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Retrospective analysis of cases with Endometrial Cancer

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Abstract
We planned this study with the aim of determining histological types, clinical, surgical stage and grade of endometrial cancer cases which were followed-up and operated on in our clinic and giving an opinion on epidemiological features. Our study was a retrospective study consisted of 298 patients who had medical operations with the diagnosis of endometrial cancer. Endometrial cancer was diagnosed via dilatation and curettage. Routine preoperative examinations were wanted from the cases. Clinical stage was determined. After the diagnosis, total abdominal hysterectomy and bilateral salpingo-ooforectomy (TAH+BSO) were applied; while only pelvic lymph node dissection was applied on the patients who had good prognostic data, total pelvic and paraaortic lymph node dissection were applied to the group with bad prognostic data. All materials were examined in the pathology laboratory of our hospital. In endometrial cancer staging, FIGO surgical staging system -2009 was used. FIGO was used in grade classification and World Health Organization Classification of Tumors system was used for the histological classification. Our study was composed of 298 patients who had endometrial cancer. Of the patients who were included in the study, average age was 56.54±9.69, BMI average was 31.47±6.20, gravida average was 4.16±2.59, and parity average was 3.41±2.15. Distributions of the patients by surgical stages were as follows; there were 32 patients whose tumor stage was in 1A (%10.7), 127 patients in 1B (42.6%), 47 patients in 1C (15.8%), 18 patients in 2A (6.0%), 7 patients in 2B (2.3%), 30 patients in 3A (10.1%), 2 patients in 3B (0.7%), 30 patients in 3C (10.1%), 2 patients in 4A (0.7%) and 3 patients in 4B (1.0%). Of the patients with endometrial cancer in our study, tumors of 102 patients were (34.2%) in grade I, 139 were (46.6%) in grade II and 57 were (19.1%) in grade III. Because endometrial cancer shows earlier symptoms than the other gynecological cancers, it can be diagnosed in early stages. There is a surgical standard treatment, but it changes according to the stages and general state of the patients.
Keywords: Endometrial cancer; Retrospective analysis; Prognosis.

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Introduction

Among the causes of post-menopausal bleeding are atrophic vaginitis, servicitis, endometritis, endometrial atrophy, myoma uteri, endometrial hyperplasia, endometrial polyps, endometrium, vulva, vagina and cervix (Burbos et al., 2010).

Top three cancer types among women around the world are breast, cervix and colorectal cancers, respectively. Of gynecological cancers, endometrial cancer is the sixth and over cancer is the seventh most common cancers. While among the cancer types seen in women in the world, endometrial cancer is the sixth in incidence and seventh in mortality (GLOBOCAN, 2008), among the causes of death from cancer, it is ranked as the ninth and second in mortality among the gynecological cancers in Turkey (Ergör, 2012).

A relation has been detected between endometrial cancer and over-weight and obesity. While fatty nourishment increase the endometrial cancer risk, fruit-vegetable weighted nourishment reduces the endometrial cancer risk (Cust, 2011). It is seen that the risk of endometrial cancer development in women who never smoked is higher than the women who smoked before or are still smoking (Viswanathan et al., 2005). In the studies with Estrogen Replacement Treatment (ERT) it was revealed that long term use of estrogen had a close relation (an increase of 10-20 times in relative risk) with endometrial cancer development (Anderson, Judd & Kaunitz, 2003). The risk is more in the individuals who have endometrial cancer history in their families. It is also reported that individuals who have colon cancer in their families are at risk of endometrial cancer (Sonoda & Barakat, 2006). Early menarch and late menopause increase the risk of endometrial cancer (Xu et al., 2004). High BMI increases the mortality rate from endometrial cancer, too (Calle, Rodriguez, Walker-Thurmond & Thun, 2003).

It is suggested to perform biopsy on the women who have risk factor in their history (American Cancer Society, 2013). In literature, screening tests for endometrial cancer are; endometrial biopsy, USG and bulk screening which is suggested in the screening of high risk groups. Especially in the studies made with the group that take tamoxifen, it was found beneficial to measure endometrial thickness with Dilatation & Curettage (D&C) or hysteroscopy in determining endometrial cancer risk. Transvaginal USG, endometrial biopsy are the other methods used for bulk screening (Sonoda & Barakat, 2006).

