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Chapter 6

Abdominal Advanced Oncologic Surgery

Enrico Maria Pasqual and Serena Bertozzi

Additional information is available at the end of the chapter

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1. Introduction

1.1. The peritoneal cavity, locoregional area

The peritoneal cavity, enclosed by visceral and parietal peritoneum , is the largest potential space in the body. With its own vascularization and lymphatic drainage, is anatomically separated from the general body system and other body compartments.

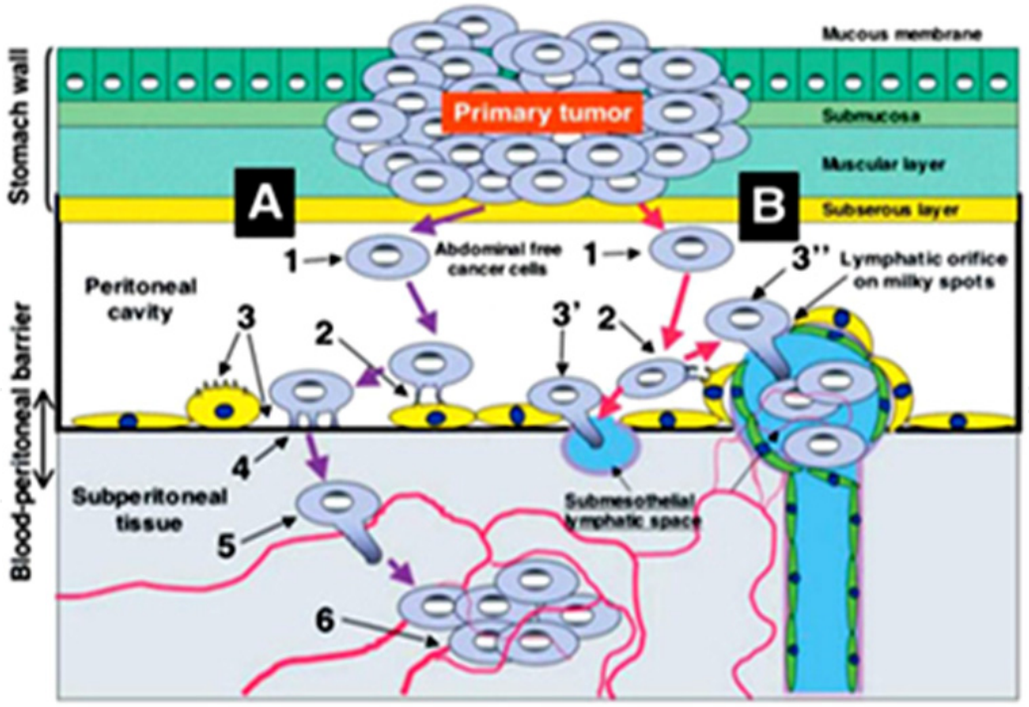


Figure 1. Mechanisms of peritoneal cancer cells seeding.

Any pathological process involving the peritoneal cavity can easily disseminate throughout this space by means of unrestricted movement of fluid and cells. Accordingly malignant

intraperitoneal tumour progression, before reaching the circulation system and developing distant metastases (pulmonary, brain and bone metastases) diffuses within and through the peritoneal cavity (Fig. 1). At this step intraperitoneal tumours must be considered in locoregional stage.

Peritoneal neoplasia can originate de novo from the peritoneal tissues (primary tumour) or invade or metastasize into the peritoneum from adjacent or remote organs (metastases).

Rare are the primitive tumours of the peritoneum: they include malignant mesothelioma, peritoneal primary carcinoma and sarcoma.

Malignant peritoneal mesothelioma is a rare but aggressive tumor derived from the peritoneal mesothelium accounting for 2 cases per 1 million population reported each year in USA. Association of malignant peritoneal mesothelioma and asbestos exposure has been reported to be as high as 83%. This locally aggressive disease is difficult to treat or palliate. Commonly, treatment regimens combine aggressive cytoreductive surgery with intraperitoneal chemotherapy. Cytoreductive surgery is the cornerstone of current treatment, while hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) is a promising strategy in suitable patients (Deraco *et al.*, 2002) (Fig. 2).

