

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1,2,3	Intraoperative intraperitoneal chemotherapy increases the incidence of anastomotic leak after anterior resection of rectal tumor
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2,3	To investigate whether intraoperative intraperitoneal chemotherapy increases the incidence of AL after anterior resection of rectal neoplasms.  Intraoperative intraperitoneal chemotherapy can improve the prognosis of patients with locally advanced rectal carcinoma, but it also increases the possibility of AL after anterior resection of rectal neoplasms.
<b>Introduction</b>				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4,5	Reports have shown that intraoperative intraperitoneal chemotherapy can reduce locoregional recurrence rate and increase long-term survival rate. Nevertheless, the effects of intraoperative intraperitoneal chemotherapy on postoperative complications have rarely been explored, which concern the safety and feasibility of this new treatment modality.

Objectives	3	State specific objectives, including any prespecified hypotheses	5	Given that AL is the most common and serious operation complication after rectal surgery, we evaluated the role of intraoperative intraperitoneal chemotherapy in the occurrence of AL.
<b>Methods</b>				
Study design	4	Present key elements of study design early in the paper	6	We extracted data from 477 consecutive patients who underwent anterior resection of rectal cancer at the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College from September 2016 to September 2017.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6	We extracted data from 477 consecutive patients who underwent anterior resection of rectal cancer at the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College from September 2016 to September 2017. Information regarding intraoperative usage of chemotherapy agents was carefully collected from medical records.
Participants	6	<p>(a) <i>Cohort study</i>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i>—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants</p>	6	The inclusion criteria were detailed as follows: (1) All patients were definitely diagnosed with rectal cancer through abdominal and pelvic enhanced computed tomography (CT) scans, rectal

				<p>magnetic resonance imaging (MRI), colonoscopy, tissue biopsy and pathological examination; (2) All patients were confirmed to be with TNM stage II-III through rectal MRI at the time of diagnosis; (3) The distal border of tumor from anal verge was less than 15 cm; (4) All patients underwent anterior resection surgery with the double stapling technique.</p> <p>The exclusion criteria were as follows: (1) Patients who were considered to be with TNM stage I or IV at the time of diagnosis; (2) Patients who received hand suture anastomosis, Hartmann's surgery, intersphincteric resection and abdominal perineal resection. (3) Patients whose information was not clearly and accurately presented in medical records.</p>
		<p>(b) <i>Cohort study</i>—For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i>—For matched studies, give matching criteria and the number of controls per case</p>	/	This is not a matched study.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6	AL was diagnosed through clinical symptoms and signs of fever, abdominal pain, peritonitis, and discharge of intestinal content from pelvic drainage. Pelvic CT scans and rectoscopy can be

				further conducted to confirm AL. The hydrops and pneumatosis in the pelvic cavity in CT images or anastomotic defect in endoscopy images can imply the existence of AL.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7	To evaluate the comparability between chemotherapy group and control group and decrease confounding bias, A total of 32 variables were included in our investigation. All factors can be roughly divided into demographic characteristics, comorbidities, preoperative oncological therapy, operative treatment and tumor staging. All these data were described in detail in the medical records. We carefully examined the accuracy of our data to reduce bias from data collection.
Bias	9	Describe any efforts to address potential sources of bias	7,8	To evaluate the comparability between chemotherapy group and control group and decrease confounding bias, A total of 32 variables were included in our investigation.  To control confounding bias, factors that were clinically regarded to be associated with AL and imbalanced factors between the two groups with a P-value <0.05 were further introduced into multivariate

				logistic regression analysis and stratification analysis to determine independent risk factors of AL.
Study size	10	Explain how the study size was arrived at	6	We extracted data from 477 consecutive patients who underwent anterior resection of rectal cancer at the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College from September 2016 to September 2017.

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7	Quantitative data that were normally distributed were presented as mean $\pm$ standard deviation and further analyzed using t-test. However, quantitative data that were not normally distributed were presented as median (range) and were compared using Mann-Whitney U tests.
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7, 8	Given that we excluded patients whose information was not clearly and accurately presented in medical records, no data were missing in this study. Quantitative data that were normally distributed were presented as mean $\pm$ standard deviation and further analyzed using t-test. However, quantitative data that were not normally distributed were presented as median (range) and were compared using Mann-Whitney U tests. Qualitative data were expressed as the number of cases and percentage and further compared using Pearson's $\chi^2$ test or Fisher's exact test. Ordinal data were also presented as cases and percentage but further examined using Mann-

