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Thromboprophylaxis, pain and organization: How do expert centers manage PIPAC's perioperative care? An international survey

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ABSTRACT

Introduction: Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) is an emerging therapeutic option for peritoneal carcinomatosis, offering improved drug distribution and tissue penetration. Although clinical outcomes have been encouraging, international guidelines for perioperative management – including pain control and thromboprophylaxis – are still lacking.

Materials and methods: A global online survey was distributed to PIPAC practitioners to corresponding authors of published PIPAC studies and members of the International Society for the Study of Pleura and Peritoneum (ISSPP). The questionnaire consisted of 24 closed-ended questions covering five domains: institutional experience, perioperative organization, thromboprophylaxis, biological monitoring, and postoperative pain management. Consensus was defined as ≥70% agreement among respondents.

Results: Out of 300 contacted experts, 125 responded (42% overall response rate), representing 68 centers across 27 countries (71.2% from Europe). Consensus was reached for four items: performing a surgical or oncological consultation before each PIPAC procedure (74.59%), conducting pre and postoperative laboratory tests (89.43% and 70.73% respectively) and the non-use of non-medicated thromboprophylaxis (70.97%). Pharmacological thromboprophylaxis was prescribed in 63.71% of centers, mainly low-molecular-weight heparin, up to 7 days in 33% of centers, up to 21 days in 33%, and limited to the in-hospital stay in 22%. Otherwise, anesthetic consultations were systematically performed in 57.26% of centers. Outpatient procedures (<24 h) were performed in 11.29%, while 41.94% and 34.68% of patients were hospitalized for one and two days respectively. Paracetamol was the first-line analgesic and was used in more than 80% of cases on postoperative day 1. A significant difference was observed regarding the use of morphine PCA, which was more frequently prescribed after oxaliplatin-based PIPAC ($p = 0.013$).

Discussion: This international survey highlights substantial heterogeneity in perioperative care practices. Although PIPAC and cytoreductive surgery are performed for peritoneal metastases, pharmacological thromboprophylaxis appears to be less frequently prescribed in the PIPAC settings. Pre-PIPAC consultation and perioperative biological monitoring are more standardized, although noteworthy variations persist. These findings underscore the need for evidence-based international guidelines to harmonize perioperative management and improve patient outcomes in PIPAC.

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1. Introduction

Pressurized intraperitoneal aerosol chemotherapy (PIPAC) was first introduced in humans in 2011(1). It represents an innovative laparoscopic approach for delivering intraperitoneal chemotherapy in patients with peritoneal carcinomatosis (PC), leveraging the physical advantages of drug aerosolization and pressurization. Administered as a therapeutic aerosol under pressure, PIPAC achieves a more homogeneous spatial distribution than conventional liquid intraperitoneal chemotherapy [1], along with deeper tissue penetration [2] and higher intratumoral drug concentrations [3] attempted. Encouraging outcomes have been reported in peritoneal metastases of gastric [4,5], ovarian [6,7], colorectal [8], pancreatic [9], and hepatobiliary origins [10], demonstrating that PIPAC is feasible, safe, and well-tolerated, with promising clinical response rates [11]. To agents commonly used include cisplatin, doxorubicin and oxaliplatin.

Consensual recommendations regarding the operative technique, safety checklists, and treatment protocols have been developed [12] to ensure standardized practices that optimize patient safety and facilitate clinical research. However, unlike other oncologic procedures and surgeries, no clear international guidelines exist for perioperative management, including pain control and thromboprophylaxis.

Therefore, the objective of the present study was to characterize current international perioperative practices in PIPAC centers, with the aim of providing a foundation for developing collaborative, evidence-based perioperative guidelines.

2. Material and methods

2.1. Data collect

The survey was developed by the authors (Marc Pocard and Jade Fawaz) and distributed electronically to PIPAC centers worldwide. Two mailing lists were used: The official ISSPP mailing list and a list compiled from all corresponding authors of PubMed-indexed articles identified using the keyword “PIPAC”. Participation was voluntary. Data were collected using a secure online survey platform (Surveymonkey Inc. SanMateo, USA).

