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## Malignant peritoneal mesothelioma literature review: past, present, and future

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### Abstract

**Background and Objective:** Malignant peritoneal mesothelioma (MPM) is an insidious neoplasm that arises from the mesothelial lining of the abdominal cavity. Historically, outcomes of MPM were dismal, as MPM is relatively resistant to cytotoxic chemotherapy. However, with advances in technology and improved understanding of tumor pathophysiology, treatments for MPM have produced encouraging 5-year survival. The standard of care for patients with resectable disease remains cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Patients with inoperable MPM can be offered several systemic treatments, including chemotherapy, immune checkpoint inhibitors, or investigational treatments. Our objective is to provide an overview of our current knowledge concerning MPM and latest advances in treatment.

**Methods:** Narrative overview of the literature published in English from database origin until January 31, 2022 relating to MPM was searched in PubMed database, Google Scholar, and [ClinicalTrials.gov](https://clinicaltrials.gov).

**Key Content and Findings:** CRS-HIPEC has offered improved survival for surgical candidates, however outcomes for inoperable MPM remains dismal. With advancements in

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technology and better understanding of underlying MPM biology, new treatment approaches are arising and imperative.

**Conclusions:** MPM is a rare and lethal disease of the peritoneum. CRS-HIPEC remains the standard of care for resectable disease. In 2022, several clinical trials are available for patients with MPM offering future advances in therapy and further understanding of this rare disease process.

### Keywords

Malignant peritoneal mesothelioma (MPM); cytoreductive surgery (CRS); heated intraperitoneal chemotherapy; peritoneal carcinomatosis

## Introduction

Malignant peritoneal mesothelioma (MPM) is a rare, aggressive, and lethal neoplasm that arises from the mesothelial lining of the abdominal cavity (1–3). MPM comprises 20–30% of all mesothelioma in developed countries (4–6). Annually, approximately 500–800 new cases of MPM are diagnosed in the United States, with 90% diagnosed in non-Hispanic whites (7–10). Unlike pleural mesothelioma (PM), patients with peritoneal disease are diagnosed at a younger age (median 63 versus 71 years), with equal disease distribution between men and women (8). At the time of diagnosis, the majority of patients will have advanced disease; without treatment, median overall survival is at best 6 months (8,9,11). Cytoreductive surgery (CRS) followed by hyperthermic intraperitoneal chemotherapy (HIPEC) is the standard of care for patients with resectable disease and good performance status (8,12,13). With advances in operative technique, CRS-HIPEC has shown encouraging five-year survival results, and in some settings this is performed with intention to cure. On the other hand, outcomes for unresectable MPM remains dismal, with median survival of 1 year (14). This review provides an overview of our current knowledge concerning MPM including epidemiology, clinical presentation, and diagnosis; as well as discussions of past, present, and future directions of treatment. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://dmr.amegroups.com/article/view/10.21037/dmr-22-19/rc>).

## Methods

A comprehensive literature review was completed by searching PubMed, Google Scholar, and ClinicalTrials.gov from database's inception until January 31, 2022. Only articles published in English were considered. All natures of studies: prospective randomized controlled trials, non-randomized prospective trials, retrospective studies, case reports, reviews, and meta-analyses were included. The search terms included singular and combinations of the following: “malignant peritoneal mesothelioma”, “mesothelioma”, “cytoreductive surgery”, “heated intraperitoneal chemotherapy”, and “peritoneal carcinomatosis” (Table 1).

## Epidemiology

MPM was first described in 1908 by Miller and Wynn; however, it gained attention during the 1960s after the effects of widespread use of asbestos during World War II were shown

to correlate with increased incidence rates of mesothelioma and disease-specific mortality (2). In the 1980s, commercial regulations were implemented to ban the use of six mineral fibers collectively defined as “asbestos”. However, many of the remaining 400 mineral fibers are unregulated; they are still commercially used today, considered carcinogenic, and have been associated with mesothelioma (15). In fact, talc-based products have been associated with mesothelioma and ovarian cancer due to containing small amounts of asbestos minerals such as chrysotile and amphiboles. Recently, Johnson & Johnson withdrew its sale of talc baby powder in the United States and Canada due to lawsuits claiming association with ovarian cancer and mesothelioma (16). Today, asbestos remains the most identifiable risk factor in MPM; however, only 10–33% of MPM cases have positively identified previous asbestos exposure. MPM takes 20 years to develop following exposure, thus recall to the exposure can be difficult (9,15,17). Talcum, historic Thorotrast angiograph dye, radiation, papovavirus, simian virus, and chronic inflammation represent additional risk factors for the development of MPM (17,18).

