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Research Article

Does Peritoneal Carcinomatosis Owing To Uterine Cancer Require Cytoreductive Surgery And Hyperthermic Intraperitoneal Chemotherapy?

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Abstract

Background: One of the most prevalent pelvic malignancies in women is uterine cancer. Although they only make up 15% of newly diagnosed cases, advanced stage uterine cancer is associated with a bad prognosis. Our goal was to evaluate the advantages of hyperthermic intraperitoneal chemotherapy and cytoreductive surgery for peritoneal carcinomatosis brought on by uterine cancer. Techniques: Morbidity, overall survival, and survival without progression were examined throughout the 5-year follow-up at the Surgical Oncology Clinic at the Istanbul Umraniye Training and Research Hospital. This study comprised twenty-two instances with uterine-peritoneal carcinomatosis who had received hyperthermic intraperitoneal chemotherapy and cytoreductive surgery. Cases were monitored for overall survival, disease-free survival, and postoperative morbidity-mortality. A cutoff score of 15 was established for the peritoneal carcinomatosis index.All patients received intraperitoneal treatment for 60 minutes following abdominal suturation, comprised of doxorubicin and cisplatin. Findings: The patients' median age was 64.6 (43–72). 12.8 was the average PCI score (3–15). 16 (72.7%) cases had a CC score of 0, 1 in 3, and 2 in 3. Twelve of these individuals had undergone surgery before. 13.1 days was the median length of stay at the hospital. There were no significant side effects from the treatment. Seven (31.8%) of the individuals had a Clavien-Dindo Grade 3 complication. There were no patient deaths while they were in the hospital. The 5-year overall survival rate was 45.3 (57%) months, whereas the 5-year disease-free survival rate was 36.8 (36%) months.Conclusions: Because uterine cancer patients have low peritoneal carcinomatosis index scores and manageable complication rates, we believe that cytoreductive surgery and hyperthermic intraperitoneal chemotherapy should be preferred in cases of peritoneal carcinomatosis due to longer disease-free survival and overall survival. However, for this topic, large-scale prospective randomized trials are required.

Keywords : *uterine cancer; peritoneal carcinomatosis; cytoreductive surgery; hyperthermic intraperitoneal chemotherapy.*

INTRODUCTION

One of the most prevalent pelvic tumors in women is uterine carcinoma (UC). In females, the lifetime risk for UC is approximately 4% [1]. Women between the ages of 60 and 70 are typically affected. After receiving surgery, chemotherapy, radiation therapy, and hormone therapy, UC has a favorable prognosis; additionally, UC accounts for just 2% of cancer-related deaths [2]. Although they only account for 15% of newly diagnosed cases, advanced stage UC is associated with a bad prognosis. Females with distant (20–25%) or local (49–66%) peritoneal metastases have lower 5-year survival rates, with a median survival of less than a year [3,4].According to the guidelines, cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can be used to treat selected patients with ovarian and colon cancers who have low peritoneal carcinomatosis index (PCI) scores, as well as cases of pseudomyxoma peritonei originating from the appendix without extra-abdominal metastases. The effectiveness of CRS and HIPEC in UC has not yet been the subject of any Randomized Controlled Trials (RCTs) in the literature. Although the modest number of cases involved restricts the credibility of the statistics, retrospective series from seasoned hospitals offer insight into the treatment of synchronous and metachronous peritoneal metastasis (PM) to the peritoneum caused by UC with CRS and HIPEC [5–8]. In light of these restrictions, our goal was to examine the 5-year outcomes of our tertiary center's patients who had peritoneal carcinomatosis (PC) brought on by UC. Analyzing the advantages of SRC and HIPEC in PC because of UC was our goal. During the 5-year follow-up, morbidity, overall survival, and survival without progression were examined.

