



Port site resection after laparoscopy in advance ovarian cancer surgery: Time to abandon?



Víctor Lago^{a,*}, Laura Gimenez^a, Luis Matute^a, Pablo Padilla-Iserte^a, José Miguel Cárdenas-Rebollo^d, Marta Gurrea^a, Beatriz Montero^b, Guillermina Montoliu^c, Santiago Domingo^a

^a Department of Gynecologic Oncology, University Hospital La Fe, Valencia, Spain

^b Department of Pathology, University Hospital La Fe, Valencia, Spain

^c Department of Radiology, University Hospital La Fe, Valencia, Spain

^d Department of Applied Mathematics and Statistics CEU San Pablo University, Madrid, Spain

ABSTRACT

Introduction: The use of laparoscopy in the treatment and management of advanced ovarian cancer is increasing among the gynaecologic oncologists. The development of port site metastases after laparoscopy is a concern and a matter of debate due to theoretical iatrogenic disease spread. Port site resection (PSR) has been proposed as an option to avoid this scenario.

Material and methods: One hundred and twenty-three patients with advanced ovarian cancer (FIGO III-IV) and with diagnostic laparoscopy were included and after cytoreductive surgery were classified into two groups: no port site resection (No-PSR) and port site resection (PSR). Based on the pathological results of all port site specimens, PSR was classified as positive port site metastasis (PSM+) and negative port site metastasis (PSM-).

Results: In 82 cases, the laparoscopic port site access was resected in the debulking surgery. At the final specimen examination, 49% presented as PSM+. No statistical differences regarding survival were found, either between the No-PSR and PSR groups ($p = 0.28$) or between the PSM+ and PSM- groups ($p = 0.92$). A higher wound complication rate was found in the PSR group (17% vs. 34%; $p = 0.047$). The RR (Relative Risk) of wound events for PSR was 2.42 (95% CI 1.09–5.35; $p = 0.0296$).

Conclusions: To date, not only there is no data supporting PSR after laparoscopy in advanced ovarian cancer, but the role of PSM+ in prognosis also remains unclear. In patients in which laparoscopy is performed prior to the debulking procedure, the PSR may not be recommended in those cases of no macroscopic port site metastasis.

1. Introduction

Optimal cytoreductive surgery and platinum/taxane-based chemotherapy are the cornerstone of treatment for advanced ovarian carcinoma. During surgery, maximal effort to achieve no residual tumour is needed, as it is key in the management of advanced disease [1,2]. Primary debulking surgery (PDS) and interval debulking surgery (IDS) are the main alternatives in the treatment scheme to obtain optimal cytoreduction [3,4].

Resources such imaging or laparoscopic scores have been proposed to assess the preoperative chance of optimal cytoreduction [5–7]. The use of laparoscopy in the treatment and management of advanced ovarian cancer is increasing among gynaecologic oncologists [8,9]. Some centres have introduced this resource in their clinical practice prior to debulking surgery. However, there is no a standardised recommendation of use. The development of port site metastases after laparoscopy is a concern and a matter of debate because of the

theoretical presence of metastasis due to iatrogenic disease spread. The reported incidence of positive port site metastasis (PSM+) in ovarian cancer after diagnostic laparoscopy in advanced ovarian cancer prior to surgery varies significantly from 17 to 47% [10–12]. Due to this fact, port site resection (PSR) has been proposed as an option to avoid this scenario.

The purpose of this study was to evaluate the impact of PSR on the oncological outcome of advanced ovarian cancer. The secondary objectives were to evaluate morbidity related to port site resection, the incidence of port site metastasis and its role as a prognostic factor.

2. Material and methods

This is a retrospective study performed at a single institution. Data from patients with advanced ovarian, primary peritoneal and fallopian cancer (FIGO III-IV) treated at the gynaecological oncology unit at the University Hospital La FE (Valencia, Spain) were reviewed from our

* Corresponding author. Avinguda de Fernando Abril Martorell, 106, 46026, Valencia. F Tower, 3rd Floor, Valencia, Spain.
E-mail address: victor.lago.leal@hotmail.com (V. Lago).

