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REVIEW PAPER

Mucinous appendiceal neoplasms: classification, imaging, and HIPEC

David J. Bartlett[1] · Paul G. Thacker Jr.[1] · Travis E. Grotz[2] · Rondell P. Graham[3] · Joel G. Fletcher[1] · Wendaline M. VanBuren[1] · Veena R. Iyer[1] · Jeff L. Fidler[1] · Christine O. Menias[4] · Nabil Wasif[5] · Shannon P. Sheedy[1]

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Abstract

Recent advances, specifically cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC), offer advantages compared to the traditional therapeutic approach of systemic chemotherapy in the treatment of peritoneal carcinomatosis from mucinous appendiceal neoplasms (MAN). This review provides an up-to-date, comprehensive summary of the histologic classification of MAN, reviews common imaging findings of mucoceles and pseudomyxoma peritonei, and describes the radiologist's role in the multidisciplinary care team in quantifying disease and in helping select patients for definitive surgery.

Keywords Mucinous appendiceal neoplasm, MAN · Hyperthermic intraperitoneal chemotherapy, HIPEC · Cytoreductive surgery · Pseudomyxoma peritonei, PMP

Introduction

Peritoneal carcinomatosis (PC) results from direct spread or metastasis to the visceral and parietal peritoneum by a variety of tumors originating from the abdominal organs, or less commonly from the peritoneal lining itself. This heterogeneous group of tumors is encompassed in the term "peritoneal surface malignancies" (PSM) as they share a common clinical evolution and treatment. On the basis of the epidemiological data, PSM have a high annual incidence, including nearly 30% of gastric cancers, 13% of colorectal cancers, 60% of ovarian cancers, nearly all appendiceal adenocarcinomas, and peritoneal mesothelioma [1–3].

In the past, systemic chemotherapy alone was employed for palliative intent of PSM. However, in the mid-1990s, thanks to the peritoneal malignancy surgical expert Paul Sugarbaker's pioneering efforts, research began into developing an integrated therapy for PSM. This integrated therapeutic scheme, termed cytoreductive surgery/hyperthermic intraperitoneal chemotherapy (CRS/HIPEC), includes a systematic intraoperative evaluation of the abdomen with aggressive resection of all visible tumor while preserving organs whenever possible, i.e., CRS, and high-dose intraperitoneal chemotherapy with intraperitoneal hyperthermia (HIPEC) [4–10]. Although CRS/HIPEC is the only effective treatment for patients with peritoneal carcinomatosis from appendiceal neoplasms, it carries high risk of morbidity. Thus, correct patient selection for the procedure is critical and requires multidisciplinary collaboration. In this review, we will discuss the pathologic classification and radiologic appearance of epithelial appendiceal neoplasms, describe the CRS/HIPEC procedure, and help define the role of the radiologist in the multidisciplinary team.

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✉ Shannon P. Sheedy
Sheedy.Shannon@mayo.edu

[1] Department of Radiology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA

[2] Department of Hepatobiliary and Pancreatic Surgery, Mayo Clinic, Rochester, MN, USA

[3] Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA

[4] Department of Radiology, Mayo Clinic, Scottsdale, AZ, USA

[5] Department of General Surgery, Mayo Clinic, Scottsdale, AZ, USA

Mucinous appendiceal neoplasm

Appendiceal neoplasms are relatively rare, reported in less than 1% of appendectomy specimens [11, 12]. Epithelial appendiceal neoplasms, about 70% of which are mucinous histologic type, and neuroendocrine neoplasms account for the majority of primary appendiceal tumors [11, 13, 14]. The majority of mucinous appendiceal neoplasms (MANs) develop in middle-aged and elderly patients and are discovered incidentally, but some patients present with non-specific signs or symptoms such as abdominal pain or distension. MANs are the most common cause of pseudomyxoma peritonei (PMP), a clinical syndrome characterized by progressive accumulation of mucinous tumor throughout the peritoneal cavity [15].

In 2016, in an attempt to achieve consistency and to enable more meaningful data sharing across institutions, the Peritoneal Surface Oncology Group International (PSOGI) issued a consensus statement regarding the nomenclature and classification of epithelial appendiceal neoplasms and PMP. According to the new consensus statement, mucinous neoplasms (excluding the goblet cell tumor, a subtype of neuroendocrine tumor which also has features of mucinous neoplasm) are classified as follows [16]:

- LAMN (low-grade appendiceal mucinous neoplasm)—extends beyond the mucosa into the appendiceal wall but without infiltrative invasion and with *low-grade* cytologic atypia
- HAMN (high-grade appendiceal mucinous neoplasm)—extends beyond the mucosa into the appendiceal wall but without infiltrative invasion and with *high-grade* cytologic atypia
- Mucinous adenocarcinoma—shows infiltrative invasion and may be well, moderately, or poorly differentiated
- Poorly differentiated mucinous adenocarcinoma with signet ring features

The specific histology of the appendiceal neoplasms predicts the biologic behavior and the penchant for specific patterns of disease spread [11]. Regardless of the degree of cellular atypia, both LAMN and HAMN can develop transmural extension or can rupture, and when this occurs, the patient is at risk for developing PMP. The presence of epithelial cells within the extra-appendiceal mucin portends a worse prognosis; thus, any extra-appendiceal mucin must be carefully inspected in appendectomy specimens. Limited data suggests that HAMN is more likely to be associated with extra-appendiceal epithelial cells than is LAMN [17–19].

A well-differentiated mucinous adenocarcinoma consists of mostly mucin pools lined by neoplastic epithelium with minimal atypia and may be more likely to develop PMP than the poorly differentiated adenocarcinoma that shows little or no gland formation [15, 16]. Because of their worse prognosis, poorly differentiated mucinous neoplasms with signet ring cells are classified separately [20–22]. The non-mucinous appendiceal adenocarcinoma is more similar histologically and radiologically to colorectal adenocarcinomas, often presenting with a focal soft tissue mass and with greater propensity to develop regional lymph node metastases and metastases to liver, lung, and peritoneum [13].

Although PMP does not generally metastasize to lymph nodes or beyond the peritoneal cavity, especially in its low-grade form, it should be considered malignant as it is characterized by relentless progression and will become fatal if not treated. The PSOGI expert panel recommends that PMP classification be based on the histology of the peritoneal disease, rather than based on the primary neoplasm [16]. The panel proposed the following categories and associated grading scheme (G1–G3) [16]:

- Acellular mucin—characterized by the absence of neoplastic epithelial cells within the peritoneal mucin (Fig. 1a)
- Low-grade mucinous carcinoma peritonei—G1 (previously referred to as disseminated peritoneal adenomucinosis [DPAM])
- High-grade mucinous carcinoma peritonei—G2 (previously referred to as peritoneal mucinous carcinomatosis [PMCA])
- High-grade mucinous carcinoma peritonei with signet ring cells—G3 (previously referred to as peritoneal mucinous carcinomatosis with signet ring cells [PMCA-S]) (Fig. 1b)

Because of the distinct natural history and prognosis of MAN, the TNM classification system is similar to, but independent of, the colorectal staging system (Online Appendix A) [23, 24].

