

# CT Differentiation of Diffuse Malignant Peritoneal Mesothelioma, Tuberculous Peritonitis, and Peritoneal Carcinomatosis

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**Abstract:** *Objective:* To investigate the significance of computed tomography findings in diffuse malignant peritoneal mesothelioma (DMPeM), tuberculous peritonitis (TBP), and peritoneal carcinomatosis (PC) to differentiate the three diseases. *Methods:* The clinical manifestation and computed tomography scans of 147 patients with diffuse malignant peritoneal mesothelioma (n = 60), tuberculous peritonitis (n = 32), and peritoneal carcinomatosis (n = 55) were retrospectively reviewed, while taking into account of ascites, pleural plaques, viscera infiltration; abnormalities in the peritoneum; involvement of the mesentery and omentum; as well as the presence and location of enlarged lymph nodes. *Results:* There was no significant difference among all three groups in terms of clinical manifestation, peritoneum, omentum, and mesentery involvement, ascites, as well as the presence and location of enlarged lymph nodes. The study found that 95% of DMPeM patients had been exposed to asbestos in the past. The patients showed significant differences in the following aspects: (1) irregular peritoneum thickening, caked omentum thickening, pleural plaques, visceral infiltration, and asbestos exposure were more common in peritoneal mesothelioma patients; (2) nodular peritoneum thickening and visceral metastasis were more common in patients with peritoneal carcinomatosis; (3) smooth peritoneal thickening, pleural effusion, and extraperitoneal tuberculosis were more common in patients with tuberculous peritonitis. *Conclusion:* A combination of computed tomography findings could improve our ability in differentiating the three diseases.

**Keywords:** Mesothelioma; Peritoneum; Computed tomography; Tuberculous peritonitis; Peritoneal carcinomatosis; Diagnosis

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## 1. Introduction

Ascitic fluid is commonly seen in many pathologic conditions. Malignancies account for 10% of all ascites [1], and patients with delayed diagnosis and treatment may have poorer prognosis. Among the malignant ascites, peritoneal carcinomatosis of the gastrointestinal tract and ovaries accounts for more than 80%, while primary neoplasms of peritoneal and subperitoneal origin are far less common than metastatic disease in these locations. Our previous study found that in patients with unexplained abdominal effusion in our district, tuberculous peritonitis was the most common cause, followed by peritoneal mesothelioma and peritoneal carcinomatosis [2]. An accurate diagnosis based on imaging alone is often impossible.

Nevertheless, high-resolution computed tomography (CT) features, combined with relevant clinical and demographic data, may help narrow the differential diagnoses for peritoneum-based neoplasms in many cases. Previous studies have validated the role of CT in identifying peritoneal mesothelioma from tuberculous peritonitis <sup>[3]</sup> or peritoneal metastatic carcinoma <sup>[4]</sup>. In clinical work, differentiating these three diseases is a problem; hence, this study was designed.

In this article, we present a review of diffuse malignant peritoneal mesothelioma (DMPeM), tuberculous peritonitis (TBP), and peritoneal carcinomatosis (PC). Being aware of the diverse clinicopathologic features as well as the CT features of these three diseases might help radiologists to narrow the differential diagnoses and increase the likelihood of an accurate radiologic diagnosis.

## 2. Materials and methods

The computed tomography scans from 60 cases of DMPeM, 32 cases of TBP, and 55 cases of PC, treated at Cangzhou Central Hospital over approximately a 3-year period (August 2012 – October 2015), were retrospectively reviewed. The eligibility criteria were as follows: (1) first-visit patients (2) with relatively complete chest and abdomen CT, (3) confirmed pathology results, (4) and a diagnosis of DMPeM based on the Guidelines for Pathologic Diagnosis of Malignant Mesothelioma: 2012 Update of the Consensus Statement from the International Mesothelioma Interest Group <sup>[5]</sup>. The diagnosis of TBP was established on the basis of at least one of the following criteria: (1) histological evidence of caseating granuloma; (2) histological demonstration of acid-fast bacilli in the lesion or ascitic fluid. The diagnosis of PC was also established on the basis of histological evidence. Each patient only suffered from the one of the aforementioned three diseases. Ethical approval was obtained from the institutional ethics committee, with the following reference number: 2012-012-01.

