Endometrial Cancer - Evaluation of Diagnostics Treatment and Prognosis in 150 Patients

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OBJECTIVE: In this study we aim to discuss diagnostic and tratment modalities and prognostic factors of 150 patients that were admitted to our clinic between October 2002 and May 2009 in a retrospective way in regard with the current literature.

STUDY DESIGN: Patients' all demographic data were recorded upon admittance, diagnostic and treatment options that were perfomed were also recorded and thus are used in this study.

RESULTS: Patients' median age was 67.1±11 ,2 (52-79) , Trans vaginal ultrasonography (TVUSG) was used to measure endometrial thickness and the median was 15.7± 4.91 mm (6-36). All patients were diagnosed with fractional curretage before admittance to the gynecological oncology clinic, all underwent total abdominal hysterectomy bilateral salpingoopherectomy and bilateral pelvic–para aortic lymphadenectomy (performed if FIGO critera are met). Surgical staging results were as follows; 78% Stage 1, 10% Stage 2, 8% Stage 3 and 4% were Stage 4. Histopathological differentiation resulted largely in favor of Endometrioid adenocarcinoma with 132 patients (88%), 6 cases of Serous papillary carcinoma (4%), 7 cases of Clear cell carcinoma (4.6%), 3 cases of Mucinous carcinoma (2%) and 2 cases of Undifferentiated carcinoma (1.3%). In terms of grading, 28 patients (18.6%) were classified as high grade and among 132 patients that were classified as endometrioid carcinoma 69 were grade I (52.2%), 52 were grade II (39.3%) and 11 were grade III (8.3). In terms of myometrial invasion beyond 50%, grade I patients were less likely to, with only 5.2%, and 39% and 76.3% for grades II and III respectively. Lymph node dissection was performed on 71 patients among which 8 had positive pelvic lymph nodes (5.3%) and 2 had positive aortic lymph nodes (1.3%). All high grade patients had positive peritoneal cytology.

Lymphovascular space invasion was present in 36 of the patients (24%) of which 3 were grade I (8.3%), 12 were grade II (33.3%) and 11 were grade III (30.5%). Among 16 patients that had cervical invasion 14 also had lymphovascular space invasion (LVSI) (87.5%).

CONLCLUSION: Survival in endometrial carcinoma depends on many factors starting with the FIGO staging, histological type of the tumour, its histological grade, lymphovascular invasion, treatment modalities and patient specific variables such as age, BMI, parity.

Key Words: Endometrial cancer, Endometrial cancer diagnosis, Endometrial Cancer Treatment

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Introduction

Endometrial carcinoma is the leading cancer of the female genital tract and is the fourth most common cancer after lung, breast and bowel in women. In Turkey it comes after cervical cancer[1] and in regard of the current literature sums up to almost half of all gynecologic cancers in total.[2] Approximately about 20 % of these patients are lost in 5 years after diagnosis despite of all known treatment options used. Endometrial carcinoma is a disease of the post menopausal period, highest incidence in the 6th decade and can originate from normal, hyperplastic or atrophic endometrium[3] dependent on estrogen (Type I) or independent of hormonal stimulus (Type II) with a worse prognosis.

In terms of viability, prognosis and recurrence surgical stage of the tumour is the main factor. Among risk factors; obesity, diet, early menarche late onset menopause, nulliparity, hypertension, diabetes mellitus (DM), tamoxifen usage,

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pelvic radiation, Lynch syndrome and chronic anovulation (.,ie PCOS) can be considered.[4]

Early diagnosis is largely possible due to tumour's behaviour to present itself with symptoms such as bleeding as the most common. Diagnosis is made possible using TVUSG and endometrial biopsy.[5,6] Tumour's histologic subtype, grade, myometrial invasion level, cervical spread, lymph node metastase, adnexial or abdominal spread, size, lymphovascular space invasion (LVSI) and patient age are considered as the main prognostic values.

