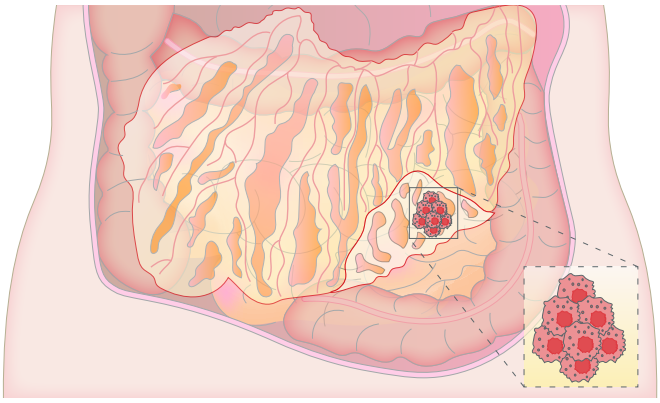
Mistakes in the management of peritoneal malignancies and how to avoid them

Francesco Saverio Papadia, Tarkan Jäger, Charlotte Rabl, Matteo Santoliquido and Andrea Barberis

Peritoneal malignancies represent a complex and often misjudged clinical challenge. Historically synonymous with a terminal diagnosis, the advent of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) radically altered the prognosis for selected patients. However, progress has been jeopardised by a series of recurring and preventable errors in diagnosis, staging, and treatment selection. This article delineates the ten most critical pitfalls in managing peritoneal surface malignancies. For each pitfall, we provide evidence-based explanations, concrete clinical examples, and strategic recommendations for avoidance. We emphasise the pivotal role of early multidisciplinary discussion, precise imaging, and timely referral to high-volume expert centres to optimise patient outcomes and offer curative intent where previously there was none.



The peritoneum is a common site of metastasis for gastrointestinal and gynaecological cancers and the primary site for rare entities like malignant peritoneal mesothelioma and primary peritoneal carcinoma. For decades, the diagnosis of peritoneal carcinomatosis signalled the end of the therapeutic road, relegating patients to palliative systemic chemotherapy with a median overall survival rarely exceeding 6–12 months. This fatalistic view was perpetuated by nonspecific symptoms, inadequate diagnostic tools, and lack of effective treatments. The paradigm shift began with Sugarbaker and others, who established CRS and HIPEC as a potentially curative multimodal strategy.[1,2] This approach, analogous to surgical treatment of liver or lung metastases,[3,4] aims for complete macroscopic resection (complete cytoreduction [CC-0]) followed by intraperitoneal chemotherapy to eradicate microscopic residues. Despite robust long-term survival data — a 10-year survival rate of 63% for pseudomyxoma peritonei (PMP) and median overall survival of 42 and 46 months for colorectal peritoneal metastases (CRPM) and ovarian peritoneal metastases, respectively[5,6,7] — this strategy remains underutilised. Management is often plagued by avoidable errors stemming from outdated beliefs, diagnostic delays, and inadequate staging. This article illuminates these common pitfalls and provides a practical framework for their avoidance, ensuring patients receive modern, standard-of-care management.

Abbreviations: CRPM, colorectal peritoneal metastases; CRS, cytoreductive surgery; DWI, diffusion-weighted imaging; HIPEC, hyperthermic intraperitoneal chemotherapy; LAMN, low-grade appendiceal mucinous neoplasm; MDT, multidisciplinary team; PCI, Peritoneal Cancer Index; PMP; pseudomyxoma peritonei; SLS, staging laparoscopy.

Mistake 1 Therapeutic nihilism — considering all peritoneal cancer incurable

The automatic classification of any peritoneal dissemination as a terminal, chemo-only condition is perhaps the most fundamental and damaging error. This therapeutic nihilism is often based on historical data and a lack of awareness of recent advances. While it holds true for aggressive histologies like pancreatic or biliary cancer with peritoneal involvement, it is profoundly incorrect for others. For low-grade appendiceal mucinous neoplasms (LAMN) and PMP, CRS/HIPEC is arguably the most compelling indication; when complete cytoreduction is achieved, 10-year survival rates exceed 70–80%,[8] making it a curative procedure. For CRPM, the PRODIGE 7 trial[5] unequivocally confirmed the role of complete cytoreduction, with a median overall survival of 41.2 months, far surpassing outcomes with palliative chemotherapy. Outcomes are even more favourable in patients with a Peritoneal Cancer Index (PCI) <12. Furthermore, selected cases of gastric cancer and epithelial ovarian cancer have also shown a survival benefit from this aggressive approach in randomised trials.[9,10,11]

