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Impact of extent of disease on 1-year healthcare costs in patients who undergo cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastases: retrospective observational cohort study

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Background: **The goal of this retrospective observational study was to determine the impact of the extent of peritoneal disease on 1-year healthcare costs in patients with colorectal peritoneal metastases (PM) who undergo cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS + HIPEC). The extent of peritoneal disease, expressed by the Peritoneal Cancer Index (PCI), directly affects the complexity of CRS + HIPEC and ultimately survival outcomes. The impact of the PCI on treatment-related healthcare costs remains unknown.**

Methods: **Data from patients with colorectal PM who underwent CRS + HIPEC between January 2012 and November 2017 were extracted retrospectively from an institutional database. Patients were divided into four subgroups with PCI scores ranging from 0 to 20. Treatment-related costs up to 1 year after CRS + HIPEC were obtained from the financial department. Differences in costs and survival outcomes were compared using the χ^2 test and Kruskal–Wallis *H* test.**

Results: **Seventy-three patients were included (PCI 0–5, 22 patients; PCI 6–10, 19 patients; PCI 11–15, 17 patients; PCI 16–20, 15 patients). Median (i.q.r.) costs were significantly increased for the PCI 11–15 and PCI 16–20 groups (€51 029 (42 500–58 575) and €46 548 (35 194–60 533) respectively) compared with those for the PCI 0–5 and PCI 6–10 groups (€33 856 (25 293–42 235) and €39 013 (30 519–51 334) respectively) ($P = 0{\cdot}009$).**

Conclusion: **Treatment-related healthcare costs are significantly increased among patients with extensive tumour burden (PCI score 10 or above) who undergo CRS + HIPEC for the treatment of colorectal PM.**

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Introduction

The effect of modern systemic chemotherapy regimens and molecular targeting agents for the treatment of colorectal peritoneal metastases (PM) remains limited and extends median overall survival (OS) by only up to 24 months[1–5]. The introduction of aggressive cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) has radically changed the survival outcomes for highly selected patients. During this surgical procedure, all macroscopically visible tumour deposits are removed from the abdominal cavity, which is subsequently flushed with a heated chemotherapeutic agent to eliminate all remaining tumour cells. In highly selected patients with limited and resectable colorectal PM, the reported median OS is up to 63 months, with 5-year survival rates of up to 54 per cent[6–9].

However, CRS + HIPEC is a complex procedure with major postoperative morbidity rates of 12–52 per cent

and mortality rates of 0·9–5·8 per cent[10]. Furthermore, a recovery time of 6–12 months is necessary to restore quality of life (QoL) to preoperative levels[11,12]. Therefore, only patients who would benefit the most in terms of survival and QoL, with an acceptable chance of treatment-related morbidity and mortality, should be selected for CRS + HIPEC.

Owing to the continuous rise in healthcare costs, greater focus is placed on balancing economic costs and possible survival gain of various oncological treatments, taking quality-adjusted life-years (QALYs) into account. Several cost–effectiveness analyses have been performed in the field of CRS + HIPEC, and up to nearly fivefold differences in total hospital costs were found in these series. The heterogeneity of disease burden might explain the wide range in hospital costs[13–24]. The extent and distribution of peritoneal disease is scored by the Peritoneal Cancer Index (PCI)[25]. Most HIPEC teams perform CRS + HIPEC only in patients with a PCI score below 20, whereas others maintain a lower threshold, leading to a debate about the true cut-off value for PCI. The main focus of this debate is survival outcomes after CRS + HIPEC, but costs are increasingly being weighed against the delivered value for the patient and should therefore also be included in this debate.

Previous studies have not analysed the financial consequences of the extent of peritoneal disease on healthcare costs. Therefore, the present study aimed to identify the impact of the extent of peritoneal disease, expressed by the PCI score, on perioperative hospital costs in patients with colorectal PM who undergo CRS + HIPEC.

Methods

All consecutive patients with histologically proven colorectal PM who were treated with CRS + HIPEC at a Dutch tertiary referral centre, University Medical Centre Groningen (UMCG), between January 2012 and November 2017 were identified from a merged, prospectively maintained, institutional database. The study was approved by the institutional ethics committee of UMCG (protocol number 201800395).

Patients were divided into four subgroups according to their PCI scored at the end of the cytoreduction during CRS + HIPEC (PCI 0–5, PCI 6–10, PCI 11–15 and PCI 16–20). These specific groups were selected before analysis as they represent the most commonly reported subdivisions of the PCI score in current scientific literature.

