Updates in Surgery

Angelo Di Giorgio
Enrico Pinto *Editors*
In collaboration with
Paolo Sammartino and Franco Roviello

Treatment of Peritoneal Surface Malignancies

State of the Art and Perspectives

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Foreword by
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Foreword

On the basis of the latest epidemiological data, peritoneal surface malignancies (PSM) represent a pathology characterized by a high annual incidence, between those of stomach and colorectal cancer.
The integration of cytoreduction surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), variously combined with other adjuvant and neoadjuvant chemotherapeutic regimens, is an example of the increasingly complex care strategy for PSM.

There is a strong rationale behind combining CRS with HIPEC to create a procedure based on the evolutionary history of PSM, once considered to be caused only by locally advanced malignancies of the abdominal cavity free of distant metastases. Over the past 20 years, the consistency of results of this integrated procedure has led to it now being considered the treatment of choice for carcinomatosis from pseudomyxoma peritonei, mesothelioma and, recently, the colon, with low peritoneal spread. Furthermore, the trend in using this procedure is increasingly being applied to treat gastric and ovarian carcinomatosis and rarer forms of peritoneal diseases, such as peritoneal metastases from breast and pancreatic cancer and sarcomatosis.

Experience to date using this treatment modality has identified the most significant prognostic parameters and the most important risk factors associated with the procedure. This monograph is thus based on contributions from some of the major Italian centers devoted to treating PSM. It provides the most significant updates on diagnosis, treatment, and outcomes obtained so far. The text thoroughly summarizes the state of the art on CRS plus HIPEC and identifies future development perspectives on related research.

Rome, September 2014

Giorgio De Toma
President, Italian Society of Surgery

Preface

A variety of tumors originating from intra- or extra-abdominal viscera and, more rarely, from the peritoneal membrane, spread or metastasize to the visceral and parietal peritoneum. The term peritoneal surface malignancy (PSM) encompasses all these forms and thus identifies a heterogeneous family of primary or metastatic tumors with epithelial or mesenchymal origin. The inclusion of various forms of primary and secondary PSM under a unique definition is justified by the substantial uniformity of their clinical evolution within the abdominal and pelvic cavity, leading to production of tumor implants and ascites until fatal obstruction occurs. Prognosis is poor, and palliative therapy has long represented the only treatment option. In the natural history of PSM, evolution can be slow and metastatic development late, so that many forms represent ideal targets for aggressive locoregional therapies.

In the 1980s, Paul Sugarbaker theorized – following countless pharmacokinetic and pharmacodynamic studies – about advantages of the association between maximal surgical cytoreduction [peritonectomy (PRT)], aimed at removing all visible implants, and hyperthermic intraperitoneal chemotherapy (HIPEC), aimed at treating microscopic or millimetric residues. Since the 1990s, this concept has gradually gained acceptance and currently is the intervention of choice for pseudomyxoma peritonei and mesothelioma, but it is also diffusely used to treat carcinomatosis from colorectal, gastric, and ovarian cancer and peritoneal sarcomatosis. For the most common forms of PSM treated with PRT plus HIPEC, experiences available to date consistently show overall results better than or highly competitive with traditional treatment modalities. PSM forms that until two decades ago were considered untreatable surgically and for which progression was fatal within months of diagnosis, today, after appropriate patient selection, are routinely treated with PRT plus HIPEC, resulting in improved patient quality of life and long-term survival rates. The combined procedure achieves acceptable postoperative morbidity and mortality rates in relation to its complexity and duration (median 10 h) similar to those of major abdominal and pelvic surgery.

However, the procedure has limited application considering the high overall incidence of various forms of PSM and is not exempt from criticism. The limited

diffusion of PRT plus HIPEC treatment is related to the long learning curve; availability of relevant human, technical, and economic resources; and skepticism toward its effectiveness, particularly in reference to HIPEC, which is considered potentially risky during the postoperative course. Furthermore, the main criticisms concern the lack of prospective randomized phase III studies to define clearly the role of HIPEC, given that the validity of maximum cytoreduction is accepted worldwide. Indeed, to date, overall results of prospective trials for HIPEC are scarce and heavily criticized for the general treatment approach, lack of homogeneity of surgical techniques, and wide dispersion of enrolled cases. Therefore, results regarding overall significance of this procedure come mainly from multi-institutional studies, reviews, meta-analyses, and studies conducted in single centres with a high volume of PRT plus HIPEC activity. While taking into account the limitations inherent in such studies, the magnitude of experience gained to date reveals the overall trend of results. The great effort made by surgeons, oncologists, and specialized centers dedicated to treating PSM using PRT plus HIPEC has brought about the possibility of successfully treating aggressive locoregional tumors such as PSMs. It now remains for the inevitable upcoming prospective studies to confirm the promising results obtained thus far with this combined treatment modality and to determine the most appropriate ways to address treatment for PSM.

The purpose of this monograph is to provide a summary of the knowledge base supporting the rationale of associating maximum cytoreduction with HIPEC, pathological assessment and diagnostic workup of patients with PSM, surgical and HIPEC techniques, and management results of the most common forms of PSM. In the world that revolves around PSM management, Italy plays a significant role, as demonstrated by case series treated by the various PSM centers in this country and the vast scientific contribution drawn from the literature and from acts of the major international conventions. Collaboration between many of the most important specialized Italian surgeons and treatment centers has helped provide an overall picture that illustrates the state of the art regarding PSM management. The topics discussed, and the opinions, experiences, and conclusions expressed by the various authors of these chapters, provide an in-depth summary of experiences pertaining to the most critical issues and outline goals to be achieved in the coming years through collective and coordinated efforts.

Rome, September 2014

Angelo Di Giorgio
Enrico Pinto

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