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Hysterectomy, Oophorectomy, and Heart Disease Risk Factors in Older Women

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ABSTRACT

Objectives. This study examined the relation of hysterectomy and oophorectomy to heart disease risk factors.

Methods. Data were collected and analyzed for 1150 women aged 50 through 89.

Results. Of these women, 21.8% reported hysterectomy with bilateral oophorectomy; 22.1%, hysterectomy with ovarian conservation. Compared with women without hysterectomy, oophorectomized women, especially those 20 or more years postmenopause, had increased lipids, lipoproteins, glucose, and insulin; blood pressures were increased among current estrogen users. Women with hysterectomies with ovarian conservation had similar or more favorable risk factors than nonhysterectomized women.

Conclusions. Bilateral oophorectomy, but not hysterectomy, may have long-term negative consequences for heart disease risk factors not totally ameliorated by estrogen use. (*Am J Public Health.* 1997;87: 676–680)

Introduction

Hysterectomy is the second most common surgical procedure in the United States[1]; approximately one third of all women have a hysterectomy by age 60.[2,3] In women who have completed their families, bilateral oophorectomy is often recommended to prevent ovarian cancer.[4]

Increased risk of heart disease and atherosclerosis after bilateral oophorectomy has been reported in several studies.[5–8] Hysterectomy with conservation of at least one ovary is less consistently associated with heart disease, with recent studies reporting no differences[5,7,9] and older studies reporting increased risk.[10,11] Studies comparing women before and after bilateral oophorectomy reported increases in low density lipoprotein (LDL).[12,13] Some studies reported no differences in high density lipoprotein (HDL) following bilateral oophorectomy[12,14,15]; others reported increases[16] or decreases.[13] Some[12,13] but not all[16,17] studies reported no differences in total cholesterol or triglycerides.

Most previous studies examined small samples close to the time of surgery, did not include hysterectomized women with ovarian conservation, and did not examine multiple heart disease risk factors. Only one large study[9] of hysterectomized women with and without bilateral oophorectomy examined lipids, glucose, and blood pressures; insulin was not examined.

We examined the association of hysterectomy and oophorectomy to lipids and lipoproteins, blood pressure, glucose, and insulin at a time relatively remote from surgery, in a large, community-based sample of older women.

Methods

Study Population

From 1972 through 1974, 82% of all adult residents in a middle-class southern California community (Rancho Bernardo) were surveyed for heart disease risk factors. Of these women, 1254 (82%) were seen from 1984 through 1987, when

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they were aged 50 through 89. After the exclusion of women who were not menopausal (n = 19), had not fasted 12 hours (n = 37), were using lipid-lowering medications (n = 12), or were missing information on hysterectomy (n = 10) or estrogen use (n = 26), there remained 1150 postmenopausal women, who form the basis of this report. All were ambulatory and gave written informed consent.

Data Collection

Participants were queried about smoking, alcohol consumption (mL per week), physical activity (exercise ≥ 3 times/wk), and menopausal history, including date of last menses, type of menopause (natural or surgical), and, in the case of hysterectomy, date and number of ovaries removed. The reason for hysterectomy or oophorectomy was not ascertained. Age at menopause was defined as age at last menses for women without hysterectomy and age at surgery for hysterectomized women with bilateral oophorectomy. In hysterectomized women with ovarian conservation, age at menopause was defined as the age when estrogen replacement was initiated or, for hysterectomized women who never used estrogen, as age 50, the average age of natural menopause in this cohort. Years postmenopausal was defined as current age minus age at menopause. Medication use was confirmed by prescriptions or pills brought to the clinic.

Body mass index (kg/m^2) and waist-hip ratio (cm/cm × 100) were used to estimate obesity and central adiposity, respectively. Blood pressure was measured twice by a certified technician using the hypertension detection follow-up protocol. A 75-g oral glucose tolerance test was performed.

Fasting cholesterol and triglycerides were measured by enzymatic techniques; HDL was measured with Lipid Research Clinic procedures[18]; and LDL was calculated using the Friedwald formula.[19] Fasting and 2-hour glucose were measured by an oxidase method and insulin by radioimmunoassay.[20] Insulin levels were available for subjects seen after November 4, 1985 (n = 824 for fasting, n = 774 for postchallenge).