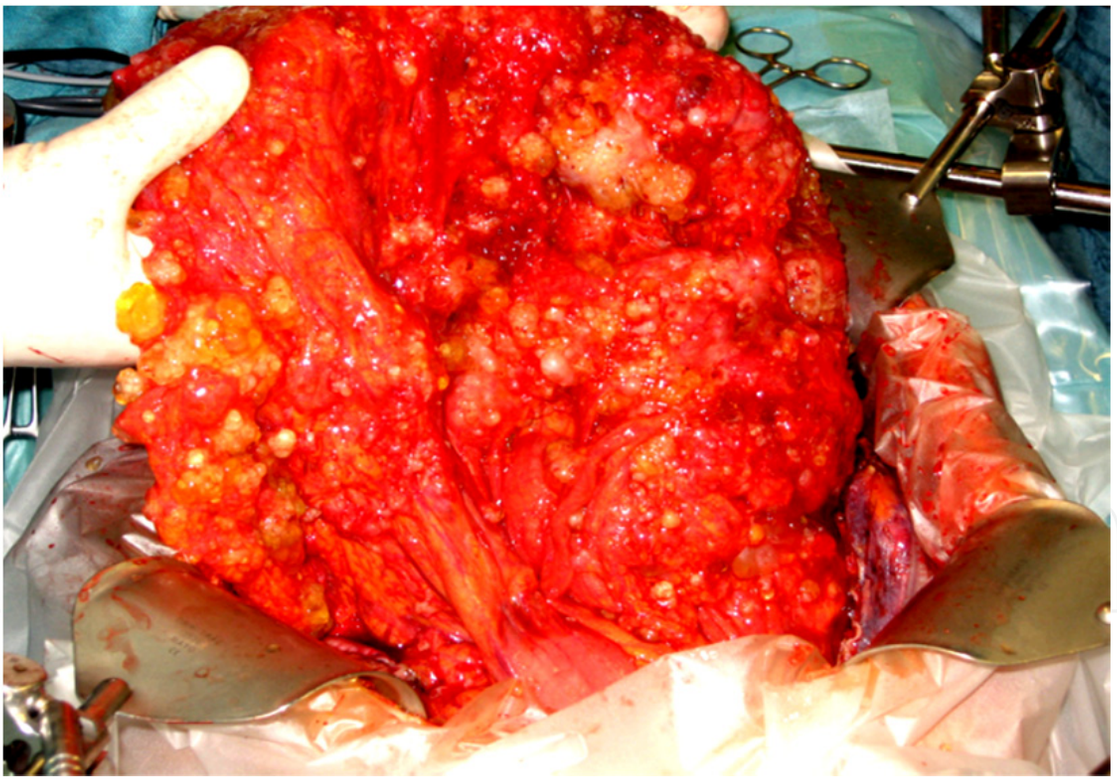
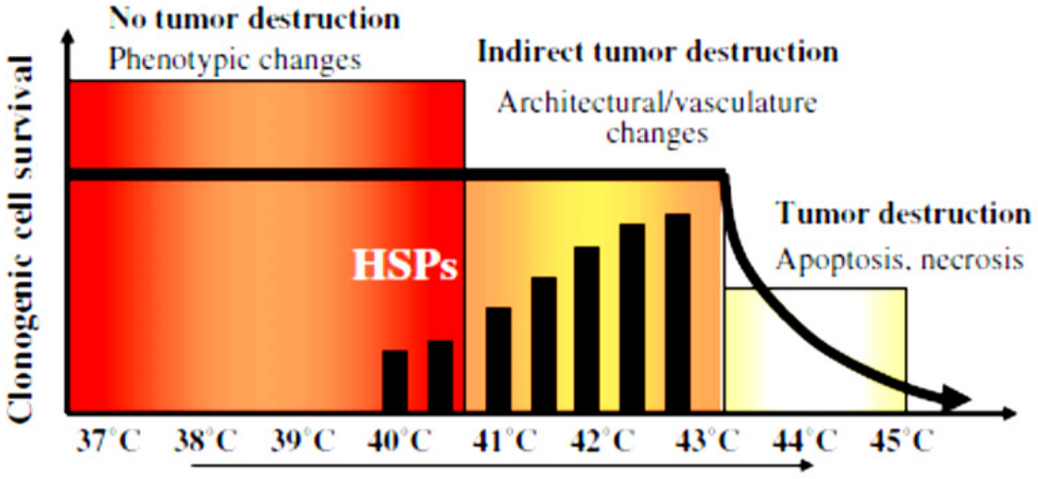


Figure 2. Omental cake.

Primary peritoneal carcinoma is a very rare tumour and (ie, serous surface papillary carcinoma) arises primarily from peritoneal cells. This malignancy predominantly affects postmenopausal women and typically displays multicentric peritoneal and omental involvement. Pathologically and clinically, it resembles papillary serous ovarian carcinoma.

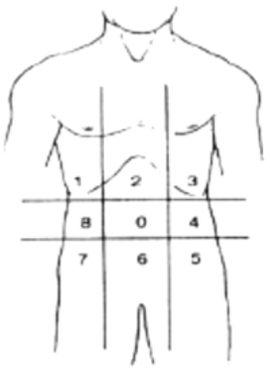
Many primary tumours, arising from organs placed within the peritoneal cavity, disseminate through it, leading patients to death. Peritoneal cavity represents the site of metastases in 50% of colorectal cancer, 50% of gastric cancer and 75% of ovarian advanced cancer. It represents the sole site of intraperitoneal metastasis in 20-25% of colorectal cancer, 30% of gastric cancer and 70% of ovarian cancer (Koppe *et al.*, 2006; Randall and Rubin, 2001; Sadeghi *et al.*, 2000). Intraperitoneal drug administration studies confirmed the existence of a peritoneal-plasma barrier which allows to concentrate the antiblastic drug within the cavity even 100-1000 times compared with that of the same drug infused through systemic circulation. Therefore a high antiblastic tumour tissue concentration and a low systemic toxicity can be achieved (Flessner, 2005). In association with intraperitoneal chemotherapy, hyperthermia has been demonstrated to enhance drug diffusion within the tumour tissue and also to have a direct antitumour activity (Issels, 2008) (Fig. 3)

