



# Imaging Recommendations for Diagnosis, Staging, and Management of Peritoneal Malignancies

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## Abstract

Peritoneum is a serosal membrane lining the solid viscera and the hollow viscus of the abdomen and is made of a single layer of mesothelial cells. The most common primaries that spread to the peritoneum include gastrointestinal, ovarian, colorectal, and peritoneal metastases can be seen at some point during the disease course in 15 to 43%, 60 to 70% and 15 to 20% of patients, respectively. Other malignancies involving the peritoneum such as primary peritoneal carcinoma, peritoneal mesothelioma, peritoneal lymphomatosis, pseudomyxoma peritonei from low-grade appendiceal mucinous neoplasm, are far less common. The review strives to provide a framework for diagnosis and management of the disease.

## Keywords

- ▶ CRS
- ▶ guidelines
- ▶ peritoneal surface malignancies
- ▶ recommendations

## Introduction

Peritoneum is a serosal membrane lining the solid viscera and the hollow viscus of the abdomen and is made of a single layer of mesothelial cells. Due to low sensitivity of imaging modalities to detected small peritoneal metastasis, the incidence of peritoneal malignancies remains unclear. Peritoneal carcinomatosis is the most common peritoneal surface malignancy and its incidence among the Czech population was 99 per 1,000,000. Primary peritoneal surface malignancies are very uncommon with an incidence of 4.36 per 1,000,000.<sup>1</sup> The most common primaries that spread to the peritoneum include gastrointestinal, ovarian, colorectal, and peritoneal metastases

can be seen at some point during the disease course in 15–43%, 60–70%, and 15–20% of patients, respectively.<sup>2</sup> Other malignancies involving the peritoneum such as primary peritoneal carcinoma, peritoneal mesothelioma, peritoneal lymphomatosis, pseudomyxoma peritonei from low grade appendiceal mucinous neoplasm are far less common.

Advanced stage of the primary tumor predisposes to peritoneal carcinomatosis. Apart from T- and N-stage, positive peritoneal fluid cytology and histological subtype of the primary are risk factors for peritoneal metastases. The most common symptoms of peritoneal surface malignancies include abdominal pain, abdominal distension from ascites or bowel obstruction. Non-specific symptoms include nausea,

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vomiting, fatigue, weight loss, and constipation. Tumor markers are used for diagnosis, prognosis, and for assessing treatment response. Carcinoembryonic antigen (CEA) and CA-19-9 are used in gastrointestinal malignancies. CA-125 is used for ovarian cancer and mesothelioma. CA-125 and CA72-4 are used for gastric cancer.

### Risk Factors and Etiopathogenesis<sup>2</sup>

Advanced stage of the primary tumor, regional lymph node involvement, histological subtype and positive peritoneal cytology, are the usual risk factors for the development of peritoneal metastases from underlying primary neoplasm.

Loss of E-cadherin, a cell-cell adhesion molecule, is responsible for the detachment of cancer cells from the primary tumor. Rapid cellular proliferation, defective lymphatic drainage, fibrosis, and contraction of the interstitial matrix, and increased osmotic pressure generated by anaerobic glycolysis and leakage of plasma proteins, result in the shading of cells, due to elevated interstitial fluid pressure. Cutting of tumor or sectioning of the vascular, lymphatic, or biliary drainage is also responsible for peritoneal seeding.

The peritoneal deposits tend to gravitate in the cul-de-sac and the right paracolic gutters. Other locations include the subdiaphragmatic area and the mesentery, owing to diaphragmatic excursions.

### Clinical/Diagnostic Workup

Clinically, the patient can present with signs and symptoms of primary malignancy.

Clinical features of peritoneal involvement are abdominal distention and pain. Patient can also have non-specific presentations such as fatigue, nausea, anorexia, weight loss, and constipation.

Serum tumor markers can be used for diagnosis, prognosis, and response assessment of peritoneal malignancy. The common tumor markers are CA 19-9 for pancreatobiliary system, CEA for GI tract, and CA 125 for ovarian primaries and mesothelioma. Cell block preparation, immunohistochemistry with appropriate markers indicate the possible primary, if not evident at presentation.

Surgical exploration using laparoscopy is the most sensitive modality for evaluation of the extent of the disease and assessment of its potential surgical resectability. Diagnostic laparoscopy is essential for the assessment of peritoneal cancer index (PCI).

### Imaging Referral Guidelines:

- Ultrasound findings might raise the suspicion of an underlying peritoneal malignancy and act as a trigger for cross-sectional imaging. However, ultrasound is not recommended as a sole imaging modality for staging peritoneal surface malignancy.
- Ultrasound is useful for image-guided biopsy of peritoneal or omental disease.

