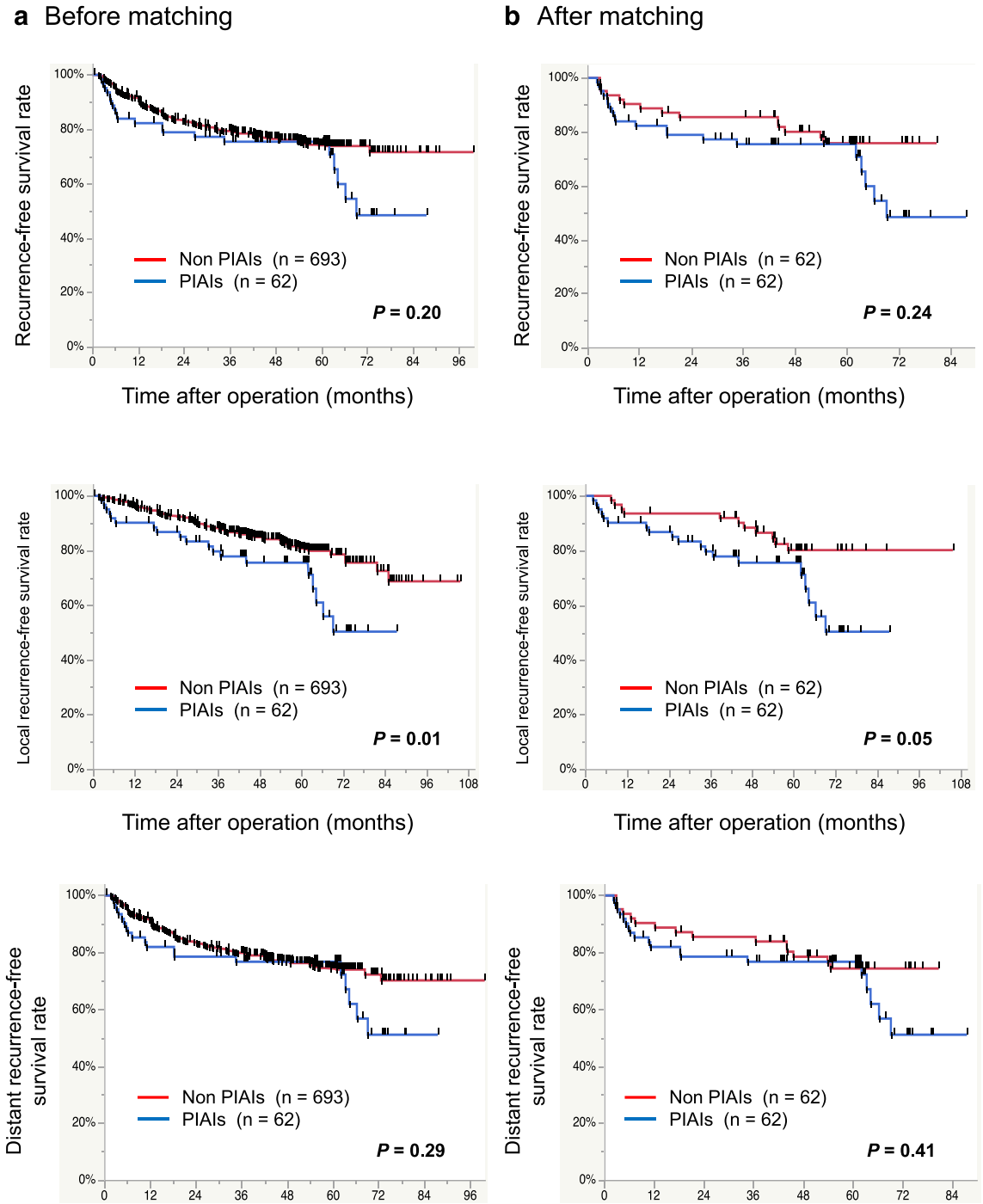

Fig. 3 Kaplan-Meier curves for recurrence-free survival, local recurrence-free survival, and distant recurrence-free survival according to PIAIs. **a** Before and **b** after matching

is that we included patients with positive drainage culture and analyzed oncological outcomes, whereas previous studies compared only patients with and without AL and/or IAA. The rationale for including patients with these complications is based on the premise that AL and/or IAA is often associated with a positive drainage culture. Some patients may have a positive drainage culture but no AL and/or IAA on image findings. If such patients are included in a "non AL" group, the results may be misleading because the differences in oncological outcomes between groups may be reduced. Clinically, in addition, it is sometimes difficult to classify AL and IAA. Therefore, we defined postoperative organ/space infections with at least one of AL, IAA, or positive drainage culture as PIAIs.

