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Cost analysis of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy and the risk factors for their increased cost in a public insurance health care system – Single centre study

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ABSTRACT

Introduction: This study aimed to evaluate the costs of CRS and HIPEC and treatment of the related postoperative complications in the public healthcare system. We also aimed to identify the risk factors that increase the cost of CRS and HIPEC.

Materials and methods: We retrospectively evaluated 80 patients who underwent CRS and HIPEC between February 2016 and November 2018 in the Department of Surgery, University Hospital of Olomouc, Czech Republic. Intraoperative factors and postoperative complications were assessed. The treatment cost included the surgery, hospital stay, intensive care unit (ICU) admission, pharmaceutical charges including medication, hospital supplies, pathology, imaging, and allied healthcare services.

Results: The postoperative morbidity rate was 50%, and the mortality rate was 2.5%. The mean length of hospitalisation and ICU admission was 15.44 ± 8.43 and 6.15 ± 4.12 for all 80 patients and 10.73 ± 2.93 and 3.73 ± 1.32, respectively, for 40 patients without complications, and 20.15 ± 13.93 and 8.58 ± 6.92, respectively, for 40 patients with complications. The total treatment cost reached €606,358, but the total reimbursement was €262,931; thus, the CRS and HIPEC profit margin was €-343,427. Multivariate analysis showed that blood loss ≥1.000 ml ($p = 0.03$) and grade I–V Clavien-Dindo complications ($p < 0.001$) were independently associated with increased costs.

Conclusion: The Czech public health insurance system does not fully compensate for the costs of CRS and HIPEC. Hospital losses remain the main limiting factor for further improving these procedures. Furthermore, treatment costs increase with increasing severity of postoperative complications.

Introduction

Peritoneal surface malignancies are a heterogeneous group of tumours. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are among the treatment modalities for peritoneal carcinomatosis since the 1990s [1]. Studies have shown the efficacy of the combination of CRS and HIPEC as a curative intent modality for selected patients with pseudomyxoma peritonei (PMP) [2], diffuse malignant peritoneal mesothelioma (DMPM) [3]. Promising outcomes have also been achieved in peritoneal metastases from colorectal cancer [4], gastric cancer [5] and ovarian cancer [6]. However, the main criticism of CRS and HIPEC is that long-term survival is only achieved in selected cases at the cost of challenging surgery associated with high morbidity and mortality rates, while a combination of cytostatic treatment and targeted biological treatment can provide comparable results in the similar patients [7]. CRS and HIPEC require experienced specialists, and gaining adequate surgical skills in cytoreductive procedures and peritonectomy requires long-term training, with suggestions that at least 140–150 procedures are required to achieve optimal

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competency [8]. The indication for CRS and HIPEC vary according to institutional protocol. As such, the extent of cytoreduction also differs and there are marked variables in HIPEC with respect to not only the approach (open vs. closed), but also the type of drugs used and the duration of hyperthermia. No international standard guideline for the use of HIPEC has been developed. In addition CRS and HIPEC are associated with a high morbidity rate of 12%–57% [9,10].

The Czech Republic is among the European countries where CRS and HIPEC is less frequently performed despite a similar incidence in peritoneal surface malignancies (GLOBOCAN). The Czech public healthcare system is funded exclusively by the state, with private funding limited only to certain types of operations. Cash payments for treatment of oncological diseases, optional fees for extra services, supplies or care by a specific surgeon/physician are forbidden.

The present study aimed to evaluate the cost of cytoreductive surgery and the costs of postoperative complications in this Czech public healthcare system and identify the risk factors that increase the cost of cytoreductive surgery and HIPEC.

Material and methods

Patients

This retrospective study evaluated 80 patients with mucinous or non-mucinous peritoneal malignancies treated with CRS and HIPEC at the Department of Surgery, University Hospital of Olomouc, Czech Republic between February 2016 and November 2018. This study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology statement [11]. Patients with extent disease who underwent palliative resection and HIPEC were excluded from the study.

