MALIGNANT PLEURAL MESOTHELIOMA TREATED IN CLINIC FOR PULMONARY DISEASES AND TUBERCULOSIS "PODHRASTOVI" IN TEN-YEAR PERIOD (FROM 1998 TO 2007)

Vesna Čukić*, Aida Ustamujić, Vladimir Lovre, Hasan Žutić, Sadika Genjac, Mina Mašić -Zečević

Clinic for Pulmonary Diseases and Tuberculosis "Podhrastovi", University of Sarajevo Clinics Centre, Bardakčije 90, 71 000 Sarajevo, Bosnia and Herzegovina

* Corresponding author

Abstract

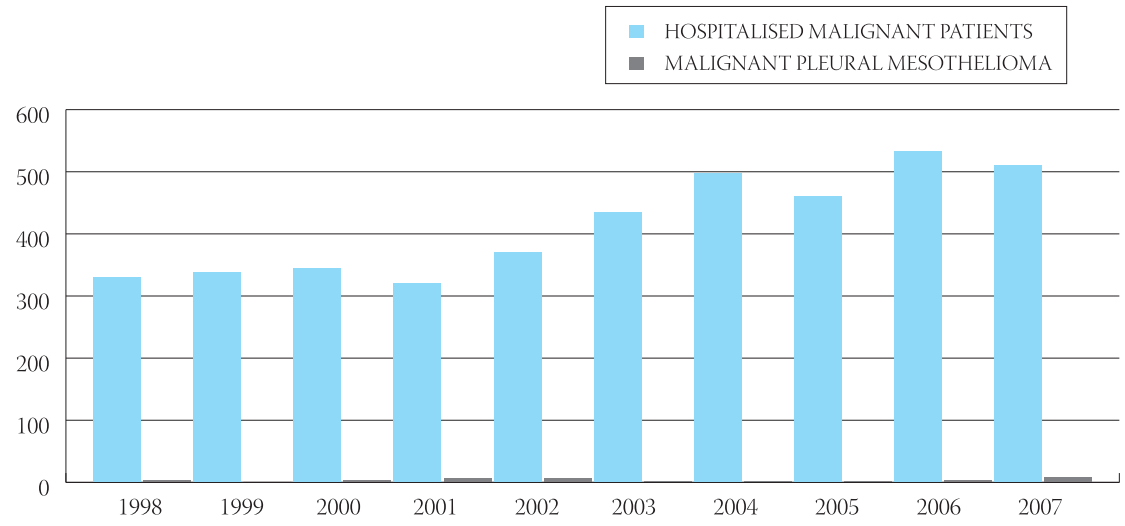
Malignant pleural mesothelioma (MPM) is the most common primary malign tumour of pleura. The aim of this study was to evaluate cases of MPM diagnosed and treated in Clinic for Pulmonary Diseases and Tuberculosis "Podhrastovi" during ten-year period (1998-2007). Study is retrospective. The patients were analysed according to age, sex, histopathologic type of the tumour, cantonal distribution in Federation of Bosnia and Herzegovina and regimen of treatment.

MPM presented 0,72% (0-1,56% per year) of all hospitalised malignant patients, and the greatest number of registered cases was in the year of 2007. The series included 16 male (57,14%) and 12 female (42,86%). Cases over 64 years old were the most frequent (14-50%) than 45-54 years (7-¬25%). Histopathology types of hospitalised cases of MPM: epitheloid form (8- 28,57%); sarcomatoid form (2- 7,14 %); other forms (18-64,29%). The most patients came from Canton Sarajevo (12-42,86%); ZE-DO canton (8-28,57%) and the UNA-SANA canton (5-17,86%). The therapy applied: chemotherapy (11-39,29%); radiotherapy (3-10,71%); chemotherapy + radiotherapy (4-14,29%); symptomatic therapy (10-35,71 %).

