Signature: © Pol J Radiol, 2014; 79(Suppl.1): S33-38
DOI: 10.12659/PJR.890563

Polish Journal of Radiology
www.PolRadiol.com
REVIEW ARTICLE

Received: 2014.02.19
Accepted: 2014.02.19
Published: 2014.05.20

The role of CT in the diagnosis of malignant pleural mesothelioma

Izabela Hoczela, Justyna Filipowska

Clinical Department of Radiology, Provincial Specialized Hospital, Rzeszów, Poland

Author's address: Izabela Hoczela, Clinical Department of Radiology in Provincial Specialized Hospital in Rzeszów, Szopena 2 Str, 35-055 Rzeszów, Poland, e-mail: izahoczela@interia.pl

Summary

Malignant pleural mesothelioma (MPM) is a rare and aggressive tumor that arises from the pleura.

A previous exposure to asbestos is the main risk factor of mesothelioma. Clinical signs are mostly late and unspecific. Chest CT shows unilateral pleurisy associated with pleural nodular thickening and tumor invasion of adjacent structures. The diagnosis of MPM is based on histology using immunohistochemistry on pleural biopsies best obtained by thoracoscopy.

The treatment of MPM relies mainly on chemotherapy. Surgery, pleurectomy/decortication or extrapleural pneumonectomy is rarely undertaken as a result of staging of tumor.

This article shows that CT has an essential role in the diagnosis, assessment and monitoring response to therapy of patients with malignant pleural mesothelioma.

MeSH Keywords: Pleural Effusion • Pleural Effusion, Malignant • Tomography Scanners, X-Ray Computed

PDF file: http://www.polradiol.com/download/index/idArt/890563

Background

Malignant mesothelioma is an invasive cancer that develops from cells of the mesothelium. In the majority of cases mesothelioma affects the pleura (90%), and it is the most common primary tumor of the pleura. Mesothelioma may also affect peritoneum (peritoneal mesothelioma accounts for about 7% of all malignant mesotheliomas) and, very rarely, pericardium and tunica vaginalis [1].

Malignant pleural mesothelioma (MPM) is a medical problem of special interest that requires multidisciplinary approach due to the increasingly growing number of cases, as well as diagnostic and therapeutic difficulties.

Computed tomography plays an important role in diagnosis, staging and monitoring of treatment effects in patients with malignant pleural mesothelioma [2,3].

Epidemiological, Pathomorphological and Symptomatological Characteristics

Malignant pleural mesothelioma is a rare form of cancer. Its estimated that there is 1 case of mesothelioma in 100 new cases of primary lung tumors. In Poland, approximately 200 patients are diagnosed with mesothelioma annually [4,5].

There is an upward trend in the incidence of pleural mesothelioma, which is attributed to a prolonged exposure to asbestos fibers (in the near past, asbestos was commonly used in construction, textile, shipbuilding and automotive industries) [4]. Because of the long latency period between first exposure to asbestos and manifestation of the disease (about 20 to 40 years), British epidemiologists predict that incidence of pleural mesothelioma will peak between 2015 and 2020 [5].

MPM is most prevalent in men, and median age at diagnosis is about 60 years. In Poland, the highest incidences of pleural mesothelioma are reported in Silesia Province (woj. śląskie) and Małopolska Province (woj. małopolskie) (Zaklady Wyrobow Azbestowo-Cementowych in Szczucin near Dabrowa Tarnowska) [4].

Apart from asbestos (particularly crocidolite is considered to be more likely to cause cancer), there are other possible risk factors for malignant mesothelioma such as:

– oncogenic polyomavirus or Simian virus (SV40) (some injectable polio vaccines given between 1955 and 1978 were contaminated with SV40),
– radiation (mesothelioma may develop in people exposed to high doses of radiation to the chest or abdomen, about 20 years after radiation therapy),
– other minerals (e.g. erionite, beryllium and silica),
– chronic inflammation and genetic predisposition [4,6].

There are 3 histological types of malignant mesothelioma: epithelioid (comprises about 55% of malignant mesothelioma cases and generally has the best prognosis), mixed (biphasic) (about 30% of cases) and sarcomatoid (comprises about 15% of cases and has the worst prognosis) [4].

