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Anesthesia Challenges During HITHOC: A Narrative Review with Institutional Experience

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Introduction

Hyperthermic intrathoracic chemotherapy (HITHOC) is an advanced multimodal therapeutic approach for malignant pleural diseases, particularly mesothelioma and advanced thymoma. This technique combines cytoreductive surgery with intrapleural perfusion of heated chemotherapeutic agents (approximately 42°C), resulting in significant physiological disturbances and substantial anesthetic challenges[1,2].

Despite its growing adoption in specialized centers, anesthetic management during HITHOC remains poorly standardized, with most available evidence derived from small case series.

At Hospital Israelita Albert Einstein, 15 procedures have been performed over the past two years, with perioperative findings consistent with those reported in the literature. This article is presented as a narrative review complemented by institutional experience. Its objective is to summarize the current evidence regarding perioperative anesthetic management during HITHOC while describing practical aspects of the protocol adopted at Hospital Israelita Albert Einstein.

Literature Search Strategy

A narrative literature review was performed using PubMed/MEDLINE and Google Scholar. The search included publications through 2025 using combinations of the terms *HITHOC*, *hyperthermic intrathoracic chemotherapy*, *cytoreductive surgery*, *anesthesia*, *perioperative management*, and *thoracic oncology*. Priority was given to clinical studies, narrative reviews, systematic reviews, and consensus publications addressing anesthetic and perioperative management. Because of the limited number of available studies, evidence from institutional case series was also considered.

Pathophysiology and Hemodynamic Challenges

Cardiovascular Instability

The intrathoracic instillation of 3–5 liters of heated perfusate leads to profound hemodynamic changes. Up to 50% of patients may experience significant reductions in arterial blood pressure, while tachycardia (>100 bpm) occurs in a subset of cases[1,3].

These alterations are primarily driven by increased intrathoracic pressure, resulting in mediastinal shift, elevated central venous

pressure, and increased airway pressures. Consequently, venous return is impaired, cardiac chambers may be compressed, and cardiac output can decrease[1].

In parallel, a hyperdynamic circulatory state may develop, characterized by reduced systemic vascular resistance, increased cardiac index, and elevated end-tidal CO_2. Although often transient, severe events such as intraoperative asystole have been reported, underscoring the potential severity of these physiological disturbances[2,3].

Our institutional experience mirrors these findings and reinforces the importance of continuous invasive hemodynamic monitoring throughout all phases of the procedure.

Temperature Management Challenges

Thermoregulation during HITHOC presents a biphasic pattern. During cytoreductive surgery, patients are at risk of hypothermia, whereas the perfusion phase induces controlled hyperthermia[1].

Hyperthermia is associated with increased metabolic demand, elevated lactate levels, and metabolic acidosis, and may lead to neurological complications at extreme temperatures (>43°C)[1,2,3].

Anesthetic Management Strategies

Monitoring and Vascular Access

Comprehensive monitoring is mandatory and should include invasive arterial pressure monitoring, central venous access, continuous core temperature monitoring, capnography, and hourly urine output assessment.

Anesthetic Technique

A combined approach using general anesthesia and thoracic epidural analgesia is widely considered optimal.

Thoracic epidural analgesia provides effective intraoperative and postoperative pain control, reduces systemic opioid requirements, and may facilitate earlier recovery. General anesthesia may be maintained using either volatile agents or total intravenous anesthesia (TIVA), depending on institutional preference[4,5].

Fluid Management and Vasoactive Support

Perioperative fluid management requires a careful balance between maintaining adequate organ perfusion and avoiding fluid overload, particularly given the risk of pulmonary complications[3,4,5].

Forced diuresis is commonly employed to reduce cisplatin-induced nephrotoxicity. However, this approach must be individualized based on hemodynamic status and renal function.

Vasoactive support is frequently necessary. In our experience, norepinephrine was required in all cases, with progressive dose escalation during the hyperthermic phase. In selected cases, vasopressin was added to achieve hemodynamic stability[1,2,3].

Blood Management

Significant intraoperative blood loss is common and often necessitates transfusion. However, in contrast to hyperthermic intraperitoneal chemotherapy (HIPEC), clinically significant coagulopathy appears to be less frequent during HITHOC[1,2].

