European Journal of Surgical Oncology 45 (2019) 383–388

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Short-term complications in elderly patients undergoing CRS and HIPEC: A single center's initial experience

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ARTICLE INFO

Article history:
Accepted 31 October 2018
Available online 2 November 2018

Keywords:
Cytoreductive surgery
Hyperthermic intraperitoneal chemotherapy
Peritoneal carcinomatosis
Elderly
Serious adverse event

ABSTRACT

Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a well-established curative treatment for patients with peritoneal carcinomatosis (PC) from colorectal cancer (CRC) and pseudomyxoma peritonei (PMP). The study's aim was to present a single center's initial experience with CRS and HIPEC and report the postoperative morbidity in elderly patients.

Methods: A retrospective observational study was conducted of all patients with peritoneally disseminated colorectal cancer or pseudomyxoma peritonei undergoing CRS and HIPEC between March 2014 and March 2017. Patient characteristics and the peri- and postoperative course were reviewed. Elderly patients were defined as those aged $\geq$ 65 years. Postoperative complications were classified according to the Serious Adverse Event (SAE) grading system.

Results: 122 patients undergoing CRS and HIPEC were split into two groups based on age (< 65 years versus $\geq$ 65 years) at the time of surgery. Both groups were comparable for ASA score, Peritoneal Cancer Index (PCI), procedure time and blood loss. Serious Adverse Event (SAE) grade > 3 morbidity was 26.7% in the elderly group as opposed to 10.4% in the younger group ($p = 0.034$). Both univariate and multivariate logistic regression analysis demonstrated that age was a significant risk factor (OR = 3.2, 95% CI 1.1–9.4, $p = 0.033$) for severe postoperative morbidity (SAE > 3).

Conclusion: This retrospective study showed advanced age to be a significant risk factor for SAE > 3, after undergoing CRS and HIPEC. The initial institutional experience resembles previously published literature in terms of severe postoperative morbidity in elderly patients.

Introduction

Over the past twenty years, cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has increasingly been used as a curative therapeutic modality in patients with peritonitis carcinomatosa from colorectal cancer (CRC) and pseudomyxoma peritonei (PMP) [1,2]. CRS and HIPEC has resulted in significantly improved outcomes with 1-year and 5-year survival rates up to 72% and 32% for colorectal cancer and 90% and 74% for PMP respectively [3,4]. It has been demonstrated that this survival benefit depends mostly on achieving an R1-resection, signifying a total cytoreduction.

To obtain total cytoreduction, extensive resections of abdominal viscera and stripping of peritoneum are sometimes performed, which affects morbidity and mortality with rates as high as 42% and 4% respectively [4]. It has been reported that these morbidity and mortality rates are increased in the elderly patient [5,6]. However, data on postoperative outcomes for this specific patient population remains limited and conflicting data have been published.

This study aimed to investigate the peri- and postoperative complications for elderly patients ($\geq$ 65 years) undergoing CRS and HIPEC in the start-up phase of a tertiary referral center and to identify the potential contributing risk factors.

Methods

Patients

Between March 2014 and March 2017, a total of 122 patients

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https://doi.org/10.1016/j.ejso.2018.10.545
0748-7983/

underwent CRS and HIPEC in the Erasmus Medical Center in Rotterdam for peritoneally disseminated colorectal cancer or pseudomyxoma peritonei. Relevant patient-, tumor-, treatment-related, and postoperative period characteristics were collected in a prospectively maintained database. This retrospective study was approved by the local medical ethics committee in the Erasmus Medical Center (registration number MEC-2018-1286).

Preoperative screening

All patients, who were referred for CRS and HIPEC, underwent a thorough preoperative screening in order to select those who would be eligible for this procedure. The screening included physical examination and imaging of the chest, abdomen and pelvis to rule out distant metastases and to determine the extent of the peritoneal dissemination. General contraindications for the procedure were >3 liver metastases, extra-abdominal metastases and a Peritoneal Cancer Index (PCI) score greater than 20 [7–9].

