

## Original Article



# Protective ostomies in ovarian cancer surgery: a systematic review and meta-analysis

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## ABSTRACT

**Objective:** To assess the benefit of protective ostomies on anastomotic leak rate, urgent re-operations, and mortality due to anastomotic leak complications in ovarian cancer surgery.

**Methods:** A systematic literature search was performed in MEDLINE, Web of Science, ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials for all studies on anastomotic leak and ostomy formation related to ovarian cancer surgery. Non-controlled studies, case series, abstracts, case reports, study protocols, and letters to the editor were excluded. Meta-analysis was performed on the primary endpoint of anastomotic leak rate. Subgroup analysis was carried out based on type of bowel resection and bevacizumab use. Secondary endpoints were urgent re-operations and mortality associated with anastomotic leak, length of hospital stay, postoperative complications, 30-day readmission rate, adjuvant chemotherapy, survival, and reversal surgery in ostomy and non-ostomy patients.

**Results:** A total of 17 studies (2,719 patients) were included: 16 retrospective cohort studies, and 1 case-control study. Meta-analysis of 17 studies did not show a decrease in anastomotic leak rate in ostomy patients (odds ratio [OR]=1.01; 95% confidence interval [CI]=0.60–1.70; p=0.980). Meta-analysis of ten studies (1,452 women) did not find a decrease in urgent re-operations in the ostomy group (OR=0.72; 95% CI=0.35–1.46; p=0.360). Other outcomes were not considered for meta-analysis due to the lack of data in included studies.

**Conclusion:** Protective ostomies did not decrease anastomotic leak rates, and urgent re-operations in ovarian cancer surgery. This evidence supports the use of ostomies in very select cases.

**Keywords:** Anastomotic Leak; Ovarian Neoplasms; Ostomy

## INTRODUCTION

Ovarian carcinoma is the most lethal gynecological cancer, and the fifth cause of cancer death in US, responsible for 13,980 deaths in US in 2019 [1]. Maximal cytoreductive surgery is the most important factor for survival among patients with stage III or IV ovarian carcinoma [2]. To achieve complete cytoreduction, it is sometimes necessary to perform bowel resections. Colorectal resection is the most frequent type [3,4].

**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**Author Contributions**

Conceptualization: N.S.B.; Data curation: N.S.B.; Formal analysis: N.S.B., V.S.J.; Investigation: N.S.B., G.T.E.; Methodology: N.S.B., G.T.E.; Resources: L.M.; Software: L.M.; Supervision: M.M.A.; Validation: V.S.J., M.M.A.; Visualization: N.S.B.; Writing — original draft: N.S.B., G.T.E.; Writing — review & editing: V.S.J., L.M., M.M.A.

Bowel resection may be associated with anastomotic leak (AL), which is a very severe complication given its significant postoperative morbidity and mortality. The incidence of AL is around 1.7%-13.9% among ovarian cancer patients [5-17]. However, in the colorectal literature it is estimated to be higher, from 2.6% to 26% [18-21].

There are some authors who confirm that a protective ostomy may reduce the risk of anastomotic leakage [8,22,23] in ovarian cancer surgery, while others report that a protective ostomy does not decrease the incidence of anastomotic leakage [5,12,24-27]. There are still other studies which confirm that ostomy placement reduces the morbidity of anastomotic breakdown [5,28].

In the colorectal literature, there are 4 meta-analysis of randomized controlled trials that have proven a decrease of anastomotic leakage and urgent re-operations due to leakage complications in the ostomy patient group [29-32]. A meta-analysis of non-randomized studies showed a decrease in mortality related to leakage in ostomy patients [32]. However, the results found in colorectal surgery must not be interpolated to ovarian cancer surgery because there are multiple procedures, larger peritonectomy, and lower rate of very low colorectal anastomoses (5 cm or less from the anal verge) performed on women with ovarian cancer as compared to patients with rectal cancer [33-35].

Therefore, there is no evidence of a lower risk of AL related to the use of ostomies during cytoreductive surgery for ovarian cancer. The aim of this study was to perform a systematic review and meta-analysis of controlled and/or comparative studies, contrasting the event rates of AL after cytoreductive surgery for ovarian cancer in patients with and without ostomy, as well as the morbidity and mortality of AL in both groups of patients.

## METHODS

### 1. Protocol and registration

We conducted this meta-analysis according to the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines [36]. The protocol was registered in the PROSPERO database (study ID CRD42021237031).

### 2. Eligibility criteria

Inclusion criteria: Controlled and/or comparative studies evaluating AL after bowel resection during cytoreductive surgery for ovarian cancer were considered.

Primary outcome was a) event rate of AL comparing patients with and without protective ostomy.

Secondary outcomes were b) number of urgent re-operations due to leakage-caused complications between the 2 comparison groups; c) mortality rate related to AL between ostomy and non-ostomy patients, d) length of hospital stay, postoperative complications, 30-day readmission rate, adjuvant chemotherapy and survival between ostomy and non-ostomy patients; and e) proportion, timing, and complications of reversal surgery in ostomy patients.