Diagnostic CT was performed with multislice CT scanners (LightSpeed VCT, GE, United States of America [USA]). Imaging of the chest, abdomen, and pelvis was performed under the following parameters: 120 KV, 150–300 mA, gantry rotation time of 0.5 seconds, collimator width of 40 mm, and section thickness of 5 mm. The images were obtained following the intravenous administration of 75–100 mL of iodinated contrast at 3 mL/s, using an automated injector (OptiVantage, Liebel-Flarsheim Company, USA). All available CT scans were submitted for randomized, independent, double reading (or triple reading in the case disagreements) with the focus on asbestos-related abnormalities. The radiologists received specific training in the interpretation of CT scans by experienced chest and abdomen radiologists and occupational physicians.

The CT findings were reviewed and classified based on several components.

- (1) Presence of ascites: ascites was considered extensive when distributed throughout the abdomen and pelvis, moderate when localized around the liver and spleen, and mild when only a small amount of fluid was present.
- (2) CT analysis of the peritoneum: abnormalities such as peritoneal thickening (divided into smooth thickening or irregular thickening) and peritoneal nodules were evaluated <sup>[6]</sup>. A thickness exceeding 2 mm was regarded as thickening <sup>[7]</sup>.
- (3) Involvement of the omentum: can be classified as nodular, smudged (infiltration with ill-defined soft tissue density), or caked thickening (cake-like thickening of the omentum mingled with the connective tissue).
- (4) Involvement of the small bowel mesentery: can be classified as nodular, thickened soft tissue strands with crowded vascular bundles or diffuse infiltration with soft tissue density masses.
- (5) Presence and location of enlarged lymph nodes: lymph nodes were considered to be enlarged if the diameter of the short axis was greater than 1 cm in the retroperitoneal and mesenteric stations and greater than 0.5 cm in the mediastinal, hilar, and cardiophrenic nodal stations.

- (6) Solid abdominal visceral infiltration or metastases.
- (7) Thoracic changes, such as pleural plaques and pleural effusion.

SPSS 25.0 was used for data analysis. The results were presented as proportions wherever applicable. Chi-square test was used to determine the associations among qualitative variables. With any differences among the three groups, further comparisons were carried out between two groups. P values less than 0.05 were considered statistically significant. Fisher’s exact test was performed when the sample size (n) was less than 40 or the theoretical frequency (T) was less than 1.

### 3. Results

#### 3.1. Clinical characteristics of the patients

In the DMPeM group, there were 19 men and 41 women, with an average age of  $60 \pm 8.5$  years. 95% of the patients with DMPeM had been exposed to asbestos in this past, while the other two groups had no history of asbestos exposure. Abdominal distention (85%) was the most common presenting symptom. Other symptoms included abdominal pain (40%) and abdominal mass (15%). Physical examination revealed the presence of ascites (40 of 60) and abdominal mass (7 of 60). In the TBP group, there were 19 men and 13 women, with an average age  $35 \pm 3.2$  years. Fever (65.2%), abdominal distention (85.2%), and abdominal pain (40.7%) were the most common presenting symptoms. In the PC group, there were 18 men and 37 women, with an average age of  $65 \pm 9.5$  years. Concerning the causes of peritoneal involvement, there were 25 patients (45%) with ovarian carcinoma, 16 (29%) with colonic cancer, 6 (11%) with pancreatic carcinoma, 3 (5%) with breast carcinoma, 2 (4%) with gastric carcinoma, and 3 (5%) with unknown primary origin. Among these patients, the main clinical manifestation was abdominal distension.