Data Analysis

Age-adjusted (1-year units) comparisons and means for each risk factor after adjustment for age and other covariates were calculated by hysterectomy and oophorectomy status with the use of analysis of covariance. For each heart-disease risk factor, regression analyses with contrast coding compared both groups of hysterectomized women with women without hysterectomy, after adjustment for covariates and after stratification by current estrogen use and by years postmenopausal (≤10, 11 through 19, ≥20). To correct skewness, triglyceride and insulin analyses were performed on log-transformed data, with antilogs presented. All statistical tests are two-tailed.

TABLE 1—Comparison of Age and Other Covariates for 1150 Women Aged 50 through 89, by Hysterectomy and Oophorectomy Status: Rancho Bernardo, Calif, 1984 through 1987

		Hysterectomy	
	No Hysterectomy (n = 645)	Ovarian Conservation (n = 254)	Bilateral Oophorectomy (n = 251)
Age, y	70.5	69.5	69.5
Body mass index, kg/m^2	24.2	24.3	24.4
Waist-hip ratio	79.5	79.9	79.2
Age at menopause, y	49.9	46.5***	48.7
Years menopausal	19.9	23.3***	20.8
Alcohol consumption, mL/wk	84.0	86.1	74.2
Regular exercise, % yes	19.7	17.7	19.9
Ever smoked, % yes	33.5	29.1	33.5
Current estrogen, % yes	20.8	40.6***	44.6***

***$P < .001$ for comparisons with women without a hysterectomy.

TABLE 2—Adjusted Means[a] for Each Heart Disease Risk Factor for 1150 Women Aged 50 through 89, by Hysterectomy and Oophorectomy Status: Rancho Bernardo, Calif, 1984 through 1987

		Hysterectomy	
	No Hysterectomy (n = 645)	Ovarian Conservation (n = 254)	Bilateral Oophorectomy (n = 251)
Cholesterol, mg/dL	228.4	229.1	229.4
High density lipoprotein, mg/dL	68.8	68.2	68.6
Low density lipoprotein, mg/dL	139.4	137.4	137.0
Triglycerides,[b] mg/dL	100.0	104.7	107.2**
Systolic blood pressure, mmHg	139.0	139.2	141.3
Diastolic blood pressure, mmHg	75.2	75.4	75.3
Fasting glucose, mg/dL	98.1	99.4	97.9
Postchallenge glucose, mg/dL	136.7	140.0	146.5***
Fasting insulin,[b,c] μ units/mL	10.5	9.8	10.0
Postchallenge insulin,[b,d] μ units/mL	75.9	70.8	81.3*

[a]Means adjusted for age, body mass index, and current estrogen use.
[b]Statistics performed on $\log_{10}$ triglycerides, fasting insulin, and postchallenge insulin; antilogs presented.
[c]Based on 450 women without hysterectomy, 192 with hysterectomy and ovarian conservation, and 182 with bilateral oophorectomy.
[d]Based on 418 women without hysterectomy, 186 with hysterectomy and ovarian conservation, and 170 with bilateral oophorectomy.
*$P < .06$ for comparisons with women without a hysterectomy.
**$P < .05$ for comparisons with women without a hysterectomy.
***$P < .01$ for comparisons with women without a hysterectomy.

Results

These 1150 women had an average age of 71 years (SD = 9.0) and were an average of 21 years postmenopause (SD = 11.4, range = <1 year to 61 years); 30% were currently using estrogen. Over-

TABLE 3—Multiply Adjusted Comparisons of Each Heart Disease Risk Factor by Hysterectomy and Oophorectomy Status for All Women and, after Stratification, by Current Estrogen Use and Years Postmenopausal, for 1150 Women Aged 50 through 89: Rancho Bernardo, Calif, 1984 through 1987