Assessments

All patients underwent preoperative computed tomography (CT) of the chest, abdomen, and pelvis. Gastroscopic and colonoscopic examinations were performed to identify the primary lesions. Most of the surgeries were a primary radical cytoreductive treatment. For patients with pseudomyxoma peritonei from low-grade appendiceal mucinous neoplasm or those with ovarian carcinomas, relapses were also operated after prior cytoreductive surgery in the abdominal cavity. Diagnosis was most frequently based on biopsy during diagnostic laparoscopy. Preoperative staging also included overall patient status, the American Society of Anesthesiologists (ASA) risk classification, and the results of echocardiography and spirometry examinations. Laboratory tests included the levels of tumour markers (CEA, CA19-9, CA72-4, CA-125).

CRS and HIPEC technique

The indication criteria for CRS and HIPEC were set based on the guidelines established by a local clinical tumour board. The criteria included potential for achieving complete cytoreduction, the type of tumour, the overall patient status, and the exclusion of extraperitoneal metastases. The extent of peritoneal involvement was evaluated according to Peritoneal Cancer Index (PCI) value [12], which was established by the surgeon at the beginning of the laparotomy. Initially, ascites and urine catheter samples and nasopharyngeal and rectal swabs were taken for microbiological examination. A prophylactic dosage of antibiotics (amoxicillin/sulbactam and metronidazole) was administered 1 h before the surgery and, every 8 h thereafter over an additional period of 24 h.

The extent of cytoreductive surgery was according to the extent of the peritoneal disease found during surgery, with an aim of achieving complete cytoreduction. All procedures during the surgery were performed by a single surgeon (D.K.) as supervised by Beate Rau of Charité Universitätsmedizin (Berlin, Germany). The completeness of cytoreduction [12] was evaluated as follows: CC0 – no visible residual tumour, CC1 – residual tumour $\leq$ 2.5 mm in diameter, CC2 – residual tumour measuring 2.5 mm-2.5 cm, and CC3 – residual tumour measuring >2.5 cm. All the anastomoses were constructed prior to the HIPEC procedure, using the closed method. Four drains were inserted prior to the closure of the abdominal cavity: two drains into the upper abdominal quadrants for inflow of the lavage fluid, and two drains into the lesser pelvis to outflow the lavage fluid. HIPEC was immediately performed after surgery for 30–90 min depending on the cytostatic used. Currently, we routinely use cisplatin for ovarian cancer, cisplatin and doxorubicin for mesothelioma, and mitomycin C for all other types of tumour. After HIPEC, only the drain in the left lesser pelvis was retained.

Risk factors for increased costs

The preoperative parameters included age, sex, comorbidities according to the ASA classification, body mass index, the number and type of surgeries, chemotherapy prior to the cytoreduction itself, and the type of tumour. Intraoperative parameters included the extent of disease through the PCI index, the extent of cytoreduction, number of anastomoses, operating room time (defined in this study as the time from the start of the incision to the completion of HIPEC rather than the total length of stay inside the operating room), blood loss, and the number of stomata. Postoperative complications were assessed in terms of the Clavien-Dindo classification [13,14]. We also assessed the overall duration length of hospitalisation and ICU admission and the mortality/morbidity rates.

Cost evaluation

The costs were evaluated based on the analysis conducted by the professionals of hospital's financial department. The cost analysis was divided into two subgroups: the first evaluated all demonstrable costs that can be reported within the Czech DRG system according to the Ministry of Health guidelines, along with separately charged supplies and services (staplers, advanced electrocoagulation technologies, blood products and antibiotics, and duration of hospitalisation and ICU admission). The second was a calculation of all costs for one case which in an ideal scenario without any postoperative complications would pay the true costs to the hospital for one CRS and HIPEC. As a scenario for CRS and HIPEC, we used a comparison of costs for CRS and HIPEC resulting from right colon carcinoma with localised peritoneal carcinomatosis, including right hemicolectomy, omentectomy, peritonectomy, and cholecystectomy with HIPEC using mitomycin for 90 min. In an ideal scenario, there was also a calculation of all the true personnel costs; costs for operation; and working time of surgeon and all operation personnel, including anaesthetist, nurses, and other staff. For revenues, each of the DRG case was evaluated with the total casemix value and the resulting amount of reimbursement from the health insurance companies. These cost/revenue indicators were correlated with the clinical data of each case.

