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## Health-Related Quality of Life and Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy

### Introduction and Background

**I**n 1982, Sugarbaker, Borofsky, and colleagues published what has become a classic study in the quality of life literature.<sup>1</sup> In their study, 26 patients were randomized to either amputation plus chemotherapy or limb-sparing surgery plus radiation therapy and chemotherapy. After all patients had stabilized following treatment, quality of life questionnaires were administered. Limb-sparing surgery plus irradiation and chemotherapy did not provide improved quality of life when compared with amputation. This challenged the common notion that any aggressive treatment was better than amputation and provided some impetus for health-related quality of life (HRQOL) studies.

Interest in HRQOL assessment in surgical oncology has been growing recently. Blazeby and colleagues identified 33 randomized clinical trials that employed psychometrically reliable and valid HRQOL questionnaires.<sup>2</sup> Of these studies, 22 (67%) concluded that HRQOL outcomes either influenced treatment decisions or provided data for informed consent. The authors recommended HRQOL assessment be included in the relevant surgical trials so the information gained could be used to inform both clinicians and patients about the impact of surgery on short- and long-term quality of life. Hyperthermic intraperitoneal chemotherapy (HIPEC) surgeons, nurses, and quality of life researchers are now establishing new territory for the collection and application of HRQOL data in surgery. The 5th International Consensus Meeting on Peritoneal Surface Malignancy (PSM) produced guidelines for baseline and ongoing assessment of patient HRQOL.<sup>3</sup>

Cytoreductive surgery (CS) + HIPEC is a surgical and a chemotherapeutic procedure that has been used to treat PSM for over 20 years; yet, to our knowledge, the first quality of life study of this procedure was published in 2001.<sup>4</sup> In this paper, we will define health-related quality of life; summarize

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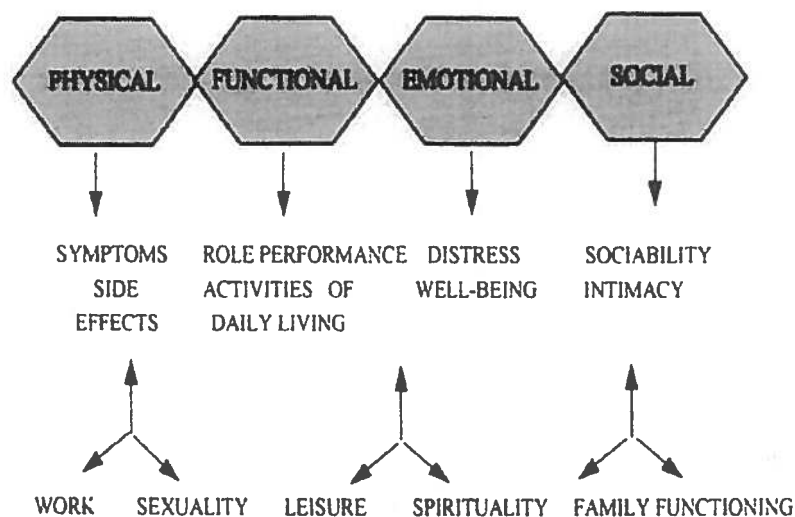


FIG 1. HRQOL domains and modifiers for the Functional Assessment of Cancer Therapy—General (FACT-G). (Reprinted by permission of Taylor & Francis Group. D. Cella & D. Tulsky: Quality of Life in Cancer: Definition, Purpose, and Method of Measurement, *Cancer Investigation* 11(3), 327-336, 1993.)

the HRQOL in PSM studies published to date; describe obstacles to conducting and applying this type of research in a clinical setting; illustrate, through a case study, how the understanding of quality of life dimensions can directly affect and improve patient care; and conclude with recommendations on ways to improve overall patient care using HRQOL data.

