Available online at www.sciencedirect.com
ScienceDirect
Gynecologic Oncology 112 (2009) 146–149
Gynecologic Oncology
www.elsevier.com/locate/ygyno

Prospective evaluation of prognostic significance of the tumor-free distance from uterine serosa in surgically staged endometrial adenocarcinoma

Katherine V. Schwab, David M. O'Malley, Jeffrey M. Fowler, Larry J. Copeland, David E. Cohn *

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, the Ohio State University College of Medicine, Columbus, Ohio 43210, USA

Received 30 July 2008
Available online 19 October 2008

Abstract

Objective. To determine if tumor-free distance (TFD) from the uterine serosa predicts surgicopathologic factors and outcome in surgically staged endometrial cancer, and to compare TFD with the traditional estimate of depth of myometrial invasion (DOI).

Methods. Patients who underwent complete surgical staging for primary endometrial cancer at a single institution were identified from 2002–2005. During this time, TFD was prospectively measured at the time of pathologic evaluation of the uterine specimen. Tumor-free distance (TFD) was defined as distance from deepest myometrial invasion to the serosal surface, whereas DOI was defined as the distance between the endomyometrial junction and deepest myometrial invasion. DOI and TFD were shown as continuous variables and compared to traditional surgicopathologic factors and evaluated for their ability to predict recurrence and death from disease. Univariate and multivariate analysis were used to examine the data. Receiver–operator characteristic curve was created to evaluate optimal TFD.

Results. We identified 99 patients that met the study criteria. Mean DOI was 0.6 cm and mean TFD was 1.3 cm. 77 patients were stage I, 11 were stage II, and 11 were stage III. Tumor grade was distributed as 68, 21 and 10 for grades 1, 2, and 3 respectively. Median follow up time was 2.7 years (1002 days) with 9 episodes of recurrence and 7 deaths. Univariate analysis demonstrated DOI to be a significant predictor of death, grade, lymph node metastasis, lymphovascular space involvement (LVSI), stage, lower uterine segment (LUS) involvement and adnexal involvement. TFD significantly predicted lymph node metastasis, LVSI, and grade. Using Cox proportional hazards model, DOI more significantly predicted recurrence (hazard ratio 3.11, $p=0.0007$). Both DOI and TFD predicted death from disease (hazard ratio 3.58, $p=0.0006$ and 0.22, $p=0.0365$, respectively). Although the performance characteristics of TFD were modest, the balance of sensitivity and specificity for TFD in predicting recurrence was 1 cm.

Conclusions. TFD, like DOI, is predictive of many surgicopathological variables and patient outcome in surgically staged endometrial cancer. Although the performance characteristics may not be as powerful as DOI, the ease and reproducibility of this measurement may justify its inclusion in synoptic reporting of endometrial cancer.

Keywords: Endometrial cancer; Surgical staging; Prognostic factors; Depth of invasion

Background

Endometrial cancer is the most common gynecological cancer and the third leading female malignancy in the United States. 39,080 cases are expected to be diagnosed this year [1]. Irregular vaginal bleeding initiates clinical evaluation at early stage disease for most patients. However, 22% of patients with clinically stage I disease will be upstaged with surgical staging [2]. In 1988, the Oncology Committee of the International Federation of Gynecology and Obstetrics outlined a surgical staging system that is based on pathologic findings including peritoneal cytology, hysterectomy, bilateral salpingo-oopherectomy, and bilateral pelvic and para-aortic lymphadenectomy [7]. Complete surgical staging, including depth of myometrial invasion (DOI) delineates prognosis and guides further management.

* Corresponding author. 320 West 10th Avenue, M-210 Starling Loving Hall, Columbus, Ohio 43210, USA. Fax: +1 614 293 3078.
E-mail address: David.Cohn@osumc.edu (D.E. Cohn).

