



Dealing with microscopic peritoneal metastases of epithelial ovarian cancer. A surgical challenge



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ABSTRACT

Understanding biology and progression mechanisms of peritoneal metastases of epithelial ovarian cancer (EOC) is a cornerstone in the knowledge and the comprehensive management of the disease. Despite clinical remission after the association of complete cytoreductive surgery and platinum-based chemotherapy, peritoneal recurrence still occurs in 60% of patients.

Eligible studies, published from 1980 to June 2016, were retrieved through ClinicalTrials.gov, MEDLINE, Cochrane databases and bibliography searches. We reviewed all publications that deals with microscopic peritoneal metastases of EOC in French and English. To discuss expected benefits of intraperitoneal (IP) chemotherapy, fluorescence-guided surgery or IP photodynamic therapy, we reviewed most recent and relevant studies. The final reference list was generated on the basis of originality and relevance to the broad scope of this review.

Published data concerning early-stage ovarian cancer suggest that occult peritoneal or epiploic metastases are present in 1.2%–15.1% of cases. In the frequent case of advanced-stage disease, residual microscopic lesions are ignored by conventional surgery. We are convinced that microscopic peritoneal metastases are a relevant surgical therapeutic target. This article discusses existing data on microscopic peritoneal metastases, the treatment indications, the diagnostic and therapeutic surgical approaches to be developed and their expected benefits.

A local therapeutic strategy to target microscopic lesions is needed in addition to complete macroscopic cytoreductive surgery to decrease the rate of peritoneal recurrence. Intraperitoneal chemotherapy, and targeted photodynamic therapy could play a role in this new paradigm. The roles of these different options must be defined by future researches.

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1. Introduction

Understanding biology and progression mechanisms of peritoneal metastases (PM) of epithelial ovarian cancer (EOC) is a cornerstone in the knowledge and the comprehensive management of the disease, as PM will occur in the majority of patients. Indeed, the goal of cytoreductive surgery (CRS) in these patients is to completely remove all visible peritoneal invasion because the absence of residual disease after surgery is known to improve the prognosis [1–8].

Despite clinical remission after the completion of complete surgery and platinum-based chemotherapy, 60% of patient develop peritoneal recurrence [9,10]. This suggests that microscopic lesions may be present that are not eradicated by surgery, not controlled by systemic chemotherapy and that may be one of the mechanisms leading to peritoneal recurrence. Peritoneal carcinomatosis is responsible for the greatest morbidity and mortality in women with EOC [11,12].

There are very few studies in the literature on microscopic peritoneal involvement in EOC, its detection and potential role in the progression of cancer. The peritoneum should be considered an organ in its own right and the surgeon must treat peritoneal metastases with the intent to cure [13]. To follow the recommendations by Elias et al. this microscopic disease must be managed, because complete CRS is now a skill that can be mastered skill and its uses is a validated guideline [9]. Moreover, “complete CRS” should be defined as “without macroscopic residual disease” thus highlighting the presence of microscopic disease [3,14].

To our knowledge, there are no published reviews that specifically deal with microscopic peritoneal metastases (mPM) in ovarian cancer and their treatment. The goal of this article is to review the scientific evidence for the role of mPM in peritoneal recurrence and to discuss potential diagnostic and therapeutic approaches.

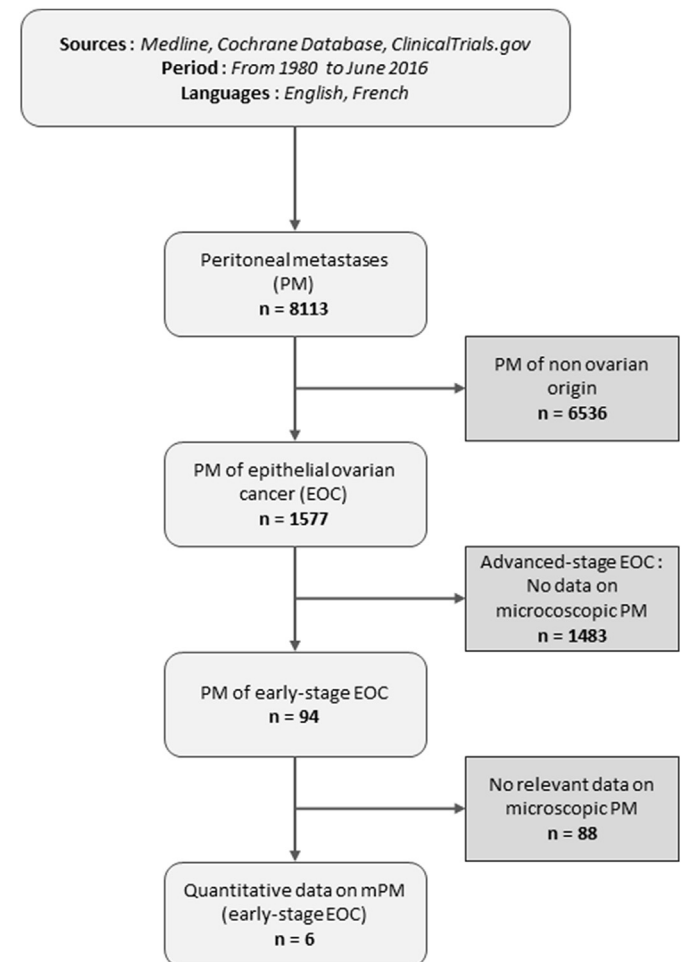
2. Sources

We reviewed all publications that deals with microscopic peritoneal metastases of epithelial ovarian cancer in French and English. Eligible studies, published from 1980 to June 2016, were retrieved through ClinicalTrials.gov, MEDLINE, Cochrane databases and bibliography searches, with the search terms “epithelial ovarian cancer”, “peritoneal metastases”, “microscopic metastases”, “peritoneal recurrences”, “HIPEC”, “intraperitoneal photodynamic therapy”.

3. Study selection

Only six publications met our inclusion criteria. No clinical trial has been found that specifically focus on the subject of this review. To discuss expected benefits of intraperitoneal chemotherapy, fluorescence-guided surgery or intraperitoneal photodynamic therapy, we reviewed most recent and relevant studies as those subjects were not the main objective of this review. Concerning intraperitoneal chemotherapy, we chose to focus only on ovarian cancer applications, although many data exist from digestive

cancer. The final reference list was generated on the basis of originality and relevance to the broad scope of this review.



Quantitative data on microscopic peritoneal metastases of epithelial ovarian cancer. Study selection.

4. Peritoneal metastases from ovarian cancer

Peritoneal metastases from EOC occur by transcoelomic route. Cells from the primary tumor detach and are disseminated through the peritoneal cavity with the peritoneal fluid leading to direct implantation on the peritoneal surface [11]. Peritoneal carcinomatosis appears in the form of numerous flat lesions on the visceral or parietal peritoneum. They are present at diagnosis in 70–75% of cases.

It has been clearly established that complete surgical removal of macroscopic lesions improves overall survival (OS) and progression-free survival (PFS). In the *Cochrane Review* published by Elattar et al., analyses showed that in the groups of women in whom complete cytoreduction could be achieved (with no residual macroscopic disease, that is no visible disease), OS and PFS were significantly prolonged. Although PFS was not reported in all of the

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