The Clinical Desire for Pressurized Intraperitoneal Aerosol Chemotherapy in South Korea: An Electronic Survey-based Study

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Abstract

Background: Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is effective for treating peritoneal metastasis. However, it is currently used in the limited areas. Thus, we performed a survey to evaluate the clinical desire for PIPAC in South Korea, one of the many countries where PIPAC has not yet been introduced.

Methods: We performed an online survey between November and December 2019. The questionnaire consisted of 20 questions, which were divided into comprehensive, procedure, and cost inquiries including five, 13 and two questions, respectively.

Results: A total of 164 respondents who answered the questionnaire. Among respondents, 41.7-50% majoring in ovarian cancer, pseudomyxoma peritonei, and malignant mesothelioma preferred PIPAC for the curative treatment of primary diseases, whereas 32.7-33.3% majoring in colorectal and hepatobiliary cancers chose it for the palliative treatment of recurrent diseases. Moreover, 66.7-95.2% considered PIPAC appropriate for the cancers the specialized in, and 76-78.7% expected a treatment response of more than 50% and considered grade 1 or 2 minor surgical complications acceptable. Finally, most of the respondents answered the reasonable costs to purchase and implement PIPAC once at between 1,000,000-5,000,000 KRW.

Conclusions: This surgery may reflect on the availability, scope, and reasonable cost of PIPAC treatment in South Korea for introducing PIPAC.

Background

Peritoneal metastasis (PM) is commonly accompanied by a variety of solid tumors showing drug resistance to intravenous (IV) chemotherapy, which leads to a poor prognosis [1-3]. To try to overcome the limitations of IV chemotherapy, the effects and safety of intraperitoneal (IP) chemotherapy and hyperthermic intraperitoneal chemotherapy (HIPEC) have been investigated in solid tumor patients with PM. However, the effects of these therapies are still controversial [4-7], and renal and hepatic toxicities, a lack of relevant IP administration cycles and the required one-time administration after cytoreductive surgery are considered as disadvantages in IP chemotherapy and HIPEC [8].

On the other hand, pressurized intraperitoneal aerosol chemotherapy (PIPAC) delivers chemotherapeutic agents as an aerosol formed by a high-pressure injector at room temperature. Chemotherapeutic agents equivalent to 10% of those used in IV chemotherapy are effectively spread diffusely throughout the abdominal cavity by PIPAC, but tissue concentrations are maintained up to 200 times that of IV chemotherapy [9]. Moreover, PIPAC can be conducted repeatedly with more diffuse distribution, deeper penetration, and fewer toxicities than IP chemotherapy and HIPEC [10, 11]. Nevertheless, PIPAC is currently considered primarily a palliative treatment [12] and is only available in the limited areas including European countries and Singapore [13].

A survey evaluating the clinical application and scope of PIPAC in countries where PIPAC has not been introduced is essential to establish the required medical foundation for future introduction. Thus, we performed a survey of surgical oncologists related to PIPAC to evaluate the clinical desire for PIPAC in South Korea.

Methods

Participation

This study was approved by the Institutional Review Board of Seoul National University Hospital in advance (No. 1907-054-104). We surveyed surgical oncologists from the following four societies between November and December 2019: the Korean Society of Gynecologic Oncology (http://www.sgo.or.kr/); the Korean Society of Surgical Oncology (http://www.sisso.or.kr/); the Korean Surgical Society (https://www.surgery.or.kr/); and the Korean Association of Hepato-Biliary-Pancreatic Surgery (http://www.kahbps.or.kr/).

Study design

The questionnaire consisted of 20 questions related to PIPAC, which were divided into the following categories: comprehensive inquiry (five questions), procedure inquiry (13 questions), and cost inquiry (two questions). The comprehensive inquiry included the following questions: How long do you have experience in treating solid tumors with PM as a surgical oncologist; what kind of hospital do you belong to; what types of solid tumors with PM do you treat mainly; how many solid tumor patients with PM do you treat annually; and what type of treatment do you approach for treating solid tumors with PM.