		<p>Whitney U tests. To control confounding bias, factors that were clinically regarded to be associated with AL and imbalanced factors between the two groups with a P-value <math>&lt;0.05</math> were further introduced into multivariate logistic regression analysis and stratification analysis to determine independent risk factors of AL. Overall survival rate and disease-free survival rate were calculated by the Kaplan-Meier method and further compared through log-rank test. All tests were two-sided, and a P-value <math>&lt;0.05</math> was regarded as statistically significant.</p>
(b) Describe any methods used to examine subgroups and interactions	/	<p>To control confounding bias, factors that were clinically regarded to be associated with AL and imbalanced factors between the two groups with a P-value <math>&lt;0.05</math> were further introduced into multivariate logistic regression analysis and stratification analysis to determine independent risk factors of AL.</p>
(c) Explain how missing data were addressed	7	<p>Given that we excluded patients whose information was not clearly and accurately presented in medical records, no data were missing in</p>

				this study.
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	6	Follow-up data were acquired by outpatient reexamination and telephones.
		(e) Describe any sensitivity analyses	/	No sensitivity analyses was done.
<b>Results</b>				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8	A total of 477 patients were included in our investigation with an average age of 58.7±10.9 years.
		(b) Give reasons for non-participation at each stage	/	No non-participation was observed in this study.
		(c) Consider use of a flow diagram	/	/
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8	A total of 477 patients were included in our investigation with an average age of 58.7±10.9 years. 301 (63.1%) and 176 (36.9%) were male and female, respectively. 171 patients received intraoperative intraperitoneal chemotherapy, including 8 patients using lobaplatin alone, 157 patients using fluorouracil implants alone and 6 patients using lobaplatin and fluorouracil implants simultaneously. 306 patients didn't receive intraoperative intraperitoneal chemotherapy.
		(b) Indicate number of participants with missing data for each variable of interest	/	No missing data was existed in our



				study.
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	10	All patients were followed up with a median period of 24 months (range 1-31 months).
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	9	The details for the occurrence of AL were presented in Table 4. In total, 18 (3.8%) individuals developed AL in our study. Higher incidence of AL was observed in the group received intraoperative intraperitoneal chemotherapy (7.6%) than in the control group (1.6%), which was significantly different (P=0.001).
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure		
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9	Descriptive analysis signified natural orifice specimen extraction surgery (P=0.035), placement of transanal tube (P=0.014), number of stapler firing (P=0.007) were imbalanced between the chemotherapy group and control group. All of these variables and other factors that were confirmed to be associated with AL in previous reports were enrolled in subsequent multivariate analyses (Table 5). After adjusting for confounding

		factors, intraoperative intraperitoneal chemotherapy was confirmed to significantly increase the incidence of AL (odds ratio [OR], 5.386; 95% confidence interval [CI], 1.808-16.042; P=0.002).
(b) Report category boundaries when continuous variables were categorized	17	Number of stapler firing, n(%):1 and 2, Above 2
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	/	

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10	Stratification analysis was also conducted to control confounding bias. The influence of intraoperative intraperitoneal chemotherapy on AL was further analysed in subgroups of gender, diabetes, incomplete intestinal obstruction, tumor location, natural orifice specimen extraction surgery, consolidation suture, defunctioning stoma, transanal tube and number of stapler firing. Intraoperative intraperitoneal chemotherapy significantly promoted the occurrence of AL in male, no diabetes, no incomplete intestinal obstruction, tumor located above the peritoneal reflection, no consolidation suture, no defunctioning stoma, no transanal tube, using 1 or 2 stapler firings and using more than 2 stapler firings subgroups.
<b>Discussion</b>				
Key results	18	Summarise key results with reference to study objectives	12	We found that AL occurred more frequently in patients who underwent intraperitoneal chemotherapy. And this tendency was verified both in the univariate and multivariate analysis.

Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13	<p>Our study has several limitations. Firstly, it's a retrospective cohort study and patients are divided into chemotherapy group and control group, selection bias, information bias and confounding bias can exist though we tried to collected variables as much as possible and performed multivariate analysis. Further large, multicenter, cohort studies or randomized control trials are necessary to assess the safety of intraoperative intraperitoneal chemotherapy. Secondly, the incidence of AL in our center is relatively low compared with most reports. Only 18 AL patients were observed in this study, which made it hard to perform dose-response relationship analysis and subgroup analysis to control bias.</p>
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13	<p>Surgeons should deliberately weigh the short-term risks of postoperative AL and the long-term benefits of improved oncological outcome and survival rate before choosing intraoperative</p>

				intraperitoneal chemotherapy.
Generalisability	21	Discuss the generalisability (external validity) of the study results	13	In conclusion, our present research determined that intraoperative intraperitoneal chemotherapy increased the incidence of postoperative AL after anterior resection of rectal carcinoma, but it also improved the DFS rate in patients with locally advanced rectal carcinoma.
<b>Other information</b>				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1	Supported by:Medicine and health technology innovation project of Chinese Academy of Medical Sciences,No.2017-12M-1-006.

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).