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Laparoscopic cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for limited peritoneal metastasis. The PSOGI international collaborative registry

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ABSTRACT

Introduction: A laparoscopic approach for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (L-CRS+HIPEC) in highly selected patients has been reported in small cohorts with a demonstrable reduction in length of stay and post-operative morbidity. This study aims to analyse individual patient data from these international centres collected through the Peritoneal Surface Oncology Group International (PSOGI) L-CRS+HIPEC registry.

Methods: An international registry was designed through a networking database (REDCAP®). All centres performing L-CRS+HIPEC were invited through PSOGI to submit data on their cases. Patient's characteristics, postoperative outcomes and survival were analysed.

Results: Ten international centres contributed a total of 143 L-CRS+HIPEC patients during the study period. The most frequent indication was low grade pseudomyxoma peritonei in 79/143 (55%). Other indications were benign multicyst mesothelioma in 21/143(14%) and peritoneal metastasis from colon carcinoma in 18/143 (12,5%) and ovarian carcinoma in 13/143 (9%). The median PCI was 3 (2-5). The median length of stay was 6 (5-10) days, with 30-day major morbidity rate of 8.3% and 30-day mortality rate of 0.7%. At a median follow-up of 37 (16-64) months 126/143 patients (88.2%) were free of disease.

Conclusions: Analysis of these data demonstrates that L-CRS+HIPEC is a safe and feasible procedure in highly selected patients with limited peritoneal disease when performed at experienced centres. While short to midterm outcomes are encouraging in patients with less invasive histology, longer follow up is required before recommending it for patients with more aggressive cancers with peritoneal dissemination.

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Introduction

The last two decades have seen an increasing role of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of peritoneal surface malignancies (PSM). Currently, the procedure has major morbidity and mortality rates that range from 22 to 34% and 0.8–4.1% [1,2] respectively. During this period, this multimodality approach has resulted in improved outcomes due to better selection of patients, progress on systemic treatments and improved perioperative management. Finally increasing awareness has led to patients with peritoneal metastases being referred for consideration of CRS + HIPEC at an earlier stage of their disease. The referral of patients with low volume peritoneal disease allow the opportunity to offer them laparoscopic CRS/HIPEC (L-CRS + HIPEC) with the potential to improve short-term outcomes and post-operative recovery without compromising long-term outcomes results [3–5].

L-CRS + HIPEC has been performed since 2011 [6] with promising results for patients with low volume peritoneal metastasis (low peritoneal cancer index (PCI)) from low grade appendiceal neoplasm with minimal morbidity and shorter length of stay. L-CRS + HIPEC involves the same procedures as open approach including peritonectomies and multivisceral resections in order to achieve a complete cytoreduction. After this, HIPEC is administered using a close technique with laparoscopic ports used for inflow and outflow catheters [7,8].

The most common indications for L-CRS + HIPEC include low grade tumours such as low grade appendiceal mucinous neoplasm (LAMN) causing low grade pseudomyxoma peritonei (LG-PMP) and multicystic peritoneal mesothelioma (MPM) [9,10]. For high-grade malignancies such as ovarian and colorectal cancer peritoneal metastasis the experience in L-CRS + HIPEC is more limited [5,11,12]. Risk Reducing (RR) L-CRS + HIPEC is a suggested approach aimed at avoiding peritoneal relapses in high risk patients such as those with perforated low grade appendiceal mucinous neoplasms (LAMN T4a) [9,13] or high risk colon cancers [14], however this indication needs further validation.

This study aims to present the results from the PSOGI L-CRS + HIPEC registry, providing an overview of worldwide trends and results from the minimally invasive approach to treat peritoneal metastasis across a range of pathologies. Collecting this data is critical to evaluating the outcomes from this technique, identifying challenges, and enabling its safe introduction.

Methods

L-CRS + HIPEC PSOGI registry

This PSOGI registry was developed in November 2019, to record the international experience from reference groups that use the laparoscopic approach for CRS and HIPEC in selected cases with PSM. A networking database (REDCAP®) was used to facilitate the introduction of cases to each collaborative group. The data were collected prospectively by groups performing the procedure and analysed retrospectively. Informed consent was obtained from all patients, with approvals from local research and ethics committees.

Study group

Consecutive patients undergoing L-CRS + HIPEC in PSOGI registered international reference centres were included in this database. In order to be considered a reference centre, the unit had to have performed at least 30 CRS/HIPEC procedures per year. L-CRS + HIPEC was defined as a procedure where the indication was to resect established low volume peritoneal metastasis. Patients underwent Risk-reducing laparoscopic HIPEC (RR-L-HIPEC) defined as a procedure where the indication was to prevent the development of peritoneal recurrence in high risk patients [13,14] without peritoneal disease (PCI = 0), were excluded from the analysis (Fig. 1).