Table 1
Characteristics of patients with epithelial ovarian cancer undergoing laparoscopy prior to debulking surgery.

	Total	No-PSR	PSR	P value	
	123	41 (33.3)	82 (66.7)		
Port site metastasis [n(%)]		–	PSM + 40 (49)	PSM – 42 (51)	
Age [n(%); year				(*) p = 0.0054	
< 65	86	22 (54)	64 (78)		
> 65	37	19 (46)	18 (22)		
BMI [n(%); kg/m ²				(*) p = 0.7502	
< 30	112	38 (93)	74 (90)		
> 30	11	3 (7)	8 (10)		
ECOG [n(%)]				(*) p = 0.2031	
0	94	29 (71)	65 (79)		
1	29	12 (29)	17 (21)		
FIGO STAGE [n(%)]				(*) p = 0.8496	
III	104	36 (88)	71 (87)		
IV	16	5 (12)	11 (13)		
Type of surgery [n(%)]				(*) p = 0.7891	
PDS	80	26 (63)	54 (66)		
IDS	43	15 (37)	28 (34)		
Ascites [n(%); ml				(*) p = 0.0662	
> 500	76	30 (73)	46 (56)		
< 500	47	11 (27)	36 (44)		
Histology [n(%)]				(*) p = 0.8844	
HGSOC	90	30 (73)	61 (74)		
Others	33	11 (27)	21 (26)		
Ca 125 [Mean ± DS (Range)];	1837 ± 3112 (0–9577)	1622 (12–22116)	1585 (14–8660)	(μ) p = 0.312	
Operating time [Mean ± DS (Range)]; min	328 ± 91 (160–730)	299 (140–855)	314 (170–730)	(μ) p = 0.343	
Cytoreduction result				(*) p = 0.5816	
R0	87	31 (76)	56 (68)		
R1	26	8 (20)	18 (22)		
R2	10	2 (4)	8 (10)		
Follow-up [Mean]; month		26,78	21,56	(μ) p = 0.24	

No-PSR: No Port-Site Resection; PSR: Port-Site Resection; PSM + : Positive Port- Site Metastasis; PSM-: Negative Port- Site Metastasis; BMI: Body Mass Index; ECOG: Eastern Cooperative Oncology Group; PDS: Primary Debulking Surgery; IDS: Interval Debulking Surgery; HGSOC: High Grade Serous Ovarian Cancer.
(*) : Chi²; (°): Fisher's Exact Test; (μ): Mann-Whitney U Test.

clinical tumour registry from 2011 to 2016. Approval was obtained from the local ethics committee.

Patients with borderline tumours or ovarian tumours at an initial stage (FIGO I-II) were excluded. Patients with a laparoscopy prior to surgery were identified (n = 123). Those cases with grossly apparent port site metastasis were also excluded. At our institution, the use of laparoscopy for the assessment of operability in patients with clinical and imaging diagnosis of advanced ovarian cancer is the standard of care in case of doubts regarding the achievement of complete cytoreduction [7]. Primary laparotomy was performed after a tumour board assessment if there were clinical and imaging findings suggesting a high chance of complete cytoreduction.

All the laparoscopic procedures were performed at our institution. For this purpose, between two and three ports were used as follows: one 12 mm trocar at the umbilicus, one 5 mm trocar at a supra-pubic location and a third optional trocar located at the epigastrium. The Hasson open technique was used in all cases. All of them were located at the midline to facilitate removal at the debulking surgery. The standard intra-abdominal pressure used was 10–12 mmHg, and at the end of the procedure, the abdomen was emptied of gas before removal of the trocar.

Regarding PSR, there is not a clinical consensus at our institution. Consequently, as the cytoreductive procedures were performed by three different gynaecologic oncologists, two of them systematically performed PSR but the third one did not perform it. The port sites were resected (full thickness abdominal wall resection) according to the surgeon's choice at the beginning of the surgical procedure before knowing the final cytoreductive result of the surgery (Image 1). Patients were classified into two groups: no port site resection (No-PSR) and port site resection (PSR). Based on the pathological results of all port site specimens, the patients were classified as positive port site metastasis

(PSM+) if there was tumour found in the path of the trocar and negative port site metastasis (PSM-) in the absence of tumour.

