Complications and risk factors for complications of implanted subcutaneous ports for intraperitoneal chemotherapy in gastric cancer with peritoneal metastasis

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Abstract

Objective: Intraperitoneal (IP) chemotherapy through subcutaneous port is an effective treatment for gastric cancer (GC) patients with peritoneal metastasis (PM). The objective of this study is to assess the port complications and risk factors for complications in GC patients with PM.

Methods: In retrospective screening of 301 patients with subcutaneous ports implantation, 249 GC patients with PM who received IP chemotherapy were screened out for analysis. Port complications and risk factors for complications were analyzed.

Results: Of the 249 analyzed patients, 57 (22.9%) experienced port complications. Subcutaneous liquid accumulation (42.1%) and infection (28.1%) were the main complications, and other complications included port rotation (14.1%), wound dehiscence (12.3%), inflow obstruction (1.7%) and subcutaneous metastasis (1.7%). The median interval between port implantation and occurrence of complications was 3.0 months. Eastern Cooperative Oncology Group (ECOG) performance status [odds ratio (OR), 1.74; 95% confidence interval (95% CI), 1.12–2.69], albumin (OR, 3.67; 95% CI, 1.96–6.86), implantation procedure optimization (OR, 0.33; 95% CI, 0.18–0.61) and implantation groups (OR, 0.37; 95% CI, 0.20–0.69) were independent risk factors for port complications (P<0.05). ECOG performance status was the only factor that related to the grades of port complications (P=0.016).

Conclusions: Port complications in GC patients who received IP chemotherapy are manageable. ECOG performance status, albumin, implantation procedure and implantation group are independent risk factors for port complications in GC patients with PM.

Keywords: Gastric cancer; peritoneal metastasis; intraperitoneal chemotherapy; paclitaxel; port complication

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Introduction

Gastric cancer (GC) is among the most common cancers with poor survival worldwide, especially in East Asia (1,2). Peritoneal metastasis (PM) is the most frequent type of metastasis of GC, and is the main cause of mortality in GC...
patients, it severely threatens the survival of patients (3). Although multiple approaches have been applied such as systemic chemotherapy (4,5), hyperthermic intraperitoneal chemotherapy (HIPEC) (6), pressurized intraperitoneal aerosol chemotherapy (PIPAC) (7), and cytoreductive surgery (8,9), the outcome of patients with PM is still worse.

Intraperitoneal (IP) infusion of chemotherapeutic drugs was attempted to expose IP tumor cells to anticancer drugs at high drug concentrations with minimal systemic toxic effects (10). To administer anticancer drugs to the peritoneal cavity, implanting a subcutaneous port is an effective approach (11). Recently, repeated IP chemotherapy has been widely applied for GC patients with PM, and chemotherapeutic drugs can be repeatedly injected into the abdominal cavity through the subcutaneous implanted port, and patients’ survival was benefited from the regimen (12,13). However, the implantation of the port may induce certain kinds of related complications, like in ovarian cancer (14). Unfortunately, there are rare reports about port complications in GC. So, the exploration of occurrence and risk factors for the port complications is meaningful for GC patients with PM.

In the present study, we retrospectively collected the information of 301 patients with subcutaneous ports implanted, 249 GC patients with PM who received port implantation and IP chemotherapy were screened out for analysis. There were 57 patients who experienced port complications, including infection, subcutaneous liquid accumulation, port rotation, wound dehiscence, inflow obstruction and subcutaneous metastasis. To define the severity of complications, we classified the complications into grades 1−4, and analyzed contributions to grades. Importantly, we optimized the port implantation procedures and revealed risk factors for the occurrence of port complications.

Materials and methods

Patients

A retrospective analysis of 301 patients with subcutaneous ports implanted at Ruijin Hospital Shanghai Jiao Tong University School of Medicine from April 2015 to March 2020 was conducted. Flow diagram that described the screening, exclusion and inclusion of the patients is showed in Figure 1. The inclusion criteria were as follows: 1) pathologically proven gastric adenocarcinoma; 2) PM visible to the naked eyes or proven by laparoscopic exploration not just positive peritoneal cytology; 3) ECOG performance status of 0−2; 4) patients without pyloric obstruction or intestinal obstruction; 5) adequate bone marrow, liver, and renal functions and an survival period of more than 6 months; and 6) port implantation and IP chemotherapy performed at Ruijin Hospital and patient’s follow-up for a minimum of 6 months after port implantation or until the development of a complication. Patients were excluded if they had any of the following criteria: 1) pathologically proven non-gastric carcinomas; 2) PM invisible to the naked eyes or just positive peritoneal cytology or with prophylactic port implantation; 3) non-adequate bone marrow, liver, and renal functions and an survival period of less than 6 months; or 4) patients loss to follow-up or follow-up time less than 6 months after port implantation or until the development of a complication. The range of PM was stratified according to peritoneal cancer index (PCI) scores (15). This study was conducted with the approval of the Ruijin Hospital Ethical Review Board and written informed consents were provided by the patients.

