Quality of life after cytoreductive surgery and intraoperative hyperthermic intraperitoneal chemotherapy for peritoneal surface malignancies: A systematic review

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Abstract

Background: Cytoreductive Surgery (CRS) accompanied by Hyperthermic Intraperitoneal Chemotherapy (HIPEC) is a promising technique in the treatment of peritoneal metastatic disease. The complexity and the potential adverse effects of the procedure can significantly affect patients’ Quality of Life (QoL). Few studies have assessed the impact of CRS + HIPEC in patients’ QoL using structured and validated tools. This is a systematic review of the currently available published data, investigating the QoL after performing CRS + HIPEC for tumours of varying primary origin.

Methods: We performed a systematic review of the studies indexed in PubMed database until July 2014, using as key phrase “quality of life” and “intraperitoneal chemotherapy”, including studies using only validated questionnaires for assessing quality of life parameters.

Results: 20 studies were identified that matched the criteria set. The results of these studies, although of significant heterogeneity, clearly demonstrate that although overall QoL scores drop in the immediate postoperative period, at an average of 3 months post procedure they recover to 80%—100% or even exceed baseline values. Furthermore, between 6 and 12 months postoperatively, overall QoL is improved in survivors compared to pre-operative status.

Conclusions: CRS and HIPEC is feasible as a treatment modality in selected patients with peritoneal metastatic disease and can preserve or even improve patients’ overall quality of life.

Keywords: Cancer; Quality of life; Intraperitoneal chemotherapy; HIPEC; Surgery

Introduction

Cytoreductive surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) for peritoneal metastases (PM) is gradually being accepted as an effective and promising treatment modality for what was until recently considered to be a terminal condition. Despite the existence of technical variations across institutions, the main concept of CRS + HIPEC can be summarized by the surgical excision of all the visible metastatic deposits in the abdominal cavity combined with heated intraperitoneal chemotherapy to attempt to destroy microscopic cancer cells in the abdominal cavity. The use of intraperitoneal chemotherapy enables high concentrations of chemotherapy agents in the abdominal compartment. The addition of hyperthermia further enhances the oncological efficacy of the technique due to its cytotoxicity and synergistic action with the chemotherapy agents, resulting in better penetration in the sites of tumour deposits. Hyperthermia also increases the vascular supply of
cancerous deposits, improving the local concentration of the chemotherapy.\(^3,4\)

There is no doubt that appropriate selection of patients for CRS + HIPEC is a crucial factor determining the success of the technique\(^5\) and this will have a significant bearing on the QoL benefits of the procedure. There are also numerous technical aspects requiring evaluation by future randomised clinical trials, predominantly in search of the optimal chemotherapy regimens, the possible intraoperative combination of intraperitoneal and systemic chemotherapy, the potential implementation of secondlook operation strategies and the emerging role of intraperitoneal administration of immunoregulation agents.\(^6\)–\(^10\)

There is mounting evidence supporting the use of CRS and HIPEC in prolonging patients’ survival from various tumour types, including gastrointestinal, ovarian and primary peritoneal malignancies.\(^11,12\) For some peritoneal surface malignancies, such as pseudomyxoma peritonei and peritoneal metastases of colorectal origin, CRS and HIPEC has become established as the standard of care.\(^13,14\) However the procedure is complex and carries high morbidity rates and long hospital stays.\(^15\)–\(^17\) The combination of multiple peritoneal and visceral resections required to achieve complete cytoreduction, as well as the local and systemic adverse effects of HIPEC, give rise to justified concerns with respect to the health-related Quality of Life-HRQoL of patients undergoing this major procedure. The aim of this systematic review is to investigate the outcomes of published studies evaluating HRQoL following CRS + HIPEC for peritoneal metastatic disease and to identify areas for future research.

### Methods

We performed a systematic review of the studies indexed in PubMed database until July 2014, using as key phrase “quality of life” and “intraperitoneal chemotherapy”. We included studies that evaluated the Quality of Life (QoL) after cytoreductive debulking surgery (CRS/DBS), followed by intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC), irrespective of the primary cancer site. In our literature search, the shortened “Quality of Life” term was used instead of the more precise “health-related Quality of Life” in alignment with the terminology used in the relevant studies. However the definition of HRQoL was not attenuated, as QoL in our reported studies refers to the extent to which one’s usual or expected physical, emotional, and social well-being are affected by a medical condition or its treatment.\(^18\)

We excluded all studies in which the evaluation of QoL was performed without structured questionnaires/validated tools, as well as studies not published in English. Citations of articles retrieved at the initial literature search were manually searched to identify further relevant studies meeting the purpose and selection criteria of this systematic review.