	Hysterectomy			
	Ovarian Conservation		Bilateral Oophorectomy	
	β	95% CI	β	95% CI
All women[a,b,c] (n = 1150)				
Cholesterol, mg/dL	−3.47	−8.1, 1.1	3.59	−1.0, 8.2
HDL, mg/dL	−0.28	−2.3, 1.7	−0.26	−1.8, 2.3
LDL, mg/dL	−3.59	−7.9, 0.8	2.38	−2.0, 6.8
Triglycerides,[d] mg/dL	1.00	−1.1, 1.1	1.10*	1.0, 1.1
Systolic blood pressure, mmHg	−1.32	−3.6, 0.9	1.58	−0.7, 3.8
Diastolic blood pressure, mmHg	0.23	−0.9, 1.3	0.19	−0.9, 1.3
Fasting glucose, mg/dL	0.04	−2.0, 2.1	0.20	−2.2, 1.8
Postchallenge glucose, mg/dL	0.43	−5.4, 6.2	4.88*	−0.9, 10.7
Fasting insulin,[d] μ units/mL (n = 824)	−1.00	−1.1, 1.1	1.00	−1.1, 1.1
Postchallenge insulin,[d] μ units/mL (n = 774)	−0.90*	−1.0, 1.0	1.10*	1.0, 1.2
Stratified analyses				
Current estrogen users[a,b] (n = 349)				
Cholesterol, mg/dL	−6.40*	−13.4, 0.5	3.08	−3.9, 10.1
HDL, mg/dL	−1.77	−5.2, 1.7	−3.21*	−6.6, 0.2
LDL, mg/dL	−6.09*	−12.8, 0.6	0.56	−7.3, 6.2
Triglycerides,[d] mg/dL	1.00	−1.0, 1.2	1.00	−1.1, 1.1
Systolic blood pressure, mmHg	−0.04	−3.4, 3.2	4.50***	1.2, 7.9
Diastolic blood pressure, mmHg	0.42	−1.3, 2.1	1.95**	0.3, 3.7
Fasting glucose, mg/dL	−0.22	−2.3, 1.9	0.22	−1.9, 2.3
Postchallenge glucose, mg/dL	4.83	−3.1, 12.8	6.86*	−0.2, 14.9
Fasting insulin,[d] μ units/mL (n = 263)	1.00	−1.1, 1.1	1.10	−1.2, 1.03
Postchallenge insulin,[d] μ units/mL (n = 247)	1.00	−1.2, 1.1	1.00	−1.1, 1.2
>20 years postmenopausal[a,c] (n = 608)				
Cholesterol, mg/dL	−7.25**	−13.9, −0.8	7.33**	0.4, 14.5
HDL, mg/dL	−0.73	−3.5, 2.1	−0.68	−3.8, 2.4
LDL, mg/dL	−7.29***	−13.4, −1.2	6.33**	0.4, 13.0
Triglycerides,[d] mg/dL	1.00	−1.1, 1.1	1.10*	−0.9, 1.2
Systolic blood pressure, mmHg	−2.80	−6.2, 0.6	2.62	−1.1, 6.3
Diastolic blood pressure, mmHg	−0.16	−1.7, 1.3	0.02	−1.6, 1.7
Fasting glucose, mg/dL	0.35	−2.8, 3.5	0.54	−3.0, 4.0
Postchallenge glucose, mg/dL	0.42	−8.3, 9.1	8.29**	1.2, 17.9
Fasting insulin,[d] μ units/mL (n = 399)	1.00	−1.1, 1.1	1.00	−1.1, 1.1
Postchallenge insulin,[d] μ units/mL (n = 367)	−1.10**	−1.3, −1.0	1.10**	1.0, 1.3

Note. β = beta weight, the difference between women in that hysterectomy group and those without hysterectomy. CI = confidence interval. HDL = high density lipoprotein. LDL = low density lipoprotein.
[a]Adjusted for age, body mass index, alcohol consumption, regular exercise, and cigarette smoking.
[b]Adjusted for years postmenopausal.
[c]Adjusted for current estrogen use.
[d]Statistics performed on $\log_{10}$ triglycerides, fasting insulin, and postchallenge insulin; antilogs presented.
*$P < .10$ for comparisons with women without a hysterectomy.
**$P < .05$ for comparisons with women without a hysterectomy.
***$P < .01$ for comparisons with women without a hysterectomy.

all, 22.1% (n = 254) reported hysterectomy with conservation of one or both ovaries, and 21.8% (n = 251) reported hysterectomy with bilateral oophorectomy.

There were no significant differences by hysterectomy or oophorectomy status in age, body mass index, waist-hip ratio, alcohol consumption, exercise, or smoking (Table 1). Hysterectomized women with ovarian conservation were younger at menopause ($P < .001$) and menopausal for more years ($P < .001$); both groups of hysterectomized women were more likely to be current estrogen users than those without hysterectomy ($P < .001$ for both groups).

After adjustment for age, body mass index, and estrogen use, women with oophorectomies had significantly higher triglycerides ($P < .05$) and postchallenge glucose ($P < .01$) and marginally higher postchallenge insulin than women without hysterectomy (Table 2). No differences were observed between hysterectomized women with ovarian conservation and women without hysterectomy ($P > .10$). Adjustment for years of estrogen use yielded similar results (data not shown).