Moreover, the procedure inquiry included questions as follows: if you apply PIPAC for treating solid tumors with PM, what point in the course of disease progression would you consider using PIPAC; when you consider PIPAC for treating primary diseases, to what extent of disease would you consider applying PIPAC; when considering PIPAC for treating primary diseases with PM, would you consider neoadjuvant chemotherapy before PIPAC; what types of solid tumors with PM do you think that PIPAC can be applied to; do advantages such as high

concentration in tissues with less drug and lower toxicities factor into the decision to use PIPAC; what factors do you think must preceded PIPAC introduction; what types and severities of complications would be considered reasonable from using PIPAC; do you think that it is appropriate to implement PIPAC repeatedly; do you think general anesthesia for 30 minutes to two hours is acceptable for performing PIPAC; what treatment response percentage would you expect from using PIPAC; what is the most critical factor that hinders the proper effect of PIPAC; and what do you think is the current level of evidence for the effects of PIPAC. Finally, the cost inquiry included questions about the reasonable cost of purchasing and implementing PIPAC (Table 1).

Statistical analysis

This survey was taken through the Elimnet Corporation (https://www.nownsurvey.com/), a commercially available web-based survey platform. All categorical variables were analyzed using the Chi-squared or Fisher's exact test. For the statistical analyses, we used SPSS software version 21.0 (SPSS Inc., Chicago, IL, USA).

This study was carried out in accordance with relevant guidelines.te the clinical desire for PIPAC in South Korea.

Results

Comprehensive inquiry

A total of 164 respondents answered the questionnaire, and 62 (37.8%), 55 (33.5%), 52 (31.7%), 48 (29.3%), 27 (16.5%), and four respondents (2.4%) treated PM accompanied by ovarian cancer, gastric cancer, colorectal cancer, pseudomyxoma peritonei, hepatobiliary cancer, malignant mesothelioma, and others.

About 60% of the respondents had more than ten years of experience and worked at university hospitals. Moreover, about 40% of the respondents said they treated more than ten solid tumor patients with PM annually and take a multidisciplinary treatment approach. However, there were no differences in periods of experience, working hospitals, and numbers of patients treated annually among the various surgical oncologists. In terms of treatment approach, the respondents majoring in gastric cancer (41.8%), colorectal cancer (50%), pseudomyxoma peritonei (37.5%), and hepatobiliary cancer (33.3%) preferred the multidisciplinary approach. In contrast, those majoring in ovarian cancer (33.9%) and malignant mesothelioma (44.4%) chose to plan their treatment by themselves (Table 2).

Procedure inquiry

In relation to the course of disease progression and the suitable point for PIPAC, 41.7-50% of respondents majoring in ovarian cancer, pseudomyxoma peritonei, and malignant mesothelioma preferred PIPAC as a curative treatment for primary diseases, whereas 32.7-33.3% of those majoring in colorectal and hepatobiliary cancers preferred PIPAC as a palliative treatment for recurrent diseases.

Moreover, 65.5% of respondents answered that advanced-stage disease among primary diseases was suitable for applying PIPAC and 55.2% would consider neoadjuvant chemotherapy before PIPAC. In particular, 66.7-95.2% of respondents answered that the cancers they majored in were appropriate for PIPAC, and 87.2% considered the advantages of high concentration in tissues and lower toxicity as decisive factors for choosing PIPAC. However, 65.5% of respondents considered results from randomized trials prerequisite for introducing PIPAC. Approximately 70% of respondents stated that they expected a treatment response of more than 50% through repeated implementation of PIPAC, and that grade 1 or 2 minor surgical complications were acceptable. About 60% of respondents answered that the patient's general status was the most important factor hindering the effect of PIPAC, and that the current level of evidence for the therapeutic effects of PIPAC was low.

However, there were no differences in the extents of primary diseases considered suitable for PIPAC treatment, the potential need for neoadjuvant chemotherapy, the decisive factors for using PIPAC, the prerequisites for introducing PIPAC, types and severities of tolerable complications, acceptability for implementing PIPAC under general anesthesia, and the expected percentage of treatment response among the various surgical oncologists (Table 3).

Cost inquiry

Most respondents answered that the reasonable cost to purchase and implement PIPAC once was between 1,000,000-5,000,000 KRW. There were no differences in the reasonable expenses to purchase and implement PIPAC among the various surgical oncologists (Table 4).

Discussion

This study was conducted to evaluate the clinical desire for PIPAC in South Korea, one of the countries where PIPAC has not yet been introduced. Through our survey, we identified the potential availability and scope of PIPAC, the expected effects and toxicity, and the expected

reasonable cost of PIPAC in South Korea.

Although PIPAC is readily used to treat PM in Europe, its use does not come without concerns. First, the relevant studies are heterogeneous concerning patients and clinical indications. Second, the assessments of treatment response differed considerably among the relevant studies. Third, the appropriate endpoints to evaluate the effect of PIPAC, such as survival, quality of life, and ascites control are ambiguous [12]. In the absence of randomized controlled trials, the clinical desire for PIPAC is expected to differ according to the medical environment of each country.