Initially, pleural mesothelioma progresses slowly and does not give any symptoms. Early symptoms, such as chest pain and increasing shortness of breath on exertion due to pleural effusion, are nonspecific. Mesothelioma signs and symptoms vary, depending on tumor location and invasion of adjacent structures, and may include superior vena cava syndrome, Horner's syndrome or difficulty swallowing. General symptoms such as fever, sweating, blood in the sputum (hemoptysis), cough, weight loss and weakness, may also occur. In severe cases tumor involves the ipsilateral chest wall leading to its deformation and immobilization. Sometimes, tumor may manifest as a palpable chest wall mass [4–7].

Computed Tomography Features in Malignant Pleural Mesothelioma

There are two morphological types of malignant pleural mesothelioma:
1. diffuse (the most common type, usually involves the right chest wall) which spreads extensively on the pleural surface; initially it forms small nodules on the parietal pleura in the posterior costophrenic angle, and subsequently progresses to a solid mass that bonds together two pleural layers, covers the lung and enters the interlobar fissures,
2. localized (with better prognosis) which forms a well-defined pedunculated tumor attached to the pleural surface [7].

MPM may also invade fatty tissue and muscles of the chest wall, involve the diaphragm, spread directly into the peritoneal cavity and spread to the lungs via the lymphatic system. The tumor frequently involves mediastinal lymph nodes, and in advanced stages it may metastasize into the liver, lungs or bones [7].

Well-differentiated papillary mesothelioma (WDPM) is a rare subtype of epithelial mesothelioma that is limited to the pleural surface and does not invade adjacent structures. WDMP affects predominantly older adults. It is characterized by a low-grade epithelial cell atypia and associated with a favorable prognosis.

On a standard chest x-ray, pleural tumors manifest by a pleural effusion and, less commonly, also pleural infiltration [6]. Spiral chest CT plays a key role in diagnosis of pleural mesothelioma, as it may detect the following symptoms:

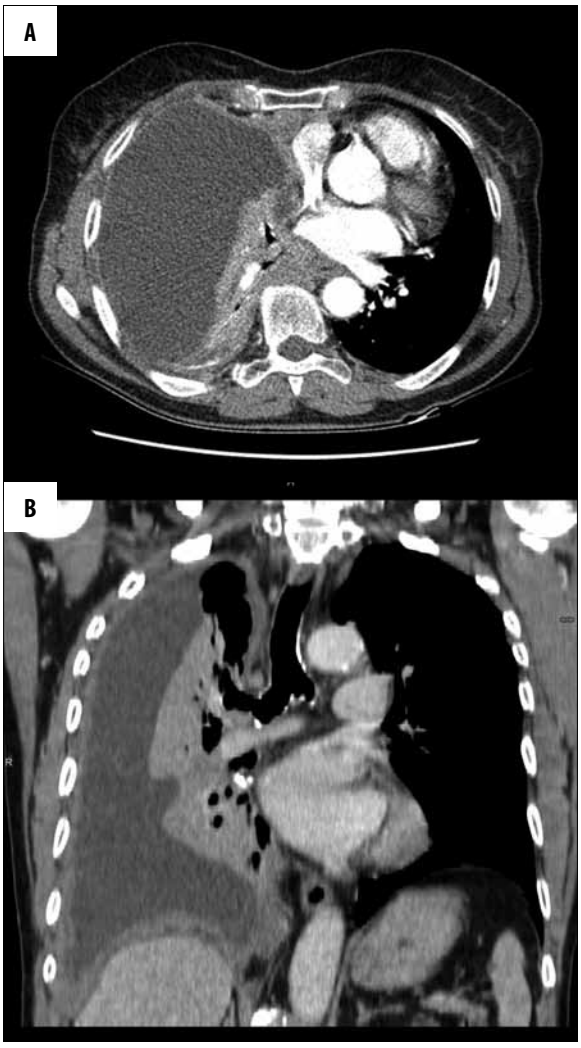

Figure 1. Chest CT. (**A**) Axial plane. (**B**) MPR reconstruction. Large right pleural effusion compressing the lung.

1. Pleural effusion

Usually, pleural mesothelioma is associated with a large one-sided pleural effusion (pale yellow or bloody) [6,7].

Exudative pleural effusions are caused by local malignant processes leading increased capillary permeability.

According to the Light's criteria, effusion is an exudates if: the ratio of fluid protein to serum protein is greater than 0.5, ratio of fluid LDH to serum LDH is greater than 0.6, pleural fluid LDH level is above 200 IU/L.

On computed tomography, the attenuation coefficient greater than 20 HU (Hounsfield units) indicates that pleural effusion is an exudate. However, the median HU values increase to 40–50 HU if there is some blood in the exudate.

