Original Article

Prevalence and Factors Related to Failure to Receive Hormonal Replacement Therapy after Bilateral Oophorectomy in Women Aged 45 Years or Younger

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Objective: To determine the prevalence and factors related to failure to receive hormonal replacement therapy (HRT) after bilateral oophorectomy in women aged 45 years or younger.

***Materials and Methods*:** A retrospective descriptive study was conducted in patients who underwent bilateral oophorectomy during January 2009 to December 2013 in Faculty of Medicine Vajira Hospital. Inclusion criteria were age 18 to 45 years old had complete ovarian tissue removed. Exclusion criteria were women who had contraindication to HRT.

Results: A total of 183 patients had some types of gynecologic surgery including bilateral oophorectomy during the study period. Eighteen patients were excluded due to the following contraindications: incomplete ovarian removal (9 patients), history of breast cancer (5 patients) or deep vein thrombosis (4 patients). The median age of 165 patients included in the study was 40.6 years (range 24 to 45 years) with the median BMI of 24.3 kg/m^2 (range 23.8 to 40.2 kg/m^2). The most common indication for surgery was adenomyosis with or without endometriosis (54.5%). The prevalence of failure to receive HRT was 52.7%. Factors significantly related to failure were having gynecologic malignancy and age older than 40 years.

Conclusion: Slightly more than half of the patients, aged younger than 45 years, who had undergone bilateral oophorectomy failed to receive HRT. Significantly related factors were gynecologic malignancy and age older than 40 years.

Keywords: Surgical menopause, Bilateral oophorectomy, Hormonal replacement therapy

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Menopausal status is condition wherein physiologic change of aging with cessation of sex hormones production occurs. On the other hand, it can be an event after bilateral oophorectomy or so called 'surgical menopause'. Menopausal status can have many unfavorable impacts to women's health presenting as cardiovascular disease[1,2], neurologic disease[3,4], osteoporosis and menopausal symptoms[5].

In 2013, International Menopause Society[6] advises all women who undergo menopause under the age of 45 years and without contraindications to hormonal replacement therapy (HRT) to use HRT until the average age of the natural menopause. HRT which can restore the body's hormonal levels can be in the form of estrogen therapy or estrogen in combination with progesterone. Pure estrogen therapy is generally used for women who have had hysterectomy (or surgical menopause) whereas estrogen with progesterone therapy for women is used in women who experience natural menopause. The combined therapy should also be considered in women who have had surgical menopause due to endometriosis.

The importance of HRT is to relieve menopausal symptoms, such as, vasomotor symptoms and to prevent health impact due to estrogen deficiency. This is especially the case in young women who had premature ovarian failure or surgical menopause. Despite the benefits of HRT, some factors may hinder its use. For example, few studies had reported that HRT might increase risk of breast cancer, endometrial cancer, venous thromboembolic events (pulmonary embolism or deep vein thrombosis) and cerebrovascular events[7-11]. These findings led some physicians to omit the prescription by prejudice, aside from the underlying diseases or contraindications of the women themselves. Furthermore, socio-economic status and education may be factors leading to failure to receive HRT. As the result, the patients continue suffering from symptoms and effects of estrogen deficiency.

The present study aimed to determine the prevalence and factors related with failure to receive HRT after bilateral oophorectomy in women aged 45 years or younger.

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Materials and Methods

Study design and participants

The retrospective descriptive study was carried out in the Gynecological clinic, Department of Obstetrics and Gynecology, Faculty of Medicine Vajira Hospital, Navamindradhiraj University. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and the Vajira Institutional Review Board approved the study protocol.

The patients who underwent bilateral oophorectomy during January 2009 and December 2013 were identified from the departmental surgical databases. The patients aged between 18 to 45 years old were included. Exclusion criteria were women who had residual ovarian tissue after surgery, had contraindications for HRT use such as breast cancer, deep venous thrombosis, poor controlled hypertension, diabetes, abnormal liver function, or had incomplete data.

Data collection

Data collection included age, height, weight, underlying diseases, history of smoking, indications for surgery, pathological results, and history of HRT use were collected from the patients' medical records and hospital databases. HRT use referred to the use of HRT starting within 3 month after the bilateral oophorectomy.