We found that the availability and scope of PIPAC were different among different types of Korean surgical oncologists. Many respondents majoring in ovarian cancer, pseudomyxoma peritonei, and malignant mesothelioma preferred PIPAC for the curative treatment of primary diseases. In contrast, those majoring in colorectal and hepatobiliary cancers chose PIPAC for the palliative treatment of recurrent diseases. These findings are similar to the results from studies related to IP chemotherapy and HIPEC. In these studies, IP chemotherapy and HIPEC improved the prognosis of ovarian cancer [6, 7], pseudomyxoma peritonei [14, 15], and malignant mesothelioma [16, 17]. In contrast, they did not show any definitive effects for treating colorectal and hepatobiliary cancers [4, 18]. This suggests Korean surgical oncologists may consider applying PIPAC in conditions similar to those that warrant IP chemotherapy and HIPEC.

Despite these differences, 66.7-95.2% of respondents considered the cancers they majored in appropriate for PIPAC. Moreover, about 70% expected a treatment response of more than 50% through repeated implementation of PIPAC and considered grade 1 or 2 minor surgical complications acceptable. These findings are in line with data from previous studies where the rate of clinical response was 36-80% and grade 3 or 4 adverse events were observed in only 12-15% of procedures [12]. These data suggest that the medical needs of Korean oncologists prior to the introduction of PIPAC are likely similar to those of their European counterparts.

Furthermore, what was considered the reasonable costs to purchase and implement PIPAC once was between 1,000,000-5,000,000 KRW, equivalent to about 1,000-5,000 USD. This is about 20-50% of the cost of implementing HIPEC and about 5-10% of the cost for purchasing it in South Korea, which seemed to be determined by considering the repeated implementation of PIPAC. However, these costs will change over time with new domestic medical devices and the status of insurance markets.

All studies have limitations and ours is no exception. First, the number of specialists who could reply appropriately to this survey from each society could not be confirmed due to the Personal Information Protection Act. Considering the e-mail was sent to all members including residents, general doctors, and specialists, we could not estimate the response rates of only specialists in this study. Second, this survey was conducted exclusively on surgical oncologists. For more meaningful results, the survey should also be performed on medical oncologists who treat solid tumors with PM. Third, it may be unreasonable to consider these results similar to those from other countries where PIPAC has not been introduced because the medical environment may be very different.

Conclusions

This is the first study to investigate the clinical desire for PIPAC in countries where PIPAC has not yet been introduced. Based on the results from this study, we believe that the introduction of PIPAC will help to further establish the availability, scope, and reasonable cost of PIPAC treatment.

Declarations

Acknowledgments

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Authors' contributions

EJL: Data curation, Formal analysis, Investigation, Writing - original draft. SJP: Data curation, Formal analysis, Investigation. JM: Data curation, Investigation. HP: Data curation, Investigation. JL: Data curation, Investigation. AS: Data curation. JK: Data curation, Investigation. NL: Data curation, Investigation. SJC: Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Writing - original draft, Writing - review & editing. HSK: Conceptualization, Data curation, Formal analysis, Investigation, Supervision, Writing - original draft, Writing - review & editing.

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Availability of data and materials

The dataset analyzed during the current study are available from the corresponding author on reasonable request, because the survey was conducted with guaranteed anonymity.

Ethics approval and consent to participate

Seoul National University Hospital Institutional Review Board (IRB) approved this study (No. 1907-054-104). The IRB waived the participants' consent. However, prior to the survey, consent to participation in the study and utilization of the survey results was additionally confirmed, and through this, it was confirmed that written consent was replaced.

Consent for publication

Not applicable.

Conflicts of Interest

The authors report no conflicts of interest.

