

The Incidence of Ovarian Involvement in Endometrioid Endometrial Adenocarcinoma: A Retrospective Analysis

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ABSTRACT

Background & Objective: Endometrial carcinoma is the most common malignancy of the female genital tract, which most often affects postmenopausal women. The ovaries may be active when a patient has endometrial cancer, so removing an ovary can worsen a patient's quality of life. On the other hand, a complete surgical staging in endometrial cancer includes oophorectomy since 1988. There has been some research to assess whether an oophorectomy should be performed and in which cases, ovaries can be preserved.

Materials & Methods: Aim of this study was to evaluate the coexistence of ovarian involvement in endometrioid endometrial carcinoma. In this study, we evaluated 180 patients with endometrioid endometrial cancer patients who were surgically staged at Imam Hossein Hospital between 2004 and 2017.

Results: Mean age of subjects of the study was 56.78 ± 10.59 . Forty-six of patients (25.6 %) were less than 50 years old and 74.4 % (134) were older than 50. Twenty out of 180 (11.1 %) of them had ovarian involvement (one of them had simultaneous ovarian tumor) and 11 (55%) of these cases were less than 50 years old. In 55 % (11) patients, the involved ovaries were less than 5 cm with grossly normal appearance, lymph nodes metastases were detected in 3 out of 20 (15 %) of them although their ovarian size were 4, 4.5 and 6.5 cm. In 10 (50 %) of them, deep myometrial invasion was detected.

Conclusion: In endometrial cancer staging, ovarian preservation could be a challenging decision and a real controversy which needs more researches.

Keywords: Endometrial cancer, Ovarian cancer, Ovarian metastasis, Synchronous ovarian cancer



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Introduction

Although mean age of endometrial cancer is at least 20 years older than cervical cancer and it is usually the cancer of postmenopausal period (1,2), it has been recently noted that the age is decreasing and 25% of patients are premenopausal. The incidence of the disease among women of less than 40 years old is 2-14% (3,4). The most prevalent histopathology in endometrial cancer is "endometrioid" type, which is usually well differentiated (grade 1) and estrogen-receptor positive in younger patients (5,6). Standard treatment for endometrial cancer is total abdominal hysterectomy, bilateral salpingo-oophorectomy with

pelvic and paraaortic lymphadenectomy as needed (7-9). Five-year survival has been reported more than 90% in early-stage endometrial carcinoma (10).

Regarding this great survival, life quality would be an important aspect for these patients; considering that, oophorectomy could result in serious side effects e.g., osteoporosis, cardiovascular disorders, psychological and sexual problems (11-13). On the other hand, simultaneous ovarian cancer has been detected almost 5% in stage I and 10% in stage II of endometrial cancer (14-15).

Therefore, it's important to consider ovarian involvement before achieving oophorectomy (16-17). For the reasons mentioned above, ovarian preservation in endometrial cancer is a challenging concept; the aim of this study was to evaluate the coexistence of ovarian involvement in endometrioid endometrial carcinoma in order to make the best clinical decision in younger patients who want to preserve their ovaries.

Materials and Methods

In this retrospective descriptive-analytical study, 191 completely surgically staged endometrial cancer cases were enrolled to the study based on the gynecology and pathology database of Imam Hossein Hospital from 2004-2017. Non-endometrioid endometrial cancers were excluded and cases with pure endometrioid pathology were included. All the slides and blocks were reviewed by an experienced gynecology pathologist, and were confirmed. Synchronous ovarian cancer was diagnosed in the following conditions: no or superficial myometrial involvement, low stage for endometrial or ovarian cancer, low grade for endometrial or ovarian cancer, different pathologic grades for endometrial and ovarian cancers or different pathologic features of endometrial and ovarian cancers.

Data were analyzed by SPSS 22 (SPSS Inc., Chicago, Ill., USA), X² and T-test. P-value<0.05 was considered statistically significant.