Statistical analysis

Complications were analysed using the Chi-square test and Fischer exact test. The Kruskal-Wallis non-parametric analysis of variance was used to analyse the treatment cost. Perioperative

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parameters and complications that predicted increased hospital cost were identified via multivariate linear regression and via the non-parametric Mann-Whitney and Kolmogorov-Smirnov tests, respectively. All analyses were performed using NCSS2019 (NCSS, USA); $p < 0.05$ was considered significant.

Results

Patients and surgical outcomes

The 80 patients were divided into those with ($n = 40$) and without ($n = 40$) complications. The demographic characteristics of the patients are shown in Table 1. The mean length of hospitalisation and ICU admission was 15.44 ± 11.07 days and 6.15 ± 5.52, respectively. The overall morbidity in our study was 50.0%. The most frequent complications were anaemia, protracted nausea, defect of the passage and anastomotic leakage, various types of infections (e.g. urinary, airway), and abdominal collections. Three patients developed an enterocutaneous fistula, and five patients exhibited significant postoperative haemorrhage from nonsurgical sources; all of them had to be re-operated. The overall mortality was 2.5% ($n = 2$). Of the two patients, one died of severe aplastic anaemia with pancytopenia. The other patient died of pulmonary embolism during protracted sepsis and acute renal failure.

The surgical procedure and postoperative course are detailed in Table 2. Only the number of patients with a history of previous surgery (2.5% vs. 15%) and mean operation time (301.33 ± 53.84 vs. 417.19 ± 59.65) differed between the patients with and without complications. We also found statistically significant differences in the total length of hospitalisation (10.73 ± 2.93 vs. 20.15 ± 13.93 days) and ICU admission (3.73 ± 1.32 vs. 8.58 ± 6.92 days).

Cost analysis

The total treatment cost for all 80 patients amounted to €606,358 (230.61%), but the total reimbursement from the public insurance company was only €262,931 (100%); hence, the total profit margin for the CRS and HIPEC procedures for the hospital was €-343,427 (−130.61%) (Table 3). The median treatment cost for all patients without complications was € 4,085.80 ± 1,111.94. Meanwhile, the median total treatment cost for patients who developed grade I, II, III, IV, and V complications was €3,478, €5,238 ± 1,798.45, €9,565.79 ± 5,136.25, €14,638 ± 32.53, and €11,145 ± 5,498.46, respectively. (Table 4). In an ideal scenario for CRS and HIPEC of right colon carcinoma with PC and without any complications, we calculated all the real costs per case under the economic conditions of our region, and the total costs is approximately €12,257.40 (€1,307 for supplies; €210, drugs and antibiotics; €6,035.80, OR time and personnel costs; €388, supplies for HIPEC; €3,252.60, median ICU stay; and €1,064, standard ward stay).

The economic impact of the complications is analysed in Table 4. We found a strong association between the severity of the complications and the treatment costs and the duration of hospitalisation and ICU admission. The median total treatment cost increased as the grade of complications increased from grade I to grade IV. The two patients who developed Grade V complications died relatively early, and thus, neither the cost nor the length of hospitalisation reached similar to that for the grade IV complication group, where all the patients survived and were discharged for home care.

