ORIGINAL ARTICLE

Prevalence and clinicopathological differences between type I and type II of endometrial cancer

SETARE AKHAVAN[1], MONA MOHSENI[1*], MITRA MODARES GILANI[1], AZAM SADAT MOUSAVI[1], SHAHRZAD SHEIKHHASANI[1], ELHAM FEIZABAD[1,2]
[1]Department of Oncologic Gynecology, Vali-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran.
[2]Department of Obstetrics and Gynecology, Yas Hospital, Tehran University of Medical Sciences, Tehran, Iran.
**Correspondence: monamohsenigyneco@gmail.com*
Department of oncologic gynecology, Vali-Asr Hospital, Tehran University of Medical Sciences, Tehran, Iran.

ABSTRACT

Background: The aim of this study was to evaluate the prevalence and clinicopathological differences between type I and type II endometrial cancer.

Methods: This retrospective study was carried out on 480 histological confirmed endometrial cancer women (362 Type I and 118 Type II patients), diagnosed and treated in Imam Khomeini hospital from March 2010 to February 2021.

Results: The average age of these 480 patients was 55.94±10.19 with the age range of 27 to 84. Of them, 72.1% were post-menopausal and 13.5% were nulliparous. The two most common presentations of EC were post-menopausal vaginal bleeding and menometrorrhagia.

The three survival rate, and five survival rate was 382 (95.3%), and 271 (83.4%), respectively with significantly (p-value<0.001) higher proportion in three and five survival rate in Type II.

The survival rate based on tumor stages demonstrated a better rate in low stages compared to high stages. In addition, disease recurrence occurred in 17.1% (82) of patients with significant (p-value<0.001) more prevalent in Type II of tumor.

Conclusions: The findings of this study recommend that the higher mortality rate of type II endometrial cancer might be due to its high stage at the time of diagnosis. Accordingly, comprehensive screening is likely to increase the survival rate in this curable cancer.

Keywords: Endometrial cancer, Cancer stage, Prognosis, Survival

BACKGROUND

Endometrial cancer (EC) is the most prevalent gynecologic cancer (1). EC is more prevalent in women who are in the sixth or seventh decade of their lives (2-4).

Prolonged estrogen exposure is a known risk factor for the beginning of the premalignant stage of EC. Fortunately, EC is one of the curable tumors if it is recognized in the primary phase (5-9).

EC is categorized into two distinct types according to its histopathology and clinical outcomes. Type I is more common and accounts for 80 to 85% of the cases. Type I is caused by prolonged estrogen exposure and includes endometrioid tumors grade I and II and its variants, such as mucinous carcinoma, villoglandolar. Its 5-year survival rate is 80% or even more (10-12).

Type II could be observed in 15-20% of the patients with EC. It consists of all non-endometrioid containing clear cell, papillary serous, undifferentiated carcinoma, squamous cell, and Grade III endometrioid. Type II of EC is very aggressive which often develops in the atrophic uterine in post-menopausal women (10, 13).

To our knowledge, no previous study evaluate the prevalence and clinicopathological differences of uterine involvement in the Iranian population. Thus, the aim of this study was to evaluate the prevalence and clinicopathological differences between type I and type II endometrial cancer.

METHODS

This retrospective study was carried out on 480 histological confirmed endometrial cancer women, diagnosed and treated in Imam Khomeini hospital from March 2010 to February 2021.

All histologically confirmed EC women who were referred to our oncology department participated in the study. The patients whose medical records were incomplete were excluded from the study.

After the diagnosis, total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO) was applied. In some patients, bilateral pelvic lymph node with or without paraaortic lymph node were dissected. In addition, omentum biopsy was only done in the patients with papillary serous carcinoma. All tissue specimens were assessed in our hospital pathology department.

Medical records were collected including age, menopausal state, obstetrics history, disease presentation, type of surgery, tumor information including its size, stage, grade, histologic type, and the involvement of other organs.

FIGO and the World Health Organization (WHO) tumor classification were used in stage and grade classification of the patients' tumors (14, 15).

The study primary outcomes were estimating the prevalence of different type of EC, the disease recurrence and participants' three and five survival rate.

Statistical analysis: All the data were analyzed using SPSS version 24.0 (IBM, New York, USA). A P-value of lower than 0.05 was considered as the level of statistical significance. We used Independent T-test and Non-parametric Mann–Whitney U-test to assess differences in means. A Chi-square test was applied to evaluate differences in proportions.