### Health-Related Quality of Life Defined

The term health-related quality of life, sometimes shortened to quality of life, has been defined and applied by a number of people in slightly different ways.<sup>5-8</sup> (We use the modifier “health related” QOL to distinguish it from other areas of life that are not directly related to health, for example, housing or quality of living circumstances.) Most definitions incorporate some measure of physical, social, and mental/emotional health. We have adopted a version of the definition provided by Cella and colleagues.<sup>9-12</sup> In this instance, HRQOL 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>13</sup> A study that reported only toxicity or performance status would therefore not qualify as a HRQOL study.

There are at least four areas, sometimes referred to as domains that can

be measured in quality of life assessment (Fig 1). These include physical well-being (symptoms and side effects, such as pain, nausea, etc), social/family well-being (sociability and intimacy, including feeling close to friends, satisfaction with family communication, etc), functional well-being (role performance and activities of daily living, such as work, sleep, etc), and emotional well-being (sadness, nervousness, etc). There are other important factors in patients’ lives that may modify how they experience their overall HRQOL. These include spirituality, financial resources, sexuality, and family functioning. There is a general consensus among researchers that the quality of life concept is measurable, multi-dimensional, and subjective or meaningful to the individual patient.

### HRQOL in the CS + HIPEC Context

The most common context for HRQOL assessment is in a phase III randomized trial where two or more treatments are being compared on both survival and quality of life. Although many studies of this type have been conducted in the general cancer patient literature,<sup>14,15</sup> we are aware of none currently published in the CS + HIPEC literature. This is because there are few randomized clinical trials in this area in general, and it takes resources, ie, a research nurse, to collect these data. The only randomized clinical trial reported in the literature to date began with a quality of life component.<sup>16</sup> Due to logistical difficulties in collecting the HRQOL data, however, this portion of the protocol was not completed and was not included in the final publication (personal communication, Verwaal 2008).

Even though no HIPEC phase III randomized trials have been published with HRQOL data, there is a growing body of literature from which patients and clinicians can draw upon to understand the quality of life costs that are associated with HIPEC treatment.

### HRQOL in CS + HIPEC: A Review of the Literature

We have been able to locate a total of eight published HRQOL studies. See Table 1 for a summary of the research. We will highlight findings from the HRQOL literature to date and indicate limitations of this research.

#### *The Wake Forest Experience*

Nurses, surgeons, and allied health care professionals at Wake Forest University/Baptist Medical Center (WFUBMC) began HRQOL research supported by a grant from the National Cancer Institute in 1995. This

TABLE 1. Summary of CS + HIPEC HRQOL studies

Author/year	N/Dx	Measures/timing	Outcomes summary
McQuellon et al. (2001)	n = 64 (pre), 48 (2 wks post-Tx), 40 (3 m), 39 (6 m), 31 (12 m)/(16 large intestine, 15 appendix, 11 gastric, 7 other, 6 mesothelioma, 5 malignant neoplasm, 4 ovarian)	FACT-C, MOS-SF36, BPI-SF, ces-D, ECOG PSR/pre, 2 wks post-Tx, 3, 6, 12 m physical functioning was severely limited in moderate activities at pre tx	Sig change on PWB, EWB, FWB scales over 1 year; FACT-G scores decreased Post-TX and returned to baseline by 3 m; 11 pts. 2 died before 3-mo. asses. (5 within 30 d); patients with ascites improved on the FACT-C scores, post tx while those w/o ascites decreased relative to baseline.
McQuellon et al. (2003)	n = 17 of 109 eligible/(10 appendix, 5 large intestine, 1 ovarian, 1 peritoneum)	FACT-C, MOS-SF36, CES-D, las, PCQ, ECOG-PSR/cross-Sectional, 3.1-8 years post tx.	Overall QoL acceptable. long-term QoL scores did not differ Sig. from 3-, 6-, 12-mo. scores; no limitations on moderate activity were reported in 94% of cases
Alexander et al. (2004)	n = 73/(50 GI cancer, 23 mesothelioma)	MOS-SF36, FACT-C/pre, 6 wks post-Tx, 3, 6, 9 m	FACT-C mean scores show Sig. improvement at 3, 6, 9 m rel. baseline; SF36 PCS score decreased Sig. at 6 wks but did not differ Sig at subsequent time points; SF36 MCS Improved at 6 weeks, 3 m, did not differ from pre-at 6, 9 m; 30% morbidity; at median f/6 of 17 m, 22 NED, 45 AWD, 6 DOD.
Schmidt et al. (2004)	n = 20/various Dx, including: appendix, ovary, colon, peritoneum, stomach, pancreas, Liver, bowel, retroperitoneal, sarcoma, uterus.	EORTC QLQ-30/cross-sectional	Mean score global health status = 62.6 (73.3 = control); mean score for patients with stoma (n = 2) = 16.7, w/o stoma (n = 18) = 67.7; highest functional symptom scores = fatigue (48.6), insomnia (38.1) and pain (35.6); 34% morbidity; 4.5% mortality rate