Preoperative evaluation and staging

All patients with colorectal PM underwent a standard preoperative assessment to evaluate suitability for CRS + HIPEC. Patients were staged by chest, abdominal and pelvic CT, and diagnostic laparoscopy to investigate the extent and resectability of the peritoneal disease and rule out other distant metastases. Afterwards, eligibility for CRS + HIPEC was determined by a multidisciplinary oncology team, which included a radiologist, medical oncologist, gastroenterologist and oncological surgeon. In the Netherlands, eligible candidates for CRS + HIPEC are, in general, those with completely resectable colorectal PM, PCI score below 20, no distant metastases, and a performance status that allows for major surgery. Up to three resectable liver metastases are not considered an absolute contraindication.

Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy

All CRS + HIPEC procedures were performed in accordance with the current national Dutch HIPEC protocol[9]. The surgical procedure started with explorative laparotomy to assess the extent and distribution of peritoneal disease according to the PCI score, to determine the possibility of achieving a complete cytoreduction. The PCI score combines lesion sizes (0–3 points) with the distribution of peritoneal deposits in nine abdominopelvic regions and four small bowel segments[26]. The score ranges from 0 to 39 points; a higher score indicates a more extensive tumour burden. In patients with signs of extensive disease (PCI above 20), no CRS was performed and the surgical procedure was terminated (non-therapeutic laparotomy). These specific patients were not included in the present study. When the colorectal PM were deemed resectable, CRS was performed to remove all macroscopically visible tumour tissue. Subsequently, the completeness of cytoreduction (CC) was determined, with a score of zero (CC-0) indicating no residual tumour was visible or palpable in the peritoneal cavity, CC-1 indicating the presence of a residual tumour smaller than 2·5 mm, CC-2 indicating the presence of residual tumour of between 2·5 mm and 2·5 cm, and CC-3 indicating the presence of a residual tumour larger than 2·5 cm or a confluence of nodules[27].

HIPEC was performed only in patients with (nearly) complete cytoreduction (CC-0 or CC-1). Mitomycin C (35 mg/m^2) was circulated with a temperature of 41–42°C in the abdominal cavity for 90 min. Reconstruction surgery was then performed as required, including bowel anastomosis and colostomy.

Neither neoadjuvant nor adjuvant chemotherapy is considered standard treatment in the Netherlands, and patients were given these treatments only when indicated according to the current national Dutch HIPEC protocol[9]. All

patients were admitted to the ICU for a minimum of 1 day after surgery until cardiac and pulmonary functions were stable.

Follow-up

Clinical follow-up occurred within 1 month after hospital discharge and continued on a regular 3–6-month basis for at least 5 years. In patients with suspected disease recurrence, based on clinical symptoms or an increase in carcinoembryonic antigen level, CT of the chest and abdomen was performed.

Treatment costs

All treatment-related incurred healthcare costs from 1 day before CRS + HIPEC to 1 year afterwards were obtained from the financial department. These costs included all components of the surgical procedure, postoperative in-hospital care, postoperative hospital visits (to the outpatient clinic and emergency department), and the in-hospital rehabilitation programme. These data concerned the actual individual patient-related costs that were incurred to treat the patient for CRS + HIPEC. Thus, a longer surgical procedure or more days in the ICU or ward translated directly into higher costs. Costs for preoperative workup were not included.

All the different components of healthcare costs were classified into eight categories: ward admission, ICU admission, surgical, diagnostic, therapeutic, consulting departments, outpatient visit and rehabilitation programme costs. Ward admission costs were defined as total ward costs (primary admission to hospital and also readmissions within the first year after treatment). ICU admission costs were defined as total ICU costs (primary admission to hospital and also readmissions within the first year after treatment). Surgical costs consisted of all costs of the operating room, use of consumables during surgery, surgical debulking, hyperthermia treatment, perfusionist labour, chemotherapeutic drugs, anaesthesiology and all reinterventions (for instance, surgical reintervention and ultrasound-guided drainage). Consulting department costs consisted of all costs of consulting by other medical specialties, physiotherapy consulting and dietetics consulting. Outpatient visit costs were defined as all costs for treatment-related visits at the outpatient clinic or emergency department. Costs of neoadjuvant and adjuvant chemotherapy were not included because these are not standard treatments in the Netherlands and, when indicated, these treatments were carried out in other local hospitals.

As all costs were incurred within 1 year, no discounting was applied. Analysis was carried out using 2017 costs in euros (€).