- CECT of the thorax, abdomen, and pelvis is the recommended imaging modality for initial assessment of patients with peritoneal malignancy.
- Administration of both intravenous and positive oral contrast are recommended as a part of an optimal CT protocol.
- MRI is not recommended for all patients with peritoneal surface malignancy. Contrast-enhanced MRI with diffusion-weighted imaging may have a role in select patients with low-volume peritoneal disease on CECT and incomplete diagnostic laparoscopy due to adhesions.<sup>3</sup>
- PET-CT is not recommended for initial assessment of peritoneal malignancy.

### Imaging Guidelines

#### a) Screening and diagnosis

Peritoneal surface malignancy is often suspected based on incidentally detected ultrasound findings such as ascites, omental, or peritoneal thickening. However, confirmation of diagnosis is with histopathology either using ultrasound-guided biopsy or by diagnostic laparoscopy and biopsy.

#### b) Staging

CECT of the thorax, abdomen, and pelvis is the imaging modality of choice for staging peritoneal surface malignancy. Studies done on new-generation CT scanners with thin section imaging and multiplanar reconstructions have improved sensitivity of 88 to 93% for detecting peritoneal disease. However, sensitivity to detect disease smaller than 1 cm and for detecting small bowel and mesenteric disease remain poor. Staging system used for primary peritoneal surface malignancy is the same as ovarian cancer and fallopian tube malignancies. Peritoneal cancer index (PCI) provides a comprehensive estimate of tumor volume within the peritoneal cavity. Imaging underestimates PCI. Despite these limitations, CECT is an effective modality for obtaining a general overview of the disease extent and exclude those who may not benefit from cytoreductive surgery and HIPEC.<sup>4</sup>

Radiology reports must mention the following<sup>5</sup>:

P – radiological estimation of PCI (rPCI), local extent of the primary malignancy in patients with peritoneal carcinomatosis.

A – presence or absence of ascites and abdominal wall disease

U – presence of disease in unfavorable sites, which make complete cytoreduction unlikely or difficult.

S – small bowel and mesenteric disease

E – presence of extraperitoneal metastases or lymph nodes.

### Peritoneal Cancer Index

Peritoneal cancer index (PCI) is a measure of the peritoneal disease burden and distribution, introduced by Jacquet and Sugarbaker.<sup>6</sup> The abdomen is divided into 13 regions (**Table 1**)<sup>7</sup> and a score is assigned depending on the disease burden in each region, resulting in minimal score of 0 to

**Table 1** Peritoneal Cancer Index

	Region	Score	Scoring	Size
0	Central		LS0	No visible tumor
1	Right upper			
2	Epigastrium			
3	Left upper		LS1	< 0.5 cm
4	Left flank			
5	Left lower			
6	Pelvis		LS2	0.5 cm–5.0 cm
7	Right lower			
8	Right flank			
9	Upper jejunum		LS3	> 5cm or caking
10	Lower jejunum			
11	Upper ileum			
12	Lower ileum			
Total				

maximum score of 39. PCI is best assessed at laparoscopy and/or laparotomy. Preoperative assessment of PCI by MDCT can arm the surgeon with surgical roadmap and act as an arbitrator for decision regarding cytoreductive surgery<sup>8</sup>

#### c) Re-staging and follow-up

- CECT is again the preferred modality for re-staging peritoneal surface malignancy following neo-adjuvant chemotherapy. Images are reassessed for similar findings as described above.
- In this setting, there is a role for PET-CT in select patients with peritoneal malignancy who are being considered for cytoreductive surgery to exclude extraperitoneal metastases.

#### d) Follow-up

Follow-up evaluation is with a combination of clinical examination, tumor markers, and CECT of the thorax, abdomen, and pelvis at 6 monthly intervals for 2 years, followed by annual evaluation for at least 5 years.

## Principles of Management

Common treatment modalities for peritoneal surface malignancies (PSM) are systemic chemotherapy, cytoreductive surgery, and intraperitoneal chemotherapy, with curative or palliative intent.

Systemic chemotherapy can be used either as neoadjuvant or adjuvant measure in either curative or palliative setting. Anti-angiogenic agents are being explored for their roles in the management of PSM to target neo-angiogenesis associated with tumor growth and peritoneal dissemination. Targeted therapy and immunotherapy also hold promise in the management of PSM. Endocrine therapy can be an option in the management of PSM, from hormone-dependent primaries.

Cytoreductive surgery (CRS) is a vital curative treatment for PSM with the objective of resecting all possible peritoneal

deposits. It can be combined with HIPEC to increase efficacy of therapy in patients with CC > 0.