RESULTS

The mean age of 480 patients was 55.94±10.19 with the age range of 27 to 84. 36.9% of the patients were older than 60. Of them, 72.1% were post-menopausal and 13.5% were nulliparous.

The two most common presentations of EC were post-menopausal hemorrhage and menometrorrhagia in 70.6% (339) and 26.7% (128) of the patients, respectively.

Past medical history (PMH) was positive in 65.5% (305) of the participants. There was diabetes in 53.1% (162), hypertension in 67.8% (207), and hypothyroidism in 17.7% (54) of the patients. There was not a significant diversity in different types of EC regarding PMH (p-value=0.141). In addition, a positive history of cancer was reported in 4.4% (21) and Lynch syndrome in one patient.

A positive first-degree family history of cancer was found in 2.1% (10) of the patients; the other one did not have any positive family history.

About 75% (362) of the patients had Type I EC, while 25% (118) had Type II with 46.5% invasion to the myometrium. The baseline characteristics according to the type of endometrial cancer are illustrated in Table 1.

The most common histology type (80.2% of the patients) was endometrioid. Furthermore, the tumors of 215 patients were (44.8%) in grade I, 149 were (31%) in grade II, and 116 were (24.2%) in grade III (Fig. 1).

There were 259 patients whose tumor stage was in 1A (54%), 101 patients in 1B (21%), 47 patients in stage 2 (9.8%), 17 patients in 3A (3.5%), 12 patients in 3B (2.5%), 21 patients in 3C1 (4.4%), 7 patients in 3C2 (1.5%), 2 patients in 4A (0.4%) and 14 patients in 4B (2.9%). There was a significant difference between the two types of EC in terms of disease stage and grade (p-value<0.001) (Fig. 2 A, B).

Comparing organ involvement according to the type of endometrial cancer showed that except for lymph nodes regrades of endometrial cancer type (Table 2).

Considering that nine patients did not refer for the follow-up visit, 70 and 146 patients did not finish three or five years after their disease diagnosis; The three, survival rate and five survival rate was 382 (95.3%), and 271 (83.4%), respectively. Comparing the survival rate according to the type of endometrial cancer is illustrated in table 3 (Table 3).

The survival rate based on tumor stages showed a better rate in low stages compared to high stages. In addition, disease recurrence occurred in 17.1% (82) of patients with significantly (p-value<0.001) higher prevalence in Type II (Fig. 3).

Table 1 Comparing baseline characteristics according to type of endometrial cancer

variables	Type of Endometrial cancer		P-value
	Type I (N=362)	Type II (N=118)	
Age, yrs.	54.86±9.94	59.25±10.31	<0.001
Parity	3.79±2.75	4.60±3.09	0.007
Post-menopausal	256 (70.7)	90 (76.2)	0.243
Size of tumor, mm	3.57±2.01	4.71±2.45	<0.001

Table 2 Comparing organ involvement according to type of endometrial cancer

Variables	Type of Endometrial cancer		P-value
	Type I (N=362)	Type II (N=118)	
LVSI*	92	87	<0.001
Lower segment involvement	61	37	0.001
Serousal involvement	4	9	<0.001
Myomertial involvement	150	73	<0.001
Parameter involvement	7	15	<0.001
Adnexa involvement	20	22	<0.001
Cervical involvement	39	36	<0.001
Peritoneal cytology involvement	4	5	0.031
Lymph node involvement	133	53	0.113

*LVSI: lympho vascular space invasion.

Table 3 Comparing survival rate according to type of endometrial cancer

Survival rate	Type I		Type II		P-value
	Total Number	Alive Number	Total Number	Alive Number	
Three years survival rate	301	295	100	87	<0.001
Five years survival rate	236	213	89	58	<0.001

Figure 1 The distributions of histological types of the patients with endometrial cancer

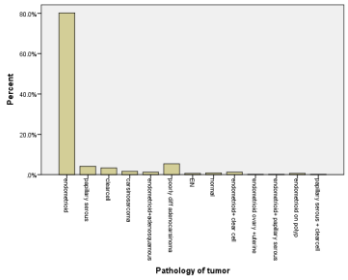
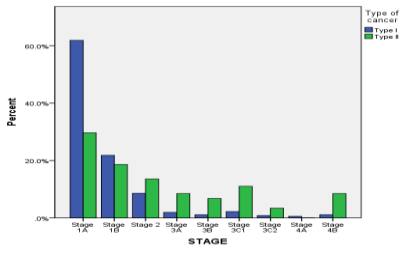


Figure 2 The distributions of tumor stage (A) and grade (B) in Type I and Type II of endometrial cancer

A.