TABLE 1. Continued

Author/year	N/Dx	Measures/timing	Outcomes summary
Tuttle et al. (2006)	n = 35/(19 appendix, 7 colon, 3 mesothelioma, 2 stomach, 2 small bowel, 1 gall bladder, 1 Unk)	FACT-C, fact-G/pre tx, 4, 8, 12 m	No Sig diff between pre- and 4-mo. fact-C data; improvement in 8 and 12 m 51% morbidity rate; 0% post-op mortality rate; morbidity associated with; Sig smaller FACT-C increases; median survival 41.4 m
McQuellon et al. (2007)	n = 96 (pre), 38 (3 m), 32 (6 m), 24 (12 m)/36 Appen, 24 colon/rectum, 9 meso, 5 ovary	FACT-C, MOS-SF36, CES-D, BPI-SF, ECOG PSR/pre, 3, 6, 12 m post-Tx	Sig improvements from pre-12 m for all FACT scales except SWB, which remained high; mean FACT-G scores were approx. 80 at pre- and 3 m (80 control); Sig effect for SE-36 scores from pre- to 12 m for PF, RF, BP scales; Sig % of pts. rated themselves as limited a "lot" on daily activities; 32% mortality rate 12 m.
Jess et al. (2008)	n = 23/pseudomyxoma peritonei	MOS-SF36, EORTC QLQ-30 CCM-38 pre-Tx, 3, 6, 12 m, 18, 24 m/	Sig decrease in SF36 PCS and role physical scores from pre-to 3 m returning to pre-levels by 6 m; other scores comparable to normal population; 70% morbidity rate; 0% 30-d mortality rate
McQuellon et al. (2008)	n = 58 (pre) 35 (3 m), 33 (6 m), 28 (12 m)/appendiceal	fact, MOS-SF36, CES-D, ECOG PSR/pre, 3, 6, 12 m, 24 m post-Tx	Sig changes over time for EWB and PWB; PWB, FWB and overall FACT returned to pre-levels or higher by 6 m; EWB increased Sig from pre-to 3 m; Sig effect for SF36 scales physical functioning, role physical, bodily pain and vitality at 6 m; morbidity: 16% (wound infection), 15% (hematologic toxicity) 10% (respiratory failure); 8% (sepsis); 3.4% 30 d Mortality rate; estimated median survival 39.6 m.

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-colon; FACT-G, functional assessment of cancer therapy-general; LAS, life appreciation scale; MOS-SF36, Medical Outcomes Study Short Form-36; PCS, physical components score, MCS, mental components score; NED, no evaluable disease; AWD, alive with disease; DOD, deceased of Disease; PCQ, psychosocial concerns questionnaire; TOI, trial outcome index. 4 Stomach, 18 misc. (80 = Control), Sig effect for SF-36 scores from pre-to 12 m for PF, RF, BP scales. Sig % of patients rated themselves as "limited a lot" on specific items, Sig depressive symptoms at all time points, 32% mortality rate at 12 m.

