



The effects of tubal sterilization on menopausal age in a cohort of postmenopausal women

Utku AKGÖR^{1,*}, Samet KİRAT², C. Ekrem TOK³

¹Department of Gynecologic Oncology, Ankara Teaching and Research Hospital, Ankara, Turkey

²Department of Obstetrics and Gynecology, Faculty of Medicine, Kafkas University, Kars, Turkey

³Department of Obstetrics and Gynecology, Private City Hospital, Mersin, Turkey

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Abstract

To evaluate whether tubal sterilization (TS) has an adverse effect on menopausal age in a cohort of postmenopausal women. The medical records on TS were gathered from 1,228 postmenopausal women in menopause clinic at a tertiary hospital. The age at menarche, the parity, smoking and secondhand smoking status and mother's age at menopause did not show any significant difference between the groups. Likewise, marital status, educational and yearly income levels were comparable ($P > 0.01$). Although the mean BMI ($P = 0.06$) and the rate of oral contraceptive use ($P = 0.09$) were tended to be higher in non-TS women than in TS group, the difference did not reach statistical significance. The ever use of intrauterine device rate was significantly lower in TS group than in non-TS group ($P < 0.001$). The TS women, in comparison with the non-TS women had undergone earlier natural menopause ($P < 0.001$). The age at menopause had an inverse correlation with TS, and positive correlation with mother's age at menopause in univariate analyses. However, there was marginally significant correlation between secondhand smoking and age at menopause. Linear stepwise regression analyses revealed that TS and mother's age at menopause were independent predictors of age at menopause ($P < 0.05$). We found an earlier age at menopause in women with TS in this study. In this regard, this is the first report about the age at menopause in women with TS, as far as we know.

Keywords: menopausal age, tubal sterilization, menopause

1. Introduction

Tubal Sterilization (TS) is an irreversible way of the contraceptive method performed at the will of patients that have completed the fertility aspect (1). Although it is a highly effective and safe procedure, the existence of a series of symptoms referred to as post tubal sterilization syndrome has been debated (2, 3). It has been suggested that diminished blood flow due to the damaged vascular supply to the ovaries may cause ovarian dysfunction and decreased estrogen/progesterone production after TS (4, 3). This may even results premature loss of ovarian function, as reported in women who undergo hysterectomy with ovarian conservation (5). Since the first report of post tubal sterilization syndrome in 1951 by Williams et al. (6), any presence of ovarian reserve change has been extensively studied by many authors (7-9).

Several ovarian reserve tests, imaging methods and questionnaires were used to assess ovarian function after TS in many studies with conflicting results. Furthermore, these methods are amenable to subjective changes, making them unreliable for the determination of any deterioration in ovarian function. Anti-mullerian hormone (AMH) level is considered

as a reliable and objective marker for prediction of ovarian reserve. However, even the studies that used AMH for the prediction of ovarian reserve after TS, yielded conflicting results (10-13).

There are also scanty reports investigating the effect of TS on women's health later in life. TS was found to be associated with decreased bone mineral density in elderly women (14, 15). Furthermore, some authors proposed increased menopausal complaints in women who had been operated on for TS (16, 17). The aim of the current study was to evaluate whether tubal ligation has an adverse effect on menopausal age in a cohort of postmenopausal women.

2. Materials and Methods

2.1. Subjects

The study included women who experienced natural menopause at an age > 40 years. Retrospective information on TS was gathered from 1,228 postmenopausal women who attended to our menopause clinics between April and October 2014. Natural menopause was defined according to the World Health Organization as at least 12 consecutive months of

* Correspondence: utkuakgor@gmail.com

amenorrhea not due to surgery or other obvious cause, such as extreme weight loss (18). Women who reported that they had had a hysterectomy or oophorectomy (unilateral vs. bilateral was not specified, since in pretests women could not distinguish between the two) were excluded. Informed consents were obtained from all participants of this study. This project was approved by the local ethical committee of Mersin University (2014) and informed consent was obtained from all patients and controls according to the Declaration of Helsinki (revised in 2013).

2.2. Data collection

All independent variables of interest were obtained by self-report during the interview. Information regarding socio-demographic status (educational attainment, employment, marital status, ability to pay for basics), reproductive (age at menopause, age at menarche, parity, and oral contraceptive (OC) use), medical history, and lifestyle factors (smoking, physical activity).

The mother's age at menopause was retrieved mainly with interview of the subjects, and 1037 women of 1228 (84.4%) could provide information about this subject. Body mass index (BMI) was calculated as weight in kg divided by height in m². Due to similar ethnic background, ethnicity was not considered in the analyses.

