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Surgical-pathological findings in type 1 and 2 endometrial cancer: An NRG Oncology/Gynecologic Oncology Group study on GOG-210 protocol☆

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Conflicts of interest

Dr. Richard Zaino receives reimbursement for travel expenses for slide reviews and semiannual meetings; consultancy fees from Repros, Inc. for review of endometrial biopsies, as well as reimbursement for travel to the International Society of Gynecological Pathologists to attend their annual board meeting. Dr. Matthew Powell receives monies from Roche Genentech, AstraZeneca and Clovis Oncology for consultancy. He also receives payment for lectures including service on speakers bureaus from AstraZeneca and Roche Genentech. Dr. Floor Backes receives consultancy monies from Advaxis, has grants/grants pending with Eisai Inc., Clovis and ImmunoGen as well as royalties for UpToDate ad hoc author. Dr. Michael Pearl receives grant funding from NRG/GOG. Dr. Shashikant Lele receives payments for lectures including service on speakers bureaus on the Genentech Advisory Board. Dr. Steven Waggoner receives money for his institution, Case Western Reserve University from an NIH grant through GOG. Dr. Virginia Filiaci receives money to her institute for an NCI grant, support for travel to meetings for the study or other purposes, fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees and the like, payment for writing or reviewing the manuscript as well as provision of writing assistance, medicines, equipment or administrative support covered under the NCTN SDMC grant. Dr. David Miller receives money to his institute from a grant to the GOG. All other co-authors have no conflicts of interest to declare.

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Abstract

Objective—To report clinical and pathologic relationships with disease spread in endometrial cancer patients.

Methods—Surgical candidates with uterine cancer (adenocarcinoma or carcinosarcoma) who were eligible to participate in a surgical pathological study to create a clinically annotated tissue biorepository to support translational and clinical research studies. All patients were to undergo a hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic and para-aortic lymphadenectomy. From 2003–2007, open eligibility enrollment was conducted, and from 2007–2011, eligibility was restricted to enrich underrepresented patients or those at high risk.

Results—This report details clinical pathological relationships associated with extra uterine disease spread of 5866 evaluable patients including those with endometrioid histology as well as papillary serous, clear cell and carcinosarcoma histologies. Review of unrestricted enrollment was constructed in an effort to capture a cross-section population representative of endometrial cancers seen by the GOG participating members. Evaluation of this group of patients suggested the more natural incidence of different surgical pathological findings as well as demographic information. The addition of 2151 patients enrolled during the restricted time interval allowed a total of 1630 poor histotype patients available for further analysis. As expected, endometrioid (E) cancers represented the largest enrollment and particularly E grade 1 and 2 (G1 and 2) were more frequently confined to the uterus. Grade 3 (G3) endometrioid cancers as well as the poor histotype (papillary serous, clear cell and carcinosarcoma) had a much greater propensity for extant disease.

Conclusions—This study confirms the previously reported surgical pathological findings for endometrioid cancers but in addition, using a large database of papillary serous, clear cell and carcinosarcoma, surgical pathological findings substantiate the categorization of poor histotypes for these cancers.

Keywords

Surgical-pathology; Poor histotypes

1. Introduction

Corpus cancer is the most commonly diagnosed gynecological cancer in the industrialized world. In 2015, the American Cancer Society (ACS) estimated almost 55,000 new cases would be diagnosed in the US and over 10,000 would die from their disease [1]. Over the last several decades, the incidence of endometrial cancer has increased some 45%; however, the deaths from this cancer have more than tripled. Some have suggested that the increased incidence is due to the fact that a larger number of our population has reached an age in which this cancer is most frequently seen and are living longer. The reason for the increased number of women dying from their disease is unknown.

For many years, endometrial cancer was clinically staged. Several retrospective studies going back into the middle of the last century suggested a large margin of error between the clinical and actual extent of the disease; however, prospective studies done by the Gynecologic Oncology Group (GOG) in the 1970s and 1980s definitively identified the true extent of the disease which was considerably more advanced than clinically suspected even with stage I disease [2]. These studies led FIGO in 1986 to change the staging of endometrial cancer from a clinical designation to one that was surgically determined. Although surgical staging can definitively be diagnostic, it did raise many questions in regards to whether or not all endometrial cancer patients need to be surgically staged, was it therapeutic and was it definitive in guiding subsequent therapy.