### Results

The initial literature search identified 247 articles,\(^20\)–\(^38\) of which met the inclusion criteria for the systematic review. The study flowchart is presented in Fig. 1. Overall, thirteen out of the eighteen studies included were prospective and the remaining seven were cross-sectional. In general, the most widely used validated tools for QoL assessment were the Functional Assessment of Cancer Therapy (FACT), with the relevant subscales depending on the origin of the primary malignancies, the Eastern Cooperative Oncology Group (ECOG) Performance Status Rating Scale, the Medical Outcomes Study Health Survey - Short Form (SF-36) and the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire. The majority of published studies evaluating QoL after cytoreductive or debulking surgery accompanied by HIPEC, included patients with various primary cancers and different HIPEC protocols implemented across the specialist centres. However, despite their heterogeneity, the use of standardised questionnaires and the use of regular follow-up time points for QoL assessment enabled the drawing of general conclusions. A summary of the methodology and demographic details, as well as the main outcomes of the studies included in the systematic review are presented in Table 1.

A consistent finding in all the studies is that QoL appears to be significantly decreased in the immediate postoperative period and/or at the first follow-up time point, which in most studies was set at 3 months postoperatively. At this time point, when the recovery from this major procedure has usually been completed, overall QoL values seem to return to 80–100% of baseline measurements.\(^20,27,30,38\) QoL scores generally returned to baseline levels at 6 months after the procedure and interestingly, in the majority of studies where follow-up was extended beyond 6 months, QoL scores exceeded baseline scores, indicating overall benefit from the procedure in the long term.\(^20,27,29,38\)

Of note, 74%—94% of patients were able to resume their normal activities to a reasonable degree 12 months following surgery, despite certain limitations to normal activities.\(^26,32,38\) The reported gastrointestinal problems do not seem to be related to the extent of bowel resection. Furthermore, no firm conclusions can be drawn regarding the question of whether stoma formation as part of the procedure impairs patients’ QoL, as the results on this were conflicting.\(^28,30,35\) With respect to pain scores, Hill et al.\(^26\) reported that although pain levels exceeded baseline values at 3 months’ follow-up, at 6 months and 12 months, pain scores were below baseline measurements. Alves et al.\(^27\) reached the same conclusion in their cohort of pseudomyxoma peritonei patients, with reduction of pain scores being observed only in the complete cytoreduction patient group. With respect to patients’ sexual function, patients appear to experience significant problems, particularly in the
immediate post-operative period. Reduced sexual function seems to persist and remain below baseline during long-term follow-up and affects both sexes, as reported by Jess et al.30 Finally, Kirby and colleagues, in a cross-sectional study evaluating QoL in patients who underwent at least one CRS + HIPEC, demonstrated that QoL scores were similar when comparing patients who had single versus multiple procedures, with almost 80% of patients amenable to having the procedure again if required.24 This is especially relevant in view of mounting data suggesting an emerging role for re-do CRS + HIPEC in selected cases of recurrent peritoneal metastases, as well as in second-look operations in cases with high risk of peritoneal metastases.

Discussion

Determining QoL following CRS + HIPEC is of paramount importance, as global acceptance of the value of the procedure cannot be based solely on superior oncological outcomes, but needs to be accompanied by solid evidence demonstrating the preservation or improvement of QoL. Despite the recognised magnitude and morbidity associated with CRS + HIPEC, this review has demonstrated clear benefits in QoL at 3–6 months following surgery.