Imaging of mucinous appendiceal neoplasm and pseudomyxoma peritonei

The general descriptor "appendiceal mucocele" refers to the presence of a mucin filled, dilated appendix (Fig. 2). The mucocele etiology may be neoplastic, most commonly related to MAN, or non-neoplastic. Non-neoplastic etiologies such as mucosal hyperplasia or a simple retention cyst as a result of luminal obstruction, e.g., from an appendicolith, only account for about 20% of mucoceles [25]. The imaging diagnosis of a MAN rests on the identification of the mucocele, and the presence of a mucocele should impel

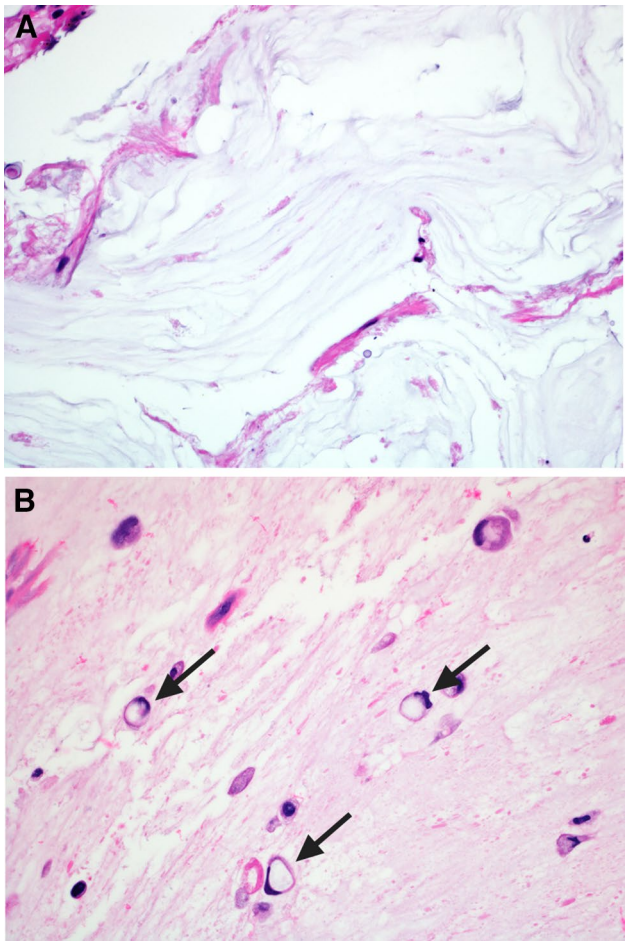


Fig. 1 **a** This photomicrograph illustrates acellular mucin. **b** In contrast, this photomicrograph shows signet ring cells (arrows) with their characteristic cytomorphology dispersed in mucin. When this is identified in the peritoneum, this confirms the diagnosis of peritoneal mucinous carcinomatosis with signet ring cells

an investigation for extra-appendiceal mucin. Only when the mucin is distributed in the peritoneal cavity beyond the right lower quadrant periappendiceal region, the patient is considered to have PMP. The prospective suggestion of MAN or PMP on imaging may help the patient receive appropriate initial care and prevent the potential need for a second, more extensive surgery, which may be required when neoplasm is discovered unexpectedly at pathology. The imaging appearance of appendiceal mucocele and PMP are well described in the radiology literature; the imaging features of mucoceles are outlined in Table 1.

PMP

Some patients with MANs remain asymptomatic until they experience progressive abdominal pain or distension, obstructive symptoms, weight loss, or new hernia related to PMP (Fig. 6). The incidence of PMP is approximately

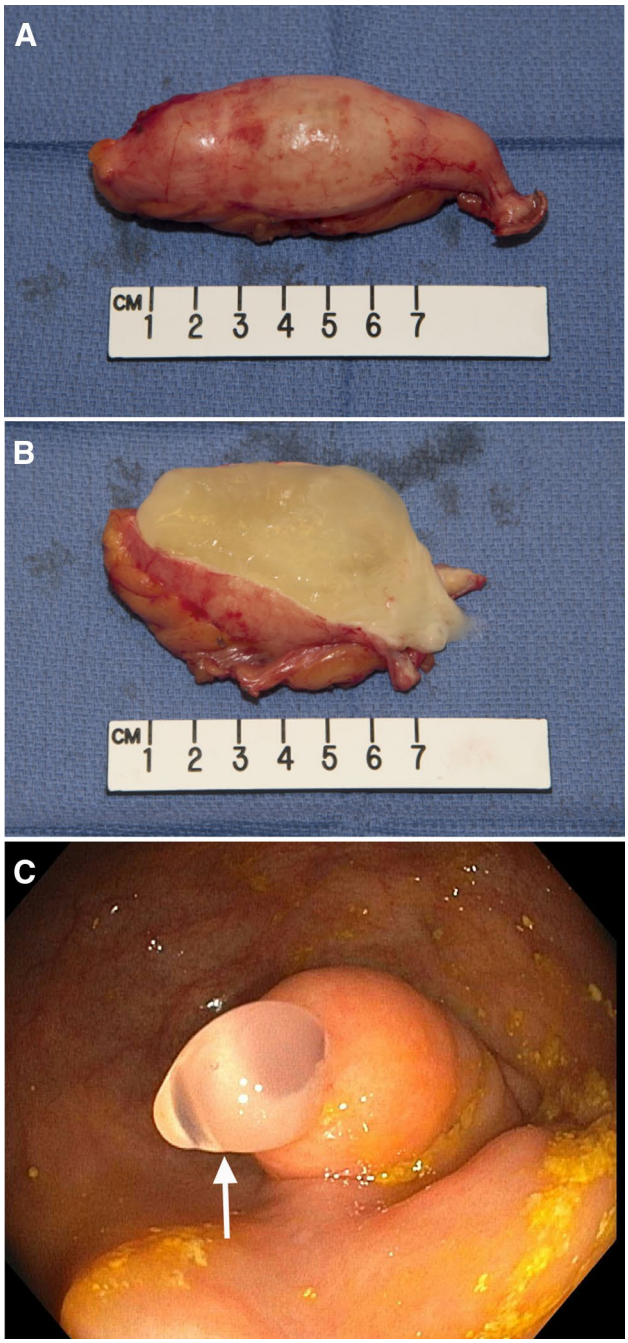


Fig. 2 A 55-year-old female found to have a mucocele on CT (not shown). **a**, **b** Intact (**a**) and cut (**b**) gross pathology specimen of an appendiceal mucocele secondary to low-grade appendiceal neoplasm. The cut specimen (**b**) demonstrates the mucin filling the dilated lumen. **c** Endoscopy in a different patient demonstrates a mucocele with mucin (arrow) being extruded from the appendiceal orifice

0.2 per 100,000 population per year [26] and develops in about 20% of patients with MANs, but in far fewer patients with non-mucinous appendiceal adenocarcinoma [15]. Left untreated, the neoplastic cells of PMP continue to proliferate and the mucus gradually fills the peritoneal cavity (hence the

Table 1 Mucocele imaging features

Imaging modality	Imaging findings
Ultrasound	• Elongated or ovoid complex mass • Echogenicity variable, often heterogeneous • "Onion skin" or lamellated appearance highly suggestive [87, 88] (Fig. 3) • Shadowing mural or intraluminal calcification is present in < 50% of mucoceles [13, 87–89] • Key: identify right ovary to exclude cystic ovarian neoplasm or tubo-ovarian abscess
CT	• Dilated appendix with low/fluid attenuation intraluminal contents • May bulge into cecum or cause intussusception (Fig. 4) • Calcification or luminal diameter > 2 cm should raise suspicion for neoplasm (Fig. 4) [17]. • Mural soft tissue nodularity and periappendiceal soft tissue density may indicate either superimposed infection or malignancy (Fig. 5) [90, 91] • Myxoglobulosis: rare morphologic variant of the mucocele, multiple intraluminal mucin globules that are best appreciated when calcified [13]
MRI	• Signal intensity is variable and dependent on the concentration of mucin, but generally hyperintense (similar to fluid) on T2-weighted imaging and hypo- to mildly hyperintense on T1-weighted imaging • Calcifications less conspicuous on MRI

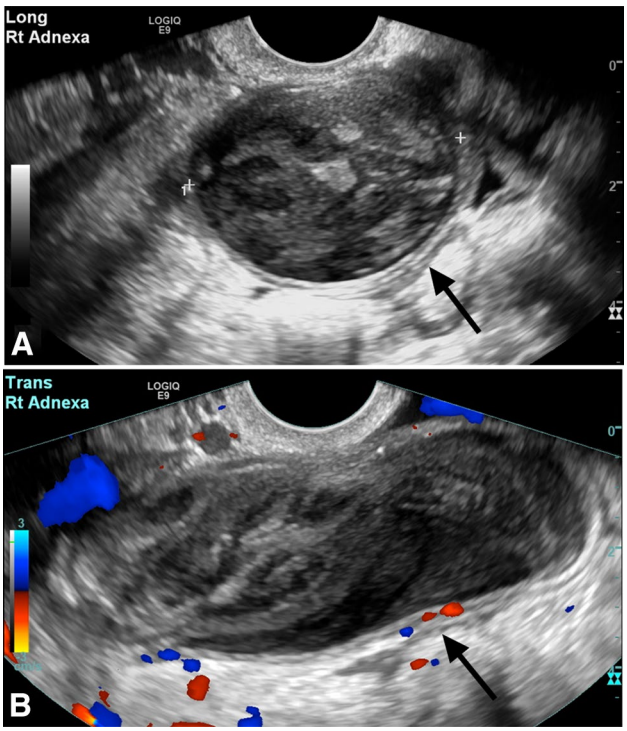


Fig. 3 A 53-year-old female who presented with pelvic pain and found to have a complex cystic pelvic mass. Longitudinal (**a**) and transverse (**b**) transvaginal, grayscale sonographic images demonstrate a heterogeneous, well-defined, cystic pelvic mass with layered "bowel signature" (arrows) surrounding the lesion, which is diagnostic of the mass being within bowel. The lamellated or "onion skin" appearance of the intraluminal contents is characteristic for a mucocele. The patient underwent surgery and was found to have a low-grade mucinous neoplasm without extra-appendiceal mucin

colloquial term, "jelly belly") (Fig. 7) [8]. Untreated disease has a 5-year survival of approximately 55–65% [13, 27, 28]. Patients with non-appendiceal neoplasms, including ovarian, colonic, urachal, and pancreatic, can develop PMP, but the appendix is the most common source and should always be carefully inspected on imaging and at surgery for a primary tumor [16, 29, 30].