Exclusion criteria: a) non-controlled studies, case series, abstracts, case reports, study protocols, letters to the editor, b) articles that addressed laparoscopic surgery, c) articles that included end colostomies or end ileostomies, d) papers that were not fully accessible, and e) articles in which the type of ostomies were not clearly defined.

Studies which included end ileostomies or end colostomies as well as many types of gynecological or non-gynecological cancers were included, but only if the data for ovarian cancer and diverting ostomies cohort could be extracted separately.

### 3. Literature search strategy

A search was done on MEDLINE (via PubMed), Web of Science, ClinicalTrials.gov and the Cochrane Central Register of Controlled Trials (last updated on February 28, 2021) to identify eligible studies. No dates of publication limits or language were applied.

The details of the search are available in **Table S1**. Restrictions by language and date were not applied. Significant studies referenced in the publications were also searched for potential inclusion. Eleven authors were contacted for further information, but a response was obtained from only 7 [5,7,8,16,22,24,37].

### 4. Study selection

A review of the literature was done independently by 2 authors (Navarro B and Garcia-Torralba E). Using Covidence Systematic review software (Covidence; Veritas Health Innovation, Melbourne, Australia), 2 authors (Navarro B and Garcia-Torralba E) screened the titles and abstracts of the gathered articles to eliminate the studies not related to the topic under investigation. Full text of the potential articles was obtained. Two authors working independently (Navarro B and Garcia-Torralba E), selected them by applying the inclusion and exclusion criteria.

Discrepancies during the selection period were resolved through consensus of the investigators (Navarro B and Garcia-Torralba E). In the event that a consensus could not be reached, a third reviewer was consulted (Martin A).

To prevent inclusion of duplicate cohorts in the meta-analysis in the case of studies from the same authors that combined exact groups of patients, only the latest and most complete studies were considered [9,12].

### 5. Data extraction

Relevant information was retrieved from selected primary studies by 2 authors working independently (Navarro B and Garcia-Torralba E). The 2 investigators filled out a previously established questionnaire. Data on the following variables were sought: year, type of study, number of ALs, number of re-operations, number of deaths in ostomy and non-ostomy patients, type of ostomy (ileostomy or colostomy), definition of AL, type of surgery (primary or recurrent), type of bowel resection, reasons for ostomy, residual disease (complete, optimal or suboptimal surgery), and International Federation of Gynecology and Obstetrics stage. Percentage, timing, and complications of reversal surgery in ostomy patients were also retrieved. Length of hospital stay was recorded, as well as time from surgery to chemotherapy, number of adjuvant chemotherapy cycles, progression-free survival, overall survival (OS), and relapse free survival (RFS) between ostomy and non-ostomy patients.

Any disagreement was resolved by discussion with a third reviewer (Martin A).

### 6. Risk of bias in individual studies

All included studies were assessed for quality of methodology following the Newcastle-Ottawa Scale (NOS) [38]. The analysis was done independently by 2 authors (Navarro B and

Garcia-Torralla E). Studies with a NOS of 7 or more were defined as low risk of bias, while studies with a score <7 were assessed as high risk for bias [39].

## 7. Statistical analysis

Pooled odds ratios (ORs) with 95% confidence interval (CI) were used as the summary statistic for the dichotomous outcome of anastomotic leakage and re-operations in the respective study arms by applying a random effects model (Mantel-Haenzel method) [40]. Subgroup analyses were carried out to evaluate the impact of rectosigmoid resection on OR for AL and re-operations. OR for AL and re-operations were calculated for a subset of patients who had undergone rectosigmoid resection with or without additional bowel resections, and another subset of patients who had had any type of bowel resections with or without rectosigmoid resection. Analysis was also performed to assess the efficacy of protective ostomy with or without adjuvant bevacizumab on OR for AL. Cochran's Q statistic and I<sup>2</sup> index were used for assessment of statistical heterogeneity. I<sup>2</sup> values of 25%, 50%, and 75% indicated low, moderate, and high heterogeneity, respectively. Publication bias was evaluated by visual inspection of funnel plots, and quantified applying the Egger's regression model [41].

All analyses were performed with Cochrane Review software (Review Manager version 5.4.1 for Windows) and STATA 14.2 version.

For ostomy reversal, the proportion of reversal surgeries among patients with ostomy formation was calculated. Timing of ostomy reversal was addressed in weeks. The median, the range, and the p-value of each study were reported for length of hospital stay, as well as time from surgery to chemotherapy between the ostomy and non-ostomy patients. We detailed the number, percentage, and p-values of postoperative complications and readmissions after 30 days of surgery between women with ostomy and without ostomy. Number of adjuvant chemotherapy cycles between both groups of patients was also noted. OS, progression free survival, and relapse-free survival were addressed in months.

## RESULTS

### 1. Study selection

The electronic search provided a total of 1,042 citations. Titles and abstracts were screened, and many studies were omitted because they were either case reports, case series, or conference abstracts, not specifically related to the topic under review, or duplications. We examined the full text of the remaining 95 articles. Seventy-eight studies were excluded because: a large proportion did not report the number of ALs separately in each group of patients (n=45); included end ostomies (n=10); analyzed morbidity of bowel resections but did not mention AL as their outcome (n=7); included many types of cancer without breaking down data by type (n=13); or had the same cohort of patients (n=2) and did not define the type of ostomy (n=1). Finally, 17 comparative studies remained suitable for data extraction [5-8,22,24-28,37,42-47] (**Fig. 1**).