The questionnaire was reviewed by nine surgeons and consisted of 24 closed-ended questions divided into five sections. The first section collected general information on the geographical location and experience of participating centers (3 questions). The second section addressed perioperative organization, including perioperative consultations (6 questions). The third section evaluated thromboprophylaxis practices (5 questions). The fourth section explored biological monitoring (4 questions) and the fifth section focused on postoperative pain management (4 questions).

The survey was conducted over a 3-month period beginning in July 2024. The study complied with the principles of the Declaration of Helsinki and the European Union General Data Regulation (GDPR).

2.2. Statistical analysis

A descriptive statistical analysis was performed. Quantitative and qualitative variables are presented as means (± standard deviation), medians (range) or percentages. Percentages were calculated based on the number of responses available for each question. An item was considered consensual when more than 70% of responses were agreed upon [13]. Comparisons of categorical variables, including the distribution of responses between groups and/or across survey items, were performed using Fisher's exact test. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Respondents

The survey was distributed to 300 PIPAC experts worldwide, and 125 responded (overall response rate 42%). Most respondents practiced in Europe (71.2%) and represented 68 PIPAC centers from 27 countries: Austria, Germany, United Kingdom, Spain, India, United States, France, Italy, Australia, Brazil, Bulgaria, Switzerland, The Netherlands, Belgium, Portugal, Singapore, Taiwan, Latvia, Poland, Marrocco, Romania, Czech Republic, Turkey, Sweden, Lithuania, Denmark and Argentina. The survey targeted healthcare professionals involved in PIPAC to describe current practices regarding perioperative care, including thromboprophylaxis, pain management and consultation organization.

Most surgeons worked in university hospitals (68%). Centers had been practicing PIPAC for more than 5 years in 43.2% of cases, for 1-5 years in 38.4%, and for less than 1 year in 18.4% (Table .1). All respondents (100%) consented to the use of their data for research purposes and to participate in collaborative authorship of future publications.

3.2. Perioperative organization

The median hospital stay intended after PIPAC was 24-48 h: 41.9% for one day and 34.7% for two days. Outpatient procedures (<24 h) were performed in only 11.3% of centers. One center adjusted the duration of hospitalization according to the chemotherapy agent used (Oxaliplatin). In others, hospitalization lasted 4 days due to national insurance requirements or Diagnosis-Related Group (DRG) regulations.

A preoperative anesthetic consultation was systematically performed before each procedure in 57.3% of centers, most often in person. When not systematic, it was generally performed only before the first PIPAC session. Twelve centers conducted the anesthetic evaluation before the first PIPAC only, after the second or third session, or performed subsequent consultations remotely.

A surgical or oncological consultation was organized before each PIPAC in 74.6% of cases. When consultations were less frequent, they generally occurred after every two or three sessions. In centers where oncological consultations were not performed systematically by the surgeon (n = 11), consultations were carried out only in the event of treatment modification, or not at all, as they were handled exclusively by the medical oncologist.

In nearly half of the centers (49.2%), no postoperative contact was established with patients. When follow-up occurred, it was performed after postoperative day 3 (20.16%) or on day 1 (16.13%) (Table .2).

Table 1
Participants profile.

In which region do you work?	
Africa	1 (0.80%)
Asia	12 (9.60%)
Europe	89 (71.20%)
MENA region	1 (0.80%)
North America	16 (12.80%)
South America	3 (2.40%)
Australia/New Zealand	3 (2.40%)
In which hospital structure do you work?	
University hospital	85 (68.00%)
Private hospital/clinic	12 (9.60%)
Anticancer center	18 (14.40%)
Public hospital	10 (8.00%)
Since when have you been carrying out PIPACs in your center?	
<1 year	23 (18.40%)
1-5 years	48 (38.40%)
>5 years	54 (43.20%)

Table 2
Perioperative organization.