For pseudomyxoma peritonei (PMP) the most recent PSOGI classification was used [15]. Patients with low-grade PMP (LG-PMP) selected for the procedure had limited peritoneal disease. For High-grade pseudomyxoma peritonei (HG-PMP) laparoscopy was undertaken to stage the patient, previously.

Patients with peritoneal metastasis from ovarian cancer were staged by laparoscopy before L-CRS + HIPEC. In order to undergo the procedure they had to have a PCI less than 10, no evidence of systemic metastasis and no evidence of large masses. For primary ovarian peritoneal metastasis (stage IIIc FIGO) an interval CRS and HIPEC was proposed after neoadjuvant therapy with carbo-taxol 3–4 cycles [16]. For limited peritoneal relapse the upfront L-CRS + HIPEC was used. For MPM with limited peritoneal disease the histologic diagnosis was confirmed at a mesothelioma reference centre [17]. Patients with colon carcinoma with localized peritoneal disease underwent to upfront L-CRS + HIPEC.

Operative technique

As this was a multicentre registry, there were some variations in equipment and operative steps in L-CRS + HIPEC between centres. In a common way, all patients were positioned in lithotomy position. Once pneumoperitoneum was achieved the entire abdominal cavity was visualized in a systemic manner for peritoneal disease using a 30–45° camera or flexible tip scope associated with table tilting to access all quadrants. The parietal and pelvic peritonectomy and total omentectomy were performed following the Sugarbaker's principles. Right parietal peritonectomy, total pelvic peritonectomy and omentectomy have previously been described [7,8].

Hyperthermic intraperitoneal chemotherapy (HIIPEC)

This was delivered using a closed technique [8]. The different HIPEC agents used are summarized in Tables 1. Centre varied slightly in the HIPEC protocols used. Oxaliplatin was delivered for

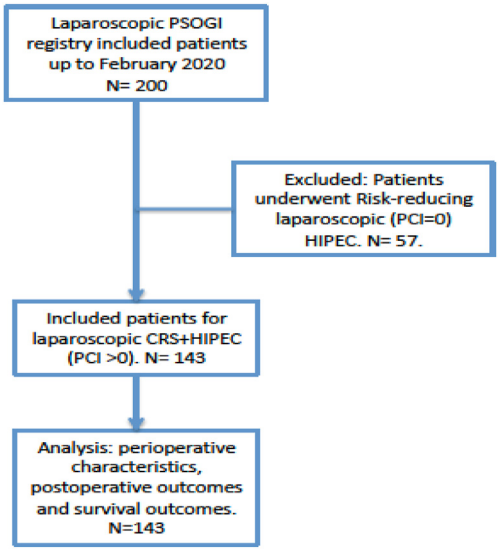

Fig. 1. Flow-chart laparoscopic PSOGI international registry.

Table 1
PCI: Peritoneal Cancer Index. BMI: Body Mass Index. CRP: C reactive Protein. PSS: Previous Surgical Score. DFS: Disease Free Survival. OS: Overall Survival. PMP: Pseudomyxoma Peritonei. MPM: Multicystic Peritoneal Mesothelioma. LAMN: Low grade appendiceal mucinous neoplasm. ♯ CRP at the second postoperative day. * 1 patient with appendiceal carcinoma, one patient with gastric carcinomatosis (PCI = 6) and one endometrial carcinomatosis.: Peritoneal relapse [1] hematogenous [8] and lymphatic [1], &: 28 patients classified by persistence were LAMN type II who had peritoneal spread with a PCI more than 0. ¶ 3 patients had peritoneal relapse. § 2 peritoneal and 1 lymphatic.: 2 peritoneal relapses.