### Clinical features

Patients with MPM most commonly present with vague symptoms such as nonspecific abdominal pain or bloating. Patients may develop abdominal distention secondary to ascites or a palpable abdominal mass (8). Patients can also exhibit signs of extensive abdominal disease such as early satiety, weight loss, and fatigue (11). Time of symptom onset to diagnosis is approximately 4–6 months, but frequently longer given the vague nature of initial associated symptoms (19).

### Diagnosis

Computed tomography (CT) is the principal imaging modality utilized for diagnosis. While positron emission tomography (PET) can be used in conjunction with CT, its value in initial diagnosis is not clear (20). Radiographically, the disease may present as mesenteric or parietal peritoneal nodules, visceral peritoneal thickening leading to foreshortening of the mesentery, ascites, or omental masses (21). Favorable radiographic findings include minimal soft tissue masses, normal intestine and mesenteric anatomy, and lack of ascites. Unfavorable findings include tumors >5 cm, especially tumors involving the lesser omentum or jejunal regions; para-aortic lymphadenopathy, and diffuse peritoneal thickening resulting in anatomic distortion of the bowel (8,22,23). A hallmark feature of MPM is its propensity to remain confined to the abdominal cavity. In fact, extra-abdominal disease is rare and typically only manifests by direct disease extension from the diaphragm across into the pleural space or via extra-abdominal lymph node metastasis (11,24) (Figure 1).

The serum protein cancer antigen (CA)-125 is frequently elevated in patients with MPM and used as a tumor marker. Due to the higher prevalence of ovarian cancer and its established association with elevated CA-125, approximately one-third of women with MPM are initially misdiagnosed with ovarian cancer (16,25). While the low specificity of CA-125 limits its utility in diagnosing MPM, it has shown some use for tumor progression and surveillance since CA-125 levels often normalize after treatment (25).

In conjunction with imaging for diagnosis, diagnostic laparoscopy has the added advantage of direct visualization of peritoneal disease burden and ability to obtain tumor biopsies (Figure 2). Diagnostic laparoscopy is imperative for staging a patient's tumor burden and identifying patients whose disease is amenable to complete cytoreduction, particularly those patients without overt radiographic evidence of disease. The peritoneal cancer index (PCI) is a systematic method of determining the distribution and burden of disease for staging (26). The PCI is calculated by dividing the peritoneal cavity into 13 regions. The peritoneal cavity is then further subdivided into 9 regions with numbering starting at the right hemidiaphragm and moving in a clockwise fashion (the umbilical region is labeled 0), followed by 4 regions of the small bowel (proximal and distal jejunum and ileum) (Figure 3). Laparoscopy, however, will underestimate to some degree the extent of disease (8). Laparoscopic port sites can also be sources for tumor deposit, so it is important to limit the number of port sites and place them in the linea alba to be excised during CRS-HIPEC if possible.

## Pathology

MPM is composed of three histological subtypes: epithelioid (56%), sarcomatoid (31%), and mixed/biphasic type (13%) (1,11). Epithelioid MPM is considered the least aggressive subtype and is associated with the most favorable prognosis in general (11,27). Borderline malignant variants of peritoneal mesothelioma have also been described, such as benign multicystic mesothelioma and well-differentiated papillary mesothelioma (WDPM). These variants are considered different biological entities and can usually be differentiated from their malignant counterparts through lack of invasion as well as no increased cellularity within the stroma or simple papillary formations if present (28,29). Of note, there is controversy in the literature regarding whether WDPM is a neoplasm or a reactive process, and there have been some case reports of WDPM with invasive foci (30,31) (Figure 4).

