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Intraperitoneal ports placed at the time of bowel resection for treatment of ovarian cancer: Complications and surgical outcomes

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HIGHLIGHTS

- Complication rates are not increased for intraperitoneal (IP) ports placed at the same time a bowel resection is done.
- Placing an IP port at the same time a bowel resection is done may help patients avoid additional surgical procedures.
- Two cycles of intravenous chemotherapy after IP port placement may allow for complete healing if a bowel resection is done.

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ABSTRACTTIENT DEMOGRAPHIC

Objectives: To determine if intraperitoneal (IP) ports placed concurrently with bowel resection during surgical treatment of ovarian cancer is associated with more complications than those ports placed without concurrent bowel resection.

Methods: The medical records of all patients who had an IP port placed at our institution between 2005 and 2016 were reviewed. Two groups were analyzed: IP ports placed with bowel resection (IP-BR) and those without (IP).

Results: Of 306 patient charts reviewed, 31% had a surgery with IP port placement and concurrent bowel resection (IP-BR). Demographics were similar except for mean BMI (25.6 IP-BR vs 27.4 IP, $p = 0.007$). More IP-BR patients had stage IIIC disease (83.3% IP-BR vs 56.9% IP, $p \leq 0.01$). Patients were cytoreduced to R0 in 48.7% IP-BR vs 56.4% IP ($p = 0.253$). For adjuvant treatment, IV chemotherapy was administered before IP chemotherapy in 90.4% IP-BR (median 2 cycles), and 50.3% IP, (median 2 cycles, $p < 0.01$). Ultimately 80.2% IP-BR (median 4 cycles) and 77.8% IP (median 5 cycles) received IP chemotherapy ($p = 0.65$). Rates of total IP port complications were similar (19.2% IP-BR vs 23.2% IP, $p = 0.397$), including IP port infections (0% IP-BR vs 0.7% IP, $p = 0.5$). Eleven percent of IP-BR patients had a bowel complication (e.g. obstruction or perforation) while IP port was in situ vs 2.7% IP ($p = 0.01$). Only 2.7% IP-BR and 6% IP discontinued IP chemotherapy due to IP port complication ($p = 0.3$).

Conclusions: Patients who have IP ports placed concurrently with a bowel resection do not appear to have more complications, nor lower rates of IP chemotherapy administration.

1. Introduction

More women die from ovarian cancer than any other gynecologic malignancy in the United States [1]. In 2006, the National Cancer Institute (NCI) recommended that the combined use of intravenous (IV) and intraperitoneal (IP) chemotherapy improves progression free survival and overall survival in optimally reduced epithelial ovarian cancer patients who have a primary debulking surgery [2]. This recommendation was based on the results of seven randomized trials conducted and published over the preceding ten years, notably including the findings of the Gynecologic Oncology Group study number 172, which demonstrated an improved median progression free survival of 5.5 months and median overall survival of 15.9 months for those patients that received IV/IP chemotherapy instead of IV chemotherapy alone [3].

Despite the recommendation of the NCI, utilization of IP chemotherapy has been lower than expected [4,5]. General concerns for IP chemotherapy toxicities and IP port complications may contribute to low utilization [6,7]. Additionally, consideration of IP chemotherapy may add additional operative procedures. There may be hesitancy to place an IP port during the same surgery in which a bowel resection has been done. This may result from concern for bowel complication or IP port infection, even though the NCI notes there is no contraindication to placing an IP port in this clinical scenario [2,8,9]. Delaying placement of an IP port subjects patients to an additional surgical procedure, and may delay initiation of chemotherapy.

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At our academic cancer center, it has been standard practice to place an IP port at the time of a debulking surgery for patients whom IP chemotherapy has been recommended, regardless of whether or not a bowel resection is done. This process has been adopted to spare patients a second procedure for our patients who are derived from a very large geographic area within the Pacific Northwest. For those who have had an IP port placed with concurrent bowel resection, their adjuvant chemotherapy course typically starts with 1–2 doses of IV chemotherapy in order to promote healing of the bowel anastomoses, followed by 4–5 cycles of IP chemotherapy. In contrast, those patients who do not have a bowel resection done at the same time as an IP port is placed typically start IP chemotherapy for their first adjuvant cycle, unless they initiated their adjuvant chemotherapy at a different institution before they were referred to our hospital for IP port placement.