Furthermore, a preoperative screening by an anesthesiologist was performed in all patients to assess physical condition and comorbidities. If the exercise tolerance was limited and/or serious comorbidities were present, a risk calculation was done and discussed with patient and surgeon to aid shared decision-making. In absence of contra-indications epidural analgesia, in addition to general anesthesia, was first choice and offered to most patients.

In most patients, a diagnostic laparoscopy was performed to estimate the PCI score to assess the extent of peritoneal carcinomatosis [7]. If the PCI was less than 20 during laparoscopy, patients were planned for an elective CRS and HIPEC procedure. Unfortunately, some patients had a higher PCI during laparotomy and therefore did not receive CRS and HIPEC.

CRS and HIPEC

CRS and HIPEC was performed in a starting tertiary medical center by a specialized surgical team of three surgeons. The starting surgeons visited an experienced HIPEC institute beforehand and the initial operations were also supervised and monitored by a visiting surgeon to ensure that protocols were followed. This period of proctorship led to the progression of the surgical learning curve. The procedures were performed according to Dutch CRS and HIPEC protocols [10,11].

After abdominal access via laparotomy, a thorough assessment of the extent of peritoneal disease was conducted by determining the PCI score according to Sugarbaker [7]. The PCI score is not relevant in patients with pseudomyxoma peritonei and was thus not assessed preoperatively. The greater omentum, primary tumor (if still present), involved visceral abdominal organs, involved parietal surfaces and all peritoneal implants were resected as able.

Administration of HIPEC was by way of the open (coliseum) technique in which the abdominal wall is attached to a retractor frame, creating an inverted funnel like cavity. This technique appears to provide optimal thermal homogeneity and spatial diffusion [7,12]. The perfusion circuit (RanD Performer) consisted of 3 inflow catheters, 2 outflow catheters, 1 roller pump and 1 heat exchanger. Thermometers were attached to the inflow- and outflow catheters. The perfusion started with the abdominal cavity being filled with a minimum of 4–6 liters isotonous saline at 2 liters per minute with an inflow temperature of 41–42 C. After reaching the desired stable abdominal temperature of > 40 C, either Mitomycin C (MMC) or Oxaliplatin was added as chemotherapeutic agent to the perfusate for a 90-min or 30-min perfusion period, respectively. If the core temperature of the patient rose above 39 C, the inflow temperature was lowered.

After the HIPEC perfusion period, intestinal bowel anastomoses and/or a stomy procedure was performed if necessary. All patients received a feeding tube (a percutaneous entero-jejunostomy till December 2015 and a naso-jejunal tube hereafter) and a tube for gastric decompression (a percutaneous gastrostomy till December 2015 or nasogastric tube hereafter). The inflow catheters were left in place as drains and the wound was closed in standard fashion.

Postoperative monitoring

After surgery, patients were transferred to the intensive care unit (ICU) for observation and stabilization. Patients were transferred to the surgical ward after this initial monitoring was completed. Postoperative complications during hospitalization were classified according to the Serious Adverse Event (SAE) grading system: SAE = 1 signifying an asymptomatic or mild complication (intervention not indicated), SAE = 2 signifying a moderate complication (local or non-invasive intervention indicated), SAE = 3 signifying a severe complication (significant but not immediately life-threatening, radiological or surgical intervention indicated), SAE = 4 signifying a life-threatening complication (reoperation and/or prolonged ICU stay indicated), and SAE = 5 signifying in-hospital death related to the adverse event. This SAE grading system is based on the NCI (National Cancer Institute) Common Terminology Criteria (CTC) for Adverse Events (version 4.0) [13,14]. The postoperative period was defined as the 30-day interval following CRS and HIPEC, or the duration of the entire hospital stay if it exceeded 30 days.

Follow up

Follow-up of patients was done in the outpatient clinic; initially 2 weeks after discharge, then at 3-month intervals for the first year and 6-month intervals thereafter with alternate CT-scans and monitoring of the Carcino-Embryonal Antigen (CEA). The follow-up is, in general, completed after a 5-year disease-free interval following CRS and HIPEC.