Once biopsies are obtained, a definite diagnosis of mesothelioma can be confirmed using a panel of immunohistochemical (IHC) antibodies. The most sensitive IHC markers for mesothelioma include calretinin, cytokeratin 5/6, and Wilm's tumor (WT-1) (8,11). IHC markers mesothelin and fibulin-3 are specific for mesothelioma (32). Negative antibody staining for carcinoembryonic antigen (CEA) and PAX8 are imperative to distinguish pathologic diagnosis of MPM from another primary such as colon cancer or ovarian cancer (17,33). IHC can also be used to look for loss of *BAP1* expression. BRCA-associated protein 1 (*BAP1*) is involved in DNA repair and apoptosis of DNA mutations (34). *BAP1* mutation is associated with uveal melanoma, clear cell renal carcinoma, cutaneous malignancies, and mesothelioma (15,35). *BAP1* mutation has been detected in 27–67% of PMs (15,36). There are few studies examining prevalence of *BAP1* mutation in peritoneal mesothelioma, but one study by Singhi *et al.* revealed a loss of *BAP1* in 57% of their patients (n=49) (36).

In fact, many molecular alterations for mesothelioma such as *NF2*, *CDK2A/B*, *TP53*, and *SETD2* have been reported in the literature for PM, but a paucity of genomic data exists for MPM (37). A recent series from Memorial Sloan Kettering used next-generation sequencing on fifty MPM tumors and revealed alterations in *BAP1* (60%), *NF2* (24%), *SETD2* (22%), and *TP53* (16%) (37). Regarding *BAP1* alterations in this study, overall survival was worse when mutations or deletions on next-generation sequencing coexisted with loss on IHC as to

compared wild-type *BAP1* or retained expression on IHC (37). In contrast, *BAP1* mutation and loss of expression has been associated with improved survival in PM, and a study in France reported better overall survival for MPM independent of tumor histological subtype, age, and sex (38,39).

## Treatment

Historically, treatment of MPM remained palliative in intent; however, systemic chemotherapy was introduced as an early alternative after the management of six patients by Brenner *et al.* (40). Decades later, the combination of surgical resection and regional intraperitoneal chemotherapy became more widespread. The first multi-institutional consensus meeting was hosted by the National Cancer Institute in Bethesda, Maryland in 2004, and the second international consensus from the Peritoneal Surface Oncology Group Biennial Meeting was held in Milan, Italy in 2006 (20,22,41). Together, these meetings resulted in the new standard of care for MPM: CRS combined with HIPEC.

## Surgery

The introduction of CRS in combination with HIPEC has improved the prognosis of selected patients with MPM to a median survival of 30–100 months and an overall 5-year survival of 40–70% (22,42). The goal for therapeutic treatment is complete or near-complete removal of all visible disease, as indicated by the Completeness of Cytoreduction (CC) score of 0 or 1 (43). In order to achieve complete cytoreduction, resections are comprised of parietal peritonectomy, selective visceral peritonectomy, greater and lesser omentectomy, and cholecystectomy. Organ resections may include splenectomy, enterectomy, or partial colectomy including low anterior resection *en bloc* with pelvic peritonectomy. Given the frequently extensive involvement of the diaphragmatic peritoneum, partial stripping of the hepatic capsule may be required. Some controversy does exist regarding selective peritonectomy of only grossly involved peritoneum versus routine complete parietal peritonectomy. One retrospective study reported a 5-year survival of 40% with selective peritonectomy, and 63.9% with complete parietal peritonectomy (P=0.027) (22,44). However, prospective randomized data are not available. Furthermore, the role of routine complete parietal peritonectomy in the setting of germline *BAP1* mutation remains undefined.

## HIPEC

Following CRS, HIPEC is performed to address the remaining microscopic disease and residual tumor deposits <2.5 mm in size (8). Intraperitoneal chemotherapy is heated to a temperature of approximately 42 degrees Celsius. The hyperthermia acts synergistically with the cytotoxic intraperitoneal chemotherapy to facilitate drug uptake as well as to denature proteins within susceptible malignant cells and thereby induce heat-shock proteins (HSP), inhibit angiogenesis, promote apoptosis, and impair DNA repair (8,45). Intraperitoneal chemotherapy can only penetrate up to 2–3 mm deep, thus reinforcing the importance of a complete cytoreduction. In cases where complete CRS cannot be obtained, HIPEC may be considered for palliation, especially in patients with ascites (22).

