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The Risk of Lymph-Node Metastasis with Positive Peritoneal Cytology in Endometrial Cancer

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Abstract

Objective—To determine the correlation between positive peritoneal cytology (PPC) and lymph node metastasis in patients with endometrial cancer grossly confined to the uterus.

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Methods—Data were extracted from the Surveillance, Epidemiology, and End Results database between 1988 and 2005. Only those patients with endometrial cancer grossly confined to the uterus who had undergone a complete staging procedure (lymph-node removal) were included. Statistical analysis used Chi-square test and logistic regression models.

Results—A total of 22,947 patients were identified. PPC was present in 3.5% of patients. The incidence of lymph node metastasis was significantly higher among patients with PPC compared to those with negative peritoneal cytology for all histologic types examined ($p<0.0001$): endometrioid adenocarcinoma; 28.7% vs. 6.9%, adenocarcinoma not otherwise specified; 35.4% vs. 5.8%, clear cell/serous carcinoma; 41.4% vs. 19.0%, and carcinosarcoma; 38.4% vs. 14.4%. After adjusting for other contributing factors in the multivariable model, PPC remained an independent predictor of lymph node metastasis ($p<0.0001$).

Conclusion—Our data indicates that patients with positive washings are at significant risk of nodal metastasis and adverse prognosis. Although, no longer a part of the current FIGO staging criteria, peritoneal cytology status should continue to inform clinical decision-making in endometrial cancer.

Keywords

Peritoneal cytology; Lymph node; Metastasis; Endometrial cancer

Introduction

Endometrial cancer is the most common gynecologic malignancy in the United States, with 46,470 new cases and 8,120 deaths estimated in 2011[1]. Most patients with endometrial cancer present with disease clinically limited to the uterus (stages I and II) and have an excellent prognosis.

Lymph node metastasis is widely recognized as a poor prognostic factor in endometrial cancer. Although, several retrospective studies have shown an improvement in survival following pelvic and para-aortic lymphadenectomy [2-6], no survival benefit could be demonstrated in either of the two recently published randomized controlled trials [7-9], questioning the routine use of complete lymphadenectomy (comprehensive staging) in early stage endometrial cancer. However, these trials mostly included women at low risk of lymph node metastasis, and it is not known if lymphadenectomy may still be beneficial in those patients known to have an increased risk of extrauterine disease. Indeed, some have proposed the use of high-risk histopathologic variables predictive of lymphatic involvement to guide the performance of lymph node dissection [10]. Several prognostic factors have been shown to be correlated with lymph node metastasis (deep myometrial invasion, cervical involvement, tumor grade, tumor diameter, serous histology, lymphovascular space invasion, and positive peritoneal cytology) [10-13]. The association of most of these factors with lymph node metastasis has been extensively studied, with the notable exception of positive peritoneal cytology.

The incidence of positive peritoneal cytology in early stage endometrial cancer has been reported to range from 5-10%. Until recently, patients with positive peritoneal cytology

were considered to have stage IIIA endometrial cancer. In 2009, the International Federation of Gynecology and Obstetrics (FIGO) eliminated positive peritoneal cytology from the staging criteria, but still required for it to be reported separately [14]. There is conflicting evidence in the literature regarding the prognostic significance of positive peritoneal cytology among patients with early stage endometrial cancer. Some studies have shown that positive peritoneal cytology is associated with poor prognosis [15-16], whereas others have not found any negative influence on survival [17-19]. The data regarding the propensity of lymph node involvement in patients with positive peritoneal cytology is also scarce. Although, there is a suggestion from previous studies that positive peritoneal cytology is associated with extrauterine disease, the actual incidence of lymph node metastasis among these patients remains unknown [10, 20-21]. In light of the above, the primary objective of this study was to determine the correlation between positive peritoneal cytology and lymphatic dissemination in patients with apparent early stage endometrial cancer. Additionally, we have evaluated the incidence of lymph node metastasis among apparent early stage endometrial cancer patients with negative and positive peritoneal cytology for different histologic types and tumor grades, utilizing a large cohort of patients from the Surveillance Epidemiology and End Results (SEER) database of the U.S. National Cancer Institute.