Variables	CRS + HIPEC n = 143	Low PMP n = 79	MPM n = 21	Colon n = 18	Ovarian n = 13
Age (y)	53 (41–61)	52 (40–63)	45 (31–52)	62 (56–65)	55 (49–60)
BMI Kg/M2	25 [22–28]	54 (68%)	17 (81%)	5 (20,8%)	13 (100%)
Gender female	107 (75%)	26 [22–27]	21 [20–25]	28 (23–31)	23 [21–28]
PSS = 0 or biopsy	50 (41,2%)	18 (22,7%)	18 89,5%	10 (41,6%)	8 (61,5%)
1 region	67 (51,3%)	49 (62%)	3 10,5%	10 (41,6%)	3 (23%)
2-5 regions	8 (6,7%)	3 (3,7%)	0	4 (16,6%)	1 (7,6%)
>5 regions	1 (0,8%)	0	0	0	1 (7,6%)
Histology					
• Low grade PMP	79 (54,5%)				
• High grade PMP	8 (5,5%)				
• MPM	20 (13,9%)				
• Colon	18 (12,5%)				
• Ovarian Carcinoma	13 (9%)				
• Others*	3 (2%)				
Indication of procedure					
• Primary	96 (67,1%)	49 (62%)	21 (100%)	14 (58,3%)	10 (76,9%)
• LAMN type II	28 (19,5%)	30 (37%) &			
• Recurrence/Persistence	19 (13,2%)			10 [6,41]%	3 (23%)
PCI	3 [2–5]	3 [2–4]	3 [3–5]	5 [3–9]	4 [4,5]
Splenectomy	6 (4,1%)	1 (1,2%)	1 (4,7%)	1 (4,1%)	2 (15%)
Intestinal resection	34,5% (small bowel 13, colon 44, rectum 3)	22 (27,8%)	5 (23,8%)	19 (79,1%)	3 (23%)
Completeness Cytoreduction					
• CC0	97%	75 (95%)	21 (100%)	24 (100%)	12 (91,7%)
• CC1	3%	4 (5%)			1 (8,3%)
HIPEC time (min)	90 (60–90)	90 (60–90)	67 (60–90)	90 (60–90)	60 (60–60)
HIPEC drug used					
• Mitomycin C	72 (50,3%)	59 (74,6%)	0	15 (62,5%)	1 (7,6%)
• Oxaliplatin	31 (21,6%)	16 (20%)	0	9 (37,5%)	1 (7,6%)
• Cisplatin	3 (2%)	1 (1,2%)	3 (14,2%)	0	0
• Paclitaxel	9 (6,2%)	0	0	0	9 (69,2%)
• Cisplatin + Doxo	21 (14,6%)	0	18 (85,8%)	0	2 (15,3%)
• Mitomycin + Cis	6 (4,1%)	3 (3,7%)	0	0	0
Num peritonectomy procedures	1 [1,2]	1 [1,2]	1 [1,2]	1 [1,2]	2 [1–4]
Time of Surgery (min)	300 (240–472)	300 (240–495)	195 (150–300)	330 (270–360)	480 (330–480)
Blood loss (ml)	50 (50–100)	50 (50–68)	100 (0–100)	115 (42–195)	250 (100–300)
CRP ♯	54 (11–101)	10 (3,5–43)	72,8 (72–93)	–	109 (49–220)
lenght Stay (days)	6 [5–10]	6 [5–10]	9 [7–12]	6,5 [4,7–10]	5 [5–8]
Morbidity 30 d					
• No	106 (74,1%)				
• Grade 1:	12 (8,3%)	4 (5%)	1 (4,8%)	1 (4,1%)	5 (38,4%)
• Grade 2:	11 (7,6%)	7 (8,8%)	2 (9,5%)	0	0
• Grade 3A:	4 (2,7%)	0	1 (4,8%)	2 (8,2%)	1 (7,6%)
• Grade 3B:	5 (3,4%)	0	0	2 (8,2%)	0
• Grade 4A:	1 (0,7%)	0	0	0	0
• Grade 4B:	1 (0,7%)	1 (1,2%)	0	0	0
• Grade 5:	1 (0,7%)	0	0	0	1 (7,6%)
Readmission 30 d	8 (5,5%)	2 (2,4%)	0	4 (16,6%)	0
Time to Chemo (w)	4 [3–7]			5 (0–20)	4 [4,5]
Follow-up (months)	37 (16–64)	39 (24–62)	40 (10–65)	22,5 (4,5–66)	12 (5–30)
DFS (months)	40,5 (12–62)	44 (19–62)	44 (10–65)	26 (4–44)	12 (5–30)
OS (months)	43 (16–63)	45 (23–62)	44 (10–65)	37 (4–66)	14 (5–30)
Relapse	17 (11,8%) (10 peritoneal)	3 (3,7%)¶	no	8 (33%):	3 (23%) §
Secondary CRS + HIPEC	6 (4,2%)	2 (2,5%)	no	no	4 (30%)

30 min at 460 mg/m^2. Mitomycin C was delivered with dose between 15 and 30 mg/m^2 for 60–90 min. Cisplatin and Doxorubicin were delivered during 60–90 min at dose of 50 mg/m^2 + 15 mg/m^2 respectively.

Variables and statistical analysis

The variables were collected and reported as medians and ranges for quantitative analysis and percentages for qualitative analysis. Morbidity was recorded according to modified Clavien-Dindo classification [18]. PCI and completeness of cytoreduction (CC) score were describing according Sugarbaker's principles [19] Kaplan–Meier analysis was used to estimate patient survival stratified by histological groups. Statistical analyses were performed using the log-rank test ($P < 0.05$ was significant). All statistical analyses were performed with SPSS version 24.0 (IBM Corp, Armonk, NY, USA).

Results

Data from 200 patients operated on in ten centres between January 2004 to February 2020 was included on the PSOGI registry. One hundred and forty three patients who underwent L-CRS + HIPEC met the inclusion criteria for this study (Fig. 1). The percentage of patients included per centre is shown in Fig. 2 (Fig. 2).