Figure 1 Flow diagram for analysis. GC, gastric cancer.
**Port implantation and procedure optimization**

The port used was the PORT-A-CATH II System (Smiths Medical ASD, Inc., St. Paul, USA), consisting of a port with a 30.5 mm portal base diameter and a 14.7 mm height and a 7.8-F single lumen silicon catheter. Port implantation was performed at the time of laparotomy or with the help of laparoscopy. A port site was designed in the right or left lower abdomen (Figure 2, Supplementary Figure S1), near the external border of the rectus abdominis, avoiding subcutaneous veins, intra-abdominal adhesions and metastatic sites.

The implantation procedure was similar to the description of previous report (16), and the catheter was placed in the pelvic cavity (Supplementary Figure S1E,F). Before the procedure optimization, only the entrance of catheter into the aponeurosis was fixed (Supplementary Figure S1D). For procedure optimization, not only the entrance of catheter into the aponeurosis was fixed, the whole catheter that exposed was embedded with nonabsorbable sutures (Figure 2C−F). The optimized implantation procedure was performed thereafter by all executive groups. Of the 249 analyzed patients, 114 were implanted before the optimization and 135 were implanted after the optimization. Among these ports, 241 were implanted immediately after laparoscopic exploration and 8 were implanted at the time of laparotomy. The specialized group consists of surgeons who have profound experience with implanting ports and focused on the IP chemotherapy for more than 3 years.

**Chemotherapy regimen**

The regimen used consisted of intravenous (iv) paclitaxel (PTX) and IP PTX and oral tegafur/gimeracil/oteracil (S-1) as reported previously (17). Specifically, PTX was administered via iv and IP at doses of 50 mg/m² and 20 mg/m², respectively, on d 1 and 8, and S-1 was given orally at doses of 80 mg/m² on d 1−14. IP infusion was achieved through a needle that was vertically inserted in the center of the port and removed when the IP infusion finished. Chemotherapy was repeated every 3 weeks until the regimen changed or toxicity was intolerable.

*Figure 2* Optimized procedures of implanting and fixing subcutaneous port. (A,B) Skin incision and subcutaneous cavity were made to accommodate the port base and catheter; (C−F) The port was fixed and catheter was embedded with nonabsorbable sutures.
Complications

Port infection was diagnosed if the port site was painful to the touch, displayed redness or felt fluctuation with or without a fever, a high white blood cell (WBC) count, or a high C-reactive protein (CRP) level. Port rotation or tilt was defined as port movement from the primary position, turnover or at an angle with the skin, resulting in difficulty with needle insertion. Wound dehiscence was defined as the dehiscence of a wound of less than 2 cm and the body of the port did not stand out of the port site. Inflow obstruction was characterized by being unable to flush saline into abdominal cavity through a catheter. Subcutaneous liquid accumulation could be induced by liquid refluxed from the abdominal cavity along the catheter and inflammatory exudate. Subcutaneous metastasis was diagnosed as nodules growing around the port position and determined by fine needle aspiration cytology.

Grading of complications

According to the degree of severity of the port complications, we classified the complications as grades 1–4 referred to the Clavien-Dindo classification (18). Grade 1 was defined as a slight volume of subcutaneous liquid accumulation or slight rotation, and the port could be used without any need for pharmacological treatment or surgical, endoscopic and radiological interventions. Grade 2 was defined as mild subcutaneous liquid accumulation, a small wound dehiscence, a mild infection or rotation, and the complication could be controlled by conservative treatments such as pharmacological treatment, and had no influence on IP chemotherapy. Grade 3 was defined as moderate subcutaneous liquid accumulation, wound dehiscence, infection, or rotation, which require pharmacological treatment, surgical, endoscopic or radiological intervention, before the port could be used again. Grade 4 was defined as severe port complications, treatments should be adopted immediately and the port could not be used again and needed to be removed or replaced.