foundational study integrated surgical care, pharmacokinetics, and quality of life research.<sup>4,17,18</sup> Subsequently, ongoing, systematic monitoring of HRQOL data has been standard of care at WFUBMC. Research nurses, physicians, data managers, HRQOL researchers, and others make up a dynamic clinical research team. Yet, even with an active HRQOL research team and nearly 300 patients accrued to the HRQOL component of HIPEC treatment, the picture of the patients' experience is far from complete. The medical/clinical HRQOL and survival data provide a developing and incomplete picture.<sup>19,20</sup> On the one hand, the HRQOL data for a significant number of patients who complete our surveys indicates reasonable functioning within 3-6 months following treatment. For some, long-term survival is possible.<sup>18</sup> By contrast, a significant proportion of patients continue to have deficits in physical functioning for months post-treatment.<sup>20</sup> Whereas these data provide evidence of the success of HIPEC, our clinical experience has taught us that some patients experience complications that significantly impair HRQOL. On the days and weeks postsurgery, a substantial minority of patients have reported that they did not expect such profound debilitation. Further complicating the picture is the fact that we have heard patients say in the early days they would never do it again, and then, some months later, reply that they are glad they went through the procedure.

Our HRQOL work has led to the following conclusions. First, patients who present with good performance status, suffer few post HIPEC complications, and who are evaluable at the follow-up time points can expect to return to near baseline levels of some dimensions of HRQOL about 3-6 months post treatment. For some people, this will take considerably longer, up to 1 year. Few people recover more quickly than 3 months. However, many patients continue to have deficits in their general physical health up to 12 months and later post-treatment. The pattern of recovery post-HIPEC varies dramatically with baseline functioning with some patients (those who enter with significant symptoms, eg. ascites) improving HRQOL quickly following surgery and others who have few symptoms at baseline worsening in the short-term post HIPEC.<sup>4</sup>

Second, as the number of patients in our HRQOL database increases, we are able to examine HRQOL data for diagnostic subtypes. Patients with PSM present a varied clinical picture. Both resection status and site of the disease portend different outcome. We have reported on HRQOL of PSM of appendiceal origin<sup>20</sup> and have additional results for colon origin in preparation. Preliminary data analysis on outcomes at 12 months suggests significant differences on role performance favoring appendiceal patients.

Third, from 20-30% of all patients monitored in our setting have significant depressive symptoms over the course of 1 year post-HIPEC. A significant portion of these can be attributed to physical symptomatology not associated with the psychological dimension of depression.<sup>21</sup>

Finally, HIPEC provides those patients who are good surgical candidates with the hope of long-term survivorship and acceptable HRQOL.<sup>18</sup> At one time this would have been inconceivable.

### *Additional HRQOL Studies*

Alexander and coworkers, from the Surgery Branch of the National Cancer Institute, are the only other researchers to conduct an HRQOL study with a significant number of patients.<sup>22</sup> Seventy-three patients (50 GI cancer, 23 mesothelioma; 41 female, mean age = 49) underwent CS plus HIPEC with 250 mg/m<sup>2</sup> cisplatin and subsequent intraperitoneal dwell with 800 mg/m<sup>2</sup> 5-FU and 125 mg/m<sup>2</sup> paclitaxel on a phase II trial. Recorded time to return to regular diet after treatment was 8 days (range 3-38), mean hospital stay = 11 days (range 9-58), and 29 complications in 22 patients (30%). At the time of study publication (median follow-up of 17 months; range 4-38), 22 reportedly had no evidence of disease; 45 were alive with disease; and 6 were deceased. The SF-36 and FACT-C were administered pretreatment, 6 weeks post-treatment, and at 3, 6, and 9 months. Physical functioning scores on the SF-36 decreased significantly from baseline to 6 weeks and, for the patients completing the surveys, returned to normal at 3 months. Mental component scores (MCS) of the SF-36 increased significantly at 6 weeks, suggesting improved emotional well-being, role functioning, energy, and social functioning. FACT-C scores declined at 6 weeks and improved to greater than baseline at 3 months ( $n = 66$ ), 6 months ( $n = 53$ ), and 9 months ( $n = 45$ ). The authors concluded that HRQOL, as measured by the FACT-C, was markedly improved in remaining patients at 3, 6, and 9 months.