Most frequently, malignant pleural mesothelioma is associated with the presence of free fluid in the pleural cavity. Sometimes, the effusion may loculate, mainly at the base of the lungs.

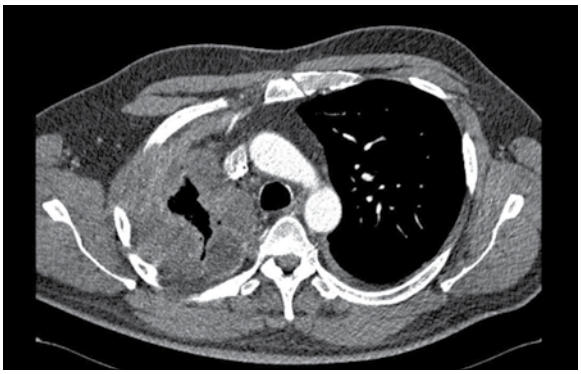

Figure 2. Chest CT, axial plane. Right nodular pleural thickening.

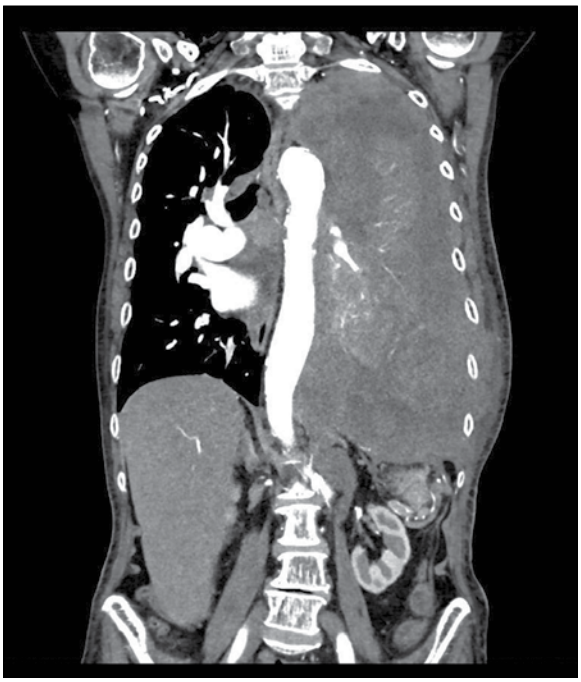

Figure 3. Chest CT, MPR reconstruction. Huge left pleural masses, that compress lung and extend to abdomen.

Malignant pleural effusions tend to recur shortly after pleurocentesis and drainage of the pleural cavity [7] (Figure 1).

2. Malignant pleural involvement

Characteristic computed tomographic (CT) features of pleural mesothelioma are specific and sufficient to make a preliminary diagnosis of MPM.

The CT scan shows diffuse pleural thickening (greater than 1 cm) with irregular, nodular outlines, where adjacent to the aerated lung area.

At early stages, focal pleural thickening may be present. Later, as MPM progresses, tumor spreads extensively and encloses the whole lung as in a shell resulting in decreased lung aeration.

Unlike benign pleural tumors, pleural mesothelioma frequently involves mediastinal pleura and interlobar fissures. It may be also associated with calcified pleural plaques.

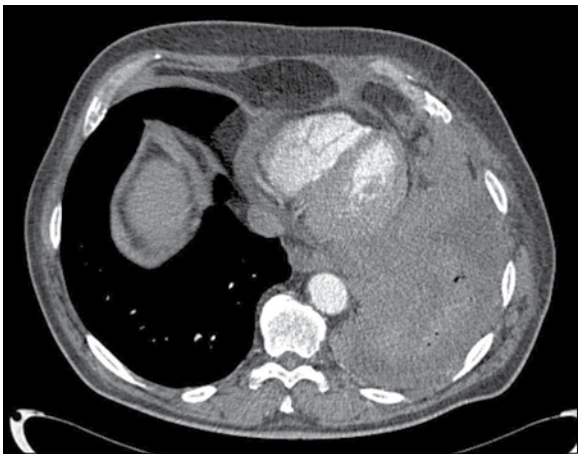

Figure 4. Chest CT, axial plane. Tumor invasion of left mediastinal adipose tissue.