Data collection

Data for patient, tumour and surgical characteristics, postoperative outcome, and OS and disease-free survival (DFS) were collected prospectively. Data on postoperative complications were collected for up to 60 days after surgery and registered according to the Clavien–Dindo classification[8]. All essential financial data for this study were collected retrospectively with assistance from the financial department.

Primary and secondary outcomes

The primary outcome was the overall healthcare costs for CRS + HIPEC for up to 1 year after the surgical procedure, divided according to the extent of peritoneal disease (PCI 0–5, PCI 6–10, PCI 11–15, PCI 16–20). Secondary outcomes included the overall costs per month of survival, the overall costs per month of DFS, and the occurrence of major postoperative complications. DFS was defined as the time between CRS + HIPEC and the date of the first recurrence of disease or the last follow-up visit in censored cases. Major postoperative complications were classified as grade III or above according to the Clavien–Dindo classification[28].

Statistical analysis

All statistical analyses were done using SPSS® Statistics version 24.0 (IBM, Armonk, New York, USA). Continuous variables with a normal distribution are expressed as mean(s.d.) values, and those without a normal distribution are expressed as median (i.q.r.) values. Categorical variables are expressed as numbers and percentages with 95 per cent confidence intervals. Patient and tumour characteristics were compared and analysed by using the χ^2 test. The Kruskal–Wallis H test was used for continuous variables without a normal distribution. All tests were two-sided, and $P < 0{\cdot}050$ was considered statistically significant.

Results

A total of 78 patients with colorectal PM underwent CRS + HIPEC between January 2012 and November 2017. Five patients (6 per cent) were excluded from further analysis because no PCI score from the surgical procedure was found in the operation report. Thus, 73 patients were included for analysis, divided into the following four subgroups according to their PCI score registered

Table 1 Baseline characteristics of patients with colorectal peritoneal metastases who had cytoreductive surgery with hyperthermic intraperitoneal chemotherapy, according to Peritoneal Cancer Index groupTable 1 Baseline characteristics of patients with colorectal peritoneal metastases who had cytoreductive surgery with hyperthermic intraperitoneal chemotherapy, according to Peritoneal Cancer Index group

	PCI 0–5 ($n = 22$)	PCI 6–10 ($n = 19$)	PCI 11–15 ($n = 17$)	PCI 16–20 ($n = 15$)	P†
Patient characteristics					
Age (years)*	61 (54–68)	63 (57–65)	61 (51–69)	64 (53–69)	0·964‡
Sex ratio (M : F)	10 : 12	11 : 8	8 : 9	9 : 6	0·755
BMI (kg/m^2)*	25·0 (24·2–26·9)	25·0 (24·2–26·9)	28·0 (25·8–31·5)	25·2 (22·8–28·6)	0·070‡
ASA grade					0·145
I	4	5	0	1	
II	15	11	14	14	
III	3	3	3	0	
Co-morbidity					
Diabetes	3	0	1	2	0·209
Hypertension	6	4	3	2	0·780
Cardiovascular disease	2	3	2	0	0·506
Pulmonary disease	6	1	2	2	0·264
Tumour characteristics					
Primary tumour location					0·576
Right colon	9	7	8	3	
Transverse colon	1	3	1	0	
Left colon	3	3	2	4	
Sigmoid	6	3	5	7	
Rectum	3	3	1	1	
Signet ring cell histology	1	1	2	2	0·478
T status of primary tumour					0·294
≤ T3	13	10	5	8	
T4	9	9	12	7	
N status of primary tumour					0·385
N0	9	8	3	2	
N1	5	5	7	5	
N2	8	6	7	8	
M status of primary tumour					0·668
M0	11	9	6	8	
M1	11	9	11	6	
Mx	0	1	0	1	
Onset of colorectal PM					0·536
Synchronous	10	8	11	7	
Metachronous	12	11	6	8	
Liver metastases	0	2	3	2	0·276

*Values are median (i.q.r.). PCI, Peritoneal Cancer Index; PM, peritoneal metastases. †χ^2 test, except ‡Kruskal–Wallis H test.

during CRS + HIPEC: PCI 0–5, 22 patients; PCI 6–10, 19 patients; PCI 11–15, 17 patients; and PCI 16–20, 15 patients.

Patient and tumour characteristics

There were no significant differences in patient and tumour characteristics at baseline between the four PCI groups (*Table 1*).