Even though surgical staging added considerable information concerning an individual cancer, yet other unknown factors probably contributed to the individual's eventual outcome. Today, it is recognized that a patient's genetically characterized tumor may provide pertinent information to detail individual risk and response to therapy and is the basis of precision

medicine. Within gynecological malignancies, molecular characterizations of ovarian and endometrial cancer have been performed. In 2003, the GOG initiated a prospective surgical pathological study (GOG-210) to create a large biorepository annotated with clinical and epidemiological information from a population of surgically staged endometrial patients. The bank tissue and data could support genomic, proteomics and immunoassay studies for the purpose of class prediction and discovery in these cancers and to identify and validate molecular characteristics associated with a risk of recurrence, clinical and histological characteristics and epidemiological factors.

2. Materials and methods

GOG-210 is a molecular and surgical pathological staging study of endometrial carcinoma. The overall goal of this protocol is to improve outcome and quality of life for patients with endometrial cancer. This fundamental goal was the development of more accurate models of risk, identification of cancer targets for therapeutic intervention and utilization of individual treatment based upon molecular characteristics identified in tumor tissue, normal tissue and/or in reality accessible biological fluids like serum and urine. Objectives were to establish a repository of clinical specimens (tissue, urine, serum) with detailed clinical and epidemiological data from patients with surgically staged endometrial carcinoma. Utilizing genomic, proteomics and immunoassay results could hopefully identify and validate molecular characteristics associated with risk of endometrial cancer recurrence, clinical and histological characteristics and epidemiological factors. These studies would hopefully improve the accuracy and resolution of the risk assessment models for predicting endometrial cancer recurrence in combination with clinical, pathological and epidemiological factors. This data then could be used to identify these characteristics that would help prevent or treat endometrial cancer and expand our current understanding of the biology progression, metastasis and responsiveness of endometrial cancer.

GOG-210 was designated to create a clinically annotated tissue biorepository. Patients were eligible if they had uterine carcinoma (adenocarcinoma or carcinosarcoma) and were appropriate surgical candidates for hysterectomy and surgical staging. Following enrollment, patients completed an epidemiological questionnaire. From September 2002 to September 2007, open eligibility enrollment was constructed in an effort to capture a cross-section population representative of endometrial cancer (EC) seen by GOG participating members. In 2007, after meeting initial enrollment and tissue goals, eligibility was restricted to enrich for previously under-represented patients or those at high risk. Restricted enrollment criteria includes non-endometrioid cancers or endometrioid cancers that were one or more of the following: G3, positive cervical biopsies, preoperative imaging suggestive of deep myometrial invasion, lymph node enlargement or extrauterine disease, non-Caucasian race, Hispanic ethnicity, and BMI below 25. The study completed total enrollment in December 2011.

All patients were to have a hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy as well as collection of pelvic washings for cytology. Intraperitoneal biopsies were collected as indicated. Patients with stage IV intraabdominal disease that could not be debulked to <2 cm did not require a lymphadenectomy (LND).

"Adequacy" of the LND was determined by review of the operative and pathology reports and was measured by the presence of at least 10 lymph nodes including at least one node from each nodal basin. Patients were not eligible if they had had prior retroperitoneal surgery or had received prior pelvic or abdominal radiation. Central pathology review was initially to be performed on all cases. After review of the first 1236 cases, it was deemed unnecessary for patients with stage IA-IC and grade 1 and 2 (G1 and 2) endometrioid (E) adenosquamous and mucinous histology to have central pathology review due to the high rate of concurrence with the institutional pathologist. An extended central pathology review was conducted by a group of GYN pathologists for patients with grade 3E histology, E histology in stage IIA-IV and all non-endometrioid histologies. Staging was assigned using the FIGO 1988 classification system. Follow-up forms, including vital status on all postoperative cancer-related treatments, were completed at the time of the postoperative clinical visits and subsequent follow-up forms were completed every three months for the first two years, every six months for the next three years, and then yearly for the next five years. Data was abstracted from evaluation forms for all patients. Descriptive statistics of the patient population and clinical pathological data were provided.

The biorepository was created by collecting up to a total of 13 specimens obtained at various time-points. Preoperative serum and urine, frozen and fixed normal tissue, frozen and fixed primary tumor, postoperative serum and three-year follow-up serums were to be obtained on all patients. In patients who subsequently recurred, serum and frozen and fixed recurrent tumors were collected when possible. Samples were collected and prepared at each GOG institution and shipped to the GOG tissue bank (Columbus, Ohio) where they are housed and distributed back to investigation for approved translational research projects.