Abbreviations

PIPAC: Pressurized intraperitoneal aerosol chemotherapy; PM: Peritoneal metastasis; IV: Intravenous; IP: Intraperitoneal; HIPEC: Hyperthermic intraperitoneal chemotherapy

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Tables

e 1. Questionnaire related to pressurized intraperitoneal aerosol chemotherapy for surgical oncologists in South Korea

Questions	Answers
nprehensive inquiry	
How long do you have experience in treating solid tumors with PM as a surgical oncologist?	☐ <5 years ☐ 5 – 10 years ☐ >10 years
What kind of hospital do you belong to?	☐ University hospital ☐ General hospital ☐ Semi hospital ☐ Cancer hospital
What types of solid tumors with PM do you treat mainly? (multiple selections is possible)	☐ Ovarian cancer ☐ Gastric cancer ☐ Colorectal cancer ☐ Pseudomyxoma peritonei ☐ Hepatobiliary cancer ☐ Malignant mesothelioma ☐ Others: _____
How many solid tumor patients with PM do you treat annually?	☐ <5 ☐ 5 – 10 ☐ 10 – 30 ☐ 30 – 50 ☐ >50
What type of treatment do you approach for treating solid tumors with PM?	☐ Multidisciplinary approach ☐ Consultation to medical oncologists ☐ Consultation to other surgical oncologists ☐ Sole care ☐ Transfer to other hospitals ☐ Others: _____
cedure inquiry	
If you apply PIPAC for treating solid tumors with PM, what point in the course of disease progression would you consider using PIPAC?	☐ Primary disease, curative ☐ Primary disease, palliative ☐ Recurrent disease, curative ☐ Recurrent disease, palliative ☐ Not applicable ☐ Not sure
When you consider PIPAC for treating primary diseases, to what extent of disease would you consider applying PIPAC?	☐ Early-stage ☐ Advanced stage ☐ Both early and advanced stages ☐ Not sure
When considering PIPAC for treating primary diseases with PM, would you consider neoadjuvant chemotherapy before PIPAC?	☐ Yes ☐ No ☐ Not sure
What types of solid tumors with PM do you think that PIPAC can be applied to? (multiple selections is possible)	☐ Ovarian cancer ☐ Gastric cancer ☐ Colorectal cancer ☐ Pseudomyxoma peritonei ☐ Hepatobiliary cancer

	☐ Malignant mesothelioma ☐ Others: _____
Do advantages such as high concentration in tissues with less drug and lower toxicities factor into the decision to use PIPAC?	☐ Yes ☐ No ☐ Not sure
What factors do you think must be preceded PIPAC introduction?	☐ Updates of treatment guidelines ☐ Reports of results from randomized trials ☐ Collaboration with specialists for IP chemotherapy ☐ Reduction of complications related to IP chemotherapy ☐ Others: _____
PIPAC is expected to have fewer complications than other types of IP chemotherapy. But all treatments have complications and PIPAC is no exception. What level of complications would you consider using PIPAC?	☐ Minor surgical complications such as postoperative pain, infection, and minor bleeding ☐ Major surgical complications such as perforation and leakage at anastomotic sites ☐ Hematologic toxicities ☐ Non-hematologic toxicities
What severity of complication from PIPAC would you consider using PIPAC at? (based on the CTCAE version 5.0)	☐ Grade 1 ☐ Grade 2 ☐ Grade 3 ☐ Possible regardless of complications ☐ Impossible regardless of complications
PIPAC is known to be repeated an average of four to six cycles to maximize the treatment response. Do you think that it is appropriate to implement PIPAC repeatedly?	☐ Acceptable if effective ☐ Willing to use it if reduced cycles ☐ Possible if only one cycle ☐ Not sure
PIPAC is performed laparoscopically under general anesthesia for 30 minutes to two hours. Do you think general anesthesia for 30 minutes to two hours is acceptable for performing PIPAC?	☐ Acceptable if patients are stable ☐ Acceptable if local or spinal anesthesia ☐ Impossible if general anesthesia is required every cycle ☐ Not sure
According to the research results, the response rate of PIPAC is known to range from 20% to 80%. What treatment response percentage would you expect from using PIPAC?	☐ >80% ☐ >50% ☐ >20% ☐ Possible regardless of response rates
What is the most critical factor that hinders the proper effect of PIPAC?	☐ Performance status of patients ☐ Suboptimal debulking surgery ☐ Burden of repetitive surgery ☐ Use of agents resistant to IV chemotherapy ☐ Others: _____
What do you think is the current level of evidence for the effects of PIPAC?	☐ Low level, and not effective ☐ Low level, but effective

	☐ High level, and effective ☐ Not sure
t inquiry	
What do you think is the reasonable cost to purchase a medical device for PIPAC?	☐ <1,000,000 KRW ☐ 1,000,000 – 5,000,000 KRW ☐ 5,000,000 – 10,000,000 KRW ☐ 10,000,000 – 50,000,000 KRW ☐ >50,000,000 KRW
How much do you think is the reasonable cost to implement PIPAC once?	☐ <1,000,000 KRW ☐ 1,000,000 – 5,000,000 KRW ☐ 5,000,000 – 10,000,000 KRW ☐ >10,000,000 KRW

·eviations: CTCAE, Common Terminology Criteria for Adverse Events; IP, intraperitoneal; IV, intravenous; PIPAC, surized intraperitoneal aerosol chemotherapy; PM, peritoneal metastasis.