Three published studies on small cohorts, ie,  $n = 23, 25,$  and  $35$ , provide additional information about post-treatment functioning of PSM patients.<sup>23-25</sup> Schmidt reported on 20/25 surviving patients from a 67-person cohort.<sup>23</sup> Of the 20 patients (PSM of multiple origins, see Table 1) who completed the EORTC-QOLQ-C30 survey, the average global health score was 62.6, somewhat lower than the global health score for the general population (75.3). Given the small number of patients in this study, finding significant differences would be unlikely. Yet, a difference of this order (ie, approximately 12 points) is probably clinically significant and would likely be statistically significant in a larger sample.

It is also important to note that the patients surveyed ranged from 1 to 8 years post treatment.

Jess and colleagues studied 23 patients diagnosed with pseudomyxoma peritonei and collected HRQOL data using the SF-36 and the EORTC-QOLQ-30, which included the colorectal cancer module.<sup>24</sup> Although the researchers studied a total of 23 patients, the number of patients surveyed at any one time point ranges from a low of 11 at 18 months to a high of 15 at 12 months. Only 13 patients were evaluated preoperatively, limiting conclusions from the data. The authors reported on trends that supported an acceptable level of HRQOL with significant deficits in physical functioning at 3 months and returning to close to normal by 6 months.

Tuttle and coworkers evaluated 35 consecutive patients with PSM (19 appendix, 7 colon, 3 mesothelioma, 2 stomach, 3 small bowel, 1 gall bladder, and 1 unknown).<sup>25</sup> Following CS, patients were administered hyperthermic mitomycin C for 90 minutes using the closed technique. The patients were administered HRQOL instruments (FACT-C) before treatment ( $n = 34$ ) and at 4 ( $n = 29$ ), 8 ( $n = 19$ ), and 12 ( $n = 12$ ) months. Statistically significant changes were recorded over time for the various subscales on the FACT (Treatment Outcome Index, Emotional Well-Being, and Functional Well-Being) as well as the overall FACT plus the colorectal subscale. It is difficult to know exactly what these data mean given so few patients for comparison at 8 and 12 months. Further, it is unclear whether a statistical analysis that can account for missing data was used. They concluded by noting early toxicity, prolonged survival, and improved HRQOL scores in survivors.

There are many limitations to these studies. First, the numbers are small, as low as 20, necessarily limiting any generalizations. Second, many different HRQOL instruments are used making comparisons across studies difficult. Third, there are many cancer diagnoses with PSM with different clinical pictures. PSM has many manifestations; it is not monolithic. Fourth, whereas all studies have a baseline measure, the exact time of this assessment is not apparent and subsequent postsurgery time points vary as well. It is likely that considerable morbidity is experienced by patients in the post surgery time period up to 6 weeks. Only two studies reviewed here measured HRQOL within 6 weeks of primary treatment. To capture significant HRQOL morbidity from this procedure, it would be necessary to conduct these assessments within 2 to 4 weeks of surgery. Although this might place an additional burden on patients, it would provide a clearer picture of the suffering encountered by nearly every patient who undergoes this procedure. Future studies should consider the ideal timing and administration of these instruments. Fifth,

most of the studies do not report nor do they control for additional therapy or counseling that could impact the multiple assessments of HRQOL post CS + HIPEC. Finally, a severe limitation of this literature is the amount of missing data. It is likely that many patients whose data are missing at follow-up assessments after treatment are deceased or ill. What happens to the HRQOL of those patients between treatment and 3 months who do not remain in the data set?

