Patients Selection For Cytoreductive surgery (CRS) and (HIPEC) in Advanced Colorectal Cancer

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- **A major component of treatment failure in colorectal cancer is cancer dissemination within the abdominal and pelvic spaces including peritoneal metastasis.**

(David et al 2017)

- **For many years, this manifestation of disease was considered to be terminal condition with no rational treatment.**

- **Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) used as combined treatment has been shown to have long term survival in selected patients with peritoneal metastases from colorectal cancer.**

(Terence et al 2016)

- **CRS defined as removal of macroscopic tumors and macroscopic peritoneal metastasis more than 5mm**
- **Hyper thermic Intraperitoneal Chemotherapy (HIPEC) if combined with CRS is the treatment that is indicated for patients with advanced colorectal cancer**

- **HIPEC : 3 advantages**

1. **Killing of microscopic malignant cells .**
2. **Potentiates the cytotoxic effect of chemotherapy .**
3. **Enhances the cell penetration of the chemotherapy .**

Review of Studies

Cytoreductive Surgery + Systemic Chemotherapy

Characteristics of the studies reporting outcomes of palliative surgery and/or systemic chemotherapy for peritoneal metastases from colorectal cancer

(5-FU = 5-fluorouracil; IRI = irinotecan; LV = leucovorin; N = number of patients; NR = not reported; OX = oxaliplatin)

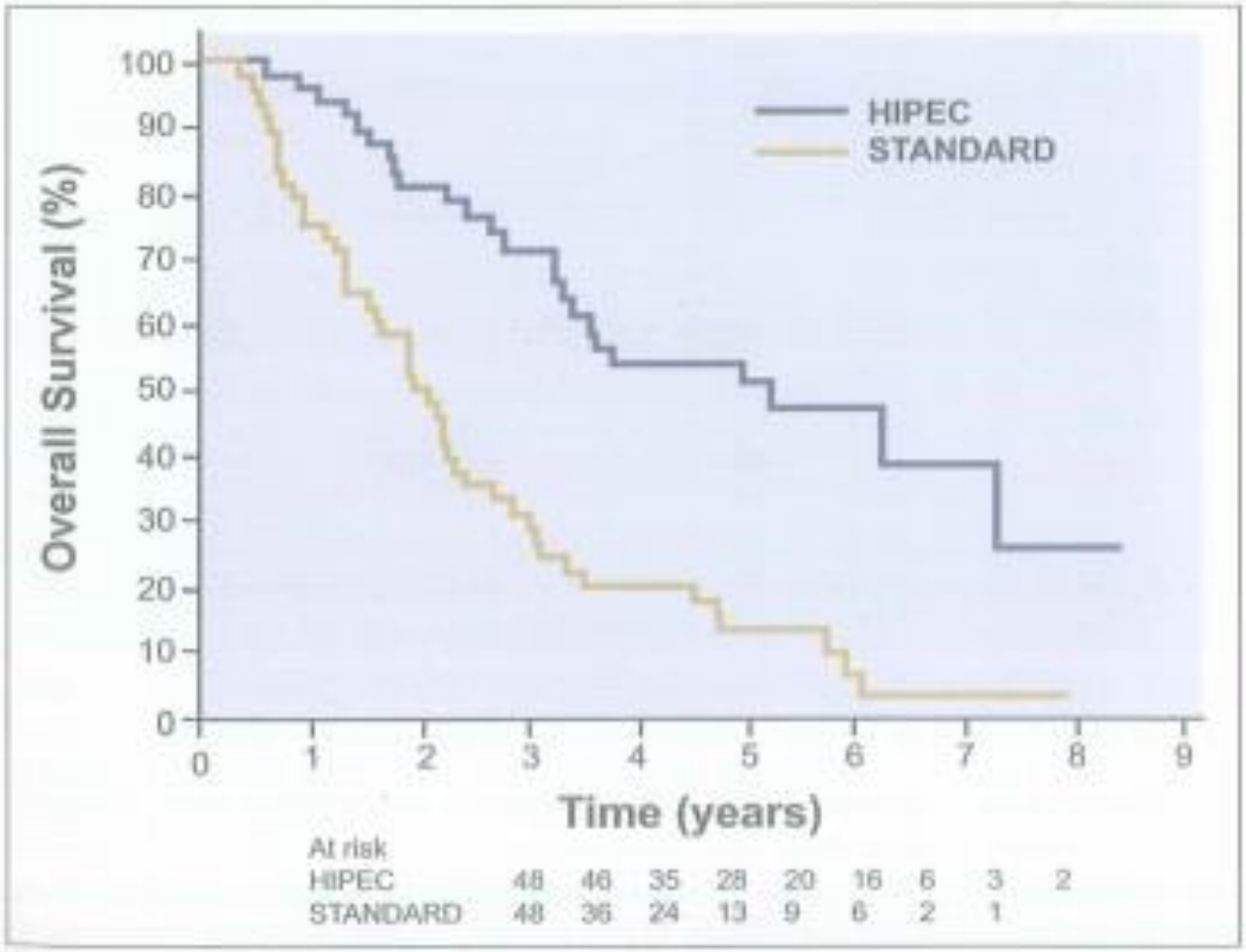
Reference	Institution/City	Year	Level of Evidence	N	Palliative Surgery	Type of Chemotherapy	Median Survival (months)	One-year Survival (%)	Two-year Survival (%)	Three-year Survival (%)	Five-year Survival (%)
Chua (73)	Multi-institutional	2011	III	114	NR	5-FU/LV/OX	11	47	NR	3	0
						IRI/OX	15	62	NR	18	6
						IRI with biological agents	23	73	NR	33	0
Lemmens	Eindhoven Comprehensive Cancer Centre	2010	III	395	NR	NR	8	36	18	10	0
Franko (75)	University of Pittsburgh	2010	III	38	NR	5-FU, LV, OX/IRI with biological agents	17	65	40	20	5
Catalano (72)	Multi-institutional	2009	III	43	Yes	5-FU, LV, OX, IRI	11	NR	NR	NR	NR
Elias (74)	Institut Gustave Roussy, Villejuif	2009	II	48	Yes	5-FU, LV, OX, IRI	24	NR	65	NR	13
Machida	Shizuoka Cancer Center	2008	III	20	Yes	5-FU, LV	12	NR	NR	NR	NR
Hasegawa	Tokai University, Tokyo	2006	III	125	Yes	5-FU, LV	15	67	25	13	13
Bloemendaal	Netherlands Cancer Institute, Amsterdam	2005	III	50	Yes	5-FU, LV, IRI	13	55	25	19	NR
Elias	Institut Gustave Roussy, Villejuif	2004	I	19	Yes	5-FU, LV	NR	NR	60	NR	22
Higashi	Tokyo Kosei Nenkin Hospital, Tokyo	2003	III	21	Yes	Yes, but type was NR	19	NR	NR	NR	NR
Verwaal (85)	Netherlands Cancer Institute, Amsterdam	2003	I	51	Yes	5-FU, LV	13	50	25	NR	NR
Kohne (76)	Multi-institutional	2002	III	660	NR	5-FU, LV	12	NR	NR	NR	NR
Jayne (29)	Singapore General Hospital Singapore	2002	III	253	Yes	NR	7	NR	NR	NR	NR
Sadeghi (66)	Multi-institutional	2000	II	118	Yes	NR	5	NR	NR	NR	NR
Total	–	–	–	1955	71%	–	–	–	–	–	–
Median							13	59	25	18	6
Range		2000 to 2011					5 to 24	36 to 73	18 to 65	3 to 33	0 to 22