PMP can look like simple ascites on CT. However, more often PMP has a slightly more heterogeneous and loculated appearance or may have septations and/or curvilinear or amorphous calcifications within the mucinous implants. The septations and the complexity of PMP are readily apparent on ultrasound (Fig. 8). PMP spreads throughout the peritoneal cavity according to the "redistribution phenomenon" whereby the mucin and/or neoplastic epithelial cells initially accumulate at sites where peritoneal fluid is resorbed, such as the omentum and the undersurface of the right hemidiaphragm, and in the dependent areas of the peritoneal cavity including the right retrohepatic space, the dependent pelvis, the paracolic gutters, and at the ligament of Treitz [8]. Omental caking is common (Fig. 9) and serosal implants on solid organs create a "scalloped" appearance on their surfaces where parenchymal invasion can occur (Fig. 8). Early on, PMP tends to spare the mobile small bowel and displaces it centrally but as the disease progresses or if left untreated, it eventually causes bowel obstruction and later in the course of disease patients often suffer from cachexia. PMP only rarely involves lymph nodes or directly spreads into the thoracic cavity. PMP appears markedly T2 hyperintense and T1 hypointense on MRI (Fig. 10).

Quantitative prognostic systems

Various quantitative prognostic scoring systems have been developed for peritoneal carcinomatosis and serve as tools for selecting optimal candidates for CRS/HIPEC [31–34]. Overall, the main objective of these systems is to predict

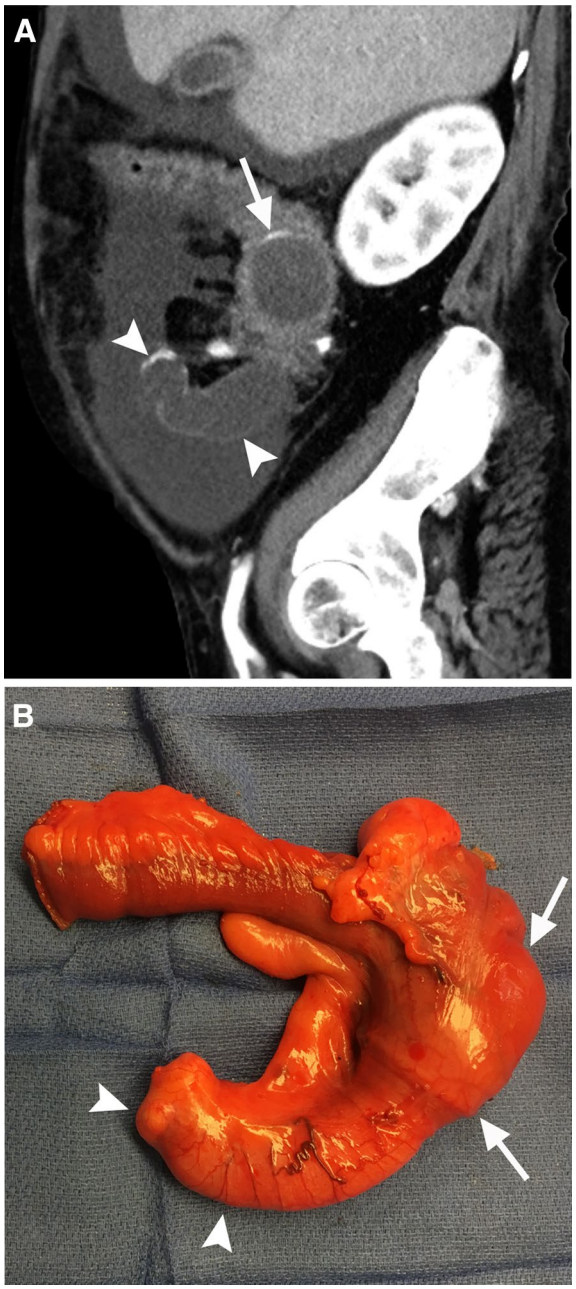


Fig. 4 A 60-year-old female who underwent a CT for vague right-sided abdominal pain and abnormal liver function tests in the setting of alcoholic cirrhosis. **a** Sagittal-enhanced soft tissue window CT image demonstrates a markedly dilated appendix (arrowheads) with discontinuous mural calcifications and intussusception into the cecum (arrow). **b** Gross pathology specimen with similar orientation as in **a** shows the dilated appendix (arrowheads) and the intussusception (arrows)

the likelihood of complete cytoreduction given that the long-term survival benefit of HIPEC is greatest in this subset of patients [32, 35–38].

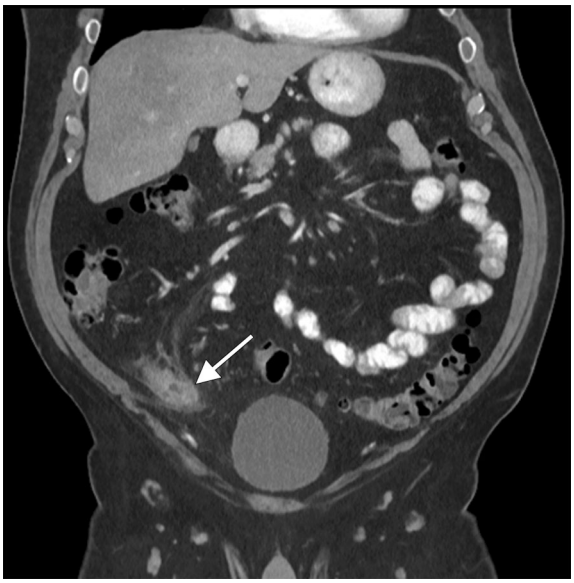


Fig. 5 A 68-year-old male who presented with right lower quadrant pain. Coronal-enhanced CT image in soft tissue window setting shows appendiceal wall thickening and heterogeneous enhancement, with increased density in the periappendiceal fat (arrow). He was thought to have uncomplicated acute appendicitis and underwent laparoscopic appendectomy. Pathology revealed low-grade appendiceal mucinous adenocarcinoma

Peritoneal cancer index

The peritoneal cancer index (PCI), developed by Jacquet and Sugarbaker, assesses tumor volume and distribution in 9 predefined abdominopelvic regions (0–8) and 4 small bowel segments (9–12) intraoperatively (Fig. 11). An intraoperative PCI greater than 20 is considered a large disease burden and a relative contraindication to CRS as the potential risks are thought to outweigh the benefits [39]. The PCI is the most widely used scoring system and has been shown in colorectal cancer to correlate with patient's long-term survival [40]. Notably, even with a very high PCI, patients with low-grade mucinous carcinoma peritonei may be successfully treated with excellent long-term outcomes if the surgeon is able to obtain complete or near complete cytoreduction [41, 42].