Materials and Methods

Demographic, clinicopathologic, and survival information for women diagnosed with endometrial cancer from January 1, 1988, to December 31, 2005, were extracted from the Surveillance, Epidemiology and End Results (SEER) database of the U.S. National Cancer Institute [22]. SEER is a population-based cancer registry that includes approximately 26% of the United States population. The demographic characteristics of the SEER registries are representative of the general population within the United States. Data from the 17 SEER registries were used. All patients with endometrial cancer were extracted in tabular format in the “Case Listing” option of the SEER* Stat software. Eligibility criteria included (1) patients with only one primary tumor, (2) patients with endometrial cancer grossly confined to the uterus who underwent a complete staging procedure (total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and/or para-aortic lymphadenectomy) (3) pathological diagnosis of endometrioid adenocarcinoma, adenocarcinoma not otherwise specified (NOS), mucinous adenocarcinoma, serous adenocarcinoma, clear cell adenocarcinoma, or carcinosarcoma (4) diagnosis between 1988 and 2005. Data recorded included date of diagnosis, age at diagnosis, race, extent of disease spread, tumor grade, histology, surgical procedure, performance of lymphadenectomy, number of lymph nodes removed, and administration of radiation treatment.

Patients were divided into three age groups: age less than 50 years, 50 to 65 years, and greater than 65 years. Race was categorized as white, black, and other. Grade, when reported, was described by a three-grade system: grade I (well differentiated), grade II (moderately differentiated), and grade III (poorly differentiated and undifferentiated). Serous carcinomas, clear cell carcinomas, and carcinosarcomas were not graded, but were all considered grade 3. “Apparent stage” was assigned from the recorded extent of disease (EOD) codes without taking into consideration the lymph node status as follows: apparent

stage IA: myometrial invasion less than 50%; apparent stage IB: myometrial invasion greater than or equal to 50%; apparent stage II: cervical stromal invasion. This was done to determine the correlation between the extent of disease and incidence of lymph node metastasis. Only patients with negative peritoneal cytology (NPC) could be classified in such manner. A separate category “positive peritoneal cytology (PPC)” was created to include those patients with apparent stage I-II endometrial cancer (disease grossly confined to the uterus) found to have positive peritoneal cytology. The “PPC group” could not be subclassified into different apparent stage categories (IA, IB, and II), because this information is not available from the SEER data. Surgical procedure data were derived from site-specific surgery codes. Data concerning the performance of lymph node dissection and lymph node metastasis were derived from pathology codes, and classified as 10 vs. >10 for lymph nodes removed. Use of adjuvant radiation therapy (none, external beam, intracavitary, combination of external beam and intracavitary, method not otherwise specified) was collected.

The distribution of demographic and clinical characteristics between patients with positive peritoneal cytology and those with negative peritoneal cytology were compared using Chi-square tests. A univariate analysis was initially performed to assess the association between various demographic and clinical characteristics and lymph node metastasis. Multivariate logistic regression was also fit to see whether PPC is independently predictive of nodal metastasis, while adjusting for the potential effects of other contributory factors. Statistical analyses were performed using SAS 9.2 (SAS Institutes, Cary, NC). All p values reported are two-tailed, and a p value of less than 0.05 was considered to be statistically significant. This study was exempt from review by the Institutional Review Board of Washington University School of Medicine.

Results

Between 1988 and 2005, 51,985 patients with “apparent” stage I-II endometrial cancer were identified. A total of 28,927 patients who did not undergo a total hysterectomy, bilateral salpingo-oophorectomy and/or lymphadenectomy were excluded. One hundred and one patients with mixed, other, and squamous histologies were also excluded, as were 10 patients in whom the lymph node status was unknown. The final cohort thus derived had a total of 22,947 patients. The mean age was 62 years (range: 20-99). Whites comprised the majority of the cohort (85.9%). Pathologically, there was a preponderance of grade I-II tumors (67.1%). While the majority of the patients had endometrioid histology (60.0%), other histologies included adenocarcinoma NOS in 29.3%, clear cell/serous carcinoma in 6.4%, and carcinosarcoma in 4.4%. Positive peritoneal cytology (PPC) was present in 3.5% of patients (n=812). Among patients with negative peritoneal cytology (n=22,135), 68.5% were apparent stage IA, 20.3% apparent stage IB, and 11.2% had apparent stage II endometrial cancer. Most patients had more than 10 lymph nodes removed (50.2%). Only 8.5% had positive lymph nodes. Adjuvant radiation was not administered in a significant number of patients (65.7%). Among those who were given radiation (33.1%), most received external beam radiation alone (52.0%).