### 2. Study characteristics

A total of 2,719 patients with bowel resection for ovarian cancer were included in our study. A protective ostomy had been done on 475. The sample size ranged from 21 to 518 women. All the studies were retrospective, 16 were cohort studies, and one was a case-control study. There were 3 multi-center, 2 bi-center and twelve single center studies. We did not identify

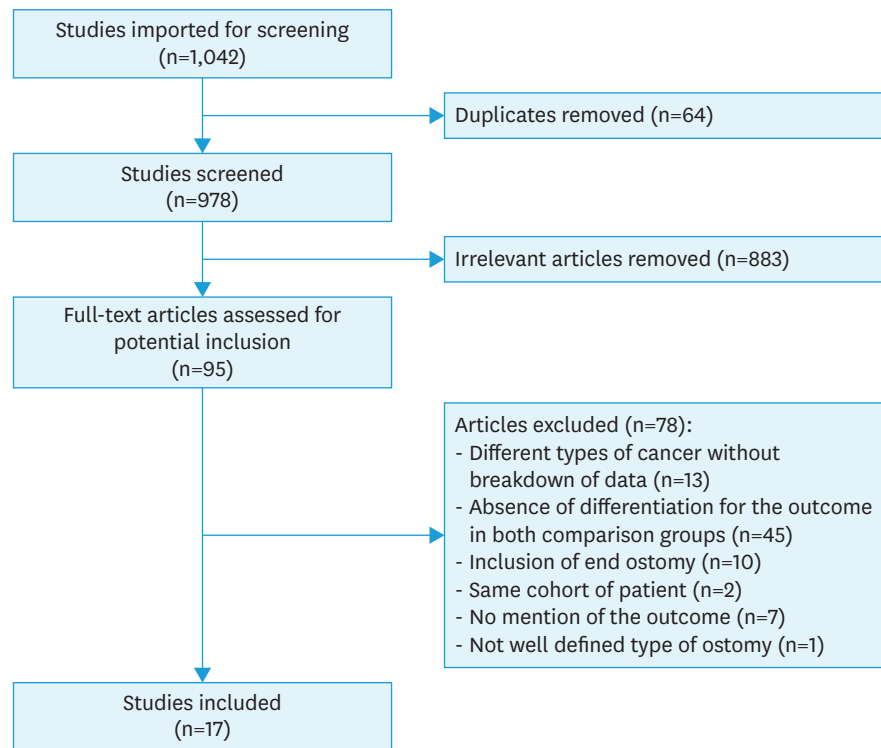


Fig. 1. Preferred Reporting Items for Systematic Review and Meta-Analysis flow diagram.

any clinical trial or prospective study. Overall, there was some clinical and methodological heterogeneity in regard to the cohort of patients included in the analysis. Five [5-8,22] studies evaluated ostomies in a combination of patients with and without rectosigmoid resection, while in twelve [24-28,37,42-47] studies all the patients had undergone a rectosigmoid resection with or without additional bowel resection. Only 3 studies [8,24,37] assessed efficacy of ostomies in patients with and without bevacizumab use. There was also heterogeneity in the type of ostomies, the reasons for ostomy and the definition of AL. Some studies did not define AL at all [5,24-28,37,42-44,47], while others defined it only clinically [46], only surgically [7], both clinically and radiologically [45], or with a combination of these 3 [6,8,22]. More information about the included studies can be seen in **Table 1**.

According to the NOS, twelve studies were assessed as having a low risk of bias with scores of 7 and more, while 5 were judged to have a high risk of bias with scores of 6 or less. Detailed information on quality assessment of included studies is shown in **Tables S2** and **S3**.

### 3. AL rate

All 17 [5-8,22,24-28,37,42-47] studies were included, involving 2,719 patients. There were 475 patients with ostomy formation and 2,244 without ostomy formation. The AL rate was 6.5% (n=31) in the ostomy group and 8.5% (n=190) in the non-ostomy group. Pooled OR for studies was 1.01 (95% CI=0.60–1.70; p=0.980), suggesting that ostomy formation was not significantly associated with less anastomotic leakage with respect to non-ostomy patients.

Subgroup analysis was performed by type of bowel resection. Concerning all the patients who had rectosigmoid resection with or without additional bowel resection, no statistical difference was observed in AL rate between the groups (OR=1.49; 95% CI=0.91–2.42;

