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Ostomy Does Not Lead to Worse Outcomes After Bowel Resection With Ovarian Cancer: A Systematic Review

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Background: Debulking cytoreduction surgery with bowel resection is a common intervention for ovarian cancer. It is controversial whether ostomy causes worse survival outcomes and how clinical physicians should choose which patients to undergo ostomy. During this study, we performed a systematic review to determine whether ostomy leads to worse outcomes after bowel resection compared to anastomosis. We also summarized the possible indications for ostomy.

Methods: We searched PubMed, Embase, and Cochrane for articles containing the phrase "ovarian cancer with bowel resection" that were published between 2016 and 2021. We included studies that compared primary anastomosis with ostomy. We mainly focused on differences in the anastomotic leakage rate, length of hospital stay, overall survival, and other survival outcomes associated with the two procedures.

Results and Conclusion: Of the 763 studies, three were ultimately included in the systematic review (N=1411). We found that ostomy did not contribute to worse survival outcomes, and that the stoma-related complications were acceptable. Indications for ostomy require further study. Bowel resection segment margins and the distance from the anastomosis to the anal verge require consideration.

Keywords: ostomy, ovarian cancer, bowel resection, meta-analysis, systematic review

INTRODUCTION

Bowel metastasis frequently occurs with advanced ovarian cancer, and debulking cytoreduction surgery, especially en bloc cytoreduction, is recommended (1–3). Bowel resection is performed when bowel metastasis is observed before or during surgery, and it is followed by primary anastomosis or ostomy (4–7). Primary anastomosis is the first choice after bowel resection, and ostomy is the alternative choice. Ostomy is not preferred because it has been shown to cause a worsened quality of life with ovarian cancer (8, 9).

Ostomy is the creation of an artificial anus in the abdomen. Because ostomy can be reversed, it can be permanent or temporary. For ovarian cancer patients, ostomy is performed to divert the feces so that the anastomosis can recover well. Anastomotic leakage (AL) is one of the most important complications associated with anastomosis because it can cause abdominal inflammation and some other issues (10). After bowel resection, ostomy can be performed instead of primary anastomosis to prevent AL. Diverting ileostomy is one of the common choices with ostomy because it is believed that it can decrease the AL rate associated with colorectal cancer (11). The AL rate has not shown any difference with permanent ostomy and temporary ostomy for colorectal cancer (12). However, patients with a stoma experience complications such as skin irritation and prefer to avoid ostomy to ensure a better quality of life (13–15). Physicians need to evaluate the problems and benefits before deciding whether to perform ostomy.

No guidelines specifically recommend follow-up interventions after bowel resection in ovarian cancer patients (1, 16, 17). Clinical physicians make decisions based on experience. There is no clear answer regarding whether ostomy will benefit patients with ovarian cancer. Few studies have concentrated on bowel surgery and its outcomes when ostomy and anastomosis are performed for ovarian cancer patients. It is still controversial whether ostomy causes worse survival outcomes and how clinical physicians should choose which patients to undergo ostomy. This review analyzed studies performed during the past 5 years to determine whether ostomy leads to worse outcomes than anastomosis. The possible indications for ostomy are also summarized.

MATERIALS AND METHODS

We searched PubMed, Embase, and Cochrane using the following MeSH terms and keywords in articles published during the past 5 years: [ovarian cancer] AND [ostomy] OR [anastomosis]. After excluding repeated studies, we screened all articles based on the title, abstract, and full text (**Figure 1**).

According to the PICO principle, P was primary or relapsed ovarian cancer, I was ostomy after bowel resection, and C was primary anastomosis after bowel resection. All meta-analyses were required to meet the following criteria: patients had primary or relapsed ovarian cancer; all patients underwent bowel resection during primary debulking surgery or interval debulking surgery, and data of ostomy patients were separated from those of anastomosis patients.

Age, body mass index, American Society of Anesthesiology score, and medical history were recorded as baseline data. Surgical information was recorded as a variable. We mainly focused on short-term and long-term outcomes such as the anastomotic leakage (AL) rate, length of hospital stay, 30-day readmission, overall survival (OS), progression-free survival (PFS), and other survival outcomes. This systematic review was not registered.