Peritoneal surface disease severity score

The Peritoneal Surface Disease Severity Score (PSDSS) stratifies patients into prognostic groups based on clinical symptoms, volume of peritoneal disease, and tumor histology [34, 43] (Table 2). The PSDSS has been shown to be an important prognostic indicator for MANs and to be a predictor of resectability for patients with PSDSS stage I and II disease [34, 44]. The disease burden used for the PSDSS is based on the PCI calculation derived from pre-operative

Fig. 6 A 59-year-old female who presented for new onset right inguinal hernia and abdominal distension. **a** Cross-table lateral photographic image of the patient's abdomen demonstrates marked abdominal distension. **b** Coronal, enhanced CT image in soft tissue window setting shows PMP with mucinous neoplasm extending into and dilating the right inguinal canal (arrow), omental caking (stars), and low-density mucin throughout the peritoneal cavity. Pathology demonstrated low-grade mucinous adenocarcinoma, likely of the appendix. The patient is scheduled for aggressive surgical debulking and hyperthermic intraperitoneal chemotherapy

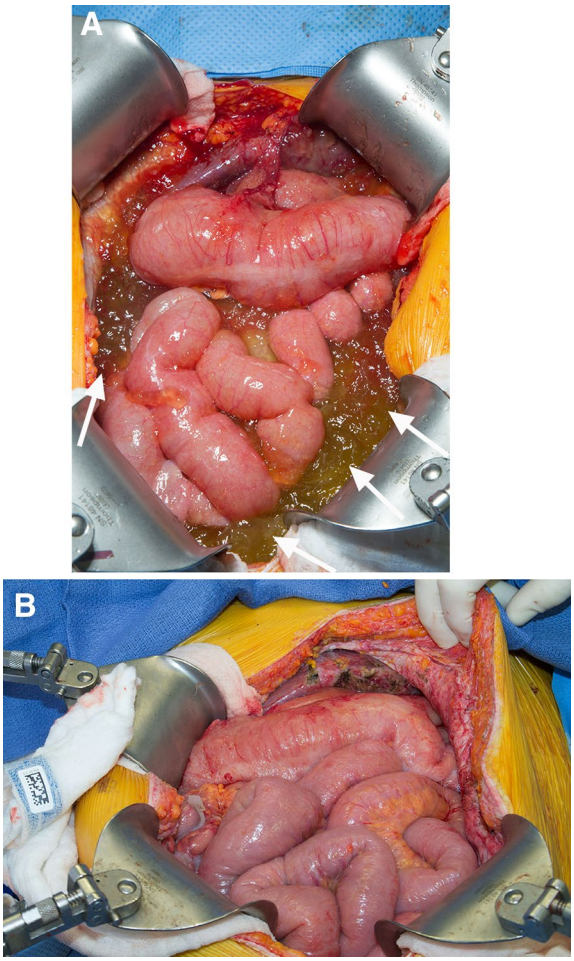


Fig. 7 Recurrent LAMN with associated PMP. **a** Intraoperative photographic image of the abdomen demonstrates diffuse gelatinous material (arrows) filling the abdomen, consistent with PMP. **b** Intraoperative photographic image of the patient's abdomen following cytoreductive surgery and hyperthermic intraperitoneal chemotherapy showing no visible residual

imaging, referred to as the radiologic PCI. Studies comparing the pre-operative radiologic PCI and the surgical PCI have shown variable results, but majority of the studies have shown that pre-operative imaging underestimates the PCI, particularly within the small bowel segments [45–49]. However, accuracy burden can be improved by using both intravenous and positive oral contrast and a standardized reporting template. [45–48].

SPAAT score

In 2015, Dineen et al. introduced the simplified pre-operative assessment for appendix tumor (SPAAT) score which relies on high-quality CT imaging to predict complete cytoreduction preoperatively for low-grade appendiceal mucinous adenocarcinoma [31]. The scoring system requires the radiologist to grade 5 anatomic regions for volume of disease. Two specific imaging features are important: visceral or porta hepatis scalloping by mucinous ascites and "mesenteric foreshortening" which occurs when tumor involves the central small bowel mesentery and causes "cauliflowering" of the small bowel (Fig. 12), sometimes referred to as "cocoon abdomen" or "frozen abdomen" in surgery. A score of 0 or 1 point is given for the absence or presence of scalloping of the liver, spleen, pancreas, or portal vein (for a maximum of 4 points) and a score of 0 or 3 is given for the absence or presence of mesenteric foreshortening, for a total maximum score of 7. In their validation cohort, 40 of 42 patients (PPV 95.2%) with a SPAAT < 3 achieved a complete cytoreduction and was also associated with disease-free interval and overall survival [31].

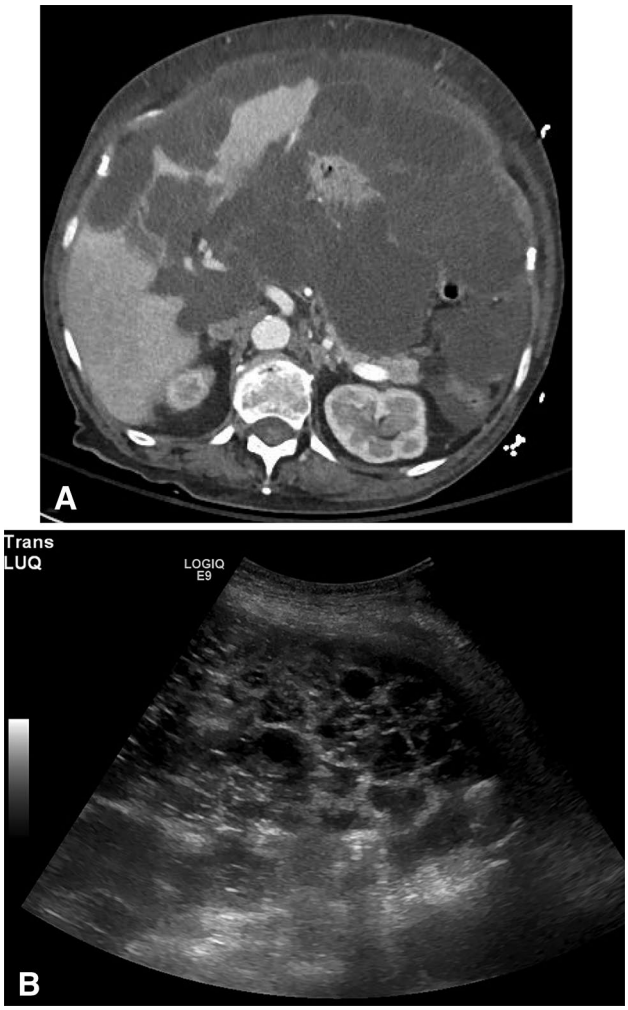


Fig. 8 A 75-year-old female presented with 6 months of progressive abdominal distension, weight loss, and decreased appetite. **a** Axial, enhanced CT image in soft tissue window setting shows extensive low-density, lobulated, and septated mucinous implants throughout the upper abdomen, with mass effect upon and scalloping of the adjacent abdominal organs. **b** Transverse, grayscale ultrasound image of the left upper quadrant demonstrates the complex mucinous material in the left upper quadrant with numerous septations

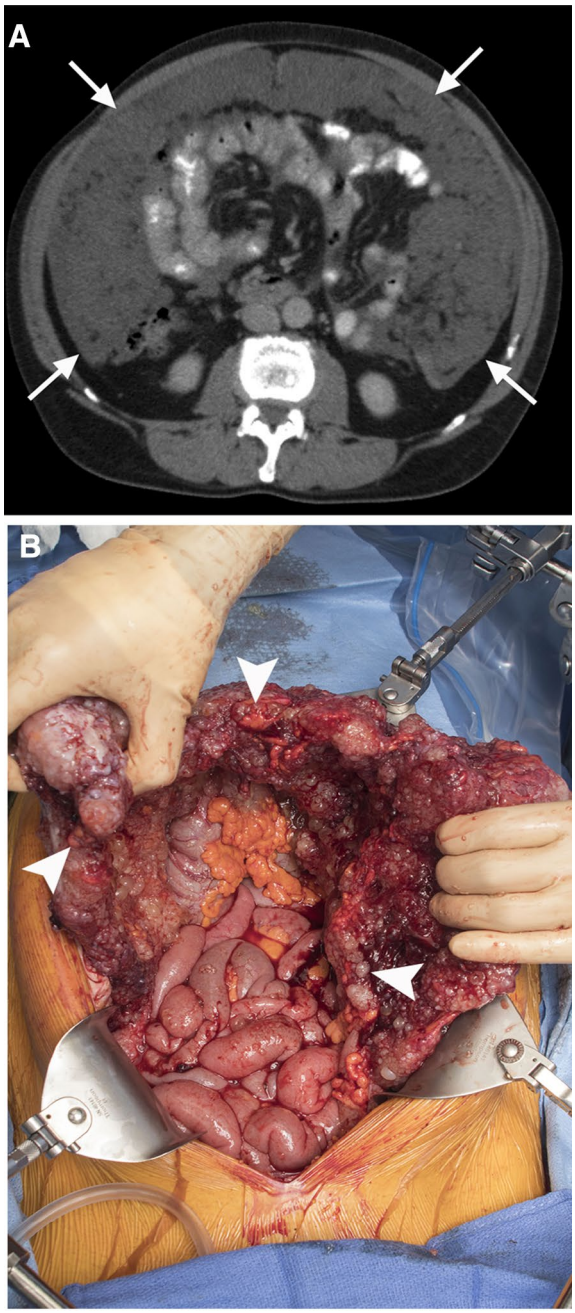


Fig. 9 A 59-year-old male presenting with abdominal distension and discomfort. **a** Axial-enhanced CT image in soft tissue window setting shows thick omental caking (arrows) with relative sparing of the centralized small bowel. **b** Intraoperative photographic image during laparotomy shows marked thickening of the omentum with innumerable tiny implants (arrowheads on a few representative implants)