MATERIALS AND METHODS

The Ümraniye Training and Research Hospital Surgical Oncology Clinic at Health Sciences University Istanbul collected prospective and retrospective data on 360 patients

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who had undergone CRS and HIPEC surgery due to intra-abdominal metastases between May 2017 and May 2022. Participants in the study provided written informed consent, and the study was authorized by the Ethics Committee of the Health Sciences University Istanbul, Ümraniye Training and Research Hospital (number 2022/192). Eight of the 30 patients who were diagnosed with UC had PCI scores greater than 15, and as a result, they were not included in the study. In terms of postoperative morbidity–mortality, disease-free survival (DFS), and overall survival (OS), the cases' demographic information, including age, comorbidities, body surface area (BSA), prior CRT story, length of surgery, PCI, completeness of cytoreduction (CC) score, fluid resuscitation during surgery, need for erythrocyte suspension and fresh frozen plasma, amount of urine, and length of intensive care unit (ICU) and hospital stay, was assessed. The interdisciplinary tumor committee gave their consent for all patient surgeries. Preoperative evaluations included oncologic PET-CT, abdominal and pelvic MRI, and tumor markers (AFP, CEA, CA 19-9, CA-125). The PCI score was determined preoperatively using diagnostic laparoscopy. The PCI score cutoff was set at 15. Patients having a PCI score of 15 or below had their operations continued. Patients who had a PCI score more than 15 were referred for neoadjuvant chemotherapy, reassessed following the treatment, and then operated on. The selection of patients for this extremely invasive procedure requires the use of multiple prognostic rating systems. The most widely used one nowadays is PCI. The higher the survival, the lower the score. Providing R0 resection—that is, removing a tumor macroscopically—was the primary goal here.Extra-abdominal metastases, low Karnofsky performance scores, and significant cardiac, pulmonary, hepatic, or renal dysfunctions are among the conditions that preclude the use of CRS and HIPEC. Furthermore, since they don't add to the survey, extensive small bowel, mesenteric involvement, multiple liver metastases, and para-aortic lymph node involvement are all regarded as contraindications. The modified lithotomy position was employed throughout the procedure. Laparoscopically, the procedure was initiated, and the PCI score was determined. A midline incision was then made, extending from the pubis to the xiphoid process. Following the incision, the PCI score was determined. Every malignant mass in the pelvic region and other abdominal locations was removed. CRS was carried out in accordance with Sugarbaker's earlier description [9]. Before HIPEC, anastomoses were created. Additionally, colostomy and ileostomy anastomoses were performed prior to HIPEC.The bilateral subdiaphragmatic, epigastric, and pelvic regions all received HIPEC surgical drainage. After inserting heat probes into the pelvic and epigastric regions, the abdomen was sutured. Following abdominal closure, intraperitoneal and intraabdominal injections of cisplatin (75 mg/m2BSA) + doxorubicin (15 mg/m2BSA) in 0.9% NaCl solution were administered in 43 and 1200 cc/h turns for 60 minutes. In every instance, HIPEC was carried out as a closed method. A probe inserted into the esophagus by the Belmont Hyperthermia Pump (Belmont Instrument Corporation, Billerica, MA, USA) was used to assess the intra-abdominal body temperature during this procedure. The patients were moved to the intensive care unit following the procedure.

Statistical Analyses

The raw data were entered into IBM SPSS Statistics 22.0 (IBM SPSS, Turkey) and subjected to analysis. The arithmetic mean ± standard deviation, minimum, maximum, and range values were used to summarize the numerical data in the tables. Frequencies and percentages were used to assess the nominal and ordinal data. Lastly, the same software's Kaplan–Meier survival analysis was used to determine overall survival.