There are two main methods for delivering intraperitoneal chemotherapy: the “open” (or “coliseum”) technique and the “closed” technique. The “open” technique involves delivering chemotherapy to an open peritoneal cavity. This is typically achieved by suturing the skin to a overlying ring retractor above the wound, which allows the surgeon’s hand to be introduced directly into the abdomen to allow for manual stirring and allocation of the peritoneal contents during HIPEC (45). The “closed” technique uses a running skin suture to bring together the laparotomy incision around the perfusing catheters to temporarily close the abdomen. Although the “closed” technique allows less exposure to operating room staff, there have been no studies directly comparing the two techniques in humans. Thus, technique is currently based on surgeon preference.

Despite its use for decades, intraperitoneal chemotherapy has not yet been standardized. Cisplatin and Mitomycin C (MMC) are most commonly reported in the literature as intraperitoneal agents used for MPM. Cisplatin is an alkylating agent that forms DNA adducts leading to apoptosis and has long been studied in its use for intraperitoneal administration (46). MMC is an alkylating agent that cross-links DNA and is recognized as one of the earliest HIPEC agents used in clinical trials of CRS-HIPEC (47). The 2018 RENAPE study was a retrospective study from France comparing the various HIPEC agents with survival outcomes after CRS-HIPEC (42). This study compared 249 patients with MPM who received either cisplatin, cisplatin plus doxorubicin, MMC, oxaliplatin, or oxaliplatin with irinotecan. No statistical differences were found among the different chemotherapy agents; however, overall survival (OS) was better in patients who received combined chemotherapy compared to a single agent [hazard ratio (HR) 0.54, 95% CI: 0.31–0.95; P=0.03] (42). In particular, patients with CC-0 resections and epithelioid histological subtype had better OS and PFS with dual-agent chemotherapy compared to single-agent treatment and had no increased postoperative morbidity (42). Another study with 211 patients with MPM observed greater overall survival with cisplatin compared to MMC in patients with CC0 or CC1 (P<0.02); there was no difference in cisplatin versus MMC for patients with CC2 disease (48). A smaller study out of Wake Forest University also published a trend towards improved survival with cisplatin versus MMC (49).

Over the past 20 years, Sugarbaker has produced results for three phase II treatment protocols for patients with MPM. In the first protocol, 42 patients were administered CRS-HIPEC with doxorubicin and cisplatin. The second protocol examined 58 patients who were treated with CRS-HIPEC, but were then followed by early postoperative intraperitoneal chemotherapy (EPIC) with daily paclitaxel for 5 days following CRS. The third protocol delivered CRS-HIPEC, EPIC, and then long-term intraperitoneal paclitaxel or pemetrexed plus IV cisplatin as adjuvant normothermic intraperitoneal chemotherapy (NIPEC) to 29 patients (50). Long-term regional chemotherapy was associated with improved survival outcomes, with 5-year overall survival of 44%, 52%, and 75% respectively for the above protocols. While no significant difference was demonstrated by the addition of EPIC to CRS-HIPEC, there was a statistically significant increase in survival among patients given NIPEC (P=0.037) (50). Despite encouraging results, the cohorts above are small, limited to a single institution, and are non-randomized. Further phase II trials and multi-institutional protocols are needed to better demonstrate the potential additional therapeutic value of NIPEC compared to HIPEC and/or EPIC alone.