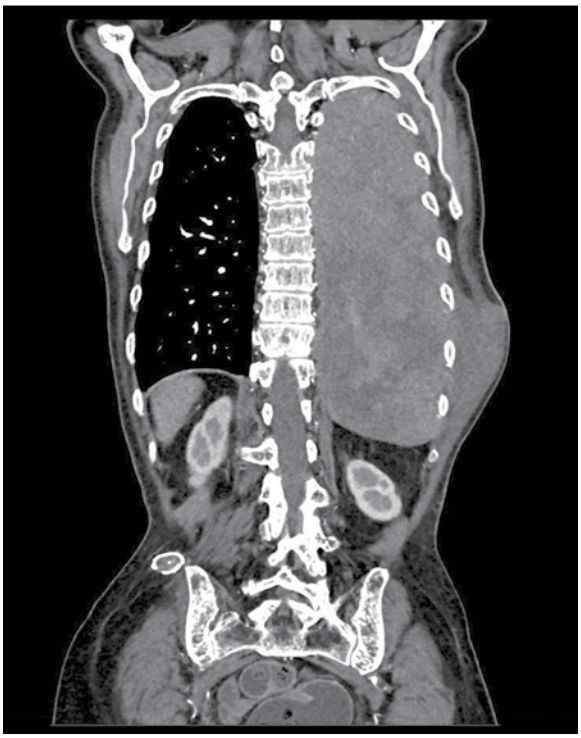

Figure 5. Chest CT, MPR reconstruction. Left chest wall invasion.

Malignant pleural mesothelioma shows heterogeneous signal enhancement on CT scans after intravenous contrast injection (Figures 2 and 3).

3. Malignant involvement of adjacent structures

Malignant pleural mesothelioma is an aggressive type of cancer. It frequently spreads directly to the adjacent structures such as chest wall (with associated rib and diaphragm destruction) or mediastinal organs (with associated pericardial effusion). In advanced MPM, tumor spreads from the posterior costophrenic angle to the abdomen along the diaphragmatic crura.

Currently, computed tomography is the diagnostic modality of choice in the evaluation of pleural tumor extent, as well

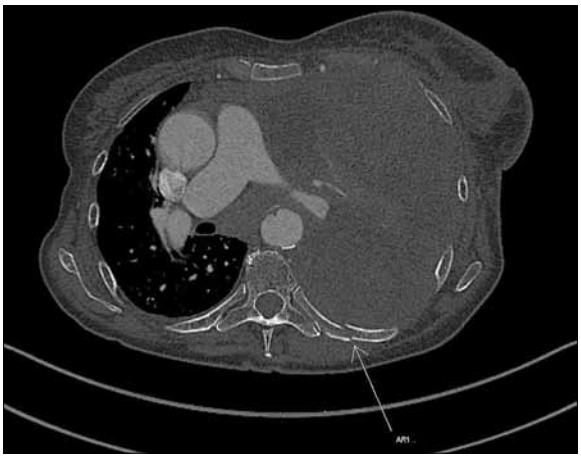

Figure 6. Chest CT, axial plane. A fracture of a left rib as extensive disease involvement (arrow).

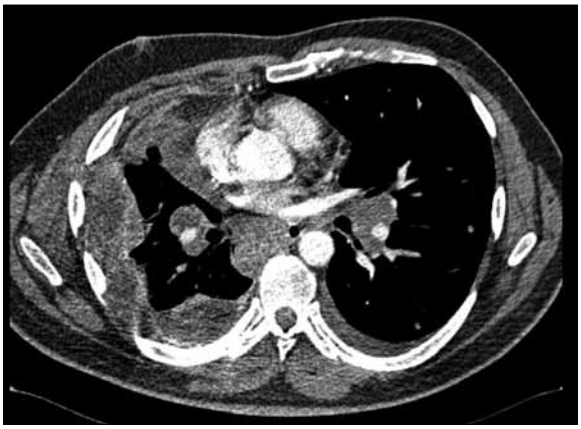

Figure 7. Chest CT, axial plane. Lymph node metastases.

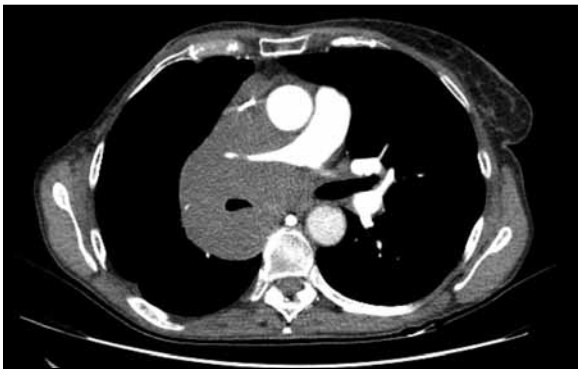

Figure 8. Chest CT, axial plane. Large right mediastinal node metastasis compressing a pulmonary artery and a bronchus.

as tumor involvement of the chest wall, mediastinum and diaphragm [2,3].