To avoid this pitfall, it is crucial to remember that histology is king; never make assumptions based on the mere presence of peritoneal disease. The primary tumour origin and its histological grade are the primary determinants of management. A common error is misclassifying an appendiceal primary as colorectal, so seeking an expert pathology review can dramatically alter the treatment pathway. Clinicians must educate themselves that CRS/HIPEC is a standard curative option for PMP/LAMN and a strong option for low-PCI CRPM and ovarian cancer. Even entities that appear histologically benign (e.g., well-differentiated papillary mesothelioma or LAMN) can occasionally show malignant transformation or coexist with malignant epithelioid implants at separate intra-abdominal sites. Plan systematic mapping, targeted biopsies of suspicious areas, and interval follow-up.

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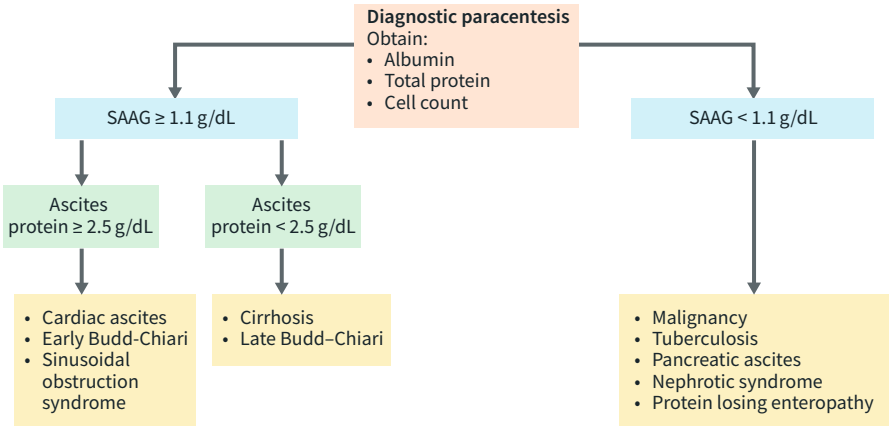

Figure 1 | Diagnostic flowchart for unexplained ascites.

► Polymorphonuclear leukocyte count (PMN) ≥ 250 cells/mm^3 represents spontaneous bacterial peritonitis (high serum-ascites albumin gradient [SAAG]) or pancreatic ascites (low SAAG). If white blood cell count (WBC) ≥ 500 x10^9 cells/L with PMN < 250 cells/mm^3, then need to rule out tuberculosis or malignancy.

Mistake 2 Diagnostic inertia — delaying or missing the diagnosis

A critical delay occurs when vague abdominal symptoms are attributed to benign conditions (e.g., irritable bowel syndrome, ascites due to cirrhosis) or previous surgery. The symptoms of peritoneal disease are insidious, with ascites being the most common presentation. However, cytology of ascitic fluid is notoriously insensitive, especially for mucinous tumours and signet-ring cell carcinomas, with sensitivity as low as <10%; relying on a negative cytology result to rule out malignancy is a mistake.[12] The Washington Cancer Institute series[13] is a stark reminder, in which none of 68 patients with peritoneal metastases from appendiceal cancer were diagnosed by cytology. Unexplained peritoneal thickening, omental caking, or localised ascites on computed tomography (CT) should raise immediate red flags, especially in a patient with a history of cancer.[14]

To circumvent this, a high index of suspicion is necessary for any patient with new-onset, unexplained ascites, abdominal distension, or obstructive symptoms. If clinical suspicion is high, one should move beyond cytology and proceed directly to more definitive diagnostic steps. Image-guided core biopsy of an omental cake or a peritoneal nodule is a minimally invasive and highly accurate tool. Furthermore, one should not fear laparoscopy but rather indicate it early; it is the gold standard for direct visualisation, targeted biopsies, and accurate PCI assessment. It is superior for detecting sub-5 mm nodules and subtle peritoneal studding that CT often misses, offering high diagnostic and staging yield with low morbidity.[15,16,17] A practical flowchart for diagnosing unexplained ascites involves a CT scan with intravenous (IV) and oral contrast, followed by an image-guided core biopsy or diagnostic laparoscopy if the CT is suspicious, culminating in histological confirmation and immediate referral to a multidisciplinary team (see Figure 1). ►