In this study we aim to evaluate the methods used for diagnosis, methods of treatment and prognostic factors in 150 patients that were admitted to our clinic between October 2002 and May 2009 in regard with the current literature.

Material and Method

Patients' all demographic data, diagnostic procedures and treatment modalities used were all recorded upon admittance. A 6.5 Mhz. frequency endo cavitary probe was used to measure endometrial thickness. All curretage material was sent to our pathology clinic for evaluation. Patients' data including age, parity, hypertension, diabetes mellitus, endometrial thickness, histopathologic diagnosis, type of operation performed, tumour stage and grade, whether or not having received post operative radiotherapy and mortality rates during follow-up were all recorded.

Student T test was used to compare the medians parametrically and Kruskal Wallis test, Mann Whitney U test and Fisher's Exact Chi-squared test was used non parametrically.

P values calculated below 0.05 were accepted as statistically significant.

Results

In regard of histopathologic differentiation of subtypes among all patients, the largest subgroup was Endometrioid Adenocarcinoma with 132 patients (88%).

Our study group's median age was 67.1±11,2 (52-79) and statistically significant difference concerning age and sub groups was between endometrioid adenocarcinoma and serous papillary carcinoma (p:0.025) along with endometrioid adenocarcinoma and undifferentiated carcinoma (p:0.023).

Diabetes mellitus and hypertension was found to have no effect on tumour's surgical stage or histologic grade to be high (.;ie III-IV and III respectively) with p values of 0.626 and 1.000 for hypertension and p values of 1.000 and 1.000 for DM respectively.

All patients were fertile with gravida 5.8± 3.6 (1-16) and para 4.5± 2.9 (1-11).

All patients admitted to our clinic complained of vaginal bleeding and all underwent fractional curretage after endometrial thickness measurement with TVUSG.

Median endometrial thickness measured with TVUSG was 15.7± 4.91 (6-36)mm. Endometrial line thickness was found to be statistically significant when compared with endometrioid adenocarcinoma 13.1± 4.9 (6-23)mm and other sub groups 33.3± 2.6 (31-36)mm (p:0.005).

Histopathological results were as follows;
142 patients were diagnosed as cancer (94.6%), 5 patients with complex hyperplasia (nuclear atypia present) (3.3%), 2 patients with complex hyperplasia without nuclear atypia (1.3%) and 1 patient had endometrial polyps (0.6%).

In terms of endometrial thickness between high grade and low grade patients we found we found it to be statistically significant (p: 0.025).

In patients with myometrial invasion less than 1/2, preoperative endometrial thickness was measured 11.8± 4.9 (6-18)mm where as those with myometrial invasion more than 1/2 were measured as 28.9± 6.6 (22-36)mm and difference is found to be statistically significant (p: 0.025).

All patients in our study group underwent total abdominal hysterectomy bilateral salpingoopherectomy and bilateral pelvic –para aortic lymphadenectomy (performed if FIGO critera are met). Surgical staging results were as follows; 78% Stage 1, 10% Stage 2, 8% Stage 3 and 4% were Stage 4. Histopathological differentiation resulted largely in favor of Endometrioid adenocarcinoma with 132 patients (88%), 6 cases of Serous papillary carcinoma (4%), 7 cases of Clear cell carcinoma (4.6%), 3 cases of Mucinous carcinoma (2%) and 2 cases of Undifferentiated carcinoma (1.3%). In terms of grading, 28 patients (18.6%) were classified as high grade and among 132 patients that were classified as endometrioid carcinoma 69 were grade I (52.2%), 52 were grade II (39.3%) and 11 were grade III (8.3%). In terms of myometrial invasion beyond 50%, grade I patients were less likely to, with only 5.2%, and 39% and 76.3% for grades II and III respectively. Lymph node dissection was performed on 71 patients among which 8 had positive pelvic lymph nodes (5.3%) and 2 had positive aortic lymph nodes (1.3%). All high grade patients had positive peritoneal cytology.