## Of What Use Is HRQOL?

There are at least three important reasons for collecting HRQOL data in the HIPEC context. First, both patient and clinician alike can benefit from additional information on post-treatment functioning for pretreatment decision making. There is evidence that patients who have clearer expectations of treatment have better psychological outcomes.<sup>26</sup> Specifically, individual patients could familiarize themselves with the literature on postsurgical morbidity, including complications and general impact on HRQOL. This could enable them to make an even more informed decision about proceeding. Although consent procedures and medical personnel do their best to provide patients with an understanding of what they are about to go through, most patients do not understand the physical, emotional, and social/family challenges that HIPEC brings; ie, almost all patients endure some level of intense suffering over the short term. Under the best of circumstances, patients often enter treatment ill prepared for complications even when directly counseled about them. A patient with major deficits in any HRQOL and performance status at the outset will likely be a higher risk candidate for treatment morbidity and mortality. Thus, nurses and physicians might be able to better prepare the patient and themselves for the aftermath of treatment. For example, patients' families could be counseled on the likely complications and be prepared to provide intense support at the bedside.

Secondly, regular, systematic monitoring could further improve patient care and symptom management. Some patients are not the best of reporters and will only endorse certain difficulties when asked very specific questions. Furthermore, once surgery is completed and patients leave the hospital, they may have only one or two follow-up appointments with their HIPEC surgeon, who may be geographically distant from them. Thus, there is the risk of being lost in transition after such highly specialized treatment. In our own studies monitoring patients post treatment, we have identified physical symptoms, such as fatigue, that contribute to overall scores on our depression-screening instruments.<sup>21</sup>

Finally, systematic collection of HRQOL data can provide a rich source of survivorship planning. The Institute of Medicine has called for survivorship care planning for all cancer patients.<sup>27</sup> Most patients who have undergone HIPEC have had a stark confrontation with their own mortality.<sup>28</sup> Such a confrontation often leaves people with psychological scars and intrusive thoughts. Focusing on survivorship planning can help patients recover some normality post-HIPEC.

### The Clinical Application of HRQOL Data in Post HIPEC Treatment Planning

The following case illustrates how HRQOL data and systematic follow-up care can be used for patient management. We start with a brief description of the patient and her situation and the reason she was referred for psychological evaluation. Subsequently, we describe the two telephone and two counseling sessions with her. The patient, CS, is a 50-year-old, white, married female currently on disability from her work as a physical therapist approximately 1 year following the diagnosis of mesothelioma and initial treatment with CS plus HIPEC. Her initial symptom presentation (vague complaints, fatigue, abdominal pain, several ER visits, CT scan-large volume of peritoneal ascites, laparoscopy/biopsy of peritoneal wall, nausea, diarrhea) preceded her diagnosis by several months. Her FACT-G score of 49 at this time reflects disruptive symptoms and significantly impaired HRQOL.

The patient had an R2A-resection which included splenectomy, omentectomy, appendectomy, and bilateral salpingo-oophorectomy. Her inpatient hospital stay was unremarkable with no complications. Subsequently, she was hospitalized for over a month in her local hospital for complications, ie. persistent nausea, poor nutritional intake, significant weight loss.

The patient completed HRQOL questionnaires at baseline before surgery, 3 months, and 6 months. (All HIPEC patients are asked to participate in our ongoing protocol Quality of Life Assessment for Intraperitoneal Hyperthermic Chemotherapy Surgery Candidates that continues HRQOL assessment at 12 and 24 months. This protocol has been described in detail elsewhere.<sup>19</sup>) She scored above our threshold of 16 on the Center for Epidemiologic Studies Depression scale (indicating further assessment was needed), so a telephone interview was conducted both before HIPEC and at approximately 4 months post HIPEC. The phone interview revealed concern about specific physical symptoms (ie. fatigue, sadness, anxiety and worry that her condition will get worse).

Fatigue, coupled with problems with balance, led to an inability to return to work and ultimately job loss. At both interviews, no subsequent psychological care was recommended. The patient was not clinically depressed, yet considerably distressed.