Although the included studies are of a heterogeneous nature, with most of them assessing QoL in patients with different primary cancers, using different QoL questionnaires, evaluating QoL at different time points and with significant variations in numbers of patients in study populations, the data consistently demonstrates a recovery of QoL 3–6 months after the procedure. It is important to mention that almost all studies which compared pre-operative to post-operative QoL scores reported that at time points of 3 or 6 months, overall QoL measures had returned to baseline levels or exceeded them.20,23,27,29,34,36,38 Furthermore, when compared to general population-matched samples or using data from general population-based normograms, patients undergoing CRS + HIPEC had equivalent or even improved QoL scores.22,30 However, it must be noted that the “expected” generally observed reduction in the number of assessed patients at long-term follow-up implies that a certain percentage of alive-with-disease patients decline participation in the QoL evaluation process. This can be due patients experiencing a general decline in health due to the development of cancer recurrence. In addition it must be noted that
<table>
<thead>
<tr>
<th>Authors/Date</th>
<th>Study Sample &amp; Primary Cancer Origin</th>
<th>Chemotherapeutic Agent Used in HIPEC/CC Status</th>
<th>QoL Assessment Tool(s) and Time Points of Assessment</th>
<th>Main Outcomes</th>
</tr>
</thead>
</table>
| Chia et al. (2014)      | n = 63/ovarian = 28, appendiceal = 13, colorectal = 12, primary peritoneal = 5, mesothelioma = 5 | Not reported/Not reported                       | EORTC QLQ-30/cross-sectional with the mean interval between QoL assessment and procedure being 1.3 years | • Median follow-up 1.08 years (0.06–9.8) & median time from surgery to the questionnaire 1.3 years (0.24–10.18)  
  • no statistical difference in QoL scores when comparing by age, gender, recurrence, gender, PCI score, presence of a complication and type of primary cancer  
  • QoL scores were highest less than 6 months after surgery, dropped subsequently but rose again after 2 years CRS + HIPEC patients had better scores compared to a control group of outpatient cancer patients at our institution & the reference EORTC group |
| Passot et al. (2014)    | Initial study sample n = 216/ovarian = 76, colorectal = 57, PMP = 40, mesothelioma = 13, gastric = 12, other = 18 | cisplatin, mitomycin C, oxaliplatin and irinotecan, alone or in combination/95% CC0/1 | Gastro-Intestinal Quality of Life Index questionnaire (GIQLI), completed preoperatively and at 1, 3, 6 and 12 months post-op (n = 175/194/192/192/192 respectively) | • Questionnaire compliance was 81%, 90%, 89%, 89% and 74% at baseline, 1, 3, 6 and 12 months respectively  
  • QoL was significantly decreased up to 6 months and returned to baseline at 12 months  
  • factors decreasing QoL were origin of PC at 3 months, presence of stoma at 6 months and length of surgery over 270 min and disease recurrence at 12 months |
| Argenta et al. (2013)   | n = 10/ovarian                        | Carboplatin/50% CC0                            | FACT-O/QoL assessed pre-op, immediately post-op and at t/up [median t/up 16mo (6–23mo)] | • QoL measures were significantly worse in the immediate post-op period compared to baseline (FACT-O score 126 vs. 108)  
  • FACT-O scores improved to 90% of baseline (median FACT-O = 113) by the 6mo time point but remained significantly below the baseline |
| Tan et al. (2013)       | n = 27/ovarian = 15, appendiceal = 5, colorectal = 4, primary peritoneal = 2, endometrial = 1 | Mitomycin C or cisplatin/100% CC0/1            | EORTC QLQ-C30/QoL assessed 6mo-18mo post-op; scores compared with disease-free cancer patients; no baseline data | • global health status and functional and symptom scores largely similar between HIPEC group and the reference group  
  • cognitive functioning and fatigue scores significantly better in the group after CRS and HIPEC  
  • post-op morbidity 48% (26% grade III-IV complications) |
| Tsilimbaris et al. (2013)| initial study sample n = 90/colorectal = 21%, ovarian = 19%, PMP = 14, gastric = 10%, mesothelioma = 19%, appendiceal = 16% | Not reported/82% CC0/1                         | EORTC QLQ-C30/QoL assessed pre-op (n = 83) and post-op at 1mo/3mo/6mo/12mo/24mo/36mo/60mo (n = 83/53/42/32/17/6 respectively) | • global health status decreasing from baseline until the 12mo t/up; increasing compared to baseline at 24mo & 36 mo t/up  
  • physical and role function recovered significantly at 6 months and were close to baseline at the 24-month measurement.  
  • cognitive and social function had slow recovery on follow-up  
  • overall acceptable QoL; no significant differences in QoL between patients who had single or re-do procedures  
  • 79% of patients positive to undergo additional CRS + HIPEC if required |
| Kirby et al. (2013)     | n = 63/all PMP (22% of patients had more than one cytoreduction) | Not reported/Not reported                       | FACT-C & FACT-TS/G/QoL assessed at median 31mo post-op (range: 6mo-161mo); no baseline data |  

