Outcome of using Combined Modality Treatment for Malignant Pleural Mesothelioma (A Retrospective Study)

Thesis

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List of Abbreviations

Abb.	Full term
ARD	Asbestos Related Disease
BFGF	Basic Fibroblast Growth Factor
CT	Computed Tomography
DNA	Deoxyribonucleic Acid
EGFR	Epidermal Growth Factor Receptor
EPP	Extra Pleural Pneumonectomy
FDA	Food and Drug Administration
FISH	Flourescence In Situ Hybridization
FNAC	Fine Needle Aspiration Cytology
Gy	Grey
IMRT	Intensity-Modulated Radiation Therapy
MPM	Malignant Pleural Mesothelioma
MRI	Magnetic Resonance Imaging
PD	pleurectomy/Decortication
PDGF	Platelet-derived Growth Factor
PET	Positron Emission Tomography
PS	Performance Status
VATS	Video-assisted Thoracoscopic Surgery
VEGFR	Vascular Endothelial Growth Factor Receptor
WHO	World Health Organization

INTRODUCTION

Malignant mesothelioma (MM) is a relatively rare cancer arising from the mesothelial lining of pleura as well as the peritoneal cavities, tunica vaginalis, and pericardium ***(Price and Ware, 2005).***

Histological subtypes of malignant pleural mesothelioma (MPM) include epithelioid (about 60%) and non-epithelioid (about 40%) variants; non-epithelioid variants include subtypes of spindle, sarcomatoid, desmoplastic, fibrous, biphasic, and not otherwise specified ***(Robinson, 2012).***

Malignant pleural mesothelioma (MPM) is caused primarily by inhalation of asbestos (about 80% of cases) Its pathogenesis is closely associated with iron overload and oxidative stress in mesothelial cells. ***(Robinson, 2012).***

Upon fiber exposure, mesothelial cells accumulate fibers simultaneously with iron, which either performs physical scissor function or catalyzes free radical generation, leading to oxidative DNA damage such as strand breaks and base modifications, followed by activation of intracellular signaling pathways and this is how asbestos cause indirect genetic damage in addition to its direct damage ***(Kamp et al., 1992).***

The incidence of MPM revealed a gradual increase in number of cases in Europe over the last 40 years with male: female ratio has changed from 1:1 to 4:1 and it is expected that

the incidence of MPM will continue to rise till approximately 2020 ***(Galateau-Salle et al., 2014)***

The relatively late discovery of most cases is due to the long interval between exposure of asbestos and development of mesothelioma with latency period of 30 to 45 years. So, because of its carcinogenic property, the use of asbestos has been banned in many developed countries, but some developing countries such as China and India still permit its usage ***(Sezer et al., 2014)***

The incidence in Egypt is expecting to rise in the following years, the total estimated cases are (207, 238, 456) in (2020, 2025, 2050) respectively ***(Ibrahim et al., 2014).***

Another cause that may account for the development of MPM is Exposure to mineral fibers as in house hold s though it's quite rare ***(Ronald et al., 2018).***

Also there are reports that suggest that ionizing radiation may also cause mesothelioma, such as in patients previously treated with mantle radiation for Hodgkin lymphoma ***(Xu et al., 2015).***

Genetic factors may also play a role in MPM, with some families carrying a germ line mutation in the BRCA1 Associated Protein 1 (BAP1) gene which increase the incidence of MPM ***(Ohar et al., 2016).***

Smoking is not a risk factor for mesothelioma, however patients who smoke and have been exposed to asbestos are at increased risk for lung cancer. In addition, patients who smoke should be encouraged to quit because smoking impedes treatment (e.g., delays wound healing after surgery) ***(Mossman et al., 2011).***

Symptoms that patients with suspected MPM often have include dyspnea and chest pain; they may also have pleural effusion, fatigue, insomnia, cough, chest wall mass, loss of appetite, and weight loss ***(Dyer et al., 2013).***

In patients with recurrent pleural effusion and/or pleural thickening, the recommended initial evaluation for suspected MPM includes:

1. Computed Tomography (CT) of the chest with contrast.
2. Thoracentesis for cytologic assessment of the effusion
3. Pleural biopsy (eg, thoracoscopic biopsy, preferred)

(van Zandwijk et al., 2013).

However, cytologic samples are often negative even when patients have MPM ***(Paintal et al., 2013)***. Fine-needle aspiration (FNA) is not recommended for diagnosis ***(van Zandwijk et al., 2013).*** Talc pleurodesis or pleural catheter may be needed for management of pleural effusion ***(Hunt et al., 2012)***. Soluble mesothelin-related peptide (SMRP) levels may

also be assessed, and these levels may correlate with disease status ***(Hollevoet et al., 2012).***

Calretinin, WT-1, D2-40, and cytokeratin (CK) 5/6 are useful immunohistochemical markers for the diagnosis of MPM, as are markers that typically are positive in pulmonary adenocarcinoma and negative in mesothelioma ***(Henderson et al., 2013).***

Because MPM is often diagnosed late, it has a poor prognosis with five-year survival is still approximately 8 %. It occurs mainly in older men (median age at diagnosis, 72 years) who have been exposed to asbestos, although it occurs decades after exposure (20-40 years later) ***(Taioli et al., 2015).***

Median survival for untreated malignant pleural mesothelioma is usually less than 1 year, survival figures must always be interpreted with caution and be compared with the average survival of nine months with supportive care alone. ***(Milano and Zhang, 2010).***

Patients that are candidate for multimodality treatment are selected according to: the clinical stage (I-III) and good performance ***(de Perrot et al., 2009).***

1- The surgical goal of MPM is cyto reductive surgery to achieve macroscopic complete resection by removing all visible or palbable tumors ***(Sugarbaker et al., 2011).***