#### 3.2. Computed tomography

The CT findings are detailed in **Table 1**.

**Table 1.** CT findings

HRCT findings	DMPeM	TBP	PC	Total	P value		
					P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
Total number	60	32	55				
<i>Peritoneum thickening</i>	55 (91.7%)	28 (87.5%)	48 (87.3%)	> 0.05	-	-	-
Smooth thickening (n)	16 (26.7%)	24 (75.0%)	2 (3.6%)		< 0.05	< 0.05	< 0.05
Irregular thickening (n)	36 (60.0%)	4 (12.5%)	18 (32.7%)	< 0.05	< 0.05	< 0.05	> 0.05
Peritoneal nodules (n)	3 (5.0%)	0	28 (50.9%)		> 0.05	< 0.05	< 0.05
<i>Omental thickening</i>	60 (100%)	30 (93.8%)	48 (87.3%)	> 0.05	-	-	-
Smudged (n)	13 (21.7%)	12 (37.0%)	4 (7.3%)		> 0.05	> 0.05	< 0.05
Nodular (n)	6 (10.0%)	9 (28.1%)	28 (50.9%)	< 0.05	> 0.05	< 0.05	< 0.05
Caked (n)	41 (68.3%)	9 (28.1%)	16 (29.1%)		< 0.05	< 0.05	> 0.05
Mesenteric involvement	31 (51.7%)	19 (59.4%)	31 (56.4%)	> 0.05	-	-	-
Intestinal wall fixation	43 (71.7%)	1 (3.1%)	26 (47.3)	< 0.05	< 0.05	< 0.05	< 0.05
<i>Ascites</i>	56 (93.3%)	32 (100%)	51 (92.7%)	> 0.05	-	-	-
Extensive	25	12	24		-	-	-
Moderate	18	8	12		-	-	-
Mild	13	12	15	> 0.05	-	-	-
None	4	0	4		-	-	-

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HRCT findings	DMPeM	TBP	PC	Total	P value		
					P <sub>1</sub>	P <sub>2</sub>	P <sub>3</sub>
Total number	60	32	55				
Visceral infiltration	51 (85.0%)	0	40 (72.7 %)	< 0.05	< 0.05	> 0.05	< 0.05
Visceral metastasis	0	0	8 (14.5%)	< 0.05	> 0.05	< 0.05	< 0.05
Pleural plaques	51 (85.0%)	0	0	< 0.05	< 0.05	< 0.05	> 0.05
Enlarged lymph nodes	20 (33.3%)	11(34.4%)	24 (43.6%)	> 0.05	-	-	-

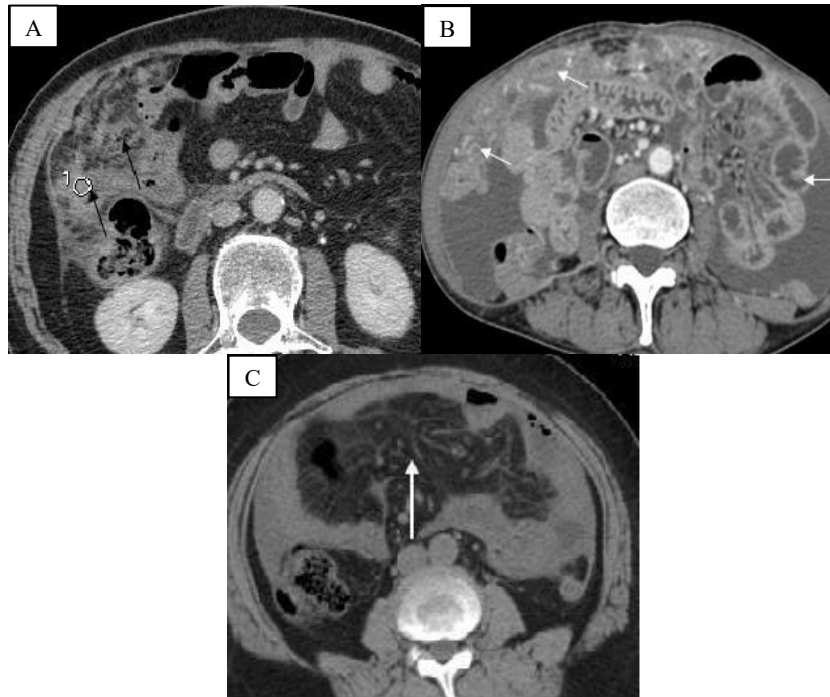
Abbreviations: DMPeM, diffuse malignant peritoneal mesothelioma; HRCT, high-resolution computed tomography; PC, peritoneal carcinomatosis; TBP, tuberculous peritonitis. P<sub>1</sub>: DMPeM and TBP group; P<sub>2</sub>: DMPeM and PC group; P<sub>3</sub>: TBP and PC group

