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Involved-field radiation therapy for locoregionally recurrent ovarian cancer ☆

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HIGHLIGHTS

- Selected ovarian cancer patients with locoregionally-confined recurrences were treated with definitive involved-field radiation therapy (IFRT).
- IFRT produced high rates of in-field disease control/prolonged disease-free intervals of up to 10 years in some patients.
- Some patients with disease progression following IFRT may benefit from RT through longer breaks from chemotherapy.

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ABSTRACT

Objective. To evaluate the effectiveness of definitive involved-field radiation therapy (IFRT) for selected patients with locoregionally-recurrent ovarian cancer.

Methods. We retrospectively reviewed records of 102 epithelial ovarian cancer patients treated with definitive IFRT (≥45 Gy). IFRT was directed to localized nodal (49%) and extranodal (51%) recurrences.

Results. The median time from diagnosis to IFRT was 36 months (range, 1–311), and the median follow-up after IFRT was 37 months (range, 1–123). Patients received a median of three chemotherapy courses before IFRT (range, 0–9). Five-year overall (OS) and progression-free survival (PFS) rates after IFRT were 40% and 24% respectively; the 5-year in-field disease control rate was 71%.

Thirty-five patients (35%) had no evidence of disease at a median of 38 months after IFRT (range, 7–122), including 25 continuously without disease for a median of 61 months (range, 17–122) and 10 with salvage treatment following disease recurrence, disease-free for a median of 39 months after salvage treatment (range, 7–92).

Eight clear cell carcinoma patients had higher 5-year OS (88% versus 37%; $p = 0.05$) and PFS (75% versus 20%; $p = 0.01$) rates than other patients. Patients sensitive to initial platinum chemotherapy had a higher 5-year OS rate than platinum-resistant patients (43% versus 27%, $p = 0.03$). Patients who required chemotherapy for recurrence after IFRT often benefitted from longer chemotherapy-free intervals after than before IFRT.

Conclusions. Definitive IFRT can yield excellent local control, protracted disease-free intervals, and even cures in carefully selected patients. RT should be considered a tool in the curative management of locoregionally-recurrent ovarian cancer.

Introduction

Most patients with ovarian cancer present with advanced disease and are treated with surgical resection followed by chemotherapy [1–3]. In the 1960s and 1970s, regional radiation therapy (RT) was used to reduce locoregional progression for early-stage ovarian cancer patients [2,4–7]. In the 1970s and 1980s, whole-abdominal irradiation emerged as a useful treatment for selected patients with small-volume disease. However, as more effective systemic treatments were developed, RT was relegated to a palliative role in the United States, rarely considered for definitive treatment [2,3,7].

Up to 70% of patients with advanced ovarian cancer experience recurrence—usually peritoneal carcinomatosis, although some patients experience predominantly locoregional recurrence without carcinomatosis or distant metastasis [2,3]. After multidisciplinary discussion, we have increasingly treated these patients with local RT, often after repeated localized recurrences despite multiple courses of chemotherapy. We retrospectively reviewed outcomes of such patients to determine the efficacy of definitive involved-field RT (IFRT) in the

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management of locoregionally-confined recurrent or persistent ovarian cancer.

Patients and methods

Patients

We identified 315 women with histologically-confirmed epithelial ovarian cancer treated consecutively with RT at MD Anderson Cancer Center during the period from January 1999 and December 2009. Patients receiving less than 39 Gy (n = 210) were considered to have received palliative treatment and were excluded. Three patients received 39 to 44 Gy, and were excluded because they were treated with palliative intent. The remaining 102 women, treated with a definitive RT dose of ≥45 Gy, were included in this study.

Patient, tumor, treatment, and follow-up information was abstracted from the medical records after Institutional Review Board approval. Ovarian cancer was staged according to the 2009 International Federation of Gynecology and Obstetrics system [8]. Disease sites were classified as pelvic, abdominal, or distant and as nodal or extranodal sites. Distant metastasis included liver metastasis and extra-abdominal disease beyond the paraaortic lymph nodes.

Treatment

All patients underwent surgical resection of the primary tumor, bilateral salpingo-oophorectomy, total abdominal hysterectomy, and selective biopsies and resections of lymph nodes, omentum, and other suspicious findings. One patient received preoperative chemotherapy for liver metastases present at diagnosis. Three high-risk patients received preoperative chemotherapy to allow time for resolution of deep vein thromboses (n = 2) and hydronephrosis with acute renal failure (n = 1) before surgery. Surgery was followed by adjuvant platinum-based chemotherapy (n = 96) or another chemotherapy regimen (n = 6). Seventeen patients underwent second-look laparotomy after adjuvant chemotherapy.