In order to compare the characteristics of these groups, the following demographic and surgical variables were recorded: age, body mass index (BMI), menopause status, performance status (ECOG), International Federation of Gynaecology and Obstetrics (FIGO) Stage, type of surgery, ascites, histology, Ca 125, operating time, cytoreduction result and time of follow up.

Cytoreduction was classified as: R0: no macroscopic residual tumour; R1: macroscopic residual tumour < 1 cm and R2: macroscopic residual tumour > 1 cm.

All complications during postoperative course were recorded, as well as the length of hospital stay. Complications were graded according to the Clavien-Dindo classification [13]. Grade I complications were not reported in this study. For each patient, only the highest complication grade was recorded when a complication clearly occurred as a consequence of a prior complication of a lower grade. Complications of the same grade, but not directly related to each other, were recorded separately. A specific complication that re-occurred was only recorded once. Regarding the wound related complications, the following disorders were specifically recorded: wound dehiscence, hematoma, seroma, abscess, edge necrosis, eventration (based on clinical or imaging criteria) and scar metastasis (Image 2). Platinum-based chemotherapy was performed after primary debulking surgery (PDS) and before interval debulking surgery (IDS) according to standard guidelines.

Descriptive statistics, such as mean, median, frequencies and percentages, were used to describe the data and compared by the chi-squares test, Fisher's exact test Mann Whitney U test or t-test as appropriate.

Univariable survival analyses were performed using Kaplan-Meier

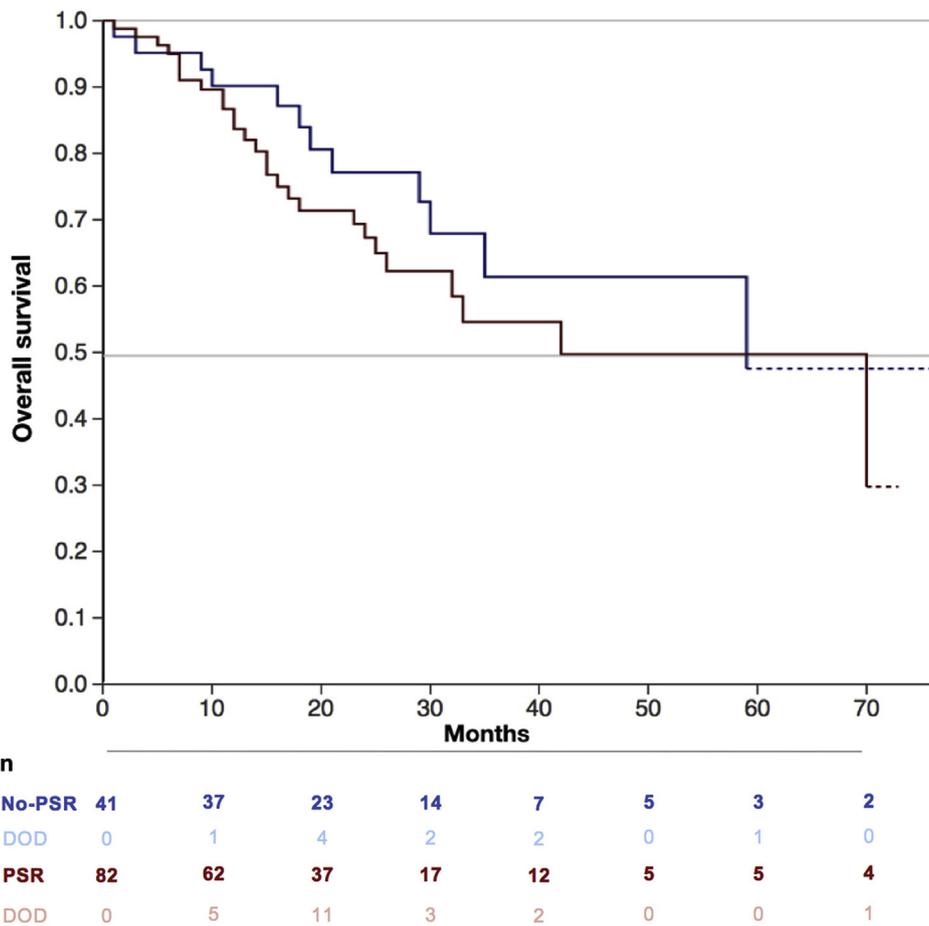


Fig. 1. No-PSR and PSR Kaplan–Meier curves. DOD: death of disease.

and Wald tests to obtain p values. Tests were two-sided at the 0.05 level. Statistical analysis was performed using SPSS version 20.0 (IBM Corporation, New York, NY).