What is the average duration of hospitalization for patients on whom you have performed a PIPAC?	
<24 h (Day care surgery)	14 (11.29%)
24 h (Day of discharge D1)	52 (41.94%)
48 h (Day of discharge D2)	43 (34.68%)
72 h (Day of discharge D3)	11 (8.87%)
Other	4 (3.23%)
Do you carry out an anesthetic consultation before each PIPAC?	
Yes, during outpatient clinic visit in person	71 (57.26%)
Yes, online or by phone	17 (13.71%)
No	36 (29.03%)
If not before each PIPAC, do you carry out an anesthetic consultation	
Only before the first PIPAC	33(70.21%)
After two PIPACs	3 (6.38%)
After three PIPACs	5 (10.64%)
Other	12 (25.53%)
Do you carry out a surgical or oncological consultation with your patient systematically before each PIPAC?	
Yes, during outpatient clinic visit in person	91 (74.59%)
Yes, online or by phone	13 (10.66%)
No	18 (14.75%)
If not before each PIPAC, do you carry out a surgical or oncological consultation with your patient:	
After two PIPACS?	8 (20.00%)
After three PIPACS?	21 (52.50%)
Other	11 (27.50%)
Does a member of your department (doctor or nurse) contact the patient after a PIPAC?	
No	61 (49.19%)
Yes, on day 1	20 (16.13%)
Yes, on day 2	12 (9.68%)
Yes, on day 3	6 (4.84%)
Yes, after day 3	25 (20.16%)

3.3. Thromboprophylaxis measures

Drug thromboprophylaxis was prescribed postoperatively by 63.7% of centers, most frequently low-molecular-weight heparin (96.3%). One center reported using unfractionated heparin. Mechanical prophylaxis (compression stockings) was used in 29% of centers. Adaptation of thromboprophylaxis based on tumor origin (gastric, colorectal, ovarian, mesothelioma, biliopancreatic) or chemotherapy regimen was uncommon, and most respondents reported no change in practice according to these criteria ($p = 0.904$) (Fig. 1).

When prescribed, the duration of pharmacological thromboprophylaxis varied widely: up to 7 days in 33% of centers, up to 21 days in 33%, and limited to the in-hospital stay in 22% (Table .3).

3.4. Biological assessment

A postoperative biological assessment was performed in 70.7% of centers, most commonly on postoperative day 1 (73.1%). The most frequently ordered tests were complete blood count (97.8%), C-reactive protein (85.7%), electrolyte panel (74.7%), renal function tests (61.5%), liver function tests (61.5%) and coagulation studies (24.2%).

Sixteen practitioners (17.2%) selected "other" for the timing of postoperative tests, indicating varied practices beyond 1, 3 or 5. Some did not prescribe tests at all (29.3%), while others performed assessments on day 7, day 14 or before the next systemic chemotherapy cycle.

Preoperative laboratory assessment was systematically performed before each PIPAC session in 89.4% of centers (Table .4)

3.5. Postoperative pain management

Paracetamol was the first-line analgesic and was used in more than 80% of cases for both oxaliplatin and doxorubicin-cisplatin regimens, on postoperative day 1 (Table.5A) and at discharge (Table.5B). Step II (tramadol) and step III analgesics (strong opioids, morphine PCA) were used less frequently. Nonsteroidal anti-inflammatory drugs were also commonly prescribed (40–48%).

A significant difference was observed regarding the use of morphine

Table 3
Thromboprophylaxis measures.

Do you prescribe non-medicated thromboprophylaxis (compression stocking) after performing a PIPAC?	
Yes	36 (29.03%)
No	88 (70.97%)
Do you prescribe drug thromboprophylaxis after performing a PIPAC?	
Yes	79 (63.71%)
No	45 (36.29%)
If yes, what type?	
LMWH (Low molecular-weight heparin)	77 (96.25%)
New direct oral anticoagulants (ex. Rivaroxaban)	3 (3.75%)
Other	2 (2.50%)
For how many days?	
≤7 days	26 (33%)
>7 days and ≤21 days	26 (33%)
>21 days	8 (10%)
During hospitalization	17 (22%)
Preop and for first 24 h	1 (1%)