More recently, pressurized intraperitoneal aerosol chemotherapy (PIPAC) has been proposed as a new technique to deliver intraperitoneal chemotherapy. Data from preclinical studies and a small three-patient study demonstrated higher local drug bioavailability and better therapeutic index after PIPAC (doxorubicin and cisplatin) versus HIPEC (51). A prospective study in France looked at the use of PIPAC in small cohort of patients with diffuse MPM (52). The purpose of this study was to determine feasibility of PIPAC as neoadjuvant treatment with intent of facilitating future CRS. Of 25 patients reviewed, 20 were considered nonresectable upfront and administered IV chemotherapy along with cisplatin and doxorubicin as PIPAC. Of the 20 patients, 11 patients underwent complete CRS after receiving PIPAC (52). Another study out of France evaluated neoadjuvant catheter-based bidirectional treatment in patients with diffuse MPM initially considered unresectable or borderline resectable. Twenty patients were given neoadjuvant IP pemetrexed with IV cisplatin or IP oxaliplatin with IV gemcitabine in effort to facilitate future CRS-HIPEC. After post-treatment laparoscopic reevaluation, 50% of the patients were able to undergo complete CRS-HIPEC. The two-year overall survival was 83.3% for patients who were able to achieve CRS-HIPEC and 44% for patients treated with bidirectional therapy only (53). These novel intraperitoneal chemotherapy approaches to otherwise high disease burdens offers the potential for downstaging MPM and facilitating surgical treatment.

### Chemotherapy

MPM renders many patients unresectable at diagnosis. The efficacy of systemic chemotherapy is poor as MPM is associated with relative chemoresistance (20). Cisplatin or carboplatin has shown some benefit as monotherapy and in combination with gemcitabine (20,54). A phase III clinical trial comparing pemetrexed with cisplatin compared to cisplatin alone showed increased response rate and median overall survival of 9.3 vs. 12.1 months in patients with PM who received combination therapy (55). Pemetrexed was well tolerated, with low rates of grade 3 or 4 side effects (56). Following this trial, the International Expanded Access Program (EAP) was created to facilitate compassionate use of pemetrexed for 109 patients with MPM. Response rates were higher when pemetrexed was combined with a platinum agent versus pemetrexed alone, and disease control rate was 78% in combination versus 50% alone (56). A phase II clinical trial revealed that the treatment with pemetrexed and gemcitabine had inferior survival results (1 year OS 67.5%), and toxicity was significant (11,57). Additionally, bevacizumab, a monoclonal antibody (mAb) against VEGF, has been shown to be associated with statistically significant overall survival ( $P=0.017$ ) when combined with cisplatin and pemetrexed in treatment of PM (58). A multicenter phase II study investigated the use of this combination in 53 patients with advanced malignant mesothelioma, including a small cohort of MPM ( $n=7$ ), however this paper largely focused on PM and the trial failed to meet the primary endpoint of 33% improvement in progression-free survival rate at 6 months compared to controls with cisplatin and pemetrexed alone (59). Further trials with the addition of bevacizumab to cisplatin and pemetrexed are needed in regards to treatment of MPM. At this point, pemetrexed with cisplatin is considered standard first line systemic treatment for patients with unresectable disease, whereas pemetrexed and gemcitabine can be used as a second line therapy for patients who cannot tolerate platinum therapy (57).

## Immunotherapy

Of late, immune checkpoint inhibitors (ICI) have been an area of interest for second-line treatment of patients with MPM who have progressed on or were intolerant to prior first-line platinum-pemetrexed chemotherapy (60). ICIs have shown efficacy in MPM and have recently been approved for first-line treatment; however, the evidence for efficacy of ICI in MPM has been limited. PD-L1 expression is observed in approximately 50% of patients with MPM compared to 30% with PM (61). In a phase II trial accruing both PM and MPM patients, pembrolizumab had an overall response rate (ORR) of 20% in pleural (n=56) versus 12.5% in peritoneal (n=8) mesothelioma (60). A second phase II trial investigated the use of “AtezoBev” (Atezolizumab, mAb against PD-L1, with bevacizumab) in 20 patients with advanced yet previously treated MPM. AtezoBev showed a promising 40% ORR with notable 1 year progression free survival (PFS) of 61% and 1 year OS of 85% (60,62). Another clinical trial looked at a total of 29 patients with MPM, with 20 treated with dual ICIs (nivolumab plus ipilimumab) and 9 treated with single agent ICI (63). This trial found no significant difference in overall response rate (ORR) when comparing dual agent with single agent ICIs (63). Head-to-head comparisons of single- or dual-agent ICI therapy versus second-line cytotoxic chemotherapy remain to be performed.