The first counseling session was approximately 2 months post-treatment. At that time, she was referred for further assessment due to depressive symptoms identified in her surgery follow-up appointment. The patient was seen in consultation by a counseling psychologist (RPM) on referral by her surgeon. At that time, she stated, "I have felt like giving up." This was the result of the tenacity of symptoms and lengthy post HIPEC hospitalization in her local hospital. Additionally, she complained of fatigue, discomfort in her abdominal area, and the nagging feeling that her cancer was coming back. Her HRQOL assessment score at 3 months post HIPEC on the FACT was 58, denoting a lack of energy, trouble meeting the needs of her family, nervousness, and remaining bothered by side effects of treatment. However, this score represents a 9-point improvement over her pretreatment score of 49. After thorough screening and discussion with the patient and spouse, it was apparent she was improving physically and emotionally, and thus, no ongoing counseling was recommended at that time.

She was subsequently seen for an additional follow-up counseling session following referral by her surgeon at 9 months post HIPEC. At this follow-up, her affect was remarkably flat even when he gave her the good news that there was no evidence of disease; he referred her to RPM for further assessment of depression. The patient was indeed distressed. She scored 14 on the Beck Depression Inventory, indicating mild depressive symptoms. Additionally, she named nine troubling symptoms, including fatigue, short-term memory loss, pain, hearing loss and tinnitus, difficulty with balance, back ache, decreased stamina, joint pain, and intrusive thoughts about her predicted life span, ie. 18-24 months. The patient's overall health status was discussed in relation to what the patient had heard from her surgeon, ie, "You are doing well medically. Everything looks good." From a surgical standpoint the patient's wounds were healed; there was no evidence of disease; and she was ambulatory and functioning reasonably well. From the patient's standpoint, her energy level was not quite 50% of normal, and she had a number of chronic problems that had developed post HIPEC. She was frustrated and disappointed in her overall quality of her life. This was reflected in her (FACT/HRQOL) score of 62 at 6 months post-HIPEC. She was showing a slow improvement (49 at baseline, 58 at 3 months) surpassing the defined minimally important difference for the FACT-G.<sup>29</sup>

Our emphasis in this case study is on the bio-psychosocial nature of the patient's problems and their profound impact on the patient's mood and outlook. Our effort is to emphasize the complexity of her situation, particularly in light of optimal healing following surgery and no evaluable residual disease. Despite this, the patient has significant challenges to overcome to return to what she considers normal.

The treatment of choice has been to develop a plan of action to help improve her overall HRQOL. This can be described as a survivorship plan, a systematic effort to rehabilitate physical, social, and emotional deficits post HIPEC.<sup>27</sup> The survivorship plan proposed by the patient included the following activities:

**Physical well-being:** (1) Diet modifications—more vegetables, no red meat, no dairy, some fish and chicken. (2) Walking. (3) Better sleep.

**Emotional well-being:** (1) Spend time with husband, family, grandchildren and friends. (2) Work on Continuing Education Credits to maintain physical therapy certification.

**Spiritual well-being:** Attend church as much as possible.

**Major obstacles to overcome:** No energy; low back and knee pain; reduced income; memory loss (cannot do Sudoku as well as I used to); tinnitus; pain in abdominal area.

This case illustrates one of the more vexing problems for patients following CS + HIPEC. They may be doing well medically but not feeling well. It often helps to explain to patients that their medical indicators look good; there are no complications; their wounds are healing; they are beginning to eat and ambulate and yet they may still feel bad, distressed, discouraged, and like giving up. CS does report great disappointment in the current quality of her living, as she has little energy, and her activities are greatly curtailed. Her scores on the FACT support her subjective sense of poor health. She wonders if she will ever recover and yet she has just been given a positive report by her medical team. This underscores the importance of HRQOL data provided by the patient— from her point of view, a "positive" medical report means little.

The current treatment for this patient is not primarily biomedical. It takes a biopsychosocial model of understanding,<sup>30</sup> or perhaps more to the point, a conceptual model that links quality of life data to active treatment interventions.<sup>31</sup> In this situation, the oncology counselor met with the patient to discuss biological, psychological, social, and spiritual dimensions of her care. The patient then developed her survivorship plan.

