Effect of Hysterectomy on Conserved Ovarian Function

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The aim of this study was to assess the impact of premenopausal Total Abdominal Hysterectomy (TAH) on the function of the remaining ovaries by reviewing the menopausal age in TAH treated patients.

We retrospectively reviewed the medical records of 510 women who had previously undergone TAH, either with or without unilateral salpingo-oophorectomy, due to benign disease at the department of Obstetrics and Gynecology, Yonsei University College of Medicine, between Jan 1989 and Dec 1992. Out of the 510 women, the 94 who were throughly followed up were included in the study, and their menopausal age based on patient symptoms was compared to that of the control group.

The mean menopausal age in TAH treated patients was significantly lower than that of the control group (P < 0.001). There was a positive correlation between age at operation and menopausal age.

From this study, we could conclude that TAH accelerated ovarian dysfunction, and that the younger the patient was at the time of operation, the earlier the onset of menopause. It is hence apparent that women treated with TAH are at risk of early menopause and should receive adequate hormone replacement therapy.

Key Words: Hysterectomy, ovarian function

INTRODUCTION

The issue of conserving the ovaries at total abdominal hysterectomy in premenopausal women with benign gynecologic disease has been the subject of considerable controversy.[1-5] On the side there is the need for prophylactic oophorectomy in menopausal women undergoing hysterectomy to prevent future development of malignant change.[6-10] On the other hand, some clinicians prefer to conserve apparently normal ovaries because if they are removed during hysterectomy, then patients will mandatory require long-term hormonal replacement therapy due to the lengthened life-span, which will eventually lower the compliance rate.[11] Futhermore, the endocrinologic function of the postmenopausal ovary-secretion of androgen and testosterone-should not be neglected.[12-14]

Bilateral oophorectomy in premenopausal women results in an abrupt decline in the serum hormonal level which leads to a severe endocrinologic imbalance and therefore the onset of sudden menopausal symptoms and decreased libido owing to the decreased levels of androgen and testosterone.[15,16] Therefore, it has become accepted to preserve the ovaries at hysterectomy, provided that the patient is not at high risk for ovarian cancer, not contraindicated for HRT, has not undergone treatment with fertility agents, and has not presented any evidence of pathologic conditions of the ovaries in the operative field.

Clinicians always question whether or not to preserve apparently normal ovaries when performing hysterectomy due to benign gynecologic disease. There have been several reports on premenopausal loss of endocrinologic function in conserved ovaries[17-20] and on the effect of simple tubal ligation on ovarian function.[21] In the study, we investigated and compared the mean menopausal age of patients treated with hysterectomy to that of a normal control group to assess the effect of hysterectomy on the function of preserved ovaries.

MATERIALS AND METHODS

The medical records of 510 premenopausal women aged between 35 and 45, who had undergone hysterectomy with or without unilateral oophorectomy for a non-malignant gynecologic disease at the department of Obstetrics and Gynecology, Yonsei University College of Medicine, between January, 1982 and December, 1992, were reviewed. Ninety-four women out of the total 510 who were followed up were selected. Total abdominal hysterectomy had been performed in all patients. Those who had previously undergone intrapelvic operations such as cesarean section, myomectomy, and benign ovarian cystectomy, as well as those with a past history of diabetes mellitus, thyroid disease, or hormonal therapy, were all excluded from the study. The control group consisted of 150 women who had undergone spontaneous menopause (hence referred as the non-hysterectomized group) and visited the postmenopausal clinic of the department of Obstetrics and Gynecology, Yonsei University College of Medicine in May, 2000.

In the study group, menopausal age was determined by measuring serum FSH concentration (> 40IU/mL) at the time of onset of acute symptoms such as hot flushes, fever, sweating, palpitation, and vaginal dryness. Comparisons and levels of significance were assessed between the average menopausal ages of the hysterectomized group and the control group, of the hysterectomized women with preserved ovaries and the hysterectomized women with unilateral oophorectomy, and of the hysterectomized women with previous tubal ligation history and those without. Also

evaluation was the correlation of Body Mass Index (BMI) to average menopausal age.