### 3.2.1. CT findings of DMPeM

In patients with DMPeM, parietal peritoneal involvement appeared as thickening of the involved region with mild to moderate enhancement (CT value increased to 34–74 HU). Irregular thickening (2–25 mm) was the most, followed by smooth thickening (2–8 mm) and nodular thickening (**Figure 1**). One patient had local peritoneal thickening of more than 1 cm. Omental involvement was observed in all DMPeM patients, in which diffuse, caked thickening was the most, followed by smudged appearance and nodular implantation (**Figure 2**). The involved mesentery showed a stellate appearance, which indicated soft tissue thickening around the mesenteric vessels. Enlarged lymph nodes with no fusion or enhancement were predominantly noted in the right cardiophrenic region (18 of 60) and the retroperitoneal para-aortic region (2 of 60). Fifty-one patients had abdominal organ involvement, which appeared as infiltration of the bowel (50 of 60), liver (28 of 60), spleen (18 of 60), and stomach (11 of 60). Thoracic changes occurred in 51 patients. Thickening (27 of 60) and plaques (51 of 60) (right, 52.9%; bilateral, 31.4%) with or without calcification were present in 51 patients, and pleural effusion was noted in 9 patients (3 with bilateral effusion). Ascites, as the most common CT finding, was noted in 56 patients (93.3%).



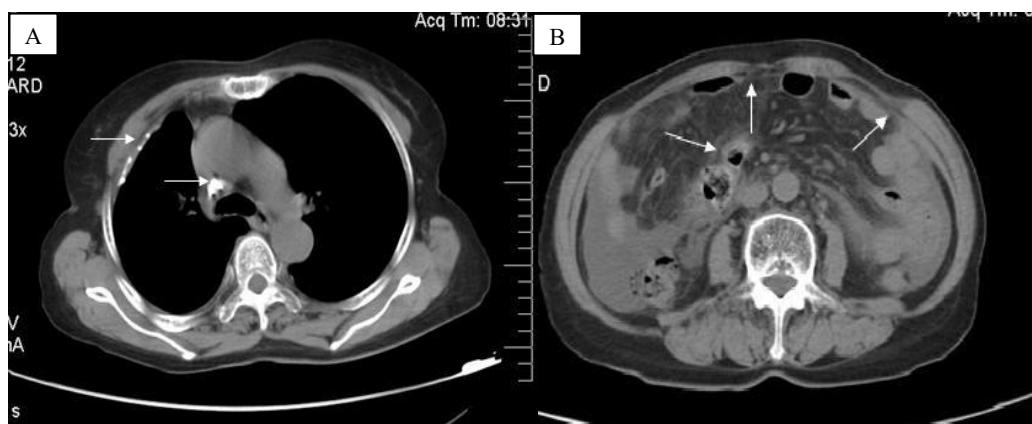
**Figure 1.** HRCT scan of DMPeM showing irregular peritoneal thickening and pleural plaque (arrows in A and B) as well as diffuse peritoneal thickening and slight enhancement (arrows in C)