Completeness of cytoreduction score (CCR score)

In the early 1990s, Sugarbaker developed an intraoperative scoring system to describe the remaining volume of disease after surgery known as the completeness of cytoreduction after surgery score (CCR score) ranging from CCR-0 through CCR-3 [50, 51]. A score of CCR-0 or CCR-1 (tumor nodules < 2.5 mm) is considered a complete cytoreduction and CCR- 2 or CCR -3 (tumor nodules > 2.5 mm) is considered incomplete cytoreduction [50]. Patients with CCR-2 and CCR-3 disease have significantly higher mortality and lower progression-free survival compared to CCR-0 and CCR-1 [37, 52].

Cytoreduction surgery and hyperthermic intraperitoneal chemotherapy

The management of LAMN and HAMN is controversial, but if LAMN is discovered following appendectomy with no evidence for extra-appendiceal neoplastic epithelial

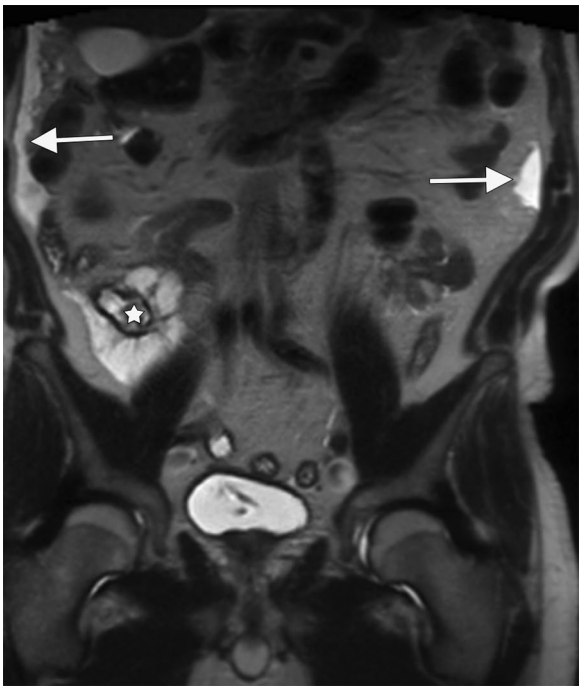


Fig. 10 A 72-year-old-male presenting to the emergency department with a one-week history of right lower quadrant pain and found to have PMP on CT (not shown). Coronal, non-fat suppressed, T2-weighted MR image shows marked T2 hyperintensity within an appendiceal mucocele (star), as well as periappendiceal mucin and hyperintense mucin in the paracolic gutters (arrows). Patient proceeded to appendectomy with right hemicolectomy, cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Pathology revealed mucinous adenocarcinoma of the appendix with extensive peritoneal metastatic disease, including involvement of the ileum, surface of the liver and spleen, omentum, and peritoneum

cells or lymph node involvement, a second surgery with right hemicolectomy is probably not warranted [15]. In these patients, the risk of developing PMP is low. Currently, there is no consensus on surveillance imaging in LAMN. However, most authors recommend follow-up CT imaging every year for at least 5 years [15, 53]. In those patients who were found to have no spread of tumor or mucin beyond the appendix, surveillance may be stopped after 5–10 years with no evidence of recurrence [15]. The optimal management of HAMN or of LAMN with peritoneal spread is even more debatable, but they may best be treated as adenocarcinomas [15, 16, 54, 55].

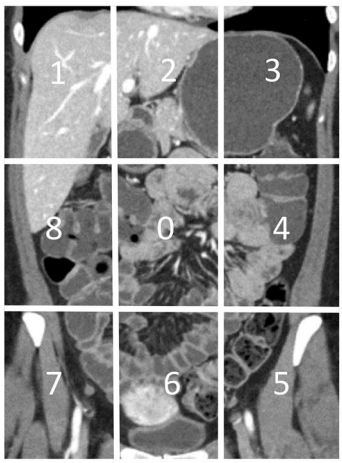
Appendiceal adenocarcinomas require treatment with a right hemicolectomy and regional lymphadenectomy, similar to colorectal adenocarcinoma [15]. The presence of peritoneal implants or PMP, depending on the extent of disease and histologic appearance of the tumor, may warrant CRS/HIPEC, with the intent for cure (Fig. 13). However, patients with extraperitoneal metastatic disease, retroperitoneal disease, or disease that is not amenable to complete cytoreduction may receive a palliative (with no intent for cure) debulking surgery or systemic chemotherapy [54].

CRS may include peritoneal stripping, small bowel and large bowel resection, partial gastrectomy, splenectomy, omentectomy, cholecystectomy, hysterectomy, and oophorectomy. The therapeutic rationale for the combined CRS/HIPEC approach is based on the fact that surgery remains the mainstay of therapy in solid peritoneal surface malignancies and a complete cytoreduction (CCR0) remains the only potentially curative treatment. However, in the presence of microscopic neoplastic cells, obtaining a true margin negative resection is likely impossible in most cases. Intraperitoneal chemotherapy is an attractive adjunct to CRS as the cancer cells have been reduced to a minimal volume and are more likely to be susceptible to cytotoxic agents. Furthermore, the chemotherapy dose can be escalated within the peritoneal cavity because of the peritoneal plasma barrier, a semipermeable membrane that allows limited drug passage into the plasma. Hyperthermia has been well documented to augment regional chemotherapy and radiotherapy [56–59]. Hyperthermia increases cancer cell susceptibility to chemotherapeutic agents; increases the depth of penetration of the chemotherapeutic agent through modulation of the tumor microenvironment, immunologic, and cell signaling pathways; and impairs DNA repair mechanisms [60, 61].

For low-grade appendiceal mucinous adenocarcinomas, CRS/HIPEC with complete cytoreduction can lead to long-term survival in $>60\%$ of patients [62, 63], with the importance of complete cytoreduction demonstrated in multiple studies [36, 52, 64]. Chua et al. reviewed over 2000 patients with appendiceal cancer from multiple institutions and demonstrated a 24% 5-year survival with incomplete cytoreduction or debulking compared with approximately 80% for patients undergoing a CCR0/1 (nil residual disease or disease ≤ 0.25 cm) resection [52]. However, in carefully selected patients in whom a complete cytoreduction is not achieved, debulking can extend survival and palliate symptoms [65]. Pre-operative imaging is critical in helping to determine which patients are candidates for complete cytoreduction and which patients would benefit from a more limited palliative debulking. This information can facilitate pre-operative discussions, allowing the surgeon to address expectations and educate patients on what organs are most likely to be removed.