This case illustrates one method of using quality of life data. Although we currently do not have the resources to intensely monitor patients'

overall HRQOL and provide timely interventions, we are collecting data on this patient population. These data could be invaluable to health care teams in the patient's home setting. Given that CS + HIPEC is a procedure that is conducted in approximately 50 centers around the US, patients are often far from the treatment site when they develop difficulties. Post treatment survivorship information and general plans may provide invaluable information to patients in the short term (3-6 months post surgery) to maximize their survivorship quantity and quality.

### *Collecting and Applying HRQOL Data*

We have described the limited literature on HRQOL in CS+ HIPEC and attempted to link one case study with a specific HRQOL instrument, namely the FACT. This connection can only be made possible by an integrated research and clinical team. Essential elements of this team include members of many disciplines. The process begins with a dedicated surgical team actively interfacing with research assistants, nurses, and psychosocial oncology professionals. It is essential to have a surgical team interested in collecting these data and dedicated data analysts and behavioral scientists to apply it. Assembling the essential pieces to a well-running surgical HRQOL team involves a significant investment of human and financial resources.

### **Conclusions and Future Direction**

Three major lessons can be gleaned from clinical experience with HIPEC and the HRQOL data. First, for patients undergoing this type of treatment, both quantity and quality of time is precious. This evolving treatment is still considered by some to be palliative. Therefore, patients are likely to be acutely aware of their predicted life span of months, even though there are longtime survivors.<sup>18</sup> Some patients tell of dire predictions made by practitioners who have no knowledge of the progress made in HIPEC treatment. In this context, there is an urgency to "first do no harm" and then provide some life of quality. The case study above illustrates how a patient can be deemed "better" and yet still have symptoms significant enough to grossly impair her overall quality of life. Secondly, the commitment to collecting HRQOL data and applying it in the clinical setting requires human and financial resources, as well as people interested in practicing bio-psychosocial medicine. The Wilson and Cleary model of linking HRQOL data to clinical variables and life enhancing treatment is yet to be realized.<sup>31</sup> Nevertheless, work at Wake Forest University and other locations provide hope that a biopsychosocial method of attending to people can work.<sup>32-34</sup> Finally, HRQOL studies in

this area should continue with an emphasis on applied HRQOL data in the clinical setting. Patients and clinicians who provide and apply HRQOL data are pioneers in the field, making way for better care for their successors. They are making a difference in the quality of life of patients with peritoneal surface malignancy.

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## Appendix A: Hyperthermic Intraperitoneal Chemotherapy: A Perfusionist's Perspective

### Introduction

**T**he objective of the perfusionist during a hyperthermic intraperitoneal chemotherapy (HIPEC) procedure is to circulate the hyperthermic chemotherapy agent into and out of the patient's peritoneum for the time period specified by the surgeon. Only two pieces of equipment are needed: a roller head pump and a heater/cooler. Although there are more complex computerized integrated systems on the market, any institution can create their own with these two pieces of equipment. The roller head pump can be placed on a designated cart for ease of mobility. A standard heater/cooler can be used but is not optimal for this procedure as it will take longer for the fluid to reach the required therapeutic temperature. A modified heater/cooler with a digital control up to 48°C capabilities (though never required) allows one to precisely regulate the outlet temperature by 0.1°C and should be allocated for HIPECs only. Also, an electrical engineer should oversee this modification. Table 1 lists all the materials needed to perform a HIPEC. Figure 1 displays the HIPEC system.

### Priming and Initiation of Therapy

The circuit is primed with 3 L crystalloid heated to 43°C and recirculated until initiation of the HIPEC. While the priming volume is recirculating, the surgeon inserts the four cannulae (2 inflows and 2 outflows). After inserting the outflow cannulae, a perforated aseptic syringe bulb is placed over both of them (Fig 2) and positioned within the abdomen before temporarily suturing the abdomen closed. Once the cannulae are in place, the 1/4" inflow tubing and 3/8" outflow tubing are passed off the sterile field, and the perfusionist connects them to the preprimed circuit after removing the recirculation loop. The air in the connected tubing and abdomen is displaced as the HIPEC circulation is initiated. The clear

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