**Figure 2.** HRCT image of DMPeM showing the thickening of the greater omentum and a nodule (arrows in A); omental cakes and intestinal distention (arrows in B); as well as thickened mesentery (arrow in C)

### 3.2.2. CT findings of TBP

Out of the 32 patients with TBP, parietal peritoneum involvement was found in 28 patients without enhancement. Smooth thickening was the most, followed by irregular thickening. None of the patients showed nodular thickening. Omental involvement was observed in 30 TBP patients, in which smudged appearance was the most, followed by caked thickening and nodular thickening. The mesentery was involved in 19 TBP cases (**Figure 3**). One patient had bowel wall fixation, while none of the patients had mesenteric shortening. Mesenteric lymphadenopathy with central necrosis was observed in 11 patients. Pleural plaques and abdominal organ involvement were not found in any of the TBP patients. However, pleural effusion (16/32) and extraperitoneal tuberculosis (24/32) were found to be more common in these patients. Ascites was also found in all of the patients.



**Figure 3.** HRCT of a patient with TBP showing mediastinal lymph node calcification, pleural calcification, and tuberculosis (arrows in A). Abdominal HRCT showing ascites and the involvement of greater omentum, peritoneum, and mesentery (arrows in B)

### 3.2.3. CT findings of PC

Out of the 55 patients with PC, peritoneal involvement was found in 48 patients with moderate to severe enhancement (CT value increased to 70–104 HU). Nodular thickening was the most, followed by irregular thickening (**Figure 4**) and smooth thickening. Omental involvement was observed in 48 PC patients, in which nodular thickening was the most, followed by smudged appearance and caked thickening. The mesentery was involved in 31 cases, and bowel wall fixation was noted in 26 patients. Mesenteric shortening was not seen. Multiple enlarged lymph nodes were found in 24 patients, in which retroperitoneal lymph nodes were more common (21/55). In addition, eight patients had lymph node fusion. Pleural plaques and extraperitoneal tuberculosis were not found in any of the patients with PC, but pleural effusion was noted in 10 cases. Fifty cases of PC had abdominal and pelvic visceral infiltration, including 28 cases involving the intestine, 13 involving the liver, 4 involving the spleen, 9 involving the stomach, and 3 involving the uterus. Eight patients had liver metastasis in addition to peritoneal involvement. Ascites was found in 51 patients, in which the most prevalent was extensive ascites.



**Figure 4.** Contrast-enhanced HRCT of a patient with peritoneal metastatic carcinomatosis from sigmoid colon tumor (arrow in A) showing irregular thickening of peritoneum (arrows in B) and large amount of ascites.

### 3.2.4. Comparison of CT findings

#### (1) Thickening and enhancement of the peritoneum

91.7% of patients with DMPeM showed mild to moderate enhancement; 87.3% of patients with PC showed moderate to severe enhancement; no TBP patients showed enhancement. The detailed results are presented in **Table 1**.

#### (2) Thickening of the omentum

The results are presented in **Table 1**.

#### (3) Mesenteric involvement

The results are presented in **Table 1**.

#### (4) Ascites

The results are presented in **Table 1**.

#### (5) Abdominal visceral infiltration or metastasis

Abdominal visceral infiltration was observed in DMPeM and PC groups, while abdominal visceral metastasis was only observed in the PC group. No abdominal visceral involvement in the TBP group.

#### (6) Presence and location of enlarged lymph nodes.

In the DMPeM group, enlarged lymph nodes with no fusion or enhancement were noted in the right cardiophrenic region (18 of 60) and the retroperitoneal para-aortic region (2 of 60); in the TBP group, mesenteric lymphadenopathy with central necrosis was observed in 11 patients; in the PC group,

multiple enlarged lymph nodes were found in 24 patients, in which retroperitoneal lymph nodes were more common (21 of 55).