ıble 2. Answers to the comprehensive inquiry

Answers	Total (n=164, %)	Ovarian cancer (n=62, %)	Gastric cancer (n=55, %)	Colorectal cancer (n=52, %)	Pseudomyxoma peritonei (n=48, %)	Hepatobiliary cancer (n=27, %)	Malignant mesothelioma (n=9, %)	Others* (n=4, %)	*P* value
riods of experience in treating solid tumors with PM									0.098
<5 years	38 (23.2)	11 (17.7)	12 (21.8)	16 (30.8)	7 (14.6)	9 (33.3)	1 (11.2)	1 (25)	
5-10 years	31 (18.9)	15 (24.2)	8 (14.6)	10 (19.2)	17 (35.4)	2 (7.4)	4 (44.4)	0 (0)	
> 10 years	95 (57.9)	36 (58.1)	35 (63.6)	26 (50)	24 (50)	16 (59.3)	4 (44.4)	3 (75)	
orking hospitals									0.578
University hospitals	101 (61.6)	38 (61.3)	27 (49.1)	28 (53.8)	31 (64.6)	18 (66.7)	8 (88.9)	4 (100)	
General hospitals	48 (29.3)	19 (30.6)	21 (38.2)	17 (32.7)	14 (29.2)	5 (18.5)	0 (0)	0 (0)	
emi hospitals	9 (5.5)	3 (4.8)	3 (5.5)	5 (9.6)	1 (2.1)	2 (7.4)	1 (11.1)	0 (0)	
ncer hospitals	6 (3.7)	2 (3.2)	4 (7.3)	2 (3.8)	2 (4.2)	2 (7.4)	0 (0)	0 (0)	
mbers of solid tumor patients with PM treated annually									0.254
< 5	25 (31.7)	19 (30.6)	18 (32.7)	20 (38.5)	14 (29.2)	13 (48.1)	2 (22.2)	0 (0)	
5-10	44 (26.8)	15 (24.2)	16 (29.1)	14 (26.9)	11 (22.9)	7 (25.9)	0 (0)	2 (50)	
10-30	44 (26.8)	18 (29)	14 (25.5)	12 (23.1)	15 (31.2)	4 (14.8)	3 (33.3)	0 (0)	
30-50	12 (7.3)	7 (11.3)	3 (5.5)	2 (3.8)	4 (8.3)	2 (7.4)	1 (11.1)	0 (0)	
> 50	12 (7.3)	3 (4.8)	4 (7.3)	4 (7.7)	4 (8.3)	1 (3.7)	3 (33.3)	2 (50)	
Treatment approach									<0.001
ıltidisciplinary approach	65 (39.6)	18 (29)	23 (41.8)	26 (50)	18 (37.5)	9 (33.3)	3 (33.3)	1 (25)	
onsultation to medical oncologists	26 (15.9)	2 (3.2)	13 (23.6)	5 (9.6)	3 (6.3)	13 (48.1)	0 (0)	1 (25)	
onsultation to ther surgical oncologists	33 (20.1)	20 (32.3)	5 (9.1)	12 (23.1)	16 (33.3)	3 (11.1)	2 (22.2)	0 (0)	
Sole care	38 (23.2)	21 (33.9)	13 (23.6)	8 (15.4)	10 (20.8)	2 (7.4)	4 (44.4)	2 (50)	
Transfer to ther hospital	2 (1.2)	1 (1.6)	1 (1.8)	1 (1.9)	1 (2.1)	0 (0)	0 (0)	0 (0)	

reviations: PIPAC, pressurized intraperitoneal aerosol chemotherapy; PM, peritoneal metastasis.

rvix and uterine cancers (n=1); cervical cancer and peritoneal metastasis with other origins (n=2); cervical cancer and coma (n=1).