Statistical analysis

Data were analyzed using SPSS statistics software version 22.0 (IBM Corporation, Armonk, NY, USA). Continuous data were tested for normality using a histogram, normal Q-Q plot, and the Kolmogorov Smirnov test. Data were presented as median with range, mean with standard deviation (SD), or number with percentage. Pearson's Chi-square test was used to compare categorical variables. Univariable and multivariable analysis was used to determine the impact of factors on the HRT receiving. The *p*-value <0.05 was considered statistical significance.

Results

A total of 183 patients aged between 18 to 45 years old who underwent bilateral oophorectomy during the study period were identified. Eighteen patients were excluded due to the following contraindications: incomplete ovarian removal (9 patients), history of breast cancer (5 patients) or deep vein thrombosis (4 patients). From 165 patients who met inclusion criteria and were included in the present study, the median age was 40.6 years (range 24 to 45 years) and the median BMI was 24.3 kg/m^2 (range 23.8 to 40.2 kg/m^2). The main indications for bilateral oophorectomy were adenomyosis and/or endometriosis (54.5%), ovarian cancer (15.8%), and endometrial cancer (10.3%). There was one patient presented with huge abdominopelvic mass suspected ovarian cancer but the final pathological diagnosis was colon cancer. The demographic and clinical data are presented in Table 1.

The authors found 78 patients (47.3%) received postoperative HRT whereas 87 (52.7%) did not have any form of HRT. The 2 most common hormonal regimens were oral estrogen alone (44.9%) and oral estrogen combined with progestin (30.8%). The factors that significantly related to failure to receive HRT were the gynecologic malignancy and age older than 40 years (Table 2). After adjusting for BMI, smoking and underlying disease, gynecologic malignancy and age older than 40 years remained significant. The odds ratios were 15.51 (95% CI, 5.92 to 40.67) and 3.81 (95% CI, 1.57 to 9.26) respectively (Table 3).

Discussion

Young patients who had surgical menopause should receive HRT to alleviate menopausal symptoms and to prevent long-term degenerative diseases[12-15]. The present study demonstrated that more than half of women who underwent bilateral oophorectomy did not have HRT. Significant factors related to the failure of receiving HRT were gynecologic malignancy and age older than 40 years.

There were a few reasons why gynecologic cancer patients did not have HRT. The general objective of physicians who treated patients with cancers is generally a cure for cancer. Surveillance of cancer recurrence after treatment was commonly practiced whereas a concern about the long-term health impact from estrogen deficiency might be lowered

Table 1. Demographic characteristic of women who underwent bilateral oophorectomy (n = 165)

Characteristic	
Age (years), median (range)	40.6 (24 to 45)
BMI (kg/m^2), median (range)	24.3 (23.8 to 40.2)
Indication for bilateral oophorectomy, n (%)	
Adenomysis and/or endometriosis	90 (54.5)
Uterine leimyoma	13 (7.9)
Tubo-ovarian abscess	5 (3.0)
Ovarian cancer	26 (15.8)
Endometrial cancer	17 (10.3)
Cervical cancer	13 (7.9)
Colon cancer	1 (0.6)
Pathological results, n (%)	
Benign	108 (65.5)
Malignant	57 (34.5)
Receive HRT, n (%)	78 (47.3)
Oral estrogen	35 (21.2)
Transdermal estrogen	1 (0.6)
Oral estrogen plus progesterone	24 (14.6)
Tibolone	18 (10.9)
Smoking, n (%)	4 (2.4)
Underlying disease, n (%)	
Hypertension	16 (9.7)
Diabetes mellitus	6 (3.6)
Dyslipidemia	8 (4.8)
Others	10 (6.1)

Other underlying diseases = acquired immune deficiency syndrome, systemic lupus erythematosus, migraine, asthma, chronic myeloid leukemia, and hypothyriodism

Table 2. Factors related with failure to receive HRT after bilateral oophorectomy (n = 165)