Demographic and clinical features were compared between patients with and without positive peritoneal cytology (Table 1). There was no significant difference between the two groups with regards to patient age at diagnosis ($p=0.36$). Patients with positive peritoneal cytology were more likely to be non-whites than those with negative peritoneal cytology (18.5% vs. 13.6%, $p=0.0006$). When compared to patients with negative peritoneal cytology, the patients with PPC were more frequently diagnosed with high-risk factors such as grade III disease (43.5% vs. 24.9%, $p<0.0001$) and unfavorable histologic types such as clear cell/serous carcinoma (17.9% vs. 6.0%, $p<0.0001$) and carcinosarcoma (9.0% vs. 4.2%, $p<0.0001$). Similarly, adjuvant radiation was administered in a significantly greater percentage of patients with positive peritoneal cytology (54.0% vs. 32.3%, $p<0.001$). Although, removal of more than 10 lymph nodes was more common among patients with positive peritoneal cytology than those with negative peritoneal cytology (54.4% vs. 50.1%), the difference was not statistically significant ($p=0.1$).

On univariate analysis, the following variables were found to be significantly associated with lymph node metastasis: age ($p=0.0001$), race ($p<0.0001$), histology ($p<0.0001$), grade ($p<0.0001$), peritoneal cytology ($p<0.0001$), and number of lymph nodes removed ($p<0.0001$) (Table 2). Patients with positive peritoneal cytology had a significantly higher incidence of lymph node metastasis compared to those in whom the peritoneal cytology was negative (32.6% vs. 7.6%). Similarly, the incidence of lymph node metastasis appeared to increase with tumor grade (3.1% in grade I, 8.0% in grade II, and 14.7% in grade III tumors) and the extent of lymph node resection (7.2% with <10 lymph nodes removed, and 9.7% with ≥ 10 lymph nodes removed). Based on the histological subtype, the incidence of metastatic lymph nodes was highest in clear cell/serous cancers (21.2%) and lowest in adenocarcinoma NOS (6.2%).

The incidence of lymph node metastasis among patients with negative and positive peritoneal cytology was further examined for different combinations of histologic types and tumor grades (Table 3). The rates of lymph node metastasis was significantly higher among patients with PPC compared to those with negative peritoneal cytology for all histologic types examined: endometrioid adenocarcinoma; 28.7% vs. 6.9%, adenocarcinoma NOS; 35.4% vs. 5.8%, clear cell/serous carcinoma; 41.4% vs. 19.0%, and carcinosarcoma; 38.4% vs. 14.4%. The rates of lymph node metastasis in the PPC group were compared to the individual stage categories of the NPC group (apparent stages IA, IB, and II). More patients with positive peritoneal cytology had positive lymph nodes compared to those with apparent stages IA and IB, across all histologic types and tumor grades. Although, there was a trend towards higher incidence of lymph node involvement among patients with positive peritoneal cytology compared to apparent stage II tumors, the incidence rates overlapped between apparent stage II and PPC for most categories examined.

Logistic regression models were then developed to examine the predictors of lymph node metastasis. When using the entire cohort, positive peritoneal cytology was found to be independently associated with an increased risk of lymph node metastasis after adjusting for other contributory factors ($P<0.0001$) (Table 4). The odds of lymph node involvement were 11 times more likely with PPC compared to apparent stage IA disease and negative peritoneal cytology, 2.2 times more likely with PPC compared to apparent stage IB disease

and negative peritoneal cytology, and 1.4 times more likely with PPC compared to apparent stage II disease and negative peritoneal cytology. Other factors significantly associated with lymph node metastasis were patient race ($p=0.003$), histology ($p<0.0001$), tumor grade ($p<0.0001$), and number of lymph nodes removed ($p<0.0001$).