The participants' educational level was divided into two levels: < high school and > high school. Marital status was categorized as: married, unmarried, widowed, or divorced or separated. The yearly income levels separated into two groups according to the national poverty line which was determined by the government: low and mid-to-high income levels.

The women were asked about current or past smoking, and women who smoked tobacco for more than one year were classified as "ever-smokers". Passive smoking status was collected by environmental tobacco smoke (ETS) questionnaire of International Agency for Research on Cancer. The questionnaire was validated by Nyberg et al. (19).

2.3. Statistical Analyses

Data were analyzed using SPSS for Windows 20.0 Demo. Data are shown as mean \pm SD or as the number and percentage of subjects. Regarding baseline characteristics, if the distribution was normal, Student's t test was used for comparisons of variables, and the Mann-Whitney U test was used for variables that showed a skewed distribution. Dichotomous variables were analyzed by X² test. Pearson correlation was used to assess associations between the variables. Linear stepwise regression analysis was used to identify variables that best predicted the age at menopause. Statistical significance was defined as an alpha level at or below 0.05.

The analysis of first 200 patients showed that about 7% of patients had chosen TS as a contraceptive method. Regarding this ratio, assuming that women with TS experience two years earlier menopause (48 years vs 46 years with an SD of

approximately 5 years), the power analysis dictated that 88 women in TS group and 1140 women in control group should be included at 5% significance level with 80% power (G*Power v3.1.7 Power Analysis Software).

3. Results

Demographic characteristics of women included in the study are shown in Table 1. The age at menarche, the parity, smoking and secondhand smoking status and mother's age at menopause did not show any significant difference between the groups. Likewise, marital status, educational and yearly income levels were comparable (Table 1, P > 0.01).

Although the mean BMI (27.9 ± 4.0 vs. 27.1 ± 3.8 , P = 0.06) and the rate of oral contraceptive use (63.5% vs. 54.6%, P = 0.09) were tended to be higher in non-TS women than in TS group, the difference did not reach statistical significance. The ever use of intrauterine device rate was significantly lower in TS group than in non-TS group (21.6% vs 43.5%, respectively, P < 0.001). The TS women, in comparison with the non-TS women had undergone earlier natural menopause (46.4 ± 2.8 vs. 48.4 ± 3.7 , respectively, P < 0.001).

Table 1. The characteristics of women with and without tubal sterilization (TS)

	TS group n = 88	Non-TS group n = 1140	P
Age at menopause (years)	46.4 \pm 2.8	48.4 \pm 3.7	<0.001
Age at menarche (years)	13.2 \pm 1.3	13.3 \pm 1.4	0.91
Body mass index (kg/m ²)	27.1 \pm 3.8	27.9 \pm 4.0	0.06
Parity	2.7 \pm 1.8	2.7 \pm 1.5	0.71
Ever oral contraceptive use	48 (54.6%)	724 (63.5%)	0.09
Ever intrauterine device use	19 (21.6%)	496 (43.5%)	<0.001
Ever-smoker	25 (28.4%)	327 (28.7%)	1.0
Secondhand smoking	53 (60.2%)	712 (62.5%)	0.68
Mother's age at menopause (years)	47.3 \pm 3.6	48.1 \pm 3.8	0.14
Marital status (married)	74 (84.1%)	1018 (89.3%)	0.13
Educational level (high school)	18 (20.5%)	223 (19.6%)	0.84
Yearly income level (medium-to-high)	74 (84.1%)	910 (79.8%)	0.93

Table 2 presents the results of Pearson correlation tests and linear stepwise regression analyses between the variables. The age at menopause had an inverse correlation with TS, and positive correlation mother's age at menopause in univariate analyses (Table 2, P < 0.05).

However, there was marginally significant correlation between secondhand smoking and age at menopause. Linear stepwise regression analysis revealed that TS and mother's age at menopause were independent predictors of age at menopause (P < 0.05, Table 2).

Table 2. Bivariate correlations and linear stepwise regression models of clinical variables on age at menopause

	Bivariate correlations		Linear stepwise regression models *		
	R	P	B-coefficient	Standard error of regression coefficient	P
Tubal sterilization	-0.135	<0.001	-2.108	0.464	0.001
Age at menarche (years)	-0.005	0.86			
Body mass index (kg/m ²)	-0.017	0.56			
Parity	-0.021	0.46			
Oral contraceptive use	-0.019	0.51			
Intrauterine device use	0.008	0.77			
Ever smoking	0.004	0.89			
Secondhand smoking	-0.051	0.07			
Mother's age at menopause	0.297	<0.001	0.279	0.034	0.001
Marital status	0.010	0.74			
Educational level	0.011	0.70			
Yearly income level	0.010	0.72			

* Only the statistically significant variables were expressed in the regression model.