Mistake 3 Inadequate radiological assessment — using suboptimal imaging

Relying on poor-quality CT scans (e.g., without contrast or low resolution) or using the wrong imaging modality leads to significant under-staging. A standard CT scan is inadequate for mapping peritoneal disease, as small lesions on the complex structures of the peritoneum and small bowel mesentery are easily missed.[18] A dedicated peritoneal protocol CT with IV contrast and positive oral contrast is mandatory, as the oral contrast distends the bowel loops, allowing for better visualisation. Diffusion-weighted imaging (DWI) magnetic resonance imaging (MRI) is superior to CT in detecting non-mucinous peritoneal deposits, while positron emission tomography (PET)/CT is excellent for detecting extraperitoneal metastatic disease but has very low sensitivity for mucinous tumours and should not be used to rule out peritoneal disease in these cases.[19]

To avoid this, clinicians must demand high-quality imaging by specifically requesting a "CT abdomen/pelvis with IV and oral contrast for peritoneal staging." Knowing the strengths of each modality is key: CT is good for mucinous disease and overall surgical planning, MRI-DWI is best for non-mucinous disease, and PET/CT is best for excluding extra-abdominal disease.[20] Involving a dedicated radiologist is crucial, and the report should comment on the Sugarbaker PCI regions and mention specific contraindications for surgery.[21]

Mistake 4 Flying blind — omitting PCI calculation and staging laparoscopy

Making treatment decisions based solely on cross-sectional imaging without a true assessment of the disease burden via the PCI is a recipe for an unnecessary exploratory surgery or an incomplete cytoreduction. Imaging consistently underestimates the PCI, particularly in the crucial areas of the small bowel and its mesentery.[22] The PCI is the single most important prognostic factor for outcomes after CRS/HIPEC.[23] Staging laparoscopy (SLS) is a minimally invasive procedure that provides the most accurate pre-treatment PCI, allowing for visualisation of all abdominal quadrants, biopsy for definitive histology, and assessment of resectability.[16] It is the crucial step that separates a planned, curative procedure from a disastrous laparotomy.

Avoidance hinges on making SLS a routine standard of care for any patient being considered for CRS/HIPEC, unless contraindicated by dense adhesions. Early referral to a multidisciplinary team (MDT) allows this decision to be made before the window of opportunity closes.

Mistake 5 The volume–outcome relationship — managing patients outside specialised centres

Underestimating the complexity of CRS/HIPEC and treating patients in low-volume centres is a dangerous pitfall. CRS/HIPEC is one of the most complex procedures in surgical oncology, involving extensive surgery across multiple organ systems followed by a complex chemoperfusion process. Data is unequivocal: high-volume centres have significantly lower morbidity and mortality rates, higher rates of complete cytoreduction, and better long-term survival.[24] The learning curve is steep, requiring profound expertise in complex surgical oncology operations and a substantial number of cases to overcome it, making centralisation of care a necessity for patient safety and efficacy.[25]

The solution is to refer early and often. At the first suspicion of a resectable peritoneal

malignancy, the patient should be referred to a certified high-volume centre for evaluation, without initiating palliative chemotherapy first. Clinicians should be aware of the designated expert centres within their national or European network.

Mistake 6 The lone wolf approach — bypassing the MDT

A surgeon, oncologist, or gastroenterologist making treatment decisions in isolation is a significant error. Peritoneal malignancies require nuanced decision-making where a fine balance must be struck between surgery and systemic therapy. The MDT, including peritoneal surgeons, surgical oncologists, medical oncologists, radiologists, pathologists, and specialised nurse coordinators, is the safeguard against inappropriate care. Key discussions include candidacy for CRS/HIPEC, the need for neoadjuvant chemotherapy, the best sequencing of therapy, and the management of recurrence.

To avoid this pitfall, an MDT review should be mandated for any patient with peritoneal metastases before starting treatment.[26] Presenting complex cases at tumour boards also serves to educate the entire team on the possibilities and limitations of modern peritoneal surface oncology.

Mistake 7 Misguided first steps — starting chemotherapy in primarily resectable cases

Immediately starting systemic chemotherapy in a patient with resectable, low-volume disease can be detrimental for certain histologies. Appendiceal tumours (either low or high grade) are largely resistant to chemotherapy; delaying surgery offers no benefit and risks disease progression to an unresectable state.[27] For low-PCI colorectal cancer, although neoadjuvant chemotherapy is often used, there is a risk of chemotherapy-induced peritoneal sclerosis, which can make subsequent surgery more difficult.[28] A 'surgery-first' strategy is a valid consideration in young, fit patients with very low PCI, and for determinate histologies (e.g., LAMN).[29]

Therefore, the decision to start chemotherapy or opt for surgery first is complex and must be made by the expert MDT based on histology, PCI, and patient factors. The automatic reflex to start chemotherapy should be challenged, as it is usually the wrong choice for appendiceal cancer.