The association of positive peritoneal cytology with lymph node metastasis was also examined for individual histologic sub-types (endometrioid/mucinous, adenocarcinoma NOS, papillary serous/clear cell, and carcinosarcoma) in different multivariable models separately (Table 5). The odds ratio for lymph node metastasis in patients with PPC compared to those with NPC and apparent stage IA disease was 12.5 for endometrioid histology, 20.5 for adenocarcinoma NOS, 6.1 for clear cell/serous cancer, and 6.8 for carcinosarcoma. The corresponding odds ratios for lymph node involvement with PPC vs. NPC and apparent stage IB disease were 2.1, 4.0, 1.5, and 2.3, respectively, and for PPC vs. NPC and apparent stage II disease, 1.4, 2.1, 1.3, and 1.4, respectively.

Discussion

This is the largest published report on the incidence of lymph node metastasis in patients with positive peritoneal cytology and endometrial cancer apparently confined to the uterus. In particular, we have determined the incidence of lymph node metastasis separately for patients with different histologic types and subcategorized by tumor grade where applicable. Our study is important because most previous studies of positive peritoneal cytology have not been large enough to allow a sub-group analysis of outcomes by histology and/or tumor grade, thus providing valuable information for patient counseling and clinical decision-making.

Our results indicate that positive peritoneal cytology is an independent risk factor for disease spread to the lymph nodes. The incidence of lymph node metastasis, in the adjusted analysis, was significantly greater in the PPC group than found in any individual clinical stage categories within the NPC group (apparent stages IA, IB, and II). Other investigators have reported similar results. Creasman et al identified those patients at particularly high risk of lymph node metastasis among women with clinical stage I disease [10]. The rate of pelvic lymph node metastasis was 25% among patients with positive peritoneal cytology and 7% among those with negative peritoneal cytology. The corresponding rates for para-aortic lymph node metastasis were 19% and 4%, respectively. In another study, by Taskiran et al, the incidence of any retroperitoneal lymph node metastasis was significantly different between patients with and without positive peritoneal cytology (53.1% vs. 8.6%, $p<0.001$) [20]. Although, positive cytology has been dropped from the revised FIGO endometrial cancer staging criteria, the above data clearly indicate that patients with positive washings are at significant risk of extrauterine disease and as such deserve to be placed in a more advanced stage category. The recent elimination of positive cytology from the FIGO staging criteria was mainly due to the uncertainty regarding the true significance of positive cytology among patients with endometrial cancer otherwise confined to the uterus. Certainly, a few small studies have failed to show a negative correlation of positive cytology with prognosis among these patients, propagating the existing controversy [17-19]. We hope that with further studies recapitulating our results in the future, peritoneal cytology will be

added back into the FIGO staging system, enabling accurate risk-stratification and clinical decision-making in these patients.

Although, multiple groups have failed to show a correlation between malignant cytology and high-risk uterine features [19, 23-25], positive washings were significantly associated with deep myometrial invasion, poorly differentiated tumors, and tumors of non-endometrioid histology in the current study. Since the presence of these adverse features can increase the risk of extrauterine disease, we performed separate multivariable analyses by individual histologic subtypes in order to confirm the independent effect of positive peritoneal cytology on lymph node metastasis. The odds ratios for lymph node metastasis with PPC compared to NPC and apparent stage IB or stage II disease were comparable for all histologic subtypes examined, however, they were disproportionately higher for PPC relative to NPC and apparent stage IA disease, among patients with endometrioid histology and adenocarcinoma NOS compared to those with clear cell/serous cancer or carcinosarcoma. These findings are important, considering that both high tumor grade and non-endometrioid histology continue to play an important role in influencing adjuvant treatment recommendations in the presence of malignant cytology in endometrial cancer, as revealed by a recent survey study of the practice patterns of members of Society of Gynecologic Oncologists in the United States [26]. In this study, in the presence of malignant cytology, adjuvant therapy was recommended for 46% with grade I tumors, 62% with grade II tumors, and 98% with uterine papillary serous carcinoma.