CYTOREDUCTION + HIPEC

Characteristics of the major studies reporting outcomes of complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal metastases from colorectal cancer
(N = number of patients; NR = not reported)

Reference	Institution/City	Year	Level of Evidence	N	Overall Survival (months)	One-year Survival (%)	Two-year Survival (%)	Three-year Survival (%)	Five-year Survival (%)
Elias (95)	French Multicentre	2010	III	439	32	85	60	45	30
Chua	St. George Hospital, Sydney	2009	III	54	33	87	70	44	NR
Elias (74)	Institut Gustave Roussy, Villejuif	2009	II	48	63	NR	81	NR	51
Shen	Wake Forest University Winston-Salem	2008	III	30	41	NR	NR	NR	NR
Franko	University of Pittsburgh Medical Center, Pittsburgh	2008	III	36	20	85	NR	45	NR
Gomes da Silva (82)	Washington Cancer Institute Washington, DC	2006	III	70	20	88	NR	44	32
Kianmanesh	Louis-Mourier University Hospital, Paris	2007	III	30	38	NR	72	NR	44
Verwaal (85)	Netherlands Cancer Institute, Amsterdam	2005	III	59	43	94	NR	56	43
Glehen (87)	Multi-institutional	2004	III	377	32	90	NR	55	40
Verwaal	Netherlands Cancer Institute, Amsterdam	2003	I	39	22	70	45	NR	NR
Total				1,084					
Median					33	86	70	48	42
Range					20 to 63	70 to 94	45 to 81	44 to 56	20 to 51

Comparison between CRS + HIPEC or +Systemic.



Comparison of similar patients with resectable peritoneal metastases, treated with CRS + HIPEC or treated with systemic chemotherapy *(from reference 74)*

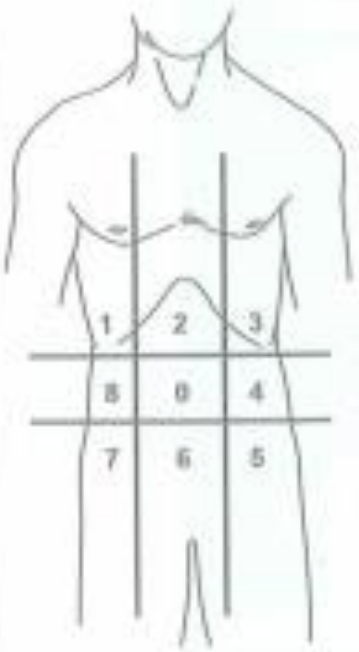
Quent et al 2021:

- **365 patients with colorectal peritoneal metastasis**
- **133 CRS with HIPEC**
- **132 CRS alone**
- **Follow up 63.8 months**
- **Concluded CRS with HIPEC of benefit to patients with isolated peritoneal carcinimatosis without extra abdominal metastasis from colorectal cancer**

NICE 2021 concluded the following:

- **Safety and efficacy of CRS and HIPEC depend on patients selection , experienced multidisciplinary team , highly specialized centers and complete macroscopic resection (with less than 5 mm residual tumor tissue) and peritoneal cancer index PCI less than 16**

Peritoneal Cancer Index



Regions	Lesion Size
0 Central	
1 Right Upper	
2 Epigastrium	
3 Left Upper	
4 Left Flank	
5 Left Lower	
6 Pelvis	
7 Right Lower	
8 Right Flank	
9 Upper Jejunum	
10 Lower Jejunum	
11 Upper Ileum	
12 Lower Ileum	

PCI ☐

Lesion Size Score

LS 0 No tumor seen
LS 1 Tumor up to 0.5 cm
LS 2 Tumor up to 5.0 cm
LS 3 Tumor >5.0 cm or confluence

The peritoneal cancer index combines a distribution assessment with a volume assessment to estimate the extent of peritoneal metastases. This estimate predicts the long-term benefits one can achieve with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy.