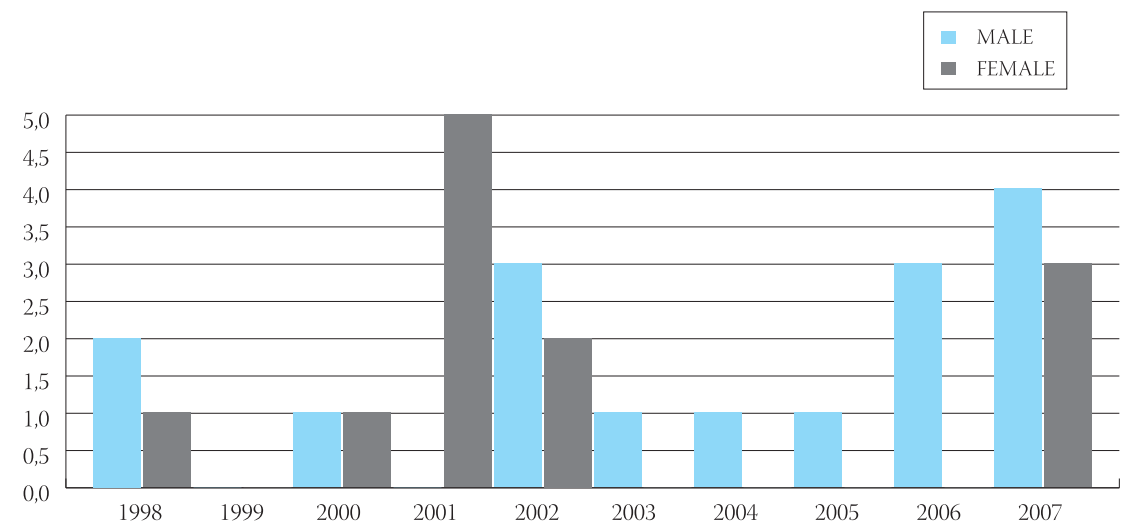
KEY WORDS: malignant pleural mesothelioma, retrospective evaluation, Clinic "Podhrastovi"