3. Results

3.1. Patient baseline characteristics and surgical data

Between January 2011 and December 2016, a total of 446 patients with ovarian cancer FIGO Stage III-IV underwent cytoreduction (Diagram 1). An initial laparoscopic assessment for resectability was performed in up to 123 patients with advanced ovarian cancer. In 82 of them, the laparoscopic port site access were resected in the PDS or IDS. At the final specimen examination, 40/82 cases (49%) presented as PSM+.

Characteristics of the patients from both groups of study (No-PSR vs. PSR) were compared (Table 1). No differences were found when BMI (> 30; 7%vs.10%; p = 0.7502), performance status (ECOG > 0; 29% vs.21%; p = 0.2031), FIGO stage (III; 88% vs. 87%; p = 0.849), type of surgery (PDS; 63% vs. 66%; p = 0.7891), ascites (> 500; 73% vs. 56%; p = 0.0662), histology type (HGSOC; 73% vs. 74%; p = 0.8844), Ca. 125 (1622 vs. 1585; p = 0.312), operating time (299 vs. 314 min; p > 0.343) or cytoreduction results (R0; 76% vs. 68%; p = 0.5816) were compared. A statistical difference was found regarding age (> 65; 46% vs. 22%; p = 0.0054). There were no differences regarding the follow-up period (26.8% vs. 21.6%; p = 0.24). In the PSM + group, there were no differences between PDS and IDS [28/54 (52%) vs. 12/28(42%); p = 0.439].

3.2. Association of port site resection and overall survival

Kaplan-Meier survival curves were calculated for the No-PSR and PSR groups (Fig. 1). No statistical differences were found when curves were compared (p = 0.28). A sub-analysis of survival adjusted for confounding variables between the PSM+ and PSM- was performed. Kaplan-Meier survival curves are shown in Fig. 2, in which no differences were found between the two groups (p = 0.92).

3.3. Association of port site resection and postoperative morbidity

Complications and inpatient data are shown in Table 2. There were statistical differences regarding the length of the post-operative inpatient period (7.1 vs 10,2 days; p = 0.0028). The rate of wound event was higher in the PSR group (17% vs 34%; p = 0.047). The relative risk (RR) of wound events for PSR was 2.42 (95% CI 1.09–5.35; p = 0.0296). The RR of ventration for PSR was 2.12 (95% CI 0.76–5.91; p = 0.1486). When post-operative complications of both groups were compared according Clavien-Dindo classification, no differences were found regarding grade II, III, IV and V complications (p = 0.066).

4. Discussion

Our study focused on two major points: the influence of PSR on survival and the wound-related complications of PRS after debulking surgery. Both groups (No-PSR vs. PSR) were comparable as no differences were found regarding the main variables. No statistical differences regarding survival were found between the No-PSR and PSR