In regression analyses adjusted for all covariates (Table 3), oophorectomized women had marginally higher triglycerides, postchallenge glucose and postchal-

lenge insulin, while hysterectomized women with ovarian conservation had marginally lower postchallenge insulin than women without hysterectomy ($P < .10$). In stratified analyses, among those 20 or more years postmenopause (Table 3), oophorectomized women had significantly higher cholesterol (7 mg/dL), LDL (6 mg/dL), postchallenge glucose (8 mg/dL), and postchallenge insulin (1.1 μ units/mL) ($P < .05$), while hysterectomized women with ovarian conservation had lower cholesterol (7 mg/dL, $P < .05$), LDL (7 mg/dL, $P < .01$), and postchallenge insulin (1.1 μ units/mL, $P < .05$) than women without hysterectomy. Among current estrogen users, oophorectomized women had higher systolic ($P < .01$) and diastolic blood pressures ($P < .05$). Patterns were similar but not statistically significant for women less than 10 years or 11 through 19 years postmenopause and for women not currently using estrogen (data not shown).

Discussion

In this study, oophorectomized women had less favorable heart-disease risk factors. This was particularly evident among women for whom more time had elapsed since menopause. Differences were not explained by age, obesity, estrogen use, alcohol consumption, cigarette smoking, or exercise.

In accord with previous small, short-term studies,[12–14,16] oophorectomized women had higher cholesterol and LDL than women without hysterectomy. In accord with Luoto et al.,[9] differences in triglycerides (but not glucose) between oophorectomized and nonhysterectomized women were seen many years after surgery. In Rancho Bernardo, oophorectomized women also had less favorable postchallenge glucose and insulin levels. In short-term prospective studies, exogenous estrogen lowers LDL and raises HDL cholesterol.[21,22] Bilaterally oophorectomized, estrogen-treated women followed for up to 2 years had decreased LDL,[13,23] increased HDL[13,15,23,24] and no change in total cholesterol, triglycerides,[24] or fasting glucose.[25]

In Rancho Bernardo, hysterectomized women with ovarian conservation either were not significantly different from or had more favorable heart disease risk factors than women without hysterectomy. These differences were significant many years after menopause and are compatible with a differential effect of preventive health behaviors. We reported that hysterectomized women were more likely than women without hysterectomy to decrease dietary fat and salt, increase exercise, and make other diet and lifestyle changes to promote health.[26] For hysterectomized women with ovarian conservation, these changes may be sufficient to improve health to the extent that they do not differ from, or even have more favorable heart disease risk factors than, women without hysterectomy. In contrast, these changes may not be sufficient to offset the very low levels of endogenous sex hormones associated with bilateral oophorectomy, and may not prevent a worsening of heart disease risk factors over time.

Potential sources of bias were considered. Misclassification of bilateral oophorectomy would have reduced the observed differences. Other studies report that women accurately recall hysterectomy and oophorectomy status.[27–29] In Rancho Bernardo women, medical-record validation showed that only 1.9% of 52 who reported bilateral oophorectomy and 11.1% of 45 who reported ovarian conservation did not know their true oophorectomy status. Estrogen use was validated at the clinic, making recall bias unlikely. Differential access to medical care is also unlikely to have introduced bias; over 90% of these women saw a physician within the previous year, and rates did not differ by hysterectomy or oophorectomy status.[26] Although the prevalence of hysterectomy appears high, the incidence in this cohort between 1972 and 1984 was 10.7%, similar to the 9.6% rate for those years for women in the western United States.[30] Numerous statistical analyses were performed; thus, chance could have affected some results. However, observed differences tended to be consistent. Finally, the addition of progestin to estrogen replacement, found to lessen or reverse the benefits of estrogen,[31,32] is unlikely to account for the observed differences; over 80% of bilaterally oophorectomized Rancho Bernardo women were taking unopposed estrogen, and proportions were similar by oophorectomy status.

Heart disease risk factors were not measured before hysterectomy or bilateral oophorectomy. Thus, we cannot exclude the possibility that observed differences existed prior to surgery. Likewise, we cannot exclude the possibility that both the need for oophorectomy and unfavorable heart disease risk factors were caused by another, unmeasured factor. Finally, this study of White, middle-class, relatively well-educated women may not generalize to other ethnic or socioeconomic groups.

Nevertheless, the observation that bilateral oophorectomy is associated with more unfavorable heart disease risk factors many years after surgery, not totally ameliorated by estrogen replacement, has significant public health implications, given the high frequency of hysterectomy in the United States and the concurrent removal of both ovaries in older women. Since hysterectomy alone does not have a negative effect, physicians should reconsider routine bilateral oophorectomy for cancer prevention, and additional studies should be done to examine the remote consequences of this surgery. □

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