Factors associated with increased treatment cost

In univariate analysis, operating time ≥350 min (vs. <350 min, $p < 0.001$), blood loss ≥1.000 ml (vs. <1.000 ml, $p < 0.001$), and Clavien-Dindo complication grades I–V (vs. no complication, $p < 0.001$) significantly increased treatment costs (Table 5). In the multivariate analysis, only blood loss ≥1.000 ml ($p = 0.03$) and complications I–V ($p < 0.001$) were independently associated with increased costs. More detailed analysis revealed that the operating room time accounted for 17.7% of the cost variability and that every additional minute increases the costs by €22.23 ($p < 0.001$). Blood was another important factor, accounting for 75.8% of the cost variability. Every additional ml of blood loss increases the costs by €7.30 ($p < 0.001$). Although the number of anastomoses showed no statistical significance (p=0.102), it accounted for 3.4% of the cost variability, each anastomose increases the cost by €796.84. Complications accounted for 39.8% of the cost variability, with each complication grade increasing the cost by €1.611,48 ($p < 0.001$).

Discussion

To our knowledge, this is the first study to examine the cost and

Table 1
Patient demographics from peritoneal malignancies.

Factor	*n=80*		No complication n = 40		Complications n = 40		*p value*
Female (%)	77,50	(62/80)	77,50	(31/40)	77,50	(31/40)	1,000
BMI (kg/m2)	23,14	±2,28	23,14	±2,31	23,13	±2,29	0,470
age (years)	56,48	±11,87	56,93	±11,50	56,03	±12,35	0,799
Tumour origin (%)							
Colorectal cancer	16,25	(13/80)	12,50	(5/40)	20,00	(8/40)	0,363
Appendiceal tumours	12,50	(10/80)	10,00	(4/80)	15,00	(6/40)	0,499
Ovarial cancer	48,75	(39/80)	57,50	(23/40)	40,00	(16/40)	0,117
Gastric Cancer	2,50	(2/80)	2,50	(1/40)	2,50	(1/40)	1,000
Mesothelioma	10,00	(8/80)	10,00	(4/40)	10,00	(4/40)	1,000
Other	10,00	(8/80)	7,50	(3/40)	12,50	(5/40)	0,456
Previous surgery							
non	8,75	(7/80)	15,00	(6/40)	2,50	(1/40)	0,047*
abdominal resection	46,25	(37/80)	42,5	(17/40)	50,00	(20/40)	0,501
biopsy	45,00	(36/80)	55,00	(22/40)	35,00	(14/40)	0,072
Previous chemotherapy %							
yes	72,50	(58/80)	77,50	(31/40)	67,50	(27/40)	0,317
non	27,50	(22/80)	22,50	(9/40)	32,50	(13/40)	0,317

*indicates $p < 0.05$, values are presented as mean ± standard deviation, number (%) or median, n.a. = not available (continous data are shown as mean and standard deviations).

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Table 2
Operation and postoperative course demographics from peritoneal malignancies.

Factor	Total n = 80		No complication n = 40		Complications n = 40		*p* value
Operation							
Operation time	359,26	±58,75	301,33	±53,84	417,19	±59,65	<0,001*
PCI	14,06	±11,50	13,85	±11,50	14,28	±11,00	0,935
CC score							
0	61,3	(49/80)	60,0	(24/40)	62,5	(25/40)	0,409
1	38,7	(31/80)	40,0	(16/40)	37.5	(15/40)	0,592
HIPEC closed system %	100,0	(80/80)	100,0	(40/40)	100,0	(40/40)	1000
Number of anastomosis	0,99	±0,83	0,93	±0,92	1,05	±0,75	0,375
Blood loss (ml)	760,00	±286,19	706	±278,43	814	±287,06	0,076
Postoperative course							
Hospital stay (days)	15,44	±11,07	10,73	±2,93	20,15	±13,93	<0.001*
ICU stay (days)	6,15	±5,52	3,73	±1,32	8,58	±6,92	<0.001*
In hospital mortality %	2,5	(2/80)	0,0	(0/80)			0,152

*indicates $p < 0.05$, values are presented as mean ± standard deviation, number (%) or median (range), n.a. = not available continous data are shown as mean and standard deviations; ICU = intensive care unit, PCI = peritoneal cancer index, CC = completeness of cytoreduction.

Table 3
Reimbursement (Euro) from public health care system in Czech Republic.