RESULTS

Of the 763 studies found during the database search, 112 remained after screening for duplicates. After screening the title, abstract, and full text based on the criteria, three studies were finally analyzed. Twenty-two other studies were used as references to support our interpretations.

Major Findings of the Three Studies

Three retrospective studies directly compared the outcomes of ostomy and primary anastomosis. These were the most important references during our analysis (**Figure 1** and **Table 1**).

The study by Canlorbe et al. included stage IIIB to IV ovarian cancer based on the International Federation of Gynecology and Obstetrics (FIGO) classification with anterior bowel resection during complete cytoreductive surgery (18). Patients were divided into groups based on whether they underwent ileostomy/colostomy (without stoma group, N=90; with stoma group, N=9). Of the nine patients with a stoma, one patient had two stomas and one was scheduled to undergo left colostomy but it was changed to ileostomy. Some baseline data, such as age and BMI, were reported. They also reported some surgery information, including the number of stomas and whether small bowel resection was performed. They compared the basic data and surgery information and found no difference between groups. A reverse rate of 88.9% and overall AL rate of 7.1% (6.7% in the primary anastomosis group and 11.1% in stoma group; not statistically compared) were reported during this study. Three adverse events (lower than Clavien–Dindo grade III) caused by the stoma were reported. The median OS was 31 months and the median PFS was 17 months. During the univariate analysis, patients with a stoma had a longer hospital stay and worse OS and PFS (log-rank test). The multivariate analysis was performed after the univariate analysis. Ileostomy and lymph node involvement were found to be risk factors for relapse. They reported two OS and PFS curves, but these were not statistically compared. This retrospective study reported worse outcomes for the stoma group; however, it did not report multivariate analysis results regarding survival outcomes and did not compare the curves of the two groups using multivariate statistics. The sample size was small, especially that of the stoma group, which made the results less reliable. The association between the surgery type and the outcomes was not reported.

The study by Fleetwood et al. included ovarian cancer patients who underwent colon resection. These patients were divided into the primary anastomosis group (N=453) and end ostomy group (N=586) (19). Some basic information was reported and the preoperative comorbidities were compared between groups (no significant difference). The primary anastomosis group seemed to have significantly more disseminated cancer, and the stoma group experienced more preoperative weight loss and received more neoadjuvant chemotherapy; however, the differences were not significant. Lower preoperative albumin and platelet levels and significantly higher preoperative leukocyte counts were observed in the ostomy group. Surgery information was not recorded in detail. Postoperative complications were almost statistically equal between groups, but the ostomy group tended to have worse complications. Severe adverse events (Clavien–Dindo grades III