Disease specific managements are summarized in **Table 2**.<sup>2</sup>

## Palliative Measures

Palliative measures and best supportive care are required in patients not amenable to curative treatment and patients developing complications such as malignant bowel obstruction (MBO), ascites, and malnutrition.

Patients with MBO present with pain, nausea, vomiting, and aspiration. Recommended measures for alleviating the symptoms include decompression using an NG tube, gastric anti-secretory therapies such as histamine-2 receptor blockers and proton pump inhibitors. Steroids, due to their anti-inflammatory can reduce pain by decreasing bowel wall and mesenteric edema. Octreotide, a somatostatin analog, and gastric anti-secretory and antimotility agent, in combination with steroids has been shown to reduce gastrointestinal secretions and vomiting, as well as morbidity associated with MBO. In the event of failure of medical management, decompressive gastrostomy tube placement is recommended.

Surgery may be required for patients with acute perforation. Resection-anastomosis can be an option in patients unresponsive to conservative management of MBO. Complete cytoreductive surgery with or without intraperitoneal chemotherapy can also be considered. However, surgery in the setting of disseminated disease is associated with high morbidity and mortality.

Malnutrition is associated with longer hospital stays, post-operative complications, and a reduction in overall survival. Patients failing to achieve adequate oral or enteral caloric intake are recommended parenteral nutrition (PN) support.

Ascites is commonly caused by ovarian, esophageal, gastric, colorectal, hepatobiliary, and primary peritoneal

**Table 2** Principles of management

Pathologies	Neoadjuvant treatments	Surgery	HIPEC	Targeted therapies	Intraperitoneal treatments	Systemic chemotherapy
<b>Pseudomyxoma peritonei and PM from appendiceal cancers</b>						
Curative	No	Upfront CC-0 or CC-1 CRS	recommended	No	Option of EPIC	Adjuvant if poor prognostic factors
Palliative	-	Upfront CC-2 or 3 CRS	recommended	Antiangiogenic* Bromelain and Acetylcysteine (BroMac) in early clinical development	PIPAC under evaluation	Palliative according to right-sided colorectal cancer*
<b>Malignant peritoneal mesothelioma</b>						
Curative	Intraperitoneal chemotherapy, NIPS and PIPAC under evaluation	Upfront CC-0 CC-1 CRS	recommended	No standard recommendation*	Option of EPIC	Adjuvant if poor prognostic factors to be considered*
Palliative	-	No	No	Immunotherapy, PARP-inhibition and other targeted agents under evaluation*	Option of long-term intraperitoneal chemotherapy or PIPAC	Palliative Platinum- /Pemetrexed-based regimens
<b>PM from Ovarian Cancer</b>						
1st line	Systemic chemotherapy if CC-0 CRS not possible	Upfront or interval CC-0 CRS	Option in interval surgery	Antiangiogenic or PARP-inhibition	No	Adjuvant Platinum- /Taxane-based
Platin sensitive Recurrence	Systemic chemotherapy if CC-0 CRS not possible	Upfront or delayed CC-0 CRS	Under evaluation into RCT	Antiangiogenic or PARP-inhibition	PIPAC under evaluation	Palliative Platinum-based
Platin resistant recurrence	Systemic chemotherapy if CC-0 CRS not possible	Option if CC-0 CRS	Option if CC-0 CRS	Antiangiogenic	PIPAC under evaluation	Palliative Topotecan or Anthracyclines
<b>PM from colorectal cancer</b>						
Curative	Option of systemic chemotherapy intraperitoneal chemotherapy, NIPS and PIPAC under evaluation	CC-0 CRS	Option into specialized centers	No standard recommendation*	PIPAC under evaluation	Adjuvant if poor prognostic factors*
Palliative	-	No	No	Antiangiogenic and anti-EGFR according to mutational status and sidedness of primary tumor Immunotherapy in MSI patients	PIPAC under evaluation	Palliative oxaliplatin/fluoro pyrimidine-based or irinotecan/fluoro pyrimidine or trifluridine-tipiracil (3rd-line)

Table 2 (Continued)

