Prognostic Factors for Outcomes and Complications for Primary Squamous Cell Carcinoma of the Vagina Treated with Radiation

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Purpose

To analyze the results and identify prognostic factors for primary squamous cell carcinoma (SCCA) of the vagina treated with radiation therapy from a single institution from 1959 to 2005.

Materials & Methods

Eighty patients with a mean follow up of 94 months were analyzed in this Stanford University Medical Center retrospective series. Mean clinical characteristics included are summarized below in Table 1.

Table 1. Patient and Treatment Characteristics (n=80).

Age, mean, y/o (range)		65 (33-99)
Pts alive, n (%)		40 (50)
F/U alive pts, mean, mo (range)		94 (3-290)
Hemoglobin mean (g/dL) (range)		12.5 (8.7-14.4)
Prior Hysterectomy, n (%)		39 (49)
Reason for Hys, n (%)	Unknown	6 (8)
	Benign	19 (24)
	Malignant	14 (18)
Primary resected, n (%)		8 (10)
Tumor size, mean, cm (range)		4 (0.3-10)
Tumor dose, mean Gy (range)		73 (6-127)
Chemoradiation, n (%)		6 (8)
Surgical salvage, n (%)		5 (6)
Stage, n (%):	0	2 (2.5)
	I	33 (41)
	II	23 (29)
	III	13 (16)
	IVA	8 (10)
	IVB	1 (1.5)

The majority of patients were treated with radiation as the primary modality (90%). A minority of patients were treated with external beam radiation (EBRT) (21%) or brachytherapy (BT) (15%) alone.

Materials & Methods (cont.)

Intracavitary and interstitial BT were performed in 38 (48%) and 24 (30%) patients, respectively. Sixty percent of patients were treated with a combination of EBRT to the pelvis and BT to the whole vagina (see Table 2).

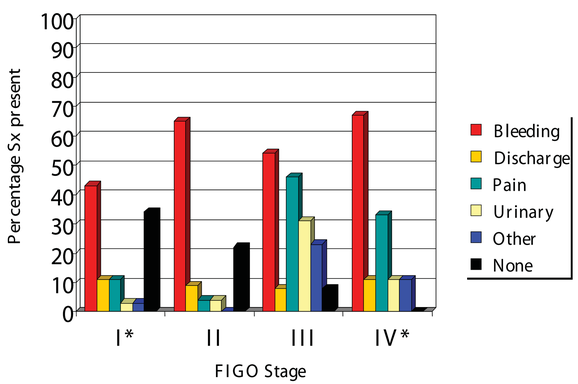
Table 2. Method of XRT by FIGO Stage.

XRT Method	FIGO Stage				Total (%)
	I*	II	III	IV*	
EBRT	4	6	3	4	17 (21)
Intracavitary (IC)†	9	0	0	0	9 (11)
Interstitial (IT)	2	0	0	0	2 (3)
Orthovoltage (TV)	0	0	0	0	0 (0)
EBRT + IC††	15	7	3	3	28 (35)
EBRT + IT	3	10	6	1	20 (25)
IC + IT	1	0	0	0	1 (1)
EBRT +TV	0	0	1	1	2 (3)
Other§	1	0	0	0	1 (1)

* - Combination of Stage 0 & I or IVA & IVB, respectively; † – High dose rate (HDR) in 1 pt.; †† –HDR IC in 8 pts & 3/8 with Intensity Modulated Radiation Therapy (IMRT); & § - Treated with EBRT+TV+IT.

Results

Vaginal bleeding was the most common symptom at presentation at 54% (Figure 1). Although, 23% of women presented without any symptoms, this occurred mostly in women with stage I & II disease, so that with increasing stage, stage III & IV, almost all women presented with at least one symptom.



Results (cont.)

Kaplan-Meier (KM) 5-year pelvic control (PC), distant metastasis free survival (DMFS) and disease specific survival (DSS) probabilities were: stage I, 85%, 100%, & 93%, respectively; stage II, 76%, 95%, & 68%, respectively; stage III, 62%, 65%, & 44%, respectively; and stage IV, 30%, 28%, & 13%, respectively.

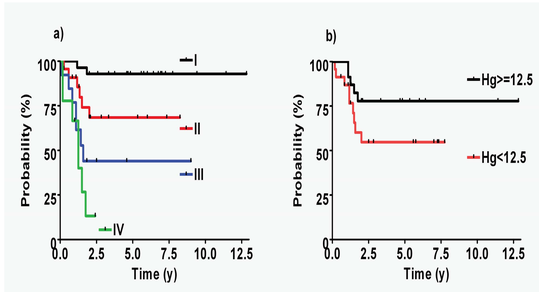


Figure 2. DSS stratified by a) FIGO Stage; & b) pre-treatment/treatment Hemoglobin (Hg).

Sites of first failure included: pelvis in 62%; distant metastases (DM) alone in 19%; and pelvis and DM in 19%. Inguinofemoral nodal (IFN) failure was seen in 1 out of 13 (8%) patients with a primary involving the lower 3rd of the vagina who did not receive IFN radiation. No IFN failures were observed in 22 patients who recieved IFN radiation.

Table 3 lists the significant prognostic factors found on multivariate analysis (MVA) for PC and DSS.

Table 3. Prognostic factors found on MVA.

Variable	PC	DSS
	p-value	p-value
Stage (I vs. II vs. III vs. IV)	<.01	.0001
Size (continuous variable)	.01	.06
Hg (continuous variable)	.01	.01
Prior Hysterectomy (No vs. Yes)	.02	.01

Prior Hysterectomy DSS HR = .37 (.05-.69) 95% CI
Prior Hysterectomy PC HR = .39 (.04-.75) 95% CI

Results (cont.)

There were eleven grade 3/4 (G3/4) complications occurring in ten patients in our cohort: fistula (3); small bowl obstructions (2); perineal skin breakdown (2); bowel perforation; rectal ulcer; proctitis; and pelvic bone necrosis. The KM 5-year G3/4 complication free estimate of our cohort was 85%. MVA for G3/4 complications revealed that patient age, size of tumor and total tumor dose were predictive (p<0.05) for complications.

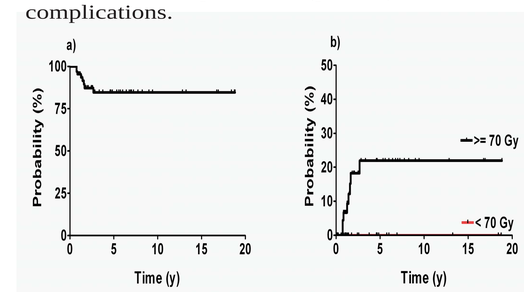


Figure 3. Complications associated with radiotherapy for vaginal SCCA. a) Complication free survivial of the entire cohort; b) Kaplan-Meier estimate of complications stratified by total tumor dose.

Conclusions

1. Radiation as a single modality for early stage (I & II) primary vaginal SCCA produces good results.
2. Advanced stage disease necessitates a combined modality treatment approach testing concurrent cisplatin-based regimens and/or new modalities (e.g. hyperthermia).
3. Pre-treatment/treatment Hg levels appear to be clinically significant and further studies on the affect of correction of anemia are warranted.

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