## Future directions

Currently, there are several ongoing and upcoming clinical trials focusing on the treatment of MPM. For instance, a phase II randomized clinical trial, [NCT05001880](#), has been accepted to compare the addition of atezolizumab with carboplatin, pemetrexed, and bevacizumab prior to surgery compared to a control group without the addition of atezolizumab treatment. Another upcoming clinical trial, [NCT05041062](#), is focusing on major pathologic response of peritoneal mesothelioma tumors to the preoperative combination of nivolumab and ipilimumab. An active clinical trial, [NCT04847068](#), is utilizing an *ex-vivo* SMART (Sample Microenvironment of Resected Metastatic Tumor) System to test tumor response to different intraperitoneal chemotherapy agents in patients with peritoneal carcinomatosis, including peritoneal mesothelioma.

Chimeric antigen receptor (CAR)-expressing T cells represent another avenue of immunotherapy that shows potential in mesothelioma. A phase I clinical trial, [NCT01583686](#), used CAR T cell receptor immunology targeting mesothelin for patients with metastatic disease. Mesothelin is a tumor differentiation antigen that is overexpressed in many malignancies including ovarian cancer and mesothelioma (64). Hassan *et al.*, investigated MORAb-009, a chimerical monoclonal antibody targeting mesothelin in patients with mesothelioma (n=13), pancreatic cancer (n=7), and ovarian cancer (n=4). This phase I study revealed MORAb-009 to be well tolerated with maximum tolerated dose (MTD) of 200 mg/m<sup>2</sup>, and 11 of 24 patients treated had stable disease (64). A phase II study was implemented, however the malignancies targeted were pancreatic cancer, ovarian cancer, and PM. Hassan *et al.*, also utilized SS1P, a recombinant mesothelin immunotoxin consisting of the anti-mesothelin Fv linked to a truncated form of the potent bacterial toxin *Pseudomonas* exotoxin A, for treatment in patients with malignant mesothelioma and other mesothelin-expressing cancers (65). A phase I clinical trial established safety and maximum MTD of SS1P, which led to a pilot trial of SS1P in combination with



pemetrexed and cisplatin in chemo-naïve patients with PM that resulted in 8 out of 13 patients having partial responses. Currently, SS1P is being combined with Pentostatin plus cyclophosphamide in clinical trial [NCT0136290](#) to study the effectiveness of suppressing the immune system in chemo-refractory malignant mesothelioma. More recently, a cell surface antigen, mesothelin Immunotoxin LMB-100, a recombinant anti-mesothelin immunotoxin composed of humanized anti-mesothelin Fab fused to a *Pseudomonas* exotoxin, has been studied in a phase I trial in patients with advanced pleural or peritoneal mesothelioma who did not respond to platinum therapy (66). Ten patients were treated with LMB-100 and then treated with either pembrolizumab (n=9) or nivolumab (n=1). Four of the ten patients had either partial response or complete response. Due to promising results, a phase II clinical trial, [NCT03644550](#), is currently recruiting patients with pleural and peritoneal mesothelioma who have progressed on platinum therapy to be treated with LMB100 followed by pembrolizumab (67). While the results are not currently available, the variation of clinical trials and advancing technology elicits hope for future treatments.

## Conclusions

MPM is a rare and lethal disease of the peritoneal lining. CRS-HIPEC remains the standard of care and is associated with long-term survival in patients who receive complete or near-complete cytoreduction. While not as effective, systemic therapy, immune checkpoint inhibitors, investigational agents, NIPEC, and PIPAC are available for patients with advanced nonresectable disease.