Introduction

Malignant mesothelioma is a tumour in origin from cells of serous membranes such as pleura, pericard, peritoneum and tunica vaginalis testis. The most common localisation is a pleura. Malignant pleural mesothelioma (MPM) almost always has a diffuse growth and involves both visceral and parietal surfaces. WHO advises that MPM should be classified into one of three main types: epitheloid, sarcomatoid (with desmoplastic being a particularly aggressive) and biphasic (1). Asbestosis fibres are the cause of the most cases of MPM. About 85 % cases of MPM may be directly attributable to occupational asbestos exposure (2,3,4). MPM can also result from para–occupational (for example–laundering worker's overalls) and environmental exposure (3). The mean latency period between first exposure to asbestos and death from MPM is 41 years (range 15- 67) (2). Clinical features - Typically, presentation is either with a chest pain, dyspnoea or both (5, 6). The pain is dull, diffuse and worsens during the course of illness. It may be described as heaviness or aching in the shoulder arm, chest wall and upper abdomen. It sometimes has neurophatic components because of entrapment of intercostal, autonomic or brachial plexus nerves. Cough is not prominent. Profuse sweating may occur. Pneumothorax is rare. The disease spreads by local extension and involves mediastinal structures. Pericardial involvement with tamponade and dysphagia may be pre-terminal events. Bilateral disease and expressive weight loss may be present in the terminal phases. Sometimes patients present with acute pleuritic chest pain and a clear radiographs or a small effusion and initial investigations may fail to give a diagnosis. Some patients may remain symptom-free for many months, some have rapid deterioration. The illness is progressive with a median survival of 8 -14 months (2, 7). Distant metastases are late and more common in the sarcomatoid variety (8). Diagnosis- It is essential to use the combination of history, examination, radiology and pathology. The history of asbestos exposure is very important. Physical signs include signs of pleural thickening and effusion with restriction of expansion of the hemithorax. Finger clubbing occurs commonly (9). Sometimes tumour tissue may be felt between the ribs. Plain chest radiographic abnormalities may strongly suggest a malignant process. The key investigations are pleural tap if an effusion is present and the fluid should be sent for cytology and immunocytochemistry; contrast -enhanced CT with a biopsy (10). In early phase the pleural fluid is serous, later it is often hemorrhagic. Although immunocytochemistry can reliably show that cells are mesothelial, it may be difficult to distinguish malignant from highly reactive mesothelial cells (11). Pathological diagnosis may be obtained from cytology or histology and interpretation should be taken in context with the history, examination findings and radiological appearance. A biopsy is required if the diagnosis is not clear after the pleural tap and CT scan. The techniques are an ultrasound or CT -guided percutaneous pleural or a thoracoscopic biopsy. Blind Abram's punch biopsy is less effective (12). Thoracoscopy is appropriate where there is a pleural fluid and it facilitates complete drainage, biopsy and immediate talc pleurodesis. Negative pleural biopsy and cytological results do not exclude MPM. Diagnostic imaging - The initial chest radiographic appearances may range from normal in early disease to complete opacification of a hemithorax. The pleural thickening may manifest as discrete pleural nodules or pleural plaques visible after the drainage of a fluid or may encase the lung. The mediastinum may be dislocated. Ultrasound -pleural effusions and thickening can be readily appreciated and discrete malignant nodules can be seen (13). Contrast-enhanced CT (computed tomography) is the primary imaging modality for evaluation of MPM. Magnetic resonance imaging (MRI) features are similar to those seen at CT but both techniques may underestimate the stage of disease. When conventional imaging and biopsy are unhelpful, PET (positron emission tomography) may be useful. As to serum markers, a recent study (14) confirmed higher levels of SRMP (soluble mesothelin related proteins) in MPM. Management - The role of surgical resection is very uncertain. The more radical is extrapleural pneumonectomy (pleuropneumonectomy)(EPP) than the debulking operation (cytoreductive surgery) performed at open thoracotomy or by video –assisted thoracic surgery (VATS). The TNM staging system proposed by the International Mesothelioma Interest Group (IMIG) is used for assessing patients with potentially resectable disease. One of the central aims is to achieve an early pleurodesis. The most effective available pleurodesis agent is sterile talc (15). Radiotherapy provides pain relief and reduces mass of tumour. Prophylactic radiotherapy may reduce chest wall implantation following invasive procedures. Chemotherapy should be used for all patients with performance status 0-2. Several chemotherapeutic agents can reduce tumour bulk, help symptoms and prolongs survival. Supportive and palliative care of patients provide relief of pain and other physical symptoms such as dyspnoea, cough and others. The aim of this work was to evaluate cases of MPM treated in Clinic for Pulmonary Diseases and Tuberculosis "Podhrastovi" during ten- year period (1998-2007).



GRAPH 1. MPM in Clinic "Podhrastovi" between 1998-2007.



GRAPH 2. Gender structure of hospitalised patients with MPM in Clinic " Podhrastovi" between 1998-2007

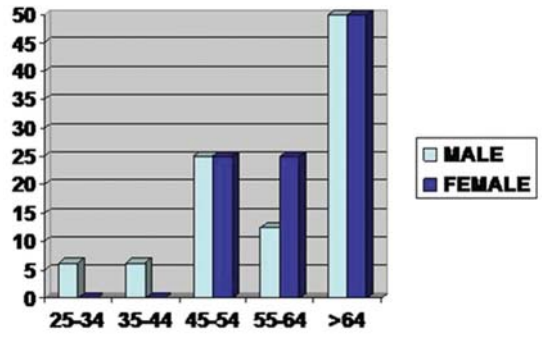
Materials and Methods

This retrospective study was performed using a database with cases of MPM diagnosed and treated in Clinic "Podhrastovi" from 1998 ¬to 2007. The patients were analysed according to age, sex, histopathologic type of the tumour, cantonal distribution and regimen of treatment.