Also all patients who had positive lymph nodes were also high grade, had deep myometrial invasion and had positive peritoneal cytology.

Lymphovascular space invasion was present in 36 of the

patients (24%) of which 3 were grade I (8.3%), 12 were grade II (33.3%) and 11 were grade III (30.5%). Among 16 patients that had cervical invasion 14 also had lymphovascular space invasion (LVSI) (87.5%).

Post operative radiotherapy is a routine process in our clinic so all patients had pelvic radiation.

Discussion

Endometrial cancer is most frequently encountered between the 6th and 7th decades of life. Median age is 60. Its been noted that over 75% of the patients are above the age 50.[2] In our study we found the median age of our patients 67.1±11,2 (52-79) to be consistence with the current literature. Diabetes Mellitus is known to increase the risk by 2.8 fold [7] hence 24% of patients in our study group who had DM prior to admittance. Hypertension is also known to increase the risk for endometrial cancer. 37% of the patients in our study group had hypertension so in regard with the current literature we also confirm that hypertension and DM are risk factors for endometrial cancer.

Endometrial cancer mainly originates from unopposed estrogenic stimulation. Nulliparous women are known to have an increased risk by 2 fold along with infertility and having anovulatory cycles, facing unopposed estrogenic stimulus is a significant risk factor.[4,6]

We also beleive this to be an important risk factor but in our study group all patients were fertile and only 12 (0.8%) patients had polycystic ovaries. Having all of the study group comprising of post menopausal patients we can't decide if these 12 patients had PCOS in their reproductive age. But when asked about their menstruel cycles, 10 of 12 revealed that they used to have irregular cycles so we can assume that, albeit fertile, these patients faced unopposed estrogen from unovulatory cycles.

In a study it was shown that almost all of the patients younger than 30 years who had endometrial cancer were all infertile.[8]

As noted before our study group were all fertile and we are currently investigating this issue in another study.

Current studies suggest that using TVUSG for endometrial evaluation is a safe method for cancer screening especially if used with endometrial sampling to increase sensitivity.[9]

Thus TVUSG is an effectice tool in discriminating the patients where endometrial sampling is necessary.[10] As noted before we have found that endometrial line measurement with TVUSG is statistically significant (p:0.005) when endometrioid adenocarcinoma is compared with other subgroups as well as endometrial line thickness and tumour grade comparison (p: 0.025).[11,12]

All patients were diagnosed with endometrial sampling prior to admittance to our clinic and our positive predictive value for cancer was 94.6% which is in consistence with the current literature.[13] Though it should be noted that a negative result does not guarantee disease abscence[14] as shown in our study group 5.6% of patients who had negative pathology results were actually cancer. Further evaluation is necessary especially in patients with complex hyperplasia and nuclear atypia. An early operation in these patients will surely benefit the patients.[15,16]

Relationship between tumour grade and prognosis were shown in previous studies. Tumour grade along with myometrial invasion which is another prognostic value is an important factor in determining lymph node metastase. Risk for deep myometrial invasion, cervical spread, lymph node metastase, local recurrence and distant metastasis increases with tumour undifferentiation.[17]

In our study 28 patients (18.6%) were classified as high grade and among 132 patients that were classified as endometrioid carcinoma 69 were grade I (52.2%), 52 were grade II (39.3%) and 11 were grade III (8.3%). In terms of myometrial invasion beyond 50%, grade I patients were less likely to, with only 5.2%, and 39% and 76.3% for grades II and III respectively. Lymph node dissection was performed on 71 patients among which 8 had positive pelvic lymph nodes (5.3%) and 2 had positive aortic lymph nodes (1.3%). All high grade patients had positive peritoneal cytology.