Ismailia Teaching Oncology Institute

- Located at Ismailia , the nice city alongside Suez canal beach
- **60** Beds
- **8** Department

1. Surgical Oncology
2. Medical Oncology
3. Radiotherapy
4. Diagnostic Radiology
5. Intervent. Radiology
6. Histopathology
7. Clinical Pathology
8. Anaeshesia and ICU

PATIENT SELECTION

I- Exclusion befor exploration:

- Extra abdominal metastases.
- Medically and psychologically unfit

This is done through:

- History and physical examination
- Psychological study
- Blood tests , tumour markers
- CT , PET-CT
- Colonoscopy and Biopsy
- Laparoscopy (the gold standard for diagnosis if possibly done) .

To detect Peritoneal Cancer Index (PCI) preoperative

II- Exclusion after exploration:

- **Frozen** pelvis
- Mesenteric **root** infiltration
- Massively infiltrated **pancreatic** capsule
- Expected **small bowel resection** for more than **half** of length
- **Unresectable** liver metastases

SURGICAL TECHNIQUES

- **Median xipho- pubic incision**

1. Peritonectomy and pelvic surgery

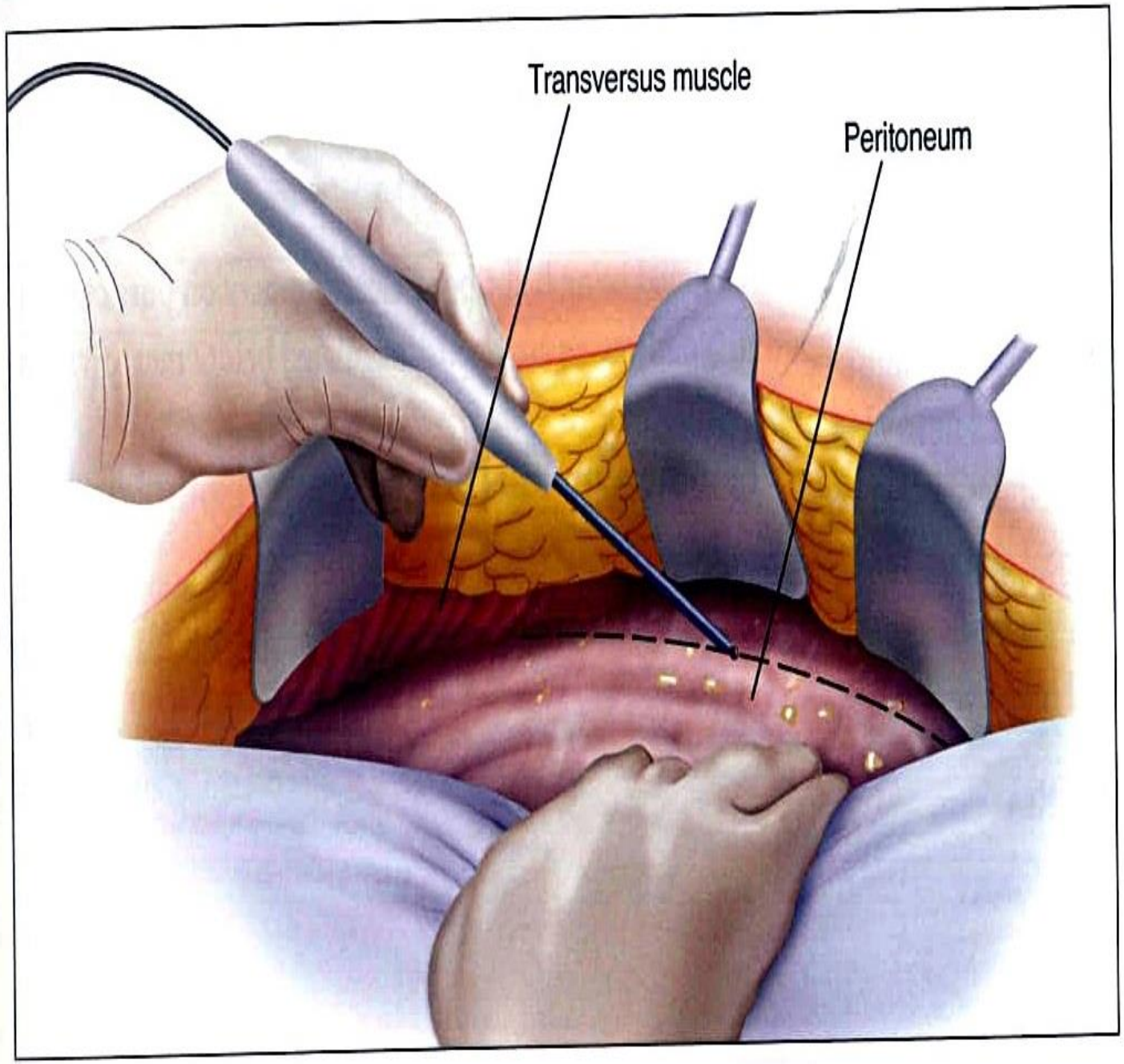
- **Evaluation and resection of colorectal pathology**
  - ★ **Resection of Uterus and ovaries if infiltrated in female**
  - ★ **Pelvic peritonectomy started on right and left side of bladder with traction on urachus**
  - ★ **If there is tumour invading seminal vesicle and prostate resection of both is necessary in male**