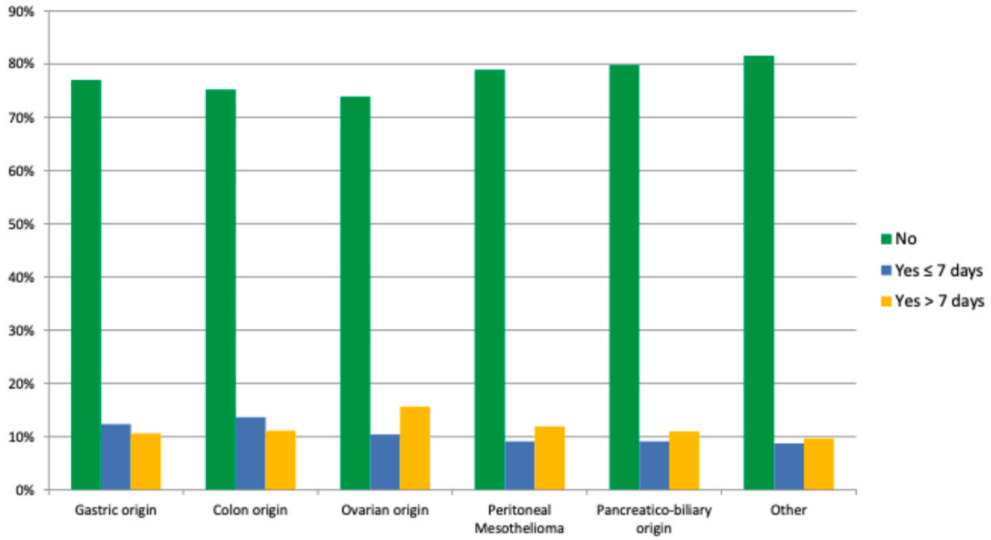

Fig. 1. Do you adapt the indication for thromboprophylaxis according to the type of peritoneal carcinomatosis or the chemotherapy used?

Table 4
Biological assessment.

Do you prescribe a biological assessment after PIPAC	
Yes	87 (70.73%)
No	36 (29.27%)
If yes, on which day?	
Day 1	68 (73.12%)
Day 3	15 (16.13%)
Day 5	10 (10.75%)
Other	16 (17.20%)
If yes, which one(s)	
Blood count	89 (97.80%)
Platelets	78 (85.71%)
C-reactive protein	60 (65.93%)
Serum electrolytes (Na+, K+, etc.)	78 (85.71%)
Urea, creatinemia	68 (74.73%)
Liver function test	56 (61.54%)
Clotting test	22 (24.18%)
Do you systematically carry out a biological assessment before each PIPAC?	
Yes	110 (89.43%)
No	13 (10.57%)

Table.5A
Pain killer prescribed at day 1 according to the PIPAC's regimen.

	Oxaliplatin	Doxo-cisplatin	*p-value*
Paracetamol	94	94	0.345
Nefopam	6	5	1.000
Tramadol	34	38	0.369
Opioid (ex Oxycontin)	37	26	0.343
Morphin PCA (Patient Controlled Analgesia)	12	2	**0.013**
Anti-inflammatory	57	49	0.825
Phloroglucinol	4	5	0.741
Total	**244**	**219**	-

Table.5B
Pain killer prescribed when discharged according to the PIPAC's regimen.

	Oxaliplatin	Doxo-cisplatin	*p-value*
Paracetamol	96	96	0.485
Nefopam	3	2	1.000
Tramadol	33	28	0.781
Opioid (ex Oxycontin)	23	15	0.307
Morphin PCA (Patient Controlled Analgesia)	1	1	1.000
Anti-inflammatory	46	46	0.722
Phloroglucinol	6	5	1.000
Total	**208**	**193**	-

PCA, which was more frequently prescribed after oxaliplatin-based PIPAC ($p = 0.013$).

4. Discussion

The response rate of this international survey was correct (42%). Among the six questions addressing perioperative organization, an agreement >70% was observed for two items: the performance of an anesthetic consultation only before the first PIPAC session (70.21%, Table 2), and the systematic surgical or oncological consultation before each PIPAC during an in-person outpatient visit (74.59%, Table 2). Other organizational aspects showed substantial heterogeneity, particularly regarding hospital length of stay and postoperative patient follow-up (Table .2).