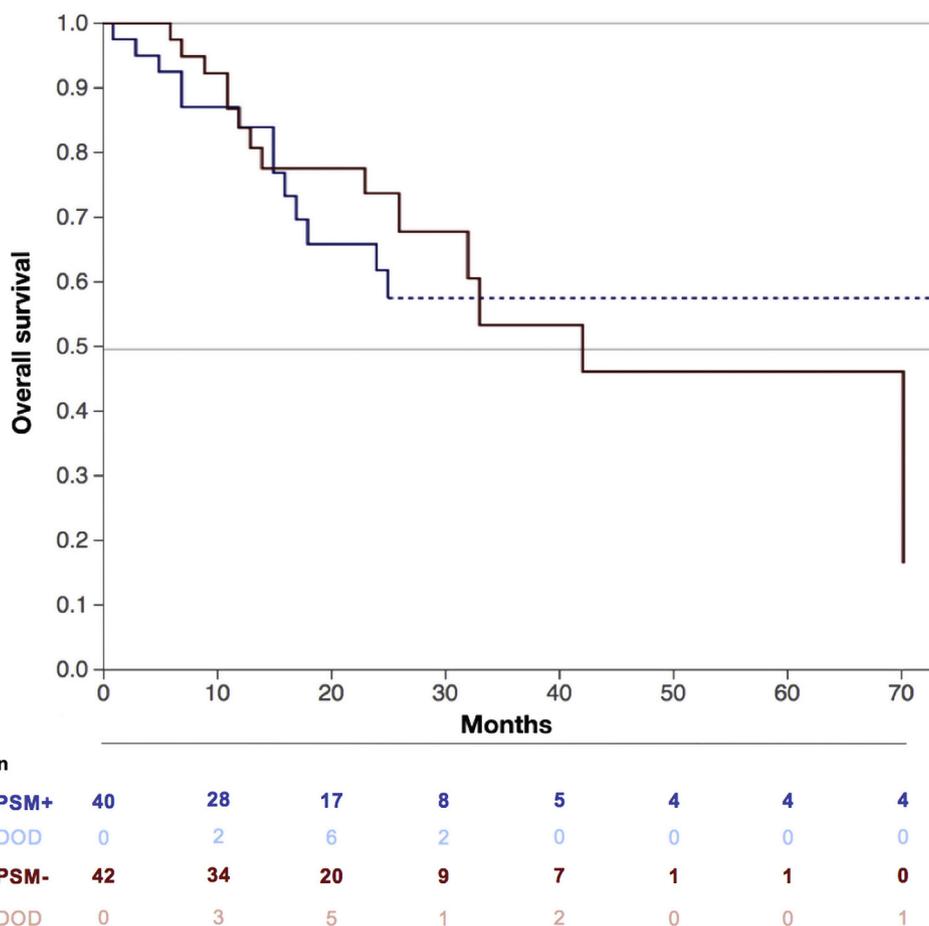


Fig. 2. PSM + and PSM- Kaplan–Meier c.

groups. A higher wound complication rate was found in the PSR group. To date, the role of PSR, independently of the presence of PSM+, has not been properly studied. Previous published articles focused on the role of PSM+ in survival and complications.

In recent years, laparoscopic assessment for resectability and tumour histology has become a common resource in ovarian cancer treatment [6]. The development of port site metastases after laparoscopy in advanced ovarian cancer has been a matter of debate. Iatrogenic disease spread during laparoscopy in ovarian cancer has been explained by the chimney effect created by the CO₂ pressure gradient, which conditions tumour cell seeding throughout the port site [14].

It has been proposed that the presence of metastases may be related to survival, and PSR may influence the oncological outcome. Nevertheless, systematic PSR during debulking surgery is a controversial issue. In fact, it is not mandatory at our institution and it depends on the surgeon's criteria. All the laparoscopic procedures were performed at our centre following the same procedure, and when PSR was performed, all port sites were routinely and systematic resected.

The published rate of PSM+ in advanced ovarian cancer after laparoscopy ranges between 16 and 47% [10–12,15,16]. The incidence of PSM+ in our cohort was as high as 49%. This may seem to be a higher incidence when we compared our rate of PSM+ with some other series [10,15,16]. Nevertheless, our rate of PSM+ is similar to those groups who reported the presence of PSM+ after performing the procedure in a standardised way (Ataseven et al. 46.7%, Heitz et al. 47%) [11,12]. Different factors have been reported to be associated with a high incidence of PSM+, such as more advanced tumour stage and ascites [12]. The prevalence of PSM+ has been found to be statistically higher depending on whether it was performed in the same institution in which the cytoreductive surgery is performed or in a different centre

(Referral). Nonetheless, given the fact that all the laparoscopy procedures were performed at our institution, this fact could not be analysed.

Regarding the presence of metastases, no statistical difference was found in the survival between both groups (PSM+ vs. PSM-). This has been the main matter of study in previous series. However, these authors also concluded that there was no significant relationship between port site metastases and survival [10,12,15,17]. The rate of PSM+ was higher in the PDS group compared with the IDS group, but no statistical differences were found (52% vs. 42%).