Statistical analysis

Data retrieval for the analysis was from a prospectively maintained electronic database. Continuous variables were expressed as a median with an interquartile range, and categorical variables were presented as percentages. Continuous variables were compared between patients with an age < 65 years and age ≥ 65 years using a Student's t-test, while categorical variables were compared using either the Chi-squared ($\chi 2$) test or Fisher's exact test. A multivariate analysis was performed for the postoperative outcomes in the overall study population with independent variables: age ≥ 65 years, gender, BMI (body mass index), ASA (American Society of Anesthesiologists) classification, procedure time, number of resected organs, number of bowel anastomoses and blood loss. All tests were performed two-sided and results were considered significant when $p < 0.05$. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS), Version 21.0 (IBM Corporation, Armonk, NY, USA).

Results

Patient cohort

Demographic data and clinico-pathological characteristics for both age groups (< 65 years versus ≥ 65 years) are described in Table 1. An overview of specifically patients with colorectal and appendix cancer is given in Table 2. From March 2014 to March 2017, 122 patients underwent elective CRS and HIPEC for peritoneal

Table 1
Demographic & clinico-pathological characteristics of patients undergoing CRS + HIPEC.

	All patients (N = 122)	<65 years (N = 77)	≥65 years (N = 45)	p-value
Age, median years [IQR]	60.5 [51–68]	53.2 [51.5–54.8]	70.5 [69.5–71.5]	**<0.001**
Gender, N (%)				NS
Male	58 (47.5%)	37 (48.1%)	21 (46.7%)	
Female	64 (52.5%)	40 (51.9%)	24 (53.3%)	
Body Mass Index, median [IQR]	25.1 [22.3–27.8]	25.1 [22.3–28.0]	25.0 [22.7–27.8]	NS
Smoking (past history/current), N (%)	65 (53.3%)	40 (51.9%)	25 (55.6%)	NS
Co-morbidities, N (%)				
Hypertension	27 (22.1%)	10 (13%)	17 (37.8%)	**0.001**
Diabetes mellitus	17 (13.9%)	7 (9.1%)	10 (22.2%)	**0.043**
Insulin-dependent diabetes mellitus	7 (5.7%)	3 (3.9%)	4 (8.9%)	NS
ASA classification, N (%)				**0.047**
1	28 (23%)	21 (27.3%)	7 (15.6%)	
2	71 (58.2%)	45 (58.4%)	26 (57.8%)	
3	23 (18.9%)	11 (14.3%)	12 (26.7%)	
Primary tumor entity & location, N (%)				
Appendix cancer	4 (3.3%)	2 (2.6%)	2 (4.4%)	
Pseudomyxoma peritonei	18 (14.8%)	12 (15.6%)	6 (13.3%)	
Colorectal cancer	99 (81.1%)			
Left colon	9 (9.1%)	6 (9.7%)	3 (8.1%)	
Right colon	42 (42.4)	23 (37.1%)	19 (51.4%)	
Transverse colon	7 (7.1%)	5 (8.1%)	2 (5.4%)	
Sigmoid	24 (24.2%)	15 (24.2%)	9 (24.3%)	
Rectum	17 (17.2%)	13 (21%)	4 (10.8%)	
Other	1 (0.8%)	1 (1.3%)	0 (0%)	
Peritoneal carcinomatosis, N (%)				NS
Synchronous	67 (54.9%)	44 (57.1%)	23 (51.1%)	
Metachronous	55 (45.1%)	33 (42.9%)	22 (48.9%)	

IQR: interquartile range; NS: not significant; ASA: American Society of Anesthesiologists.

Table 2
Clinico-pathological characteristics of patients with colorectal and appendix cancers (N = 103).

