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Functional Anatomy in Relation to Peritoneal Surface Malignancies (PSM): Lessons Learnt after 254 Cases of Peritonectomy at a Tertiary Oncology Centre in India

Research Article

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Abstract

Introduction: Peritoneal Surface Malignancies (PSMs) are a heterogenous group of diseases. They are still considered terminal in many tertiary care centers in India. Cytoreductive Surgery (CRS) including peritonectomy has been the main stay of treatment of PSMs. In this article, we elaborate the applied anatomy of peritoneum from macroscopic to microscopic structure, the mechanism of spread, common sites of involvements and the techniques of perfection in CRS leading to better surgical outcomes based on our experience.

Methods: We have performed 254 cases of peritonectomy-Total Parietal Peritonectomy (TPP) in 104 cases (40.9%) and disease selective in 150 cases (59.1%) from 2014 to 2021. We have performed TPP in cases of Pseudomyxoma Peritonei (PMP), Malignant Peritoneal Mesothelioma (MPM) and post NACT cytoreduction in all patients of PSMs

Results: In all cases of CRS we removed the primary tumor as per standard oncological principles. Apart from this we removed total greater omentum, lesser omentum, omental bursa and all lymph nodes pertaining to respective diseases. The distribution of our patients was Ovarian carcinoma (n = 152), Colorectal (n = 43), PMP (n = 34), MPM (n = 11), Sarcomatosis (n = 7), Gastric Cancer (n = 3) and Miscellaneous (n = 4). With our 7 years' experience we share our inputs on the anatomical basis of peritoneal carcinomatosis and sarcomatosis.

Conclusion: We have performed 254 peritonectomy procedures. On the basis of our experience and evidence, we conclude that anatomy of peritoneum is very important as it is the most common site of recurrence in PSMs after CRS. We recommend TPP in all cases of PMP, MPM and in interval cytoreduction setting.

Keywords: CRS; HIPEC; Peritoneum; Peritoneal carcinomatosis; Sarcomatosis

Abbreviations: PSM: Peritoneal Surface Malignancy; CRS: Cytoreductive Surgery; PMP: Pseudo Myxoma Peritoneii; MPM: Malignant Peritoneal Mesothelioma; HIPEC: Hyperthermic Intraperitoneal Chemotherapy; NACT: Neo Adjuvant Chemotherapy; TPP: Total Parietal Peritonectomy; PC: Peritoneal Carcinomatosis

Introduction

Peritoneal Surface Malignancies (PSMs) are a heterogenous group of diseases including Pseudomyxoma Peritonei (PMP), Malignant Peritoneal Mesothelioma (MPM), Ovarian Carcinoma, Colorectal cancer with synchronous or metachronous peritoneal metastasis, Gastric cancer with limited metastasis and selected cases of Sarcomatosis. PSMs used to be considered as terminal disease a decade back and still remains terminal in many tertiary care centers in India. With the advent of Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC), the prognosis has significantly changed over the last decade. CRS including peritonectomy has been the main stay of treatment for patients of PSMs. In this article, we elaborate the applied anatomy of peritoneum from macroscopic to microscopic structure, the mechanism of spread, common sites of involvements and the techniques of perfection in CRS leading to better surgical outcomes based on our experience.

Materials and Methods

We have performed 254 cases of peritonectomy – total parietal peritonectomy in 104 cases (40.9%) and disease selective in 150 cases (59.1%) from 2014 to 2021. Total parietal peritonectomy was done in cases of PMP, MPM and post Neoadjuvant Chemotherapy (NACT) cytoreduction in all patients of PSMs. In primary cases we performed total peritonectomy and remaining were disease specific peritonectomy such as pelvic peritonectomy in ovarian carcinoma and right parietal peritonectomy in right sided colon cancer (Table 1).

Table 1: Types of selective peritonectomy procedures done.