Statistical analysis

This study was designed to assess the port complications and risk factors for complications in GC patients with PM. Totally, 301 patients with subcutaneous ports implantation were retrospectively analyzed, and 249 patients who met the inclusion criteria were included for the analysis. All patients were followed up at least for 6 months after the port implantation. The interval between port implantation and complications was defined as the time from port implantation and the appearance of the sign of complications. For statistical analysis, the patients were grouped into 2 categories with respect to sex (male or female), age (<60 or ≥60 years), BMI (<23 or ≥23 kg/m²), ascites (present or absent), prior chemotherapy (present or absent), simultaneous surgery (yes or no), albumin (<35 or ≥35 g/L), hemoglobin (normal: 131–172 g/L, anemia: <131 g/L for male; normal: 113–151 g/L, anemia: <113 g/L for female), glucose (euglycemia: 3.9–6.1 mmol/L or hyperglycemia: >6.1 mmol/L), implantation approach (laparoscopic exploration surgery or open surgery), implantation procedure (before or after optimization of port implantation) and implantation group (specialized or other groups). Similarly, the patients were divided into 3 categories with respect to ECOG performance status (0, 1 or 2) and PCI (0–10, 11–20 or 21–39).

The correlation between clinical characteristics and port complications was analyzed using the Chi-squared test and Fisher’s exact test. Logistic regression analyses were used to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) of complications. Mann-Whitney U test and Goodman-Kruskal Gamma test were used to analyze whether the clinical characteristics were correlated with the complication grades. IBM SPSS Statistics (Version 20.0; IBM Corp., New York, USA) was used for the analyses. Two-tailed P<0.05 was considered a statistically significant difference.

Results

Port complications and grading and correlation with clinical characteristics

During the observation period of this study, 301 patients with subcutaneous ports implanted were retrospectively analyzed. Six patients with other carcinomas were excluded. Twenty-three GC patients with T4 stage tumors but without visible metastasis were implanted with ports for prophylactic IP chemotherapy were also excluded. And 7 patients lost to follow-up. Sixteen patients were excluded for the follow-up time less than 6 months. Therefore, 249 patients who underwent port implantation and met the inclusion criteria were included, 57 (22.9%) port-related complications were recorded (Figure 1). When analyzing the clinical characteristics, we found that sex, age, BMI,
PCI, ascites, history of prior chemotherapeutic treatment, simultaneous surgery, hemoglobin, glucose and port implantation approach were not significantly associated with port complications, but ECOG performance status, albumin, implantation procedure and implantation group experience were significantly associated with port complications (Table 1). Specifically, ECOG performance status was significantly related to infection, wound dehiscence and subcutaneous liquid accumulation; albumin was related to infection, rotation and wound dehiscence; implantation procedure optimization was related to the occurrence of infection and subcutaneous liquid accumulation; implantation group was related to the occurrence of wound dehiscence and subcutaneous liquid accumulation (Supplementary Table S1). The median interval between port implantation and complications occurrence was 3.0 months (Table 2). The median times for the occurrence of infection, port rotation, wound dehiscence, inflow obstruction, subcutaneous liquid accumulation, and subcutaneous metastasis were 3.3 months, 2.6 months, 1.0 month, 2.0 months, 4.0 months and 5.5 months, respectively. As demonstrated, subcutaneous liquid accumulation and infection were the main complications, accounting for 42.1% and 28.1%, respectively. To clearly describe the severity of port complications and adopt effective treatments, we first formed a classification of complications according to the degree of severity. All 57 complications were classified into grades 1–4. Impressively, in 18 cases of grade 4 complications, 9 cases were induced by infection (Supplementary Table S2). Next, we explored the relationship between clinical characteristics and complication grades, and found that ECOG performance status was the only factor that was significantly related (Table 3).

Clinical manifestations of port complications

When patients presented with infection symptoms such as port site pain, skin redness or fluctuation (Supplementary Figure S2A,B), with or without a high WBC count, or a high CRP level, according to the guidelines on the prevention of surgical site infection (SSI) (19), systemic and local treatments were given immediately. Due to these efforts, 7 port infections were controlled, and the IP chemotherapy could be continued afterwards; however, 9 ports were removed with 3 patients having new ports implanted and the other 6 patients ceasing IP chemotherapy.

Subcutaneous liquid accumulation around the port was the most common complication (Supplementary Figure S2C,D), and it was identified in 24 patients. Fortunately, most cases were in the grade 1 and 2 groups and resolved by aspiration of the liquid with a syringe before continued administration of IP chemotherapy. Only 3 patients presented with grade 4 complications and had their ports removed and abandoned IP chemotherapies (Supplementary Table S2).

Port rotation, tilt or turnover was observed in 8 patients (14.0%) (Supplementary Figure S2E,F, Supplementary Table S2). This complication may hamper the insertion of needles into ports. However, most cases were grade 1 and 2 complications and did not cause serious discomfort, so after adjustments, needles could still be inserted into the ports, except in 1 case the port had to be removed and IP chemotherapy abandoned.