Material and Methods

Our study was a retrospective study consisted of 298 patients who had medical operations with the diagnosis of endometrial cancer in Istanbul Kanuni Sultan Süleyman Hospital, Clinic of Obstetrics and Gynecology between the years of 2001-2011. Approval of Education and Planning Board and Ethical Committee of the Hospital was received. Endometrial cancer was diagnosed via dilatation and curettage. Routine preoperative examinations were asked from the patients. All patients were examined via ultrasonography (Siemens Sonoline G50 and Voluson730 Expert) and depth of myometrial invasion was evaluated. Clinical stage was determined.

After the diagnosis, first of all, abdomen fluid sampling was made for cytological examination following abdomen exploration in all patients. Then, total abdominal hysterectomy and bilateral salpingo-ooforectomy (TAH+BSO), bilateral pelvic lymph node dissection ± paraaortic lymph node dissection were applied. Biopsies were taken from the suspicious lesions in the abdomen if there is any. Hysterectomy specimen was cut in the middle and interpretation was made about the presence of myometrial invasion and grade, tumor volume and cervical dimension. While only pelvic lymph node dissection was applied on the patients who had good prognostic data, total pelvic and paraaortic lymph node dissection were applied on the group with bad prognostic data. Omentum biopsy was also added in that group of patients. In the surgically suitable cases,

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dissection was made on the renal veins level. All materials were examined in the pathology laboratory of our hospital.

FIGO surgical staging system-2009 was used in the staging of endometrial cancer. FIGO was used in grade classification and World Health Organization Classification of Tumors system was used for the histological classification. Age average, menopause state, body mass index, gravida-parities, additional diseases, smoking, tumor types, histological grades, surgical and clinical stages, existence of lymphovascular invasion, myometrial invasion and its degree, cervical involvement and lymph node involvement of all patients were evaluated.

In the statistical analysis of our study, SPSS 11.0 packaged software (Statistical Package for the Social Sciences Inc; Chicago, IL, USA) was used. Continuous variables were figured as, average (average) ± Standard deviation (SS); discrete variables were figured as, frequency (n) and percentage distribution.

Results

Our study was composed of 298 patients who had endometrial cancer. Of the patients in the study, average of age was 56.54±9.69, BMI average was 31.47±6.20, gravida average was 4.16±2.59, and parity average was 3.41±2.15. While 223 (74.8%) of the patients were in menopause, 75 (25.2%) of them were not in menopause, 34 (11.4%) were smoking, 264 (88.6%) were not smoking, 130 (43.6%) had hypertension, while 168 (56.4%) did not have hypertension. 64 (21.5%) had Diabetes Mellitus, while 234 (78.5%) did not have Diabetes Mellitus. Demographic characteristics of the patients are demonstrated in Table 1.

Table 1. Demographic characteristics

Demographic characteristics		**M ± SD**	**Min.**	**Max.**
Age (year)		56.54 ± 9.69	33.00	80.00
Gravida		4.16 ± 2.59	0.00	14.00
Parity		3.41 ± 2.15	0.00	11.00
BMI (kg/m^2)		31.47 ± 6.20	18.00	61.00
		n	%	
Smoking	Using	34	11.4	
	Not using	264	88.6	
Hypertension	Present	130	43.6	
	Absent	168	56.4	
Diabetes Mellitus	Present	64	21.5	
	Absent	234	78.5	
Menopause status	In Menopause	223	74.8	
	Not in Menopause	75	25.2	

Mean±SD:Standard deviation, BMI: Body Mass Index

262 (87.9%) of the patients in our study had endometrial adenocarcinoma, 4 (1.3%) had endometrial clear cell carcinoma, 5 (1.7%) had endometrial adeno squamous carcinoma, 1 (0.3%) had endometrial stromal sarcoma, 20 (6.7%) had endometrial serous papillary carcinoma, 3 (1.0%) had endometrial carcinosarcoma and 3 (1.0%) had endometrial mixed mesodermal sarcoma. The

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distributions of histological types of the patients with endometrial cancer are demonstrated in Table 2.

Table 2. The distributions of histological types of the patients with endometrial cancer

Histological Type of the Cancer	n	%
Endometrial Adenocarcinoma (EAC)	262	87.9
Endometrial Clear Cell Carcinoma (ECCC)	4	1.3
Endometrial Adenosquamous Carcinoma (EASC)	5	1.7
Endometrial Stromal Sarcoma (ESS)	1	0.3
Endometrial Serous Papillary Carcinoma (ESPC)	20	6.7
Endometrial Carcinosarcoma (ECS)	3	1.0
Endometrial Mixed Mesodermal Sarcoma (EMMS)	3	1.0

Distributions of the patients with endometrial cancer in our study, by clinical stages, were as follows; there were 66 (22.1%)patients whose tumor stage were 1A, 127 (42.6%) patients in 1B, 89 (29.9%) patients in 1C, 6 (2.0%) patients in 2A, 3 (1.0%) patients in 2B, 2 (0.7%) patients in 3A, 1 (0.3%) patient in 3B, 3 (1.0%) patients in 3C and 1 (0.3%) patient in 4A. There were not any patients whose tumor stage was in 4B.