Type of Selective Peritonectomy	No of Patients (n = 150)
Pelvic Peritonectomy	135 (90%)
Right Subdiaphragmatic Peritonectomy	112 (75%)
Lesser Omentectomy	87 (58%)
Peritonectomy of Morrison's Pouch	37 (25%)
Left Subdiaphragmatic Peritonectomy	33 (22%)
Parietal Peritonectomy	16 (11%)
Mesentery with Small Bowel Serosa	13 (9%)

Results

In all cases of CRS we removed the primary tumor as per standard oncological principles. Apart from this we removed total greater omentum, lesser omentum, omental bursa and all lymph nodes pertaining to respective diseases. The distribution of our patients was Ovarian carcinoma (n = 152), Colorectal (n = 43), PMP (n = 34), MPM (n = 11), Sarcomatosis (n = 7), Gastric Cancer (n = 3) and Miscellaneous (n = 4) (Table 2). Glisson capsulectomy, pancreatic capsulectomy, cholecystectomy, distal gastrectomy, sigmoidectomy, ileocecal resection, splenectomy, segmental liver resection, hepatic bridge resection, metastatectomy were performed as and when required to achieve complete CRS. Analysis of the pattern of recurrences opened our eyes to revisit applied anatomy of peritoneum and metastatic spread of Peritoneal Carcinomatosis (PC) as peritoneum was the most common site of recurrence (27%, n = 41/150) where total parietal peritonectomy was not performed. With our 7 years of experience we share these inputs on the anatomical basis of Peritoneal carcinomatosis and sarcomatosis.

Table 2: Summary of the cases where peritonectomy was performed.

Disease	No of Patients (Total n = 254)
Ovarian Carcinoma	152
Colorectal Carcinoma	43
Pseudo Myxoma Peritonei	34
Malignant Peritoneal Mesothelioma	11
Sarcomatosis	7
Gastric Cancer	3
Miscellaneous	4

Discussion

In primary cases, we performed disease specific peritonectomy. In our practice CC1 was considered only when multiple small nodules ≤ 2.5mm involving small bowel wall in multiple sites were present. Otherwise we don't believe in CC1 disease as everywhere these are removable. Organ resection either total, partial/segmental in selective cases were performed to achieve optimal cytoreduction. We have studied that peritoneum is one of the largest organs in our body with a surface area of 1.2 - 2m2 [1].

Controversies still persist regarding the choice of total vs selective parietal peritonectomy. Some authors preferred Total Parietal Peritonectomy (TPP) in all cases with acceptable morbidity and mortality and showed significant recurrence free and overall survival [2-4]. On the contrary, other authors have stated that parietal peritoneum constitutes only 10% of total surface area of peritoneum and the remaining 90% is visceral peritoneum, thereby no role of removing only parietal peritoneum [5]. Sugar baker, et al also supported disease specific peritonectomy [6,7].

But we suggest that TPP is mandatory in:

- All cases of malignant mesothelioma as the site of origin is from the peritoneum itself.
- PMP as there is diffuse involvement of peritoneum.
- Interval setting because of two reasons (i) NACT was offered when disease burden is more which could not be properly assessed during surgery after the response to NACT (ii) Post NACT site of disease detection is difficult because of desmoplastic reaction [8].

Mechanism of Peritoneal Involvement

Peritoneal Carcinomatosis may be primary like malignant mesothelioma, PMP and ovarian carcinoma, or secondary from colorectal cancers, gall bladder, pancreatic, endocervical and even from lung and breast cancers. Peritoneal Sarcomatosis may occur from endometrial stromal sarcoma, liposarcoma or leiomyosarcoma. Grossly the dislodged free tumor cells from the primary sites float with peritoneal fluid under gravitation, posture of the patient, peritoneal folding pattern, recesses and mesenteric reflections which may lead to development of peritoneal carcinomatosis/sarcomatosis. We should know about the microanatomy of peritoneum for better understanding of the disease and pattern of peritoneal and other sites involvement. Peritoneum consists of five distinct layers [9,10] (Figure 1):