Wound dehiscence was observed in 7 patients (12.3%) (Supplementary Figure S2G,H). Five patients were classified as having grade 2 complications, and only 2 patients had grade 4 complications and removed their ports and abandoned IP chemotherapies (Supplementary Table S2). Incisions with relatively mild symptoms in the 5 patients were sterilized and re-sutured with absorbable sutures and continued to be used for IP chemotherapies with reduced dose of PTX.

Inflow obstruction was diagnosed in only 1 patient (1.8%) (Supplementary Table S2). After 2 cycles of IP chemotherapy, the liquid could not be injected into the port of this patient, and exploration was performed. We found that the catheter slipped out of the abdomen and wound around the port base (Supplementary Figure S2I); debridement was performed, and the port was replaced by a new port.

Subcutaneous metastasis was observed in 1 patient (1.7%) (Supplementary Table S2, Supplementary Figure S2J). Five and a half months after the placement of the port, hard nodules were felt at the port site, and a fine needle aspiration cytology examination was performed. To avoid dissemination the port was abandoned and systemic chemotherapy was continued.

Among the 57 patients with complications, 18 patients had their ports taken out or abandoned, and 7 of these had their ports replaced. All patients with port complications continued their IP chemotherapies or changed to systemic chemotherapies after the symptoms were controlled.
Table 1 Correlation between port complications and patient clinical characteristics (N=249)

| Variables                  | N   | With complications [n (%)] | Without complications [n (%)] | P   |
|----------------------------|-----|----------------------------|-------------------------------|-----|
| Sex                        |     |                            |                               |     |
| Male                       | 109 | 20 (8.0)                   | 89 (35.7)                     | 0.132 |
| Female                     | 140 | 37 (14.9)                  | 103 (41.4)                    |     |
| Age (year)                 |     |                            |                               |     |
| <60                        | 166 | 42 (16.9)                  | 124 (49.8)                    | 0.201 |
| ≥60                        | 83  | 15 (6.0)                   | 68 (27.3)                     |     |
| BMI (kg/m$^2$)             |     |                            |                               |     |
| <23                        | 174 | 36 (14.5)                  | 138 (55.4)                    | 0.208 |
| ≥23                        | 75  | 21 (8.4)                   | 54 (21.7)                     |     |
| ECOG PS                    |     |                            |                               |     |
| 0                          | 102 | 11 (4.4)                   | 91 (36.5)                     | 0.001 |
| 1                          | 114 | 35 (14.1)                  | 79 (31.7)                     |     |
| 2                          | 33  | 11 (4.4)                   | 22 (8.8)                      |     |
| PCI                        |     |                            |                               | 0.113 |
| 0–10                       | 65  | 9 (3.6)                    | 56 (22.5)                     |     |
| 11–20                      | 71  | 20 (8.0)                   | 51 (20.5)                     |     |
| 21–39                      | 113 | 28 (11.2)                  | 85 (34.1)                     |     |
| Ascites                    |     |                            |                               | 0.381 |
| Present                    | 229 | 54 (21.7)                  | 175 (70.3)                    |     |
| Absent                     | 20  | 3 (1.2)                    | 17 (6.8)                      |     |
| Prior chemotherapy         |     |                            |                               | 0.710 |
| Present                    | 78  | 19 (7.6)                   | 59 (23.7)                     |     |
| Absent                     | 171 | 38 (15.3)                  | 133 (53.4)                    |     |
| Simultaneous surgery       |     |                            |                               | 0.322 |
| Yes                        | 10  | 1 (0.4)                    | 9 (3.6)                       |     |
| No                         | 239 | 56 (22.5)                  | 183 (73.5)                    |     |
| Albumin (g/L)              |     |                            |                               | <0.001 |
| <35                        | 68  | 28 (11.2)                  | 40 (16.1)                     |     |
| ≥35                        | 181 | 29 (11.6)                  | 152 (61.0)                    |     |
| Hemoglobin                 |     |                            |                               | 0.168 |
| Anemia                     | 133 | 35 (14.1)                  | 98 (38.4)                     |     |
| Normal                     | 116 | 22 (8.8)                   | 94 (37.8)                     |     |
| Glucose                    |     |                            |                               | 0.441 |
| Euglycemia                 | 225 | 50 (20.1)                  | 175 (70.3)                    |     |
| Hyperglycemia              | 24  | 7 (2.8)                    | 17 (6.8)                      |     |
| Implantation approach      |     |                            |                               | 0.477 |
| LS                         | 241 | 56 (22.5)                  | 185 (74.3)                    |     |
| Open                       | 8   | 1 (0.4)                    | 7 (2.8)                       |     |
| Implantation procedure     |     |                            |                               | <0.001 |
| Before                     | 114 | 38 (15.3)                  | 76 (30.5)                     |     |
| After                      | 135 | 19 (7.6)                   | 116 (46.6)                    |     |
| Implantation group         |     |                            |                               | 0.001 |
| Specialized group          | 181 | 32 (12.9)                  | 149 (59.8)                    |     |
| Other groups               | 68  | 25 (10.0)                  | 43 (17.3)                     |     |