Chest MRI may also be performed in patients potentially eligible for curative surgery to further assess overall tumor burden (Figures 4–6).

4. Enlargement of mediastinal lymph nodes

Tumor involves ipsilateral hilar and mediastinal lymph nodes in about 50% of patients (Figures 7 and 8).

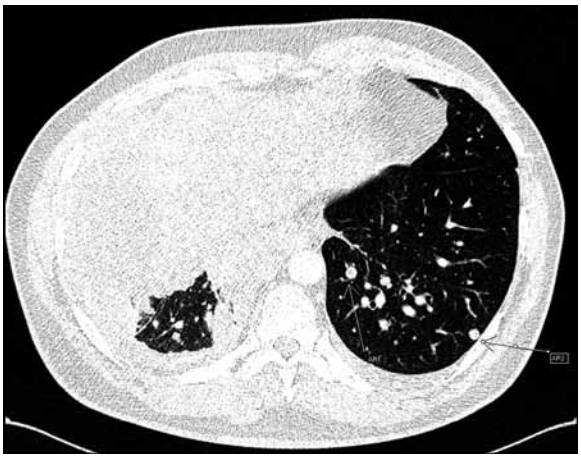

Figure 9. Chest CT, axial plane. Left pulmonary metastases manifested as nodules (arrows).

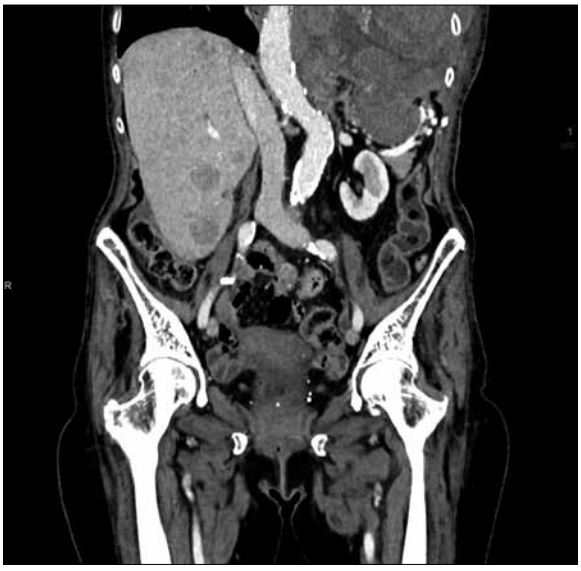

Figure 10. Abdominal CT, MPR reconstruction. Metastases in the liver.

5. Lung metastases

Lung metastases are common and may be found in about 60% of patients (Figure 9).

6. Metastases to other organs

Computed tomography is routinely used to detect distant metastatic disease. However, PET/CT is not widely used in diagnosis of metastatic mesothelioma (Figure 10).

Definite diagnosis is based on histological analysis of specimens collected during videothoracoscopy. Videothoracoscopy enables the surgeon not only to collect tissue specimens for analysis, but also to asses pleural lesions and perform pleurodesis. Pleurodesis is a procedure that obliterates the pleural space to prevent recurrent pleural effusion in patients receiving palliative treatment, and facilitates surgical intervention in patients eligible for surgery [8].

Computed tomography is also useful in assessing extent of disease. International Union Against Cancer (UICC

Table 1. Assessment of staging among patients with malignant pleural mesothelioma (UICC 2009).

Characteristic	Description
Primary tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor limited to the ipsilateral parietal pleura with or without visceral pleura involvement
T1a	Tumor limited to the ipsilateral parietal pleura (mediastinum and diaphragm) without visceral pleura involvement
T1b	Tumor limited to the ipsilateral parietal pleura (mediastinum and diaphragm) with focal visceral pleura involvement
T2	Tumor involving ipsilateral parietal pleura with at least 1 of the following: – involvement of visceral pleura (including fissures) – involvement of underlying pulmonary parenchyma – involvement of the diaphragmatic muscle
T3	Tumor involving ipsilateral pleura with at least 1 of the following: – involvement of the endothoracic fascia – extension into the mediastinal fat – solitary focus of tumor extending into the soft tissue of the chest wall – nontransmural involvement of the pericardium
T4	Tumor involving ipsilateral pleura with at least 1 of the following: – diffuse extension or multifocal masses of tumor in the chest wall with rib involvement – direct diaphragmatic extension of the tumor to the peritoneum – direct extension of the tumor to a mediastinal organs – direct extension of the tumor to the contralateral pleura – direct extension of the tumor into the spine – tumor extending through to the internal surface of the pericardium with pericardial effusion – tumor involving the myocardium – tumor involving brachial plexus
Lymph nodes	
NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastases
N1	Metastases in the bronchopulmonary or hilar lymph node(s)
N2	Metastases in the subcarinal and/or in the ipsilateral mediastinal/parasternal lymph nodes
N3	Metastases in the contralateral mediastinal and parasternal lymph nodes, ipsilateral or contralateral supraclavicular and/or internal mammary lymph nodes
Distant metastases	
M0	No distant metastasis
M1	Distant metastasis