The Student's t-test was used to compare the differences in means between the groups, Pearson correlation analysis to compare BMI and menopausal age, and regression analysis to determine the correlation between age at hysterectomy and menopausal age. $P < 0.05$ was considered significant.

RESULTS

Mean menopausal age for the control and study groups

The mean menopausal ages in the control group and the hysterectomized group were 48.1 ± 3.2 years and 46.3 ± 3.0 years, respectively; the latter being significantly lower ($p < 0.001$) (Fig. 1).

Mean menopausal age following unilateral oophorectomy

The mean menopausal age of the 19 patients who had undergone hysterectomy only was 45.4 ± 2.6 years and that of the 75 patients who had undergone unilateral salpingo-oophorectomy was 46.5 ± 3.1 years, a difference that was not significant ($p > 0.05$) (Table 1).

Mean menopausal age following tubal ligation

The mean menopausal ages of the 29 women who had received tubal ligation and the 65 women who had not were 46.8 ± 3.0 years, and
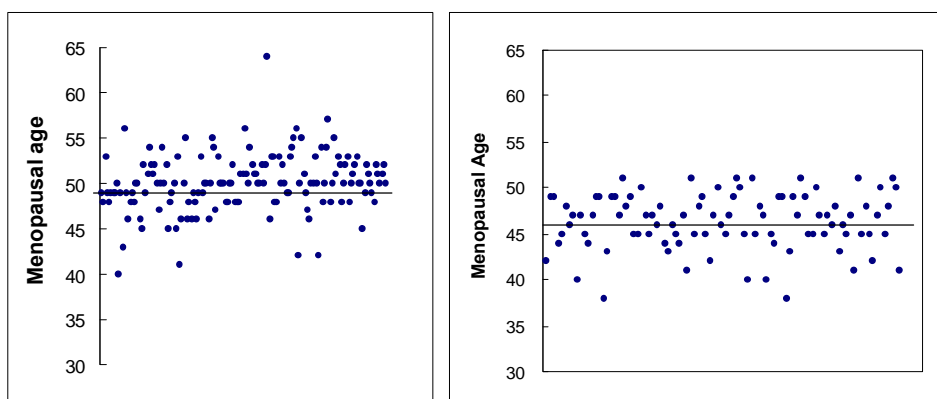

Fig. 1. Scattergram of the age at menopause in 150 women who had undergone a spontaneous menopause and in 94 women after TAH / TAH with USO ($p < 0.01$)

Table 1. The Age Distribution of the Patients Group and the Ages at Menopause after TAH/TAH with USO

Age at operation*	TAH	TAH with USO	Age at menopause*
35	0		
		3	46,38,38
36	6		44,40,40,44,45,45
		4	45,45,42,42
37	3		44,46,46
		5	42,41,40,41,41
38	0		
		4	46,46,47,47
39	2		47,47
		9	46,43,45,45,43,45,45,47,47
40	2		47,47
		2	48,49
41	6		50,50,45,45,45,45
		12	45,45,45,45,49,49,47,45,49,49,44,44
42	0		
		10	48,48,49,47,47,43,43,51,51,48
43	0		
		16	47,45,47,45,49,49,48,48,47,48,48,49,51,49,51,51
44	0		
		8	51,51,50,50,49,47,50,50
45	0		
		2	49,49
Mean age*	45.4 ± 2.6	46.5 ± 3.1	46.3 ± 3.0

*Age: years.

46.0 ± 6.0yrs, respectively, a difference which showed no statistical significance (Table 1).

Mean menopausal age and body mass index

No statistical significant difference was found between the increase in BMI and menopausal age ($p > 0.05$) (Fig. 2).