Treatment characteristics

Table 2 presents the treatment characteristics of CRS + HIPEC for the four PCI groups. Higher PCI scores were associated with a prolonged median duration of surgery ($P < 0·001$) and a significant increase in the number of anatomical resections needed to achieve complete cytoreduction ($P < 0·001$). In addition, a stoma following HIPEC was more common in the higher PCI groups ($P = 0·005$); seven of 22 patients (32 per

Table 2 Treatment characteristics for patients with colorectal peritoneal metastases who had cytoreductive surgery with hyperthermic intraperitoneal chemotherapy, according to Peritoneal Cancer Index group

	PCI 0–5 ($n = 22$)	PCI 6–10 ($n = 19$)	PCI 11–15 ($n = 17$)	PCI 16–20 ($n = 15$)	P‡
Duration of surgery (time)*	437 (377–480)	490 (453–551)	515 (482–584)	557 (494–641)	< 0·001§
No. of anatomical resections*	3 (2–4)	5 (4–7)	7 (5–8)	7 (5–10)	< 0·001§
No. of anastomoses					0·013§
0	13	4	3	7	
1	7	6	10	6	
≥ 2	2	9	4	2	
Stoma after HIPEC	7	9	12	13	0·005
Blood loss (ml)*	500 (300–1000)	1100 (425–1875)	1000 (700–1500)	1000 (500–1750)	0·065§
Resection status					0·342
CC-0	22	19	16	15	
CC-1	0	0	1	0	
Hospital stay (days)*	14 (11–19)	22 (13–35)	21 (18–30)	17 (13–38)	0·102§
Reoperation	1	2	6	2	0·053
In-hospital mortality	1	0	0	0	0·503
Clavien–Dindo complication grade					0·328
I–II	7	6	8	6	
III–IV	4	5	7	4	
Complication type (grade III–V)					
Anastomotic leak	1	2	1	1	0·813
Intra-abdominal abscess	1	3	4	3	0·549
Wound infection	0	1	0	0	0·539
Wound dehiscence	0	0	2	0	0·100
Pneumonia	1	0	1	1	0·566
Bacteraemia (cause unknown)	0	0	1	1	0·369
Electrolyte disorder	1	0	0	1	0·151
Fistula formation	1	0	1	0	0·654
Urinoma	0	0	1	0	0·342
Cardiac disease	1	0	1	0	0·518
Neoadjuvant chemotherapy (CRS + HIPEC)	6	4	3	2	0·783
Adjuvant chemotherapy (CRS + HIPEC)	4	3	5	5	0·628
Overall survival (months)†	35 (26, 44)	32 (25, 38)	27 (20, 33)	23 (15, 31)	0·112§
Disease-free survival (months)†	22 (13, 30)	17 (11, 23)	15 (9, 21)	13 (5, 20)	0·300§

Values are *median (i.q.r.) and †mean (95 per cent c.i.). PCI, Peritoneal Cancer Index; CC, completeness of cytoreduction score; CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy. ‡χ^2 test, except §Kruskal–Wallis H test.

cent) in the PCI 0–5 group required a stoma, increasing to 13 of 15 (87 per cent) in the PCI 16–20 group. However, the occurrence of major postoperative complications and median hospital stay were similar between the groups ($P = 0·328$ and $P = 0·102$ respectively). Overall, the in-hospital mortality rate was 1·4 per cent (1 of 73 patients) and did not differ between the PCI groups ($P = 0·503$).

Overall and disease-free survival

The mean OS for the entire cohort was 30 (95 per cent c.i. 7 to 60) months and the mean DFS was 17 (2 to 52) months. Ten patients (14 per cent) died within the first year after CRS + HIPEC (PCI 0–5, 4 patients; PCI 6–10, 1 patient; PCI 16–20, 5 patients).

Table 2 shows a trend towards a decreased OS after CRS + HIPEC in the higher PCI groups, but this trend was not statistically significant ($P = 0·112$). This same non-significant trend was found for DFS ($P = 0·300$).

Treatment costs

For the entire cohort, the total median (i.q.r.) hospital costs were €40 779 (32 465–53 137). The majority of hospital costs were determined by the surgical costs (39 per cent), ward admission costs (34 per cent) and ICU admission costs (12 per cent) (*Fig. 1*).