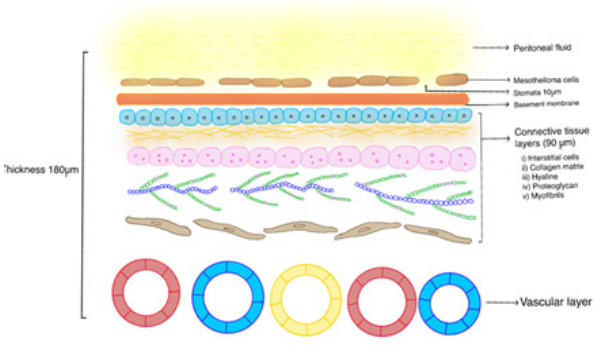

Figure 1: Plasma Peritoneal Barrier.

Plasma Peritoneal Barrier consisting of Peritoneal fluid, mesothelium, basement membrane, connective tissue (5 layers) being the strongest barrier, and the vascular layer.

I. Single layer of mesothelioma cells

II. Basal membrane

III. Connective tissue layer consisting of 5 components - (a) Interstitial cells, (b) Collagen matrix, (c) Hyaline (d) Proteoglycans and (e) Myofibrils. A total thickness of 90µm.

IV. Pericytes, parenchymal cells

V. Blood capillaries, vessels, lymphatics.

VI. Maximum thickness of peritoneum is 180µm but thickness varies from site to site [10].

Mechanism of Microscopic Spread

Free cancer cells either spontaneously or as result of treatment, propagates the peritoneal surface usually or depending upon the disease burden enter the systemic circulation via sub peritoneal lymphatic lacunae. Free tumor cells may also attach to mesothelial layer of peritoneum through a variety of adhesion molecules such as ICAM1, VCAM, PECAM1 and start proliferating [10,11]. Another mechanism of spread is due to the presence of stroma in between mesothelial cells measuring 10µm in thickness (Figure 2).

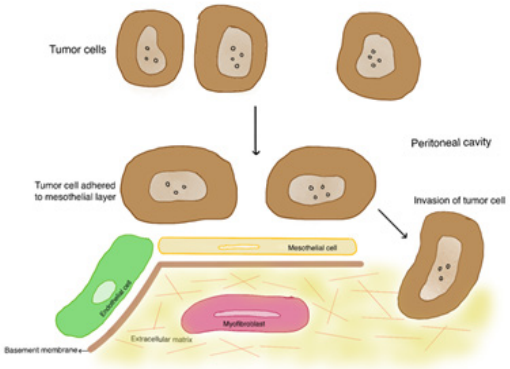

Figure 2: Pathways of spread and mechanism of peritoneal carcinomatosis.

Floating tumor cells in the peritoneal cavity adhere to the mesothelial cells and gain entry through the stomata (10µm thick) and then reach the capillary, vessels and lymphatics.

Cancer cells gain entry through the stroma and reach the capillaries, vessels and lymphatic layers also called 'Peritoneal Membrane' and get absorbed by vessels and lymphatics resulting in metastasis mainly to the liver (80%) and other organs including peritoneum (20%) [12,13]. Through the stomata (10µm) of mesothelial cell layers, cancer cells along with peritoneal fluid enter into substernal, parasternal, mediastinal, epiphrenic lymph nodes [11]. Cancer cells spread to the para aortic and renal hilum nodes occur through the same pathway particularly in colorectal cancer.

Mechanism of Macroscopic Spread

There is flow of free cancer cells with peritoneal fluid towards pelvic cavity first, being the most dependent part of the body on standing and the pouch of Morrison being the most dependent part while lying down. This may explain why pelvic peritonectomy was most commonly performed in 90% (n = 135) and peritonectomy at the pouch of Morison in 25% cases (n = 37) in our series.