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; PCI, peritoneal cancer index; Yes, gastrectomy plus with port implantation; No, port implantation only; LS, laparoscopic exploration surgery; Open, port implanted with open surgery; Before, before the optimization of port implantation procedure; After, after the optimization of port implantation procedure.
First, the study demonstrated that port complications were controllable and that IP chemotherapy for GC using a port is safe and feasible compared with previous reports (11,22-24).

In this study, we screened 301 patients with ports implantation and 249 GC patients met the inclusion criteria for the analysis, and 57 patients (22.9%) presented with port-related complications. Subcutaneous liquid accumulation (42.1%) and infection (28.1%) were the main complications. Subcutaneous liquid accumulation occurred at any time during IP chemotherapy. To some extent, subcutaneous liquid accumulation was not avoidable, but the symptoms were relatively mild, so they did not delay the progression of IP chemotherapy. Similar to the previous report (16), we did not find obvious relationships between infection and gastrectomy (Table 1). Staphylococcus aureus, Escherichia coli or Klebsiella pneumoniae, which are resident bacteria of the skin and upper respiratory system, were found in the fester of some patients. Bacterial translocation, immunocompromise, bacterial contamination and drug reflux may be the causes of infection and should be studied in the future.

Other complications such as wound dehiscence, inflow obstruction and subcutaneous metastasis, did not cause serious consequences, and IP chemotherapy could be continued after treatment. Inflow obstruction and bowel fistula were reported as the main complications (16), but there was only one case in our study, which may be due to the fine diameter catheter used. The port we used was a large central venous access system with a more tenuous catheter than the abdominal access system. The system we used has several advantages for abdominal use. First, the port has a higher polysulfone base, which could be easily used compared with previous reports (11,22-24).

Analysis of risk factors for port complications

To find out which kind of port complications could be reduced by the optimization of implantation procedures, we analyzed all complications before and after optimization, and the results demonstrated that subcutaneous liquid accumulation could be reduced after implantation procedure optimization (Supplementary Table S3). Similarly, subcutaneous liquid accumulation could also be decreased in the specialized group (Supplementary Table S4).

For an in-depth understanding of the risk factors for the occurrence of port complications, we performed a logistic regression analysis to reveal risk factors. Logistic regression analysis demonstrated that ECOG performance status (OR, 1.74; 95% CI, 1.12–2.69), albumin (OR, 3.67; 95% CI, 1.96–6.86), implantation procedure (OR, 0.33; 95% CI, 0.18–0.61) and implantation groups (OR, 0.37; 95% CI, 0.20–0.69) were independent risk factors for port complications (Table 4).

Discussion

IP chemotherapy was originally used in ovarian cancer after tumor resection, so port complications were mostly reported in ovarian cancer (14,20). There are less reports about port complications in other tumors. Recently, Ishigami et al. reported GC patients with PM received port implantation and IP chemotherapy, and showed an improved survival rate for these patients (17,21). In addition, they also reported the occurrence of port complications (16). In total, 131 GC patients with PM who received IP PTX infusion were analyzed, and 24 patients experienced port complications. In these 24 cases, inflow obstruction and infection were the main complications, and subcutaneous liquid accumulation, subcutaneous masses, fistula also occurred (16). Importantly, the study

