Gynecologic Oncology 133 (2014) 216–220

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Tumor size, depth of invasion, and histologic grade as prognostic factors of lymph node involvement in endometrial cancer: A SEER analysis ☆

Roberto Vargas [a,b], J. Alejandro Rauh-Hain [a], Joel Clemmer [a], Rachel M. Clark [a], Annekathryn Goodman [a], Whitfield B. Growdon [a], John O. Schorge [a], Marcela G. del Carmen [a], Neil S. Horowitz [b], David M. Boruta II [a,*]

[a] Division of Gynecologic Oncology, Vincent Obstetrics and Gynecology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
[b] Division of Gynecologic Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

HIGHLIGHTS

- In a population analysis using Mayo criteria, low-risk endometrial cancers have a low rate of lymph node metastasis.
- Grade 1 tumors with <50% invasion have a low risk of lymph node metastasis, irrespective of tumor size.

ARTICLE INFO

Article history:
Received 17 January 2014
Accepted 8 February 2014
Available online 16 February 2014

Keywords:
Endometrial neoplasms
Lymph node excision

ABSTRACT

Objectives. The objective of this investigation was to evaluate the risk of nodal metastasis in patients with endometrial cancer, using the Mayo criteria, in a population-based analysis.

Materials and methods. Data from the SEER registry was reviewed for endometrial cancer cases diagnosed between 1988 and 2010. Patients were considered at low-risk for nodal metastasis if their tumors were histologic grade 1 or 2, myometrial invasion was less than 50%, and tumor size equal to or less than 2 cm. Patients not meeting these criteria were considered at high-risk for nodal involvement.

Results. The final study group consisted of 19,329 women with surgically staged endometrial cancer. Of these, 1035 (5.3%) had lymph node involvement. Based on Mayo criteria, 4095 (21.1%) patients were found to be at low-risk and 15,234 (78.9%) at high-risk for nodal metastasis. Low-risk features were associated with a 1.4% risk for lymph node metastasis, compared to 6.4% in patients with high-risk features ($p < 0.001$). When myometrial invasion was removed from the analysis, low-risk pathologic features were associated with a 2.4% risk of lymph node metastasis, compared to 10.4% in patients with high-risk features ($p < 0.001$).

Conclusions. In a population-based analysis, women with low-risk endometrial cancer, as defined by the Mayo criteria, have a low rate of lymph node metastasis.

Introduction

In the United States, endometrial cancer remains the most prevalent of all gynecological malignancies. It is estimated that 49,560 new cases of endometrial cancer will be diagnosed in 2013, accounting for an estimated 8190 deaths [1]. Along with hysterectomy and bilateral salpingo-oophorectomy, comprehensive lymph node dissection remains the standard of care in the staging of most endometrial cancers [2]. However, some studies questioned the role of lymph node dissection in patients with low risk endometrial carcinomas [3–9]. Two randomized trials and retrospective population-based studies failed to demonstrate a survival benefit when routine lymphadenectomy is performed for low risk endometrial carcinomas [10–14]. Moreover, routine lymphadenectomy has been associated with increased operative time, blood loss, and 30-day patient morbidity [15,16]. Despite these compelling facts, a significant number of practitioners still perform lymphadenectomy for low risk malignancies at the time of hysterectomy. In a recent survey of GOG (Gynecologic Oncology Group) members, up to 35% of practitioners surveyed performed both pelvic and para-aortic lymphadenectomy for grade 1 endometrial carcinomas [17].

Several models for predicting the likelihood of lymph node metastasis using histopathologic parameters in women with endometrial cancer have been proposed. In a series from the Mayo clinic, 187 patients with low-risk endometrial cancer underwent comprehensive lymphadenectomy as part of their surgical staging. Only 9 out of 187

☆ This abstract has been accepted as a poster presentation at the Society of Gynecologic Oncology Annual Meeting in Tampa, Florida on March 22, 2013.

* Corresponding author at: Division of Gynecologic Oncology, Vincent Obstetrics and Gynecology, Massachusetts General Hospital, 55 Fruit Street, Yawkey 9 E, Boston, MA 02114, USA. Fax: +1 617 724 6898.
E-mail address: dboruta@partners.org (D.M. Boruta).

http://dx.doi.org/10.1016/j.ygyno.2014.02.011
0090-8258/

(5%) had evidence of lymph node metastases. Within this low risk group there were no patients with lymph node involvement if tumor size was less than 2 cm [4]. Other retrospective analyses, including a recent review of the LAP2 cohort, have demonstrated similar results in patients with low-risk characteristics [5,6,18–20].

While retrospective studies have defined a low-risk group of endometrial cancer patients, most rely on single institution experience. Due to relatively small sample sizes, these studies fail to analyze tumor grades separately and small incremental changes in tumor size. The objective of this investigation is to evaluate the risk of nodal metastasis in patients with endometrial cancer using the Mayo criteria, utilizing data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) registry.

Materials and methods

Data from the National Cancer Institute's SEER registry for endometrial cancer cases diagnosed between 1988 and 2010 was the source for this analysis. The SEER database is a tumor registry that collects data from approximately 28% of the United States population and includes incidence and population data grouped by age, sex, race, year of diagnosis, and geographic area, and provides information regarding stage of disease; tumor grade, size, and histology; lymph node status; and overall survival for each registered patient [21]. All data regarding tumor size, histologic grade, and myometrial invasion were as recorded in database based on final pathology. Our study was granted exemption by the Institutional Review Board.