<table>
<thead>
<tr>
<th>Study Details</th>
<th>Sample Size</th>
<th>Treatment</th>
<th>QoL Assessment</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duckworth et al. (2012)</td>
<td>n = 102</td>
<td>primary origin not stated</td>
<td>FACT-C, SF-36 &amp; Pittsburg Sleep Quality Index/QoL assessed after at least 12mo post-op</td>
<td>SF-36 Physical Component scores significantly lower than general population; Mental Component scores significantly higher; FACT scores higher than general FACT normative scores. Significant sleep quality impairment in 56% of cases.</td>
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<tr>
<td>Hill et al. (2011)</td>
<td>Initial sample n = 61</td>
<td>all colorectal</td>
<td>FACT-C, BPI, SF-36, CES-D, ECOG/QoL assessed pre-op (n = 61) and post-op at 3mo/6mo/12mo (n = 32/27/19 respectively)</td>
<td>Emotional well-being improved after HIPEC; social/family well-being and colon subscale of FACT worsened at 3mo, recovered at 6mo and 12mo; pain scores above baseline at 3mo; below baseline at 6mo &amp; 12mo; at 3mo, 6mo, 12mo f/up patients resumed 56%/70%/75% of normal activities resp.</td>
</tr>
<tr>
<td>Alves et al. (2010)</td>
<td>n = 49</td>
<td>all PMP</td>
<td>EORTC QLQ-C30/QoL assessed pre-op (n = 49) and post-op at 1mo/3mo/6mo/12mo (n = 48/47/46/45)</td>
<td>Global QoL decreased at 1mo f/up, gradually increasing and exceeding baseline at 12mo f/up for both CRS and debulking groups. Significant improvement of appetite at 12mo for all patients; significant improvement of pain at 12mo for cytoreduction group, not for debulking group; fatigue and nausea or vomiting marginally improved at 12mo; post-op mortality 0%, post-op 9% (grade III/IV complications).</td>
</tr>
<tr>
<td>Zenasni et al. (2009)</td>
<td>n = 68</td>
<td>PMP = 32, mesothelioma = 11, colorectal = 13, appendiceal = 2, other = 10</td>
<td>Oxaliplatin + Irinotecan or oxaliplatin or cisplatin or Mitomycin C or Mitomycin C + cisplatin/Not reported</td>
<td>Global QoL decreased at 1mo f/up using EORTC QLQ-C30 was75 (16.7–100). HIPEC did not result in exhibition of emotional disorders. Gastrointestinal problems not related to extended bowel resection, total colectomy, or short bowel syndrome.</td>
</tr>
<tr>
<td>Marci et al. (2009)</td>
<td>n = 18</td>
<td>colorectal = 8, gastric = 5, ovarian = 5</td>
<td>Cisplatin + Mitomycin C or cisplatin + doxorubicin/100% CC0/1</td>
<td>Overall QoL scores at 3mo f/up decreased compared to baseline; returning to pre-op levels at 6mo f/up. 27.7% post-op morbidity and 0% post-op mortality rates.</td>
</tr>
<tr>
<td>Jess et al. (2008)</td>
<td>Initial sample n = 23</td>
<td>pseudomyxoma peritonei</td>
<td>MOS-SF36, EORTC QLQ-30, CCM-38 QoL assessed pre-op (n = 13) and post-op at 3mo/6mo/12mo/18mo/24mo (n = 12/14/15/11/14 respectively)</td>
<td>Significant decrease in SF-36 PCS and role physical scores at 3mo; returning to baseline at 6mo f/up; other scores comparable to normal population. Permanent stoma did not influence QoL. 70% morbidity rate; 0% 30-d mortality rate.</td>
</tr>
<tr>
<td>McQuellon et al. (2008)</td>
<td>Initial sample n = 58</td>
<td>appendiceal</td>
<td>FACT-C, MOS-SF36, CES-D, ECOG, PSR/QoL assessed pre-op (n = 58) and at 3mo/6mo/12mo post-op (n = 55/33/28)</td>
<td>SF36 scores decreasing at 3mo f/up — improved above baseline at 6mo. Morbidity: 16%–3.4% 30-d mortality rate; estimated median survival 39.6 m.</td>
</tr>
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| McQuellon et al. (2007) | Initial sample $n = 96$/ appendiceal = 36, colorectal = 24, PMP = 9, ovarian = 5, gastric = 4, miscellaneous = 18 | Mitomycin C/Not reported | FACT-C, MOS-SF36, CES-D, BPI-SF, ECOG PSR/QoL assessed pre-op ($n = 96$) and at 3mo/6mo/12mo post-op ($n = 38/32/24$ respectively) | • significant improvements from pre-12 m for all FACT scales except SWB  
• mean FACT-G scores returned to baseline at the 3mo f/up  
• improvement of physical well-being at 6mo; patients resume 80% of activities  
• significant percentage of patients rated themselves as limited a “lot” on daily activities  
• 32% mortality rate at 12mo f/up  
• QoL scores at 6–8 weeks following HIPEC were 15–25% lower than the baseline scores  
• scores returned to baseline values at 3–6 months f/up  
• physical and mental component scores of SF-36 at 3–6 months post-op were slightly higher than baseline |
| Lim et al. (2007) | $n = 28$/peritoneal sarcoma | Cisplatin or Cisplatin + Mitoxantrone/ 95% & 100% CC0/1 | FACT-G score, SF-36, VAS/QoL assessed pre-op, 6–8w post-op & 3–6mo post-op | • FACT-C scores returned to baseline at 4mo post-op and improved significantly at the 8mo & 12mo f/up  
• post-op mortality 0%, morbidity 51%, median survival 41.4mo |
| Tuttle et al. (2006) | Initial sample $n = 35$/ appendiceal = 19, colon = 7, mesothelioma = 3, gastric = 2, 2 small intestine = 2, gallbladder = 1, unknown origin = 1 | Mitomycin C/57% CC0/1 | FACT-C, FACT-G/QoL assessed pre-op ($n = 35$) and post-op at 4mo/8mo/12mo, ($n = 29/19/12$ respectively) | • FACT-C scores returned to baseline at 4mo post-op and improved significantly at the 8mo & 12mo f/up  
• post-op mortality 0%, morbidity 51%, median survival 41.4mo |
| Schmidt et al. (2005) | $n = 20$ (initial study sample $n = 67$/appendix, ovary, peritoneum, stomach, liver, small intestine, colon, sarcoma, uterus, pancreatic, retroperitoneal, unknown origin = 1) | Cisplatin,Mitomycin C, Mitoxantrone/67% CC0/CC1 | EORTC QLQ-30/cross-sectional with the mean interval between QoL assessment and procedure being 4 years | • Mean score global health status = 62.6 vs 73.3 for control group  
• Mean score for patients with stoma 16.7 vs 67.7 for patients without stoma  
• Highest functional symptom scores: fatigue (48.6), insomnia (38.1), pain (35.6)  
• 34% morbidity and 4.5% post-op mortality |
| Alexander et al. (2004) | $n = 73$/peritoneal mesothelioma = 23, gastrointestinal = 50) | Cisplatin/not stated | MOS-SF36, FACT-C/QoL assessed pre-op/6w/3mo/6mo/9mo post-op | • FACT-C mean scores improved significant at 3, 6, 9 mo compared to baseline  
• PCS decreased significantly at 6 weeks but did not differ at 3, 6 and 9 mo compared to baseline.  
• MCS increased significantly at 6 weeks and 3 mo but did not differ at 6 and 9 mo compared to baseline  
• 30% morbidity at median f/up of 17 mo  
• long-term QoL scores did not differ significantly from 3mo/6mo/12mo.  
• recovery occurring early at 3mo, progressing to peak at 6–12mo post-op  
• mean SF-36 score comparable to controls  
• no limitations on moderate activity in 94% of cases |
| McQuellon et al. (2003) | $n = 17$ of 109 eligible/ appendiceal = 10, colorectal = 5, ovarian = 1, primary peritoneal = 1 | Mitomycin C/59% R0/1 resection | FACT-C, MOS-SF36, CES-D, LAS, PCQ, ECOG-PSR/QoL assessed 3.1–8 years post-op | • mean SF-36 score comparable to controls  
• no limitations on moderate activity in 94% of cases |
FACT-C scores decreased 2 weeks post-op and returned to baseline at 3 mo and 6 mo follow-up; greater than 50% of their normal activities post-op at 3, 6, and 12 months respectively.

