

Consensus Statement on Peritoneal Mesothelioma

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Diffuse malignant peritoneal mesothelioma (DMPM) has been traditionally regarded as a rapidly lethal disease. Recently, several independent prospective trials have reported improved survival with an intensive loco-regional treatment strategy including cytoreductive surgery (CRS) along with peri-operative intra-peritoneal chemotherapy (PIC). However, most of the surgical data comes from mono-institutional phase I or II studies and there is a broad range of variability regarding inclusion criteria, cytoreductive surgical procedures, drugs, temperatures and methods of delivering the heated chemotherapy (open vs. closed abdomen). This manuscript critically analyze and discuss the results of a group of health care providers trying to achieve a consensus statement in the management of this group of patients. The main conflicting points regarding preoperative evaluation, patient eligibility, combined treatment methodology, postoperative follow-up and future investigational perspectives were summarized as a list of multiple-choice questions. A questionnaire was placed on the website of the "5th International Workshop on Peritoneal Surface Malignancies" and the group members voted via internet. The results were presented for further debate during a dedicated session of the Workshop. The general treatment guidelines and future investigational perspectives were defined.
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INTRODUCTION

Malignant mesothelioma is an uncommon tumor arising from the serosal layer of pleura, peritoneum, pericardium, and tunica vaginalis testis [1]. The incidence of the disease has been rising worldwide since 1970 and is not expected to peak for another 10–20 years, due to the widespread exposure to asbestos during the last decades [2].

In the United States, where the incidence peak has likely already been reached, about 2,500 new cases of DPM are registered each year [3]. Diffuse malignant peritoneal mesothelioma (DMPM) accounts for 10–20% of all forms of malignant mesothelioma [3].

In the past, DMPM has been regarded as rapidly lethal disease. Clinical results of conventional treatments, such as palliative surgery, systemic or intra-peritoneal chemotherapy, have been far from satisfactory in terms of both cure or palliation. Recently, several independent phase I/II prospective trials have reported improved survival with an intensive loco-regional treatment strategy including cytoreductive surgery (CRS) along with peri-operative intra-peritoneal chemotherapy (PIC) in the form of hyperthermic intra-peritoneal chemotherapy (HIPEC) +/- early post-operative intra-peritoneal chemotherapy (EPIC).

There are objective difficulties in planning a phase III clinical trial in this setting, since DMPM is a rare disease and a randomized study would compare a potentially curative treatment with a palliative one. Nevertheless, an extensive literature search of the available retrospective historical series has shown that the median survival after palliative surgery and systemic and/or intra-peritoneal chemotherapy is about 1 year, ranging from 9 to 15 months [4–11]. Conversely, the median survival after aggressive surgery combined with HIPEC has approached 5 years and seems to improve with subsequent reports [4,12–19].

Taken together the aforementioned data suggest that treatment of PMP by means of CRS and PIC is supported by "Type 3 evidence," as scientific evidence is available from non-randomized studies, with external controls allowing comparisons [20].

The present paper focuses on the results of a group of health care providers trying to achieve a consensus statement in the management of peritoneal mesothelioma.

PREOPERATIVE EVALUATION

Early diagnosis of DMPM is traditionally challenging [21,22]. Due to its rarity and unspecific presentation, the disease is commonly diagnosed at advanced stage or confused with ovarian cancer or other peritoneal disseminations, often resulting in disease mistreatment. The goal of a rationale diagnostic pathway is to start an adequate and timely treatment, thus optimizing the clinical results. Since DMPM has a great propensity to implant at needle tracts, laparoscopic port sites or surgical incisions, preventing disease dissemination as a consequence of inappropriate invasive procedures is an additional primary objective [15].

CT-scan is the imaging test of choice for DMPM. The findings associated to the disease have been recently reviewed. Diffuse disease distribution throughout the peritoneal cavity with large tumor volume in the mid-abdomen and in the pelvis may increase the level of clinical suspicion. Additional findings that could be of help in the differential diagnosis from other gastrointestinal or gynaecologic malignancies are the lack of a primary site and the absence of lymph node or distant metastases [23]. The role of other imaging studies, such as magnetic resonance or positron emission tomography is presently unclear.

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