Regarding thromboprophylaxis, the only consensus observed was the non-use of compression stockings (70.97%) and the absence of adaptation of pharmacological thromboprophylaxis according to the origin of peritoneal carcinomatosis. Drug thromboprophylaxis was prescribed in fewer than two-thirds of centers, and its duration varied widely (Table .3). These findings are noteworthy given the relatively low rate of pharmacologic prophylaxis. If we are looking for information about patients also treated for peritoneal carcinomatosis, the literature demonstrates a substantial thrombotic risk in patients undergoing cytoreductive surgery and HIPEC of 30 to 50% [14,15]. Although the level of mechanical and pharmacological thromboprophylaxis recommendation is strong, the evidence level remains low to moderate [16]. To date, no studies have specifically evaluated thrombotic risk associated with PIPAC. In the study published by Khan et al. [17], venous thromboembolism (VTE) risk after cytoreductive surgery and HIPEC was evaluated using the Caprini score. This score incorporates factors such as type of surgery, venous disease or coagulation disorder, and presence of malignancy. In the context of PIPAC, the typical patient would almost systematically fall into a high-risk category (≥1.8%), thereby warranting 7 – 10 days of pharmacologic thromboprophylaxis. However, our results highlight an underuse of pharmacological prophylaxis, and when administered, it was often limited to the duration of hospitalization in 22% of centers – substantially shorter than what would be proposed by extrapolation from existing evidence. Some practitioners may consider PIPAC treatment as part of a palliative care strategy and therefore may not deem a painful and burdensome intervention such as heparin injections to be justified.

Biological monitoring practices showed a greater degree of homogeneity. Preoperative laboratory assessment was nearly systematic (89.43%), and postoperative testing was performed on day 1 in 70.73% of centers (Table .4). These practices aim to prevent or detect possible complications, particularly hemorrhagic events, which – although infrequent – represent the most common postoperative complication. In the systematic review and meta-analysis by Lundbech et al.'s [18], the 30-day postoperative bleeding rate was 4.2 [95% CI; 2.6-6.2], a relatively low incidence. Liver and kidney function were evaluated in 61.5% and 74.7% of centers, respectively. Blanco et al. [19] reported minimal PIPAC-related toxicity, with no clinically relevant hepatic cytolysis, no significant alteration in hepatic metabolic or synthetic function and preserved renal function. These findings support that PIPAC induces less hepatic and renal toxicity than other chemotherapy delivery modalities, likely due to lower drug doses and favorable pharmacokinetics [20].

Postoperative pain management in our survey partially aligns with published data. We observed that experts prescribed stronger analgesics after oxaliplatin-based PIPAC, particularly on postoperative day 1 (Table.5A). This is consistent with the findings of Tidadini et al. [21], who evaluated postoperative pain after PIPAC and found that moderate-to-severe pain occurred more frequently with Oxaliplatin than with Cisplatin-Doxorubicin ($p = 0.010$). In this study, hospital stay was longer for patients reporting higher pain intensity ($p = 0.004$) and in multivariate analysis, oxaliplatin was identified as a factor associated with increased pain (OR 2.95, 95% CI 1.10-7.89). At discharge, no significant differences in analgesic prescriptions were observed between oxaliplatin or cisplatin-doxorubicin regimens (Table.5B).

In conclusion, this survey reveals significant variability in perioperative organization, thromboprophylaxis, biological monitoring, and postoperative pain management practices across PIPAC centers worldwide. To our knowledge, this is the first study to examine these aspects. Notable findings include the underuse of pharmacologic thromboprophylaxis, despite thrombotic risk factors in patients with peritoneal metastases. Further research is warranted to evaluate the specific risk of thrombosis in the context of PIPAC. These results provide an essential foundation for developing evidence-based international guidelines aimed at standardizing perioperative care and improving patient outcomes.

Authors' contribution (CRediT)

- **Conceptualization:** Marc Pocard, Jade Fawaz, Anne Cécile Ezanno.

- Data collection: Jade Fawaz.
- Formal analysis: Jade Fawaz.
- Funding acquisition: None.
- **Investigation:** Marc Pocard and Jade Fawaz.
- **Methodology:** Marc Pocard and Jade Fawaz.
- **Project administration:** Marc Pocard and Jade Fawaz.
- **Resources:** Marc Pocard and Jade Fawaz.
- **Software:** Jade Fawaz.
- **Supervision:** Marc Pocard and Jade Fawaz.
- **Validation:** All authors.
- Visualization: All authors.
- Writing-original draft: Jade Fawaz.
- Writing-review and editing: All authors.

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Declaration of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2026.111874.

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