**Table 1.** Characteristics of included studies

Study	Study period	Study design	Patients	Ostomy/ no ostomy	AL no ostomy/ no ostomy	Type of ostomy	Stage	Type of bowel resection	Defined criteria for anastomotic leakage	Reasons for ostomy	Residual disease	Type of surgery
Canlorbe et al. [25]	2006-2011	Cohort retrospective single center	99	9/90	1/6	Transitory, protective ileostomy/colostomy	IIIB-IVA	Rectosigmoid resection in all the patients with or without 1 or 2 other bowel resections	NR	* Inadequate quality of the tissues * Multiple anastomoses * Short distance between 2 anastomoses and previous colostomy * Colorectal anastomoses created with the right colon	Complete	Primary interval
Lago et al. [24]	2010-2018	Cohort retrospective multi-center	457	108/349	15/31	Protective ileostomy	II-IV	Rectosigmoid resection in all cases with or without additional bowel resection	NR	No	NR	Primary/interval and relapse
Tseng et al. [5]	2005-2014	Cohort retrospective single center	331	44/287	2/19	Protective ileostomy	II-IV	Rectosigmoid resection with or without descending colon/bowel resections other than rectosigmoid	NR	* Low rectosigmoid anastomoses * Extensive colon resection * Anastomotic operative defect noted on intraoperative testing	Complete/optimal/suboptimal	Primary
Grimm et al. [6]	1999-2015	Cohort retrospective bi-center	518	74/444	3/33	Protective ostomy	III-IV	Rectosigmoid with or without another bowel resection (small or large w/o small bowel)/bowel resection without rectosigmoid resection	*Feculent fluid from drains, vaginal vault or wound * Extravasation from anastomotic site verified by computer tomography * Revision surgery	* More than 2 bowel resections, * Low performance status, * Very long duration of surgery (>480 min), * Anastomoses <8 cm from anal verge and/or * Inflammatory bowel disease on surgeon's discretion	NR	Primary/interval
Bartl et al. [7]	2003-2017	Cohort retrospective single center	192	14/178	4/5	Protective ostomy	IIB-IV	Rectosigmoid with or without another bowel resection (small or large or small+large)/bowel resection without rectosigmoid	* Revision surgery	NR	Complete/other than complete	Primary
Kalogera et al. [22]	1994-2011	Case-control retrospective single center	126	9/117	0/42	Protective ileostomy/colostomy	III-IV	Rectosigmoid alone with or without large bowel/large bowel resection without rectosigmoid	*Feculent fluid from drains, wound, or vagina, * Definitive radiographic evidence of extravasation at the anastomotic site, * Revision surgery	NR	Complete/optimal/suboptimal	Primary/interval/recurrent
Koscielny et al. [8]	2010-2017	Cohort retrospective single center	136	22/114	0/23	Protective ileostomy	II/IVA	Any type of bowel resection	*Feculent secretion from drains, wound or vagina, * Extravasation from anastomotic site verified by computed tomography, * Air exiting from drains during diagnostic rectoscopy or * Revision surgery	* More than one simultaneous bowel resection, * Low performance status, * Estimated high blood loss (>1,000 mL), * Low anastomosis <8 cm from anal verge and * Long operating time (>8 hr)	NR	Primary/interval/recurrent
Moutardier et al. [28]	1980-2001	Cohort retrospective single center	28	7/21	1/0	Protective ileostomy/colostomy	NR	All patients had Posterior pelvic exenteration	NR	At the discretion of the attending surgeon	NR	Primary/recurrent

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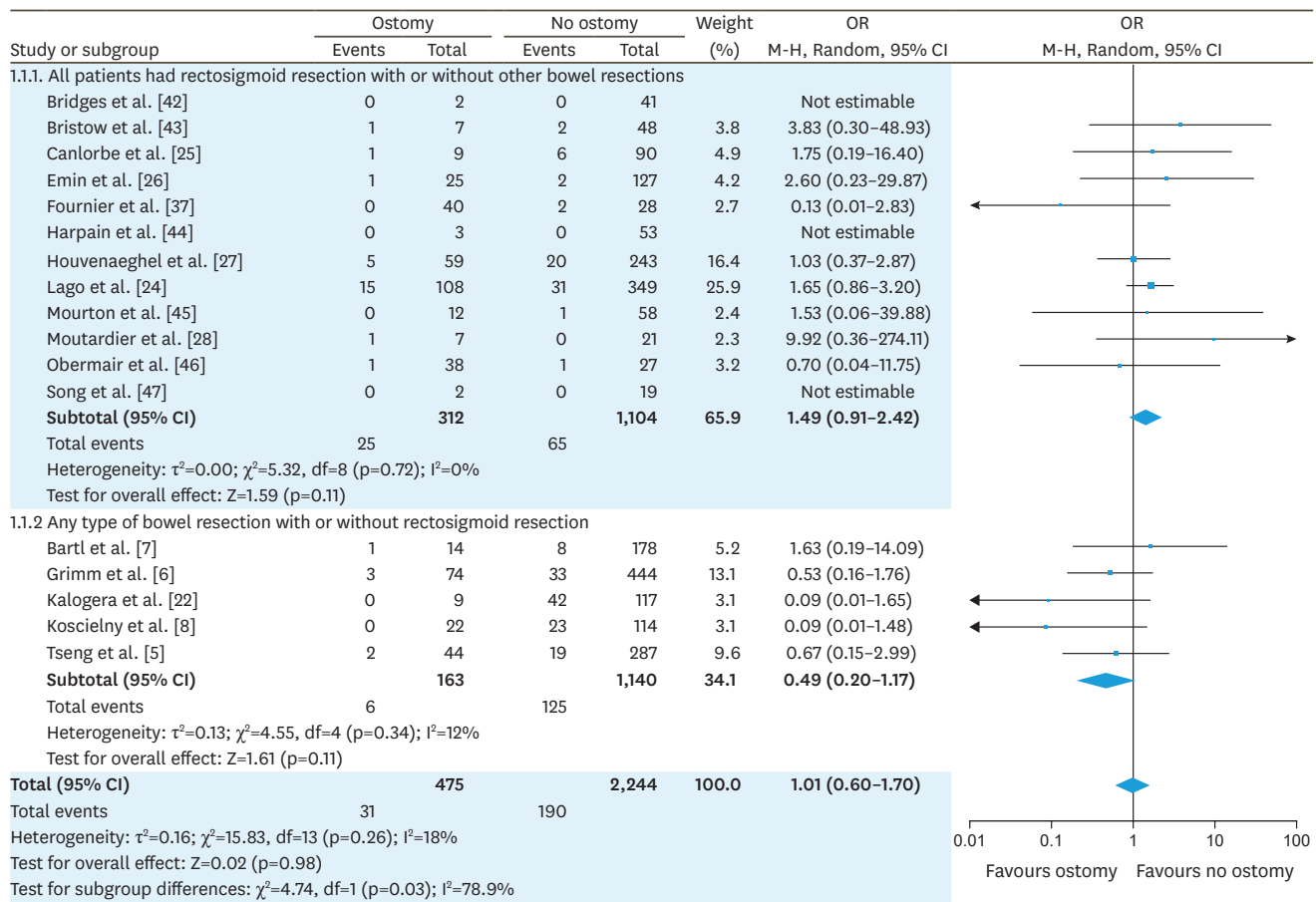


