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Intraoperative electron beam radiotherapy and extended surgical resection for gynecological pelvic recurrent malignancies with and without external beam radiation therapy: Long-term outcomes

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HIGHLIGHTS

- Patients with locally recurrent gynecological cancers have a high-risk of local re-recurrence and death.
- EBRT reduces the risk of LRR compensating some adverse disease features.
- Patients with tumor fragmentation experienced the largest benefit with EBRT treatment.

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ABSTRACT

Objective. To analyze prognostic factors in patients treated with intraoperative electrons containing resective surgical rescue of locally recurrent gynecological cancer (LRGC).

Methods. From January 1995 to December 2012, 35 patients with LRGC [uterine cervix (57%), endometrial (20%), ovarian (17%), vagina (6%)] underwent extended [multiorgan (54%), bone (9%), soft tissue (54%), vascular (14%)] surgery and intraoperative electron-beam radiation therapy [IOERT (10–15 Gy)] to the pelvic recurrence tumor bed. Sixteen (46%) patients also received external beam radiation therapy [EBRT (30.6–50.4 Gy)]. Survival outcomes were estimated using the Kaplan–Meier method, and risk factors were identified by univariate and multivariate analyses.

Results. Median follow-up time for the entire cohort of patients was 46 months (range, 3–169). Ten-year rates for locoregional control (LRC) and overall survival (OS) were 58 and 16%, respectively. On multivariate analysis non-EBRT at the time of pelvic re-recurrence [HR 4.15; $p = 0.02$], no tumor fragmentation [HR 0.13; $p = 0.05$] and time interval from primary tumor to LRR < 24 months [HR 5.16; $p = 0.01$], retained significance with regard to LRR. Non-EBRT at the time of pelvic re-recurrence [HR 4.18; $p = 0.02$] and time interval from primary tumor to LRR < 24 months [HR 6.67; $p = 0.02$] showed a significant association with OS after adjustment for other covariates.

Conclusions. EBRT treatment integrated for rescue, time interval for relapse ≥ 24 months, and not multi-involved fragmented resection specimens are associated with improved LRC in patients with LRGC in the pelvis. Present results suggest that a significant group of patients may benefit from EBRT treatment integrated with extended surgery and IOERT.

Introduction

Patients with a gynecologic central pelvic recurrence, historically have had a rescue opportunity, with exenteration providing pelvic control in approximately one third [1]. Conversely, a noncentral recurrence presents a dismal prognosis. The long-term survival with

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Table 1
Patient, tumor and treatment characteristics.

Characteristics	All patients N = 35 (%)	EBRT group N = 16 (%)	Non-EBRT group N = 19 (%)	P-value
Patient variables				
Median age (range)	53 (38–67)	54 (38–65)	52 (42–67)	0.57
Karnofsky performance status ≥90/<90	24 (69)/11 (31)	11/5	13/6	0.55
Time interval (months) from primary to LR (range) ≥24/<24	19 (54)/16 (46)	9/7	10/9	0.60
Macroscopic tumor variables				
Primary site Endometrial/uterine cervix/ovarian/vagina	7 (20)/20 (57)/6 (17)/2 (6)	3/9/3/1	4/11/3/1	0.44
Extent of infiltration of the recurrence on the pelvic sidewall F0/F1/F2/F3/F4	0 (0)/9 (26)/11 (31)/8 (23)/7 (20)	0/4/3/6/3	0/5/8/2/5	0.22
Pelvic relapse topography Posterior/posterolateral/antero-central	6 (17)/9 (26)/20 (57)	4/3/9	2/6/11	0.23
Maximum recurrent tumor diameter ≥5 cm vs < 5 cm	17 (45)/18 (55)	7/9	10/9	0.72
Tumor multifragmentation involvement Yes vs no	21 (60)/14 (40)	9/7	12/7	0.51
Microscopic tumor variables				
Initial primary tumor histologic grade I–II vs III	26 (74)/9 (26)	12/4	14/5	0.71
Histologic subtype Adenocarcinoma/squamous carcinoma	20 (57)/15 (43)	8/8	12/7	0.24
Margin status R0 vs R1	19 (54)/16 (46)	9/7	10/9	0.71
Recurrent tumor lymph node status Positive vs negative	11 (31)/24 (69)	6/10	5/14	0.28
Surgical variables				
Multiorgan resection Yes vs no	19 (54)/16 (46)	8/8	11/8	0.43
Bone resection Yes vs no	6 (17)/29 (83)	3/13	3/16	0.56
Vascular resection Yes vs no	5 (14)/30 (86)	3/13	2/17	0.42
Soft tissue resection Yes vs no	20 (57)/15 (43)	9/7	11/8	0.43
Radiation therapy and chemotherapy variables				
Surgical resection treatment for initial primary tumor Yes vs no	26 (74)/9 (26)	12/4	14/5	0.93
Adjuvant chemotherapy initial primary tumor Yes vs no	21 (60)/14 (40)	9/7	12/7	0.68
EBRT for initial primary tumor Yes vs no	25 (71)/10 (29)	11/5	14/5	0.75
Adjuvant chemotherapy for recurrent tumor Yes vs no	13 (37)/22 (63)	7/9	6/13	0.46
IOERT dose ≥12.5 Gy vs < 12.5 Gy	22 (63)/13 (37)	9/7	13/6	0.46
Hospitalization				
Median time (minutes) of surgery	452 (205–950)	424 (205–950)	476 (228–765)	0.52
Median time (days) admitted to the intensive care unit	2.57 (0–9)	3.0 (0–9)	2.2 (0–7)	0.24
Median time (days) of overall hospitalization	20 (4–138)	19 (5–120)	21 (4–138)	0.35
Toxicity				
RTOG chronic toxicity ≥ 3				
Gastrointestinal (fistula n = 3; abscess n = 2)	5	2	3	0.38
Genitourinary (ureteral stenosis n = 2)	2	1	1	
Nervous (peripheral neuropathy n = 1)	1	1	0	
Clavien–Dindo perioperative complications	20 (57)	7 (44)	13 (68)	0.14
RTOG acute toxicity ≥ 3	14 (40)	6 (38)	8 (42)	0.71
Gastrointestinal (n = 3)				
Genitourinary (n = 5)				
Soft tissue (n = 1)				
Wound infection (n = 3)				
Cardiac (n = 1)				
Pulmonary (n = 1)				

EBRT, external beam radiation therapy. RTOG, radiation therapy oncology group.
Multiorgan resection (≥2 pelvic organs): anterior exenteration with lateral extended endopelvic resection (LEER) (n = 1), anterior exenteration (n = 5), posterior exenteration (n = 3), total pelvic exenteration (n = 7), sacroexenteration (n = 3). Bone resection: LEER (n = 3), sacroexenteration (n = 3). Soft tissue resection: 19 anterior exenteration with LEER (n = 1), LEER (n = 11), and sacroexenteration (n = 3), LEER with vascular en bloc resection of the local recurrence (n = 5).