ble 3. Answers to the procedure inquiry

Answers	Total (n=164, %)	Ovarian cancer (n=62, %)	Gastric cancer (n=55, %)	Colorectal cancer (n=52, %)	Pseudomyxoma peritonei (n=48, %)	Hepatobiliary cancer (n=27, %)	Malignant mesothelioma (n=9, %)	Others* (n=4, %)	*P* value
ints in the course of disease progression suitable to PIPAC									0.018
Primary disease, curative	58 (35.4)	31 (50)	17 (30.9)	8 (15.4)	20 (41.7)	4 (14.8)	4 (44.4)	0 (0)	
Primary disease, palliative	27 (16.5)	5 (8.1)	12 (21.8)	14 (26.9)	3 (6.3)	8 (29.6)	2 (22.2)	0 (0)	
Recurrent disease, curative	18 (11)	6 (9.7)	7 (12.7)	10 (19.2)	7 (14.6)	2 (7.4)	0 (0)	0 (0)	
Recurrent disease, palliative	47 (28.7)	15 (24.2)	17 (30.9)	17 (32.7)	14 (27.1)	9 (33.3)	2 (22.2)	3 (75)	
ɔt applicable	6 (3.7)	3 (4.8)	1 (1.8)	1 (1.9)	2 (4.2)	1 (3.7)	1 (11.1)	0 (0)	
Not sure	8 (4.9)	2 (3.2)	1 (1.8)	2 (3.8)	3 (6.3)	3 (11.1)	0 (0)	1 (25)	
tents of primary diseases suitable to PIPAC									0.682
Early stage	4 (6.9)	3 (9.7)	1 (5.9)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	
Advanced stage	38 (65.5)	18 (58.1)	13 (76.5)	7 (87.5)	15 (75)	2 (50)	4 (100)	0 (0)	
ɔth early and advanced stages	16 (27.6)	10 (32.3)	3 (17.6)	1 (12.5)	4 (20)	2 (50)	0 (0)	0 (0)	
ed for neoadjuvant chemotherapy before PIPAC									0.303
Yes	32 (55.2)	13 (41.9)	13 (79.5)	6 (75)	12 (60)	2 (50)	1 (25)	0 (0)	
No	17 (29.3)	10 (32.3)	3 (17.6)	2 (25)	6 (30)	2 (50)	2 (50)	0 (0)	
Not sure	9 (15.5)	8 (25.8)	1 (5.9)	0 (0)	2 (10)	0 (0)	1 (25)	0 (0)	
pes of solid tumors with peritoneal neoplasms that PIPAC can be applied									<0.01
arian cancer	123 (75)	59 (95.2)	33 (60)	29 (55.8)	39 (81.3)	17 (63)	8 (88.9)	0 (0)	
Stomach cancer	82 (50)	12 (19.4)	50 (90.9)	33 (63.5)	19 (39.6)	13 (48.1)	7 (77.8)	0 (0)	
Colorectal cancer	93 (56.7)	20 (32.3)	40 (72.7)	48 (92.3)	24 (50)	16 (59.3)	6 (66.7)	0 (0)	
eudomyxoma peritonei	119 (72.6)	49 (79)	33 (60)	35 (67.3)	43 (89.6)	16 (59.3)	6 (66.7)	0 (0)	
epatobiliary cancer	32 (19.5)	9 (14.5)	10 (18.2)	11 (21.2)	5 (10.4)	19 (70.4)	2 (22.2)	0 (0)	
Malignant esothelioma	50 (30.5)	20 (32.3)	15 (27.3)	12 (23.1)	17 (35.4)	3 (11.1)	6 (66.7)	0 (0)	
ssibility to consider the advantage of high concentration in tissues and fewer toxicities as decisive factors for ing PIPAC									0.08
Yes	143 (87.2)	52 (83.9)	52 (94.5)	47 (90.4)	38 (79.2)	24 (88.9)	5 (55.6)	2 (50)	
No	9 (5.5)	3 (4.8)	2 (3.6)	2 (3.8)	3 (6.3)	1 (3.7)	2 (22.2)	1 (25)	
Not sure	12 (7.3)	7 (11.3)	1 (1.8)	3 (5.8)	7 (14.6)	2 (7.4)	2 (22.2)	1 (25)	
erequisites for introducing PIPAC									0.61