(7) Thoracic changes

Pleural plaques were only observed in patients with DMPeM, whereas pulmonary metastasis was only observed in patients with PC. Tuberculosis was found in the TBP group.

#### 4. Discussion

Determining the cause of ascites in an oncologic case has always been a challenge. Peritoneal carcinomatosis accounts for 8% of all ascites. Peritoneal mesothelioma is far less common than metastatic disease, except in patients with a history of asbestos exposure. Peritoneal tuberculosis (PTB), which accounts for 4% of all patients with tuberculosis [7], is a condition that is difficult to diagnose due to its non-specific clinical presentation. The clinicopathologic and CT features vary among the three diseases. The aim of this retrospective analysis was to confirm the direct and indirect signs for differentiating DMPeM from TBP and PC.

Mesotheliomas are rare neoplasms that arise from mesothelial cells, which form the serosal membranes of body cavities. Secondary to the pleural cavity, mesotheliomas commonly involve the peritoneal cavity, either solely or in combination with the pleura.

In approximately half of the reported cases, there is a history of asbestos exposure [8,9]. It has been reported that diffuse malignant peritoneal mesotheliomas might be related to more prolonged and heavy asbestos exposure than pleural mesotheliomas [10]. In our study, 95% of the patients with DMPeM had a history of asbestos exposure. Our previous study reported that 93.2% of 162 patients with malignant pleural mesothelioma (MPM) had a history of asbestos exposure, in which the majority was exposed to chrysotile [11]. The risk is higher in some areas in our district due to the presence of hand-spun asbestos yarn in the 1970s. The incidence of peritoneal mesothelioma in the region is 4.5 cases per million [11].

A history of asbestos exposure is an important basis for the diagnosis of DMPeM. When a patient with DMPeM has no history of asbestos exposure, distinguishing a typical DMPeM from peritoneal carcinomatosis or tuberculosis can be challenging based on CT findings alone.

Unlike many neoplasms, diffuse malignant peritoneal mesotheliomas tend to spread in sheets of tissue over the parietal and visceral peritoneal surfaces, thereby encasing the abdominal organs to become confluent. Certainly, the location with rich peritoneal blood supply will expand. Such extensive lesions could be accompanied by ascites. Therefore, ascites, irregular peritoneal thickening, caked omental masses, and intestinal wall fixation occur more frequently in DMPeM patients. The scalloping or direct invasion of adjacent abdominal organs supports the diagnosis of DMPeM. As shown in our results, the three diseases were characterized by peritoneal, omental, and mesentery involvement although there was no statistical significance; However, the type of thickening was different and had statistical significance. Similarly, viscera infiltrates were found in patients with DMPeM and PC, but there was no incidence of DMPeM patients with visceral metastasis through observation. This is in line with the reported results of a study conducted by Su SS *et al.* [12]. Although several investigators have reported that the amount of ascites is disproportionately small relative to the degree of tumor dissemination in diffuse malignant peritoneal mesotheliomas compared with peritoneal carcinomatosis [13], in our study, there was no difference in the extent of ascites. It is worth noting that 28.3% of patients with DMPeM had no or mild ascites, which could be used to distinguish DMPeM from other diseases with diffuse peritoneal involvement, such as PC and TBP, although there is no statistical support. Localized uniform peritoneal thickening greater than 1 cm appeared only in patients with DMPeM, which is a rare but of typical characteristics.

In addition to the above CT findings, right cardiophrenic node enlargement was found in 18 cases in our study. To our knowledge, there have been a few reports on lymph node metastases in DMPeM cases

[14,15]. The enlarged lymph nodes that were found, without fusion or enhancement, might have been caused by asbestos stimulation rather than metastasis. Changes in the pleura, such as the development of pleural plaques and asbestosis, were observed in 85% of our patients. These asbestos-related thoracic changes are signs that could be used for diagnosing DMPeM [16].