Recurrences before RT were treated with a variety of chemotherapy regimens and/or secondary cytoreduction. Patients were selected to receive definitive IFRT on a case-by-case basis after multidisciplinary discussion. Factors taken into consideration in deciding whether to offer IFRT included the ability to encompass disease by a RT field, timing and pattern of disease progression, length of disease-free intervals, response to prior treatments, resectability of disease, performance status, and limitations of other treatment options, including toxicity. Twenty-seven patients had positron emission tomography (PET) before RT.

Most patients had IFRT for treatment of gross disease (n = 73; median dose 59.2 Gy, range, 45–68.2); however, some patients were treated after gross total resection (n = 16; median dose 54.5 Gy, range, 45–64.2) or for consolidation following complete response to chemotherapy (n = 13; median dose 48 Gy, range, 45–57.6). Five patients received RT immediately following initial surgery—three for gross residual disease after surgery, one for concurrent endometrial cancer, and one for adenosquamous histology. Twenty patients were treated with high-dose chemotherapy and bone marrow transplant (BMT) for recurrence on an institutional protocol. Of these, 12 patients received IFRT for consolidation after complete response following BMT; the remaining eight had residual or recurrent disease after BMT treated with definitive IFRT (n = 5), or resection followed by postoperative RT (n = 3).

IFRT was directed to gross disease plus a high-risk clinical target volume (CTV) that included the postoperative bed or the prechemotherapy extent of disease with a 1- to 1.5-cm margin, excluding uninvolved clinical structures. Additional CTVs were designated according to the risks of microscopic disease spread, proximity to critical structures, and other risk factors for complications. Nodal CTVs included grossly involved lymph node sites, extending to cover adjacent uninvolved regions. For example, CTVs for patients with paraaortic node recurrence included the entire paraaortic nodal chain, and CTVs for patients with pelvic node recurrence included unilateral or bilateral pelvic nodes. Patients were treated using intensity-modulated RT (n = 63), 3-dimensional conformal RT (n = 35), appositional electrons (n = 3), or proton beam RT (n = 1). Four patients received both external beam RT and vaginal cuff brachytherapy. Eighteen patients received at least one cycle of concurrent systemic chemotherapy with RT; 14 with platinum-based chemotherapy, three with taxol and one with capecitabine.

Statistical analysis

Overall survival (OS), progression-free survival (PFS), and in-field disease control were evaluated using Kaplan–Meier estimates and compared using the log-rank test. Clinical and patient factors were compared using Pearson's chi-squared, Mann–Whitney–Wilcoxon, or Wilcoxon ranked-sign tests as appropriate. Ninety-five percent confidence intervals (CI) are reported. Statistical analysis was performed using the Stata software package (StataCorp. 2011. *Stata Statistical Software*: *Release 12*. College Station, TX).

Results

Patient, tumor, and treatment characteristics are shown in Table 1. The median follow-up time after IFRT was 37 months (range, 1–123), and the median follow-up time after diagnosis was 88 months (range, 8–368). The median time from diagnosis to definitive IFRT was

Table 1
Patient, tumor, and treatment characteristics (N = 102).

Characteristic		
Age at diagnosis, years, median (range)		53 (29–78)
Age at RT, years, median (range)		58 (30–81)
Time to first recurrence, months, median (range)		19 (0–288)
Time to RT, months, median (range)		36 (1–311)
Histology, no (%)		
	Serous	55 (54)
	Mixed	17 (17)
	Endometrioid	10 (10)
	Clear cell	8 (8)
	Mucinous	5 (5)
	Other	7 (7)
Stage, no (%)		
	I	15 (15)
	II	18 (18)
	III	58 (57)
	IV	4 (4)
	Unknown	7 (7)
Grade, no (%)		
	1	5 (5)
	2	8 (8)
	3	84 (82)
	Unknown	5 (5)
Sites treated with RT, no (%)		
	Pelvis	
	Pelvic LN	10 (10)
	Vaginal cuff	21 (21)
	Other pelvic mass	23 (23)
	Abdomen	
	Paraaortic LN	27 (26)
	Abdominal wall mass	2 (2)
	Other abdominal mass	6 (6)
	Inguinal LN	10 (10)
	Supraclavicular LN	2 (2)
	Mediastinal LN	1 (1)
RT indication, no (%)		
	Treatment of gross disease	73 (71)
	Postoperative treatment	16 (16)
	Consolidation after chemotherapy	13 (13)
Endocrine therapy		41 (40)
Secondary cytoreduction		46 (45)

RT = radiation therapy; LN = lymph node.