Eligible women were 18 years or older with endometrial cancer of endometrioid histology, limited to the uterine corpus or lymph nodes. Women who were diagnosed at autopsy, those with a previous diagnosis of cancer or evidence of disease involving the cervix, adnexa, or peritoneal cavity were excluded from the analysis. Patients for whom data regarding tumor invasion, size, and histologic grade were not available were also excluded from the analyses. The low-risk group, as per the Mayo criteria, was defined by: grade 1 or 2 tumor histology; less than 50% myometrial invasion; and tumor size ≤2 cm. The high risk group was comprised of tumors with myometrial invasion >50%, grade 3 histology, or tumor size >2 cm [4].

Distribution of demographic, clinical, and treatment characteristics was compared using chi-square tests. Student *t* tests were used to assess the significance of differences in the mean values of continuous variables. Logistic regression was used to determine the effect of variables (histologic grade, size, depth of invasion, age, and race) on lymph node involvement. All statistical tests were 2 sided and differences were considered statistically significant at $p < 0.05$.

Results

The 2012 submission of the SEER dataset included 126,039 women diagnosed with endometrial cancer. Of these, 60,736 patients were excluded for unknown tumor size, 19,433 were excluded for unknown lymph node status, 3808 were excluded for unknown histologic grade, and 3700 were excluded for unknown depth of invasion. Additionally, 19,093 patients were excluded if endometrial cancer was not the solitary primary tumor, was diagnosed at autopsy, tumor involved the cervix or adnexa, or tumor stage was not determinable. The final study group therefore consisted of 19,329 women with endometrial cancer diagnosed between 1988 and 2010 that had complete tumor characteristics available for analysis.

Of these 19,033 patients, 94.65% (n = 18,294) had disease confined to the uterine corpus compared to 5.35% (n = 1035) that had lymph node involvement (Table 1). The mean age at diagnosis was 61.9 (±11.4) and 62.2 (±11.1) years for patients with and without nodal involvement, respectively ($p = 0.3$). The median number of lymph nodes examined was 12 in patients without lymph node involvement, compared to 14 in patients with positive lymph nodes ($p < 0.001$).

Table 1
Patient demographics by lymph node involvement.

	Negative lymph nodes	Positive lymph nodes	p value
Number of patients	18,294 (94.65%)	1035 (5.35%)	
Age at diagnosis (years)			
Median	61 (55–70)	62 (55–70)	0.377
Race			0.016
White	15,457 (84.5%)	840 (81.2%)	
African American	1085 (5.9%)	76 (7.3%)	
Other	1752 (9.6%)	119 (11.5%)	
Grade			<0.001
I	7438 (40.7%)	217 (21.0%)	
II	7250 (39.6%)	442 (42.7%)	
III	3606 (19.7%)	376 (36.3%)	
Tumor size			<0.001
None	9 (0%)	0 (0%)	
Micro (<0.1)	351 (1.9%)	0 (0%)	
≤1 cm (0.1–1.0)	1622 (8.9%)	42 (4.1%)	
≤2 cm (1.1–2.0)	3400 (18.6%)	106 (10.2%)	
≤3 cm (2.1–3.0)	4195 (22.9%)	161 (15.6%)	
≤4 cm (3.1–4.0)	2334 (12.8%)	187 (18.1%)	
≤5 cm (4.1–5.0)	5053 (27.6%)	519 (49.1%)	
>5 cm (5.1+)	2719 (14.9%)	322 (31.1%)	
Lymph node status			<0.001
Negative	18,294 (100%)	0 (0%)	
Positive	0 (0%)	1035 (5.3%)	
Tumor invasion			<0.001
≤50%	13,967 (76.3%)	395 (38.2%)	
>50%	4327 (23.7%)	640 (61.8%)	

Women classified as white were more likely to have disease confined to the uterus compared to African-Americans or other/mixed races (94.9% vs. 93.1%, $p = 0.005$). A greater proportion of patients without lymph node involvement were found to have grade 1 or 2 tumors, as opposed to grade 3 tumors (80.3% vs. 19.7%, $p < 0.001$). Likewise, patients with disease confined to the uterine corpus were less likely to have >50% myometrial invasion, compared to patients with nodal disease (23.7% vs. 61.8%, $p < 0.001$).

Table 2
Patient demographics by Mayo criteria risk grouping.

	Low-risk group	High-risk group	P value
Number of patients	4095 (21.19%)	15,234 (78.81%)	
Age at diagnosis (years)			
Median	59 (53–67)	62 (55–70)	<0.001
Race			<0.001
White	3485 (85.1%)	12,812 (84.1%)	
African American	192 (4.7%)	969 (6.4%)	
Other	418 (10.2%)	1453 (9.5%)	
Grade			<0.001
I	2399 (58.6%)	5256 (34.5%)	
II	1696 (41.4%)	5996 (39.4%)	
III	0 (0%)	3982 (26.1%)	
Tumor size			<0.001
None	6 (0.1%)	3 (0%)	
Micro (<0.1)	321 (7.8%)	30 (0.2%)	
≤1 cm (0.1–1.0)	1308 (31.9%)	356 (2.3%)	
≤2 cm (1.1–2.0)	2460 (60.1%)	1046 (6.9%)	
≤3 cm (2.1–3.0)	0 (0%)	4356 (28.6%)	
≤4 cm (3.1–4.0)	0 (0%)	3881 (25.5%)	
≤5 cm (4.1–5.0)	0 (0.0%)	2521 (16.5%)	
>5 cm (5.1+)	0 (0.0%)	3041 (20.0%)	
Lymph node status			<0.001
Negative	4037 (98.6%)	14,257 (93.6%)	
Positive	58 (1.4%)	977 (6.4%)	
Tumor invasion			<0.001
≤50%	4095 (100.0%)	10,267 (67.4%)	
>50%	0 (0%)	4967 (32.6%)	

Low risk group = grade 1 or 2 histology, myometrial invasion <50%, and tumor size ≤2 cm.
High risk group = grade 3 histology, or myometrial invasion >50%, or tumor size >2 cm.