B.

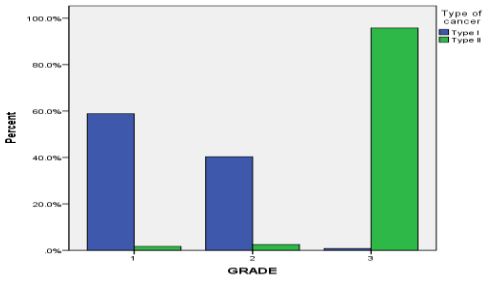
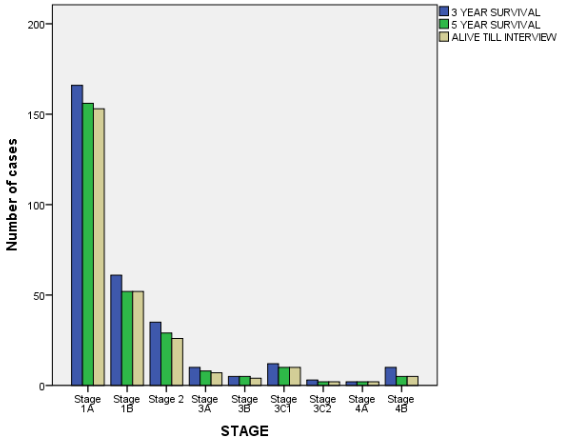


Figure 3 Comparing survival rate according to surgical stages



DISCUSSION

This study was with consistency by previous studies in terms of the prevalence of endometrial cancer. Former researches have shown type I of EC is nearly three folds more common compared to type II, however, Type II is more aggressive and lethal. Furthermore, Type II of EC is more prevalent in post-menopausal, older age, and multiparous females (5, 11, 13).

As our study showed, more than 90% of the patients with endometrial cancer poss abnormal uterine bleeding including post-menopausal vaginal bleeding and menometrorrhagia as a warning symptom (16).

By considering these complaints, we could make the early diagnosis of the disease in the majority of the cases. Consequently, most females with endometrial cancer may have an acceptable good prognosis (17, 18).

On the other hand, EC has several risk factors that influenced its prognosis and mortality. For example, old age, overweight/obesity, and diabetes were associated with increasing the overall mortality. In addition, parity, oral contraceptive agent consumption, and smoking are among other risk factors (19).

Although most of these risk factors are apparently similar in both types of EC, the several genetic changes detected in type I and type II tumors offer that these subtypes may have different etiologies (20, 21).

Although we could not assess all risk factors, our study showed a significant difference in parity numbers between the two types of EC. In addition, it is worth mentioning that in women with type I EC, the greater number of parity was significantly (p-value<0.001) considered as a risk factor for cancer mortality. However, no significant differences in regards to PMH were observed among women with different types of EC and also in survivors or dead women.

The large sample size and low loss to follow-up rate were the strength of the study. Although our findings had some limitations such as a short time of follow-up in some patients, a lack of evaluating known risk factor effect on the patients' survival rate.

CONCLUSIONS

The findings of this study recommend that the higher mortality rate of type II endometrial cancer might be due to its high stage at the time of diagnosis.

Therefore, doing comprehensive screening increases the survival rate in this curable cancer.

Acknowledgements: Not applicable.

Authors' Contributions: "S.A. Project development, M.M. and AS.M. Data collection and management, M.MG. and S.S. Manuscript writing and E.F. Data analysis and Manuscript editing. All authors reviewed the manuscript."

Funding: No funding was received.

Availability of data and materials: The datasets used and/or analyzed in this study will be made attainable from the corresponding author upon request.

Ethics approval and consent to participate: All methods were performed in accordance with the relevant guidelines and regulations (Declaration of Helsinki). Ethical approval was received by the Imam Khomeini hospital ethics board (IR.TUMS.IKHC.REC.1399.268). The patients' data were used anonymously and confidentially and all participants signed informed consent.

Consent for publication: The study patients filled informed consent for the publication of their data anonymously.

Competing interests: The authors declare they have no competing interests.