For descriptive purposes, type 1 cancers are endometrioid histology and type 2 (poor histotype) are papillary serous, clear cell and carcinosarcomas. Although not yet categorized "mixed" and "others", they have surgical pathologic findings similar to the type 1 cancers.

3. Results

A total of 6124 patients were enrolled with 5866 being evaluable. During the initial unrestricted enrollment period, 3838 patients were enrolled, 123 were excluded, and 3715 patients were evaluable. For the restricted category, 2286 patients were enrolled, 135 were excluded and 2151 patients were evaluable. A total of 41,450 specimens were collected and deposited in the cytology tissue bank.

During the unrestricted enrollment time, there were 3715 patients entered into this protocol (Table 1). The median age at enrollment was 63.1 years, with 90% of patients being 50 years of age or older and with the vast majority being presumed postmenopausal. The white race was represented by 89% of patients enrolled with African-Americans represented only by 7.9%. When type 1 and 2 were evaluated in regards to race, 76.1% of Caucasians were type 1 cancers and 23.9% were type 2. In contrast, only 46.5% of African-Americans had type 1 cancers and 53.4% were type 2. As expected, over 80% of the women were overweight or obese. About three-fourths of the patients had a surgical stage I cancer as noted by the FIGO 1988 staging. Almost three-fourths of the patients had an endometrioid histological type

with the largest number being grade 1. Serous carcinomas were represented by 11.4%, clear cell 3.5%, carcinosarcomas 4.1% and other 7.2%. Again, almost three-fourths of the patients had disease limited to the endometrium or inner one-half of the myometrium. Positive peritoneal cytology was present in 8.9%, adnexal involvement in 8.6%. Pelvic node metastasis (PNM) was noted in 9.8% and the aortic nodes involvement (PANM) was 5.1%. Lymph vascular space involvement (LVSI) was present in 22.7%. It was felt important to report separately the unrestricted population as this reflected more of the natural status of the patients who were entered into the protocol from the respective institutions.

As noted, after the initial enrollment and tissue goals were met, eligibility was restricted to enrich previously unrepresented patients or those at high risk. Subsequent tables will include both the unrestricted (3715) and the restricted (2151) patient population for a total of 5866 patients. By combining the two, certain high-interest areas such as nodal metastasis were enriched. Serous carcinomas now represented 15.5% of the patient population, clear cell 5.3% and carcinosarcoma at 6.6%. The number of women with positive peritoneal cytology increased from 8.9% to 11.3%. Pelvic node metastasis increased from 9.8% in the unrestricted group to 12.6% in the combined group and aortic metastasis from 5.1% to 7.2%. Lymph vascular space involvement increased from 22.7% to 26.0%. As previous studies have noted, as the grade became more poorly differentiated, the chances of deep invasion increased considerably (Table 2). In grade 1 endometrioid cancer, 16% had outer one-half or serosal involvement compared with 26% for grade 2 and 46% for grade 3. The poor histotypes also mirrored grade 3 endometrioid cancers. In the papillary serous group, 34% had outer one-half or serosal involvement, clear cell 33% and carcinosarcomas 44%.

Table 3 details the relationship of pelvic and para-aortic node metastasis with other risk factors. As the grade in the endometrial cancer becomes more poorly differentiated, pelvic node metastasis increases from 4% in grade 1 to 17.8% in grade 3 (G3) while para-aortic node metastasis increases from 2% to 9% respectively. Lymph node metastasis occurs to a greater degree with the poor histotypes. To a certain degree, G3 endometrioid cancers closely mirror the poor histotypes although the latter do have higher lymph node metastasis (LNM) rates. Serous lesions have pelvic node metastasis in 25% and para-aortic node metastasis in 17.5%, clear cell cancer rates are 20.1% and 12.4%, and carcinosarcomas have 21.1% and 15.2% nodal metastasis respectively. Of interest is the fact that the mixed cancers mirror the higher rate of nodal metastasis as seen with G3 endometrioid and the poor histotypes. These lesions as well as the “others” are being further categorized by the GOG expert GYN pathology panel. As depth of myometrial invasion increases, the chances of lymph node metastasis (LNM) increase considerably. Only 2.6% of pelvic lymph node metastasis (PLNM) and 1.2% of para-aortic node metastasis (PANM) was present if only endometrium was involved, but increased to 31% and 20% respectively with outer one-half of the myometrium or serosa involved.