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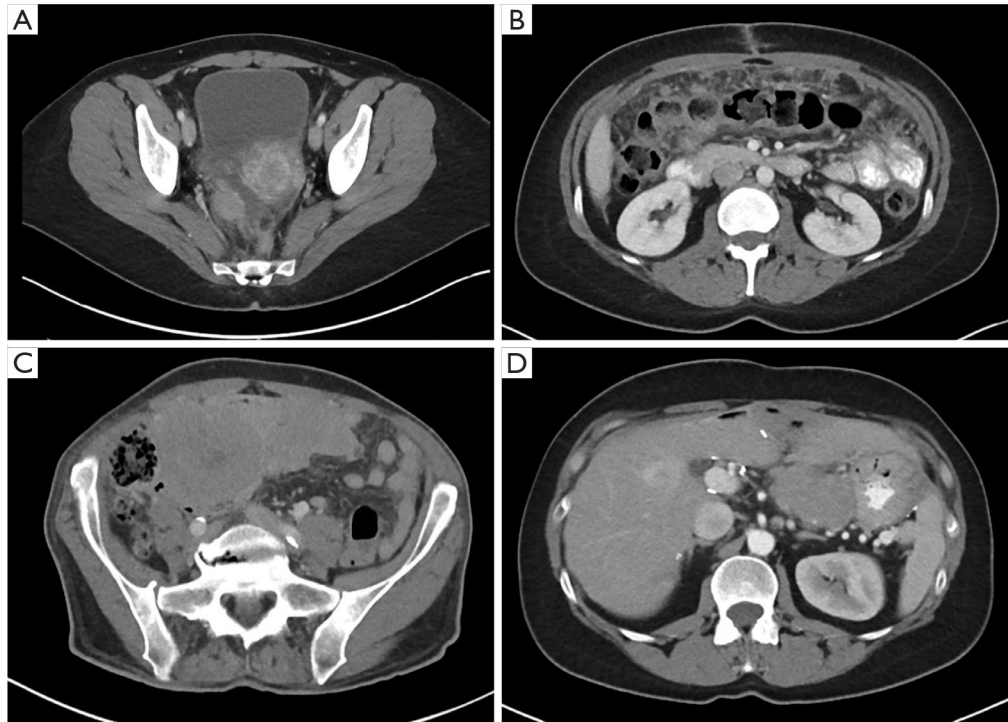
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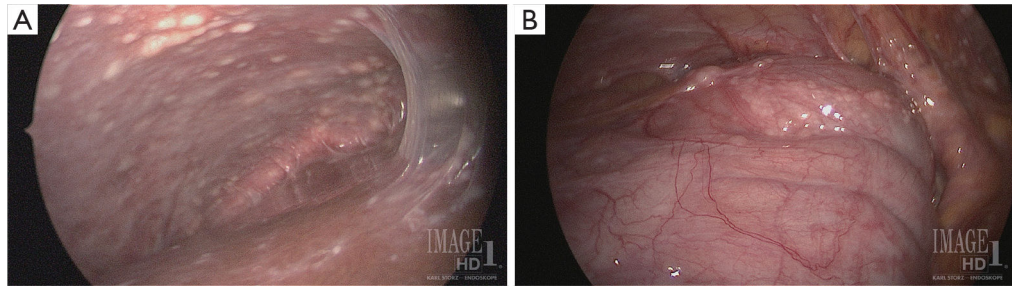
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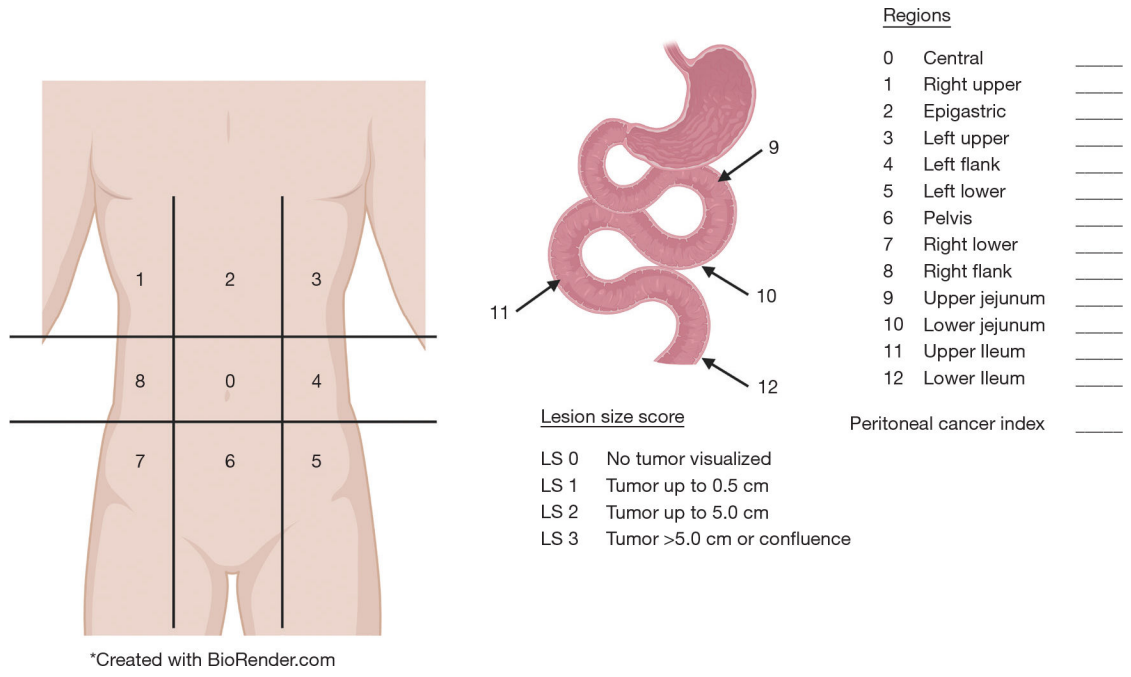
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**Figure 1.** CT images of peritoneal mesothelioma: (A) pelvic implant with associated pelvic ascites; (B) omental caking; (C) bulky omental and mesenteric disease; (D) lesser sac mass. CT, computed tomography.