SURGICAL TECHNIQUES

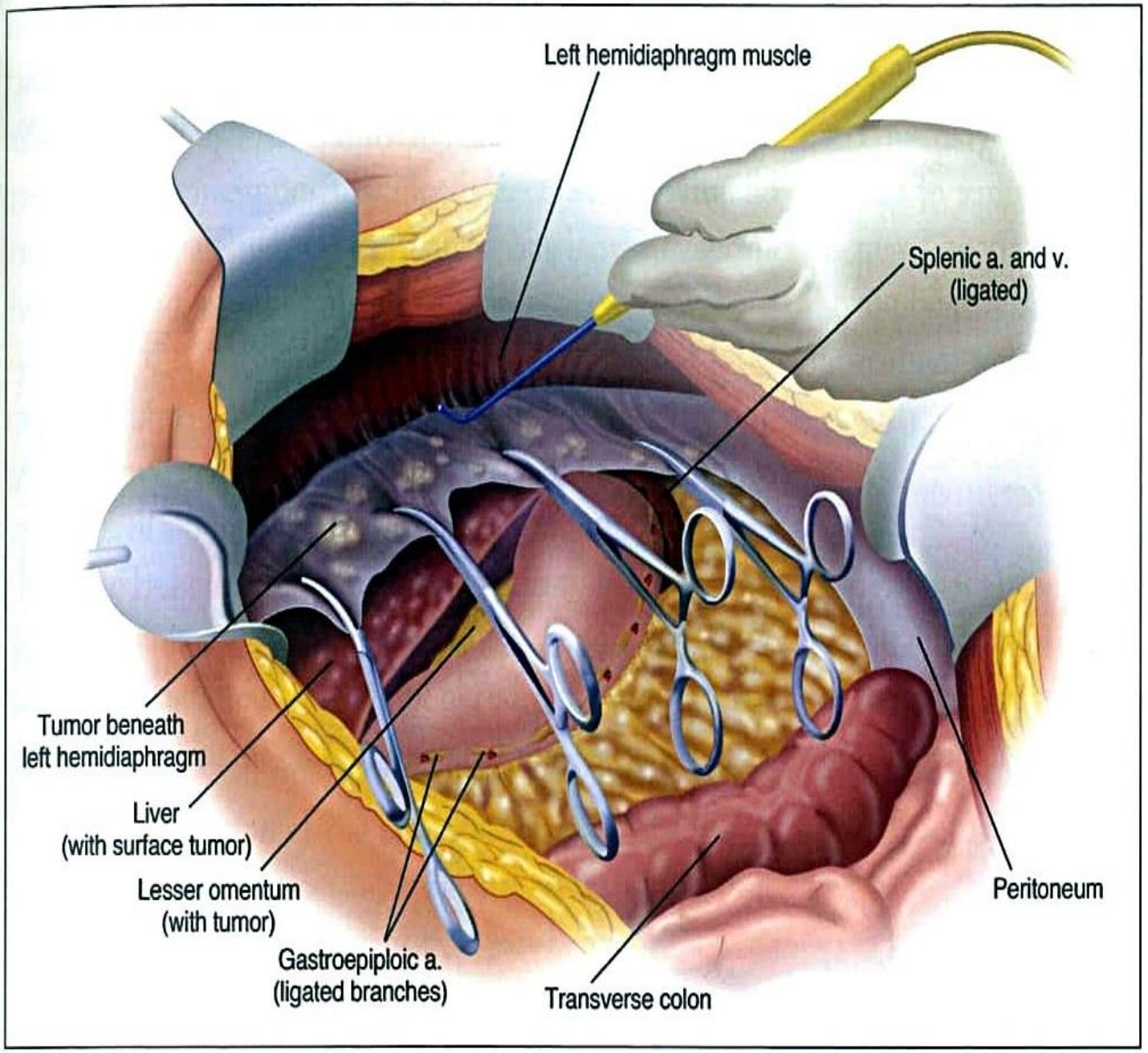
2. Peritonectomy and abdominal surgery

- **Dissection of the parietal peritoneum from the anterior abdominal wall .**
- **Left subphrenic peritonectomy**
- **Greater omentectomy and sometimes splenectomy avoiding trauma of the body or tail of the pancreas**
- **Lesser omentectomy and cholecystectomy with stripping of the hepatoduodenal ligament**
- **Resection of umbilical ligament after division of hepatic bridge (important)**
- **Right subphrenic peritonectomy and stripping of Glisson's capsule of liver**
- **Metastectomy 0f liver mets according to the rules**