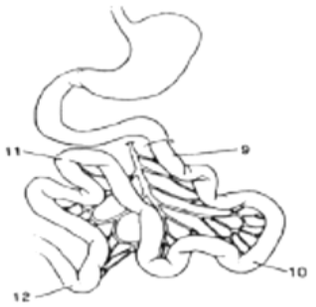


Molecular response	Cell cycle; DNA repair Apoptosis/Necrosis Induction of heat shock proteins/HSP-70 membrane expression
Clinical setting	Thermosensitisation for chemotherapy and/or radiation

Figure 3. Hyperthermia effects on tumour cells.

Therefore cytoreduction and HIPEC procedure have been suggested to treat metastases from colorectal , gastric and gynaecological tumors (Sugarbaker, 1995). Results after treatment are encouraging in particular in cases of colorectal and gynaecological cancer with median 5 years survival respectively of 40% and 45%. Less satisfactory results have been obtained in case of gastric and pancreatic cancer with a minimal percentage of patient still living far from initial diagnosis (Elias *et al.*, 2006; Roviello *et al.*, 2011). The aggressive tumour surgical removal (tumour cytoreduction) coupled with intraperitoneal chemotherapy nowadays represents the cornerstone of advanced abdominal oncologic surgery (Glehen *et al.*, 2006; Glockzin *et al.*, 2009). A large international experience was therefore made through the last decades with the goal of allowing treatment and possibly cure of intraperitoneal tumours in advanced stage (Levine *et al.*, 2007; Roviello *et al.*, 2011).





Regions		Lesion Size	Lesion SizeScore (the largest implants scored in each regions)
0	central	_____	**LS 0** No tumor seen
1	Right upper	_____	**LS 1** ≤ 0.5 cm
2	Epigastrium	_____	**LS 2** > 0.5 cm to ≤ 5.0 cm
3	Left upper	_____	**LS 3** > 5 cm or confluence
4	Left flank	_____	
5	Left lower	_____	
6	Pelvis	_____	
7	Right lower	_____	
8	Right flank	_____	
9	Upper jejunum	_____	
10	Lower jejunum	_____	
11	Upper ileum	_____	
12	Lower ileum	_____	
	PCI	**0-39**	

Figure 4. Peritoneal cancer index to map carcinosis localization.

2. Cytoreduction and intraperitoneal hyperthermic chemotherapy (HIPEC)

Advanced metastatic tumour can therefore be treated with surgery and hyperthermic chemotherapy contemporarily, during the same surgical operating work up. The first step is to carry out an aggressive cytoreduction in order to remove the whole macroscopic intracavitary tumour tissue and then to complete the procedure with HIPEC, to kill residual neoplastic cells floating within the peritoneal cavity or adherent to intraperitoneal tissue.

2.1. Cytoreduction

The surgical procedure of cytoreduction is now well standardized . Sugarbaker's classification is still the reference for abdominal oncologic surgery and goes under the definition of peritonectomy. The surgical procedure was classified according to specific different areas of the abdominal cavity and it has been tailored by Milan 's panel workshop, defining (Fig. 4):

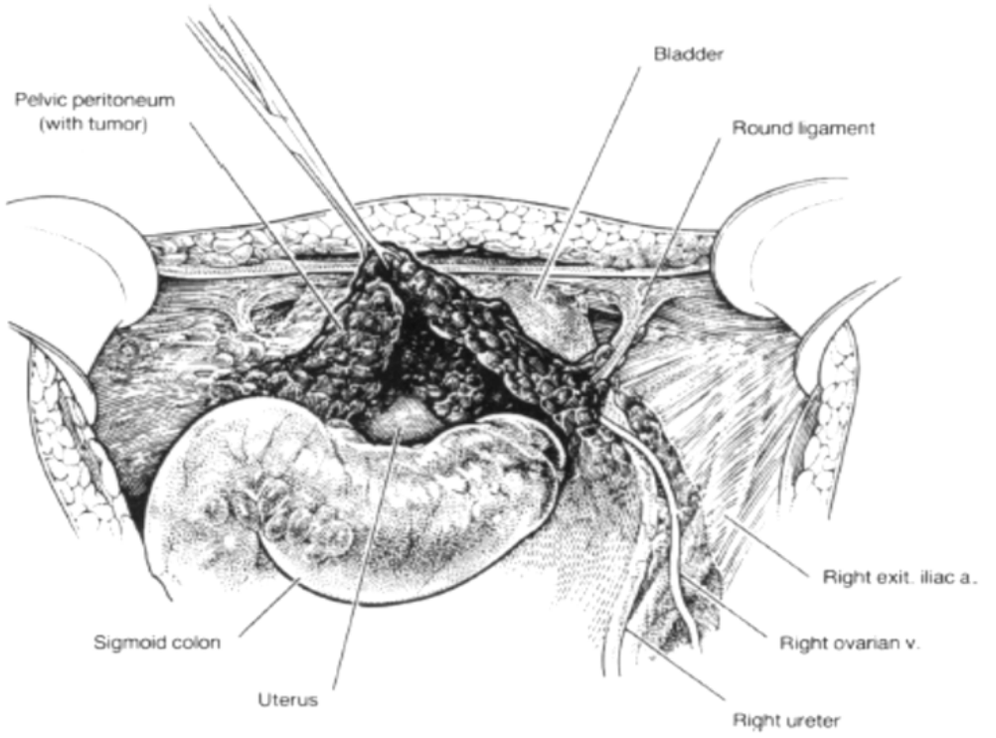


Figure 5. Surgical cytoreduction.