A higher rate of wound complication was found in the PSR group with an RR of wound events of 2.42 (95% CI 1.09–5.35). The rate of eventration in the PSR group was as high as 21%, and was 8% in the No-PSR with an eventration RR in the PSR group of 2.12 (95% CI 0.76–5.91).

Other authors have also concluded that the presence of PSM+ is associated with greater wound related comorbidity [12]. The direct consequence of PSR is that a large area of the abdominal wall is excised. It has been reported that there are differences in the surface of the resected area, i.e. this is higher in the PSR with PSM+ group [11]. There was a case of relapse at the scar site in each group (No-PSR vs. PSR). Given this low incidence, a statistical analysis could not be performed. Nevertheless, the presence of a relapse in the PSR group is contrary to the previously described theory. This finding does not confirm the observations of other groups [10].

Regarding the limitations, the retrospective design of the study, the absence of randomisation for PSR and the single institution character may represent a risk of bias. On the other hand, this is the first study in which PSR has been compared regardless of the presence of PSM. Regarding the patients who underwent PSR and the evaluation of metastases, our study represents the second largest cohort.

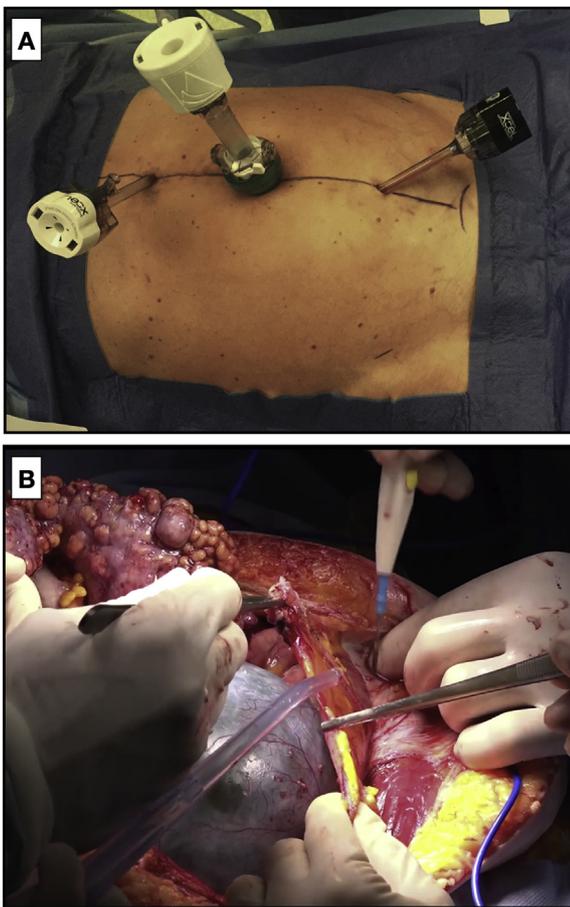


Image 1. A) Placement of the trocar along the midline to facilitate its removal at the debulking surgery (one 12 mm trocar at the umbilicus, one 5 mm trocar at supra-pubic location and a third optional trocar located at the epigastrium). B) Port site resection (PSR) during primary debulking surgery (PDS).

5. Conclusion

No statistical differences regarding survival were found, either between the No-PSR and PSR groups or between the PSM+ and PSM- groups. The incidence of PSM+ was high (49%). A higher wound complication rate was found in the PSR group. To date, not only there is no data supporting PSR after laparoscopy in advanced ovarian cancer but also the role of PSM+ in prognosis remains unclear. In conclusion, in patients in which laparoscopy is performed prior to the debulking procedure, the PSR may not be recommended in those cases of no