Mistake 8 The failed mission — accepting incomplete cytoreduction

Proceeding with CRS when a complete cytoreduction (CC-0/1) is not achievable subjects the patient to the full morbidity of a major operation without the survival benefit, which is almost entirely dependent on achieving CC-0/1.[30] An incomplete resection (CC-2/3) offers no survival benefit over chemotherapy alone. This underscores the critical role of high-quality imaging and SLS in preoperative prediction. The MDT must honestly assess the likelihood of completeness. 'Life-buying' debulking is rarely indicated and should only be considered in specific palliative scenarios, not with the illusion of providing an oncological benefit.[31] Table 1 offers an overview of the completeness of the cytoreduction score.

The cardinal rule must be "complete cytoreduction or do not start". The preoperative plan must be for CC-0/1, and if SLS or laparotomy reveals this is impossible, the procedure should be aborted without HIPEC. Patients must be counselled preoperatively about this possibility.

Mistake 9 Protocol deviation — misusing and overusing HIPEC

Applying HIPEC outside of its evidence-based indications turns a potentially curative treatment into a harmful one. HIPEC is not a 'magic bullet' that can compensate for poor patient selection or incomplete surgery. Established contraindications include a PCI above 20 for colorectal cancer, incomplete cytoreduction (CC-2/3), poor performance status (ECOG >2), presence of extra-abdominal disease, and non-indicated histologies (e.g., pancreatic or biliary cancer), where data shows high morbidity and mortality with no proven survival benefit.[32] The PRODIGE 7 trial[5] has led to a re-evaluation of HIPEC in colorectal cancer, suggesting its benefit may be agent-specific and that CRS is the critical component, making its use now more selective.

To avoid this, strict adherence to national and international guidelines on HIPEC indications is essential. HIPEC should never be used as a 'salvage' procedure in a hopeless situation, and clinicians must stay updated as the evidence base evolves.

Mistake 10 The forgotten patient — neglecting structured follow-up and reintervention

Discharging patients after CRS/HIPEC without a clear, proactive surveillance plan leads to missed opportunities for curative reintervention upon recurrence. Recurrence is common, but unlike many other metastatic cancers, isolated peritoneal recurrence can often be treated with curative intent again.[33] A structured follow-up protocol is vital, including CT or MRI every 3–4 months for the first 2 years, every 6 months for years 3–5, then annually, with tumour markers (cancer embryonic antigen [CEA], cancer antigen 19-9 [CA-19-9] and cancer antigen 125 [CA-125]) assessed at every visit.[34] Carefully selected patients with recurrent disease can undergo a second, or even third, procedure, with median survival after repeat CRS/HIPEC reaching 40–60 months.[35]

Therefore, follow-up should not be improvised but should follow a standardised, tumour-specific schedule. At the first sign of recurrence, a full re-staging process within the MDT should be initiated to evaluate for repeat intervention. The mindset should be that recurrence is a new problem to be solved, not a final verdict.

In conclusion, the management of peritoneal malignancies has been revolutionised, moving from universal palliation to potential cure. Navigating this complex field requires avoiding ten critical pitfalls. The central themes are accurate diagnosis, precise staging, meticulous patient selection, centralisation of care, multidisciplinary decision-making, and life-long structured follow-up. By adhering to these principles, gastroenterologists, surgeons, and oncologists can offer hope and significantly prolonged survival to a growing number of patients with peritoneal surface malignancies.

CC-0	CC-1	CC-2	CC-3
Complete cytoreduction	Complete cytoreduction	Incomplete cytoreduction	Incomplete cytoreduction
No visible disease	Tumour nodules <0.25 cm	Tumour residual 0.25– 2.5 cm	Tumour residual >2.5 cm

Table 1 | Completeness of cytoreduction (CC) score.

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Your management of peritoneal malignancies briefing

UEG Week

- Metastasised colorectal cancer (Complete Session). Presentation at UEG Week 2023 [https://gutflix.eu/r/HAP0OWI88hvB]
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Guidelines

- Imaging of peritoneal metastases of ovarian and colorectal cancer: joint recommendations of ESGAR, ESUR, PSOGI, and EANM [https://gutflix.eu/r/2JKcekBYNgGj]