FIGURE 1 | PRISMA diagram.
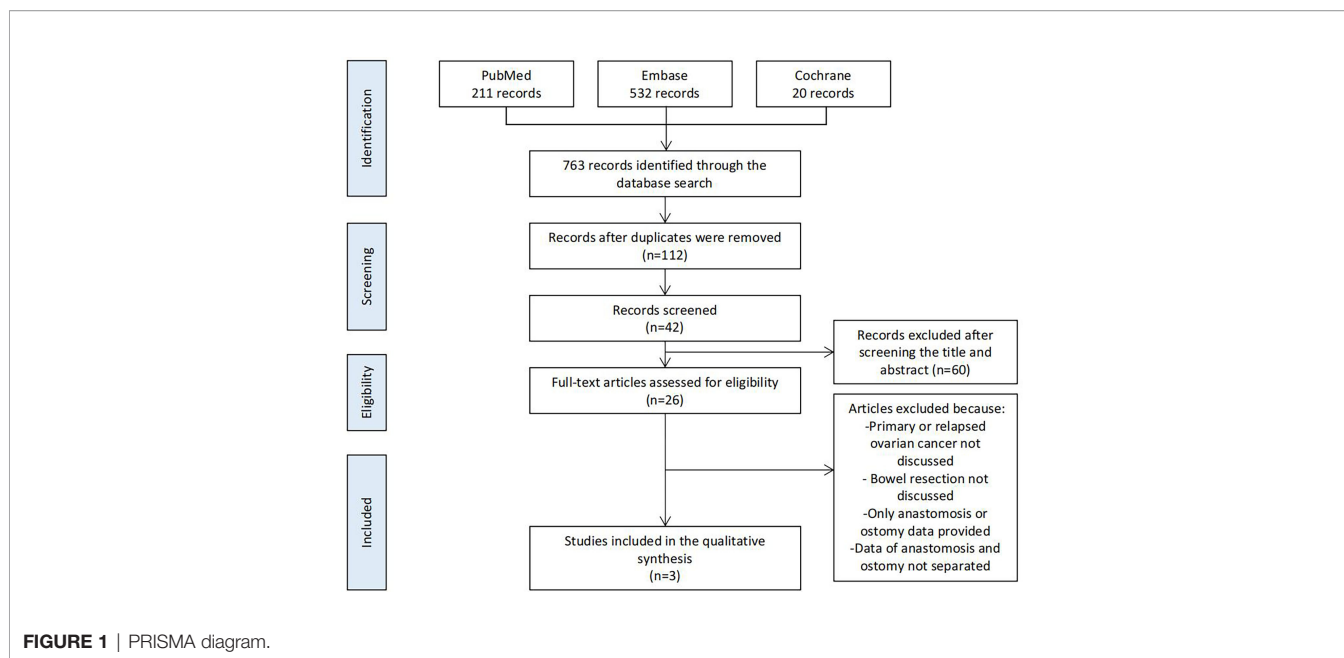
and IV) were equal between groups. However, the ostomy group had more grade II adverse events. The 30-day mortality rate was higher in the ostomy group in this study (3.1% in the primary anastomosis group and 6.2% in the stoma group). However, ostomy was not an independent risk factor when the preoperative laboratory values were controlled in the logistic regression. The blood urea nitrogen, creatinine, and preoperative albumin levels contributed to death. This retrospective study reported worse outcomes for the stoma group; however, the results changed after performing the multivariate analysis. The baseline data were compared and multivariate analysis was performed, which made these study results more reliable. However, surgery information was not recorded in detail, making the study results less reliable. It is unknown whether equal numbers of surgery types were performed. Furthermore, the reversal rate and AL rate were not reported.

The study by Lago et al. included patients with FIGO stages II to IV (20). These patients underwent colorectal resection after anastomosis and were divided into three groups (wait and see group, N=72; diverting ileostomy group, N=19; ghost ileostomy group, N=42). Ghost ileostomy involved the cutaneous placement of a portion of the terminal ileum. If no AL was observed by 7 days after surgery, then the ileum was reversed. If any AL occurred, then an ileum incision was performed without repeat laparotomy. Colonoscopy at 3 days and colonoscopy at 7 days after surgery was performed to find the AL. Some baseline information, including the albumin level, was recorded. There were no statistical differences among the three groups. Surgery information was recorded in detail. Statistical differences were observed in the estimated blood loss and intraoperative transfusion rate among groups (both were higher in the ileostomy group). The AL rate was equal among the three groups (5.6% in the primary anastomosis group; 5.3% in the ileostomy group; 4.8% in the ghost ileostomy group). The ileostomy group had a reversal rate of 73.7%; however, the ghost ileostomy group had a reversal rate of 100%. The median hospital stay and the

interval between surgery and chemotherapy were not different between the ileostomy group and the ghost ileostomy group. The ileostomy group had a higher rate of stoma-related complications than the ghost ileostomy group. This retrospective study compared the baseline data and surgery information among three groups, thus making its results more reliable. Colonoscopy was beneficial for finding asymptomatic AL and resulted in a more reliable AL rate. However, no multivariate analysis was performed and the sample size was small, thus making the results less reliable. Survival outcomes were not reported by this study.

These three studies reported different AL rates and survival outcomes for the primary anastomosis group and ostomy group. To further analyze these three studies, we used other studies as a reference.

Interpretation of the Major Finds

Higher AL rates contributed to worse OS (21). Hypoalbuminemia was an independent risk factor for AL, as reported by many studies (21–24). In fact, clinical physicians believed that the albumin level indicated whether ostomy should be performed (18–20). It was suggested that preoperative hypoalbuminemia might contribute to worse OS. According to the studies by Canlorbe et al. and Fleetwood et al., OS was worse for the ostomy group (18, 19). However, the study by Canlorbe et al. did not mention the albumin levels of the groups (18). The study by Fleetwood et al., after controlling the albumin level, reported no difference in the OS of the primary anastomosis group and ostomy group (19). The study by Lago et al. also reported no differences in the AL rates and albumin levels of the two groups; however, the survival outcomes were not directly compared (20). Therefore, ostomy itself would not contribute to worse OS with ovarian cancer.