Pain Management

Thoracic epidural analgesia remains the gold standard for postoperative pain control. It provides superior analgesia compared to systemic strategies, reduces opioid consumption, and may contribute to earlier extubation and improved respiratory outcomes[3,4].

Respiratory Management

One-lung ventilation is required and should follow lung-protective strategies, including low tidal volumes (approximately 5 mL/kg), limitation of plateau pressures, and moderate levels of PEEP (5–10 cmH_2O)[1,4,5].

During the perfusion phase, appropriate PEEP may help prevent atelectasis and improve distribution of chemotherapeutic agents.

Postoperative Considerations

Extubation and Recovery

Early extubation is feasible in most patients, provided that hemodynamic and respiratory stability are achieved. ICU stay typically ranges from 1 to 4 days, with overall hospital stay varying between 2 and 4 weeks[1,4].

Complications

Although severe complications are relatively uncommon, they may require surgical reintervention. Renal toxicity remains a major concern but can be minimized through optimized fluid management and protective strategies[1,4,6].

Institutional Experience

Between 2024 and 2026, 15 patients underwent HITHOC at Hospital Israelita Albert Einstein.

All procedures were performed using combined thoracic epidural anesthesia and TIVA with target-controlled infusion of propofol and remifentanil. The epidural solution consisted of ropivacaine 0.375% (20 mL), fentanyl (100 μg), and morphine (2 mg).

Norepinephrine infusion was required during all

PERIOPERATIVE ANESTHETIC MANAGEMENT ALGORITHM FOR HITHOC
1. PREOPERATIVE EVALUATION
2. INDUCTION AND PREPARATION
3. CYTOREDUCTIVE SURGERY (ONE-LUNG VENTILATION)
4. HITHOC PERFUSION (HYPERTHERMIC PHASE)
5. POSTOPERATIVE MANAGEMENT
PATIENT ASSESSMENT
Detailed medical history and comorbidities
Cardiorespiratory evaluation (ECG, ECHO, PFTs)
Renal function assessment
Nutritional status
Performance status (ECOG)
LABORATORY TESTS
Complete blood count
Coagulation profile
Renal and liver function
Electrolytes
Arterial blood gas
OPTIMIZATION
Treat comorbidities
Smoking cessation
Pulmonary physiotherapy
Anemia correction
Nutritional support
INFORMED CONSENT
Discuss risks, benefits and alternatives
MONITORING AND ACCESS
Standard monitoring (ECG, NIBP, SpO2, EtCO2)
Invasive arterial line
Central venous catheter
Temperature monitoring (esophageal and/or buccal)
Urinary catheter
Large-bore IV access
ANESTHETIC TECHNIQUE
THORACIC EPIDURAL
Ropivacaine 0.375% 20 mL
Fentanyl 100 µg
Morphine 2 mg
GENERAL ANESTHESIA (TIVA)
Propofol (TCI)
Remifentanil (TCI)
Rocuronium (neuromuscular blockade)
PREPARATION
Active warming to maintain normothermia
Antibiotic prophylaxis
Antiemetic prophylaxis
Blood products available
Chemotherapy circuit check
VENTILATION STRATEGY
One-lung ventilation (double-lumen tube)
Tidal volume 5 mL/kg (IBW)
Plateau pressure < 25 cmH2O
PEEP 5–10 cmH2O
FiO2 to maintain SpO2 > 92%
Permissive hypercapnia (pH ≥ 7.20)
HEMODYNAMIC MANAGEMENT
Maintain MAP ≥ 65 mmHg
Fluid therapy guided by dynamic assessment
Blood loss management
Vasoactive drugs as needed
TEMPERATURE MANAGEMENT
Risk of hypothermia during surgery
Maintain core temperature 35.0–36.0 °C before perfusion
Goal: Optimal surgical conditions and patient stability before starting perfusion
PERFUSION PHASE
Instillation of 3–5 L of chemotherapeutic solution at 42 °C
Perfusion time: 60–90 min (as per protocol)
ANTICIPATED PHYSIOLOGIC EFFECTS
↑ Intrathoracic pressure
↑ CVP and airway pressure
↓ Venous return
↓ Cardiac output
Systemic vasodilation
↑ Cardiac index
↑ EtCO2
Risk of arrhythmias
MANAGEMENT STRATEGIES
Close hemodynamic monitoring
Titrate norepinephrine (first-line)
Add vasopressin if needed (0.01–0.04 U/min)
Maintain adequate diuresis (>100 mL/h)
Monitor lactate and ABG
Maintain core temperature ≤ 41–42 °C
Goal: Maintain hemodynamic stability, adequate oxygenation and target temperature
IMMEDIATE POSTOPERATIVE CARE
Assess hemodynamic stability
Adequate analgesia (epidural infusion)
Lung recruitment and physiotherapy
Early goal-directed extubation (if criteria met)
FLUID AND RENAL MANAGEMENT
Continue forced diuresis
Maintain urine output > 100 mL/h
Monitor renal function
Avoid nephrotoxic drugs
Hydration for cisplatin protection (24–72 h)
PAIN MANAGEMENT
Thoracic epidural infusion (ropivacaine/opioid)
Multimodal analgesia
Regular pain assessment
SAFETY CONSIDERATIONS
Handle body fluids as cytotoxic for 48 h
Use appropriate PPE
Proper waste disposal
Staff training and protocols
KEY POINTS AT A GLANCE
Hemodynamic instability is expected and requires proactive management
Temperature management is crucial: prevent hypothermia and avoid excessive hyperthermia
Lung-protective ventilation and one-lung ventilation are mandatory
Epidural analgesia reduces opioid consumption and improves recovery
Careful fluid balance and diuresis protect renal function
Multidisciplinary teamwork is essential for optimal outcomes
SUMMARY FLOW
Preoperative Evaluation and Optimization
Induction and Monitoring Setup
Cytoreductive Surgery (One-Lung Ventilation)
HITHOC Perfusion (Hyperthermic Phase)
Postoperative Care and Recovery
MULTIDISCIPLINARY TEAM
Anesthesiologist
Surgeon
Perfusionist
Nursing Team
Pharmacist
Intensivist
ABG: arterial blood gas; CVP: central venous pressure; ECG: electrocardiogram; EtCO2: end-tidal carbon dioxide;
ECOG: Eastern Cooperative Oncology Group; FiO2: fraction of inspired oxygen; MAP: mean arterial pressure;
NIBP: non-invasive blood pressure; PPE: personal protective equipment; PFTs: pulmonary function tests; SpO2: peripheral oxygen saturation; TCI: target-controlled infusion.