Other risk factors also are correlated to LNM. Those with negative peritoneal cytology had PNM of 10.5% and 6.1% PANM compared with 31.8% and 22.7% respectively if peritoneal cytology was positive. Lymph vascular space involvement if negative had 4.1% PNM and 2.3% PANM compared with 37.5% and 23.8% respectively if LVSI was present.

The relationship of positive pelvic nodes to positive para-aortic nodes in the total population is noted in Table 4. There were 662 patients with positive pelvic node metastasis of which 327 also had metastasis to the para-aortic area. In addition, there were 86 patients with negative pelvic nodes and metastasis to the para-aortic area. When only the endometrioid cancers were considered, 151 (4.7%) had metastasis to the pelvic nodes with 94 (2.9%) also had PALN (Table 5). There were in addition 29 (0.9%) with negative PNM but PANM. Overall, 7.6% had PNM and 3.8% also had PANM. In evaluating the type 2 cancers (serous, clear cell and carcinosarcoma), PNM was 21.9% of which over one-half also had PANM (Table 6). In addition, there were 2.3% of the patients with negative PNM with PANM. Overall, 13.9% had PANM.

As expected, when grade of endometrioid cancers and depth of invasion were evaluated, the chances of PNM increased dramatically (Table 7). Grade 1 with endometrium-only involved had only 0.8% metastasis whereas involvement of the outer one-half of myometrium, 15.4% had PNM. The same relationship is present with G3 but to a greater degree (1.7% endometrium-only versus 29.1% with the outer one-half myometrial involvement). All of the type 2 cancers had a greater incidence of pelvic node metastasis than endometrioid types. This relationship was also present when evaluating PANM. The PANM is appreciable with type 2 cancers (25.9%–32.4%) (Table 8).

4. Discussion

This report details the surgical pathological findings of a large study of endometrial cancer, which is important in order to have precise information so that specific basic science data can be individually identified. Tumor heterogeneity is an important feature within endometrial cancer and its different cell types which demonstrate differences in greater signatures, frequency of disease spread, rates of response to therapy and outcome. We report here the largest prospective collected series of women with detailed surgical pathological findings and the collection of tissue, serum and urine that will allow detailed translational and clinical research studies.

The clinical findings confirm previous GOG surgical pathological findings of endometrial cancer. What this study adds to previous reports is a large number of poor histotype cancers that have been evaluated which has not been previously reported. As noted, the study was amended after an initial net goal of over 3000 women. An additional 2151 patients were enrolled which were restricted to those under-represented or those at high risk. The contrast between endometrioid, particularly grade 1 and 2, and the poor histotypes in regards to prognostic factors is stark.

What has been considered by some to be a “good” cancer, in fact has a wide spectrum of poor prognostic factors, depending somewhat on the histology of the disease. E-type, as expected, represents the largest number of patients in this study with almost three-fourths of the patients reported in the unrestricted enrollment. Almost two-thirds are G1 and 2 with G3 present in <10%. Certainly, G1 and 2 represent a good prognosis as 84% and 74% respectively have less than one-half myometrial invasion compared with 55% of G3. PLNM

was 4% for G1 and 7.3% for G2, and 2.0% and 3.6% respectively for PANM. This is in contrast to G3 in which 17.8% had PNM and 9.0% had PANM.

When the so-called poor histotypes (type 2) cancers are evaluated, this group of patient represents a larger number than previously noted with 26.2% in the unrestricted enrollment; however, when total enrollment is considered, 2175 poor histotype patients were analyzed. These tumors tend to have a greater number of patients with >50% myometrial invasion (33–44%) similar to the 46% seen in E3. PNM occurred in 21–25% of patients and PANM of 15–17%. Extent of disease to a great degree determines overall survival and this will be reported in a subsequent publication.

With tripling of the deaths in corpus cancer over the last several decades, it appears that there are other factors that can determine prognosis. Why do some E1 based on known good prognostic surgical pathological factors still recur and succumb to their disease while those with E3 or type 2 cancers, despite poor prognostic factors, remain tumor-free? The answer goes to the heart of this study (GOG-210). By providing a resource for investigators of tissue and surgical pathological information, multiple translational research projects to date are ongoing to evaluate molecular and biomarkers based evaluation of tumor to ideally allow better selection for optimal management (precision medicine). Already there have been 30 published or submitted manuscripts or abstracts.

