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HIPEC in Gynecological Oncology (Hyperthermic Intraperitoneal Chemotherapy)

1. Rationale / Principle

- Many gynecologic cancers (especially ovarian) spread within the peritoneal cavity
- HIPEC delivers high concentrations of chemotherapy locally with minimal systemic toxicity
- Heat (41–43°C) enhances drug penetration, increases tumor cell death, and potentiates chemotherapy activity
- Aims to kill microscopic residual disease after maximal cytoreduction (CC-0/CC-1)

2. Mechanism of Action

Role of hyperthermia

- Increases cell membrane permeability
- Induces protein denaturation
- Enhances cytotoxicity of many drugs
- Selectively affects malignant cells more than normal tissue

Chemotherapy effect

- High intraperitoneal concentration
- Reduced systemic absorption → fewer systemic side effects
- Longer tumor exposure time

3. Indications in Gynecologic Oncology

a) Ovarian Cancer (Major Indication)

1. Primary advanced ovarian cancer

- Stage III disease after interval cytoreduction (post-NACT)
- Supported by the OVHIPEC-1 trial, showing improved recurrence-free and overall survival when HIPEC with cisplatin was added to interval debulking.

2. Recurrent ovarian cancer

- Considered for platinum-sensitive recurrent disease undergoing secondary cytoreduction
- Data evolving; used in specialized centers

b) Endometrial Cancer

- Very limited role
- Only considered in highly selected patients with peritoneal carcinomatosis

4. Common Chemotherapeutic Agents Used

- Cisplatin (most common)
- Paclitaxel
- Doxorubicin
- Mitomycin-C

Typical parameters

- Temperature: 41–43°C
- Duration: 60–90 minutes
- Perfusion volume: 2–3 L
- Open (“Coliseum”) or closed technique

5. Advantages of HIPEC

- Targets microscopic residual disease after surgery
- Higher local drug concentration with lower systemic toxicity
- Hyperthermia improves drug uptake
- May improve PFS and OS in selected ovarian cancer patients
- Reduces risk of peritoneal recurrence

6. Limitations

- Requires highly skilled CRS surgery and specialized equipment
- High perioperative morbidity if cytoreduction is extensive
- Long operative time
- Not suitable for non-operable or bulky residual disease
- Evidence strong for interval debulking but still evolving for primary upfront surgery or recurrence

7. Morbidity / Complications

- Renal toxicity (especially cisplatin → requires vigorous hydration)
- Bone marrow suppression
- Anastomotic leak
- Infection, sepsis
- Electrolyte imbalance
- Thermal injury (rare)

8. Contraindications

- Poor performance status
- Extra-abdominal metastasis (liver parenchymal, lung, brain)
- Incomplete cytoreduction (residual tumor >2.5 mm)
- Severe renal dysfunction
- Extensive mesenteric involvement (prevents bowel reconstruction)

9. Evidence Summary

OVHIPEC-1 Trial (2018)

- HIPEC + Interval Cytoreduction showed:
  - ↑ Progression-free survival
  - ↑ Overall survival
  - No increase in major morbidity

Ongoing Trials

- OVHIPEC-2 (role in primary upfront surgery)
- Trials in recurrence and other cancers

10. Current Role

HIPEC is not standard for all patients, but is recommended for:

- Stage III ovarian cancer undergoing interval cytoreductive surgery
- Select cases of recurrent ovarian cancer
- Rarely, metastatic endometrial or cervical cancer with peritoneal spread

Usually carried out only in high-volume tertiary cancer centers.