**Figure 2.**  
Diagnostic laparoscopy demonstrating: (A) peritoneal implants above liver; (B) right colon serosal implants.



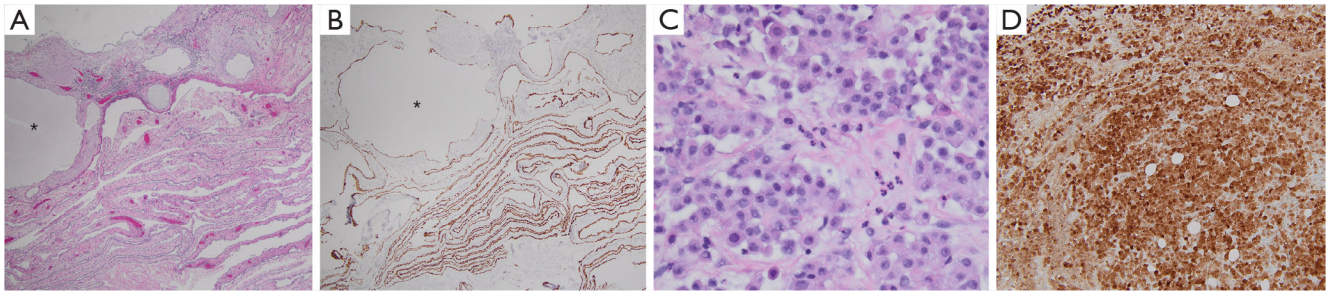
**Figure 3.**  
Peritoneal cancer index.

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**Figure 4.** Histopathology slides: (A) H&E staining of benign multicystic mesothelioma showing simple cyst encased with benign mesothelin lining (\*); (B) calretinin staining of mesothelin lining of benign multicystic mesothelioma (\*); (C) H&E staining of epithelioid type MPM showing nuclear pleomorphism and invasion into stroma; (D) calretinin staining of epithelioid type MPM. Magnification: 20× for (A,B), 40× for (C,D). H&E, hematoxylin and eosin; MPM, malignant peritoneal mesothelioma.



**Table 1**

The search strategy summary

Items	Specification
Date of search	January 31,2022
Databases and other sources searched	PubMed, Google Scholar, and <a href="http://ClinicalTrials.gov">ClinicalTrials.gov</a>
Search terms used	Search terms: malignant peritoneal mesothelioma, mesothelioma, cytoreductive surgery, heated intraperitoneal chemotherapy, and peritoneal carcinomatosis
Timeframe	From origin until January 31,2022
Inclusion and exclusion criteria	Inclusion and exclusion criteria: (D) articles in English languages; (II) article types: prospective randomized controlled trials, non-randomized prospective trials, retrospective studies, case reports, reviews, and meta-analyses
Selection process	Selection was conducted by all authors