Mean menopausal age and the age at the time of operation

Younger patients at the time of surgery experienced earlier menopause, and this relationship showed as a positive correlation between the age at the time of surgery and the age at menopause ($p < 0.05$). Menopausal age was significantly correlated to the age at hysterectomy (r=0.7841, $p <$

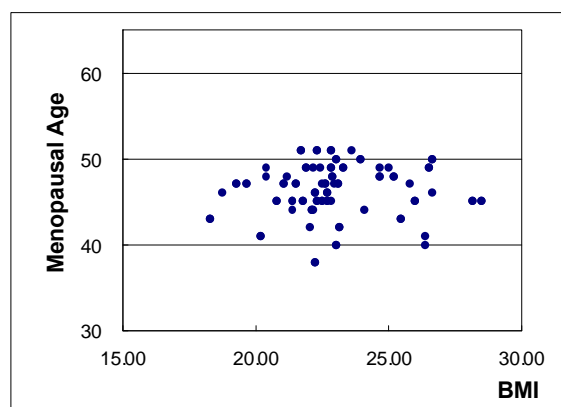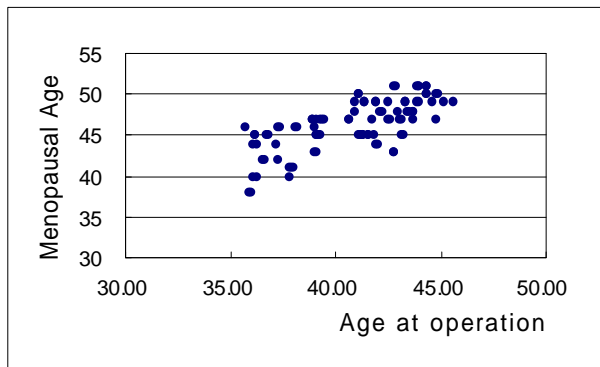0.01). The average time interval between surgery and the age at menopause was 5.5 ± 2.2 years (Fig. 3).

Fig. 2. Relationship between menopausal age and BMI in patients treated with TAH. ($p > 0.05$)

Table 2. Menopausal Age in Patients Treated with TAH, TAH with Unilateral Salpingo-oophorectomy and Tubal Ligation (TL)

	TAH	TAH c USO	TL	Non-TL
Menopause*	45.3 ± 2.6	46.5 ± 3.1	46.8 ± 3.0	46.0 ± 3.0
p-value†	$p > 0.05$		$p > 0.05$	

*age; mean ± SD.
†student t-test.

Fig. 3. Relationship between menopausal age and age at operation ($p < 0.05$, coefficient variants=0.7841, p=0.01).

DISCUSSION

The average menopausal age of women who had undergone hysterectomy with preservation of bilateral or unilateral ovary, 46.3 ± 3.0 years, was significantly younger than the natural menopausal age of 49.1 ± 3.2 years ($p < 0.001$). The patients, all under 45 years of age, were at premenopausal status at the time of surgery, which suggests that hysterectomy hastens the onset of menopause.

The precise mechanism of premature menopause in women treated by hysterectomy has not been clarified but it is thought to involve an acceleration of ovarian dysfunction. There are studies documenting close utero-ovarian association and functional alteration following hysterectomy via its effect on ovarian blood flow.[22]

Souza et al.[23] reported hypertrophied tunica albuginea in ovarian tissues obtained both during hysterectomy and laparoscopically 1 year following hysterectomy. They also reported stromal hypertrophy with decreased follicular reserve. Biro et al.[24] demonstrated higher FSH concentration in plasma from ovohysterectomized rats than from ovariectomized rats, without an equivalent

alteration in the plasma LH concentration, suggesting the presence of FSH-inhibiting substance in the uterine extract. When the endometrium was intact and menstruated in the case of partial hysterectomy, the ovary showed better function. Based on this observation, Sessume et al.[19,25] extracted the uterus from a rabbit and subsequently implanted endometrial tissue in the abdomen. One year after the operation, the ovaries were examined. The ovaries of the rabbits with the implanted endometrium had a 40% higher number of follicles.

Derksen et al.[26] supported Sessume's report by demonstrating increased serum FSH levels at 6 weeks, 6 months, and 1 year following either simple hysterectomy or endometrial ablation in premenopausal women. On the contrary, Ylikorkala et al.[27] reported normal cyclic variation in the levels of serum LH, FSH, estradiol, and progesterone, in women with Mayer-Rokitansky-Kuster-Hauser syndrome; a syndrome characterized by congenitally absent uterus and anatomically normal ovaries. They concluded that uterus presence does not affect the ovarian function.