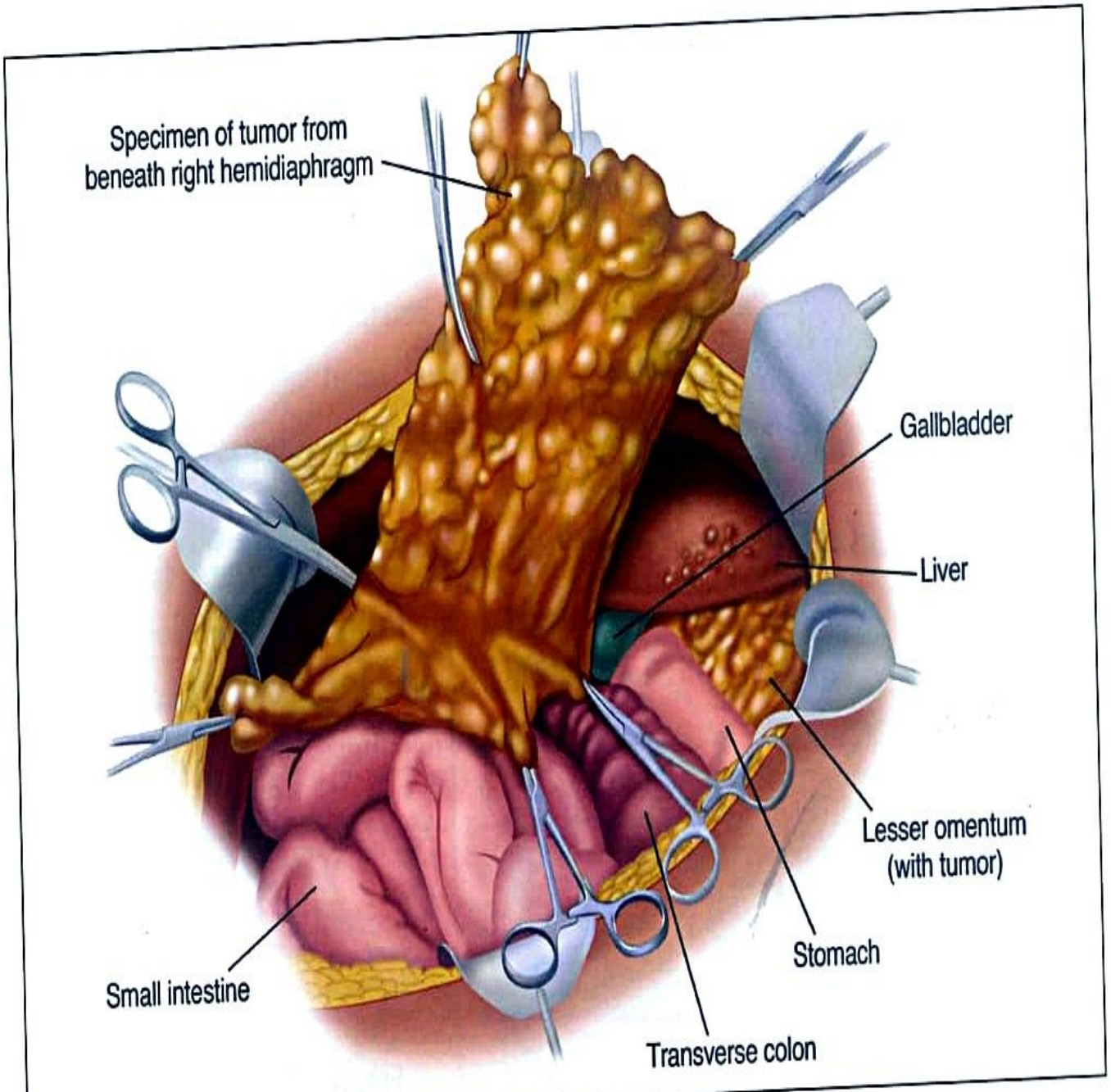
Modified lithotomy position and maximal midline incision for cytoreductive surgery.