**Table 1. (Continued) Characteristics of included studies**

Study	Study period	Study design	Patients	Ostomy/ no ostomy/ ostomy	AL ostomy/ no ostomy	Type of ostomy	Stage	Type of bowel resection	Defined criteria for anastomotic leakage	Reasons for ostomy	Residual disease	Type of surgery
Fournier et al. [37]	2005-2013	Cohort retrospective single center	68	40/28	0/2	Protective ileostomy	II-IV	All the patients had Rectosigmoid resection with or without small or large bowel	NR	* Systematically before 2010 * Then only when risk factors of leakage were present (low anastomosis, multiple suboptimal bowel resection, ascites >500 mL)	Complete/optimal/suboptimal	Primary/interval
Mourton et al. [45]	1994-2004	Cohort retrospective single center	70	12/58	0/1	Protective ileostomy	IIIC-IV	All the patients had low anterior resection with or without (large or small bowel resection)	* Clinical (pelvic pain and fever) and radiological	* Preoperative bowel obstruction * Tenuous anastomosis * Low anastomosis * Intraoperative blood loss * Poor bowel preparation * Extensive bowel resection * Presacral bleeding * Long term steroid use	Complete/optimal/suboptimal	Primary
Obermair et al. [46]	1996-2000	Cohort retrospective single center	65	38/27	1/1	Protective ileostomy and colostomy	IIB-IV	All the patients had low anterior resection	* Bowel contents drained from the abdominal wound * Clinical (fever, leukocytosis and peritoneal signs)	NR	Complete/optimal/suboptimal	Primary
Emin et al. [26]	2000-2013	Cohort retrospective single center	152	25/127	1/2	Protective ileostomy/colostomy	II-IV	All patients had rectosigmoid resection with or without large or small bowel resection	NR	NR	Complete/optimal/complete	Primary/interval/recurrent
Houvenaeghel et al. [27]	1990-2004	Cohort retrospective multi-center	302	59/243	5/20	Protective ileostomy/colostomy	II-IV	All patients had rectosigmoid resection with or without large or small bowel resection	Surgeon's decision	NR	Complete/optimal/suboptimal	Primary/interval/recurrent
Bridges et al. [42]	1984-1988	Cohort retrospective single center	43	2/41	0/0	Protective colostomy	II-IV	All patients had rectosigmoid resection with or without other bowel resection	NR	NR	Optimal/suboptimal	Primary
Harpain et al. [44]	2008-2018	Cohort retrospective multi-center	56	3/53	0/0	Protective ileostomy	II-IV	All patients had low anterior resection with or without large or small bowel resection	Surgeon's decision	NR	NR	Primary/interval
Bristow et al. [43]	2004-2007	Cohort retrospective bi-center	55	7/48	1/2	Protective colostomy/ileostomy	I/IV	All patients had rectosigmoid resection with or without large or small bowel or ileocecal resection	NR	* Tension at the anastomotic staple line * Concerns over adequate vascularization of the anastomosis * Local contamination from spillage of bowel contents	NR	Recurrent
Song et al. [47]	2003-2007	Cohort retrospective single center	21	2/19	0/0	Protective ileostomy	IIIC-IV	Total colectomy	NR	* Leak detected by air leakage testing * Incomplete anastomotic stapler ring	Complete/optimal	Primary/interval

NR, not reported.

**Ostomies do not decrease anastomotic leak**



**Fig. 2.** Anastomotic leak rate between ostomy and non-ostomy patients. CI, confidence interval; OR, odds ratio.

$p=0.110$ ). Similarly, focusing on patients who had any type of bowel resection with or without rectosigmoid resection, AL rate was statistically similar when comparing ostomy and non-ostomy patients (OR=0.49; 95% CI=0.20–1.17;  $p=0.110$ ) (**Fig. 2**).