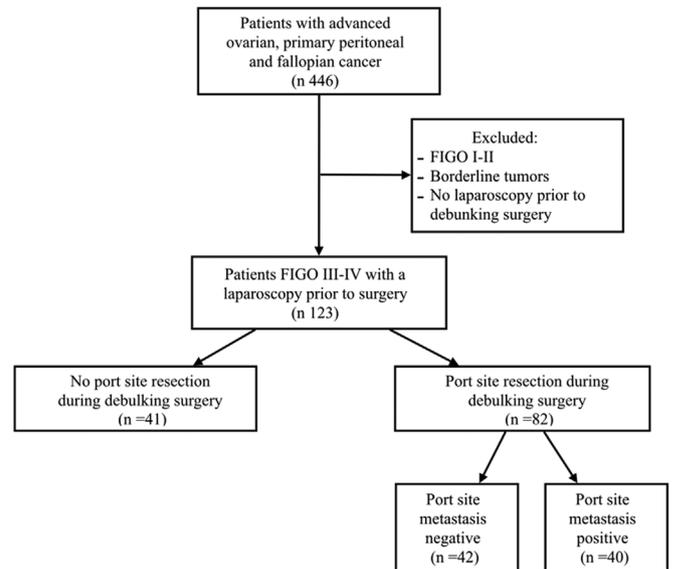


Diagram 1. CONSORT diagram describing the flow of patients through study enrolment.

Table 2
Association of Port-Site resection and postoperative morbidity.

	Total	No-PSR	PSR	P value
Inpatient days [Mean ± DS (Range)]; day	9.9 ± 3.1 (4–87)	7.1 ± 4.4 (4–28)	10.2 + /9.4 (3–87)	(μ)p = 0.0028
Wound complication [n(%); year				(*)p = 0.047
Wound dehiscence	7	1 (2)	6 (7)	
Hematoma/ seroma/abscess	10	1 (2)	9 (11)	
Necrosis	1	1 (2)	0 (0)	
Eventration	21	4 (8)	17 (21)	
Sacar metastasis	2	1 (1)	1 (1)	
Clavien-Dindo [n(%)]				(*)p = 0.066
II	59	15 (37)	44 (54)	
III	10	1 (2)	9 (11)	
IV	2	1 (2)	1 (1)	
V	1	1 (2)	0	

No-PSR: No Port-Site Resection; PSR: Port-Site Resection.
(*): Chi²; (°): Fisher's Exact Test; (μ): Mann-Whitney U Test.

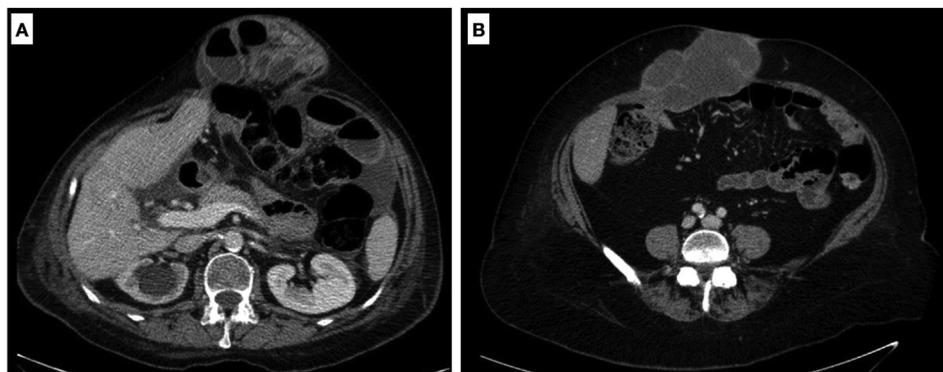


Image 2. A) Eventration after laparotomy. B) Abdominal wall metastasis (Relapse).

macroscopic port site metastasis.

Author contribution

Víctor Lago: Conception & Design of Study, Data Collection, Responsible Surgeon, Statistical Analysis, Data Analysis & Interpretation, Manuscript Preparation.

Laura Gimenez: Data Collection.

Luis Matute: Responsible Surgeon.

Pablo Padilla-Iserte: Conception & Design of Study, Responsible Surgeon.

Marta Gurrea: Responsible Surgeon or Imager.

Beatriz Montero: Responsible pathologist.

Guillermina Montoliu: Responsible Imaging.

Jose Miguel Cárdenas: Statistics review.

Santiago Domingo: Conception & Design of Study, Responsible Surgeon, Data Interpretation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.suronc.2019.01.007>.

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