A notable finding of this more rigorous analysis using propensity score-matching revealed that PIAIs are associated

Table 3 Prognostic factors of survival on univariate and multivariate analyses, overall and matched cohort

Variables	Overall cohort ($n = 755$)				Matched cohort ($n = 124$)			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Overall survival								
Non-PIAIs	*1*		1		1		-	-
PIAIs	**1.65 (0.96–2.67)**	**0.0686**	1.53 (0.88–2.50)	0.1250	1.72 (0.81–3.80)	0.1559	-	-
Cancer-specific survival								
Non-PIAIs	1		-	-	1		-	-
PIAIs	1.16 (0.45–2.47)	0.7251	-	-	1.22 (0.38–3.92)	0.7246	-	-
Recurrence-free survival								
Non-PIAIs	1		-	-	1		-	-
PIAIs	1.34 (0.81–2.08)	0.2291	-	-	1.49 (0.76–3.03)	0.2430	-	-
Local recurrence-free survival								
Non-PIAIs	**1**		1		*1*		*1*	
PIAIs	**1.80 (1.07–2.84)**	**0.0260**	**1.65 (0.97–2.63)**	**0.0479**	**1.98 (0.95–4.32)**	**0.0651**	**2.29 (1.04–5.28)**	**0.0388**
Distant recurrence-free survival								
Non-PIAIs	1		-	-	1		-	-
PIAIs	1.28 (0.77–2.01)	0.3153	-	-	1.49 (0.76–3.03)	0.2430	-	-

PIAIs, postoperative intra-abdominal infections; *HR*, hazard ratio; *CI*, confidence interval

with a higher LR rate and poorer LRFS, but not with other oncological outcomes. Hence, it has been suggested that LR may be influenced not only by tumor-related factors and surgical techniques but also by local inflammatory response associated with PIAIs. Reasons for poorer LRFS are uncertain, but various authors have attempted to explain why CRC patients who develop PIAIs may have worsened survival and recurrence. One example is inadvertent perforation of the bowel during surgery [14, 15]. It is suggested that perforation of the bowel during surgery may lead to extraluminal implantation of exfoliated cancer cells from the bowel lumen. If there is a PIAIs caused by spreading bacteria during surgery, the possibility may be high. However, in this study, there was no patient with inadvertent perforation of the bowel during surgery. In addition, there is also evidence that the inflammatory response in patients with postoperative peritoneal infection affects the oncological survival and recurrence [16–19]. Alonso et al. [19] noted that the inflammatory reaction to infection leads to increased expression of local and circulating proinflammatory and proangiogenic factors that may facilitate the oncological outcomes and growth of residual tumor cells. Several authors have attributed these mechanisms to an inflammation-based immunological pathway [20–22]. AL and IAA enhance and prolong the inflammatory response. Continual exposure to endotoxins results in tolerance and a reduced host immune response that impedes effective tumoricidal activity [23]. This creates a permissive microenvironment that allows circulating tumor cells to progress to LR and metastases, possibly through inflammatory oncotaxis [24, 25]. In the present study, inflammation response, including WBC and CRP was investigated to assess whether local inflammation response was associated with LR (supplementary Table 2), but no significant difference was found between the groups. However, a variety of acute phase reactants and proinflammatory mediators such as interleukin and the tumor necrosis factor family of proteins could be released during the acute and subsequent chronic inflammation that accompanies PIAIs, and hence the local inflammatory response associated with PIAIs might facilitate cancer recurrence. Concerning pathophysiological aspects, Salvans et al. [26] evaluated the effect of postoperative peritoneal infection (AL or IAA) on the proliferation, migration, and invasion capacities of cancer cell lines in vitro after resection for CRC. They investigated the association between postoperative peritoneal infection and tumor recurrence after surgery using cell proliferation and cell migration/invasion activity assays. Postoperative peritoneal infection was showed to enhance the invasive capacity of residual tumor cells after CRC resection, facilitating their growth to recurrent tumors [26]. The role of PIAIs and oncological outcomes remain uncertain, but these mechanisms may account for the association between poor LRFS and PIAIs.

Our study has some limitations. First, it had a non-randomized and retrospective design. Second, our study cohort was relatively limited by the nature of being a monocentric study. Therefore, univariate and multivariate

analyses may not detect factors correlated with long-term survival and recurrence. The univariate and multivariate analysis in the matched cohort revealed no differences between the patients with and without lymph node metastasis, which was expected to influence long-term outcomes. However, our application of a propensity score-matching method balanced the characteristics of our respective patient groups, though at the cost of a reduced number of patients. Finally, our study combined colon and rectal cancers rather than comparing at the influences on colon cancer and rectal cancer separately. However, a distinction is not always made between LR after PIAIs from colonic anastomoses and LR after PIAIs from rectal anastomoses [27]. In fact, most studies evaluating the influence of AL and/or IAA after surgery for CRC have investigated how these complications affect colon and rectal cancers combined rather than individually.

Conclusions

The current study minimized the imbalance in terms of group size and bias in patient backgrounds and characteristics by performing a propensity score-matched analysis, and investigated whether combing AL/IAA and positive drainage culture influences oncological outcomes. Our data showed that PIAIs are associated with higher LR and poor LRFS, but not with OS, CSS, RFS, or DRFS. Further studies are needed to evaluate the potential influence of PIAIs on oncological outcomes.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethics approval and informed consent The Institutional Review Board of Osaka Rosai Hospital approved the study (approval number 31-32). This study was eligible for exemption of informed consent. No animal experiments were performed in this study.

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