Characteristic	n = 165		
	HRT (%)	No HRT (%)	*p**
Age group (years)			0.047
≤40	34 (43.6)	25 (28.7)	
>40	44 (56.4)	62 (71.3)	
BMI (kg/m^2)			0.181
<25	51 (65.4)	48 (55.2)	
≥25	27 (34.6)	39 (44.8)	
Pathological result			<0.001
Benign	70 (89.7)	38 (43.7)	
Malignancy	8 (10.3)	49 (56.3)	
Smoking	1 (1.3)	3 (3.4)	0.366
Hypertension	4 (5.1)	12 (13.8)	0.060
Diabetes mellitus	1 (1.3)	5 (5.8)	0.126
Dyslipidemia	6 (7.7)	2 (2.3)	0.107

* χ^2 test
BMI = body mass index

priority. Furthermore, the risks and benefits of HRT in hormone responsive gynecologic malignancy after surgical treatment had not been well elucidated with inadequate evidence-based data[16-18]. Hence, some doctors may be reluctant to prescribe the HRT to patients with gynecologic cancers.

Regarding the age older than 40 years as another significant factor related to failure to have HRT, one possible factor was the awareness of the physician about the relationship of the duration of estrogen deficiency and degree of health impact: the longer estrogen deficiency, the greater health impact. Another possible reason was older women may readily have relative contraindications for HRT use.

The authors were aware of some limitations in this study. First, number of patients in the present study was quite limited. This was due to a limitation in data collection in the remote past because of the administrative management of the hospital's archive of patients' records. Second, being a retrospective study, some data which might relate to the outcome of interest were not available in the patients' record e.g. socio-economic and education backgrounds, and attitude of the women. Few studies reported that Thai patients declined to receive HRT because they lacked sufficient knowledge on surgical menopause and HRT or they had some personal misbelief toward HRT[19-21].

Nevertheless, the present study added more data regarding the prevalence and related factors of failure to receive HRT among Thai women. Further study in a large group of Thai women is needed to add information for the optimal patient's care. Other factors that might affect failure to receive HRT-such as the patients' attitude toward HRT, knowledge and socioeconomic status should also be assessed in a prospective study.

Table 3. Univariable and multivariable analyses to determine odds ratio for risk factors related with failure to receive HRT after bilateral oophorectomy

	Crude OR (95% CI)	Adjusted OR* (95% CI)
Age group (years)		
≤40**	1	1
>40	1.916 (1.006 to 3.652)	3.807 (1.565 to 9.259)
BMI (kg/m^2)		
<25**	1	1
≥25	1.535 (0.818 to 2.880)	1.360 (0.606 to 3.054)
Pathological result		
Benign**	1	1
Malignant	11.283 (4.845 to 26.274)	15.510 (5.915 to 40.672)
Smoking		
No**	1	1
Yes	2.750 (0.280 to 26.999)	1.925 (0.159 to 23.327)
Hypertension		
No**	1	1
Yes	2.960 (0.913 to 9.597)	3.693 (0.848 to 16.086)
Diabetes mellitus		
No**	1	1
Yes	4.695 (0.536 to 41.098)	7.112 (0.294 to 172.268)
Dyslipidemia		
No**	1	1
Yes	0.282 (0.055 to 1.442)	0.122 (0.012 to 1.265)

* Adjusted for other variables in table, ** Reference group
CI = confidence interval; OR = odds ratio

Conclusion

The prevalence of failure to receive HRT after bilateral oophorectomy in women younger than 45 years was 52.7%. Factors related with this situation were gynecologic malignancy and age older than 40 years. Other factors that might affect failure to receive HRT-such as the patients' attitude toward HRT, knowledge and socioeconomic status should be further explored.

What is already known on this topic?

Menopausal status can affect women's health in terms of menopausal symptoms, cardiovascular or neurologic diseases, and osteoporosis. Expert panels recommended that all women who undergo menopause under the age of 45 years and without contraindications to hormonal therapy to use HRT until the average age of the natural menopause to prevent health impact due to estrogen deficiency.

What this study adds?

As many as half of the patients aged younger than

45 years, who had undergone bilateral oophorectomy failed to receive HRT. Factors that were significantly related to failure to receive HRT included gynecologic malignancy and age older than 40 years.

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Potential conflicts of interest

The authors declare no conflict of interest.

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