Update of treatment guidelines	34 (20.7)	15 (24.2)	10 (18.2)	10 (19.2)	10 (20.8)	5 (18.5)	3 (33.3)	1 (25)	
Reports of esults from andomized trials	107 (65.2)	52 (67.7)	33 (60)	34 (65.4)	30 (62.5)	17 (63)	6 (66.7)	2 (50)	
ollaboration th specialists for IP iemotherapy	10 (6.1)	3 (4.8)	5 (9.1)	6 (11.5)	2 (4.2)	3 (11.1)	0 (0)	0 (0)	
Reduction of omplications elated to IP iemotherapy	13 (7.9)	2 (3.2)	7 (12.7)	2 (3.8)	6 (12.5)	2 (7.4)	0 (0)	1 (25)	
pes of tolerable complications considerable to use PIPAC									0.94
inor surgical mplications†	118 (72)	44 (71)	42 (76.4)	36 (69.2)	38 (79.2)	19 (70.4)	7 (77.8)	3 (75)	
ajor surgical mplications‡	18 (11)	7 (11.3)	4 (7.3)	8 (15.4)	6 (12.5)	3 (11.1)	1 (11.1)	1 (25)	
Hematologic toxicities	23 (14)	10 (16.1)	8 (14.5)	5 (9.6)	2 (4.2)	4 (14.8)	1 (11.1)	0 (0)	
Non-iematologic toxicities	5 (3)	1 (1.6)	1 (1.8)	3 (5.8)	2 (4.2)	1 (3.7)	0 (0)	0 (0)	
verities of tolerable complications considerable to use PIPAC (based on the CTCAE version 5.0)									0.65
Grade 1	67 (40.9)	23 (37.1)	27 (49.1)	20 (38.5)	22 (45.8)	15 (55.6)	5 (55.6)	3 (75)	
Grade 2	62 (37.8)	24 (38.7)	18 (32.7)	22 (42.3)	15 (31.3)	10 (37)	2 (22.2)	1 (25)	
Grade 3	29 (17.7)	15 (24.2)	7 (12.7)	8 (15.4)	9 (18.8)	1 (3.7)	2 (22.2)	0 (0)	
Possible egardless of omplications	6 (3.7)	0 (0)	3 (5.5)	2 (3.8)	2 (4.2)	1 (3.7)	0 (0)	0 (0)	
Impossible egardless of omplications	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
ceptability for implementing PIPAC repeatedly									<0.01
cceptable if effective	116 (70.7)	40 (64.5)	43 (78.2)	37 (71.2)	36 (75)	19 (70.4)	7 (77.8)	0 (0)	
lling to use it if reduced cycles	27 (16.5)	9 (14.5)	8 (14.5)	10 (19.2)	4 (8.3)	5 (18.5)	0 (0)	0 (0)	
ssible if only one cycle	14 (8.5)	9 (14.5)	2 (3.6)	2 (3.8)	5 (10.4)	3 (11.1)	1 (11.1)	4 (100)	
Not sure	7 (4.3)	7 (4.3)	2 (3.6)	3 (5.8)	3 (6.3)	0 (0)	1 (11.1)	0 (0)	
ceptability for implementing PIPAC under general anesthesia									0.08
cceptable if atients are stable	111 (67.7)	34 (54.8)	42 (76.4)	36 (69.2)	34 (70.8)	21 (77.8)	5 (55.6)	4 (100)	
cceptable if cal or spinal anesthesia	30 (18.3)	16 (25.8)	6 (10.9)	11 (21.2)	9 (18.8)	3 (11.1)	0 (0)	0 (0)	
mpossible if	16 (9.8)	8 (12.9)	4 (7.3)	3 (5.8)	4 (8.3)	3 (11.1)	4 (44.4)	0 (0)	