RESULTS

22 patients with PC from UC underwent CRS and HIPEC. Three (13.6%) of these patients had recurrent metastatic disease, thus CRS was repeated and HIPEC was carried out on them. The 12th month following surgery saw the earliest recurrence. Twelve of these patients had undergone total abdominal hysterectomy (TAH) surgery in the past. The patients' median ASA score was 1.7 (1–3), median body surface area (BSA) was 180.4 (142–199), median age was 64.6 (43–72), and median Karnofsky performance score was 82 (70–100). Fourteen (63.6%) of these patients had chemotherapy before to surgery. Table 1 shows that the median hospital stay was 13.1 days (5–49).The average PCI score was 12.8 (3–15), and the average operating duration was 5.6 hours (3–8). 16 (72.7%) cases had a CCscore of 0, 1 in 3, and 2 in 3. Anastomosis rates for the small intestine and colon were 1 in 7 (31.8%) and 2 in 5 (22.7%), respectively. Patients received 1.1 units (0–4) of erythrocyte suspension, 0.6 units of fresh frozen plasma, 3400 cc (2000–5500) crystalloids, and 650 cc (500–1000) colloids on average during the perioperative period.Table 2 shows that the average blood loss was 590 cc (200–2400) and the average urine production was 740 cc (280–2100). With the exception of two patients, macroscopic tumors were not left behind following full organ resections in CRS (Table 3). Intraperitoneal treatment with doxorubicin and cisplatin was administered to each patient for 60 minutes following abdominal suturation. There were no significant side effects from the treatment. The problems were categorized using the Clavien–Dindo (CD) grading method. Seven individuals (31.8%) experienced a CD grade 3 complication during the postoperative phase. Two patients had a colorectal anastomosis leak (CD grade 3b), which led to a Hartmann colostomy and subsequent reoperation. One case (CD grade 3b) required a second operation because of bleeding. In one

instance, bilateral nephrostomy was used to address urine leakage from the bladder wall (CD grade 3a). Under local anesthetic, the abdomen was sutured in one instance of evisceration (CD grade 3a). Two incidences of pleural effusion (CD grade 3a) were noted, and was treated by interventional radiology with the implantation of drainage catheters. There were no CD grade 4 complications found. Table 4 shows that no patient deaths occurred while they were hospitalized. Seven cases (31.8%) were identified as endometrial carcinoma in the pathology reports, five cases (22.7%) as carcinosarcoma, five cases (22.7%) as leiomyosarcoma, three cases (13.6%) as endometrial stromal sarcoma, one case (4.5%) as undifferentiated sarcoma, and one case (4.5%) as serous carcinoma. Following the completion of their medical and radiological treatment, all subjects were monitored postoperatively (Table 5). Three patients experienced a locoregional relapse; these relapses occurred at the 8th, 10th, and 12th months after surgery, respectively, and these patients underwent another operation. Table 6 shows that the overall survival rate was 45.3 (57%) months and the disease-free survival rate was 36.8 (36%) months after five years.