From the pelvis along with right paracolic gutter free cancer cells move towards right sub diaphragmatic space as it is broader than the left side and also without any ligamental barrier. The left paracolic gutter is cut off from the left sub diaphragmatic space by phrenicocolic ligament [14]. Almost 80% of lymphatic lacunae are located between the muscle fibers of the right hemi diaphragm, therefore many a times a full thickness diaphragmatic resection is required to achieve complete (CC0) cytoreduction. Due to the above anatomical and physiological mechanisms, the disease involvement is less in the left sub diaphragmatic space than the right side and the same was observed in our series where the right sub diaphragmatic area was more commonly involved (75% vs 22%) than the left. We have performed the removal of parietal peritoneum in 11% patients (n = 16) and removal of the mesentery with bowel serosa in 9% patients (n = 13).

In ovarian cancers the main pathway to involve retroperitoneal lymph nodes are through the infundibulopelvic ligaments. The disease also spreads to pelvic nodes through the broad ligament and to the groin nodes through the round ligament. In females there is 10% extra peritoneum compared to males. Peritoneal cavity is completely closed in male but in female fallopian tubes open into peritoneal cavity - thereby cancer cells may easily spread to the peritoneum from female genital tract. The ovaries are also directly related to the peritoneal surface. Hence the FIGO staging of ovarian cancer always includes the peritoneum [15].

In Colorectal cancer there is involvement of the epicolic, pericolic, intermediate and principal nodes. In gastric cancers D1 (Station 1-6) D2 (Station 7-11) lymph nodes involvement occurs. Through the Epiploic foramen (foramen of Winslow), disease may spread to the lesser sac from the greater sac with some studies having involvement in almost 2/3rd of cases [16,17]. In our series the involvement of lesser omentum was 58% (87 patients) thereby we recommend that lesser omentectomy along with lesser sac should be a part of CRS.

The transverse mesocolon divides the abdomen into supramesocolic and inframesocolic spaces [18]. Root of mesentery is the junction between parietal peritoneum and retroperitoneum. In right infra mesocolic space, fluid is impeded from draining into pelvis via the mesentery. Because of anatomical holding up of fluid along with cancer cells, the root of small bowel mesentery and sigmoid mesocolon are usually predisposed to serosal involvement. Pyloric antrum, ligament of Treitz, ileocecal and rectosigmoid junctions are more prone to be involved by the disease because of their variation and fixity in nature.

Peritoneal Spaces

The transverse colon and the transverse mesocolon are the major landmarks which divide the peritoneal cavity into supramesocolic and inframesocolic compartments. Anterior to the liver, the supramesocolic compartment is divided by the falciform ligament into the left and right subphrenic spaces [18]. The subhepatic space including the lesser sac is located inferior to the liver. The inframesocolic compartment is divided by the root of the mesentery of small intestine into the right and the left inframesocolic space and the pelvis [19]. The left and right paracolic gutters are continuations of the pelvis cranially. The left paracolic gutter is comparatively narrower than the right. The right paracolic gutter cranially is in continuity with the right subphrenic space. The pelvis is divided into five fossae by the median umbilical ligament (remnant of urachus), two medial umbilical ligaments (obliterated umbilical arteries) and two lateral umbilical ligaments (inferior epigastric vessels) [20].

Peritoneal Fluid

Under physiological conditions, about 1L of peritoneal fluid is produced within 24 hrs. The peritoneal fluid is reabsorbed by the subperitoneal lymphatic channels. The parietal and visceral layers of peritoneum are separated from each other by approximately 50-100mL of peritoneal fluid which helps in lubrication of the peritoneal surfaces. The peritoneal fluid volume increases under pathological conditions such as portal hypertension, abdominal tuberculosis, alcoholic cirrhosis, portal venous thrombosis, malignant ascites, peritonitis etc. [14].

Peritoneal fluid is drawn into the upper abdomen by low subdiaphragmatic pressures and pulled into the pelvis due to gravity. It

pools in dependent recesses, such as the pouch of Douglas in females and the recto vesical recess in males, and also along the superior portion of the sigmoid mesocolon, ileocolic region, right paracolic gutter and Morison's pouch [21].