Overall, there was a low statistical heterogeneity in AL rate ( $I^2=18\%$  and  $p=0.260$ ). A Funnel plot showed a symmetrical shape declaring a low risk of publication bias in the meta-analysis (Egger’s regression  $p=0.768$ ) (**Fig. S1**).

**4. AL rate in patients with and without bevacizumab**

The analysis of the use of bevacizumab or not would be clinically useful. And the question to be addressed here is whether prophylactic ostomy should be instituted when bevacizumab is used. In that sense, 3 studies including 661 patients reported data regarding bevacizumab use: 71 subjects received bevacizumab (39 with ostomy and 32 without ostomy), while 590 did not received bevacizumab (131 with ostomy and 459 without ostomy) [8,,24, 37]. The results of these 3 trials varied, but the OR was lower in the prophylactic ostomy group with or without bevacizumab. On the other hand, the use of bevacizumab did not indicate a risk of increased leakage without ostomy. Overall, there was moderate statistical heterogeneity ( $I^2=59\%$  and  $p=0.040$ ) (**Fig. S2**).



### 5. Urgent re-operation due to AL complications

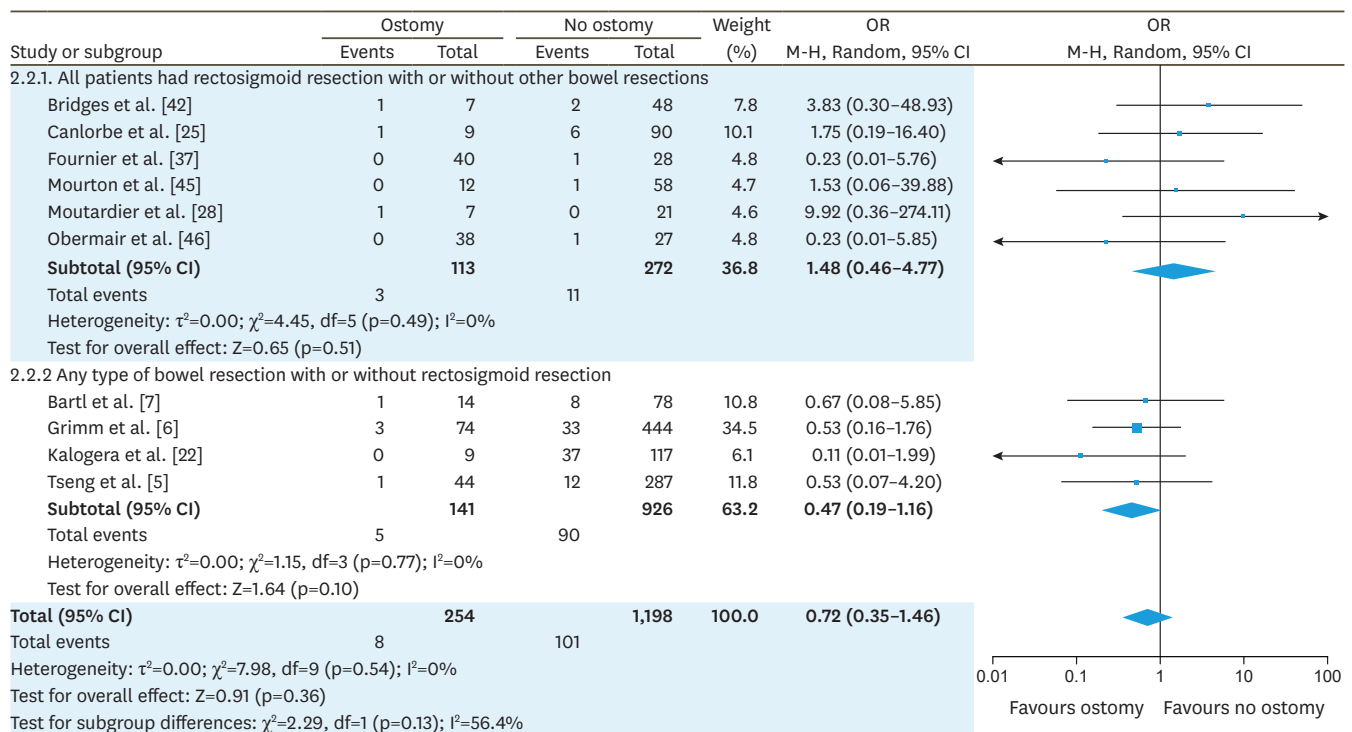
Nine [5-7,22,25,28,37,43,45,46] studies representing 1,452 women were included in the meta-analysis, with 254 patients having undergone ostomy formation, while 1,198 did not have ostomy formation. Urgent re-operation rate in the ostomy group was 3.1% (n=8) and 8.4% (n=101) in non-ostomy patients. Overall OR was 0.72 (95% CI=0.35–1.46; p=0.360) suggesting that ostomy formation is not significantly associated with less urgent re-operations for AL compared to non-ostomy patients.