DISCUSSION

One of the most important aspects of treating UC is surgery. In order to advise adjuvant chemo-radiotherapy, the underlying malignancy must be treated, which often entails a hysterectomy and bilateral salpingo-oophorectomy. Additionally, the surgical stage pertaining to lymph node excision must be evaluated [10,11]. Due to illness recurrence, two out of every three patients who have UC surgery are readmitted to the hospital within an average of two years [3]. Most of these patients have a PC diagnosis, and the traditional treatments for these patients include targeted therapy, salvage radiation, chemotherapy, or chemoradiotherapy [12]. Over the past 20 years, CRS and HIPEC have demonstrated effectiveness in treating PC patients, colon and ovarian cancers, mesothelioma, and pseudomyxoma peritonei [13]. In a multicentric phase 3 randomized controlled trial, Van Driel et al. discovered that patients with Stage III epithelial ovarian cancer who received HIPEC in addition to intermittent cytoreductive surgery had longer overall and relapse-free survival times and no higher rates of adverse events than those who received surgery alone [14]. One of these treatments is PC brought on by UC. Since the uterus is situated in the pelvic region, there is no universal agreement regarding the use of CRS + HIPEC in PC for ovarian malignancies, despite the fact that it is a recently adopted treatment approach.PC and local recurrences can be challenging to diagnose and treat. Radiologists with experience in diagnostic laparoscopy, PET-CT, and MRIs can overcome these challenges.We intended to highlight in our work that PC resulting from UC may benefit from CRS and HIPEC. Finding the patient population that would benefit from CRS and HIPEC was the primary objective here. This surgery is beneficial for patients who have a Karnofsky performance score greater than 70, are younger than 70, and have a low PCI score. CRS and HIPEC were utilized in patients with PC because of UC, albeit in a limited series. Through their review of eight studies, Tempfer and colleagues identified 68 cases in the literature. Seventy percent of the patients in this group got CC-0 resection, and they reported an OS of 12–33 months and a DFS of 7–18 months. They came to the conclusion that individuals with PC brought on by UC can safely use CRS and HIPEC [1].The 5-year DFS and OS were reported by Navarro Barios et al. to be 23% and 34%, respectively, after performing CC-0 resection on 41 out of 43 patients [15]. A median overall survival of 33 months was reported by Cornali et al. after performing CC-0 resection on 22 out of 33 patients [16]. In the study by Gomes David et al., they examined two groups: 90 patients in which CRS was the only procedure performed, and 44 patients in which both CRS and HIPEC were performed.They came to the conclusion that there was no discernible difference between the two groups' DFS and OS [17]. Of the 22 patients we conducted CRS and HIPEC on, 16 (72%) had CC-0 resection. The 5-year findings showed an OS of 57% and a DFS of 36%. Our DFS and OS were found to be slightly higher than the literature, and our CC-0 resection score was consistent with the literature. We came to the conclusion that these outcomes were because we only performed surgery on patients whose PCI scores were less than 15, and we performed diagnostic laparoscopy on each patient before surgery. Additionally, the same surgeon performed on every patient at our facility.One uncommon mesenchymal tumor is uterine corpus sarcoma. It makes up 7% of all EC.High recurrence rates are a characteristic of uterine sarcomas, which also react poorly to systemic chemotherapy. Many facilities worldwide acknowledge CRS and HIPEC as a primary treatment technique for peritoneal sarcomatosis, despite the fact that their use is disputed [18,19]. Diaz Montes et al. conducted an 11-year retrospective single-centered investigation in which they administered CRS and HIPEC to 7 instances out of a 26-case series. In contrast to 35 months of survival with traditional therapy, they reported that CRS plus HIPEC treatment resulted in a superior 43-month survival rate [20]. Uterine sarcomas accounted for 13 (59%) of the patients in our series.Cisplatin or cisplatin with doxorubicin are often used treatments for intraperitoneal sarcomas and gynecologic-originated malignancies. The temperature fluctuates from center to center between 41 and 43 degrees, the length ranges from 60 to 90 minutes, and the dosage varies based on 50 to 75 mg/body surface area M2. There is disagreement on the HIPEC dosage, duration, and chemotherapy type as a result of these differences [1]. Consistent with previous research, we administered cisplatin

75 mg/BSA plus doxorubicin 15 mg/BSA intraperitoneally throughout a 60-minute period.High rates of morbidity are a major issue with CRS and HIPEC treatment for PC patients with intra-abdominal malignancies. These morbidity rates decreased from 50% to 20% over the past ten years. It is necessary to reduce mortality rates to 5%. According to Gomes David et al.'s retrospective multicentric dataset, 20% of complications were CD grade 3 or higher. Mortality was not reported [17]. In contrast to Delotte et al., who did not record a CD grade 3 or above complication rate, Cornaliet al. reported a 3% complication rate and a 0% mortality rate in their 33 case series [7,16]. Seven (31%) of the patients at our center had a grade 3 or higher complication, and one (4.5%) of our Because of COVID 19, the instances were deemed exitus. We believe that the reason for our higher complication rate than that reported in the literature is the intestine and organ resections that were done. This article has a number of limitations. There was no control group to compare with, the study was retrospective, there were few cases, and the diseases were not selected uniformly, which raised the risk of bias. Furthermore, it was challenging to distinguish between the progression-free survival rate and the local effect of HIPEC due to differences in PCI scores and prior surgical and chemotherapy histories.

CONCLUSION

Because UC patients have low PCI scores and acceptable complication rates, we believe that CRS and HIPEC should be favored in PC due to the prolonged DFS and OS. For this topic, however, large-scale prospective randomized trials are required.

Author Contributions

Conceptualization, writing—editing and review, writing—creation of the first draft, Ö.D.; verification, data collection, and research—M.K. The published version of the manuscript has been read and approved by all authors.

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Institutional Review Board Statement

The study was authorized by the Ümraniye Training and Research Hospital's ethics committee at Health Sciences University Istanbul (number 2022/192).

Informed Consent Statement

Every participant in the study gave their informed consent.

Data Availability Statement

No data were reported by the study.

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Conflicts of Interest

No conflicts of interest are disclosed by the authors.

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