A better understanding of the genomic information that may provide better assessment is illustrated by the data provided by The Cancer Genomic Atlas (TCGA) project, of which many specimens were contributed from GOG 210 [3]. The initial study classified endometrial cancer into four categories: POLE, ultra-mutated, microsatellite instability hyper mutated, copy-number low, and copy-number high. Subsequent studies have suggested that these categories may predict additional prognostic factors in addition to long-known surgical pathological factors. These and other areas are what will be further evaluated using the GOG-210 well-defined patient population and tissue database.

One of the interesting factors which is apparent from this study is the fact that based on surgical pathological findings, E3 resembles the finding of type 2 cancers more so than E1 and 2. In Bokhman’s designation of type I and II cancers, his review was presumably based on endometrioid cancers as papillary serous, clear cell and carcinosarcomas were not mentioned although poorly differentiated cancers were included [4–8]. Based on clinical as well as pathological features, there were poor prognostic (type 2) in E1 patients and good prognosis (type 1) with E3. More recently, type 1 has been categorized as E1–3 and type 2 being what is considered poor histotypes; papillary serous, clear cell and carcinosarcoma. Maybe it is time to redefine type 1 and type 2 cancers based on current knowledge with additional refinement when genomic analysis has been completed.

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HIGHLIGHTS

- The largest prospective surgical pathologic evaluation of endometrioid cancer
- The first surgical pathologic evaluation of Type 2 endometrial cancer
- Endometrial grade 3 cancers resemble findings of Type 2 cancers.

Table 1

Patient and tumor characteristics.

Characteristic	Enrollment period				Total	
	Unrestricted		Restricted			
	n	%	*n*	%	*n*	%
Age (years)						
<40	92	2.5	45	2.1	137	2.3
40–49	293	7.9	124	5.8	417	7.1
50–59	1165	31.4	530	24.6	1695	28.9
60–69	1212	32.6	780	36.3	1992	34.0
70–79	698	18.8	469	21.8	1167	19.9
≥80	255	6.9	203	9.4	458	7.8
Ethnicity						
Hispanic or Latino	92	2.5	169	7.9	261	4.4
Non-Hispanic	3065	82.5	1797	83.5	4862	82.9
Unknown, not reported	558	15.0	185	8.6	743	12.7
Race						
Asian	50	1.3	64	3.0	114	1.9
Black/African American	294	7.9	438	20.4	732	12.5
White	3307	89.0	1529	71.1	4836	82.4
Other	25	0.7	38	1.8	63	1.1
Unknown	39	1.0	82	3.8	121	2.1
BMI (kg/m^2)						
<18.5	20	0.5	31	1.4	51	0.9
18.5–24.9	609	16.4	544	25.3	1153	19.7
25.0–29.9	833	22.4	457	21.2	1290	22.0
30.0–34.9	786	21.2	435	20.2	1221	20.8
≥35	1449	39.0	682	31.7	2131	36.3
Prior cancers						
No	3402	91.6	1906	88.6	5308	90.5
Yes	305	8.2	245	11.4	550	9.4

Table 2

Histologic grade and depth of invasion.

Depth	EG1		EG2		EG3		SER		CLC		SAR		OMX		OTH		Total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Endo. only	592	34	199	16	69	11	245	27	87	28	55	15	74	21	46	21	1367	24
Inner half	875	50	712	58	288	44	360	39	121	39	159	42	175	49	78	36	2768	48
Outer half	269	15	311	25	251	38	255	28	88	29	128	34	90	25	65	30	1457	25
Serosa	8	1	15	1	52	8	57	6	12	4	36	10	16	5	28	13	224	4
Total	1744	100	1237	100	660	100	917	100	308	100	378	100	355	100	217	100	5816	100

Chi-square test, p value < 0.001.

Table 3

Frequency of nodal metastases by risk factors[a].