4. Discussion

The most consistent finding on age of menopause is that smokers have about 1.5 years earlier menopause before nonsmokers. Available studies are less clear regarding the relation of other factors to age at menopause. With varying frequency, studies have found less education, low relative weight, nulliparity or having few children, and not using oral contraceptives to be associated with an earlier menopause (20). In this study, we found TS as another possible cause of earlier menopause in both correlation and regression analyses. Women with TS in their history had experienced about 2 years earlier menopause than women without TS (46.4 ± 2.8 vs. 48.4 ± 3.7 , respectively, $P < 0.001$). Regression analyses also showed TS as an independent risk factor for earlier menopause along with the mother's age at menopause.

Existing studies in the literature investigated short term effects of TS on menopausal age. Dede et al. (21) followed the patients for three months and found that there was no statistically significant difference in the serum FSH, LH and estradiol levels in preoperative and postoperative assessments, in fact, they proposed an improvement in ovulatory rate after

the procedure. In another study from Turkey, on short-term follow-up (3 months), laparoscopic bipolar electrodesiccation and transection of tubes does not have a negative impact on ovarian reserve, revealed by insignificant changes in AMH, FSH, LH, and E2 levels, ovarian volume, and AFCs (10). Contrary, LH levels were found significantly higher, and progesterone levels significantly lower in another study with the observation period of three months. The authors tied this low level of progesterone to deficient production by the corpus luteum, probably caused by vascular changes after TS (22).

Changes in menstrual patterns and ovarian reserve after TS have been attributed to damage to the ovarian blood vessels leading to reduced ovarian blood supply. Earlier studies raised this question of ovarian vascular deterioration after the procedure. Sixteen laparoscopic tubal sterilizations using filshie clips were performed, and ovarian and uterine artery Doppler measurements were evaluated before and after surgery with 90 days follow-up. They found an increased vascular resistance both in ovarian and uterine arteries following the sterilization procedure (23). However, many aftercoming studies failed to reveal any vascular flow disorders by Doppler analyses (24, 25). But, Doppler studies may not be sensitive enough to reveal any disturbances to ovarian vascular blood supply due to tubal sterilization.

Many cohort and case control studies about menstrual function after tubal sterilization often failed to control for confounding factors such as previous contraceptive use, previous menstrual pattern, and advancing age, all of which can affect menstrual patterns. Furthermore, observation period changed generally from 3 to 12 months which may not be capable enough to reveal any distortion to ovarian function. The Collaborative Review of Sterilization study found that, over a 5-year follow-up period, women who had undergone tubal ligation were more likely to experience a shortening of the duration of menses, a decrease in volume of menstrual flow, greater dysmenorrheal pain and an increase in cycle irregularity compared with those whose partners were sterilized (26). As a continuum of this study, the patients were followed-up to 14 years after sterilization, and it was found that women who underwent sterilization were likely to have decreases in the amount of bleeding, the number of days of bleeding, and the amount of menstrual pain and an increase in cycle irregularity (27).

Four years later, the subjects with tubal sterilization, who were now closer to the perimenopausal age range of 45–54 years were re-examined with respect to menopausal status, vasomotor and somatic symptoms and changes in menstrual patterns associated with the perimenopausal period (17). The author reported that women with TS had more flushing, they had higher psychological distress. Furthermore, the lifetime history of physician diagnosed depression was found marginally higher in those women. However, Nelson et al. (28) found that perimenopausal women with TS were not

significantly more likely to experience hormonal changes (FSH, LH, estradiol, testosterone, inhibin B) indicative of the transition to menopause or an increased severity of menopausal symptoms compared to the group of women without TS. Lastly, Wyshak (15) followed-up 3940 women for 15 years and observed that 3% of women with TS experienced vertebral fracture after age 20, whereas this rate was 1.6% in women without sterilization ($P = 0.027$). Among women aged 50 years and older, for the association between TS and vertebral fractures, the odds ratio was 2.7, for the association of chronic back pain was 3.3.

In conclusion; short-term follow-up studies could not reveal any conclusion in terms of ovarian function in women with tubal sterilization, because the end point in this situation is the menopausal age. We found an earlier age at menopause in women with TS in this study. In this regard, this is the first report about the age at menopause in women with TS, as far as we know. There are several reports indicating adverse outcomes of this procedure in perimenopausal women. However, prospective longitudinal studies have to be planned to reveal any association between TS and menopausal age.

Conflict of interest

None to declare.

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None to declare.

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