

# Anesthetic Management During PIPAC: Clinical and Practical Aspects

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Received: 2025-09-10.

Accepted: 2026-04-12.



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J Clin Med Kaz 2026; 23(2): 39-44

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## ABSTRACT

**Background:** Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) is a novel minimally invasive technique for the treatment of peritoneal carcinomatosis that allows localized delivery of cytotoxic drugs under pressure. Despite its clinical potential, this procedure presents unique anesthetic challenges due to increased intra-abdominal pressure, limited access to the patient during aerosolization, and the need for strict safety measures to prevent occupational exposure.

**Objective:** The objective of this study was to evaluate the specific features of anesthetic management during Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) procedures and to determine the safety and tolerability of this method.

**Methods:** This retrospective analysis included 26 PIPAC procedures performed under general anesthesia. The study focused on parameters related to anesthesia induction, mechanical ventilation, depth of neuromuscular blockade, integrity of the breathing system, and intraoperative monitoring. Given the unique conditions of PIPAC, such as increased intra-abdominal pressure, limited access to the patient during the procedure, and the risk of occupational exposure to aerosolized cytotoxic agents, anesthetic management was tailored accordingly. Particular attention was paid to ensuring an airtight respiratory circuit, preventing aerosol leakage, and controlling carbon dioxide levels throughout the procedure.

**Results:** All patients received adequate general anesthesia with stable hemodynamic and respiratory parameters throughout the procedure. No major anesthesia-related complications were observed. The procedure was well tolerated by all patients. Effective neuromuscular blockade was achieved in each case to facilitate laparoscopic access and ensure immobility during the aerosol chemotherapy phase. End-tidal carbon dioxide levels were closely monitored, and hypercapnia was successfully controlled through ventilatory adjustments. The use of a closed anesthetic circuit and appropriate filtration systems ensured both patient and staff safety by minimizing aerosol exposure.

**Conclusion:** PIPAC is a safe and well-tolerated procedure when performed with adherence to specific anesthetic requirements. Successful anesthetic management includes deep neuromuscular blockade, advanced monitoring, strict respiratory circuit integrity, and readiness to manage potential hypercapnia. There is a clear need to develop and implement standardized anesthetic protocols for PIPAC procedures in order to optimize clinical outcomes and minimize associated risks.

**Keywords:** Pressurized Intraperitoneal Aerosol Chemotherapy, anesthetic management, aerosol chemotherapy, hypercapnia, general anesthesia, peritoneal carcinomatosis, laparoscopy.

## Introduction

PIPAC (Pressurized Intraperitoneal Aerosol Chemotherapy) is an innovative method of locoregional chemotherapy for peritoneal carcinomatosis, characterized by increased efficiency of cytostatic delivery with minimal systemic toxicity. The method requires a special approach to anesthetic management due to the effect of increased intra-abdominal pressure, the aerosol nature of chemotherapy and the need for hermetic isolation of the surgical field. This article discusses the current aspects of preoperative assessment, anesthesia features, intraoperative monitoring and postoperative management of patients undergoing PIPAC. [1]

Peritoneal carcinomatosis is an aggressive form of metastatic disease in which malignant cells spread throughout the peritoneum to form multiple tumor implants. Most often, this condition is observed in tumors of the gastrointestinal tract (in particular, gastric, colon and rectal cancer), as well as in serous ovarian adenocarcinoma. Mechanisms of dissemination include direct tumor penetration through the serous membrane, transcoelomic spread with the flow of ascitic fluid, and possible implantation during surgical interventions. Peritoneal carcinomatosis is accompanied by a pronounced inflammatory reaction, disruption of the barrier function of the peritoneum and the development of malignant ascites, which further aggravates the clinical course of the disease. The prognosis for peritoneal carcinomatosis is extremely unfavorable, with a median survival of less than one year without specific treatment. The effectiveness of systemic chemotherapy is limited due to poor vascularization of peritoneal structures, reduced drug penetration, and high drug resistance of tumor cells in this location.