0090-8258/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.ygyno.2008.09.009

Depth of invasion has demonstrated significant prognostic factors for extrauterine disease and recurrence rate [3]. However, there is difficulty in determining accurate DOI due to adenomyosis and irregular endomyometrial junction often leading to overestimation of DOI [4]. Overestimating DOI can lead to overly aggressive treatment with unnecessary morbidity. The distance between the deepest myometrial invasion and uterine serosa may increase accuracy of measurements and improve prediction of prognosis [5,6]. Given the potential difficulty in determining DOI in cases of endometrial cancer coexisting with adenomyosis or leiomyomata, we investigated the inverse of depth of myometrial invasion, called the "tumor-free distance" (TFD) between the uterine serosa and the nearest invasive cancer.

Previously, our group had retrospectively established that this TFD was predictive of traditional surgicopathologic variables, and was more predictive of patient outcome than the more commonly reported depth of myometrial invasion [5]. In this report, we evaluate the value of TFD when prospectively collected in a large group of surgically staged endometrioid endometrial cancers.

Methods

All patients undergoing comprehensive surgical staging for primary endometrial cancer at the James Cancer Hospital at The Ohio State University from January 2002 until December 2005 were identified. During this interval, TFD was calculated prospectively by the reviewing pathologist. In our institution, 3 pathologists were primarily responsible for signing out gynecologic cancer cases; 1 of these pathologists was fellowship trained in gynecologic pathology.

Patients included in the study had undergone complete surgical staging with hysterectomy, bilateral salpingo-oophorectomy, cytology and lymph node dissection. Surgicopathologic data were collected from pathology and operative reports. Standard of care follow up and treatment were completed with adjuvant radiation and chemotherapy based on prognostic evaluation. Recurrence and survival were extracted from chart review. Exclusion occurred for patients with incomplete pathologic information for review, no follow up care documented one year post operatively, and for any percentage of clear cell, serous, or mixed epithelial cell type on pathological report.

Tumor-free distance (TFD) was defined as distance from deepest myometrial invasion to the serosal surface, whereas DOI was defined as the distance between the endomyometrial junction and deepest myometrial invasion. DOI and TFD were expressed as continuous variables and compared to traditional surgicopathologic factors and evaluated for their ability to predict recurrence and death from disease. Univariable and multivariable analysis were used to examine the data. Receiver–operator characteristic curve was created to evaluate optimal TFD.

Results

150 patients were identified with endometrial adenocarcinoma from pathological results search. 122 patients had complete surgicopathological data for review. 99 patients had appropriate follow up greater than one year and represent the basis of this report (Table 1). Average age was 60.4 years old. Median follow up time was 1002 days (approximately 2.7 years) with 9 patients experiencing recurrence and 7 patients dying. Most patient were diagnosed at Stage 1 (77.8%) with FIGO grade 1 (68.7%). Positive lymph nodes were identified in 9 (9.1%) of patients, 4 with pelvic metastasis alone, 3 with both pelvic and para-aortic metastasis, and 2 with para-aortic metastasis alone. Lymphovascular space involvement

Table 1
Summary of surgicopathologic features and outcomes of 99 patients with endometrial cancer

Continuous variables	
Age mean (range)	60.4 years (32–86)
Tumor size mean (range)	3.4 cm (0.1–9.2)
DOI mean (range)	0.6 cm (0–5.0)
TFD mean (range)	1.3 cm (0–8.0)
FIGO grade	
1	68 (68.7%)
2	21 (21.2%)
3	10 (10.1%)
FIGO stage	
1	77 (77.8%)
2	11 (11.1%)
3	11 (11.1%)
4	0
Positive washings	
Present	1 (1%)
Absent	98 (99%)
Cervical involvement	
Present	15 (15.2%)
Absent	84 (84.8%)
Adnexal involvement	
Present	7 (7.1%)
Absent	92 (92.9%)
LVSI	
Present	16 (16.2%)
Absent	83 (83.8%)
LUS involvement	
Present	29 (29.3%)
Absent	70 (70.7%)
Positive nodes	
Present	9 (9.1%)
Absent	90 (90.9%)
Recurrence	
Yes	9 (9.1%)
No	90 (90.9%)
Death	
Yes	7 (7.1%)
No	92 (92.9%)

Note: FIGO = International Federation of Gynecology and Obstetrics, LVSI = lymph vascular space involvement; LUS = lower uterine segment.