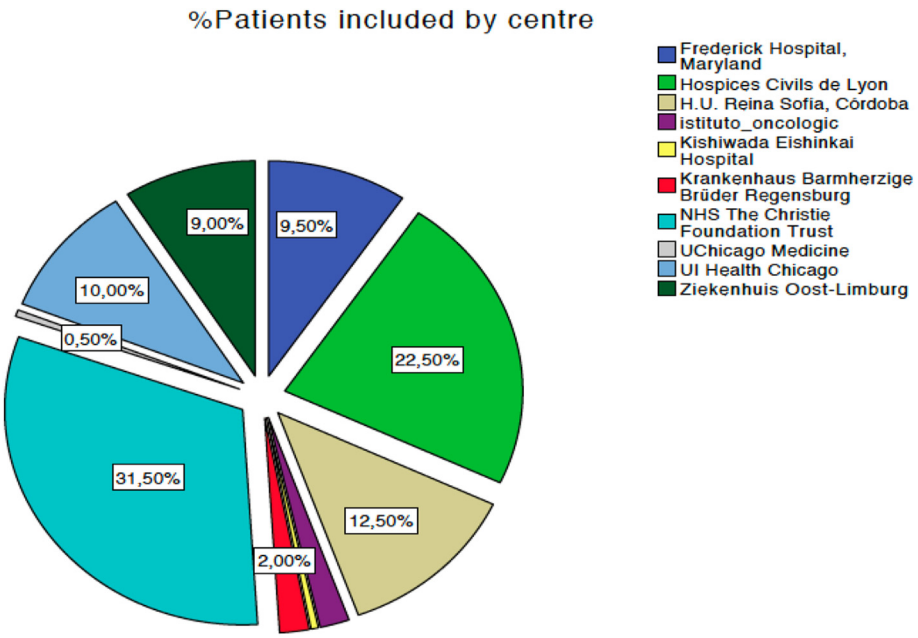

Fig. 2. Percentage of patients included in the Lap-CRS + HIPEC PSOGI registry per centre.

Patient characteristics

Patient demographics are described in Table 1. The median age was 53 (41–61) years, the median BMI was 25 [22–28], the median PCI was 3 [2–5] and the PSS was 0 or 1 predominantly. LG-PMP was the most common histology.

Surgical outcomes

The median duration for the complete procedure was 300 (240–472) minutes and CC0 was achieved in the 139/143 (97%) of cases. Intestinal resections were performed in 50/143 (34,5%). The median duration of HIPEC was 90 (60–90) minutes, and the drug most used was mitomycin C. The median number of peritonectomy procedures was 1 with a maximum of 4. The median length of stay was 6 days [5–10]. Major morbidity (Dindo Clavien ≥ 3) occurred in 12/143 (8,3%). Only one patient died secondary to serious heart insufficiency at 12th postoperative day. Hospital readmission occurred in 8 (5,5%) cases.

Survival outcomes

For the entire cohort of patients underwent L-CRS + HIPEC the median DFS in CC0 patients was 40.5 (12–62) and the median OS was 43 (16–63) months. The median return to intended oncological treatment (RIOT) was 4 [3–7] weeks for aggressive histology. Relapse occurred in 17/143 (11,8%) and the first site of relapse was the peritoneum in 10/143 (6.9%) cases. Six of them underwent to secondary open CRS + HIPEC.

Histopathologic groups (Table 1)

Pseudomyxoma peritonei

Eighty-seven patients diagnosed with pseudomyxoma peritonei underwent lap-CRS + HIPEC. Eight were diagnosed with HG-PMP and 79 LG-PMP. For LG-PMP the median PCI was 3 [1–15]. In 28 patients the surgery was indicated for a previous LAMN T4a without any suspicious of PMP in the preoperative workup, but peritoneal spread (PMP) was observed during the initial exploration. An intestinal resection was performed in 22/79 (27,8%) and the most frequent procedure was the caecectomy or appendiceal stump resection (15/22) and (7/22) right colectomy. CC0 was achieved in 75/79 (95%). The most frequently used drug for HIPEC was mitomycin C 59/79 (74,6%). The length of stay was 6 [5–10] days and major morbidity occurred in only one patient. The 5y DFS was 95% (Fig. 3.) The 5 y OS was 100% (Fig. 4.) For HG-PMP the median PCI was 4 [2–5] and in all of them right colectomy was performed. Two major complications occurred. Only one peritoneal relapse was identified at 102 months after surgery.