**Table 2** Interval between port implantation and port complications

| Complications               | Interval [median (range)] (month) | <1 month | 1–3 months | 3–6 months | 6–12 months | >12 months |
|-----------------------------|-----------------------------------|---------|------------|------------|-------------|------------|
| Infection                   | 3.3 (0.5–9.0)                     | 2       | 6          | 5          | 3           | 0          |
| Port rotation               | 2.6 (1.3–6.0)                     | 0       | 4          | 2          | 1           | 1          |
| Wound dehiscence            | 1.0 (0.5–26.0)                    | 1       | 4          | 0          | 1           | 1          |
| Inflow obstruction          | 2.0 (2.0)                         | 0       | 1          | 0          | 0           | 0          |
| Liquid accumulation         | 4.0 (0.5–16.0)                    | 2       | 12         | 3          | 5           | 2          |
| Subcutaneous metastasis     | 5.5 (5.5)                         | 0       | 0          | 0          | 1           | 0          |
| All complications           | 3.0 (0.5–26.0)                    | 5       | 27         | 10         | 11          | 4          |
Table 3 Grades of port complications and their correlation with clinical characteristics (N=57)

| Variables            | N | Complications [n (%)] |     |
|----------------------|---|-----------------------|-----|
|                      |   | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|                      |   |          |          |          |          |
| Sex                  |   |          |          |          |          |
| Male                 | 20 | 4 (7.0)  | 7 (12.3) | 2 (3.5)  | 7 (12.3) |
| Female               | 37 | 16 (28.1)| 5 (8.8)  | 5 (8.8)  | 11 (19.3)|
| Age (year)           |   |          |          |          |          |
| <60                  | 42 | 18 (31.6)| 6 (10.5) | 6 (10.5) | 12 (21.1)|
| ≥60                  | 15 | 2 (3.5)  | 6 (10.5) | 1 (1.8)  | 6 (10.5) |
| BMI (kg/m²)          |   |          |          |          |          |
| <23                  | 36 | 14 (24.6)| 8 (14.0) | 4 (7.0)  | 10 (17.5)|
| ≥23                  | 21 | 6 (10.5)| 4 (7.0)  | 3 (5.3)  | 8 (14.0) |
| ECOG PS              |   |          |          |          |          |
| 0                    | 11 | 9 (15.8)| 1 (1.8)  | 0 (0)    | 1 (1.8) |
| 1                    | 36 | 9 (15.8)| 8 (14.0) | 5 (8.8)  | 14 (24.6)|
| 2                    | 10 | 2 (3.5) | 3 (5.3)  | 2 (3.5)  | 3 (5.3) |
| PCI                  |   |          |          |          |          |
| 0–10                 | 9  | 2 (3.5) | 2 (3.5)  | 0 (0)    | 5 (8.8) |
| 11–20                | 20 | 9 (15.8)| 4 (7.0)  | 3 (5.3)  | 4 (7.0) |
| 21–39                | 28 | 9 (15.8)| 6 (10.5) | 4 (7.0)  | 9 (15.8)|
| Ascites              |   |          |          |          |          |
| Present              | 54 | 20 (35.1)| 11 (19.3)| 7 (12.3)| 16 (28.1)|
| Absent               | 3  | 0 (0)   | 1 (1.8)  | 0 (0)    | 2 (3.5) |
| Prior chemotherapy   |   |          |          |          |          |
| Present              | 19 | 6 (10.5)| 3 (5.3)  | 5 (8.8)  | 5 (8.8) |
| Absent               | 38 | 14 (24.6)| 9 (15.8)| 2 (3.5)  | 13 (22.8)|
| Simultaneous surgery |   |          |          |          |          |
| Yes                  | 1  | 0 (0)   | 0 (0)    | 0 (0)    | 1 (1.8) |
| No                   | 56 | 20 (35.1)| 12 (21.1)| 7 (12.3)| 17 (29.8)|
| Albumin (g/L)        |   |          |          |          |          |
| <35                  | 28 | 11 (19.3)| 5 (8.8)  | 3 (5.3)  | 9 (15.8)|
| ≥35                  | 29 | 9 (15.8)| 7 (12.3) | 4 (7.0)  | 9 (15.8)|
| Hemoglobin           |   |          |          |          |          |
| Anemia               | 35 | 11 (19.3)| 7 (12.3) | 4 (7.0)  | 13 (22.8)|
| Normal               | 22 | 9 (15.8)| 5 (8.8)  | 3 (5.3)  | 5 (8.8) |
| Glucose              |   |          |          |          |          |
| Euglycemia           | 50 | 20 (35.1)| 8 (14.0)| 6 (10.5) | 16 (28.1)|
| Hyperglycemia        | 7  | 0 (0)   | 4 (7.0)  | 1 (1.8)  | 2 (3.6) |
| Implantation approach|   |          |          |          |          |
| LS                   | 56 | 20 (35.1)| 12 (21.1)| 7 (12.3)| 17 (29.8)|
| Open                 | 1  | 0 (0)   | 0 (0)    | 0 (0)    | 1 (1.8) |
| Implantation period  |   |          |          |          |          |
| Before               | 38 | 15 (26.3)| 6 (10.5)| 5 (8.8)  | 12 (21.1)|
| After                | 19 | 5 (8.8) | 6 (10.5) | 2 (3.6)  | 6 (10.5) |
| Implantation group   |   |          |          |          |          |
| Specialized group    | 32 | 12 (21.1)| 6 (10.5)| 2 (3.6)  | 12 (21.1)|
| Other groups         | 25 | 8 (14.0)| 6 (10.5) | 5 (8.8)  | 6 (10.5) |