Distributions of the patients by surgical stages were as follows; there were 32 (10.7%)patients whose tumor stage was in 1A, 127 (42.6%)patients in 1B, 47 (15.8%) patients in 1C, 18 (6.0%)patients in 2A, 7 (2.3%) patients in 2B, 30 (%10.1)patients in 3A, 2 (0.7%)patients in 3B, 30 (10.1%)patients in 3C, 2 (0.7%) patients in 4A and 3 (1.0%)patients in 4B. Of the patients with endometrial cancer in our study, tumors of 102 patients (34.2%) were in grade I, 139 tumors (46.6%) were in grade II and 57 tumors (19.1%) were in grade III. Number of patients by clinical or surgical stage and grade of endometrial cancer are given in Table 3.

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Table 3. Number of patients by clinical or surgical stage and grade of endometrial cancer

Clinical or Surgical stage and Grade of Endometrial Cancer		n	%
Clinical stage (n=298)	1A	66	22.2
	1B	127	42.6
	1C	89	29.9
	2A	6	2.0
	2B	3	1.0
	3A	2	0.7
	3B	1	0.3
	3C	3	1.0
	4A	1	0.3
	4B	0	0
Surgical stage (n=298)	1A	32	10.7
	1B	127	42.6
	1C	47	15.8
	2A	18	6.0
	2B	7	2.3
	3A	30	10.1
	3B	2	0.7
	3C	30	10.1
	4A	2	0.7
	4B	3	1.0
Grade (n=298)	I	102	34.3
	II	139	46.6
	III	57	19.1

There were 71 (23.8%) patients who had lymphovasculer invasion and 227 (76.2%) patients who did not have lymphovasculer invasion in our study. In 265 (88.9%) of the patients lymph node involvement did not exist. There were 13 (4.4%) patients who had pelvic lymph node involvement and there were 20 (6.7%) patients who had pelvic and paraaortic lymph node involvement. Lymphovasculer invasion and lymph node involvement frequencies of the patients are demonstrated in Table 4.

Table 4. Lymphovasculer invasion and lymph node involvement frequencies of the patients

Lymphovasculer invasion and lymph node involvement of the patients		n	%
Lymphovasculer Invasion	Present	71	23.8
	Absent	227	76.2
Lymph node involvement	There is not lymph node involvement	265	88.9
	Pelvic lymph node involvement	13	4.4
	Pelvic and paraaortic lymph node involvement	20	6.7

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Discussion

Endometrial cancer is the most common cancer among gynecological cancers and the 7th most common cause of death from cancer (Greenlee, Murray & Bolden, 2000). Endometrial cancer is a disease which is generally seen among postmenopausal women and the course of disease gets worse with increasing age. 25% of the patients are seen in premenopausal period, only 5 %of them are seen before 40 and 70% are seen in postmenopausal period. Incidence age of the disease is 60 (Greenlee, Murray & Bolden, 2000; AJCC, 2010). In our study, while 223 (74.8%) of the patients were in menopause, 75 (25.2%) of them were not in menopause, average of age was 56.54±9.69, BMI average was 31.47±6.20, gravida average was 4.16±2.59, parity average was calculated as 3.41±2.15.

In cases where endometrial cancer is detected, surgery is the first treatment choice in 92-96% of the cases. Tumor is detected during the first diagnosis in uterus in a limited way in 75% of the patients who are diagnosed to have endometrial cancer (Çiçek, Akyürek, Çelik & Haberal, 2004). In a study conducted by Kars et al. in our country, it was observed that 82% of the patients were in Stage 1, 8% were in Stage 2, 8% were in Stage 3, 2% were in Stage 4 (Kars, Ünal & Kalender, 2010). Standard surgical approach is staging surgery, and it contains peritoneal cytology, total hysterectomy, bilateral salpingo-ooferectomy and retroperitoneal lymphadenectomy. According to the surgical pathological staging, Kösebay et al. found survival rate to be 89% in stage I, 66% in stage II, 70% in stage III and 0 in stage IV (Kösebay, Beşe & Erkün, 1996).