The study by Canlorbe et al. reported that ileostomy and lymph node involvement were risk factors for relapse and observed higher PFS in the ostomy group (18). Gallotta et al. performed a multivariate analysis and indicated that metastatic mesenteric

TABLE 1 | Information collected from the three studies.

	Canlorbe et al.		Fleetwood et al.		Lago et al.	
	Primary anastomosis	**Ostomy**	**Primary anastomosis**	**Ostomy**	**Primary anastomosis / Ghost ileostomy**	**Ostomy**
Basic information						
Age (mean)	53	53	60.1 (overall)		55.7 / 54.5	60.9
BMI (mean)	24	23	Not reported		25.1 / 24.8	25.1
ASA score			Not reported		81.9% / 92.9% (combined scores 1 and 2)	63.2% (combined scores 1 and 2)
1	7.8%	0				
2	67.8%	55.6%				
3	18.9%	44.4%				
Unknown	5.6%	0				
Comorbidities			86.3%	85.9%		
Hypertension	18.9%	3.3%	41.4%	40.6%	Not reported	
Diabetes	12.2%	11.1%	Not reported		2.8% / 2.4%	10.5%
Corticoid/steroid use	1.1%	0	3.1%	3.6%	2.8% / 7.1%	0
FIGO stage						
Not applicable (relapse)			Not reported		8.3% / 9.5%	10.5%
II					6.9% / 9.5%	0
III	92.2%	100%			59.7% / 61.9%	84.2%
IV	7.8%	0			25.0% / 19.0%	15.8%
Preoperative serum results						
CA125 (>500 U/mL)	35.6%	22.2%	Not reported		Not reported	
Hyperalbuminemia (<3.5 g/dL)	Not reported				25.0% / 23.8%	10.5%
Mean albumin level (g/dl)			3.73	3.58		
Compared the baseline data between groups	Yes		Yes		Yes	
Surgery information						
Mean operative time (min)	466	557	Not reported		363 / 360	402
Intraoperative transfusion	Not reported				61.1% / 42.9%	78.9%
Mean intraoperative blood loss (mL)	1508	1100			446 / 557	683
Repeat bowel resection	32.2%	66.7%			18.1% / 14.3%	31.6%
Additional surgery						
Lymphadenectomy	85.6%	66.7%			55.6% / 69.0%	47.4%
Omentectomy	Not reported				90.3% / 88.1%	84.2%
Low anastomosis from the anal verge (<5 cm)	Not reported				6.9% / 14.3%	5.3%
Compared the surgery information	Yes		No		Yes	
Outcomes						
Mean hospital stay (day)	18	20	Not reported		10 (ghost ileostomy)	11
Adverse events (grade III or higher)	27.8%	22.2%	36.5%	36.9%		
Stoma-related adverse event					7.1% (ghost ileostomy)	78.9%
AL rate	6.7%(in Grade III)	11.1%(in Grade III)	Not reported		5.6% / 4.8%	5.3%
Reverse rate		88.9%	Not reported			73.7%
Median overall survival	31 months				Not reported	
Progression-free survival	17 months					
30-day morbidity			Ostomy status: OR, 1.97 (univariate)			

AL, anastomotic leakage; ASA, American Society of Anesthesiology; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; OR, odds ratio.

lymph nodes were associated with high rates of isolated aortic and celiac trunk lymph node recurrences (25). However, we did not find any other studies that supported ostomy as an independent risk factor for relapse. Canlorbe et al. explained that patients with a stoma received fewer cycles of adjuvant chemotherapy because of poorer compliance (18). However, their small sample size and lack of a multivariate analysis made the results less reliable.