1. Upper RightPeritonectomy: right diaphragmatic peritonectomy with Glisson's capsule dissection; lesser omentectomy, stripping of the omental bursa and cholecystectomy plus gastric antrectomy or total gastrectomy.
2. Upper Left Peritonectomy: left diaphragmatic and parietal peritonectomy with splenectomy and greater omentectomy.
3. Pelvic Peritonectomy: pelvic parietal peritonectomy, sigmoidectomy, hysterectomy and salpingo-ovariectomy.
4. Right Parietal Peritonectomy, right/total colectomy; left parietal peritonectomy.
5. Mesenteric implants on visceral surfaces could be removed surgically or by electrosurgical local dissection. Performing cytoreduction for peritoneal tumour dissemination, not all the procedures are necessary and made, usually necessitating one – three of the different peritonectomy procedures (Fig. 4 and 5).

2.2. Intraperitoneal hyperthermic chemotherapy

After having made complete surgical cytoreduction with an absent or minimal residual disease (less than 2.5 mm tumour diameter) some catheters are inserted into the abdominal cavity and a perfusion of 2 liters of a saline solution with a determined quantity of antiblastic drug (Mytomycin, Oxaliplatin for digestive cancer and Cisplatin, Taxol for ovarian cancer) is made . The peritoneal perfusion may lasts 30-90 minutes and it can be performed in condition of closed abdomen or open abdomen (Coliseum technique) or a compromise between the two, with an abdominal- wall small entrance suitable for the handling by the operator. (Fig. 6).

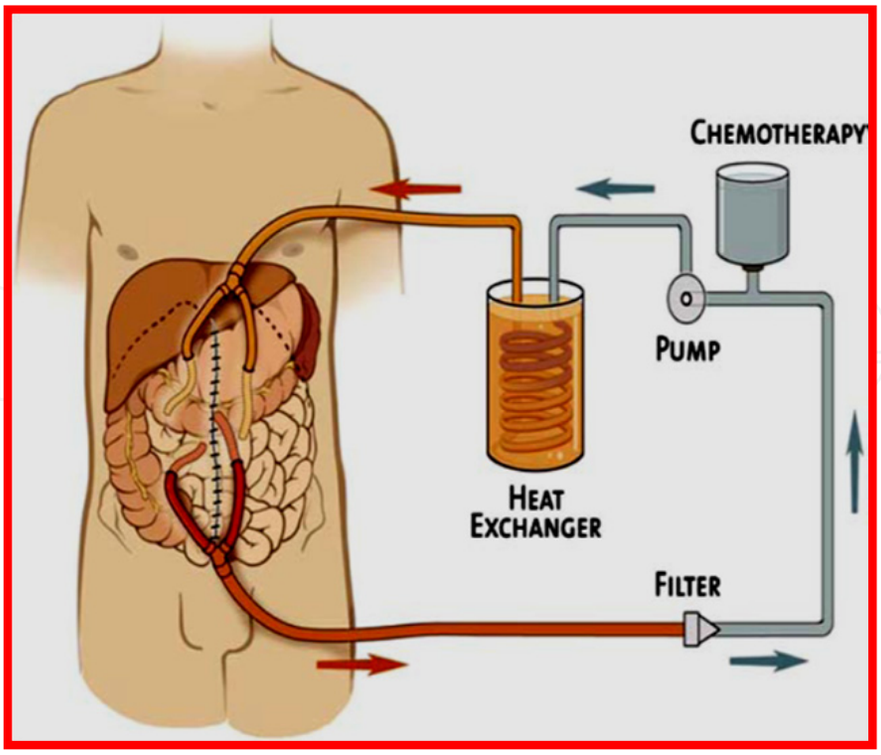


Figure 6. Hyperthermic intraperitoneal chemotherapy

Hyperthermic perfusion can be obtained by heating the perfusion medium with a heat exchanger connected to the perfusion pump. The peritoneal cavity temperature considered optimal in terms of antitumor activity and antiblastic tumour tissue diffusion is 41,5-42,5 °C (Sugarbaker and Chang, 1999; Sugarbaker, 1996; Van der Speeten *et al.*, 2009). It is of absolute importance to control the temperature of organs and bowels during the procedure. Excessive temperature of intraperitoneal tissue, more than 43 °C, is strongly correlated with lesions of the bowel wall and perforation, and also with necrosis of nerves, bladder or vases. To prevent excessive intraperitoneal temperature multiple temperature probes are placed within the peritoneal cavity to monitorate the temperature. At the end of the procedure the perfused medium is usually removed from the peritoneal cavity.