Morbidity and outcomes

CRS/HIPEC is a complex procedure that can take 6–12 h and involve multiple organ resections. The rates of perioperative morbidity and mortality range widely in the literature. A meta-analysis in 2009 reported the incidence of severe grade III/IV morbidity rates (requiring surgical, endoscopic, or radiologic intervention or life-threatening complication



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

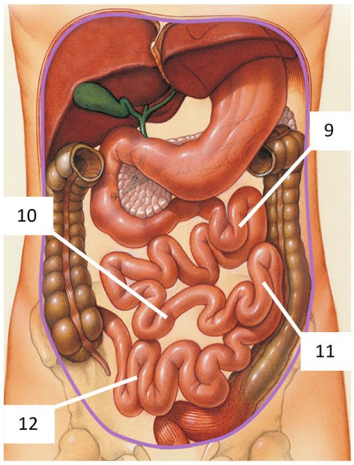


Fig. 11 Schematic diagram and regional scoring sheet for Peritoneal Cancer Index scoring

Table 2 Modified PSDSS for peritoneal carcinomatosis of appendiceal origins (PSDSS I < 4; PSDSS II = 4-7; PSDSS III = 8-10; PSDSS IV > 10) [34, 43]

Clinical symptoms	Extent of carcinomatosis	Primary tumor pathology
No symptoms (0 point)	PCI < 10 (1 point)	Low-grade mucinous neoplasm (1 point)
Mild (1 point)	PCI 10–20 (3 points)	Mucinous adenocarcinoma (3 points)
Severe (6 points)	PCI > 20 (7 points)	High-grade mixed adenocarcinoma and goblet cell carcinoid (9 points)

Mild symptoms = weight loss < 10% of body weight, mild abdominal pain, asymptomatic ascites

Severe symptoms = weight loss ≥ 10% of body weight, unremitting pain, bowel obstruction, symptomatic ascites

Table modified from Yoon et al. [34]

requiring intermediate or intensive care unit management) ranging from 0 to 52% with overall mortality rates ranging from 0 to 17% [66]. The most common complications include bleeding (15%), sepsis (15%), and surgical site infection (11%) [67]. Prior studies have identified the number of prior operations, extent of carcinomatosis, number of intraoperative procedures, number of anastomoses, operative time, extent of cytoreduction, and chemotherapy dose as significantly associated with increased risk of morbidity.

Cross-sectional imaging for CRS and HIPEC

Imaging modalities

At our institution, we routinely use CT to detect and stage PC and PMP because of its high spatial resolution, the ability to obtain high-quality multiplanar reformatted imaging in a single breath-hold scan acquisition, and because of its ready availability and consistent image quality. Positive oral contrast material increases the conspicuity of bowel serosal disease and disease in the adjacent mesentery or peritoneum. We administer a total of 1–1.5 L of oral contrast material over 60 min. We do not routinely administer rectal contrast material as the rectum and colon are often adequately distended with stool and/or air.

Despite its advantages, CT is not a panacea for PMP or PC imaging. CT is severely limited in its ability to detect nodules < 5 mm, with reported sensitivities ranging from 11 to 28% [48, 68]. This becomes problematic because miliary disease (Fig. 14) is a contraindication to HIPEC [47]. Other limitations of CT imaging occur in the presence of mucinous ascites because the proteinaceous fluid can obscure and/or mimic solid metastases or can be mistaken for simple

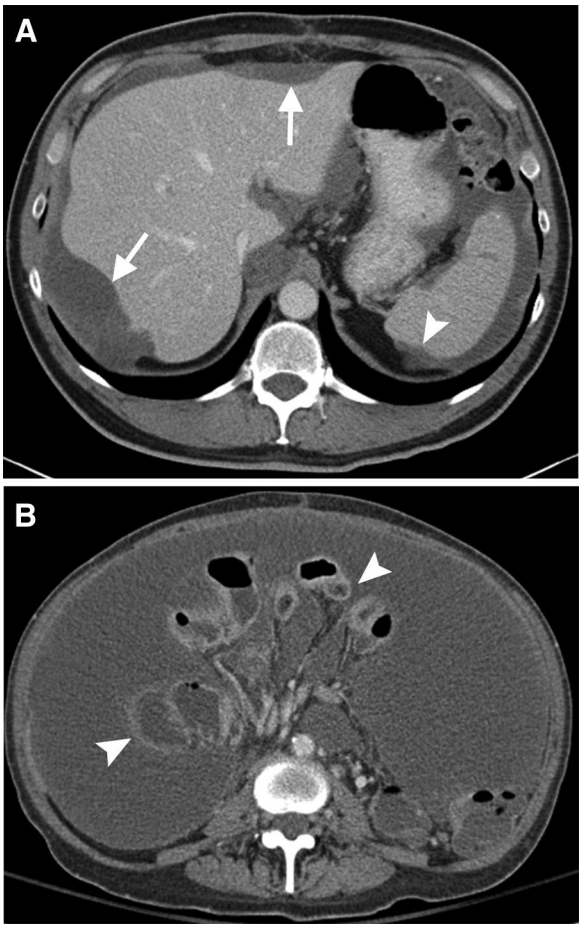


Fig. 12 SPAAT Scoring. **a** Axial-enhanced CT image in soft tissue window setting shows scalloping of the liver (arrows) and spleen (arrowhead) representing a CT finding that would score 1 point for each organ. **b** Axial-enhanced CT image in soft tissue window setting demonstrates mesenteric foreshortening and cauliflowering (arrowheads) of the small bowel, a CT finding that would score 3 points

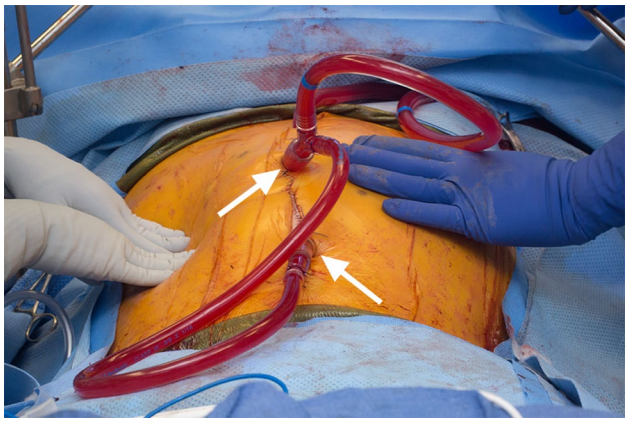


Fig. 13 HIPEC (hyperthermic intraperitoneal chemotherapy) is performed following CRS (cytoreductive surgery) with the intent to treat microscopic malignant cells that may be present. Temperature probes are inserted to monitor temperature. In-flow and out-flow catheters (arrows) are placed in the abdomen. The abdomen is sutured closed. Plasmalyte solution is used to rinse the abdomen, and then heated chemotherapy (about 42.5 °C or 108°F) is added. The surgeon gently massages the abdomen to help disperse the chemotherapy for 60–90 min. The chemotherapy is drained and the abdomen is rinsed with the saline solution once more. The patient is reopened, the catheters and probes are removed, and the abdomen is again closed

ascites [47]. Lastly, the presence of omental caking, tumor plaques, and prior surgical scars make the interpretation of the PCI difficult due to unclear boundaries and overlapping pathologies.

With its superior contrast resolution, delayed post-contrast-enhanced MRI coupled with diffusion-weighted imaging (DWI) has been shown to have high sensitivity for detection of small peritoneal implants and is potentially helpful for differentiation of acellular mucin from more cellular disease [69, 70]. Tumors enhance slowly and become much more conspicuous with delayed post-contrast material-enhanced imaging (Fig. 15) as compared to pre-contrast material T1-weighted images, where they demonstrate intermediate to low signal intensity and may be imperceptible from adjacent normal structures [69, 70]. T2 signal intensity is variable. Owing to high tumor cellularity, even small deposits are readily identifiable as hyperintense foci (Fig. 16) on diffusion-weighted imaging with corresponding dark signal on apparent diffusion coefficient mapping [69, 70]. When abdominopelvic MRI is performed for PMP or PC, the use of glucagon and oral contrast material should be considered to inhibit bowel peristalsis and to increase conspicuity of bowel serosal and mesenteric disease, respectively.

As discussed above, CT remains an imperfect tool for the pre-operative evaluation of PC [48, 68, 71–74]. In comparison to positron emission tomography co-registered with computed tomography (PET/CT), contrast-enhanced CT has been found to be superior in the pre-operative assessment of disease extent [73, 75]. In fact, recent evidence has suggested that when PET is co-registered with contrast-enhanced CT, the combination of the two modalities is more accurate than PET/CT (without intravenous contrast material) but no more accurate than contrast-enhanced CT alone for the pre-operative assessment of disease extent [76]. It is important to note that these comparisons are limited due to the small sample sizes and retrospective nature of the studies performed, and a prospective study with a larger sample size would be of value for a more accurate comparison. Furthermore, there is a definitive correlation between radiologist expertise in PC imaging, modern scanner usage with thin collimation and multiplanar reformations, as well as overall tumor burden in improved detection of peritoneal implants [71, 77].