	All patients (N = 103)	<65 years (N = 64)	≥65 years (N = 39)	p-value
Neo-adjuvant chemotherapy before CRS + HIPEC, N (%)	9 (8.7%)	6 (9.4%)	3 (7.7%)	NS
Intraoperative PCI of appendix cancer and CRC patients, median (IQR)	10 [5–16]	10 [5–16]	10 [6–16]	NS
Primary tumor TNM classification of CRC & appendix, N (%)				NS
T1/T2	5 (4.9%)	2 (3.1%)	3 (7.7%)	
T3/T4	95 (92.2%)	60 (93.8%)	35 (89.7%)	
N0	32 (31.1%)	18 (28.1%)	14 (35.9%)	
N1/N2	67 (65%)	44 (68.8%)	23 (59%)	
M0	43 (41.7%)	24 (37.5%)	19 (48.7%)	
M1	50 (48.5%)	32 (50%)	18 (46.2%)	
Adjuvant chemotherapy after CRS + HIPEC, N (%)	35 (34%)	26 (40.6%)	9 (23.1%)	NS

IQR: interquartile range; NS: not significant.

carcinomatosis for either CRC or PMP, among which 45 (36.9%) patients were elderly. Median time from primary tumor diagnosis to CRS and HIPEC was 6 months (IQR 2–20). Two patients underwent re-cytoreduction and re-HIPEC for recurrence of disease during follow-up. These two additional procedures were excluded from this study. The median follow-up time was 11.5 months (6–18). There was no statistical difference in gender distribution between both age groups. Only hypertension was statistically more prevalent in the elderly group as compared to the younger group; diabetes did not reach statistical significance. Both comorbidities were considered potential confounders and were used as independent predictor variables in uni- and multivariate analysis, as will be discussed later. The distribution of primary tumors encompassed 99 (81.1%) colorectal carcinomas, 18 (14.8%) pseudomyxoma peritonei, 4 (3.3%) appendiceal carcinomas and 1 (0.8%) cystic endosalpingiosis.

Surgical procedure

The median duration of CRS and HIPEC was 426.5 min (375.8–508). There was no statistical difference in procedure time between both age groups. The extent of peritoneal carcinomatosis, as determined with the PCI-score, was not significantly different between both groups. Most patients underwent a bowel resection with at least one bowel anastomosis. A colostomy was required for 42/122 (34.4%) patients, and 8/122 (6.6%) patients required an ileostomy. All patients received an omentectomy, either during the primary surgery or during CRS and HIPEC. The median blood loss was higher in the elderly group compared to the younger group but it was not statistically significant. No patients died during CRS and HIPEC.

Postoperative course

Table 3 reports the intra- and postoperative characteristics of patients. Major complications (SAE grade > 3) occurred in 20 (16.4%) patients in the entire cohort (N = 122). In the elderly group (N = 45), the rate of major complications was 26.7% as compared to the 10.4% in the younger group (N = 77). The most frequently occurred major complications in the entire cohort were intra-abdominal abscesses (9.8%), anastomotic leakages (4.9%), postoperative bleeding (4.1%) and pulmonary embolisms (4.1%).

Table 3
Intra- and postoperative characteristics of patients undergoing CRS + HIPEC.