Colorectal cancer

L-CRS + HIPEC was performed in 18 patients with colorectal cancer peritoneal metastasis, with a median of PCI of 5 [3–9]. In 10 (41,6%) patients the indication was a limited peritoneal recurrence. The drug used for HIPEC was mitomycin C [9] and oxaliplatin [9]. The median number of peritonectomy procedures was 1 [1,2]. The length of stay was 6,5 [4–10] days with a major morbidity in 4 cases. Eight patients (33%) had a relapse during the follow-up, which was peritoneal in one patient. Five-year DFS was 43% (Fig. 3) and 5y-OS was 54% (Fig. 4).

Multicystic peritoneal mesothelioma. (MPM)

The median PCI was 3 [3–5] and in 5 cases (23,8%) intestinal resection was performed. CC0 was achieved in 100% and the combination of cisplatin + doxorrubicin was the elected protocol for HIPEC. The median length stay was 9 [7–12] days. Major morbidity occurred in one patient. With a median of 39 months of follow-up no relapses were identified.

Ovarian peritoneal metastasis

Thirteen patients were treated by L-CRS-HIPEC. Eleven cases were an interval primary surgery after neoadjuvant chemotherapy with carboplatin and paclitaxel for 3–4 cycles. The median PCI was 4 [4,5]. The most commonly used drug for HIPEC was paclitaxel 9 (69.2%). In 12 (91.7%) patients a CC0 was achieved. Median number of peritonectomy procedures performed was 2 [1–3], including

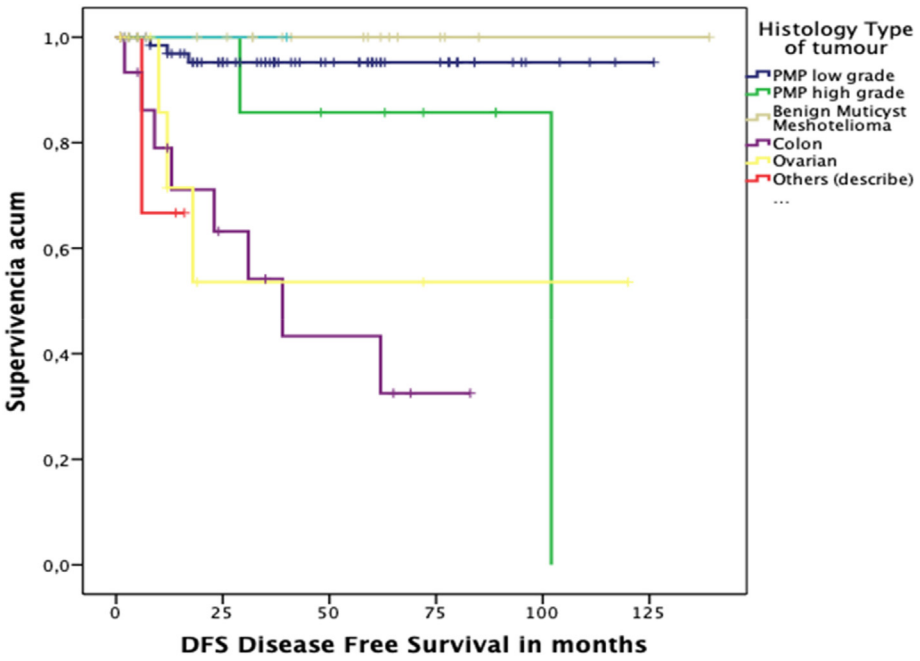

Fig. 3. L-CRS + HIPEC Disease free survival Kaplan-Meier curve sorted by type of tumours. Log-Rank test, p = 0,01.