In search of more effective methods of locoregional treatment, an innovative approach was developed – pressurized intraperitoneal aerosol chemotherapy (PIPAC) [2]. This method, proposed by Mark Ruedli and colleagues in the early 2000s, is based on the laparoscopic introduction of chemotherapy drugs into the abdominal cavity in the form of an aerosol under pressure, which contributes to a more uniform distribution of the drug and better penetration. Although the PIPAC procedure is minimally invasive, it places special demands on anesthetic management. These include the need to maintain stable ventilation with increased intra-abdominal pressure, limited access to the patient during the aerosol exposure phase, requirements for the tightness of breathing circuits and ensuring the safety of the operating personnel. In addition, most patients undergoing PIPAC are cancer patients with concomitant pathology and weakened somatic status, which requires an individualized approach to anesthesia.

This article is devoted to an overview of the anesthetic aspects of the PIPAC procedure, risk analysis and methods for their minimization, as well as practical recommendations for ensuring the safety and effectiveness of the intervention.

## Methods

The purpose of anesthetic management during the PIPAC procedure is to maintain a safe and stable course of the intraoperative period under conditions of increased physiological stress and limited access to the patient at critical stages of the intervention. Anesthetic tactics should ensure adequate depth of general anesthesia with controlled artificial ventilation under pneumoperitoneum conditions, stability of respiratory and hemodynamic functions, as well as prevention of complications



**Figure 1** – Operating room labeling to ensure staff safety during PIPAC

*The operating room must be marked in a special way*

associated with increased intra-abdominal pressure and the use of aerosol cytostatics. Compliance with biological safety measures to protect medical personnel from potential cytotoxic effects is of no small importance. The operating room must be marked in a special way (Figure 1). Given the limitations of physical access to the patient during the phase of spraying the chemotherapy drug, it is necessary to organize continuous monitoring of vital functions and be ready for immediate correction of possible critical conditions.

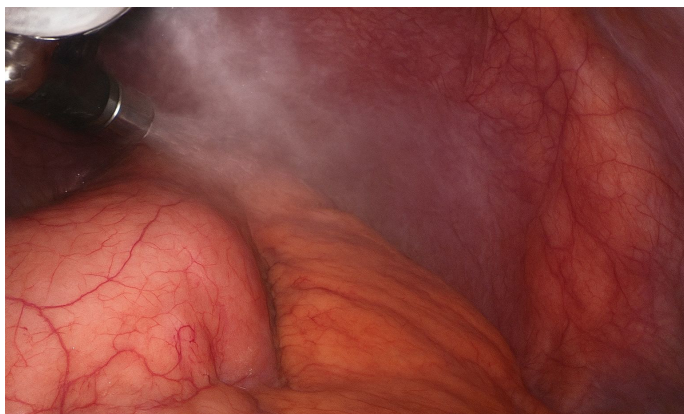
This study is a retrospective single-center analysis including data from 26 patients who underwent Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) performed at the National Scientific Oncology Center, Astana, Republic of Kazakhstan in 2024–2025. The mean age of patients was 59.35 years. All included patients had a confirmed diagnosis of peritoneal carcinomatosis associated with locally advanced adenocarcinoma of the stomach or sigmoid colon [4-5]. The selection was carried out among patients with an intact general somatic status (ECOG score 0–2) and without signs of intestinal obstruction.

Inclusion criteria were age from 18 to 70 years and the presence of peritoneal carcinomatosis associated with locally advanced gastric cancer.

All patients received neoadjuvant systemic chemotherapy according to the FLOT regimen before PIPAC. Intraperitoneal administration of cytostatics was carried out in accordance with international recommendations [6], using cisplatin at a dose of 10 mg / m<sup>2</sup> and doxorubicin at a dose of 2.1 mg / m<sup>2</sup> [1-7-14].

The chemotherapy agent is sprayed into the abdominal cavity using a special device through a nozzle (Figure 2-3).