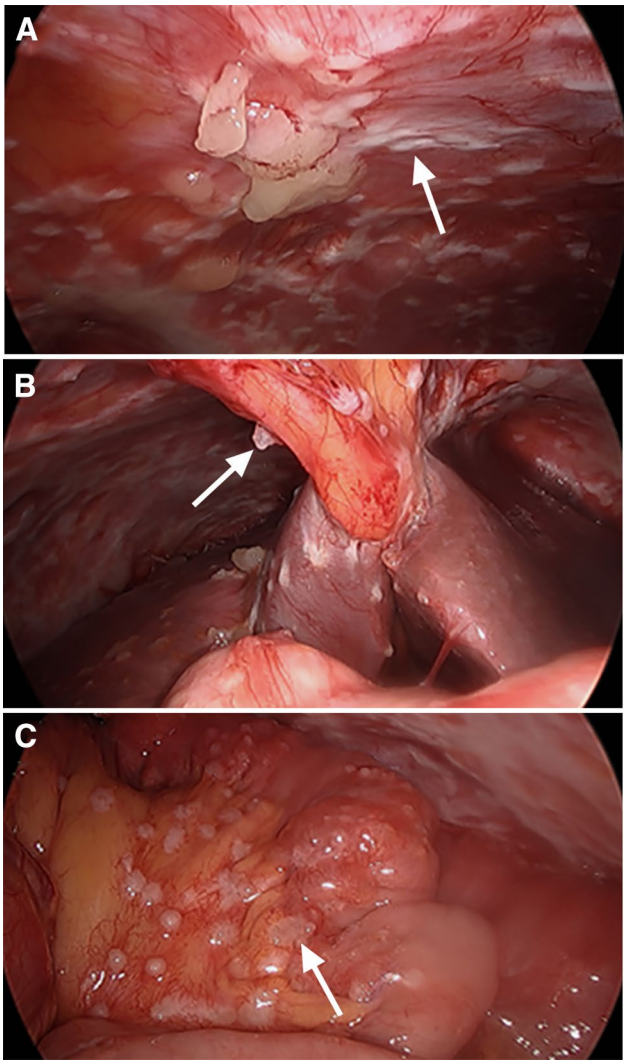


Fig. 14 A 48-year-old male with peritoneal carcinomatosis from poorly differentiated adenocarcinoma with signet ring cells who presented with large bowel obstruction. **a–c** Photographic images during laparoscopy demonstrates nearly innumerable nodular and plaque like implants (arrows on representative examples) most of which were not visible on CT, consistent with miliary disease in this patient with peritoneal carcinomatosis. The patient had a surgical PCI score of 39 and was deemed inoperable

How imaging helps the surgeon

Given the known limitations of cross-sectional imaging, diagnostic laparoscopy has been advocated by some authors as a means to help select patients who would be amenable to complete cytoreduction. In fact, Laterza et al. reported 100% sensitivity, 75% specificity, 96.6% positive predictive value, and 100% negative predictive value of diagnostic laparoscopy for predicting complete cytoreduction in 33 patients [78]. Nevertheless, several areas within the peritoneal cavity are poorly assessed with laparoscopy because of poor visibility, including intrahepatic metastases (Fig. 17), splenic and pancreatic parenchymal metastases, metastases to the lesser sac and porta hepatis (Fig. 17), and intraluminal gastrointestinal tract implants (Fig. 17) [79, 80]. Thus, cross-sectional imaging is valuable in alerting the surgeon to the presence of disease in these areas.

The radiologist must also be familiar with what constitutes resectable or unresectable disease at cytoreduction. Whereas parietal peritoneal tumor resection, including excision of disease beneath the hemidiaphragms, along posterior portions of the lesser sac, in the pelvis and along the paracolic sulci, can be completed in most patients, other sites of disease can be more problematic. [81]. For example, in a recently published paper, Sugarbaker, et al., describe several findings on pre-operative CT which portend a poorer prognosis and/or may predict incomplete cytoreduction. These findings include (1) small bowel/mesentery: multifocal small bowel obstruction (termed "chaotic bowel pattern"), mesenteric retraction which draws bowel into distinct clusters (i.e., "cocoon" bowel) (Fig. 12b), tumor infiltration within the small bowel mesentery (Fig. 18), and jejunal involvement with a mass measuring ≥ 5 cm; (2) retroperitoneum: hydroureter, psoas invasion, and retroperitoneal lymphadenopathy; (3) pelvis: seminal vesicle and pelvic sidewall invasion; (4) gastrohepatic/hepatoduodenal ligaments: infiltration of the porta hepatis and bile duct obstruction, tumor within the subpyloric space, and gastrohepatic ligament disease measuring ≥ 5 cm; (5) ascites: hemorrhagic ascites or serous ascites.

Ultimately, the pre-operative evaluation of patients with peritoneal carcinomatosis involves a multi-specialty team approach and all team members should be familiar with the strengths and limitations of the different components of the pre-operative work-up.

Reporting

Uniform and consistent reporting is helpful in clearly articulating the imaging findings to the surgeon and oncologist, allowing for the determination of a pre-operative score and accurately estimated therapeutic prognosis. Despite these benefits, reporting tends to be quite variable and poorly standardized. In order to address this variability, one recent publication describes the use of the acronym "PAUSE" for reporting the key imaging features determining surgical feasibility and pre-operative prognosis [82]. This acronym stands for (p)rimary tumor and PCI; (a)bdominal wall involvement and ascites; involvement of (u)nfavorable sites; (s)mall bowel/small bowel mesentery disease; and (e)xtra-peritoneal disease. At our institution, a collaboration between our abdominal radiologists and cytoreductive oncologic surgeons was established. A standardized template utilizing multiple "pick list" options for each anatomic

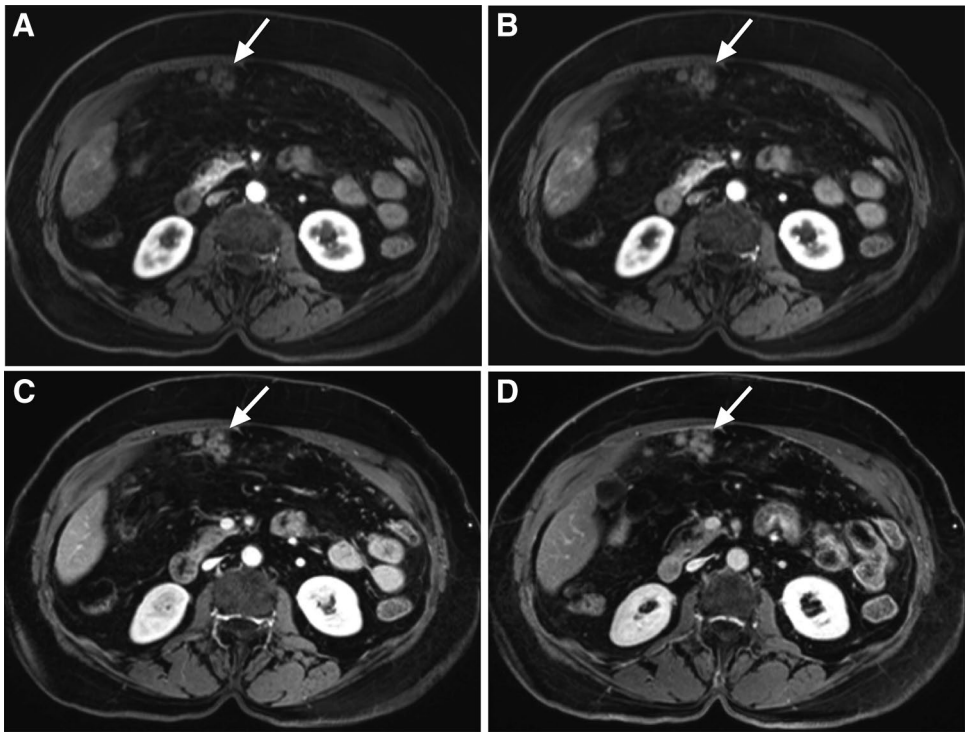


Fig. 15 A 72-year-old female with appendiceal adenocarcinoma and peritoneal carcinomatosis. Serial axial fat-suppressed T1-weighted post-gadolinium MR images demonstrate a small, grape-like cluster of peritoneal deposits in the anterior abdomen. Little if any enhancement is present on the initial image (**a**) with the metastatic deposits enhancing progressively on delayed serial images (**b**–**d**)

location was developed, which incorporated elements of the "PAUSE" method as well as certain nuances to our practice. For example, we do not routinely calculate and report PCI in our imaging reports, but some institutions may choose to do so.