	All patients (N = 122)	<65 years (N = 77)	≥65 years (N = 45)	p-value
Resected organs				
Omentum	118 (96.7%)	73 (94.8%)	45 (100%)	NS
Ovaries	48 (39.3%)	30 (39%)	18 (40%)	NS
Uterus	30 (24.6%)	21 (27.3%)	9 (20%)	NS
Rectum	37 (30.3%)	24 (31.2%)	13 (28.9%)	NS
Sigmoid	39 (32%)	24 (31.2%)	15 (33.3%)	NS
Left peritoneum	38 (31.1%)	19 (24.7%)	19 (42.2%)	NS
Right peritoneum	48 (39.3%)	28 (36.4%)	20 (44.4%)	NS
Left diaphragm	13 (10.7%)	10 (13%)	3 (6.7%)	NS
Right diaphragm	32 (26.2%)	20 (26%)	12 (26.7%)	NS
Spleen	9 (7.4%)	5 (6.5%)	4 (8.9%)	NS
Gallbladder	8 (6.6%)	2 (2.6%)	6 (13.3%)	NS
Bladder	4 (3.3%)	4 (5.2%)	0 (0%)	NS
Pelvic peritoneum	61 (50%)	41 (53.2%)	20 (44.4%)	NS
Number of anastomosis				NS
0	50 (41%)	29 (37.7%)	21 (46.7%)	
1	58 (47.5%)	40 (51.9%)	18 (40%)	
2	9 (7.4%)	6 (7.8%)	3 (6.7%)	
3	3 (2.5%)	1 (1.3%)	2 (4.4%)	
4	2 (1.6%)	1 (1.3%)	1 (2.2%)	
Stoma post-HIPEC	50 (41%)	35 (45.5%)	15 (33.3%)	NS
Procedure time, median minutes [IQR]	426.5 [375.8–508]	426 [372–509]	427 [382–504]	NS
Blood loss, median millimeters [IQR]	1300 [800–2350]	1200 [810–2175]	1500 [743–2545]	NS
SAE classification				
SAE grade 0	34 (27.9%)	25 (32.5%)	9 (20%)	NS
SAE grade 1-3	68 (55.7%)	44 (57.1%)	24 (53.3%)	NS
SAE grade >3	20 (16.4%)	8 (10.4%)	12 (26.7%)	**0.019**
Complications during hospital stay				
Anastomotic leakage	6 (4.9%)	4 (5.2%)	2 (4.4%)	NS
Intra-abdominal bleeding	5 (4.1%)	5 (6.5%)	0 (0%)	NS
Abscess	12 (9.8%)	9 (11.7%)	3 (6.7%)	NS
Wound infection	17 (13.9%)	13 (16.9%)	4 (8.9%)	NS
Wound dehiscence	4 (3.3%)	1 (1.3%)	3 (6.7%)	NS
Pneumonia	4 (3.3%)	4 (5.2%)	0 (0%)	NS
Pulmonary embolism	5 (4.1%)	1 (1.3%)	4 (8.9%)	NS
Urinary tract infection	14 (11.5%)	7 (9.1%)	7 (15.6%)	NS
Other infections	18 (14.8%)	9 (11.7%)	9 (20%)	NS
Reoperation	17 (13.9%)	11 (14.3%)	6 (13.3%)	NS
In-hospital mortality	5 (4.1%)	1 (1.3%)	4 (8.9%)	NS
Intensive Care Unit stay, median days [IQR]	3 [2–3]	3 [2–3]	3 [2.5–3.5]	NS
Hospital stay, median days [IQR]	17 [14–23]	18 [15–23]	17 [13.3–25]	NS

IQR: interquartile range; NS: not significant; SAE: Serious Adverse Event.

Table 4 reports *every* occurred complication in elderly patients who experienced *at least one major* postoperative complication. 6/45 patients (13.3%) in the elderly group and 11/77 (14.3%) younger patients underwent a reoperation during the postoperative course. The in-hospital mortality rate was 5/45 (8.9%) in the elderly group versus 1/77 (1.3%) in the younger group, but not statistically significant.

Risk factors for postoperative complications

Table 5 shows the univariate and multivariate analyses. Univariate analysis, performed on the entire cohort, demonstrated that elderly age (OR = 3.14, 95% CI 1.17–8.41, p = 0.023) was a significant risk factor associated with major postoperative complications. Other factors such as gender, body mass index and number of resected organs were not statistically significant. Stepwise multivariate models were developed with patient- and procedure-related characteristics as independent predictor variables. Multivariate analysis showed elderly age (OR = 3.21, 95% CI 1.1–9.39, p = 0.033) as a remaining significant risk factor for major postoperative complications. Although blood loss (OR = 1.001, 95% CI 1.0–1.001, p = 0.045) reached significance, the effect size was minimal.