At the preoperative stage, patients underwent a comprehensive clinical and diagnostic assessment, including general and biochemical blood tests, coagulogram, electrocardiography, echocardiography, as well as visualization



**Figure 2** – Intraoperative view during PIPAC showing pressurized aerosol distribution

*The operating room must be marked in a special way*



**Figure 3** – Medical equipment for intraperitoneal administration of a chemotherapeutic agent (PIPAC system setup)

*The chemotherapy agent is sprayed into the abdominal cavity using a special device through a nozzle.*

studies (CT or MRI of the abdominal organs) [8-9]. In the presence of signs of respiratory disorders, spirometry was performed. Consultations with specialized specialists were also carried out according to indications.

Contraindications to the procedure were decompensated somatic conditions, severe ascites (volume over 4 liters), as well as the presence of massive intra-abdominal adhesions identified by imaging methods. In 69.2% of cases, patients had concomitant diseases, primarily arterial hypertension, type 2 diabetes mellitus,

and toxic effects of previous systemic chemotherapy. According to the ASA classification, 73.1% of patients belonged to class II anesthetic risk, 26.9% to class III anesthetic risk.

The preoperative period included a mandatory informed discussion with the patient of all aspects of the upcoming intervention, including potential risks (intra-abdominal perforation, chemical peritonitis), features of anesthetic management, and the need to use a sealed operating room with a personnel protection system. Premedication included antiemetic drugs, including serotonin receptor antagonists (ondansetron), dopamine receptor antagonists (metoclopramide, cerucal), corticosteroids (dexamethasone), and proton pump inhibitors (omeprazole, pantoprazole).

Anesthetic management was performed according to the standard protocol of general anesthesia with tracheal intubation and controlled artificial ventilation. Induction of anesthesia included the administration of propofol (1.5–2 mg/kg), fentanyl (1–2 µg/kg), and rocuronium (0.6 mg/kg). Anesthesia was maintained either with total intravenous anesthesia (TIVA) or with the inhalation anesthetic sevoflurane. Deep neuromuscular blockade (TOF = 0) was provided in all cases. Intraoperative intra-abdominal pressure was maintained at 12–15 mmHg. [10].

Monitoring of vital functions was performed in an expanded volume and included noninvasive blood pressure, capnography, assessment of the depth of anesthesia using BIS, as well as control of the degree of neuromuscular blockade using TOF stimulation. [11].

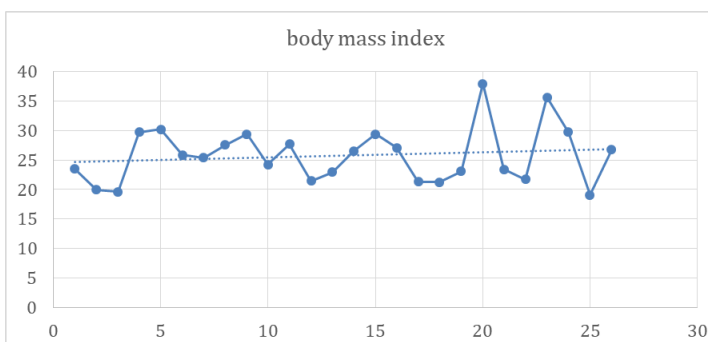
The main characteristics of the patients who took part in the observation are described in Table 1.

The observation involved 26 patients, including 17 men and 9 women. The median age was 61.5±9.7 years. The minimum age was 35 years, the maximum age was 70 years.

Figure 4 shows the BMI values with its median value for the group and standard deviation pages.

**Table 1** Main characteristics of patients who underwent PIPAC

Characteristic	Men	Women
Gender	17	9
Age, years, Median ± standard deviation	61±9,4	62±10,9
BMI, kg/m <sup>2</sup> , Median ± standard deviation	25,65±4,72	
ASA Class		
ASA 2	19	
ASA 3	6	
ECOG stage 2	2	
Oncology stages		
Stage 2	9	
Stage 2 9	17	