Total reimbursement	262,931	(100) %
Overall costs	606,358	(230,61) %
drugs and materials	*148,347*	
stay, OR	*458,011*	
Loss margin total	−343,427	
Reimbursement for each case average	3,287	
Cost for each case average	7,634	

Table 4
Cost (Euro) of treatment.

Complication	Total/Euro	Hospital stay/day	ICU stay/day
0	4 085,8 (1 111,94)	10,73 (2,93)	3,73 (1,32)
I	3 478,00 (-)	13,00 (-)	5,00 (-)
II	5 238,24 (1 798,45)	13,90 (5,54)	4,90 (1,92)
III	9 565,79 (5 136,25)	26,79 (18,22)	11,36 (7,88)
IV	14,638 (32,53)	39,00 (4,24)	24,00 (4,24)
V	11,145 (5 498,46)	24,00 (19,80)	14,00 (5,66)

Values are presented as mean ± standard deviation.

financial consequences of postoperative complications following CRS and HIPEC and its sustainability in the public insurance health care system in Central/East Europe in the post-communist area. Our study shows that the costs of CRS and HIPEC markedly limits any further development and implementation of these procedures in the Czech Republic. The total cost of surgery for the 80 patients included in the study reached €606,358 (230.61%), whereas the total reimbursement from health insurance companies was only €262,931 (100%). Thus, the institution ended up with a loss of €-343,427, and this department had to cover this sum from revenues gained from other types of surgery. The financial gap is thus −130.61%, indicating that the reimbursement covers less than one-half of the cost of CRS and HIPEC. The cost per case is €7,634 (100%), while the reimbursement is only €3,287 (43%) according to the Ministry of Health guidelines in current Czech DRG system. Currently, the real total cost for standard CRS and HIPEC is approximately €12, 257.40. Although the amount may be high, this total cost for CRS and HIPEC as a potential curative treatment of advanced colic cancer is still lower compared to that for palliative systemic chemotherapy for 6 months (cetuximab + FOLFIRI), which is approximately €28,846.

The post-communist healthcare systems are characterised by limited sources and rigidity of launching any new approaches and treatment methods. The fundamental achievements included the free healthcare services covered in the form of public health insurance either directly from the state budget or re-allocating the funds into the budgets of the public health insurance companies. Currently, the systems are confronted with an extreme increase in

Table 5
Risk factors for increased costs.

Variable	Univariate		Multivariate	
	Standardized beta	*p*-value	Standardized beta	*p*- value
Age≥60	−611,88	0,452	−2,498	0,926
Previous surgery	−449,80	0,481	605,83	0,254
Previous chemotherapy	−390,78	0,668	1470,3	0,073
Sex (female ref)	242,80	0,803	532,74	0,538
Operating time ≥350 min	22,23	<0.001*	11,56	0,082
Blood loss ≥1000 ml	7,30	<0.001*	2,62	0,03*
Number of anastomosis ≥2	796,84	0,102	357,55	0,471
Colorectal anastomosis	68,64	0,933	−840,68	0,313
Complication 1-5	1 611,48	<0.001*	1505,62	<0.001*

*indicates $p < 0.05$.

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the costs of innovative treatments, particularly biological treatment of cancer, while the revenues of the public health insurance system are limited.

The problem is that the current Czech DRG system lacks a specific item to cover the cost of CRS and HIPEC. This system does not know and cannot assess the cost of peritonectomy; it knows only certain types of resection procedures that are part of cytoreduction (e.g. intestine resection, gastrectomy, splenectomy, cholecystectomy, and omentectomy). Similarly, the system is unable to estimate the cost of HIPEC. The current reimbursement patterns are based on the following codes: (1) ***06011–3***: major surgeries of the large/small intestines without complications/with complications/with life-threatening complications; (2) ***06021–3***: major surgeries of the stomach/oesophagus/duodenum without complications/with complications/with life-threatening complications; and (3) ***13012–13***: exenteration of the lesser pelvis with radical hysterectomy without complications/with complications.