Although our study benefits from inclusion of a large number of patients, several limitations must be acknowledged. Due to SEER classification schema, the PPC group could not be further classified into the individual “apparent stage” categories (stages IA, IB, and II), unlike the patients with negative peritoneal cytology. As a result, a stage matched comparison between patients with negative cytology and those with positive cytology, although ideal, could not be performed. Instead, outcomes in the PPC group were individually compared to the different “apparent” stage categories within the NPC group (apparent stages IA, IB, and II). Additionally, data regarding the depth of myometrial invasion or cervical stromal invasion were not available independent of the stage at diagnosis and for patients with PPC, hence not included in the multivariate model. However, even if one presumes that most patients in the PPC group in the current study had deep myometrial invasion and/or cervical stromal invasion, the fact that their odds of lymph node metastasis was higher compared to the corresponding patients with negative peritoneal cytology after adjusting for other important clinico-pathologic variables including tumor grade and histology, indirectly suggests that positive cytology is indeed an independent predictor of lymph node metastasis in these patients. Although radiation use was recorded, it was not possible to determine the dose of radiation, fields that were treated, or compliance with radiation. Similarly, information regarding the administration of chemotherapy or hormone therapy was also not available. Finally, as with any registry study, centralized pathology review was not performed.

In conclusion, our study shows that positive peritoneal cytology is an independent risk factor for lymph-node metastasis in patients with endometrial cancer apparently confined to the uterus. The risk of lymph node metastasis is increased considerably (nearly two-fold) for all

histologies in the presence of positive peritoneal cytology. Therefore, although, no longer a part of the current FIGO staging criteria, peritoneal cytology status should continue to inform clinical decision-making in endometrial cancer.

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References

1. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA: a cancer journal for clinicians*. 2011; 61(4):212–36. [PubMed: 21685461]
2. Kilgore LC, Partridge EE, Alvarez RD, et al. Adenocarcinoma of the endometrium: survival comparisons of patients with and without pelvic node sampling. *Gynecologic oncology*. 1995; 56(1):29–33. [PubMed: 7821843]
3. Trimble EL, Kosary C, Park RC. Lymph node sampling and survival in endometrial cancer. *Gynecologic oncology*. 1998; 71(3):340–3. [PubMed: 9887227]
4. Cragun JM, Havrilesky LJ, Calingaert B, et al. Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2005; 23(16):3668–75. [PubMed: 15738538]
5. Mohan DS, Samuels MA, Selim MA, et al. Long-term outcomes of therapeutic pelvic lymphadenectomy for stage I endometrial adenocarcinoma. *Gynecologic oncology*. 1998; 70(2):165–71. [PubMed: 9740684]
6. Chan JK, Cheung MK, Huh WK, et al. Therapeutic role of lymph node resection in endometrioid corpus cancer: a study of 12,333 patients. *Cancer*. 2006; 107(8):1823–30. [PubMed: 16977653]
7. Uccella S, Podratz KC, Aletti GD, Mariani A. Re: Systematic pelvic lymphadenectomy vs no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. *Journal of the National Cancer Institute*. 2009; 101(12):897–8. author reply 8-9. [PubMed: 19509367]
8. Amant F, Neven P, Vergote I. Lymphadenectomy in endometrial cancer. *Lancet*. 2009; 373(9670):1169–70. author reply 70-1. [PubMed: 19345819]
9. Uccella S, Podratz KC, Aletti GD, Mariani A. Lymphadenectomy in endometrial cancer. *Lancet*. 2009; 373(9670):1170. author reply -1. [PubMed: 19345823]
10. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. *Cancer*. 1987; 60(8 Suppl):2035–41. [PubMed: 3652025]
11. Lampe B, Kurzl R, Hantschmann P. Prognostic factors that predict pelvic lymph node metastasis from endometrial carcinoma. *Cancer*. 1994; 74(9):2502–8. [PubMed: 7923007]
12. Kamura T, Yahata H, Shigematsu T, et al. Predicting pelvic lymph node metastasis in endometrial carcinoma. *Gynecologic oncology*. 1999; 72(3):387–91. [PubMed: 10053111]
13. Mariani A, Webb MJ, Keeney GL, Aletti G, Podratz KC. Predictors of lymphatic failure in endometrial cancer. *Gynecologic oncology*. 2002; 84(3):437–42. [PubMed: 11855884]
14. Kim HS, Song YS. International Federation of Gynecology and Obstetrics (FIGO) staging system revised: what should be considered critically for gynecologic cancer? *Journal of gynecologic oncology*. 2009; 20(3):135–6. [PubMed: 19809545]
15. Havrilesky LJ, Cragun JM, Calingaert B, et al. The prognostic significance of positive peritoneal cytology and adnexal/serosal metastasis in stage IIIA endometrial cancer. *Gynecologic oncology*. 2007; 104(2):401–5. [PubMed: 17014898]
16. Bansal S, Buck AM, Herzog TJ, Deutsch I, Burke WM, Wright JD. Stage IIIA endometrial carcinoma: outcome and predictors of survival. *Obstetrics and gynecology*. 2009; 114(1):100–5. [PubMed: 19546765]