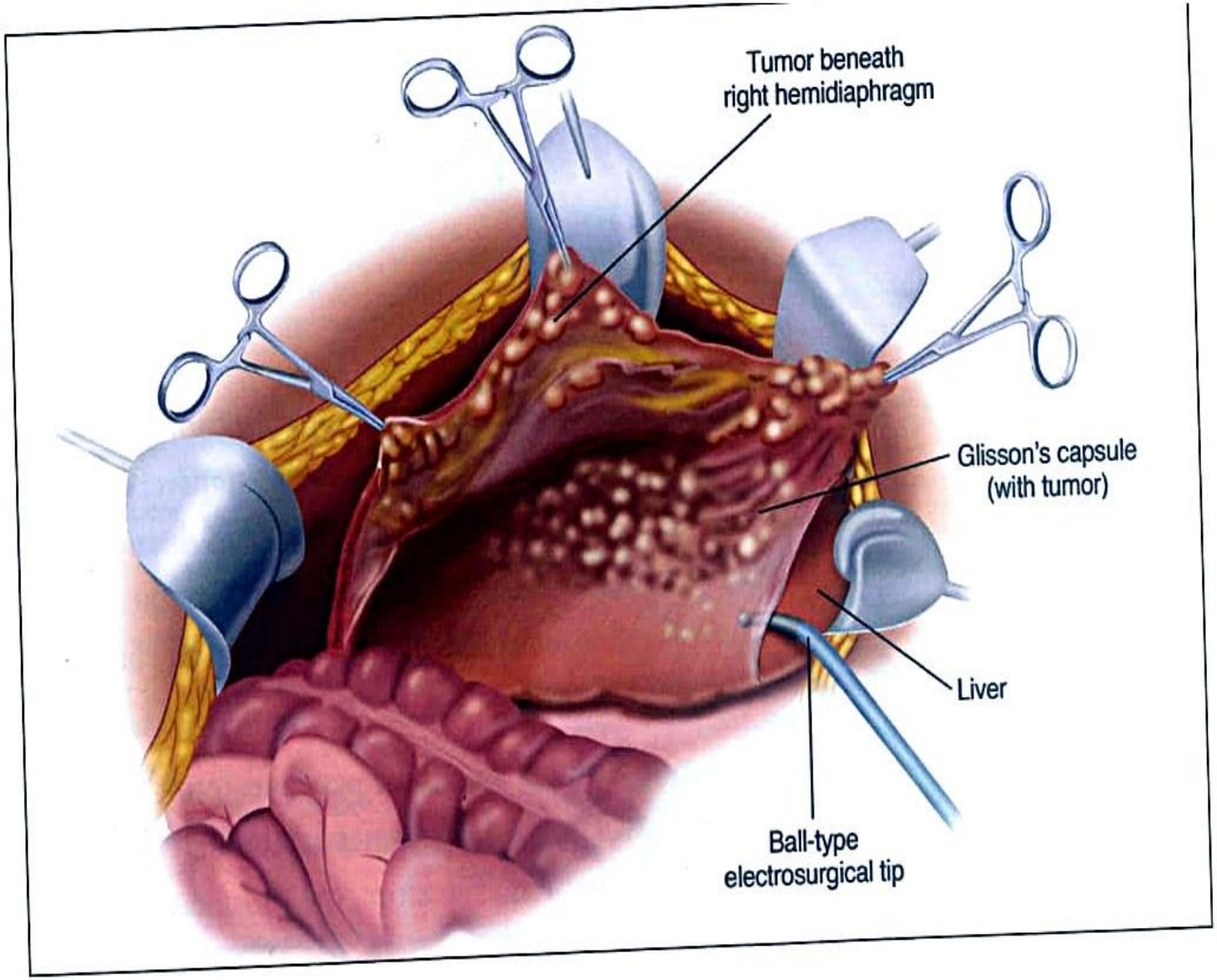
Lateral dissection of the parietal peritoneum away from the posterior rectus sheath and the abdominal wall musculature completes the anterior parietal peritonectomy.



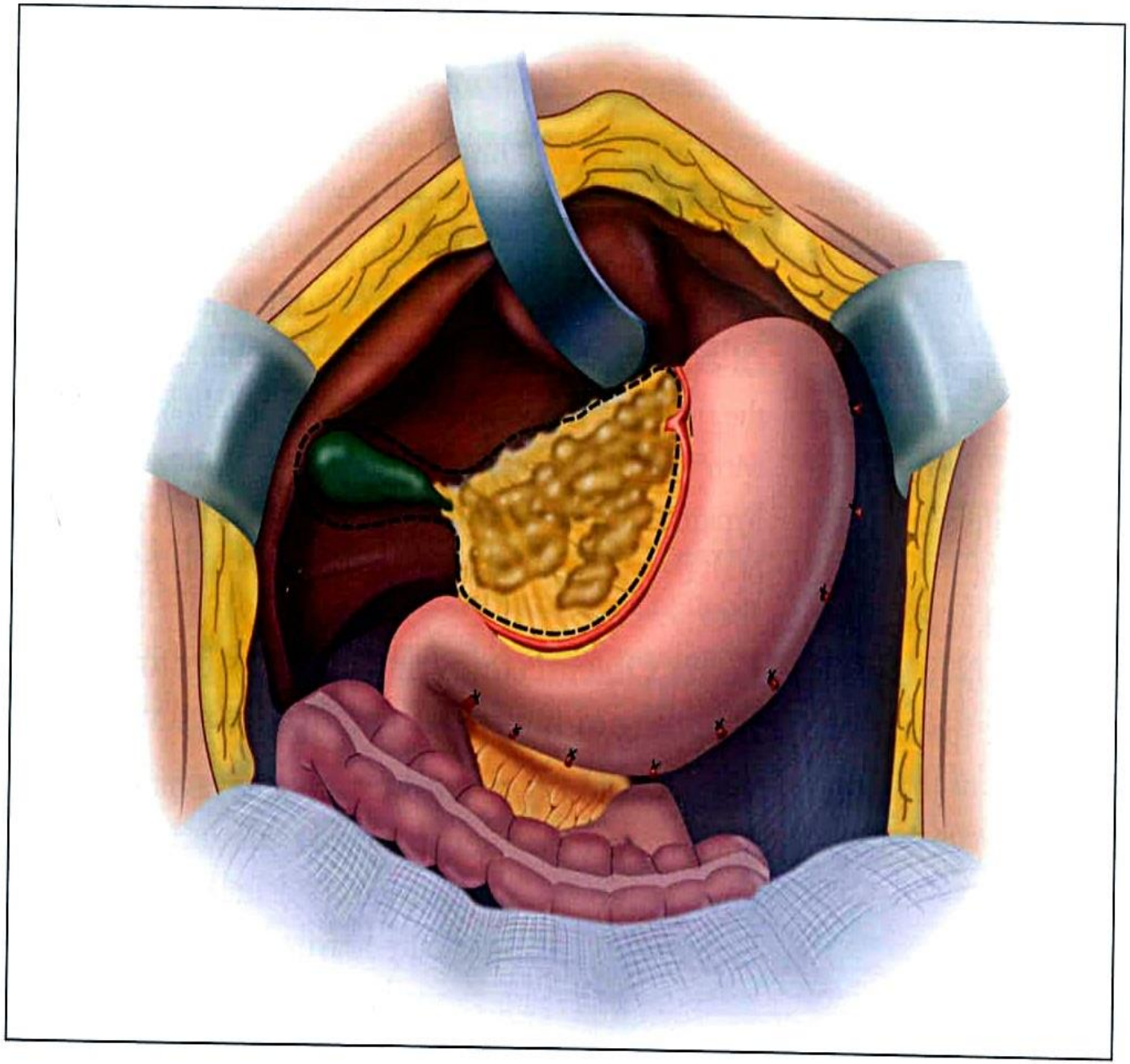
Peritoneal stripping of the undersurface of the left diaphragm.