The objective of this study was to review our clinical experience to determine the safety and outcomes when an IP port is placed in patients with or without a concurrent bowel resection. We hypothesize that placement of IP ports with concurrent bowel resection does not further increase the risk of IP port complications or limit a patient's ability to complete the indicated IP chemotherapy regimen.

2. Methods

After Institutional Review Board approval, a retrospective chart review was done of all patients who had an IP port placed between the years of 2005–2016 by the Gynecology Oncology department at the University of Washington. These patients were identified by surgical billing codes for IP port placement. The decision to place an IP port and the type of IP port used was per the discretion of the surgeon. The ports were placed at the time of a debulking surgery, or at a later date.

Patient charts were reviewed for general demographic information, components of the debulking surgeries done and the surgery when the IP port was placed (if it was placed at a later time), hospital course prior to discharge from the hospital, postoperative complications, and chemotherapy treatment courses (including type of chemotherapy given and mode and frequency). Two groups were analyzed: IP ports placed with concurrent bowel resection (IP-BR) and those without (IP). Two-tailed *t*-tests and chi-squared computations were used for analysis. When analyzing catheter complications and treatment outcomes, those patients who were lost to follow-up were excluded from the final analysis.

3. Results

Between 2005 and 2016, 306 IP ports were placed at our institution by providers in the Gynecologic Oncology department (Fig. 1). Three of these were for patients that had an IP port placed twice for different chemotherapy courses (initial treatment, and then for recurrent disease treatment). These were counted as separate encounters. Ninety-five of the IP ports (31.1%) were placed during the same surgery in which a bowel resection was performed (IP-BR cohort). Two hundred eleven (69.0%) ports were placed without a concurrent bowel resection (IP cohort). There were similar rates of non-epithelial ovarian cancer (EOC) histology between IP-BR and IP groups (Table 1). There was one patient in each group with endometrial cancer ($p = 0.56$), two patients in the IP-BR group and one in the IP group with colorectal cancer ($p = 0.18$), and one patient in each group with borderline neoplasm ($p = 0.56$). Thirteen of the ports in the IP-BR group (13.7%) and twenty of the ports in the IP group (9.5%) were placed for treatment of recurrent EOC ($p = 0.27$).

The groups were similar in terms of mean age, Caucasian race, non-smokers, current and former tobacco users, median number of prior abdominopelvic surgeries (open or minimally invasive), diabetes, known genetic mutation, and history of other malignancy diagnosis (Table 1). The only difference in the demographics was for mean BMI, which was lower in the IP-BR group, 25.6 IP-BR versus 27.4 for IP ($p < 0.01$). Approximately a third of patients lived in the same county as our institution (31.6% IP-BR vs 28.9% IP, $p = 0.64$) with similar rates of patients traveling from out of state (9.5% IP-BR vs 13.3% IP, $p = 0.35$).

Of the IP ports placed, 243 ports (98.7% IP-BR vs 84.6% IP, $p < 0.01$) were placed during a primary or interval debulking surgery. Twenty-two ports (0% IP-BR vs 10.43% IP, $p < 0.01$) were placed without additional surgical procedures done for the sole purpose of initiating IP chemotherapy. The remaining forty-one ports were placed at the time of surgery for a secondary debulking for recurrent disease. The vast majority of the primary and interval debulking surgeries done were optimal cytoreductions