Fig 1 Pie chart showing breakdown of overall healthcare costs for cytoreductive surgery with hyperthermic intraperitoneal chemotherapy for up to 1 year after the surgical procedure

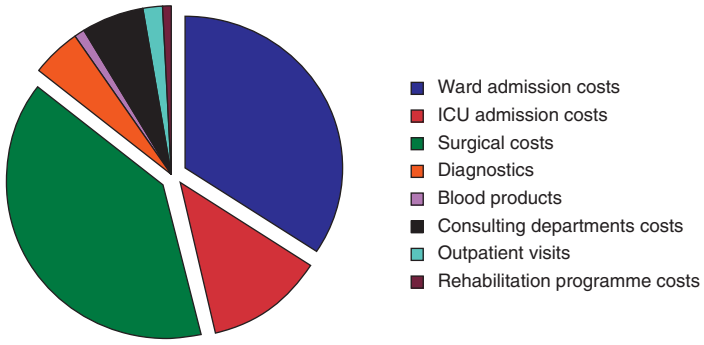

Table 3 Total costs and components of the combined procedure of cytoreduction and hyperthermic intraperitoneal chemotherapy 1 day before surgery to 1 year afterwards

	PCI 0–5 ($n = 22$)	PCI 6–10 ($n = 19$)	PCI 11–15 ($n = 17$)	PCI 16–20 ($n = 15$)	P†
Total costs (€)*	33 856 (25 293–42 235)	39 013 (30 519–51 334)	51 029 (42 500–58 575)	46 548 (35 194–60 533)	0·009
Items (€)*					
Ward admission costs	9444 (7349–17 610)	14 360 (7792–19 624)	14 604 (11 408–19 366)	13 083 (7045–17 379)	0·396
ICU admission costs	4407 (4312–6610)	4407 (4312–6610)	4407 (4359–6468)	6468 (4312–8625)	0·767
Surgical costs	11 657 (9712–15 504)	13 651 (11 716–16 788)	17 503 (15 751–21 504)	14 835 (13 392–17 166)	0·001
Diagnostics					
Laboratory costs	582 (456–760)	644 (511–832)	785 (590–965)	721 (487–1046)	0·088
Radiology costs	445 (326–884)	733 (159–1481)	1413 (649–2007)	605 (480–1498)	0·034
Microbiology costs	202 (0–576)	220 (57–399)	405 (42–837)	168 (72–428)	0·612
Pathology costs	910 (501–1207)	670 (473–1185)	620 (229–994)	560 (115–1369)	0·532
Other costs	25 (14–788)	135 (9–1126)	1021 (141–2206)	95 (16–521)	0·097
Therapeutic costs					
Blood products	0 (0–287)	459 (0–690)	459 (0–460)	690 (0–1381)	0·015
Consulting departments costs	1205 (741–2031)	2321 (729–3601)	2889 (1003–4511)	3307 (1973–6205)	0·024
Outpatient visits	545 (293–1716)	731 (361–1410)	1291 (605–2507)	2015 (1016–2762)	0·016
Rehabilitation programme costs	172 (69–422)	151 (92–277)	319 (151–541)	193 (143–680)	0·389
Costs per month of OS	950 (690–2352)	1288 (1054–1924)	2079 (1264–3451)	2101 (1424–5347)	0·010
Costs per month of DFS	2089 (823–6078)	2538 (1317–5451)	4990 (1997–7513)	7129 (2216–9966)	0·095

*Values are median (i.q.r.). PCI, Peritoneal Cancer Index; OS, overall survival; DFS, disease-free survival. †Kruskal–Wallis H test.

Table 3 presents an overview of the total median hospital costs from 1 day before CRS + HIPEC to 1 year afterwards, according to the four PCI groups. Median (i.q.r.) hospital costs were significantly increased for PCI 11–15 and PCI 16–20 groups (€51 029 (42 500–58 575) and €46 548 (35 194–60 533) respectively) compared with those for PCI 0–5 and PCI 6–10 groups (€33 856 (25 293–42 235) and €39 013 (30 519–51 334)) respectively ($P = 0·009$).

Total median hospital costs were increased in the PCI 11–15 and PCI 16–20 groups compared with those in the PCI 0–5 and PCI 6–10 groups, because of a significant increase in surgical costs ($P = 0·001$), radiology costs ($P = 0·034$), therapeutic costs ($P = 0·015$), consulting departments costs ($P = 0·024$) and costs for outpatient visits ($P = 0·016$). The remaining costs, including ICU and ward admission costs, were similar between the PCI groups.

Table 3 also provides an overview of the median hospital costs per month of OS and per month of DFS. Median (i.q.r.) hospital costs per month of OS were significantly increased in the PCI 11–15 and PCI 16–20 groups (€2079 (1264–3451) and €2101 (1424–5347) respectively) compared with those in the PCI 0–5 and PCI 6–10 groups (€950 (690–2352) and €1288 (1054–1924)) respectively ($P = 0·010$). The same trend was found for median hospital

costs per month of DFS, but this was not statistically significant ($P = 0{\cdot}095$).