general nesthesia is quired every cycle									
Not sure	7 (4.3)	4 (6.5)	3 (5.5)	2 (3.8)	1 (2.1)	0 (0)	0 (0)	0 (0)	
eatmet response percentage considerable for using PIPAC									0.94
> 80%	22 (13.4)	9 (14.5)	7 (12.7)	11 (21.2)	5 (10.4)	4 (14.8)	1 (11.1)	0 (0)	
> 50%	119 (72.6)	41 (66.1)	39 (70.9)	34 (65.4)	34 (70.8)	18 (66.7)	5 (55.6)	3 (75)	
> 20%	21 (12.8)	11 (17.7)	9 (16.4)	6 (11.5)	7 (14.6)	5 (18.5)	3 (33.3)	1 (25)	
Possible egardless of sponse rates	2 (1.2)	1 (1.6)	0 (0)	1 (1.9)	2 (4.2)	0 (0)	0 (0)	0 (0)	
e most impediment to the proper effectiveness of PIPAC									0.24
eneral status of patients	93 (56.7)	27 (43.5)	38 (69.1)	35 (67.3)	30 (62.5)	18 (66.7)	6 (66.7)	4 (100)	
Suboptimal debulking surgery	32 (19.5)	19 (30.6)	5 (9.1)	6 (11.5)	6 (12.5)	4 (14.8)	0 (0)	0 (0)	
he burden of performing repetitive surgery	29 (17.8)	13 (21.1)	8 (14.5)	9 (17.3)	7 (14.5)	4 (14.8)	1 (11.1)	0 (0)	
Use of drugs sistant to IV hemotherapy	5 (3)	1 (1.6)	3 (5.5)	1 (1.9)	2 (4.2)	0 (0)	1 (11.1)	0 (0)	
Others‖	5 (3)	2 (3.2)	1 (1.8)	1 (1.9)	3 (6.3)	1 (3.7)	1 (11.1)	0 (0)	
vels of evidence for the effects of PIPAC									0.06
ow level, and ot effective	39 (23.8)	15 (24.2)	14 (25.5)	9 (17.3)	8 (16.7)	13 (48.1)	3 (33.3)	1 (25)	
ow level, but effective	64 (39)	21 (33.9)	26 (47.3)	24 (46.2)	20 (41.7)	5 (18.5)	4 (44.4)	1 (25)	
gh level, and effective	8 (4.9)	3 (4.8)	5 (9.1)	0 (0)	6 (12.5)	1 (3.7)	1 (11.1)	0 (0)	
Not sure	53 (32.3)	23 (37.1)	10 (18.2)	19 (36.5)	14 (29.2)	8 (29.6)	1 (11.1)	2 (50)	

reviations: CTCAE, Common Terminology Criteria for Adverse Events; IP, intraperitoneal; IV, intravenous; PIPAC, ssurized intraperitoneal aerosol chemotherapy.

rvix and uterine cancers (n=1); cervical cancer and peritoneal neoplasms with other origins (n=2); cervical cancer and coma (n=1);

stoperative pain, infection and minor bleeding; ‡ perforation and leakage at anastomotic sites;

terogeneous distribution of drugs due to adhesion (n=3), less effective in hematogenous or lymphatic metastasis (n=1); risk abdominal compartment syndrome by pressurized intraperitoneal aerosol chemotherapy (n=1)

able 4. Answers to the cost inquiry

Answers	Total (n=164, %)	Ovarian cancer (n=62, %)	Gastric cancer (n=55, %)	Colorectal cancer (n=52, %)	Pseudomyxoma peritonei (n=48, %)	Hepatobiliary cancer (n=27, %)	Malignant mesothelioma (n=9, %)	Others* (n=4, %)	*P* value
e appropriate cost to purchase PIPAC									0.402
1,000,000 KRW	15 (9.1)	5 (8.1)	6 (10.9)	5 (9.6)	3 (6.3)	4 (14.8)	0 (0)	0 (0)	
,000,000- ,000,000 KRW	56 (34.1)	15 (24.2)	21 (38.2)	16 (30.8)	15 (31.3)	13 (48.1)	2 (22.2)	0 (0)	
,000,000-),000,000 KRW	45 (27.4)	20 (32.3)	14 (25.5)	16 (30.8)	12 (25)	5 (18.5)	1 (11.1)	3 (75)	
),000,000-),000,000 KRW	45 (27.4)	19 (30.6)	14 (25.5)	14 (26.9)	16 (33.3)	5 (18.5)	6 (66.7)	1 (25)	
>),000,000 KRW	3 (1.8)	3 (4.8)	0 (0)	1 (1.9)	2 (4.2)	0 (0)	0 (0)	0 (0)	
e appropriate cost to implement PIPAC once									0.184
1,000,000 KRW	71 (43.3)	25 (40.3)	26 (47.3)	21 (40.4)	14 (29.2)	16 (59.3)	0 (0)	1 (25)	
,000,000- ,000,000 KRW	84 (51.2)	34 (54.8)	28 (50.9)	23 (48.1)	30 (62.5)	11 (40.7)	9 (100)	3 (75)	
,000,000-),000,000 KRW	8 (4.9)	3 (4.8)	1 (1.8)	5 (9.6)	3 (6.3)	0 (0)	0 (0)	0 (0)	
>),000,000 KRW	1 (0.6)	0 (0)	0 (0)	1 (1.9)	1 (2.1)	0 (0)	0 (0)	0 (0)	

)reviation: KRW, Korean Won; PIPAC, pressurized intraperitoneal aerosol chemotherapy.

ervix and uterine cancers (n=1); cervical cancer and peritoneal neoplasms with other origins (n=2); cervical cancer and coma (n=1)