17. Tebeu PM, Popowski Y, Verkooijen HM, et al. Positive peritoneal cytology in early-stage endometrial cancer does not influence prognosis. *British journal of cancer*. 2004; 91(4):720–4. [PubMed: 15266316]
18. Fadare O, Mariappan MR, Hileeto D, Wang S, McAlpine JN, Rimm DL. Upstaging based solely on positive peritoneal washing does not affect outcome in endometrial cancer. *Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc*. 2005; 18(5): 673–80.
19. Takeshima N, Nishida H, Tabata T, Hirai Y, Hasumi K. Positive peritoneal cytology in endometrial cancer: enhancement of other prognostic indicators. *Gynecologic oncology*. 2001; 82(3):470–3. [PubMed: 11520142]
20. Taskiran C, Yuce K, Geyik PO, Kucukali T, Ayhan A. Predictability of retroperitoneal lymph node metastasis by using clinicopathologic variables in surgically staged endometrial cancer. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*. 2006; 16(3):1342–7. [PubMed: 16803527]
21. Imachi M, Tsukamoto N, Matsuyama T, Nakano H. Peritoneal cytology in patients with endometrial carcinoma. *Gynecologic oncology*. 1988; 30(1):76–86. [PubMed: 3366396]
22. Surveillance E, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 17 Regs Limited-Use + Hurricane Katrina Impacted Louisiana Cases, Nov 2008 Sub (1973-2006 varying) - Linked To County Attributes - Total U.S., 1969-2006 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch released April 2009, based on the November 2008 submission.
23. Obermair A, Geramou M, Tripcony L, Nicklin JL, Perrin L, Crandon AJ. Peritoneal cytology: impact on disease-free survival in clinical stage I endometrioid adenocarcinoma of the uterus. *Cancer Letter*. 2001; 164:105–10.
24. Kasamatsu T, Onda T, Katsumata N, et al. Prognostic significance of positive peritoneal cytology in endometrial carcinoma confined to the uterus. *British Journal of Cancer*. 2003; 88:245–50. [PubMed: 12610496]
25. Saga Y, Imai M, Jobo T, et al. Is peritoneal cytology a prognostic factor of endometrial cancer confined to the uterus? *Gynecologic Oncology*. 2006; 103:277–80. [PubMed: 16678244]
26. Lee CM, Slomovitz BM, Greer M, et al. Practice patterns of SGO members for stage IIIA endometrial cancer. *Gynecologic Oncology*. 2005; 98:77–83. [PubMed: 15907988]

Table 1

Comparison of Demographic and Clinical Features between Endometrial Cancer Patients with Negative Peritoneal Cytology and those with Positive Peritoneal Cytology.