The peritoneal fluid preferentially flows in certain directions due to its anatomical and physiological constraints. Peritoneal fluid from the pelvis primarily goes up the right paracolic gutter. From the right paracolic gutter, fluid enters the right subhepatic space (Morison's pouch) and subsequently to the lesser sac via the epiploic foramen [19]. Fluid also goes superiorly into the right subphrenic space but the falciform ligament limits flow from the right to the left subphrenic space. On the left, the phrenicocolic ligament limits the left paracolic gutter (recess) to the left subphrenic space. Abscesses secondary to intraperitoneal infections and tumour deposits are therefore common in the pouch of Douglas, right subhepatic space, right paracolic gutter and right subphrenic space. Fluid flow patterns are usually bidirectional [19]. Although the falciform and phrenicocolic ligaments serve as anatomical boundaries and limit the flow of fluid, large volumes of fluid can overflow under the free edges of these ligaments.

Peritoneal Ligaments

Peritoneal ligaments are double layers or folds of peritoneum that support the structures within the peritoneal cavity [20]. Peritoneal ligaments play important role in spreading peritoneal disease. We all know upper abdominal viscera are interconnected by six ligaments: Gastro hepatic, hepatoduodenal ligament (lesser omentum), Gastro Splenic, Splenorenal, Gastrocolic ligaments and Transverse mesocolon [14].

Part of each ligament bridges to the retroperitoneum. Thus, disease from the abdominal viscera may spread to retroperitoneum or vice versa. Gastrohepatic ligament is connected with sub peritoneal areolar tissue and with Glisson capsule of the liver. Because of this unique feature of gastro hepatic ligament, disease can spread from lesser curvature into both lobes of liver. Through hepatoduodenal ligament, disease may spread from porta hepatis to hepatic bridge (segment 3 and 4B) as well as retroperitoneum. Antegrade flow of lymphatic fluid from liver and biliary tree involves surrounding duodenum and pancreas.

Greater omentum is the main depot of the metastatic disease because of its police man nature. Omental cake formation occurs owing to changing of barely discernible fatty band to a mass that can spread the disease to abdominal wall [22]. Omental bursa, the floor of lesser omentum may be involved through the greater omentum and the bursa is continued to the capsule of pancreas.

Gastrocolic ligament (greater omentum) forms the left wall of lesser sac and provides a conduit for the spread of metastatic disease from greater curvature of the stomach to retroperitoneum. As 2/3rd of the greater omentum is attached to transverse colon, disease involving the stomach may involve transverse colon and vice versa and to retroperitoneum in the mid abdomen. The disease involving transverse colon may involve retroperitoneum, pancreas via transverse mesocolon.

Clinical Application

CRS includes resection of organ of origin, greater omentectomy, lesser omentectomy, total peritonectomy, clearance of all nodes and involved structures. To simplify, no macroscopic disease should be left behind. As per our practice, we consider lymph nodes dissection as an integral part of the CRS and in our series, post NACT nodal positivity in carcinoma ovary was 56%. As lymph nodes are the part and parcel of the disease, without removal of lymph nodes HIPEC is not justified. Therefore, not performing lymph node dissection violates the basic principles of HIPEC and surgical oncology. Lymph nodes are the second most common site of recurrence after peritoneum following CRS or CRS+HIPEC [23,24].

Basis of HIPEC- because of Plasma Peritoneal Barrier (PPB) systemic chemotherapy is not much effective in peritoneal carcinomatosis [25]. The PPB consisting of peritoneal fluid itself, mesothelium, basement membrane, connective tissue being the strongest barrier consists of five distinct layers, and the capillary, vascular and lymphatic layers. 80% of this circulation drain to the liver via portal system and intraperitoneal chemotherapy (CIP) is detoxified by the liver, hence systemic side effects are less and microscopic deposits in liver may be destroyed by the absorbed CIP itself. In Low- and Middle-Income countries like India it is always a challenge to deliver complex and intensive treatments like CRS and HIPEC. The key to success is multidisciplinary team approach, protocol-based treatment delivery with strict adherence to patient selection criteria, surgical quality control, and optimal perioperative care [26].