REFERENCES

1. Heidari F, Rabizadeh S, Sadat Salehi S, Akhavan S, Khaloo P, Alemi H, et al. Serum HSP70 level in patients with endometrial cancer with and without diabetes. Gynecological Endocrinology. 2020;36(4):351-5.
2. Creasman WT, Odicino F, Maisonneuve P, Beller U, Benedet JL, Heintz AP, et al. Carcinoma of the corpus uteri. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2003;83 Suppl 1:79-118.
3. El-Bolkainy MN, Mokhtar NM, Ghoneim MA, Hussein MH. The impact of schistosomiasis on the pathology of bladder carcinoma. Cancer. 1981;48(12):2643-8.
4. Sarvi F, Alleyassin A, Aghahosseini M, Ghasemi M, Gity S. Hysteroscopy: A necessary method for detecting uterine pathologies in post-menopausal women with abnormal uterine bleeding or increased endometrial thickness. Turkish journal of obstetrics and gynecology. 2016;13(4):183.
5. Binesh F, Akhavan A, Behniafard N, Jalilian S. Endometrial adenocarcinoma: clinicopathologic and survival characteristics in Yazd, Iran. Asian Pacific journal of cancer prevention : APJCP. 2014;15(6):2797-801.
6. Sherman ME. Theories of endometrial carcinogenesis: a multidisciplinary approach. Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc. 2000;13(3):295-308.

7. Hecht JL, Mutter GL. Molecular and pathologic aspects of endometrial carcinogenesis. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2006;24(29):4783-91.
8. Emons G, Fleckenstein G, Hinney B, Huschmand A, Heyl W. Hormonal interactions in endometrial cancer. Endocrine-related cancer. 2000;7(4):227-42.
9. Bokhman JV. Two pathogenetic types of endometrial carcinoma. Gynecologic oncology. 1983;15(1):10-7.
10. Moore KN, Fader AN. Uterine papillary serous carcinoma. Clinical obstetrics and gynecology. 2011;54(2):278-91.
11. Felix AS, Weissfeld JL, Stone RA, Bowser R, Chivukula M, Edwards RP, et al. Factors associated with Type I and Type II endometrial cancer. Cancer causes & control : CCC. 2010;21(11):1851-6.
12. Silverberg S, Kurman R, Nogales F, Mutter G, Kubik-Huch R, Tavassoli F. Epithelial tumors and related lesions of endometrium. Tumors of the breast and female genital organs: IARC Press Lyon; 2003. p. 221-32.
13. Esteller M, Xercavins J, Reventos J. Advances in the molecular genetics of endometrial cancer (Review). Oncology reports. 1999;6(6):1377-82.
14. Lax SF, Kurman RJ, Pizer ES, Wu L, Ronnett BM. A binary architectural grading system for uterine endometrial endometrioid carcinoma has superior reproducibility compared with FIGO grading and identifies subsets of advance-stage tumors with favorable and unfavorable prognosis. The American journal of surgical pathology. 2000;24(9):1201-8.
15. Lewin S. Comparative performance of the new versus old FIGO staging system for endometrial cancer. Gynecologic oncology. 2010;116:S10.
16. Arab M, Noghabaei G, Kazemi SN. Comparison of crude and age-specific incidence rates of breast, ovary, endometrium and cervix cancers in Iran, 2005. Asian Pacific Journal of Cancer Prevention. 2014;15(6):2461-4.
17. Colombo N, Preti E, Landoni F, Carinelli S, Colombo A, Marini C, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of oncology : official journal of the European Society for Medical Oncology. 2011;22 Suppl 6:vi35-9.
18. Oaknin A, Rodríguez-Freixinós V, Díaz de Corcuera I, Rivera F, del Campo JM. SEOM guidelines for endometrial cancer. Clinical & translational oncology : official publication of the Federation of Spanish Oncology Societies and of the National Cancer Institute of Mexico. 2012;14(7):512-5.
19. Heidari F, Rabizadeh S, Mansournia MA, Mirmiranpoor H, Salehi SS, Akhavan S, et al. Inflammatory, oxidative stress and anti-oxidative markers in patients with endometrial carcinoma and diabetes. Cytokine. 2019;120:186-90.
20. Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type I and II endometrial cancers: have they different risk factors? Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2013;31(20):2607-18.
21. Prat J, Gallardo A, Cuatrecasas M, Catasús L. Endometrial carcinoma: pathology and genetics. Pathology. 2007;39(1):72-87.