3. Advanced oncological surgery in colorectal cancer

Every year about 400.000 new cases of colorectal cancer (CRC) are diagnosed in Europe and 210.000 are believed to die of disease (Boyle and Ferlay, 2005). Peritoneal carcinosis (PC) has an incidence about 13% of CRC, in 58% of cases is synchronus with primary disease and in most cases is not diffused to the entire abdominal cavity but limited to an area (Jayne *et al.*, 2002). Peritoneal cavity recurrence is the only site of relapse in about 25% of cases (Chu *et al.*, 1989). The principal mechanism of peritoneal cancer diffusion through the abdominal cavity is the esfoliation of cancer cells following bowel-serosa tumour infiltration. Also lymphatic channel infiltration by the tumour followed by breaking of the lymphatic channel wall and subsequently loss of neoplastic cells within the abdominal cavity is a mechanism of PC formation. Furthermore at the time of surgical work up tumour manipulation and blood loss

are also intracavitary mechanism of PC formation. Facing PC, both synchronous or metachronous, the usual treatment is systemic chemotherapy but median survival is usually not longer than 6 months even after the advent of new drugs and treatment scheme (Sadeghi *et al.*, 2000). More recently Dominique Elias has published an experience with patients with PC and absence of extra-abdominal disease by using modern scheme of chemotherapy FOLFOX (5-FU, AF and oxaliplatin) and FOLFIRI (5-FU, AF and irinotecan) obtaining a median survival of 23,9 months and a 2 and 5 years survival of 65% and 13% respectively (Elias *et al.*, 2009). The advent of CRS with HIPEC have ameliorated the prognosis in these patients (Elias *et al.*, 2006; Verwaal *et al.*, 2005; Yan and Morris, 2008).

During the last decade a randomized study , two multicentric comparative studies and a numbers of observational studies have tested the CRS and HIPEC activity against PC from CRC with encouraging results: mortality and postoperative morbidity of 0-8% and 39-72% respectively and 5 years survival of 40-51% (Verwaal *et al.*, 2003, 2005; Elias *et al.*, 2009, 2006; Franko *et al.*, 2010). Main indications for application of the procedure are the presence of PC both synchronous or metachronous , therefore defining it a therapeutic procedure. But recent experiences also suggest the possible use of HIPEC in adjuvant setting after radical surgery work up. Not all patients with CRC could benefits from this approach. A number of risk factors for PC development have been demonstrated: minimal PC which was macroscopically visible, completely resected or ovarian metastasis (also resected), synchronous with the primary tumour or a perforated primary tumor inside the peritoneal cavity, primary CRC presenting with occlusion or haemorrhagia. Patients bearing these risk factors and treated with cytoreduction and HIPEC at the end of cytoreduction (no residual tumour disease was present - R0 resection) showed, in preliminary experiences, impressive results with a 5 years survival percentage reaching 90% and a 5 years disease free survival of more than 40% (Elias *et al.*, 2009). This preliminary experience supports a large number of multi-istitutional ongoing worldwide studies to confirm the role of cytoreduction and hyperthermic intraperitoneal chemoperfusion in adjuvant setting at the same time of primary surgery or after a planned second look exploration. This new therapeutic approach even if after a long maturation phase lasting more than a decade, now seems to be accepted as a new frontier to treat advanced CRC and world wide surgical units have been created to coordinate and carry on the associated medical activity.

4. Advanced oncological surgery in gastric cancer

PC from gastric cancer arises following tumours invasion of the gastric serosa as depicted in Fig. 7. Also histological type can be crucial in PC gastric developing. Gastric tumours of the diffused type seems to represent a risk factor for PC and it has been demonstrated to relapse in about 50% of cases even after curative surgical resection (Marrelli *et al.*, 2002). It has been shown that the serosal tumor invasion is correlated to the detection rate of intraperitoneal free cancer cells. The treatment of peritoneal carcinomatosis from gastric cancer by peritonectomy and HIPEC has demonstrated not so good long-term results when compared with the treatment of PC from other causes (Stewart *et al.*, 2005). Anyway conventional treatment using palliative systemic chemotherapy showed a very dismal prognosis

(Hanazaki *et al.*, 1999). Long survival after peritonectomy and HIPEC for carcinomatosis arising from gastric cancer are possible if the extension of the carcinosis is low and the cytoreduction is complete. 3-year survival of 41% and 5-year survival rates of 11% was reported (Sayag-Beaujard *et al.*, 1999; Yonemura *et al.*, 2001, 1996). CRS and HIPEC of the PC seems to allow longer survival even if hyperthermic intraperitoneal chemoperfusion role is still under evaluation.