Subgroup analysis was done by type of bowel resection. Taking into account all the patients who had rectosigmoid resection with or without additional bowel resection, no statistical difference was observed in AL rate between the 2 comparison groups (OR=1.48; 95% CI=0.46–4.77; p=0.510). Regarding patients who had any type of bowel resection with or without rectosigmoid resection, urgent re-operation rate was statistically similar when comparing ostomy and non-ostomy patients (OR=0.47; 95% CI=0.19–1.16; p=0.100) (**Fig. 3**).

Overall, there was a low heterogeneity in urgent re-operation rate ( $I^2=0$  and  $p=0.540$ ). For re-operations, funnel plot was symmetric, assessing a low risk of publication bias (Egger's regression  $p=0.316$ ) (**Fig. S3**).

### 6. Mortality for AL due to AL complications

Although 8 studies were included for this outcome [5,22,26,28,37,43,45,46], only 2 studies [22,43] show events over the non-ostomy group. In the case of Bristow et al. [43] only one case of AL was found in the non-ostomy group (OR=2.11; 95% CI=0.08–56.78; p=0.660). Kalogera et al. [22] found 8 deaths in the non-ostomy group (OR=0.68; 95% CI=0.04–12.68).



**Fig. 3.** Urgent re-operations due to anastomotic leak complications in ostomy and non-ostomy patients. CI, confidence interval; OR, odds ratio.

Therefore, a meta-analysis was not performed due to lack of data. However, it appears that no evidence was obtained in favor of one group or the other.

### 7. Morbidity, adjuvant chemotherapy, and survival between ostomy and non-ostomy

Three studies found no significant differences in length of hospital stay and in the time period from surgery to adjuvant chemotherapy between ostomy and non-ostomy patients [5,22,25].

Two studies showed similar rates of grade III–V postoperative complications [5,25] between the 2 groups of patients. One of these studies [5] presented similar 30-day and 60-day readmission rate between the 2 groups of patients.

One cohort study [25] reported that patients with ostomy received significantly fewer cycles of chemotherapy (median of 2 cycles) compared to patients without ostomy (median of 6 cycles). In addition, adherence to chemotherapy schedule was less frequent in ostomy patients compared to non-ostomy patients ( $p < 0.050$ ). They also reported a decrease in OS ( $p < 0.030$ ) and RFS ( $p < 0.001$ ) in both comparison groups.

However, 2 cohort studies [5,8] and 1 case-control study [22] showed that OS was similar in the 2 groups (**Table 2**).

### 8. Ostomy reversal

Eight studies [5,8,22,25,27,42,45-47] representing 198 patients with ostomies presented data concerning the rate of ostomy reversal. Overall, 82.6% ( $n = 161/198$ ) of women had their ostomy reversed at between 2 and 50 weeks. One study [5] reported a rate of 8% of grade III Clavien-Dindo complications after reversal surgery (**Table 3**).

## DISCUSSION

This meta-analysis did not demonstrate a reduction in the rate of ALs, urgent re-operations and mortality caused by AL in ostomy patients compared to non-ostomy patients. Likewise, the use of bevacizumab did not show a risk of increased AL in non-ostomy patients. Statistical heterogeneity in this meta-analysis was low (except for bevacizumab analysis), and funnel plots also demonstrated that there was low risk of reporting publication bias.

Few studies compared time from surgery to chemotherapy, morbidity, length of hospital stay, and survival between ostomy and non-ostomy patients. The lack of data on this topic made a meta-analysis impossible.

Many studies did not compare the 2 cohorts of patients correctly (ostomy vs non-ostomy), which lead to a lower quality of the included studies. Clinical heterogeneity among studies was high due to inclusion of different types of bowel resections, types of ostomies, types of surgery, types of cytoreductive surgery and definition of AL. To decrease clinical heterogeneity, we decided to exclude end ostomies, and perform a subgroup analysis by type of bowel resection: one subgroup in which all the patients had undergone rectosigmoid resection, and another subgroup in which patients had undergone any kind of bowel resection with or without rectosigmoid resection. Therefore, the present study represents a varied patient population.

**Table 2.** Morbidity, adjuvant chemotherapy and survival between ostomy and non-ostomy patients

Study	Days of hospital stay	Grade III-V postoperative complications	30-day readmission after surgery	Days to chemotherapy	Postoperative chemotherapy cycles	Overall survival, OS (mo)	Progression free survival, PFS (mo)	Relapse free survival RFS (mo)
Canlorbe et al. [25]	Ostomy: 20 (14-27) No ostomy: 13 (7-86)	Ostomy: 2 (22) No ostomy: 25 (27.7)	Ostomy: 10 (22.7) No ostomy: 48 (17)	Ostomy: 35 (27-90) No ostomy: 33 (14-136)	Stoma: 2 cycles (1-6) No ostomy: 6 cycles (1-9)	Ileostomy is associated with a decreased OS (p<0.030)	NR	Ileostomy is associated with a decreased RFS (p=0.001)
Tseng et al. [5]	Ostomy: 10 (5-30) No ostomy: 9 (3-69)	Ostomy: 13 (30) No ostomy: 67 (23)	Ostomy: 10 (22.7) No ostomy: 48 (17)	Ostomy: 41 (11-75) No ostomy: 40 (9-115)	Ostomy: 2 (4.8) patients received 0-4 cycles and 40 (95.2) patients received 5 or more cycles No ostomy: 10 (3.6) patients received 0-4 cycles and 269 (96.4) patients received 5 or more cycles	Ostomy: Median OS 48.7 (95% CI=34.5-63) No ostomy: Median OS 63.8 (95% CI=52.2-75.3)	Ostomy: Median PFS 17.9 (95% CI=14.1-21.8) No ostomy: Median PFS 18.6 (95% CI=16.1-21.2)	Ostomy: p=0.250 No ostomy: p=0.880
No ostomy (n=287)			Ostomy: 10 (23)					
Kalogera et al. [22]	Ostomy: 11 No ostomy: 9	NR		Ostomy: 36.5 (30-54) No ostomy: 34 (9-136)	NR	Ostomy is not associated with a reduced OS (p=0.89)	NR	NR
No ostomy (n=75)								
Koscielny et al. [8]	NR	NR		NR	NR	Ostomy: Mean OS 47.4 (95% CI=25-69.8) No ostomy: Mean OS 49.5 (95% CI=42.3-56.7)	NR	NR
Ostomy (n=22)								
No ostomy (n=114)								