Results

In this study, the data of 191 endometrial cancer cases who were surgically staged in this center between 2004 and 2017 were collected. Eleven cases with non-endometrioid pathology (e.g., Papillary serous, clear cell, mixed) were excluded and 180 cases participated in the study. Mean age of patients with endometrial cancer was 56.78 ± 10.59 ranging from 27 to 82 years old. Forty-six (25.6 %) were less than 50 years old and 134 (74.4 %) were older than 50 (Table 1). A total of 109 cases (60%) were FIGO stage IA of which 26 (23.9%) cases were less than 50 years. A total of 113 (62.7%) of cases were G1 among whom, 31 (27.4 %) were less than 50 years old (Table 2).

Of the patients, 20 (11.1%) were reported as subjects with ovarian involvement 11 (55%) of whom were less than 50 years old (Table 3).

Among 11 cases with non-endometrioid pathology, 5 (45.5%) had ovarian involvement; in endometrioid cases, 20 out of 180 (11.1%) had ovarian involvement of which, one had simultaneous ovarian cancer and was less than 50 years old. Eleven cases (55%) were less than 50 who are listed in Table 4. In 11 (55%) of these cases the largest ovarian size was 5 cm, with grossly normal appearance, although microscopically involved. Lymph nodes metastasis was detected in 3 out of 20 (15%) of ovarian involved cases, with ovarian sizes of 4, 4.5 and 6.5 cm. Among 50% (10) of ovarian involved patients, myometrial invasion was deep and more than half the thickness.

Table 1. Prevalence of different stages in less than 50 and ≥ 50 years of age ($P=0.068$)

Age-Stage	IA	IB	II	IIIA	IIIB	IIIC and higher	Total
< 50 Y. O	26 56.5 %	5 10.9 %	1 2.2 %	7 15.2 %	1 2.2 %	6 13 %	46 25.6 %
≥ 50 Y. O	83 61.9 %	30 22.4 %	4 3 %	9 6.7 %	0 0 %	8 5.9 %	134 74.4 %

Table 2. Prevalence of different grades in less than 50 and ≥ 50 years of age ($P=0.71$)

Age-Grade	G1	G2	G3	Total
< 50 Y. O	31 67.4 %	10 21.7 %	5 10.9 %	46 22.6 %
≥ 50 Y. O	82 61.2 %	32 23.9 %	20 14.9 %	134 74.4 %

Table 3. Ovarian involvement prevalence in less than 50 and ≥ 50 years of age ($P=0.000$)

Age- Ovarian Involvement	Ovarian Involvement +	Ovarian Involvement -	No oophorectomy	Total
< 50	11 23.9 %	33 71.7 %	2 4.3 %	46 100 %
≥ 50	9	125	0	134

Age- Ovarian Involvement	Ovarian Involvement +	Ovarian Involvement -	No oophorectomy	Total
	6.7 %	93.3 %	0 %	100 %

Table 4. List of cases with ovarian involvement and less than 50 years old

Ovarian involvement	Age	Ovarian mass size (cm)	Myometrial involvement (%)	Lymph node involvement
Case 1	33	18	< 50	-
Case 2	45	3	≥ 50	-
Case 3	36	8	≥ 50	-
Case 4	47	22	< 50	-
Case 5	48	4	≥ 50	+
Case 6	48	6.5	≥ 50	+
Case 7	42	4.5	≥ 50	-
Case 8	40	20	< 50	-
Case 9	40	9	≥ 50	-
Case 10	28	4.5	< 50	-
Case 11	46	3	< 50	-

Discussion

From 191 endometrial cancer patients who were surgically staged in this center, 180 cases were included in this research. In 20 (11.1%) of patients, ovarian involvement was detected and 11 (55%) of whom were less than 50 years old. Therefore, due to its importance in younger people and in the early stages, which also have a long survival, ovarian preservation is a challenging decision. However, an involved ovary is not necessarily enlarged. Due to our study, in 11 of 20 (55%) of endometrioid endometrial cancer patients with ovarian involvement, the largest ovarian size was 5 cm with grossly normal appearance, but microscopic involvement.