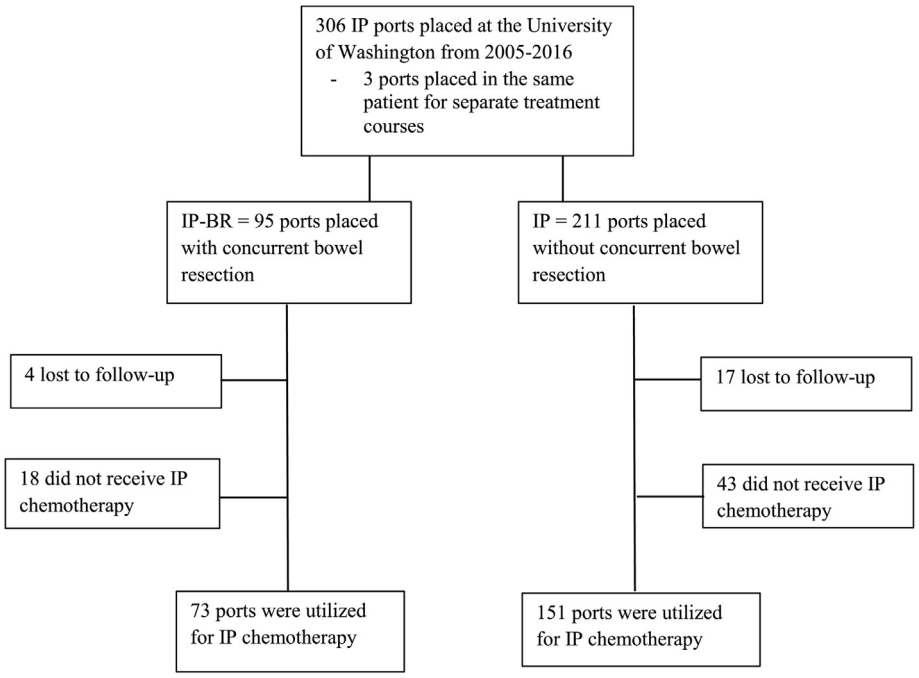

Fig. 1. Flowchart of IP ports.

Table 1
Patient demographics.

Demographic	IP-BR ($N = 95$)	IP ($N = 211$)	p-Value
Mean age	60 years	59 years	0.497
Mean BMI	25.6	27.4	0.007
Caucasian	88/92 (95.7%)	177/189 (93.7%)	0.497
Non-smoker	56 (59.0%)	143 (67.8%)	0.134
Former or current smoker	36 (37.9%)	64 (30.3%)	0.192
Median number of prior abdominopelvic surgeries	1	1	n/a
Diabetes	5 (5.3%)	21 (10.0%)	0.173
Known genetic mutation	12 (12.6%)	27 (12.8%)	0.968
History of cancer	14 (14.7%)	29 (13.7%)	0.817
Lives out of state	9 (9.5%)	28 (13.3%)	0.346
From King County	30 (31.6%)	61 (28.9%)	0.637
Endometrial cancer	1 (1.1%)	1 (0.5%)	0.561
Colorectal cancer	2 (2.1%)	1 (0.5%)	0.180
Borderline ovarian disease	1 (1.1%)	1 (0.5%)	0.561
Recurrent EOC	13 (13.7%)	20 (9.5%)	0.272

(97.4% IP-BR vs 95.2% IP, $p = 0.40$), with high rates of cytoreduction to R0 (48.7% IP-BR vs 56.4% IP, $p = 0.25$). The IP-BR group had more patients with stage III disease (87.2% IP-BR vs 68.6% IP, $p < 0.01$), including more patients with stage IIIC disease (83.3% IP-BR vs 56.9% IP, $p \leq 0.01$). The IP-BR group included fewer patients with stage II disease (2.6% IP-BR vs 14.9%, $p < 0.01$) but similar rates of stage IV (10.3% IP-BR vs 13.3% IP, $p = 0.49$).

The median number of bowel resections done at the time of IP port placement in the IP-BR group was one (range 1–3 resections done at separate intestinal sites). Sixty-eight percent of the bowel resections were of the descending colon (including rectosigmoid), 12.5% of the transverse colon, 8.7% of the ascending colon and 8.7% of the small bowel.

The groups were similar in regards to percentage of patients that received neoadjuvant chemotherapy administration (16.7% IP-BR vs 25% IP, $p = 0.14$) with median receipt of three chemotherapy cycles. After IP port placement, twenty-one patients were lost to follow-up and their adjuvant chemotherapy treatment regimen is unknown. These patients were excluded from the remaining analysis. Only 3.3% of the IP-BR ports and 4.1% of the IP ports were not utilized for IP chemotherapy due to a surgical or IP port complication ($p = 0.74$). There was also no difference between the two groups in regards to not initiating IP chemotherapy because IP chemotherapy was not indicated for the stage of the disease (1.1% IP-BR vs 3.1% IP, $p = 0.31$) or IP chemotherapy was not available where the patient received adjuvant treatment (1.1% IP-BR vs 1.6% IP, $p = 0.77$).

Ultimately 80.2% of the IP-BR ports and 77.8% of the IP ports were utilized for IP chemotherapy ($p = 0.65$). Those patients who did not receive IP chemotherapy were also excluded from the remaining analysis. The IP-BR group was more likely to receive adjuvant IV chemotherapy initially before receiving IP chemotherapy (90.4% IP-BR vs 50.3% IP, $p < 0.01$). Of those that received adjuvant IV chemotherapy before IP chemotherapy, a median of two cycles (range 1–6 cycles) was given to the IP-BR group and a median of two cycles (range 1–7 cycles) for the IP group. Three percent of the IP-BR ports and 3.3% of the IP ports were given IV chemotherapy before IP chemotherapy because of a port complication that was later addressed ($p = 0.82$) or until the IP port was placed at a later date (1.4% IP-BR vs 9.9% IP, $p = 0.02$).