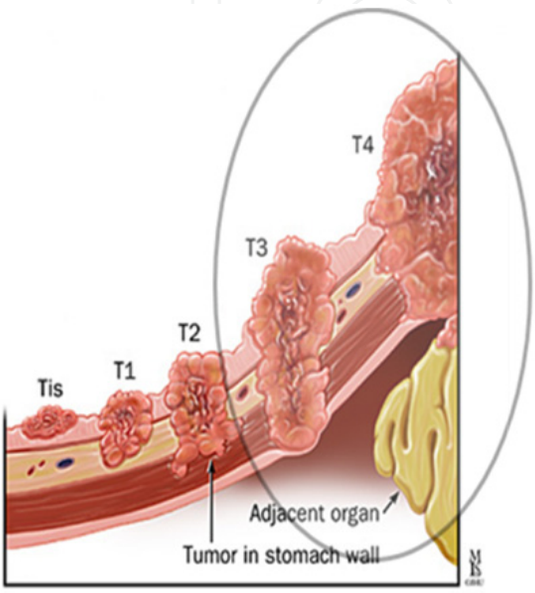


Figure 7. Invasion of the gastric serosa.

Recent experiences with HIPEC have shown quite encouraging results in case of prevention of peritoneal recurrence after radical surgery for primary carcinoma, the adjuvant role. When curative gastrectomy is performed, in fact, peritoneal recurrence develops in nearly 50% of patients , therefore prevention of PC developing represent a fundamental goal in this setting (Yonemura *et al.*, 2001, 1996; Fujimoto *et al.*, 1999; Shen *et al.*, 2009). Worldwide experiences are ongoing to ascertain the role of HIPEC in adjuvant setting and definitive results will be available in a short time.

5. Advanced oncological surgery in ovarian cancer

Epithelial ovarian cancers account for 80% to 90% of all ovarian malignancies and are the main cause of death for all gynaecological tumors (Yancik, 1993). Despite being diagnosed frequently at an advanced stage, dissemination is often confined to the peritoneal cavity (Randall and Rubin, 2001). It presents with vague gastrointestinal and constitutional symptoms of abdominal bloating, distension, weight loss, and fatigue (Goff *et al.*, 2000). Late presentation results in the majority of patients being diagnosed with advanced disease (Stage III/IV). The 5-year survival rate of patients with advanced ovarian cancer is <25% (Ozols, 2005). In the final stages of this disease, patients suffer from severe anorexia, dyspnea and pain from malignant bowel obstruction, ascites, and pleural effusion as a result of the extensive burden of tumor.

Epithelial ovarian tumor arises from the serosal lining of the ovary. This covering of the ovary communicates with the serosal lining of the abdominopelvic cavity, and is known as the peritoneum. Tumor growth results in the exfoliation of malignant cells into the peritoneal fluid. They circulate freely and typically implant in the pelvis and subdiaphramatic recesses owing to gravity and the incumbent position. Intraoperatively, it is characterized by the extensive presence of macroscopic whitish tumor nodules of variable sizes and consistency that may coalesce to form plaques or masses within the abdominopelvic cavity.

Tumor dissemination from the primary tumour may also occur through the lymphatic channel disrupted by the tumour and the direction of neoplastic cell diffusion is all through the abdominal cavity.

CRS using limited peritonectomy procedures to resect peritoneal implants and HIPEC aims to allow both macroscopic cytoreduction through surgery and cytotoxic cytoreduction through loco-regional administration of heated chemotherapy. Cytoreduction and HIPEC has been tested in different routes; front line when treating the primary cancer, as interval surgery after neoadjuvat chemotherapy in case of unresectable cancer, as treatment of ovarian cancer relapses and even in case of salvage therapy (Look *et al.*, 2004).

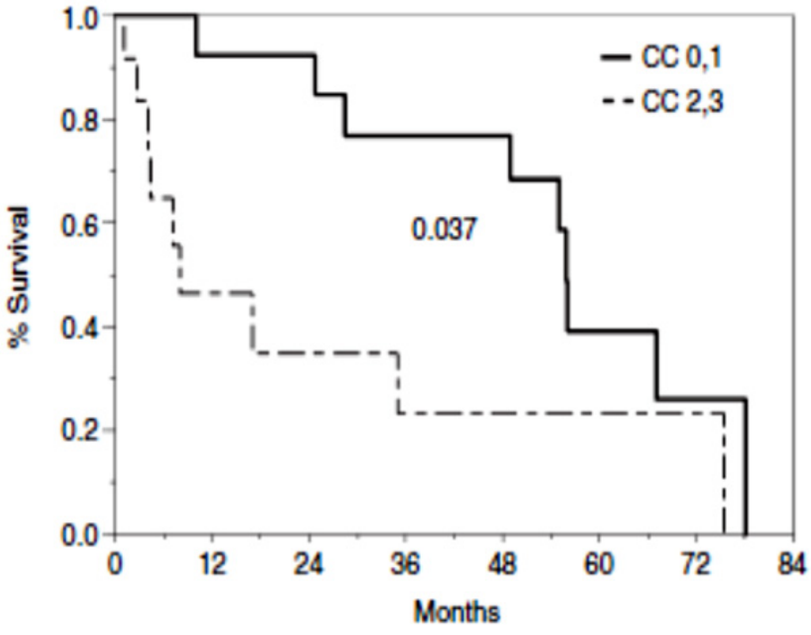


Figure 8. Ovarian cancer survival in compete and non complete cytoreduction.