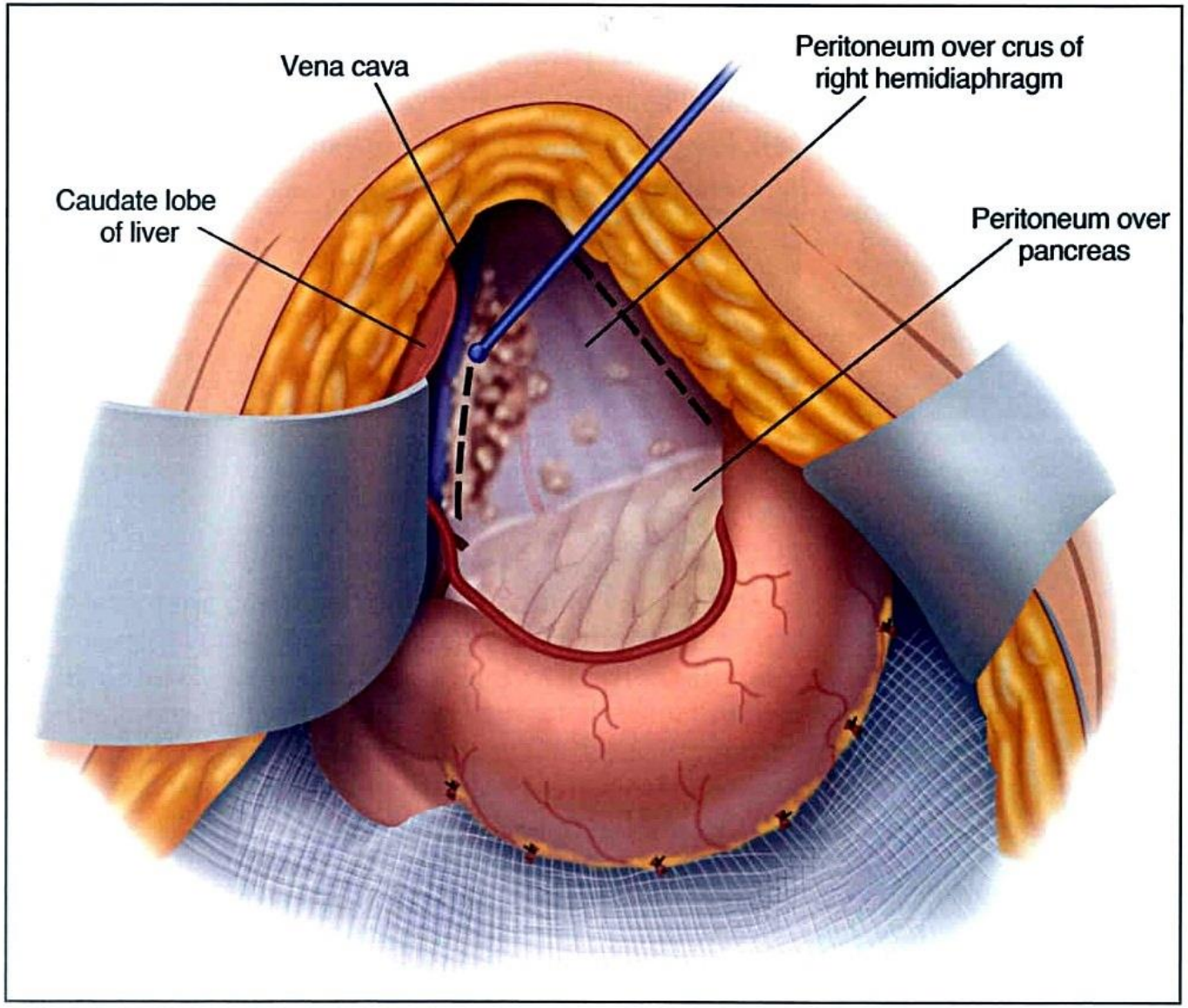
Peritoneal stripping of the undersurface of the right hemidiaphragm.



Electroevaporation of tumor from the liver surface with resection of Glisson's capsule.