Taek Sang lee *et al.* in Korea studied 260 endometrial cancer patients who received surgical treatment between 1992 and 2004. They described 19 of 260 (7.3%) simultaneous ovarian involvement cases in their study. Two of 206 (0.97%) cases with no extrauterine disease, had ovarian involvement and none of them were less than 45 years old (1). However, in our study, ovarian involvement was 11.1% (20 of 180) and almost half of them were less than 50 years old and one case (0.5%) of simultaneous ovarian cancer.

Christine Walsh *et al.* studied 102 endometrial cancer cases who underwent hysterectomy from 1996 to 2004 in the United States. In 26 (25%) of them epithelial ovarian cancer was detected at the same time, 23 were synchronous and 3 were metastatic with mostly endometrioid histology and 12 of 26 (46%) with G1 (well differentiated) and 4 of 26 (15%) with normal appearance at laparotomy. Fifteen of 26 (58%) of ovarian cancers were associated with deep endometrial invasion (14). In our study, 113 (62.7%) of cases were G1 among whom, 31 (27.4 %) were less than 50 years old. One out of 20 cases with ovarian cancer were synchronous who was less than 50 years old. Eleven of 20 (55 %) were less than 50 years old. Ovarian size

ranged from 3 to 20 cm and 5 of 11 (55 %) were less than 5 cm and grossly normal.

In France, Martin Koskas *et al.* evaluated endometrial cancer patients from 1983 to 2008. Participants with endometrioid endometrial carcinoma FIGO stage IA, G1 and less than 40 years old were included in their study. Of the participants, 184 received ovarian preservation surgery and 204 achieved hysterectomy plus oophorectomy. They were followed 5 to 10 years and demonstrated that ovarian preservation had no correlation with cancer-related mortality increment. Although they recommended a larger follow-up for confirmation (18).

Chaoyang *et al.* in China studied patients with endometrial cancer from 2000 to 2010 and evaluated ovarian preservation effect on survival in 203, less than 45 years old women with early-stage cancer. Extrauterine involvement was declared as the most important risk factor for ovarian involvement. According to their study, ovarian preservation had no influence on overall survival. Two of 163 (1.2 %) of ovarian involved cases had no extrauterine involvement (16).

Kinjyo *et al.* studied 88 women less than or equal to 45 years old with endometrial cancer of only endometrioid histology in Japan from 1990 to 2011. The mean age was 39 years and cases were FIGO stage I. Ovarian involvement was observed in 4 (4.5 %) of them and only lymphatic metastasis was described as the risk factor for ovarian cancer. Deep myometrial invasion was demonstrated as the sole predictive factor for lymph node metastasis. In our research, 109 of 180 (60.6 %) of cases were stage IA and 35 of 180 (19.4 %) were diagnosed to be stage IB. The mean age in patients under 50 years old with ovarian involvement was 41 years old. Simultaneous lymphatic and ovarian involvement were reported in 3 of 20 (15 %) of cases and in 10 of 20 (50

%) of ovarian involved participants, deep myometrial invasion was detected (5).

A meta-analysis from 10 retrospective cohort studies by Peng Jia *et al.* in 2017, demonstrated that ovarian preservation in early stage of endometrial cancer, would not influence the disease-free survival and it could be a safe and effective choice in low-risk patients (4).

Conclusion

Throughout endometrial cancer surgery, considering ovarian gross appearance and its size, extrauterine involvement and macroscopic myometrial invasion, it might be helpful to decide the ovarian preservation. In our study, ovarian cancer was detected even in normal

appearing ovaries. Therefore, accurate evaluation pre- and intra-operation is important, before making decision, especially in younger patients with no extrauterine involvement.

Regarding the controversy among ovarian involvement and its preservation in the studies, more researches with larger sample size and meta-analysis could be helpful.

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Conflict of Interest

The authors have no conflict of interest.

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