7th Edition, 2009) classification is well established staging system for malignant pleural mesothelioma. The system is based on the TNM classification in which T describes the primary tumor, N describes lymph node involvement and M describes distant metastasis (Table 1).

Pleural mesothelioma is considered poorly chemosensitive and radiation resistant tumor. Therefore, surgery is the only potentially curative treatment option. MPM surgery involves extrapleural pneumonectomy (EPP) or pleurectomy with decortication (P/D). Unfortunately, in the majority of cases, the disease is only detected when it is already in an advanced stage and only 15–20% of patients are eligible for curative treatment. The 5-year survival rate for surgically resected patients is less than 15%. Patients with unresectable tumors receive palliative chemotherapy and have a median overall survival of 6–7 months [5].

Computed tomography plays a key role in monitoring treatment effects in patients with MPM.

Assessment of response to chemotherapy is difficult in patients with advanced malignant pleural mesothelioma, since the tumor tends to spread longitudinally along the

pleura and rarely grows as an oval 2-dimensional tumor mass. Therefore, modified RECIST (response evaluation criteria in solid tumours) criteria are recommended to assess treatment response in malignant pleural mesothelioma. RECIST scale is based on the sum of the longest perpendicular (to the chest wall or mediastinum) diameters (LDs) measured at three levels in two planes (6 diameters in total) [5,9].

Conclusions

Currently, computed tomography is most commonly used to diagnose pleural malignant mesothelioma, to assess tumor extent and response to treatment.

CT may underestimate the extent of disease in patients with early chest wall and peritoneum involvement. Its usefulness is also limited in patients with early mediastinal lymph node involvement. MRI is a valuable diagnostic tool to assess the involvement of adjacent structures and to differentiate between benign and malignant pleural tumors [3].

PET is not widely used in routine diagnosis of malignant pleural mesothelioma. However, it can provide important information for differentiation between benign and malignant pleural tumors and may help detect mediastinal lymph node involvement or occult distant metastases [2,3].

References:

1. Robinson BW, Musk AW, Lake RA: Malignant mesothelioma. Lancet, 2005; 366: 397–408
2. Marom EM, Erasmus JJ, Pass HI et al: The role of imaging in malignant pleural mesothelioma. Semin Oncol, 2002; 29(1): 26–35
3. Yamamuro M, Gerbaudo VH, Gill RR et al: Morphologic and functional imaging of malignant pleural mesothelioma. Eur J Radiol, 2007; 64(3): 356–66
4. Krzakowski M: Postępy w leczeniu złośliwego międzybłoniaka opłucnej. Onkologia w Praktyce Klinicznej, 2005; 1: 132–40 [in Polish]
5. Krzakowski M: Nowotwory śródpiersia i opłucnej. Adv Clin Exp Med, 2004; 13(6): 1103–10 [in Polish]
6. Drozdowska A: Złośliwy miedzybłoniak opłucnej – postępy w rozpoznawaniu i leczeniu. Współczesna Onkologia, 2003; 7(9): 676–83 [in Polish]
7. Szołkowska M, Langfort R, Burakowska B et al: Wrzecionowatokomórkowe rozrosty nowotworowe i nienowotworowe opłucnej. Kardiochirurgia i Torakochirurgia Polska, 2012; 3: 340–51 [in Polish]
8. Stahel RA, Weder W, Lievens Y et al: Malignant pleural mesothelioma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Anna Oncol, 2010; 21 (Suppl.5): 126–28
9. Byrne MJ, Nowak AK: Modified RECIST criteria for assessment of response in malignant pleural mesothelioma. Ann Oncol, 2004; 15: 257–60