The largest experience to date was reported by Bereder who reported a median overall survival of 46 months in patients with first relapsed ovarian cancer of which a proportion are chemoresistant. In their institutions, the mortality rate was under 1% and the morbidity rates were about 10%.The treatment related complications is considered acceptable and further large volume peritonectomy units have low morality rates that range from 0 to 2% (Raspagliesi *et al.*, 2006; Bereder *et al.*, 2009; Look *et al.*, 2004). Nowadays there is large

agreement on the role of extreme cytoreduction of peritoneal carcinosis in case of ovarian cancer. Two groups of patients are then obtained: those with residual disease no more than 2.5 mm in diameter corresponding to the completeness cytoreduction rate CC0-1 and those with residual disease more than 2.5 mm CC2-3. The first group with a complete tumour eradication shows a significative better survival (Fig. 8).

Promising results have been published during this decade improving survival and disease free survival. This particular indication for this complex procedure represents a very promising but also conflicting tool because of the high drug Platinum sensitivity of ovarian cancer which makes medical oncologist to be confident with systemic chemotherapy results. Unfortunately despite a great number of patients optimally treated in this way a significant fraction of them relapse (50-70%) and in this case it is reasonable to think that extreme cytoreduction and HIPEC can be helpful.

6. Advanced oncological surgery in malignant peritoneal mesothelioma

Diffuse malignant peritoneal mesothelioma (DMPM) is a relatively uncommon peritoneal malignancy, representing 20-30% of 2.200-2.500 new cases diagnosed every year in USA, but its incidence has been rising worldwide since 1970s and is not expected to peak for another 5 to 20 years. The reason lays in its recognized association with asbestos exposure, which has been extensively used in the past as building material (Battifora, 1995; Robinson and Lake, 2005). Along with the occupational exposure, DMPM has been reported following radiation therapy, mica exposure, recurrent peritonitis and thorium dioxide administration (Maurer and Egloff, 1975; Antman *et al.*, 1983; Chahinian *et al.*, 1982; Riddell *et al.*, 1981).

It is characterized macroscopically by thousands of whitish tumor nodules of variable size and consistency that may coalesce to form plaques or masses that may layer out to uniformly cover the entire peritoneal surface. Traditionally, DMPM was considered a preterminal condition, as the majority of patients died from intestinal obstruction or terminal starvation within the first year from the diagnosis (Yan *et al.*, 2007). Despite its generally local spread without lymphoadenopathy or distant organ metastases, its poor prognosis may be explained by late diagnosis, due to the aspecificity of presenting symptoms (abdominal pain, girth, ascitis,...) and the inadequateness of most imaging tools in detecting small nodules on the whole peritoneal surface. Furthermore, no uniform treatment was initially suggested for this kind of malignancy, systemic chemotherapy and abdominal radiation therapy showed scarce results and were used only in selected patients, and surgery had only a palliative role to resolve intestinal obstruction in urgency without any significant effect on patients prognosis (Chailleux *et al.*, 1988; Antman *et al.*, 1983; Eltabbakh *et al.*, 1999; Markman and Kelsen, 1992; Neumann *et al.*, 1999; Sridhar *et al.*, 1992; Yates *et al.*, 1997). Recently, diagnostic and therapeutic aspects of the disease have been re-evaluated as encouraging reports from several centers worldwide on a combined locoregional treatment approach that uses cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have emerged. This new treatment strategy has shown favorable prognosis and has achieved in selected patients a median survival of up to

60 months and a 5-year survival of 50% using different antiblastic sequence (Deraco *et al.*, 2006; Nonaka *et al.*, 2005; Park *et al.*, 1999; Sugarbaker *et al.*, 2003; Yan *et al.*, 2007).

Given its tendency to remain confined to the peritoneal surface, the prognosis of DMPM has been significantly improved by the combined treatment with CRS and HIPEC. In particular, while CRS reduces the tumoral mass (an optimal cytoreduction aims to residual disease smaller than 2,5mm), HIPEC maximizes loco-regional chemotherapy cytotoxicity while limiting the systemic side effects (Vlasveld *et al.*, 1991; Markman, 1990; Markman and Kelsen, 1992). In this perspective, some encouraging experiences in numerous centers demonstrated a median survival of 40 to 90 months and a 5-ys-OS of 30 to 60% (Yan *et al.*, 2007; Brigand *et al.*, 2006; Deraco *et al.*, 2006; Feldman *et al.*, 2003; Loggie *et al.*, 2001; Nonaka *et al.*, 2005; Park *et al.*, 1999; Sugarbaker *et al.*, 2003). All peritonetomy center agree that complete cytoreduction is the prognostic principal factor for clinical success and that complete cytoreduction is correlated to the initial extent of intrabdominal disease and to the ability of the surgical team. Despite the data available, the role of HIPEC in this setting represents one of the strongest indications, particularly in view of considerable survival improvement over the best systemic therapy to date offered (Munkholm-Larsen *et al.*, 2009; Shen *et al.*, 2009).

7. Advanced oncological surgery in pseudomyxoma peritonei

Appendiceal tumors are uncommon neoplasms accounting for about 1% of all colorectal malignancies.