Variable		Negative Peritoneal Cytology (NPC) (N=22,135)	Positive Peritoneal Cytology (PPC)(N=812)	P value
Age at diagnosis	<50	2915 (13.2%)	99 (12.2%)	0.36
	50-65	10213 (46.1%)	363(44.7%)	
	>65	9007 (40.7%)	350(43.1%)	
Race	White	19039 (86.0%)	661 (81.4%)	0.0006
	Black	1315 (6.0%)	68 (8.4%)	
	Other	1692 (7.6%)	82 (10.1%)	
	Unknown	89 (0.4%)	1 (0.1%)	
Grade	I	6906 (31.2%)	107 (13.2%)	<0.0001
	II	8103 (36.6%)	266 (32.8%)	
	III	5509 (24.9%)	353 (43.5%)	
	Unknown	1617 (7.3%)	86 (10.5%)	
Histology	Endometrioid/Mucinous	13267 (60.0%)	498 (61.3%)	<0.0001
	Clear cell/Serous	1319 (6.0%)	145 (17.9%)	
	Adenocarcinoma NOS	6618 (29.8%)	96 (11.8%)	
	Carcinosarcoma	931 (4.2%)	73 (9.0%)	
Radiation	None	14708 (66.4%)	357 (44.0%)	<0.0001
	External Beam	3676 (16.6%)	275 (33.9%)	
	Intracavitary	1506 (6.8%)	53 (6.5%)	
	Combination	1842 (8.3%)	105 (12.9%)	
	Method NOS	124 (0.6%)	6 (0.7%)	
	Unknown	279 (1.3%)	16 (2.0%)	
Lymph node removed	<10	8782 (39.7%)	310 (38.2%)	0.1
	10	11088 (50.1%)	442 (54.4%)	
	Unknown	2265 (10.2%)	60 (7.4%)	

NOS: Not otherwise specified

Table 2

Univariate analysis of factors associated with lymph node metastasis.

Variable	Negative lymph nodes (N=21,000)	Positive lymph nodes (N=1,947)	P value
Age at diagnosis	<50	219 (7.3)	0.0001
	50-65	851 (8.0)	
	>65	877 (9.4)	
Race	White	1593 (8.1)	<0.0001
	Black	172 (12.4)	
	Other	178 (10.0)	
Marital Status	Single	953 (9.8)	<0.0001
	Married	955 (7.6)	
Grade	I	216 (3.1)	<0.0001
	II	670 (8.0)	
	III	861 (14.7)	
Histology	Endometrioid/Mucinous	1056 (7.7)	<0.0001
	Clear cell/Serous	311 (21.2)	
	Adenocarcinoma NOS	418 (6.2)	
	Carcinosarcoma	162 (16.1)	
Lymph node removed	<10	656 (7.2)	<0.0001
	10	1124 (9.7)	
Peritoneal cytology	Negative	459 (3.0)	<0.0001
		654 (14.6)	
		569 (23.0)	
	Positive	265 (32.6)	