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; PCI, peritoneal cancer index; Yes, gastrectomy plus with port implantation; No, port implantation only; LS, laparoscopic exploration surgery; Open, port implanted with open surgery; Before, before the optimization of port implantation procedure; After, after the optimization of port implantation procedure; *, Mann-Whitney U test; **, Goodman-Kruskal Gamma test.
fine diameter catheter rarely generates bowel fistula and perforation. However, due to its fine diameter, it always moves in the abdominal cavity, and it is sometimes difficult to drain the small volume of ascites.

We first proposed the grading of port complications, and grades 1−4 were designed according to the degree of severity. We identified that infection caused the most cases of grade 4 complications, resulting in the port being removed or abandoned. Further analysis revealed that ECOG performance status was the only factor associated with the grade of complications (Table 3). ECOG performance status is a reliable indicator for the patient’s general condition, and ranges from 0 to 5 (25). In this study, we demonstrated that ECOG performance status was significantly associated with port complications (Table 4). It can be easily accepted that patients with a worse health status are prone to occur complications. Patients with high ECOG performance scores should have their physical conditions adjusted, such as applying enteral nutrition support and albumin infusion before port implantation. If the ECOG performance scores are too high to improve, the doctors should adjust their strategy and suggest adoption of systemic chemotherapies instead. Implantation procedure optimization was necessary as it obviously reduced port complications and was also an independent risk factor for port complications. Another important independent risk factor for complications was the implantation group. The specialized group had rich experience and may pay more attention to details such as the size of the subcutaneous cavity, the depth of subcutaneous fat, etc.

Interestingly, both procedure optimization and specialized group could reduce the occurrence of complication of subcutaneous liquid accumulation (Supplementary Table S3,S4). Furthermore, to prove that the specialized group experience was not affected by the procedure optimization, we analyzed the complications before and after the optimization, and the results demonstrated that regardless of whether the procedure was optimized, the specialized group was significantly associated with reduced port complications (Supplementary Table S5).

Conclusions

Subcutaneous implantation of port is feasible, and the complications are manageable. For the first time, we found that independent risk factors for port complications in GC with PM were ECOG performance status, albumin level, the implantation procedure and implantation groups. ECOG performance status is especially important, as it is
also correlated with the severity of port complications. So, we propose that an optimized implantation procedure should be a standard procedure that is generalized for use and the operator should be trained.

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**Footnote**

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

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Figure S1  Procedures of implanting and fixing port before optimization. (A) Port site was designed in the right or left lower abdomen; (B,C) Skin incision and subcutaneous cavity were made to accommodate the port base and catheter; (D) Entrance of catheter into aponeurosis was fixed; (E,F) Catheter was placed in the pelvic cavity.