Tuberculous peritonitis is a rare manifestation of TB, which occurs in fewer than 4% of all TB patients [17]. It is considered to be a result of the rupture of mesenteric lymph nodes seeded by hematogenous dissemination from a distant primary focus (usually the lung) or lymphatic spread from the primary lesion site. It is difficult to establish a diagnosis of tuberculous peritonitis due to its variable clinical manifestations and non-specific laboratory investigations. CT serves as an important non-invasive diagnostic tool for assessing the extent of the disease [18].

In our study, the smooth thickening of peritoneum and smudged thickening of omentum was the most common findings in TBP patients. This is similar to previous studies conducted by Yin WJ *et al.* [3] and Na-ChiangMai W *et al.* [19]. In our TBP group, ascites was observed in all cases. Ascites could be clear in earlier stages or cloudy when the fluid has high protein and cellular content. Extraperitoneal tuberculosis is a characteristic manifestation of TBP. The presence of mesenteric lymphadenopathy with central necrosis may aid the diagnosis of TBP [19]. Lymph node calcification constitutes a remaining trace of TB infection after recovery. The diagnosis of tuberculous peritonitis is favored when there is smooth peritoneal thickening, mesenteric lymphadenopathy with central necrosis, and ascites with high attenuation [20,21].

Peritoneal carcinomatosis is a relatively common metastatic manifestation of various organ-based malignancies, particularly of the gastrointestinal tract and ovaries.

Generally speaking, PC is formed through a multi-step process: (1) detachment of cancer cells from the primary tumor; (2) attachment of intraperitoneal free cancer cells to the distant peritoneum and their invasion of the subperitoneal space; (3) infiltration into the subperitoneal space; and (4) proliferation with vascular neogenesis. The incidence of liver metastasis and lymphadenopathy is higher in peritoneal carcinomatosis [22]. As shown in this study, the nodular thickening of peritoneum or omentum with moderate to severe enhancement and visceral metastasis showed statistical significance in distinguishing DMPeM from PC and TBP. This is similar to a prior study conducted by Liang YF *et al.* [4]. The CT findings of PC include a variable amount of fluid in the serosal cavity, thickening of the peritoneal or omental lining (often irregular and nodular), and peritoneal or omental implants. The diagnosis of PC is favored when there is less severe peritoneal thickening, a higher incidence of liver metastasis and lymphadenopathy, as well as prominent ascites. These findings may be non-specific and can mimic other neoplastic and non-neoplastic conditions involving the serosal membrane, such as tuberculosis [23]. However, the possibility of secondary tumors of the serosal membrane should be considered when there is any identifiable primary tumor in the serosal cavity.

The radiologic characteristics of DMPeM, TBP, and PC are summarized in **Table 2**.

**Table 2.** CT characterization of DMPeM, TBP, and PC

CT characterization of DMPeM	Diffuse involvement of the peritoneum, mesentery, and omentum Frequent irregular peritoneal thickening with mild to moderate enhancement and caked omentum thickening No or mild ascites with obvious peritoneal tumor Scalloping or direct invasion of adjacent abdominal organs Frequent pleural changes, such as calcification or thickening Frequent bowel wall fixation and mesenteric shortening
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CT characterization of TBP	Diffuse involvement of the peritoneum, mesentery, and omentum Smooth peritoneal thickening Ascites with high attenuation Pulmonary and extrapulmonary tuberculosis Mesenteric lymphadenopathy with central necrosis
CT characterization of PC	Diffuse involvement of the peritoneum, mesentery, and omentum Nodular thickening with moderate to severe enhancement Few pleural changes unless metastasis has occurred Frequent lymph node involvement and metastasis or infiltration Original site may be identified at times

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In conclusion, there are overlapping CT findings in relation to peritoneal, omental, or mesenteric involvement, ascites, and enlarged lymph nodes in these diseases. However, they also have their own characteristics. A combination of CT findings could improve our ability in distinguishing DMPeM from TBP or PC.

#### Disclosure statement

The authors declare no conflict of interest.

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