Discussion

This observational cohort study, consisting of 73 patients with colorectal PM who underwent CRS + HIPEC, revealed that treatment-related healthcare costs increased significantly among patients with extensive tumour burden (PCI score of 10 or more). This increase is explained mainly by a prolonged duration of surgery, as well as the significantly higher costs from consulting departments and additional outpatient visits during the postoperative recovery period. This financial approach to the extent of peritoneal disease might help further to balance economic healthcare costs with the associated survival gain in the near future.

The study shows that treatment-related healthcare costs increase by one-third in patients with a high PCI (score of 10 or above) compared with costs in patients with a low PCI (score below 10). One of the main reasons for this increase seems to be the complexity of the surgical procedure itself, as surgical costs, operation time, radiology costs, and costs from consulting departments and outpatient visits increased significantly with higher PCI scores. In addition, patients with a high PCI score appear to need more intensive postoperative monitoring during the first year by their own surgical oncologist, because of the occurrence of late postoperative complications, nutritional issues, conditional problems and mental health problems.

Quite unexpectedly, no significant differences were found between the different PCI groups regarding postoperative complications, length of hospital stay or survival outcomes, although this might be explained by the limited number of patients in the present study. Nevertheless, the extent of cytoreductive surgery is a well known risk factor for treatment-related morbidity and mortality, which are associated with a diminished survival gain and a serious increase in hospital costs of approximately 320 per cent[22,29–33].

Overall, 11 cost–effectiveness analyses[13–20,22–24] and one comprehensive review[21] have reported data on the impact of CRS + HIPEC on hospital costs and up to fivefold differences were found between these studies. It should be noted that most studies[14–19,24] also included patients with primary tumour types other than colorectal in origin. Only six studies[15–18,20,22] reported a median PCI score (ranging from 8 to 22), but the PCI scores of patients with colorectal PM could not be extracted. Median hospital costs ranged from €9406 to €46 351. Only Bagnoli and colleagues[18] suggested a possible impact of the PCI score (ranging from 1 to 13) on total hospital costs. Moreover, differences in patient populations, tumour types, healthcare systems and definitions for hospital costs make it challenging to compare the present results with those in the current scientific literature. In addition, the present study analysed total healthcare costs up to 1 year after CRS + HIPEC to provide a more accurate overview of the actual healthcare costs, including those incurred during the recovery period.

Apart from extending life, QoL associated with life-years gained is an important reason for performing CRS + HIPEC. A QALY is a generic measure of disease burden that includes both the quality and quantity of life lived, and is also used to assess the value for money[34]. Two studies[21,24] have taken QALYs into consideration, and both considered CRS + HIPEC to be cost-effective. Hamilton and co-workers[24] directly compared HIPEC with palliative systematic chemotherapy, and HIPEC was deemed cost-effective. However, this conclusion was not subdivided into different PCI groups, and therefore a definitive conclusion for high-volume cases could not be made. Nowadays, the authors' institution monitors the QoL of patients undergoing HIPEC with various standardized questionnaires to enable a cost–effectiveness study to be conducted in the near future.

Complex CRS + HIPEC procedures have provided hope for a prolonged survival with acceptable QoL for patients with colorectal PM. However, the optimal cut-off value of the PCI score to perform CRS + HIPEC remains a topic of debate. PCI-associated healthcare costs have never been assessed and included in this debate. This highlights the importance of the present study, demonstrating the financial impact of the PCI on treatment-related healthcare costs, which can assist in future healthcare policy decisions.

This study has potential limitations. All patients were those from a highly experienced tertiary referral centre with 15 years of experience with CRS + HIPEC procedures. Therefore, it might not be possible to generalize these results to other medical centres, although in the Netherlands today most CRS + HIPEC procedures are performed in highly experienced HIPEC centres. Moreover, only healthcare costs incurred in the authors' own centre were available for analysis; a small number of patients received neoadjuvant or adjuvant chemotherapy in another hospital and therefore these costs were unavailable. In addition, unplanned readmissions within the first year after CRS + HIPEC could have taken place in non-index hospitals. Finally, the number of included patients was too small to perform several subanalyses in the PCI subgroups. This might also explain the higher healthcare costs for the PCI 10–15 group compared with costs in the PCI 16–20 group. Nevertheless, treatment-related healthcare costs remained significantly increased among

patients with extensive tumour burden who underwent CRS + HIPEC.

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