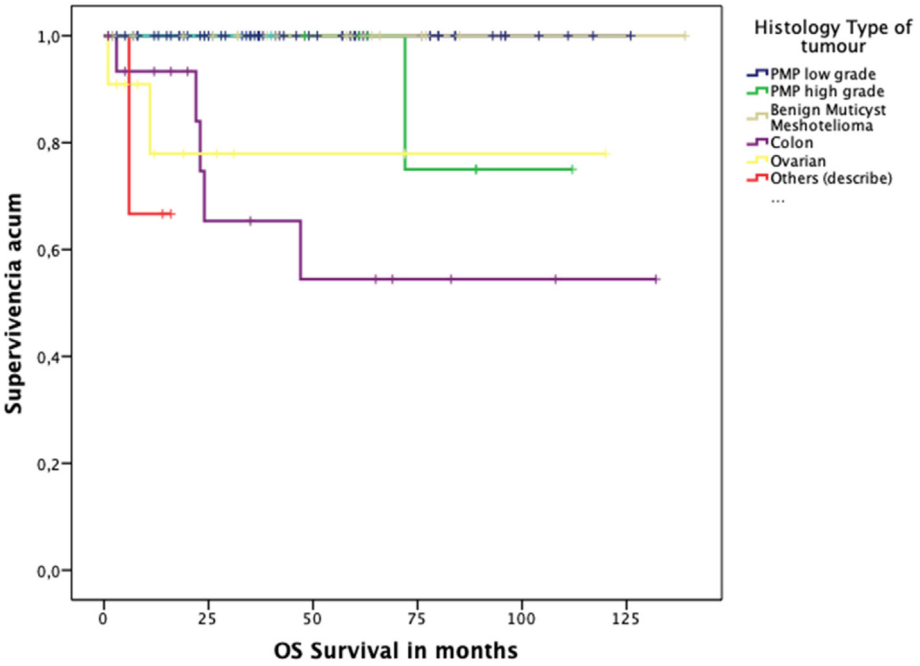

Fig. 4. L-CRS + HIPEC Overall survival Kaplan–Meier curve sorted by types of tumours. Log-Rank test p = 0,01.

total pelvic peritonectomy with extraction through natural orifices in 9 patients. Intestinal resection was needed in 3 (23%) cases. The median hospital length of stay hospital was 5 [5–8] days and the RIOT was 4 [4,5] weeks. Two patients had major complications. One required a minor operation because of trocar hernia, and the second patient died at 12th POD from a heart failure due to a severe heart insufficiency undiagnosed in the preoperative workup. The 5 years DFS was 53% (Fig. 3) and the 5y OS was 78% (Fig. 4), with no early peritoneal relapses (within 12 months after surgery).

Other indications

One case presented with appendiceal adenocarcinoma, one case with gastric peritoneal metastasis and one case with endometrial peritoneal carcinomatosis. For the patient with appendiceal adenocarcinoma the indication was an incomplete previous surgery (only appendicectomy) and limited peritoneal recurrence (PCI = 1) underwent to L-CRS + HIPEC associating right colectomy. No relapse was observed. For the case with limited gastric peritoneal metastasis (PCI = 6), the patient died at 6 months

postoperatively with early peritoneal recurrence. Patient with endometrial peritoneal metastasis underwent L-CRS + HIPEC and no relapse was identified after 16 months.

Discussion

The use of international registries allows cumulative experience on surgical procedures to be collected and analysis of outcomes from rare treatments, which would be impossible using only single-centre retrospective cohorts. The objective of the Lap-HIPEC PSOGI registry is to collect as much experience as possible in the use of minimally invasive approach for cytoreductive surgery and HIPEC. This registry constitutes the largest accumulated experience of laparoscopic CRS + HIPEC with a total of 200 treated patients, of which 143 were included in this study as they had established peritoneal disease (L-CRS + HIPEC). The remaining 57 patients excluded from this study were undergone 'risk reduction laparoscopic CRS + HIPEC (RR-L-CRS/HIPEC) for T4a LAMNs with extravasation of mucin or rupture at previous surgery (LAMN T4a) [12] and colon adenocarcinoma with a high risk of peritoneal seeding or loco-regional relapse (T4 perforated tumours or ovarian metastases) [16,20]. These indications are controversial and further data on long-term outcomes in this group is awaited.

The benefits of the minimally invasive approach for performing L-CRS + HIPEC have been described [6,10,11] with minimal morbidity and similar oncologic outcomes in patients with limited PCI score (less than 10) and low grade tumours such as LG-PMP or MPM. A more extensive and current experience has described satisfactory oncologic results in more aggressive and prevalent tumours such as colon or ovarian carcinomatosis, in which the L-CRS + HIPEC group achieved a shorter hospital stay and a shorter time to return back to chemotherapy than the matched control group. No differences in the short-term oncological prognosis and no early recurrences (less than 12 months) were showed in the laparoscopic group [6]. There are some standard steps in laparoscopic cytoreductive surgery required to achieve a complete peritoneal exploration, which are time consuming but required to avoid missing peritoneal disease. Intervention and exploration of multiple abdominal compartments require the necessary equipment (at least two or more screens) and position changes for which the patient has to be secured to the operating table. It is also requires a HIPEC perfusion machine that is able to perform a closed HIPEC technique [6–9]. In that sense, the incorporation of PIPAC as a closed technique to Lap-CRS could be an option based in its promising results [21].

In patients with high-grade colon carcinomatosis the L-CRS + HIPEC could be used for patients with limited disease reducing hospital stay and shortening the RIOT which in turn may impact survival [5]. The described survival was 54% at 5 years and DFS 43% at 5 years. Of the 18 patients operated on, only one peritoneal recurrence was identified. A recent review established a maximum survival rate of 44% at 5 years in the most favourable population [22], when the PCI was less than 7 [23].