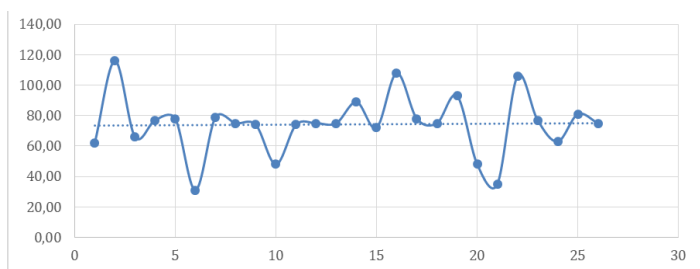


**Figure 4** – BMI values of the observation group

The body mass index was  $25.64 \pm 4.72$  kg/m<sup>2</sup>, with a maximum of 38.01 kg/m<sup>2</sup> and a minimum of 19.07 kg/m<sup>2</sup>. This factor is important because nutritional status is critical for prognosis of further treatment, risk of complications, and patient outcome. Subsequently, 13 patients underwent gastrectomy surgery. In general, patients undergoing PIPAC had no complications either during or postoperatively. [12-13].

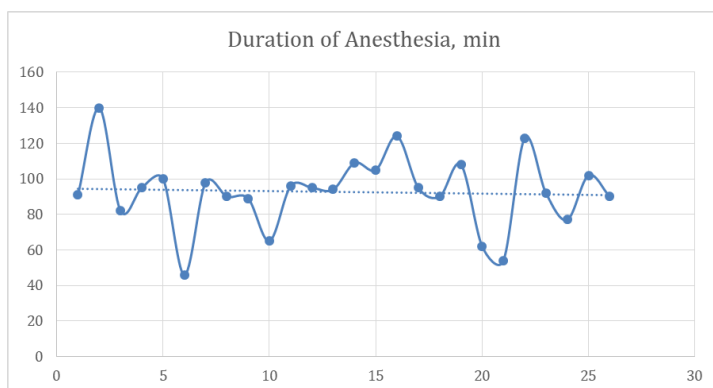
## Results

The median duration of the surgical stage was  $75.0 \pm 19.7$  minutes, with the minimum duration being 31 minutes and the maximum being 116 minutes. Figure 5 shows a diagram of the duration of the surgical intervention.



**Figure 5** – Duration of surgical intervention

All procedures were performed under general anesthesia with tracheal intubation and controlled ventilation. A deep neuromuscular block (TOF 0) was provided throughout the procedure, with PCV or VCV ventilation using a high-end anesthesia machine. The duration of anesthesia care is shown in Figure 6.



**Figure 6** – Duration of anesthesia, min

The median duration of anesthesia was  $94.5 \pm 20.75$  minutes. The minimum duration was 46 minutes, the maximum – 140 minutes.

The duration of operations and anesthesia was mainly due to three factors: individual characteristics of the oncological process, high body mass index, high risk of complications (a combination of risk factors in 1 patient: ASA 3, heart rhythm disturbances, high body mass index, etc.).

Intra-abdominal pressure was maintained at a level of up to 12 mm Hg [12], with mandatory monitoring of gas exchange parameters (EtCO<sub>2</sub>, SpO<sub>2</sub>, FiO<sub>2</sub>). Transient hypercapnia (EtCO<sub>2</sub> > 50 mm Hg) was recorded in 20% of patients, which was successfully stopped by increasing the minute ventilation

volume. Before the aerosol spray phase of chemotherapy drugs, hyperventilation and preoxygenation with 100% oxygen were performed, which allowed for the creation of an oxygen reserve in the lungs and the safe conduct of the apnea phase lasting 2–5 minutes. During spraying, the mechanical ventilation was turned off and the breathing circuit was sealed, in accordance with international safety standards [15-16].

In order to protect the operating personnel from the effects of cytostatics, biological safety protocols were strictly followed: remote control of the spray phase, complete sealing of all ports, and the use of certified filtration systems [14-15-18]. In the postoperative period, 28% of patients experienced episodes of nausea and vomiting, which were successfully relieved by ondansetron. The need for analgesia was moderate: non-steroidal anti-inflammatory drugs and promedol were used according to indications. None of the patients required transfer to the intensive care unit. Hospitalization after the procedure averaged 2–3 days; complications requiring repeated intervention or prolonged therapy were not registered.