Distributions of the patients with endometrial cancer in our study by clinical stages were as follows; there were 66 (22.1%)patients whose tumor stage were 1A, 127 (42.6%) patients in 1B, 89 (29.9%) patients in 1C, 6 (2.0%) patients in 2A, 3 (1.0%) patients in 2B, 2 (0.7%) patients in 3A, 1 (0.3%) patient in 3B, 3 (1.0%) patients in 3C and 1 (0.3%) patient in 4A. There were not any patients whose tumor stage was in 4B.

Distributions of the patients by surgical stages were as follows; there were 32 (10.7%)patients whose tumor stage was in 1A, 127 (42.6%)patients in 1B, 47 (15.8%) patients in 1C, 18 (6.0%)patients in 2A, 7 (2.3%) patients in 2B, 30 (10.1%)patients in 3A, 2 (0.7%)patients in 3B, 30 (10.1%)patients in 3C, 2 (0.7%) patients in 4A and 3 (1.0%)patients in 4B. Of the patients with endometrial cancer in our study, tumors of 102 patients (34.2%) were in grade I, 139 tumors (46.6%) were in grade II and 57 tumors (19.1%) were in grade III.

Treatment protocols of the patients vary by myometrial invasion depth of the tumor in endometrial cancer. Intra operative detection of the myometrial invasion depth is made via the macroscopic evaluation of uterus cross section or via the histological examination of the frozen sections. The extent of the surgical treatment is decided by considering the myometrial invasion depth during the operation. In the presence of deep myometrial invasion, patients need wider lymph node dissection (Varpula & Klemi, 1993). Deciding the extent of the surgical treatment after the operation starts is a significant drawback in this case. The exact invasion depth of the tumor is detected via the histopathological examinations after the operation. Although surgical-pathological staging detects the invasion depth of the tumor accurately, it has a risk of morbidity and may negatively affect optimal radiotherapy practice (Hriack, Rubinstein, Gherman & Karstaedt, 1991).

Lymphadenectomy indication and its limits are discussed nowadays. Pelvic lymph node involvement rate in patients who underwent lymphadenectomy varies between 5-18% (Chi, Barakat & Palayekar, 2008). In Creasman's classical study, pelvic paraaortic lymph node involvement was not observed when histologically grade 1 patients did not have myometrial invasion in endometrial

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cancer, still in cases that were in grade 1 but had inner 1/2 myometrial invasion, pelvic lymph node involvement was observed at the rate of 3%, and paraaortic lymph involvement was observed at the rate of 1% (Creasman, Morrow & Bundy, 1987).

There is not a clear opinion on lymph node dissection. There are people who assert that lymph dissection needs to be applied on all patients and there are also people who assert that only hysterectomy is enough for the early stages and lymph dissection should be added in the advanced stages (Doğan, Güngör & Özgü, 2008: 56). The study conducted by Chan et al. involves a very wide serial. In this study, staging surgery was performed on 12333 patients while 27063 patients did not have lymphadenectomy. In patients whose final pathology was stage 1 and grade 1, 2 there were no difference between the survival rates in both groups. However, in diseases that were further than stage 1 or in cases that were independent from stage, were in grade 3, survival rate was higher in patients who took staging (Chan, Wu & Cheung, 2007:286). In a study conducted by Ayhan et al., patients who did not have preoperative cancer diagnosis and those who were diagnosed to have cancer in final pathology after hysterectomy (incomplete surgery) were investigated in two groups. Difference was not observed between the groups who underwent lymphadenectomy and who did not in terms of recurrence, survival, disease-free survival, most of the patient group consisted of patients in early stage 1 (Ayhan, Kart & Guven, 2006:373). In our study, there were 71 (23.8%) patients who had lymphovasculer invasion and 227 (76.2%) patients who did not. 265 (88.9%) of the patients did not have lymph node involvement. There were 13 (4.4%) patients who had pelvic lymph node involvement and 20 (6.7%) patients who had pelvic and paraaortic lymph node involvement.

Aggressive treatment is redundant in patients whose tumor dissemination is low; lymphadenectomy may cause really serious complications. Among these complications are lymphocyst, bleeding, vascular injury, gastrointestinal and urogenital injuries. Morbidity and mortality decrease by avoiding unnecessary processes in especially old, obese and patients with systemic medical problems.

Conclusion

Endometrial cancer is the most frequently increasing gynecological cancer in recent years in our country. Obesity that increases with the causes such as malnutrition and rise in socioeconomic level may be related to the increase in endometrial cancer frequency. Because endometrial cancer shows earlier symptoms than the other gynecological cancers, it can be diagnosed in early stages. There is a surgical standard treatment, but it changes according to the stages and general state of the patients.

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