Many stoma-related complications, such as dehydration and malnutrition, decrease the quality of life (26). Many patients do not prefer ostomy because it is associated with a worse quality of life. However, stoma-related complications rarely cause Clavien–Dindo grade III or higher adverse events with ovarian cancer, which is acceptable (18–20). It has been reported that the reverse rate varies from 43.3% to 88.9% (18, 20, 27). Enhancing postoperative care and increasing the reverse rate might result in patients being more receptive to ostomy.

We summarized and analyzed three studies that directly compared primary anastomosis and ostomy. We found that

ostomy alone did not contribute to worse survival outcomes and that the stoma-related complications were acceptable.

Indications for Ostomy

Ostomy, especially diverting ileostomy, is believed to reduce the AL rate and may result in better survival outcomes; however, these results were not reported by the three aforementioned studies (18–20). The indications for ostomy might contribute to the AL rate, thereby rendering the difference between primary anastomosis and ostomy not significant. A decreased AL rate was reported for ostomy by Kalogera et al., who compared the AL rate before and after determining the indications for ostomy (26).

For ovarian cancer, there are no guidelines that specifically recommend ostomy after bowel resection (1, 14, 15). Indications causing physicians to perform ostomy have been partially different from the real risk factors for AL (28). Some studies have reported that hypoalbuminemia (<3.5 g/dL), additional bowel resection, more extensive rectosigmoid resection, previous treatment with bevacizumab, longer operative time, and intraoperative red blood transfusion might lead physicians to perform ostomy (27–29). However, in other studies of the risk factors for AL, age, preoperative albumin level, small intestine resection, positive resection margins, additional bowel resection, manual anastomosis, and the distance from the anastomosis to the anal verge were independent risk factors for AL (21–23, 30–33). Clinical physicians chose patients with a worse preoperative status, such as malnutrition and elderly age, to undergo ostomy, which were proven to be risk factors for AL (22, 28). Regarding the surgery information, additional bowel resection and additional small intestine resection were proven to be risk factors for AL and were evaluated by physicians to decide whether to perform ostomy (21, 22, 27, 31, 32). However, physicians in the gynecology field might ignore some surgical factors, such as bowel resection margins and the distance from the anastomosis to the anal verge. Furthermore, risk factors for AL were not unanimous in all of these studies; different potential factors were included in the aforementioned studies. It should be proven whether risk factors for AL affect outcomes of ovarian cancer by directly comparing them using multivariate analysis.

No clear indications for ostomy have been suggested by the guidelines for ovarian cancer. We suggest that clinical physicians should evaluate the preoperative status and surgery information of patients before deciding whether to perform ostomy. The preoperative albumin level and age were the most important preoperative characteristics. However, additional bowel resection, additional small bowel resection, bowel resection margins, and the distance from the anastomosis should be considered. Furthermore, a multivariate analysis of all possible indications is needed to prove the conclusions of these studies.

DISCUSSION

The aforementioned studies did not allow us to perform a meta-analysis to obtain a more precise and statistical conclusion. We were only able to review the literature and report our suggestions.

Ostomy itself did not contribute to worse outcomes, and the AL rate decreased after considering the indications for ostomy (26). Further investigations of the indications for ostomy with ovarian cancer are needed. Because the AL rate is reportedly low for ovarian cancer (approximately 5%), larger sample sizes are needed for future studies. Some studies of the risk factors for AL showed that postoperative colonoscopy might be useful for identifying asymptomatic AL (34–36) after surgery. Moreover, studies of colorectal cancer might suggest some factors that could affect decision-making when ovarian cancer is involved. For example, the distance from the tumor to the anal verge was associated with the AL rate and survival outcomes of colon cancer; this has been proven but is not usually considered an indication by physicians treating ovarian cancer (23, 37).

CONCLUSION

Ostomy did not contribute to worse survival outcomes after bowel resection compared with primary anastomosis with ovarian cancer. The stoma-related complications were considered acceptable. The basic characteristics of patients (age and preoperative albumin level) and surgery information (operative time, intestine resection, additional bowel resection, manual anastomosis, bowel resection margins, and the distance from the anastomosis to the anal verge) should be considered before performing ostomy and require further investigation.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

XH searched the database and did the statistic analysis, as well as wrote this manuscript. ZY provided practical suggestions and critically revised the manuscript. All authors contributed to the article and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2022.892376/full#supplementary-material

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