It is known that LVSI is associated with a worse prognosis and higher risk of recurrence.[18]

Lymphovascular space invasion was present in 36 of the patients (24%) of which 3 were grade I (8.3%), 12 were grade II (33.3%) and 11 were grade III (30.5%). Among 16 patients that had cervical invasion 14 also had lymphovascular space invasion (87.5%).

LVSI is more commonly associated with cervical spread and higher grade tumours as shown in our study.

Cervical spread increases the risk for lymph node metastase, recurrence and extrauterine disease. Patients with cervical spread is associated with high grade tumours and histologic subtypes causing a worse prognosis.[19]

Usually patients with cervical spread are of higher grade and have deep myometrial invasion.

Surgery is the most important factor in all stages of the disease and is comprised of total abdominal hysterectomy bilat-

eral salpingoopherectomy and bilateral pelvic - para aortic lymphadenectomy (performed if FIGO critera are met), peritoneal cytology and omental biopsy or removal.

In our study group lymphadenectomy was performed on 71 patients of which 8 had positive lymph nodes (5.3%). Decision for lymphadenectomy was based on FIGO criteria. But as a side note we are also investigating, in another study group, the effectiveness of lymphadenectomy in all patients with endometrial cancer regardless of deep myometrial invasion and tumour grade to further maximize correct staging and prognosis evaluation as noted by other studies.[20,21]

Although post operative radiotherapy is a routine treatment for all stages of the disease in our clinic we have seen that it may be considered as overtreatment since it doesn't affect survival, albeit known to reduce local recurrence in early stage (I or II) disease. Thus it is more appropriate to use post operative pelvic radiation on patients with a higher risk or recurrence.[22,23]

Conclusion

Survival in endometrial carcinoma depends on many factors starting with the FIGO staging, histological type of the tumour, its histological grade, lymphovascular invasion, treatment modalities and patient specific variables such as age, BMI, parity.

Endometrial Kanser - 150 Hastada Tanı Tedavi ve Prognozun Değerlendirilmesi

AMAÇ: Bu çalışmada amacımız 150 hasta üzerinden Endometrium CA tanısı almış hastaların üzerinden literatür bilgisini gözden geçirmektir. Hastalar geriye dönük olarak 2002-2009 tarihleri arasında kliniğimize başvuran hastalardır.

GEREÇ VE YÖNTEM: Tüm hastaların demografik bilgileri kaydedilerek bu çalışmada kullanılmıştır.

BULGULAR: Hastaların ortalama yaşı 67.1±11,2 (52-79)'di, Trans vaginal ultrasonografi (TVUSG) endometriyal kalınlığı ölçmede kullanıldı ve ortalama 15.7±4.91 mm'di (6-36). Tüm hastalara kliniğe kabul edilmeden önce fraksiyone küretaj yapıldı, hepsine total abdominal histerektomi iki taraflı ooferektomi, iki taraflı pelvik paraaortik lenf nodu diseksiyonu yapıldı. Cerrahi evrelemede; %78 Stage %1,10 Stage %2,8 Stage %3 and %4 Stage 4 hasta vardı. Endometrioid adenocarcinoma 132 hastada (%88), 6 hasta serous papillary carcinoma (%4), 7 hasta clear cell carcinoma (%4.6), 3 hasta mucinous carcinoma (%2) ve 2 hasta undifferentiated carcinoma (%1.3) olarak patolojik tanı aldı.

Lenfovasküler invazyon bulunan 36 hastanın 3'ü Grade I, 12'si Grade II ve 11'i Grade III idi. Servikal invazyonu olan 16 hastanın 14'ünde aynı zamanda lenfovasküler invazyon vardı.

SONUÇ: Endometrium CA'da yaşam süresini birçok parametre etkiler. Tümörün histolojik tipi, FİGO evresi, histolojik grade, lenfovasküler invazyon, tedavi şekli, yaş, vücut kitle indeksi gibi.

Anahtar Kelimeler: Endometrial kanser, Endometrial kanser tanısı, Endometrial kanser tedavisi

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