

Review

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



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Accepted 13 August 2014

Available online 6 September 2014

**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 “intraoperative 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.

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

**Introduction**

Cytoreductive surgery (CRS) and Hyperthermic Intra-peritoneal 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.<sup>1</sup> 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.<sup>2</sup> 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

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cancerous deposits, improving the local concentration of the chemotherapy.<sup>3,4</sup>

There is no doubt that appropriate selection of patients for CRS + HIPEC is a crucial factor determining the success of the technique<sup>5</sup> 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 second-look operation strategies and the emerging role of intraperitoneal administration of immunoregulation agents.<sup>6–10</sup>

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.<sup>11,12</sup> 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.<sup>13,14</sup> However the procedure is complex and carries high morbidity rates and long hospital stays.<sup>15–17</sup> 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.<sup>18</sup>

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<sup>19–38</sup> 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 post-operative period and/or at the first follow-up time point, which in most studies was set at 3 months post-operatively. 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.<sup>20,27,30,38</sup> 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.<sup>20,23,26,27,29–38</sup>

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.<sup>26,32,38</sup> 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.<sup>28,30,35</sup> With respect to pain scores, Hill et al.<sup>26</sup> 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.<sup>27</sup> 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

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