## Discussion

The Pressurized IntraPeritoneal Aerosol Chemotherapy (PIPAC) procedure is an innovative method of locoregional chemotherapy, which is increasingly being introduced into clinical practice for the treatment of peritoneal carcinomatosis. Despite its clinical promise, this method remains a technically and organizationally complex intervention that requires coordinated work of a multidisciplinary team. Of particular importance in the process of PIPAC is anesthesiological management, which goes beyond standard general anesthesia and involves a deep understanding of the physiological changes caused by intra-abdominal pressure, exposure to chemoaerosol, and limited access to the patient at key stages of the intervention.

One of the central tasks of the anesthesiologist in PIPAC is to ensure adequate gas exchange under pneumoperitoneum conditions. Increased intra-abdominal pressure (usually up to 12–15 mm Hg). leads to limited diaphragm excursion, decreased pulmonary compliance and the risk of hypercapnia [15-17]. According to the data of the present study, 20% of patients experienced transient hypercapnia (EtCO<sub>2</sub> > 50 mm Hg), which requires dynamic correction of mechanical ventilation parameters, including an increase in minute volume and optimization of the level of positive end-expiratory pressure (PEEP). These features emphasize the need for individual selection of ventilation strategies depending on the patient's respiratory reserve and the volume of surgical intervention.

In addition, an important aspect of anesthesiological management is maintaining stable hemodynamics against the background of possible vasodilation associated with systemic resorption of cytostatics and their potential cardio- and nephrotoxicity. Administration of drugs such as cisplatin and doxorubicin requires special attention to renal and cardiovascular function, especially in patients with comorbidities. Monitoring of hemodynamic parameters and timely correction of perfusion disorders should be part of the basic management algorithm.

Prevention of postoperative nausea and vomiting (PONV) is another key component, especially in high-risk patients (women, patients with previous courses of systemic chemotherapy, use of inhalational anesthetics and opioids). In our study, the use of a multicomponent premedication regimen, including serotonin and dopamine receptor antagonists, as well as corticosteroids, provided effective prevention of PONV in most cases.

The PIPAC procedure places high demands on the qualifications of the anesthesiologist, his readiness to respond quickly in conditions of limited access to the patient and interaction with the surgical team. Given the relatively small accumulated clinical experience in the use of this technology, the development and implementation of standardized anesthetic protocols adapted to PIPAC conditions seems relevant. Further accumulation of clinical data is necessary to assess safety, identify risks and optimize the tactics of managing patients undergoing this treatment [20].

## Conclusion

Anesthetic care for PIPAC is a complex measure that requires the use of extended monitoring, deep neuromuscular blockade and specific ventilation tactics. Compliance with safety standards when working with aerosol forms of chemotherapy drugs can significantly reduce the risks for staff and patients, increasing the effectiveness of the treatment of peritoneal carcinomatosis [21].

**Author Contributions:** Conceptualization, M.B., H.B. and K.S.; methodology, M.B., H.B., and A.S., K.S.; validation, E.U., M.B., Z.B. and H.B.. A.S.; formal analysis, M.B., H.B.,

Z.B. and K.S., A.S.; investigation, K.S., and A.S.; resources, M.B., and E.U.; data curation, K.S., and A.S.; writing — original draft, M.B., H.B., and K.S.; writing — review and editing, M.B., H.B., and K.S.; visualization, K.S.; supervision, E.U.; project administration, M.B; funding acquisition, M.B. All authors have read and agreed to the published version of the manuscript.

**Disclosures:** The authors have no conflicts of interest.

**Acknowledgments:** None.

**Funding:** This publication was published within the framework of the program-targeted funding of the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan, IRN: BR24992950. Agreement No. 386/PCF24-26.

**Data availability statement:** The corresponding author can provide the data supporting the study's conclusions upon request. Due to ethical and privacy constraints, the data are not publicly accessible.

**Artificial Intelligence (AI) Disclosure Statement:** The authors declare no AI Tools used for preparation of this work.

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