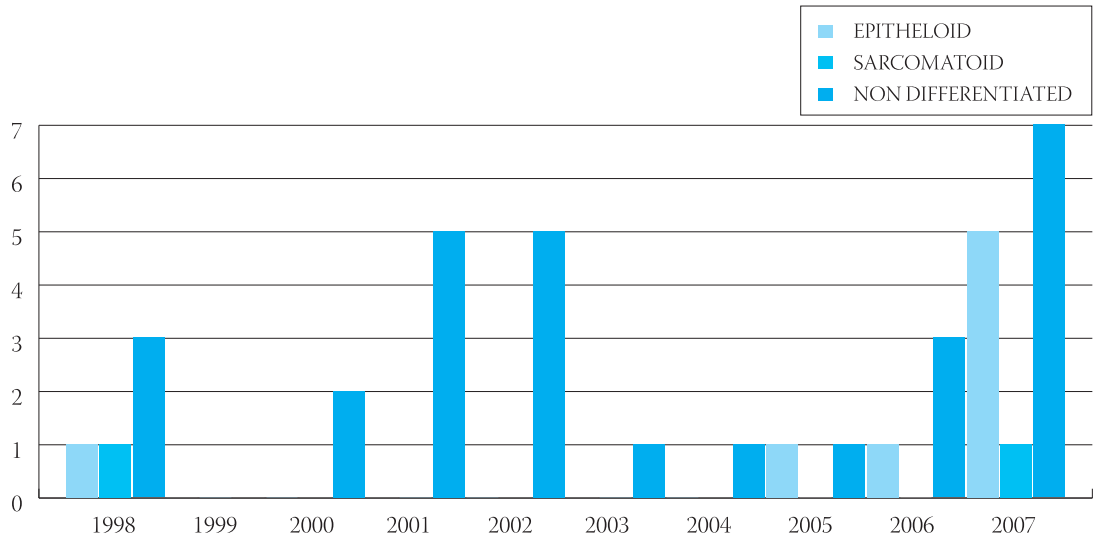
Results

The results of our study are showed on the following graphics.

MPM presents 0,72% (range 0-1,56% per year) of all hospitalised patients with a malign disease, and the greatest number was in the year 2007 (Graphic 1). The series included 16 male (57,14%) and 12 female (42,86%) (Graphic 2).



GRAPH 3. Age groups of hospitalised patients with MPM a in Clinic "Podhrastovi" between 1998¬-2007.

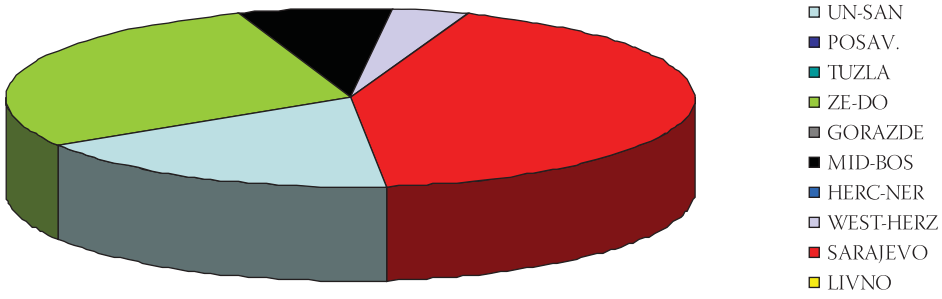


GRAPH 4. Histopathologic types of MPM in patients hospitalised Clinic " Podhrastovi" between 1998-2007.

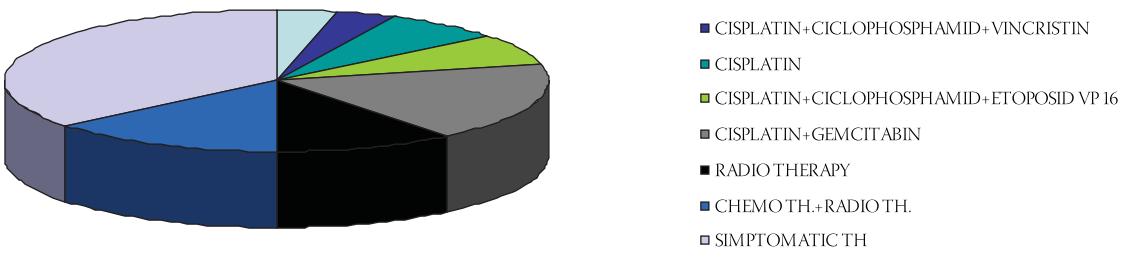
Patients over 64 years old are the most frequent (14-¬50%) , than 45-54 years (7-25%) (Graphic 3).