Values are presented as median (range) or number (%).

CI, confidence interval; NR, not reported; OS, overall survival; PFS, progression-free survival; RFS, relapse free survival.

## Ostomies do not decrease anastomotic leak

**Table 3.** Proportion, timing, and complications of reversal surgery

Study	Total of ostomies	Ostomy reversal	Time to reversal surgery (wk)	Complications of reversal surgery
Canlorbe et al. [25]	9	8 (88)	25 (5–40)	No grade III or more (Clavien-Dindo classification) complications occurred
Kalogera et al. [22]	9	5 (55)	37 (25–50)	NR
Tseng et al. [5]	44	39 (88)	26 (6–50)	Three patients (8%) had intraabdominal abscesses. Two were managed conservatively with radiological drainage and one was managed surgically. Another patient presented with stricture at the anastomotic site which became symptomatic after ileostomy reversal.
Koscielny et al. [8]	22	20 (90)	Within 26	NR
Mourton et al. [45]	12	11 (92)	26 (13–43)	NR
Obermair et al. [46]	38	25 (65)	NR	NR
Houvenaeghel et al. [27]	59	51 (86)	5 (2–43)	NR
Bridges et al. [42]	2	2	Within 26	NR
Song et al. [47]	2	0	-	NR
Total	197	161/197 (81.7)	2–50	

Values are presented as median (range) or number (%).

NR, not reported.

This permits us to generalize our findings to ovarian cancer surgery, but at the same time it is responsible for a clinical heterogeneity in our meta-analysis.

In addition, no randomized controlled studies related to the topic of investigation were found. Only one prospective [23] study was identified. However, we could not include it in our analysis because it comprised both gynecological and non-gynecological cancers without breakdown of data by type of cancer. This study affirms that utilizing strict criteria to perform an ostomy in patients with rectosigmoid resections reduces the frequency of ALs.

Two studies [11,48] not included in our review must be discussed: one that assessed end ostomies and one that was a case series. Gockley et al. [11] included all types of ostomies. They stated that ostomy patients had higher rates of postoperative complications compared to non-ostomy patients. However, they did not find significant differences in hospital length of stay, 30-day readmission rate after surgery, ability to receive chemotherapy and progression free survival between patients with ostomy and without ostomy. Tozzi et al. [48] collected data from patients with rectosigmoid resection and diverting ileostomies to investigate the morbidity of diverting ileostomies. They described 46.8% of ostomy-related complications of grade  $\geq 2$ . They reported that thirty-day readmission rate after surgery was 17% due to dehydration caused by ostomies. Delay of adjuvant chemotherapy was caused by dehydration (caused by ostomy) in 12.7% of cases.

The main strength of this study was the large number of patients included. By contacting authors for further information, more studies could be added to the review. Limitations of this meta-analysis are the clinical heterogeneity of included studies and the absence of randomized controlled studies, which may limit the extrapolation of these results to daily practice. We did not have the necessary data to evaluate morbidity, adjuvant chemotherapy, length of hospital stay, and survival of patients who had undergone ostomies compared to those who had not. Complications of reversal surgery could not be analyzed due to scarcity of data.

## CONCLUSIONS

In conclusion, in this meta-analysis involving patients with bowel resection during cytoreductive surgery for ovarian cancer, ostomy formation is not associated to a reduced rate

of ALs and urgent re-operations due to AL complications. With respect to mortality due to AL complications, a meta-analysis was not performed because of the paucity of data. However, it appears that ostomy formation does not offer advantages in term of mortality. This information might be useful to limit the use of ostomy formation in ovarian cancer surgery to very select cases. More prospective multi-center or randomized controlled trials are needed to evaluate ostomy use in patients at increased risk of anastomotic leakage.

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## SUPPLEMENTARY MATERIALS

### Table S1

Search strategy

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### Table S2

Quality of included studies I

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### Table S3

Quality of included studies II

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### Fig. S1

Funnel plot for anastomotic leak.

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### Fig. S2

Efficacy of ostomy in patients with and without bevacizumab.

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### Fig. S3

Funnel plot for urgent re-operations.

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