**Abbreviations:** BPI-SF, Brief Pain Inventory-Short Form; CES-D, Center for Epidemiologic Studies-Depression Scale; ECOG PSR, Eastern Cooperative Oncology Group performance status rating; EORTC, European Organization for Research and Treatment of Cancer; QLQ-C30, Quality-of-Life Questionnaire; CCM-38, Colorectal Cancer module 38; FACT, functional assessment of cancer therapy; FACT-C, functional assessment of cancer therapy colorectal; FACT-G, functional assessment of cancer therapy general; FACT-O, functional assessment of cancer therapy ovarian; LAS, life appreciation scale; BPI, brief pain inventory; MOS-SF36, Medical Outcomes Study Short Form-36; PMP, pseudomyxoma peritonei; pre-op, pre-operatively; post-op, postoperatively; EDC, early post-operative intraperitoneal chemotherapy; CRS, cytoreductive surgery; HIPEC, hyperthermic intraperitoneal chemotherapy; CC, completeness of cytoreduction.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Number of Patients</th>
<th>QoL Assessment Time Points</th>
<th>Mitrionycin C/Not reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>n = 64 (preop)</td>
<td>Post-op (n = 48), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Appendiceal</td>
<td>n = 15</td>
<td>Post-op (n = 12), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Gastric</td>
<td>n = 19%</td>
<td>Post-op (n = 11), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Colon</td>
<td>n = 46%</td>
<td>Post-op (n = 16), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>n = 59%</td>
<td>Post-op (n = 6), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>n = 74%</td>
<td>Post-op (n = 4), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Ovarian</td>
<td>n = 6, 40%</td>
<td>Post-op (n = 3), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>n = 1, 23%</td>
<td>Post-op (n = 1), 2 w, 3 mo, 6 mo, 12 mo</td>
<td>C15</td>
</tr>
</tbody>
</table>