Future directions

Additional studies are required to further define the role of CRS and HIPEC in appendiceal neoplasms. Currently, there are 57 active clinical trials investigating the role of CRS/HIPEC in PC from various malignancies and 6 of those trials include patients with PC from appendiceal neoplasms [83]. There is increasing interest in developing molecular targeted compounds for personalized treatment of PC. In fact, many formulations of tumor-homing peptides designed for treatment and as imaging agents already exist and will become available in years to come, creating new opportunities to improve imaging sensitivity/specificity and overall treatment outcomes [84]. Molecular imaging agents have also been used intraoperatively, e.g., fluorescence image-guided surgery, and may show promise to improve the rate of complete cytoreduction [85]. There is also need for further optimization and standardization of available imaging protocols, better coordination of imaging modalities, and further revision of the available scoring systems given the heterogeneity of results among the studies available [49, 81, 86].

Conclusion

Appendiceal neoplasms are rare, with initial presentations ranging from a localized appendiceal mucocele to an aggressive malignancy with peritoneal spread. Cooperative multidisciplinary teamwork is required to provide each patient the most appropriate, personalized treatment plan. The radiologist must be familiar with the strengths and limitations of cross-sectional imaging techniques; should be familiar with the various imaging appearance of appendiceal neoplasms, peritoneal carcinomatosis, and PMP; should be aware of the different scoring systems for estimating the extent of peritoneal disease; and should be aware of key anatomic locations that may preclude or complicate surgery or that may be inaccessible at diagnostic laparoscopy. The appended report template can be used as a tool to provide a detailed account of the disease locations, thereby helping facilitate therapeutic

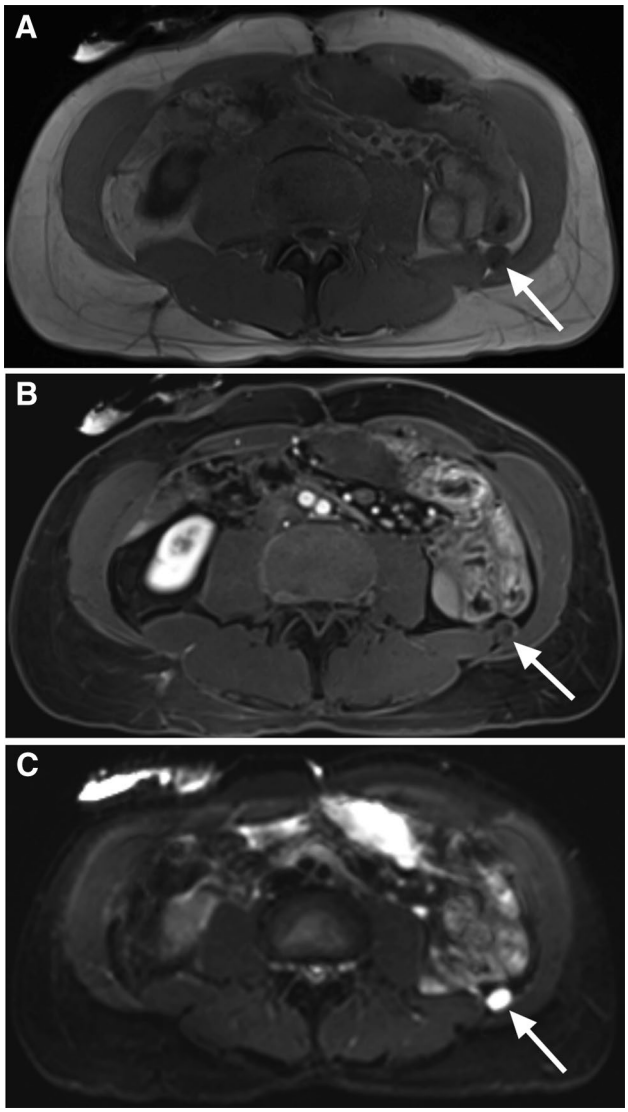


Fig. 16 A 51-year-old male with appendiceal adenocarcinoma and peritoneal carcinomatosis. **a** Axial T1-weighted MR image without fat suppression demonstrates a focal hypointense nodule in the left paracolic gutter. **b** Axial T1-weighted fat-suppressed image following gadolinium administration shows very mild peripheral enhancement. **c** Axial diffusion-weighted image demonstrates marked restricted diffusion in the lesion, making the nodule very conspicuous

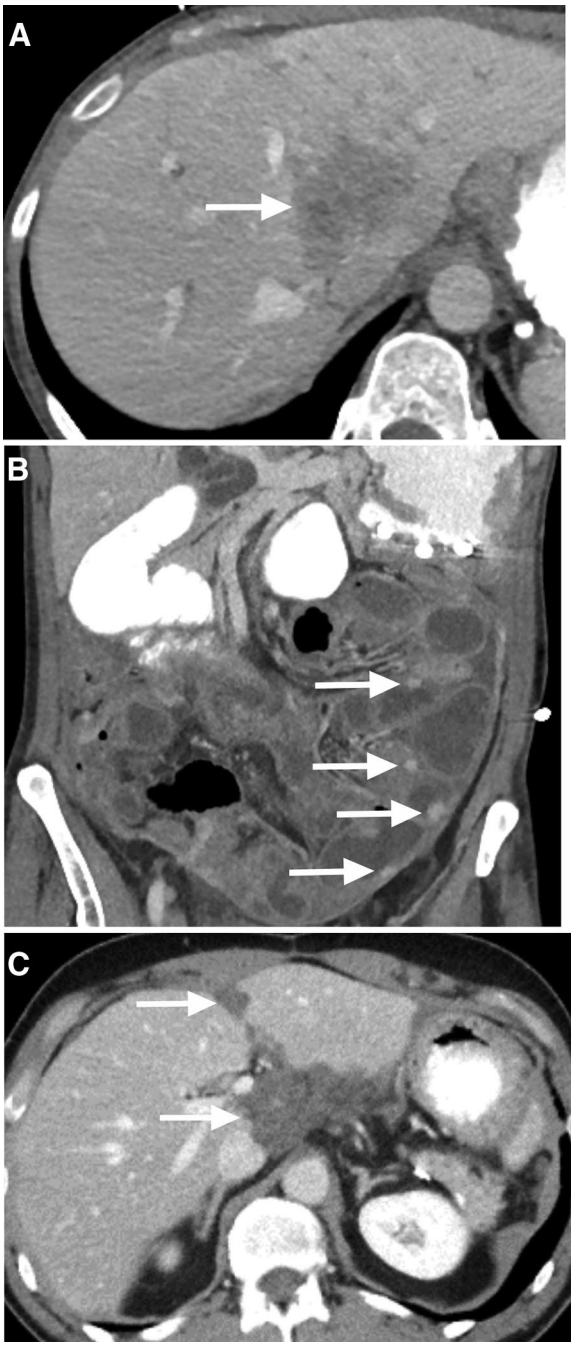


Fig. 17 Disease that may be inaccessible by laparoscopy. **a**, **b** A 60-year-old female with metastatic appendiceal adenocarcinoma. Axial- (**a**) and coronal- (**b**) enhanced CT images demonstrate intrahepatic metastases (**a**, arrow) and small bowel metastases, including numerous small mural and intraluminal metastases (**b**, arrows). **c** A 57-year-old male with extensive metastatic disease in the porta hepatis and extending along the falciform ligament (arrows)

Fig. 18 A 52-year-old female with peritoneal carcinomatosis from poorly differentiated appendiceal adenocarcinoma with signet ring cells. Axial-enhanced CT image in soft tissue window settings demonstrates multifocal peritoneal implants in the small bowel mesentery and involving small bowel (arrows)

decision making and potentially serving as a roadmap for the oncologic surgeon during diagnostic laparoscopy or the CRS/HIPEC procedure.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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