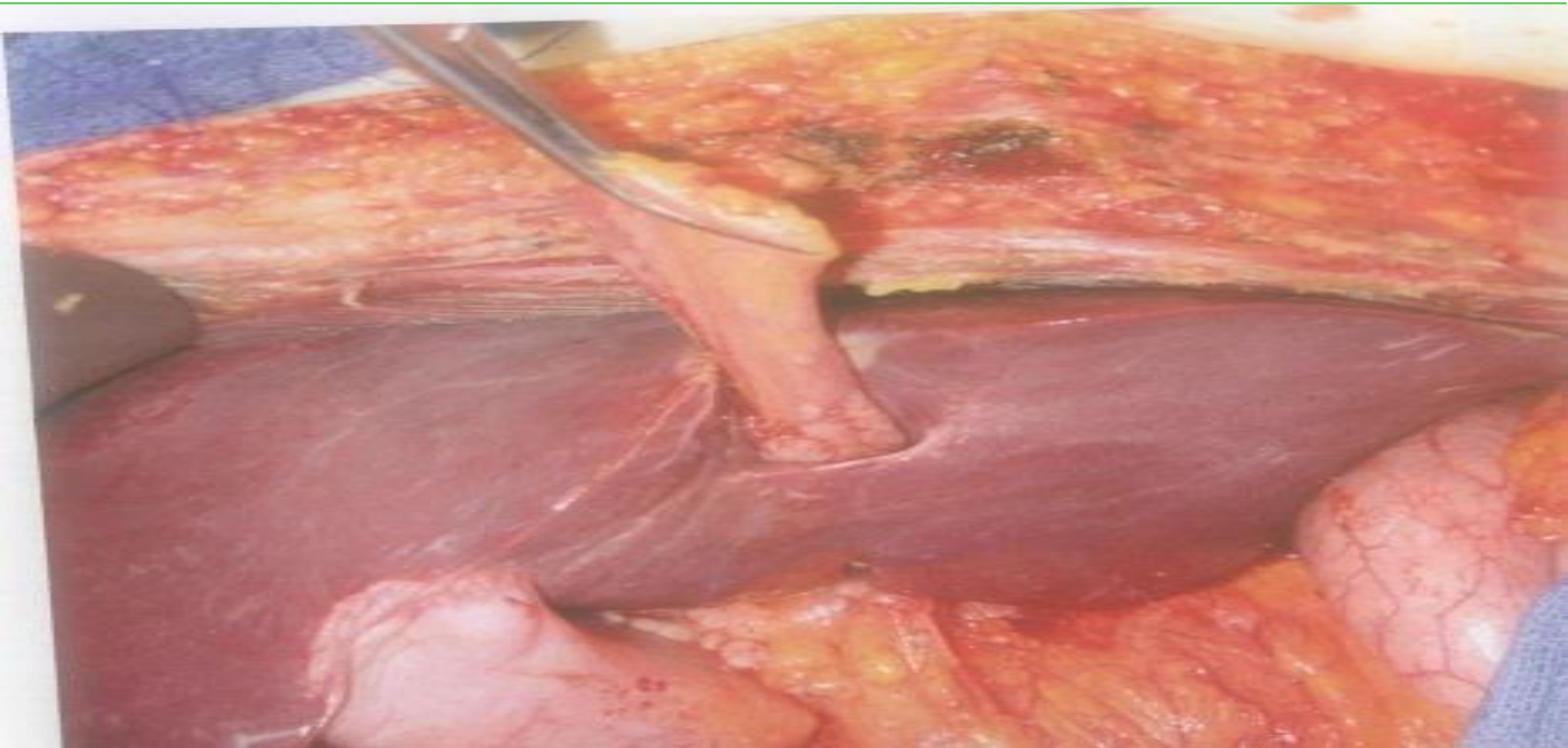


Lesser omentectomy and cholecystectomy with stripping of the anterior and posterior (if necessary) aspect of the hepatoduodenal ligament.



Stripping of the omental bursa after dividing the peritoneal reflection between left caudate lobe and superior vena cava.

Hepatic Bridge



TECHNIQUE of HIPEC

- **Delivery of HIPEC is performed by using HIPEC Delivery Set.**
- **Our drug delivered is Mytomycin**
- **Delivery of HIPEC is by two methods:**
  1. **Open abdomenal technique**
  2. **Closed abdomenal technique.**
- **Open and Closed techniques are both safe and feasible.**

Our Results

- 12 cases from jun 2018 till April 2021
- 9 males and 3females
- Age ranging between 42-60 years
- Mortality 4 :
  1. Early 1 case from pulmonary embolism
  2. Late 3 one case pancreatic fistula and the two other complex high output small intestinal fistula with redo surgery

- **Morbidity:**

1. **1 case fecal fistula treated conservatively**
2. **2 cases developed incisional hernia**
3. **1 case recurrent attacks of adhesive intestinal obstruction to be managed conservatively**

CONCLUSIONS.

- **CRS and HIPEC are an option for selected patients with Peritoneal Metastasis from colorectal origin which may result in long-term survival .**
- **Adequate patient selection is one of the major challenges**
- **So This technique needs a multidisciplinary team**

CONCLUSION

- Our target was to develop a model or protocol to predict and improve survival
- CRS and HIPEC should be avoided in patients who are unlikely to undergo a complete macroscopic resection and medically and psychologically unfit
- Patients free from cardiopulmonary disease , free of obstructive symptoms , with low peritoneal carcinimatosis index less than 16 are the best candidates for this technique of surgery

CONCLUSIONS.

- **This technique needs a multidisciplinary team of surgical oncology , medical oncology , anaesthesia , intensive care , high quality operating room nurses and biomedical engineering.**

THANK YOU