The use of interval CRS + HIPEC using cisplatin for primary peritoneal ovarian carcinomatosis has shown benefits in survival compared to not adding HIPEC [16]. However, the complete resection of all macroscopic disease continues to be the most important prognostic factor in these patients. The use of neoadjuvant carbo-taxol in stage IIIc–IV of FIGO has been shown not be inferior to upfront surgery improving the ability to achieve a complete cytoreduction being the most important prognostic factor (24–27). The neoadjuvant chemotherapy can reduce tumour burden allowing a CRS to be performed through a minimally invasive approach, associating the application of HIPEC. Laparoscopic CRS without HIPEC in primary advanced ovarian cancer has been described with excellent perioperative results [12,28]. More experience has been described for L-CRS + HIPEC in limited peritoneal recurrence with excellent results in terms of morbidity and RIOT [28]. Thirteen patients were included in our study, of which 10 were interval L-CRS + HIPEC and 3 with recurrent disease. The mean hospital stay was 5 days and the return back to chemotherapy was 4 weeks. No early relapse (less than 12 months) occurred in this group of patients. L-CRS + HIPEC may be a feasible option for limited peritoneal carcinomatosis ovarian for both, interval surgery and localized recurrent disease, however the experience is limited to recommend it, and further studies are needed. The laparoscopic approach brings with it some challenges that should be appreciated. First, laparoscopic surgery loses the ability to feel the nodules the peritoneal cavity increasing the risk of leaving peritoneal implants behind which may lead to early relapses and decreased survival [29]. This is particulary important in high grade pathologies such as colorectal or ovarian cancer. It is important to note that the number of patients with these pathologies was low in our study and the follow-up short, however, no early recurrences (within 12 months) were reported. Second, the estimation of the PCI by laparoscopy can be difficult as it requires significant patient tilting and the use of 30–45° cameras to access to hidden spaces with the aim of accurately calculating the PCI score. Thirsty, access to all quadrants of the abdomen in an ergonomic manner requires multiple port placements. Finally a number of specimens need to be carefully collected and extracted.

A number of limitations of the study should be considered. First, this was a based on retrospective analysis of a prospectively collected registry. Second, there was some variation in surgical techniques and definitions of the procedures that required categorisation. Third, due to the number of cases performed per centre surgeons in different centres were at different stages in their learning curve for the procedure.

Conclusions

The minimally invasive approach to treat the PSM is a promising option that reduces hospital stay and leads to early recovery with limited postopeartive morbidity and mortality. The indications are represented by L-CRS + HIPEC for limited peritoneal carcinomatosis (PCI <10) for LG-PMP and MPM. Limited peritoneal metastasis from colon and ovarian cancer may be treated by this minimally invasive approach, but additional studies or accumulate more experience with longer follow-up should be performed.

Conflicts of interest and source of funding

The authors declare that they have no conflict of interest.

Ethical approval

All the procedures performed in this study were in accordance with the local ethical committees.

Informed consent

Informed consent was obtained from all individual participants included in the registry.

Contribution Author(s)

- Study concepts: ASA, AO, EJ, GO.
- Study design: ASA, AO, EJ, GO.
- Data acquisition: ASA, AO, PG, SG, EJ, VSK, PP, NS, SA, YY, TK, SCR, ROL, SHJ, CAA, RPS, BJ and GO.

- Quality control of data and algorithms.
- Data analysis and interpretation: ASA, AO, EJ, ROL, SHJ, RPS, CAA, BJ and GO.
- Statistical analysis:ASA.
- Manuscript preparation: ASA, AO, EJ, OG, GS, VSK, PP and SA.
- Manuscript editing: ASA, OA, JE
- Manuscript review: OA, PG, SG, EJ, VSK, PP, NS, SA, YY, TK, SCR, ROL, SHJ, RPS, CAA, BJ and GO.