NOS: Not otherwise specified

Table 3

Incidence of Lymph Node Metastasis by Histology and Tumor Grade

Clinical Stage	Endometrioid/Mucinous				Adenocarcinoma NOS				Clear cell/Serous	Carcinosarcoma
	Overall	Grade I	Grade II	Grade III	Overall	Grade I	Grade II	Grade III		
Negative Peritoneal Cytology	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)	Positive Lymph Nodes Point Estimates (Top) and 95% CI (Bottom)
	Overall (stages I-II)	6.9% (6.5%-7.3%)	3.1% (2.6%-3.6%)	12.0% (10.8%-13.3%)	5.8% (5.3%-6.4%)	2.2% (1.6%-2.9%)	5.7% (4.9%-6.7%)	10.7% (9.3%-12.4%)	19.0% (16.9%-21.3%)	14.4% (12.2%-16.8%)
	IA	2.5% (2.2%-2.9%)	1.1% (0.8%-1.5%)	5.4% (4.3%-6.7%)	2.1% (1.7%-2.5%)	0.9% (0.5%-1.4%)	2.3% (1.7%-3.1%)	3.8% (2.7%-5.3%)	10.3% (8.3%-12.5%)	8.4% (6.2%-11.0%)
	IB	14.5% (13.2%-15.8%)	8.4% (6.5%-10.7%)	15.8% (13.8%-18.0%)	11.3% (9.6%-13.2%)	7.0% (4.4%-10.5%)	11.3% (8.8%-14.3%)	14.8% (11.4%-18.7%)	30.2% (24.1%-36.8%)	19.6% (14.6%-25.5%)
	II	21.2% (19.0%-23.5%)	15.7% (11.7%-20.5%)	21.3% (18.0%-24.8%)	19.9% (17.1%-23.0%)	8.3% (4.2%-14.4%)	15.7% (11.9%-20.2%)	30.0% (24.4%-36.1%)	36.6% (30.9%-42.5%)	27.8% (21.0%-35.4%)
Positive Peritoneal Cytology (Stages I-II)	28.7% (24.8%-32.9%)	18.4% (10.9%-28.1%)	26.9% (21.1%-33.3%)	35.3% (28.1%-43.1%)	35.4% (25.9%-45.8%)	10.5% (1.3%-33.1%)	41.7% (25.5%-59.2%)	42.1% (26.3%-59.2%)	41.4% (33.3%-49.8%)	38.4% (27.2%-50.5%)

Table 4

Multivariate Analysis of Factors Associated with Lymph Node Metastasis in Patients with “Apparent” Stage I-II Endometrial Cancer.

	Variables		Odds Ratio (95% CI)
Age	<50		Referent
	50-65		1.02 (0.85-1.21)
	>65		0.91 (0.76-1.09)
Race	White		Referent
	Black		*1.28 (1.05-1.55)
	Other		*1.33 (1.10-1.60)
Histology	Endometrioid/Mucinous		Referent
	Adenocarcinoma NOS		0.88 (0.77-1.00)
	Clear cell/Serous		*2.05 (1.72-2.43)
	Carcinosarcoma		*1.45 (1.17-1.81)
Grade	I		Referent
	II		*2.00 (1.69-2.36)
	III		*2.88 (2.42-3.41)
Stage	Negative Peritoneal Cytology	IA	Referent
		IB	*5.08 (4.44-5.81)
		II	*7.91 (6.87-9.10)
	Positive Peritoneal Cytology		*11.00 (9.13-13.26)
Lymph Nodes Removed	<10		Referent
	10		*1.33 (1.19-1.48)

*
p<0.05

Table 5
Multivariate Analysis of Factors Associated with Lymph Node Metastasis by Histologic Sub-type.

Variables	Endometrioid/Mucinous		Adenocarcinoma NOS		Clear cell/Serous Cancer		Carcinosarcoma	
	Odds Ratio (95% CI)	Referent	Odds Ratio (95% CI)	Referent	Odds Ratio (95% CI)	Referent	Odds Ratio (95% CI)	Referent
Age	<50							
	50-65	0.99 (0.80-1.23)		0.88 (0.61-1.28)	1.37 (0.72-2.58)		1.54 (0.61-3.92)	
	>65	0.85 (0.68-1.06)		0.93 (0.65-1.34)	1.15 (0.62-2.05)		1.29 (0.52-3.21)	
Race	White							
	Black	0.95 (0.68-1.32)		*1.62 (1.06-2.48)	1.30 (0.88-1.91)		*1.67 (1.04-2.71)	
	Other	*1.38 (1.08-1.75)		1.27 (0.85-1.90)	1.21 (0.71-2.05)		1.15 (0.52-2.55)	
Grade	I							
	II	*1.95 (1.61-2.37)		*2.11 (1.49-3.01)	--		--	
	III	*2.78 (2.26-3.41)		*3.41 (2.39-4.86)	--		--	
Stage	Negative Peritoneal Cytology	IA						
		IB						
		II						
Lymph Nodes Removed	Positive Peritoneal Cytology							
Lymph Nodes Removed	<10							
	10	*1.28 (1.11-1.48)		*1.50 (1.19-1.88)	1.15 (0.87-1.53)		1.38 (0.94-2.02)	

* p<0.05