Figure A

procedures, with progressive dose escalation during the hyperthermic phase. Vasopressin was added in selected patients presenting persistent vasodilatory hypotension.

Based on our institutional protocol, perfusion was initiated with a target core temperature of approximately 35°C, allowing gradual warming to approximately 37°C by the end of perfusion. Although this strategy has provided satisfactory temperature control in our experience, it represents an institutional practice and has not been validated in comparative clinical studies.

Overall, the physiological responses observed at our institution were consistent with those reported in published case series.

Although complete perioperative data were not available for all patients who underwent HITHOC at our institution, we included a concise summary of our institutional experience to illustrate that the overall perioperative characteristics and anesthetic challenges observed in our practice are consistent with those reported in the published literature. This section is intended to provide clinical context rather than to present a comprehensive case series or comparative analysis.

Proposed Perioperative Management Algorithm

The proposed management algorithm was developed by integrating findings from the available literature with the institutional protocol currently employed at Hospital Israelita Albert Einstein. It is intended as a practical framework rather than an evidence-based guideline and should be adapted according to institutional resources, surgical technique, and patient characteristics. (Figure A)

Safety Considerations

Strict safety protocols are essential to protect healthcare personnel from exposure to cytotoxic agents. The use of appropriate personal protective equipment and adherence to safe handling protocols are mandatory, as patient body fluids may remain contaminated for up to 48 hours post-procedure[1,3,4].

Conclusion

HITHOC is a highly complex procedure requiring comprehensive perioperative planning, meticulous monitoring, individualized hemodynamic management, and close multidisciplinary collaboration.

Current recommendations are supported primarily by observational studies and institutional experiences. Our institutional findings are consistent with the published literature but should be interpreted as complementary clinical experience rather than confirmatory evidence.

Our experience at Hospital Israelita Albert Einstein aligns with the existing literature and highlights the need for further research aimed at standardizing anesthetic protocols and improving perioperative outcomes.

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