There are reports explaining the reason for premature menopause following hysterectomy as being due to alterations in the hemodynamics of ovarian circulation resulting from the intervention. The ovarian function in hormone production depends on the ovarian blood supply.[19,21] By ligating the uterine artery during hysterectomy, the blood flow to the medial aspect of the ovary is affected. The ovarian arteriole pressure increases, leading to vascular hypertension followed by constriction of arterioles which results a progressive decrease in ovarian circulation and consequent ovarian tissue damage. Stone et al.[28] reported a decrease in circulating serum estradiol level from 60 pg/mL to 20 pg/mL following

hysterectomy but not after diagnostic laparoscopy. Janson et al.[29] measured the change in ovarian blood flow before and immediately after hysterectomy using the [133]Xenon clearance method and found a blood flow reduction from 89% to 52%. -which supports the hypothesis that vascular damage results in ovarian dysfunction.

Sessume et al.[19] observed an earlier onset of ovarian dysfunction in their unilateral oophorectomy group than the bilateral ovary-conserved group and concluded that ovarian function is correlated with the amount of ovarian tissue preserved. To the contrary, in our own study, we found no significant difference in menopause age between patients who had bilateral ovaries preserved and those who had unilateral ovary preserved. Therefore, the results of our study do not support any correlation between endocrinologic function and the amount of ovarian tissue preserved. They support the hypothesis that the conservation of a small amount of ovarian tissue has its own endocrinologic function.[30]

Because the ovarian artery derived from the uterine artery runs adjacent to the fallopian tube at the isthmus portion, Some studies have reported that it could be damaged or accidentally ligated with the fallopian tube at the time of tubal ligation, and so lead to ovarian dysfunction via vascular hypertension.[21] But based on our study, no statistically significant difference in menopausal age was noted between hysterectomized patients who had had previous tubal ligation and those who had not (46.1 yrs vs. 46.9 yrs, $p > 0.005$). This lack of correlation may be due to the performance of hysterectomy before the ovarian dysfunction related to tubal ligation could take place.

Serum estrogen level decreases from 50 - 300 pg/mL before menopause to below 100 pg/mL following menopause. After menopause, androgen and testosterone produced from the adrenal gland and climacteric ovary are converted into estrogen in fat cells and muscle cells. It is generally expected that women with increased body mass index will experience delayed onset of menopause due to increased conversion of androgen to estrogen.[28] However, our study showed no significant correlation between the body mass index and age of onset of menopausal symptoms.

The body weight of the study group did not vary throughout the 10 years of follow up. The following reasons amy account for this result. Firstly, obesity is generally defined as a BMI of greater than 30, but the study group was lacking in obese patients. Secondly, the premenopausal serum estrogen level in the high BMI group was lower than that in the low BMI group, and also lower than the postmenopausal level in the high BMI group. Although the postmenopausal serum level of estrogen was higher than that in the low BMI group, its absolute level was not high enough to have any effect on the menopausal age.[31]

Our study supports the many previous study findings that patients who are younger at operation go on to experience a younger age of menopause onset.[19,22] The women in our study experienced menopause 3 to 7 years following operation (mean 5.5 ± 2.2 years). Ovarian tissue damage caused by disturbances in ovarian microcirculation may induce compensatory hormone production which reaches a limit at 3 - 7 years following surgery, thus enabling the depletion of follicular reserve to lead to menopause. From the results of this study it is apparent that hysterectomy has a negative effect on preserved ovarian function. Consideration should also be given the patients, especially younger ones may experience premature menopause following surgery. Although ovarian dysfunction is expected after surgery, the endocrinologic function is still preserved for a certain period of time. Therefore, conserving both ovaries represents a better approach than prescribing long term hormonal replacement therapy following bilateral oophorectomy, unless the patient is at a high risk for ovarian cancer.

We advocate education of the patient, prior to surgery, about the possible occurrence of premature ovarian failure and the associated symptoms, in order to ensure that effective hormonal replacement therapy is started at the onset of menopausal symptoms.

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