Practical Tips and Tricks

- For total parietal peritonectomy extraperitoneal approach is advisable, specifically in cases of PMP, MPM and post NACT cytoreduction.
- Parietal peritoneum to be removed from anterior, lateral, posterior abdominal wall surfaces, inferior surfaces of diaphragm and pelvis.
- Complete hepatic mobilization is required for subdiaphragmatic peritonectomy and disease removal. Take care about IVC, right hepatic vein and diaphragmatic injury. Diaphragm is thinner at its posterior costal attachments - more precautions to be taken at this area to avoid diaphragmatic rent formation.
- Know the detailed anatomy of peritoneal structure, function and mechanism of PC. It is necessary to have adequate knowledge about lesser sac, greater omentum, lesser omentum, peritoneal folds of the anterior abdominal wall, peritoneal compartments, retroperitoneal spaces - aorta and its branches, IVCs and its tributaries, cisterna chyli, lymphatic channels and nodes, lumbar vessels, nerves including sympathetic trunks, kidney, course of both ureters, pancreas, ascending and descending colon, duodenum, suprarenal gland [27].
- Detailed anatomical knowledge and the surgical skill are the keys to successful outcomes of any complex surgery. We read anatomy repeatedly and correlate practically.

Lessons Learnt after 254 Cases

- Peritoneum is a complex and the largest organ in our body and the root of mesenteric attachment (15cm) is the gateway between intraperitoneum and retroperitoneum.
- In the retroperitoneal tissue at the root of mesentery there are numerous pacinian corpuscles and over stretching of mesentery and peritoneal fold causes undue stimulation of these encapsulated mechano receptors leading to hypotension and tachycardia.
- Constant pressure over IVC during hepatic mobilization may lead to sudden bradycardia.
- Laparoscopy has an important role before opening the abdomen in selected cases as CT or PET CT has >30% discordance.
- MRI is a better imaging modality for mucinous disease and assessment of bowel and subdiaphragmatic deposits.
- Apart from the small bowel transmural infiltration, there is no CC1 disease as all are resectable. Hence, we check for transmural infiltration throughout the length of small bowel beforehand especially when we find small bowel mesenteric disease burden is high.
- Diseased peritoneum is thickened and it can easily be stripped off from posterior rectus sheath, bladder, diaphragm etc. Prophylactic peritonectomy is a patience game and most of the time posterior rectus sheath is removed along with non-diseased peritoneum.

- Hemostasis is the most important part after peritonectomy. Keep one eye always to achieve complete hemostasis repeatedly.

- Peritonectomy using ball electrosurgical cautery at the setting of 75-100W to destroy microscopic cancer cells and achieve hemostasis.

- Abdominal mop coverage over all dependent surfaces after peritonectomy to prevent cancer cells adhesion.

- Minimum three times large volume (4.5L) saline irrigation after CRS to eliminate blood clots and tumor cell adhesive molecules. Sugarbaker advised usage of 0.25% Hydrogen peroxide for the same purpose in addition to hemostasis [28].

- Reconstruction like intestinal anastomoses before or after HIPEC depends upon experience of the surgeon. We do before HIPEC and keep the anastomotic site away from the inflow tubings. Many other HIPEC surgeons prefer the anastomoses after HIPEC.

- In a word, peritoneum is the largest and complex organ in our body.

- Prehabilitation, good anatomical knowledge and gentle intra operative handling of peritoneal cavity is mandate as we believe the origin of post-operative complications start during surgery.

Conclusion

We have performed 254 peritonectomy procedures. On the basis of our experience and evidence, we conclude that anatomy of peritoneum is very important as it is the most common site of recurrence in PSM patients undergoing CRS. We recommend TPP in all cases of PMP, MPM and in interval cytoreduction setting. Decision making, multidisciplinary approach, standard setup and overall skill of the surgeon matters for optimal outcomes.

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