The median number of IP chemotherapy cycles administered was four for the IP-BR group (range 1–7 cycles) and five for the IP group (range 1–6 cycles). Fifty-three percent of the IP-BR group and 45% of the IP group received IV chemotherapy after receiving IP chemotherapy ($p = 0.24$). In total (including neoadjuvant and adjuvant chemotherapy treatment, IP chemotherapy with or without IV chemotherapy), the IP-BR and IP groups received a median of six chemotherapy cycles (range 5–12 cycles for the IP-BR group, and a range of 3–12 cycles for the IP group). Time from IP port placement to first adjuvant chemotherapy cycle (whether IV or IP) was no different for the two groups (32.3 days IP-BR vs 28.7 days IP, $p = 0.08$).

In regards to IP port complications (Table 2), there was a higher incidence of a major small or large bowel complication (obstruction or perforation) occurring while an IP port was in place in the IP-BR group (11% IP-BR vs 2.7% IP, $p = 0.01$). Otherwise, there was no difference between the two groups in terms of: abdominal pain though to be secondary to the port, cellulitis, catheter/reservoir leakage, IP infusion leaking from the vagina, catheter was obstructed, dislodged or migrated, port access challenges (e.g. unable to access, or requiring fluoroscopy to access), port erosion, and catheter infection requiring removal. In the IP-BR group, 14 ports had a total of 17 complications, and 35 ports in the IP group had a total of 42 complications, for a total rate of IP port complications of 19.2% for the IP-BR group and 23.2% for the IP group ($p = 0.40$). Use of only 2.7% of the IP-BR ports and 6% of the IP ports was discontinued earlier than intended due to a port complication ($p = 0.30$). Two of the IP-BR ports and 4 of the IP ports required surgical revision ($p = 0.97$).

4. Discussion

This retrospective review did not detect a difference in total rates of IP port complication between ports placed at the same time a bowel resection was done and those ports placed in the absence of a bowel resection for advanced ovarian cancer. Additionally, there was no difference in rates of administering IP chemotherapy between the two cohorts, and these rates were higher than prior studies assessing utilization of IP chemotherapy: approximately 80% of both cohorts started IP chemotherapy and completed a median of 4 cycles of IP chemotherapy in the IP-BR group and 5 cycles in the IP group. This is in part because the vast majority of the IP-BR patients were first given IV chemotherapy, as is our typical institutional practice in order to allow for complete healing of the bowel anastomoses before IP chemotherapy is initiated. In total, both groups received a similar number of chemotherapy cycles, regardless of route of administration.

There was a statistically significant difference in the rate of major bowel complications while an IP port was in place. Eleven percent of IP-BR patients experienced a bowel obstruction or perforation versus 2.7% of the IP group. One possible confounding factor is that all of the IP-BR patients underwent a bowel resection. Additionally, the IP-BR group had more patients with stage III disease, such that the underlying burden of disease may also have contributed to this finding. While there were more bowel complications in the IP-BR group, there was no difference between the two groups in terms of discontinuing use of the IP port for IP chemotherapy.

All charts that were available at the time this study was conducted were analyzed (i.e. all charts of IP ports placed from 2005 to 2016). Based on the baseline rate of 23% for IP port complication rates found

Table 2
IP port complications.

Type of IP port complication	IP-BR ($N = 73$)	IP ($N = 151$)	p-Value
Abdominal pain	2.7%	8.0%	0.131
Superficial cellulitis	0%	1.3%	0.323
Catheter/reservoir leakage	1.4%	1.3%	0.978
IP infusion leaking from the vagina	0%	1.3%	0.323
Catheter obstructed, dislodged, or migrated	3.3%	4.6%	0.858
Port access challenges	4.1%	7.3%	0.357
Port erosion	0%	0.7%	0.486
Catheter infection requiring removal	0%	0.7%	0.486
Major bowel complication while IP port still in place	11%	2.7%	0.010
All IP ports with any complication	19.2%	23.2%	0.397

in our study (for those ports placed in the absence of a bowel resection), post hoc analysis showed that this study was powered to detect a difference of at least 8% (power > 0.80 and alpha of 0.05). Thus, while we did not find a difference between the groups in terms of IP port complications, the sample size was insufficient to adequately assess this finding. Nonetheless, we feel that the large sample size analyzed in this report has produced clinically relevant findings showing that there is likely no increased risk of placing an IP port at the same time that a bowel resection was done, particularly when the patient is first given two doses of IV chemotherapy to allow for full healing of the bowel anastomoses.