Pathologies	Neoadjuvant treatments	Surgery	HIPEC	Targeted therapies	Intraperitoneal treatments	Systemic chemotherapy
<b>PM from gastric cancer</b>						
Curative	Option of systemic chemotherapy Intraperitoneal chemotherapy and NIPS, PIPAC under evaluation	CC-0 CRS in patients with low PCI	Option in combination with CC-0 CRS	No standard recommendation*	PIPAC under evaluation	Adjuvant
Palliative	PIPAC under evaluation	No	Under evaluation	Trastuzumab in Her 2 positive patients Immunotherapy in MSI and under further evaluation in MSS	PIPAC under evaluation	Palliative Platinum/Fluoropyrimidine based 1st-line, Taxane (2nd-line) or irinotecan or trifluridine-tipiracil (3rd-line)
<b>PM from others malignancies</b>						
Curative	To select adequate candidate	Only in case of CC-0 CRS	Option in combination with CC-0 CRS	-		Optional
Palliative	-	No	Option in malignant ascites	-	Optional	Registered and established disease specific regimens

Abbreviations: CC, Completeness of cytoreduction surgery; CC0, no residual nodule; CC1, <2.5 mm; CC2, <25 mm; and CC3, >25 mm; CRS, cytoreductive surgery; EPIC, early postoperative intraperitoneal chemotherapy; HIPEC, hyperthermic intraperitoneal chemotherapy; MSI, microsatellite instability; MSS, microsatellite stable; NIPS, n intraperitoneal and systemic chemotherapy; PAMP, poly (ADP-ribose) polymerase; PCI, Peritoneal Cancer Index; PIPAC, pressurized intraperitoneal aerosol chemotherapy; PM, peritoneal metastasis.  
 \*No definitive evidence from controlled trials available.

carcinomatosis. Lung, pancreatic, endometrial, breast primaries are less likely to be associated with ascites. Malignancy related ascites should be confirmed with diagnostic paracentesis and cytology, esophagogastroduodenoscopy, colonoscopy, contrast-enhanced CT/magnetic resonance imaging of the abdomen and pelvis, and pelvic ultrasound (in female patients). These investigations can also help in establishing the diagnosis of primary malignancy. In the event of negative results, diagnostic laparoscopy and biopsy with PCI scoring is recommended, in addition to ruling out other causes of ascites such as cirrhosis or infectious diseases such as peritoneal tuberculosis. Supportive paracentesis can be effective for relieving ascites related symptoms.

### Summary of Recommendations: 100 Words

- i) Contrast-enhanced CT of the abdomen and pelvis is the imaging modality of choice for peritoneal disease.
- ii) Review of thin sections (1–2 mm) in both axial and coronal planes is recommended for assessing the extent of peritoneal disease.
- iii) Use of positive oral contrast is recommended to improve the detection of disease in the small bowel mesentery and serosa.
- iv) PET-CT is recommended to exclude extraperitoneal disease before considering major surgical management such as cytoreductive surgery and HIPEC.
- v) Radiology reports must include a succinct description of the volume of peritoneal disease in terms of PCI and address specific sites of disease that might hinder completeness of cytoreduction.

### Synoptic Reporting CT, MRI, and PET-CECT

*Synoptic reporting of peritoneal surface malignancy must address the following*

Is there an obvious primary? Gastrointestinal/ovarian/-colorectal/appendix/pancreaticobiliary/urachal  
Fluid: ascites (yes/no), mild/moderate/severe  
Peritoneal or omental thickening: (yes/no)

Is ultrasound-guided biopsy possible? (yes/no)

Bowel, mesentery:

- Bowel wall thickening/dilatation/obstruction (yes/no)

- Mesenteric fold thickening (yes/no)

- Mesenteric tethering (yes/no)

- Root of mesenteric disease (yes/no)

Upper abdomen: subphrenic spaces, lesser omentum, gastro-splenic ligament, porta, portocaval space (yes/no)

Liver and biliary system: Focal lesions in the liver (- yes/no); biliary dilatation (yes/no)

Spleen: focal lesions in the spleen, splenic hilar disease

KUB:

Hydronephrosis (yes/no)

Pelvis:

- Plane between pelvic masses and recto-sigmoid colon (lost/maintained)

- Iliac vessel encasement (yes/no)

- Ureteric encasement (yes/no)

- Presacral space or pelvic side wall infiltration (yes/no)

Abdominal wall: surgical scars/port site metastases

Nodes:

Metastases: liver, lungs, bones, spleen, adrenals, etc.

Impression:

P – Radiological PCI

A – Ascites/abdominal wall disease

U – Unfavorable sites of disease

S – Small bowel and mesenteric disease

E – Extraperitoneal disease

### Authors' Contributions

The manuscript has been read and approved by all the authors, that the requirements for authorship have been met, and that each author believes that the manuscript represents honest work. All authors have contributed equally towards concept, design, definition of intellectual content, literature search, clinical studies, experimental studies, data acquisition, manuscript preparation, manuscript editing and manuscript review.

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### Conflict of Interest

None declared.

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