The majority of appendix cancers are carcinoid tumors; the second most common are epithelial neoplasms. The latter frequently present with mucinous ascites and mucinous tumor implants throughout the abdominal cavity. Such rare condition, with an incidence of approximately 1/1,000,000/year, is known as pseudomyxoma peritonei (PMP). Mucinous adenocarcinoma originating from large bowel, ovary, or other intra-abdominal sites may mimic PMP (Baratti *et al.*, 2008). According to Ronnett, PMP was histologically classified into disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinomatosis (PMCA), and intermediate or discordant feature group (ID). Appendiceal tumors were classified into low-grade appendiceal mucinous neoplasm (LAMN) and mucinous adenocarcinoma (MACA) (Misdraji). Pseudomyxoma peritonei (PMP) represents a rare peritoneal malignancy with a controversial bordeline behavior. Although a possible ovarian origin was initially suggested in the female sex, the over-expression of determined molecular markers has finally demonstrated a more probable PMP origin from a perforated appendiceal epithelial tumor. Undoubtedly, a small proportion of cases originate anyway from other organs, which ovarian primary is likely to be the more commonest of, followed by colon and rectum, stomach, gallbladder and biliary ducts, small bowel, urinary bladder, lung, breast, falloppian tube and pancreas (Smeenk *et al.*, 2006, 2007; de Bree *et al.*, 2000).

PMP is clinically characterized by diffuse intra-abdominal gelatinous collections with mucinous implants on peritoneal surfaces. Its pathognomonic accumulation at specific abdominal and pelvic sites is due to the so-called phenomenon of “redistribution” within

the peritoneal cavity, which is determined by physical factors, such as the movement and absorption of peritoneal fluid and gravity (Sugarbaker, 1994). Despite its usually indolent behavior, its natural history is characterized by a slow progression to terminal starvation through intestinal obstruction by mucinous ascitis. Recent pathological (Ronnett *et al.*, 1995) molecular genetic (Szych *et al.*, 1999) and immunohistochemical studies (Carr *et al.*, 2002) have provided substantial evidence that most cases of PMP originate from ruptured low grade appendiceal tumors and that mucin-producing epithelial cells accumulate into the abdominal cavity as a result of a distribution process.Therefore, surgical management consisted in repeated interval debulking for symptomatic relief (Sugarbaker, 1996). Based on recent prospective trials, CRS and HIPEC has been proposed as the standard of care for PMP. Results are encouraging with a 5-ys-OS ranging from 62.5 to 100% for low grade PMP and from 0 to 65% for high grade disease . This differentiation is crucial for the evolution of disease; low grade tumours are slow growing and indolent differently from those high grade, fast growing and aggressive (Sugarbaker and Chang, 1999; Witkamp *et al.*, 2001; Güner *et al.*, 2005; Moran *et al.*, 2008; Moran and Cecil, 2003; Murphy *et al.*, 2007; Baratti *et al.*, 2008; Elias *et al.*, 2008; Loungnarath *et al.*, 2005; Smeenk *et al.*, 2007; Stewart *et al.*, 2005; Yan *et al.*, 2006). The goal of the surgical cytoreduction is to remove all the visible tumor by the following procedures: right subdiaphragmatic and parietal peritonectomy, left subdiaphragmatic and parietal peritonectomy,greater omentectomy with splenectomy, lesser omentectomy and stripping of the omental bursa, andpelvic peritonectomy with salpingo-oophorectomy in women. Depending on disease extent, implants on visceral serosa were removed by electrosurgical local dissection or multivisceral resections including Glisson's capsule dissection, cholecystectomy, partial or total gastrectomy, sigmoid, right or total colectomy. According to several phase I and II prospective trials, 5-year survivals have ranged between 66% and 97% (Stewart *et al.*, 2005). It must be taken in mind that, because of the limited data on prognostic factors for this procedure in the setting of appendiceal primary tumors, further well designed, prospective, multi-institutional study are required (Bevan *et al.*, 2010; Roviello *et al.*, 2011).

8. Conclusion

CRS and HIPEC is a complex therapeutic systems which require highly specialized human resources, complex technological facilities, very much depending from expertize of the team involved. Literature refers to a learning curve of more than 100 procedures underscoring the crucial importance of treatment center experience. A continuous comparison must be done with new systemic and locoregional treatment possibility in order to verify new advantages in term of patient survival. This is the reason why a biannual international meeting is planned for comparing results, verify indications and planning of further studies regard to indications, duration and temperature of the perfusion, open or closed perfusion models or type and dosage of chemotherapeutic agents.

The future of treatment of peritoneal carcinosis appears correlated to the strong cooperation with medical oncologists to select patients and focusing on the timing of treatment which in our experience is crucial. The development of new scheme treatment must be approached as in treating ovarian peritoneal carcinosis with front line, interval, or salvage procedures.

Therefore creating regional centers dedicated to peritoneal carcinosis treatment that investigate not only response and survival, but also standardization of technique and methods to do CRS and deliver HIPEC remains crucial.

Author details

Enrico Maria Pasqual and Serena Bertozzi
University of Udine, Italy

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