Risk Factor		Pelvic			Aortic		
		N+	%	*p*-Value	*N*+	%	*p*-Value
Histology				<0.001			<0.001
Endometrioid, grade 1	(*N* = 1516)	60	4.0		30	2.0	
Endometrioid, grade 2	(*N* = 1129)	82	7.3		41	3.6	
Endometrioid, grade 2	(*N* = 580)	103	17.8		52	9.0	
Serous (SER)	(*N* = 805)	201	25.0		141	17.5	
Clear cell (CLC)	(*N* = 274)	55	20.1		34	12.4	
Carcinosarcoma (CLC)	(*N* = 322)	68	21.1		49	15.2	
Mixed, nos. (OMX)	(*N* = 318)	64	20.1		42	13.2	
Other (OTH)	(*N* = 188)	29	15.4		24	12.8	
Myometrial invasion				<0.001			<0.001
Endometrium only (EN)	(*N* = 1184)	31	2.6		14	1.2	
Inner half (IN)	(*N* = 2477)	172	6.9		93	3.8	
Outer half (OU)	(*N* = 1304)	361	27.7		229	17.6	
Serosa (SE)	(*N* = 156)	95	60.9		74	47.4	
Peritoneal cytology				<0.001			<0.001
Negative	(*N* = 4364)	459	10.5		266	6.1	
Positive	(*N* = 532)	169	31.8		121	22.7	
Adnexal involvement				<0.001			<0.001
Negative	(*N* = 4629)	464	10.0		261	5.6	
Positive	(*N* = 475)	195	41.0		149	31.4	
Other extra-uterine metastasis				<0.001			<0.001
Negative	(*N* = 4567)	404	8.9		237	5.2	
Positive	(*N* = 565)	258	45.7		176	31.2	
Lympho-vascular space involvement				<0.001			<0.001
Negative	(*N* = 3722)	151	4.1		85	2.3	
Positive	(*N* = 1323)	496	37.5		315	23.8	
Menopausal status				<0.001			<0.001

Risk Factor		Pelvic			Aortic		
		N+	%	*p*-Value	*N*+	%	*p*-Value
Pre-menopause	(*N* = 389)	30	7.7		18	4.6	
Post-menopause	(*N* = 3366)	441	13.1		289	8.6	

[a]Patients with both pelvic and aortic node status and variable information.

Table 4

Relationship of positive pelvic nodes to aortic nodes[a].

Pelvic	Aortic				Total	
	Negative		Positive			
	n	%	*n*	%	*n*	%
Negative	4384	85.4	86	1.7	4470	87.1
Positive	335	6.5	327	6.4	662	12.9
Total	4719	92.0	413	8.1	5132	100.0

[a]Patients with both pelvic and aortic nodal information.

Gynecol Oncol. Author manuscript; available in PMC 2017 November 27.

Table 5

(On-line only) relationship of positive pelvic nodes to aortic nodes, endometrioid[a].

Pelvic	Aortic				Total	
	Negative		Positive			
	n	%	*n*	%	*n*	%
Negative	2951	91.5	29	0.9	2980	92.4
Positive	151	4.7	94	2.9	245	7.6
Total	3102	96.2	123	3.8	3225	100.0

[a]Nodal status as reported by institute pathologist.

Gynecol Oncol. Author manuscript; available in PMC 2017 November 27.

Table 6

(On-line only) relationship of positive pelvic nodes to aortic nodes, type II cancers[a].

Pelvic	Aortic				Total	
	Negative		Positive			
	n	%	*n*	%	*n*	%
Negative	1732	75.7	56	2.5	1788	78.1
Positive	237	10.4	263	11.5	500	21.9
Total	1969	86.1	319	13.9	2288	100.0

[a]Nodal status as reported by institute pathologist.

Table 7

Histology, depth of invasion, and pelvic node metastasis[a].

Depth of invasion	Histology							
	EG1 %	EG2 %	EG3 %	SER %	CLC %	SAR %	OMX %	OTH %
Endometrium only	0.8	1.6	1.7	7.9	1.3	2.0	6.3	0.0
Inner half	2.0	3.9	3.9	18.3	15.5	14.4	11.8	8.3
Outer half	15.4	16.8	29.1	44.3	40.5	29.6	42.2	24.6
Serosa	42.9	50.0	67.6	66.7	70.0	58.3	60.0	47.1

[a]Among patients with both pelvic and aortic node status and myometrial invasion info ($N = 5121$).

Table 8

Histology, depth of invasion, and aortic node metastasis[a].

Depth of invasion	Histology							
	EG1	EG2	EG3	SER	CLC	SAR	OMX	OTH
Endometrium only	0.0%	1.1%	0.0%	4.2%	0.0%	2.0%	3.1%	0.0%
Inner half	1.3%	1.7%	0.8%	11.3%	6.4%	8.6%	5.6%	6.9%
Outer half	6.9%	8.4%	14.5%	32.4%	28.4%	25.9%	30.1%	16.4%
Serosa	28.6%	33.3%	43.2%	61.5%	60.0%	33.3%	60.0%	47.1%

[a]Among patients with both pelvic and aortic node status and myometrial invasion info ($N = 5121$).