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References

[1] Newton AD, Barlett EK, Karakousis GC, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: a review of factors contributing to morbidity and mortality. J Gastrointest Oncol 2016;7(1):99–111.
[2] Foster J, Sleightholm M, Patel A, et al. Morbidity and mortality rates following cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy compared with other high-risk surgical oncology procedures. JAMA Netw Open 2019;2(1):e186847.
[3] van der Pas MH, Haglind E, Cuesta MA, et al. Colorectal cancer laparoscopic or open resection II (COLOR II) study group. Laparoscopic versus open surgery for rectal cancer (COLOR II): short term outcomes of a randomized phase 3 trial. Lancet Oncol 2013;14:210–8.
[4] Sommariva A, Zagonel V, Rossi CR. Rossi CR the role of laparoscopy in peritoneal surface malignancies selected for hyperthermic intraperitoneal chemotherapy (HIPEC). Ann Surg Oncol 2012;19:3737–44.
[5] Rodriguez-Ortiz L, Arjona-Sanchez A, Ibañez-Rubio M, et al. Laparoscopic cytoreductive surgery and HIPEC: a comparative matched analysis. Surg Endosc Apr 2020. https://doi.org/10.1007/s00464-020-07572-x.
[6] Esquivel J, Averbach A, Chua T. Chua TC Laparoscopic cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in patients with limited peritoneal surface malignancies: feasibility, morbidity and outcome in an early experience. Ann Surg 2011;253:764–8.
[7] Arjona-Sanchez A, Duran-Martinez M, Sanchez-Hidalgo JM. Peritoneal carcinomatosis from ovarian carcinoma treated by interval laparoscopic complete cytoreduction and HIPEC with extraction through natural orifice. Surg Oncol 2019;31:14–5.
[8] Laparoscopic cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (L-CRS/HIPEC) for perforated low-grade Appendiceal mucinous neoplasm (LAMN II)Parkin CS, Wilson Malcolm, et al., editors. Ann Surg Oncol 2019;26:2285.
[9] Abudeeb HSC, O'Dwyer ST, et al. Laparoscopic cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for perforated low-grade appendiceal mucinous neoplasms. Surg Endosc 2020.
[10] Frederic Mercier GJ, Alyami M, et al. Long-term results of laparoscopic cytoreductive surgery and HIPEC for the curative treatment of low-grade pseudomyxoma peritonei and multicystic mesothelioma. Surg Endosc 2019.
[11] Arjona-Sanchez A, Esquivel J, Glehen O, et al. A minimally invasive approach for peritonectomy procedures and hyperthermic intraperitoneal chemotherapy (HIPEC) in limited peritoneal carcinomatosis: the American Society of Peritoneal Surface Malignancies (ASPSM) multi-institution analysis. Surg Endosc 2019;33(3):854–60.
[12] Fagotti A, Alleti SG, Corrado G, et al. The INTERNATIONAL MISSION study: minimally invasive surgery in ovarian neoplasms after neoadjuvant chemotherapy. Int J Gynecol Canc 2019;29:5–9.
[13] Amin MB, Edge SB, Greene FL, et al. AJCC cancer staging manual. eighth ed. New York: Springer; 2017.
[14] Honoré C, Goere D, Souadka A, et al. Definition of patients presenting a high risk of developing peritoneal carcinomatosis after curative surgery for colorectal cancer: a systematic review. Ann Surg Oncol 2013;20:183–92.
[15] Carr NJCT, Mohamed F, et al. A consensus for classification and pathologic reporting of pseudomyxoma peritonei and associated appendiceal neoplasia: the results of the peritoneal surface oncology group international (PSOGI) modified Delphi process. Am J Surg Pathol 2016;40:14–26.
[16] van Driel WJ, Ksn, Sikorska K, et al. Hyperthermic intraperitoneal chemotherapy in ovarian cancer. N Engl J Med 2018;378:230–40.
[17] Kusamura SKV, Villeneuve L, et al. Peritoneal mesothelioma: PSOGI/EURACAN clinical practice guidelines for diagnosis, treatment and follow-up. Eur J Surg Oncol 2020;12.
[18] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240(2):205–13.
[19] Jacquet P, Sugarbaker P. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Canc Treat Res 1996;82:359–74.
[20] Arjona-Sánchez A, Barrios P, Boldo E, et al. HIPECT4: multicentre, randomized clinical trial to evaluate safety and efficacy of Hyperthermic intra-peritoneal chemotherapy (HIPEC) with Mitomycin C used during surgery for treatment of locally advanced colorectal carcinoma. BMC Canc 2018;18:183.
[21] Alyami M, Hübner M, Grass F, et al. Pressurised intraperitoneal aerosol chemotherapy: rationale, evidence, and potential indications. Lancet Oncol 2019;20:e368–77.
[22] Sánchez-Hidalgo JM, Rodriguez-Ortiz L, Arjona-Sanchez A, et al. Colorectal peritoneal metastases: optimal management review. World J Gastroenterol 2019;25:3484.
[23] Elias Dominique, Boutitie Florent, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. J Clin Oncol 2009;28:63–8.
[24] du Bois A, Reuss A, Pujade-Lauraine E, et al. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux pour les Etudes des Cancers de l'Ovaire (GINECO). Cancer 2015;115:1234–44.
[25] Kehoe S, Hook J, Nankivell M, et al. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): an open-label, randomised, controlled, non-inferiority trial. Lancet 2015;386:249–57.
[26] Vergote I, Trope C, Amant F, et al. Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. N Engl J Med 2010;363:943–53.
[27] Gallotta V, Ghezzi F, et al. Laparoscopic management of ovarian cancer patients with localized carcinomatosis and lymph node metastases: results of A retrospective multi-institutional series. J Minim Invasive Gynecol 2016.
[28] Fagotti A, Petrillo M, Costantini B. Minimally invasive secondary cytoreduction plus HIPEC for recurrent ovarian cancer: a case series. Gynecol Oncol 2014;132:303–6.
[29] Passot G, Goéré D, et al. Multicentre study of laparoscopic or open assessment of the peritoneal cancer index (BIG-RENAPE). BJS 2018;105:663–7.