Histopathologic types of MPM: Epitheloid form (8-¬28,57%); Sarcomatoid form(2-7,14%); Non –differentiated (18-64,29%) (Graphic 4).

The greatest number of patients came from Canton Sarajevo (12¬-42,86%); followed by ZE-DO canton (8-28,57%) and the UNA-SANA canton (5-17,86%) (Graphic 5). The chemotherapy was predominated, but there was also a great number of patients with only symptomatic therapy because of a bad performance status at the time of diagnosis (Graphic 6). The median survival for all patients was 8,5 months after the diagnosis of MPM



GRAPH 5. Cantonal distribution of patients with MPM hospitalised in Clinic "Podhrastovi" between 1998-2007.



GRAPH 6. The regimen of treatment of hospitalised patients with MPM in Clinic "Podhrastovi " between 1998¬-2007.

Discussion

The established cause of MPM is inhalation of asbestos in occupational, para-occupational or environmental exposure. The highest risks are in workers in shipbuilding, railway engineering, asbestos product manufacture; but also in subjects with less obvious occupations such as decorator and plumber. The risk is higher for amphibole asbestos fibre type than chrysotile (16). Genetic predisposition may explain why fewer than 5% of asbestos-exposed individuals develop MPM (17). MPM can be induced by non-asbestos fibres such as erionite found in rocks in some areas in Turkey (18) but only some families within only three villages develop MPM which show the role of genetic factors (17). Our study is retrospective and we were not able to establish real exposure to asbestos fibres in the past. Between 1998-2007 in Clinic "Podhrastovi" 28 patients with MPM were hospitalised (16 male and 12 female) which presents 0,72% (range 0-1,56% per year) of all hospitalised malignant patients in that period. The relative high number of women indicate the importance of para occupational or environmental asbestos exposure. Patients more than 64 years old were the most frequent. In the United States there were 2550 mesothelioma cases (2000 males and 550 females) in 2000. The incidence was 0,92 cases of mesothelioma (pleural and peritoneal) per 100.000 population (1,4 males; and 0,4 females) (19). Pathologist should attempt to specify the histological type of MPM but it is often difficult (11). Histopathology types of hospitalised MPM in our Clinic: epitheloid form (8-28,57%); sarcomatoid form (2-7,14%); non differentiated (18-64,29%). Therapy of MPM is very uncertain. One of the central aims is to achieve an early pleurodesis which is done in all our patients with sterile talc. Different modalities of therapy are available- surgery, radiotherapy, chemotherapy, or combination. In our patients chemotherapy was predominated (11-39,28%) particularly Gemcitabin + Cisplatin shedule (5-17,86%); combination of chemotherapy and radiotherapy (4-14,29%); radiotherapy (3¬-10,71%); palliative simptomatic therapy (10-35,71%). There are big expectations from new chemoterapeutic - pemetrexed which has been on trial from the beginning of 2008. Several studies have reported survival data. A series in England showed median survival from symptoms onset of 14 months and a worse prognosis in sarcomatoid type (2). A study in the USA showed that, among 141 cases, the median survival from onset of symptoms was 10 and from diagnosis 5 months (7). The few patients who survived over 3 years had epitheloid form (20). The median survival for all patients in our study was 8,5 months after the diagnosis. In the developed countries such as United Kingdom there are responsibilities of employers of workers, who might be exposed to asbestos, laid out in Control of Asbestos Regulations (21).