There is a firm association between QoL and factors that are known to affect morbidity, mortality, and survival rates. These can be generally grouped as factors related to the underlying malignancy (primary origin, histology, extension of peritoneal spread), patient selection protocols and technical variations across peritoneal surface malignancy units. The majority of studies included in this review are heterogeneous even when referring to individual study samples and they did not discriminate QoL outcomes according to the factors mentioned above. As previously noted, there are significant variations regarding sample sizes of the included studies, spanning from 10 to 216 patients, which results in different “weighting” of each of the studies when drawing general conclusions. However, the general trend of QoL recovery to baseline after 3–6 months is a consistent conclusion in the clinical studies, both in studies looking at patients with different primary cancers and also in studies investigating a specific primary cancer type, regardless of the number of patients enrolled.

Overall, our conclusions confirm the presence of a clear trend of recovery and possible improvement of QoL after CRS + HIPEC, which was demonstrated in the previously conducted literature reviews of 2009. Four years after these reviews, the number of clinical studies evaluating QoL after CRS + HIPEC has doubled. Despite the radical nature of the operation and the significant adverse effects of HIPEC, this review provides further evidence regarding the safety, tolerability and the long-term beneficial impact of the procedure on patients’ QoL.

As the presented studies indicate, the early and short-term post-operative period is when QoL is most impaired. This would indicate that efforts to reduce surgical complications, postoperative pain and stoma formation could all contribute to improvements in QoL in this early post-operative period. Although not backed up by any firm evidence, possible contributions to improving QoL in the early post-operative period could come from a well-structured patient support team, comprising different health and allied professionals to ensure the provision of optimal care to patients during this important post-operative phase. Of particular importance are the surgeon, anaesthetist, postoperative pain team, specialist nurses, physiotherapists, stoma therapists, psychosocial oncologists and clinical psychologists, whose roles can all have a positive impact on patients’ recovery following surgery. Optimizing the delivery of intraperitoneal chemotherapy in ways that will minimize adverse systemic effects may also contribute to a reduction in post-operative morbidity and mortality.

Heterogeneity of the included studies, in terms of primary cancer origin, technical variations in the HIPEC regimes and different time points of QoL assessment are the main limitations of this systematic review. Significant
variations regarding the number of patients included in each of the included studies, as well as limiting the literature search to PubMed database and English studies only are further possible limitations. Despite this, only studies with validated and structured QoL questionnaires were included in the review, enabling the interpretation of results as objectively as possible.

In summary, this review has demonstrated that Cytoreductive Surgery and HIPEC seems to preserve patients’ QoL, and in some cases results in its overall improvement at 3–6 months following surgery. In view of the establishment of CRS + HIPEC in the treatment of selected patients with peritoneal metastatic and the possible expansion of its indications, we believe that clinical studies should encompass the assessment of QoL as a standard parameter whenever possible. QoL should ideally be assessed as part of multicenter randomized controlled trials and optimally with the incorporation of validated QoL assessment tools.

Funding

There is no financial sponsorship of the study.

References

8. Trial comparing Simple Follow-up to Exploratory Laparotomy Plus “in Principle” (Hyperthermic Intraperitoneal Chemotherapy) HIPEC in Colorectal Patients (ProphyloCHIP). ClinicalTrials.gov Identifier: NCT01226394.