Figure S2  Typical pictures of port complications. (A,B) Infection of ports; (C,D) Subcutaneous liquid accumulation of ports; (E,F) Rotation and tilt of ports; (G,H) Wound dehiscence of ports; (I) Catheter wound around the port base and induced obstruction; (J) Metastasis of port site.
| Variables                        | N Without | Infection With | Rotation With | Dehiscence With | Obstruction With | Liquid With | Metastasis With |
|---------------------------------|-----------|----------------|---------------|-----------------|------------------|-------------|-----------------|
| Sex                             |           | With P         | With P        | With P          | With P           | With P      | With P          |
| Male                            | 109       | 0.49           | 0.62          | 0.86            | 0.28             | 0.11        | 0.35            |
| Female                          | 140       |                |               |                 |                  |             |                 |
| Age (year)                      |           | 0.87           | 0.18          | 0.71            | 0.46             | 0.31        | 0.46            |
| <60                             | 166       | 0.07           | 0.18          | 0.42            | 0.53             | 0.60        | 0.53            |
| ≥60                             | 83        |                |               |                 |                  |             |                 |
| BMI (kg/m²)                     |           | 0.07           | 0.18          | 0.42            | 0.53             | 0.60        | 0.53            |
| ECOG PS                         |           | 0.01           | 0.21          | 0.01            | 0.49             | 0.04        | 0.49            |
| PCI                             |           | 0.67           | 0.52          | 0.21            | 0.54             | 0.12        | 0.56            |
| Simultaneous surgery            |           | 0.38           | 0.53          | 0.56            | 0.83             | 0.91        | 0.83            |
| Glucose                         |           | 0.06           | 0.63          | 0.14            | 0.33             | 0.50        | 0.33            |
| Hemoglobin                      |           | 0.07           | 0.53          | 0.24            | 0.33             | 0.50        | 0.33            |
| Anemia                          |           | 0.06           | 0.63          | 0.14            | 0.33             | 0.50        | 0.33            |
| Normal                          | 116       | 0.22           | 0.14          | 0.76            | 0.70             | 0.76        |                 |
| Hyperglycemia                   | 24        | 0.15           | 0.50          | 0.33            | 0.50             | 0.33        |                 |
| Glucose                         |           | 0.06           | 0.63          | 0.14            | 0.33             | 0.50        | 0.33            |
| Hyperglycemia                   | 24        | 0.15           | 0.50          | 0.33            | 0.50             | 0.33        |                 |
| Infection                       |           | 0.66           | 0.58          | 0.61            | 0.85             | 0.90        | 0.85            |
| Rotation                        |           | 0.08           | 0.70          | 0.14            | 0.33             | 0.50        | 0.33            |
| Dehiscence                      |           | 0.07           | 0.53          | 0.24            | 0.33             | 0.50        | 0.33            |
| Obstruction                     |           | 0.06           | 0.63          | 0.14            | 0.33             | 0.50        | 0.33            |
| Liquid                          |           | 0.66           | 0.58          | 0.61            | 0.85             | 0.90        | 0.85            |
| Metastasis                      |           | 0.66           | 0.58          | 0.61            | 0.85             | 0.90        | 0.85            |

BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; PCI, peritoneal cancer index; Yes, gastrectomy plus with port implantation; No, port implantation only; LS, laparoscopic exploration surgery; Open, port implanted with open surgery; Before, before the optimization of port implantation procedure; After, after the optimization of port implantation procedure.
### Table S2 Grading of port complications

| Complications         | Grade (n) | 1 | 2 | 3 | 4 | [n (%)] |
|-----------------------|-----------|---|---|---|---|---------|
| Infection             |           | 0 | 3 | 4 | 9 | 16 (28.1) |
| Port rotation         |           | 5 | 2 | 0 | 1 | 8 (14.0)  |
| Wound dehiscence      |           | 0 | 4 | 1 | 2 | 7 (12.3)  |
| Inflow obstruction    |           | 0 | 0 | 0 | 1 | 1 (1.8)   |
| Liquid accumulation   |           | 15| 3 | 2 | 4 | 24 (42.1) |
| Subcutaneous metastasis|        | 0 | 0 | 0 | 1 | 1 (1.8)   |

### Table S3 Port complications in groups before and after implantation procedure optimization

| Complications         | Before optimized | After optimized | P   |
|-----------------------|------------------|-----------------|-----|
|                       | With             | Without         | With | Without |
| Infection             | 9                | 105             | 7    | 128     | 0.385 |
| Port rotation         | 5                | 109             | 3    | 132     | 0.335 |
| Wound dehiscence      | 5                | 109             | 2    | 133     | 0.167 |
| Inflow obstruction    | 1                | 113             | 0    | 135     | 0.458 |
| Liquid accumulation   | 17               | 97              | 7    | 128     | 0.010 |
| Subcutaneous metastasis| 1             | 113             | 0    | 135     | 0.458 |

### Table S4 Port complications in specialized treatment group and other groups

| Complications         | Specialized group | Other groups | P   |
|-----------------------|-------------------|--------------|-----|
|                       | With              | Without      | With | Without |
| Infection             | 11                | 170          | 5    | 63      | 0.715 |
| Port rotation         | 4                 | 177          | 4    | 64      | 0.143 |
| Wound dehiscence      | 3                 | 178          | 4    | 64      | 0.072 |
| Inflow obstruction    | 1                 | 180          | 0    | 68      | 0.539 |
| Liquid accumulation   | 12                | 169          | 12   | 56      | 0.009 |
| Subcutaneous metastasis| 1              | 180          | 0    | 68      | 0.539 |

### Table S5 Relationship between implantation group and port complications

| Groups                | With complications | Without complications | P   |
|-----------------------|--------------------|------------------------|-----|
| Before optimization   |                    |                        | 0.048 |
| Specialized group     | 21                 | 56                     |     |
| Other groups          | 17                 | 20                     |     |
| After optimization    |                    |                        | 0.032 |
| Specialized group     | 11                 | 93                     |     |
| Other groups          | 8                  | 23                     |     |