Conclusion

MPM is the most common primary malign tumour of pleura with a very poor survival because all of therapy modalities have limited results. The established cause in the development of disease is exposure to asbestos, but a genetic predisposition has a big role. Preventive measures, such exists in developed countries would be of the greatest significance. Malignant mesothelioma presents 0,72% of all hospitalised malignant patients in Clinic "Podhrastovi" in ten-year period (1998-2007). Male and female at the age of more 64 were the most frequent, particularly men. The most number of patients came from Sarajevo. Non-differentiated patohistological forms were the most frequent. Chemotherapy was predominated form of treatment. MMP should be considered in any patient with either pleural fluid or pleural thickening, especially if chest pain is present.

References

(1) Travis W. Histopathological types of lung cancer and pleural tumours. WHO, Springer, 1999.

(2) Yates D.H., Corrin B., Stidolf P.N. et al. Malignant mesothelioma in south and east England: clinocopathological experience of 272 cases. Thorax 1997; 52-12.

(3) Howel D., Arblaster L., Swinburne L. et al. Routes of asbestos exposure and the development of mesothelioma in an English region. Occup. Environ. Med. 2006; 63:390-395

(4) Goldberg M., Imberon E., Rolland P. et al. The French National Mesothelioma Surveillance Program. Occup. Environ. Med. 2006; 63: 390-395.

(5) Elmes P.C., Simpson M.J.C. The clinical aspects of mesothelioma. QJ Med. 1976;427-449.

(6) Hillderdahl G. Malignant mesothelioma: a review of 4710 published cases. Br. J. Dis. Chest 1983; 77: 321-343.

(7) Ribak J., Selikoff JJ. Survival of asbstos isulation workers with mesothelioma. Br. J. Ind. Med.1992; 49:732-735.

(8) Law M.R., Hodgson M., Heard B.E. Malignant mesothelioma of the pleura: relation between histological type and clinical behaviour. Thorax 1982 ; 37:810-815.

(9) McGavin C.R., Hughes P.D. Finger clubbing in malignant mesothelioma and benign asbestos pleural disease. Respir. Med. 1998; 691-692

(10) British Thoracic Society. BTS guidelines for the management of pleural disease. Thorax 2003; 58 (Suppl . II): 1-59.

(11) Trawis W.D.,Brambilla E.,Muller-Hermelink H.K.et al. Tumours of the lung, pleura, thymus and heart. Lyon: IARC Press (distributed by WHO Press), 2004.

(12) Maskell N., Gleeson F.V., Davies R.J. et al. Standard pleural biopsy vs CT guided cutting needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. Lancet 2003; 361: 1326-1330.

(13) Herth F. Diagnosis and staging of mesothelioma transthoracic ultrasound. Lung Cancer 2000; 45 (Suppl 1): S 63-67

(14) Schepereel A., Grigoriu B., Conti M.,et al. Soluble mesothelin-related peptides in the diagnosis of malignant mesothelioma. Am. J. Respir. Crit. Care Med. 2006;173:1155-1160.

(15) Shaw P., Agarwal R. Pleurodesis for malignant pleural effusions. In: Cochrane Library, Issue1, Oxford: Update Publications, 2004.

(16) Berman D.W., Crump K. Technical support document for a protocol to assess asbestos-related risk. Draft prepared for US Department of Transportation and US Environmental Protection Agency 2004.

(17) Broaddus V.C. Advances in Mesothelioma Research (Report of the IMIG Meeting): International Pleural Newsletter, A publication of the International Pleural Network, 2004; 2(3): 10-11

(18) McDonald J.C., McDonald A.D. Mesothelioma: is there a background? In: Bignon J.. Jaurand M.C., eds. The mesothelial cell and mesothelioma. New York: Marcel Dekker, 1994: Chapter 3., 268-270.

(19) Price B., Ware A. Mesothelioma trends in the United States: An update based on SEER data for 1973 through 2003. Am. J. Epidemiol .2004;159:107-112.

(20) Van Gelder T., Damhuis R.A., Hoogstedon H.C. Prognostic factors and survival in a malignant pleural mesothelioma. Eur. Respir. J. 1994; 7 1035-1038.

(21) Anonymous. Control of Asbestos Regulations 2006,.Statutory Instrument 2006 No.2739, UK