Our analysis revealed clearly countable costs with respect to the length of hospitalisation, length of ICU admission, medication, and medical supplies. Similar detailed calculations can be made for the operating room costs including supplies, antibiotics, blood products, and specific devices for electrocoagulation and for HIPEC. Limited results were obtained for the HR cost per surgery because no specific codes for this type of procedure exist in the Czech reimbursement system, making it impossible to report cases such as peritonectomy and diaphragm stripping.

These quantified costs, however, are still multiply lower than those covered for CRS and HIPEC procedures in other healthcare systems. For example, in Germany, the costs per surgery reach €21,072 while reimbursement from the insurance company is € 20,474, and thus the loss per case is only roughly €598 [16]. Further, in Italy is similar only 38.5% of costs reimbursed [17]. Similarly, Baratti reported an average cost per case of €36,015 [18]. Still higher CRS and HIPEC costs have been described for the Australian system, where Chua et al. [19] calculated the average cost per case to be AUD55,000 for malignant mesothelioma, AUD66,000 for colorectal carcinoma, AUD88,000 for carcinoma of the appendix, and AUD92,000 for pseudomyxoma peritonei. The significantly lower costs of CRS and HIPEC in the Czech Republic should be considered in the context of the overall economic situation, with significantly lower personnel costs and lower prices of energy inputs, among others.

However, it remains unclear how other HIPEC centres can be established under public healthcare systems worldwide when in our experience not even half of the costs for one operation are reimbursed. CRS and HIPEC is an expensive treatment, as has been established by many studies. However, in our system, the cost for CRS and HIPEC are still lower than that for systemic treatment. During the opening of our centre, we secured sufficient financial and personnel resources to offer this treatment in our region under oversight of our hospital management. We have used all the hospital's resources, as well as grants of our university and the Ministry of Health. Our cost analyses has been helpful for the Ministry of Health to initiate a complete change of financing under our DRG system. Called the DRG restart, the system will commence in 2020–2023 and will already include all types of operations. Our site serves as a reference centre for designating CRS and HIPEC costs in the Czech Republic, thus ensuring complete financial compensation in the context of our healthcare system.

The high rate of morbidity of this procedure not only raises the treatment costs, but it can also discourage the surgical team and hospital when considering the cost effectiveness of these procedures. In this study, we observed an overall morbidity and mortality rate of 50% and 2.5%, respectively, which is comparable to that in major centres treating patients with peritoneal carcinomatosis [20–24]. Further, we found that postoperative complications following CRS and HIPEC are associated with increased morbidity rates, extended length of hospitalisation, and higher hospital costs. The significant predictors of increased costs were operating time ≥350 min, blood loss ≥1,000 ml, and grade I-IV Clavien-Dindo complications.

Mizumoto et al. [20] suggested that PCI >20, operation room time >5 h, and blood loss >2.5 l were risk factors for complications. Casado-Adam et al. [21] also found a significant correlation between morbidity and the histological grade, PCI, small-bowel resections, colorectal anastomosis, and the number of anastomoses.

Clinically, the aim is to reduce the risk of postoperative complications, and this can be achieved primarily via precise nutritional preparation and pre-operative optimisation termed "prehabilitation" [15]. A key component of prehabilitation is prescribing exercise interventions such as aerobic exercise and specific deep breathing techniques for optimal cardiovascular system function and nutritional status to ultimately improve the patient's overall condition [6,23,24].

Conclusions

The actual cost of CRS and HIPEC exceeded the reimbursed amount from the public health insurance system by approximately 130%. The treatment costs increased with the severity of postoperative complications. The risk factors for increased costs were operating room time ≥350 min, blood loss ≥1,000 ml, and grade I-IV Clavien-Dindo complications. Thus, a comprehensive review and adjustment of the reporting patterns for CRS and HIPEC in the DRG system are crucial for the sustainability and development of these procedures in the Czech Republic.

Declaration of competing interest

All authors declare that they have no conflicts of interests.

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