Discussion

CRS and HIPEC is a curative treatment for selected patients with peritoneal carcinomatosis. This current study focuses primarily on a tertiary center's initial experience with CRS and HIPEC including the postoperative complications. Sixty-five years was chosen as a cut-off point to distinguish between “younger” and “elderly” patients and even though this has been done by others as well, the definition of elderly patients remains arbitrary [15–18]. The results of this study support the general opinion. They suggest that, even after thorough patient selection, age ≥65 years is a significant risk factor for major postoperative complications after CRS and HIPEC. Age, in general, is known to be directly related with increased comorbidities and a reduced capacity to recover after extensive surgery [5,19,20].

The postoperative major morbidity (SAE > 3) rates were significantly higher in elderly patients (26.7% versus 10.4%, p = 0.034) and, although not significant, there was a trend in higher mortality rates (8.9% versus 1.3%, p = 0.061) as well. Multivariate analysis demonstrated that age remained a significant risk factor for developing major postoperative complications. Gagnière et al. [21] recently published a meta-analysis on outcomes of elderly patients undergoing CRS and HIPEC in various experienced centers. Overall postoperative 30-day morbidity was not affected by age, however

Table 4
Postoperative complications (at least one SAE > 3) and hospital stay in elderly patients (N = 12).

Patient	Diagnosis	Postoperative complications	Intervention	Outcome	Hospital stay (days)
#1	Pseudomyxoma peritonei	Basilar artery thrombosis	Conservative management during ICU stay	In-hospital death	6
#2	Pseudomyxoma peritonei	Severe abdominal sepsis based on bowel ischemia, GI-leakage and intra-abdominal abscess	Relaparotomy with small bowel resection and primary anastomosis, intravenous antibiotics, radiological drainage of abscess, renal replacement therapy & ultimately conservative management	In-hospital death	40
#3	Pseudomyxoma peritonei	Abdominal sepsis; delirium; vocal cord dysfunction; urinary retention	"Negative" relaparotomy; antipsychotic medication; conservative management; urinary catheterization	Discharged	81
#4	Appendix carcinoma	Septic shock based on liver abscess	Radiological drainage of abscess, intravenous antibiotics & re-admission intensive care unit	Discharged	30
#5	Pseudomyxoma peritonei	Sepsis with suspicion of pneumatosis intestinalis; delirium; electrolyte imbalances	"Negative" relaparotomy & intravenous antibiotics; antipsychotic medication	Discharged	32
#6	Pseudomyxoma peritonei	Abdominal sepsis based on GI-leakage; peri-operative cardiac arrest during relaparotomy; acute kidney injury with electrolyte imbalances; delirium; aspiration pneumonia, fascial dehiscence	Relaparotomy twice with ileostomy constructed; cardio-pulmonary resuscitation; temporary renal replacement therapy; antipsychotic medication; antibiotics; implantation of mesh	Discharged	64
#7	Colorectal cancer	Metabolic disorder; pulmonary insufficiency based on aspiration; delirium; urinary retention with UTI	Re-admission intensive care unit; insertion of tracheostomy tube; antipsychotic medication; antibiotics & urinary catheterization	Discharged	79
#8	Colorectal cancer	Suspicion of GI-leakage; intra-abdominal abscess; pulmonary embolism	"Negative" relaparotomy; radiological drainage of abscess; low molecular weight heparin	Discharged	33
#9	Colorectal cancer	Stomach perforation; abdominal wound evisceration; contained anastomotic leakage; electrolyte imbalance	Relaparotomy; conservative management with drainage	Discharged	44
#10	Colorectal cancer	Massive pulmonary aspiration with hypoxemia and cardiac arrest	Attempted cardio-pulmonary resuscitation	In-hospital death	13
#11	Colorectal cancer	Bradycardia followed by cardiac arrest; urinary tract infection	Short & uncomplicated cardio-pulmonary resuscitation on the ICU; oral antibiotics	Discharged	22
#12	Colorectal cancer	Delirium; massive pulmonary aspiration with cardiac arrest	Attempted cardio-pulmonary resuscitation	In-hospital death	11

ICU: intensive care unit; GI: gastro-intestinal; UTI: urinary tract infection.