Other studies looking at rates of IP port complications have found rates ranging from 9 to 34% [8,10–12]. In GOG 172, only 42% of the IP group completed all 6 cycles of the prescribed chemotherapy regimen, and 34% of this cohort discontinued IP chemotherapy due to catheter complication (including infection, blocked catheter or leaking catheter, port access difficulty, and patient desire) [3,8]. There was no association between small bowel and ileocecal resection and ability to complete 6 cycles of IP chemotherapy, however there was an association between a left colonic resection (including rectosigmoid resection) and not initiating IP chemotherapy.

In comparison, other studies demonstrated lower rates of IP catheter complication than what was described from GOG 172. An analysis of IP port catheters placed at one institution found a catheter complication rate of only 9.6% [11]. This rate of catheter complications was hypothesized to be lower in part due to less IP ports being placed at the same time a bowel resection is done. However, a later analysis of fenestrated IP ports placed at the same institution demonstrated that rates of initiating and completing IP chemotherapy was no different for those that had bowel resection performed at the same time that an IP port was placed and those that did not [10]. In a study done in Japan, a catheter complication rate of only 9.7% was found [12].

Our finding of a 19–23% total complication rate is well within the previously described analyses. Importantly, the rates of discontinuing IP port chemotherapy due to a port complication in our study were 2.7–6%, which is significantly less than what has been previously reported by Walker et al. [8].

The strengths of this study include the large patient population that was analyzed over an eleven-year time span which allows for a comprehensive review of our perioperative outcomes. The demographics of both groups were similar with the exception of BMI, which, although a statistically significant difference, was only a small difference of 1.8. Additionally, this study was completed at one institution where practices are typically standardized across the department, particularly in regards to placement of and use of IP ports.

There are inherent limitations of this study as it is a retrospective cohort study. Most of the data abstracted was extracted from clinician notes, which are not standardized and thus some data was missing. In addition, many of the patients treated at our institution travel great distances for surgical management, but then have their chemotherapy completed elsewhere and monitored by an outside provider. Those patients for whom we did not have follow-up data were excluded from the analysis of adjuvant chemotherapy treatment and IP port complication. This study reviewed charts over a long period of time, during which there may have been adjustments to IP port placement surgical techniques decreasing the rates of IP port erosion or access challenges. Lastly, the administration of bevacizumab, which is associated with an increased risk of bowel perforation, was not accounted for in this study. However, bevacizumab was not approved by the Food Drug and Administration for adjuvant treatment of ovarian cancer until 2018, and thus utilization was likely low during our study time period.

Our data shows that there is no significant increased risk to placing an IP port at the same time as a bowel resection is done. Additionally, our results suggest that after ovarian cancer surgery that includes a bowel resection, adjuvant IP chemotherapy can be safely and consistently administered if preceded by 2 cycles of adjuvant IV chemotherapy. These high rates of initiating IP chemotherapy and adherence to recommended treatment regimens were greater than what has been previously reported by Wright et al. and Bowles et al. They found IP chemotherapy administration rates ranged from 20 to 50% in community and academic settings [4,5].

The recently published results of GOG 252 demonstrated no improvement in progression free survival with use of an IP platinum agent in combination with bevacizumab and IV paclitaxel versus IV carboplatin. As such, we anticipate continued evolution of the chemotherapy treatment options recommended to patients with advanced, optimally debulked ovarian cancer [13]. However, should IP chemotherapy be utilized, the results of our study suggest that patients are able to tolerate IP port placement and chemotherapy well, are able to utilize IP ports with minimal complications, and are able to avoid a second procedure under general anesthesia if an IP port is placed at the time of a debulking surgery.

Author contribution

HG and RU conceived of the project idea. HG obtained institutional review board approval. All three authors performed a comprehensive electronic medical record review of all included medical charts. AK conducted the data analysis, and all three authors contributed to the writing of the manuscript.

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None.

Declaration of competing interest

The authors have no conflicts of interest.

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