Table 5
Univariate & multivariate analysis of risk factors for major complications (SAE grade > 3) following CRS + HIPEC for all patients (N = 122).

Risk factor	Univariate		Multivariate	
	Odds ratio	p-value	Odds ratio	p-value
Age ≥ 65 years	3.136	**0.023**	3.621	**0.036**
Gender	2.352	NS	3.135	NS
BMI	1.058	NS	1.087	NS
Hypertension	1.653	NS	1.309	NS
Diabetes	0.644	NS	0.581	NS
ASA score > 2	1.092	NS	0.654	NS
Number of resected organs	1.058	NS	0.954	NS
Bowel anastomosis	1.050	NS	1.958	NS
Blood loss	1.000	**0.024**	1.001	**0.045**
Procedure time	1.003	NS	0.998	NS

NS: not significant; ASA: American Society of Anesthesiologists.

Clavien-Dindo grade 3 or higher postoperative morbidity did increase with age. Gagnière did not find a significant difference in 90-day postoperative mortality in the elderly patient. As the authors suggest, these results should be interpreted with caution considering the heterogeneous and retrospective nature of the studies included in the meta-analysis.

There are various risk factors associated with age so the significant difference in postoperative outcomes between elderly patients and their younger counterparts could be due to risk factors related to age instead of solely age. This study also found blood loss to be a risk factor for major complications, which is in concordance with previously published research [22]. On the other hand, other variables (e.g. procedure time) that were previously reported to be associated with major complications, did not turn out to be significantly related to them in this study. Therefore, it has to be noted that because the statistical difference in the major complication (SAE > 3) rate between both age groups could not be explained through a difference in comorbidities or ASA classification, as demonstrated in the multivariate analysis, it can be assumed that age by itself remains an important risk factor that should be taken into consideration during preoperative screening.

We acknowledge that this study has its limitations. Similar to other published studies on this subject, the main limitations are the retrospective nature and relatively small sample size [16,23,24]. Due to the study's retrospective design, one needs to address the possible selection bias (internal validity) in the results: because the decision to perform CRS and HIPEC on patients was based on pre-operative clinical assessment of the performance status and not randomized, one could argue that (elderly) patients who were eligible but less fit were excluded from undergoing this extensive procedure. Because the excluded patients were not recorded in the database, it was not possible to look at their patient characteristics and (statistically) compare them to the operated patients. This phenomenon could have led to a biased estimation, in this case an underestimation, of the complication rate in elderly patients in this study, but also of the effect between exposure (age) and outcome (postoperative complication). In order to correct for this, possible confounders in the relation between age and postoperative complications were compared between both age groups, and those that were significantly different were added to the multivariate analysis to produce an "adjusted" effect size (odds ratio).

The limited sample size and therefore amount of clinical data might especially impact the multivariate analysis – although the fit of the model was good, the selection of too many independent predictor variables relative to the small sample size could lead to overfitting of the model and thus moderate external validity [25]. The model will have to be applied to other datasets to better determine its predictive power.

Conclusion

This article describes a starting tertiary center introducing CRS and HIPEC as a curative surgical treatment for selected (elderly) patients with peritoneal carcinomatosis. The postoperative morbidity in this cohort is comparable to various more experienced centers. Proctoring and intensive collaboration with experienced institutions is paramount to achieving similar or lower morbidity and mortality rates after CRS and HIPEC. This study shows elderly age as a significant risk factor for major postoperative morbidity (SAE > 3), in accordance with previously published literature. However, therapeutic decisions in elderly patients should not be made based on chronological age alone. Selected elderly patients with a good performance status might still benefit from undergoing CRS and HIPEC. Careful patient selection is therefore crucial, especially in this specific population, to maintain low morbidity and mortality rates.

Acknowledgments/Disclosure

The authors declare no acknowledgements and no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2018.10.545.

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