Risks of Bilateral Oophorectomy-Symptoms, Disease, and Mortality

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Disclosure

• Philip Sarrel, M.D. is the Founder and President of The Advancing Health After Hysterectomy Foundation, Inc. (a non-profit corporation registered in Connecticut)
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Bilateral Salpingo-Oophorectomy (BSO)

• Most BSOS are done at the time of hysterectomy and most occur before age 50.¹ There are more than 1 million women who have undergone BSO at age 45 or younger.


Oophorectomy: 1998-2011

• Mikhail E AJOG, 2015;213:713-721.
The Age at which women undergo Hysterectomy Overall BSO

<table>
<thead>
<tr>
<th>Age (n-24)</th>
<th>n (%)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>23,722 (0.4)</td>
<td>4079 (17.2)</td>
</tr>
<tr>
<td>25-34</td>
<td>577,636 (9.6)</td>
<td>111,548 (19.3)</td>
</tr>
<tr>
<td>35-44</td>
<td>2,382,001 (39.7)</td>
<td>699,080 (29.4)</td>
</tr>
<tr>
<td>45-54</td>
<td>2,146,887 (35.8)</td>
<td>1,310,043 (61.0)</td>
</tr>
<tr>
<td>55-64</td>
<td>459,338 (7.7)</td>
<td>301,061 (65.5)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>409,733 (6.8)</td>
<td>195,661 (47.8)</td>
</tr>
</tbody>
</table>

1.0 million women age 45 and under had their ovaries removed between 1998-2011


BSO: Adverse Effects

- The major concern about women whose ovaries are removed before age 45 is that the benefits of BSO are outweighed by increased frequency and severity of symptoms, and increase in disease risk and mortality rates. For this reason, ACOG has advocated ovarian conservation and bilateral salpingectomy (BS) in these women.

Mikhail E AJOG, 2015;213:713-721.

Symptoms Are More Frequent and Severe After Surgical Menopause

- Hot flashes
- Fatigue
- Cardiac symptoms
- Depressed affect


Symptoms Due to Ovarian Hormone Insufficiency Are More Severe After Hysterectomy/BSO

Oldenhave A reported 90% vs 50% with severe hot flashes comparing surgical vs. natural menopause.

Kronenberg F reported findings from more than 900 women comparing natural and surgical menopause:

- The incidence of chest pressure and change in heart rate is doubled in women with surgical menopause (22%-47%).
- Depression with suicidal thoughts are also doubled (10%).

Rosenberg G reported hospitalization for suicide attempt was more than doubled in women who had BSO at age 35 and younger.
Disease and Mortality After Surgical Menopause: A 75-Year Saga  

1. Albright F, Smith DH, Richardson AM. Postmenopausal osteoporosis. JAMA 1941;116:2465  

Increase in Disease Associated With Surgical Menopause

- Osteoporosis
- Cardiovascular disease/myocardial infarction
- Hypertension and Stroke
- Dementia and Alzheimer's Disease


Oophorectomy and Osteoporosis

Bone density after >24 months estrogen therapy vs deprivation:

T score < -1.0 (osteopenia or osteoporosis): 16% vs 47% of those with > 24 mos deprivation (p=0.03);  

By age 50, 13% with >24 mos of deprivation prior to age 50 had osteoporosis compared to 3% who received estrogen therapy

BSO, Hot Flashes and Hypertension

Increased sympathetic tone with hot flashes\(^1\)\(^3\)-\(^5\)

5. Franco OH, et al. Vasomotor symptoms...cvd risk...meta-analysis. Maturitas 2015;83:353-361

Surgical menopause at age 45 or younger without hormone replacement shows increased risks for: (Mayo Clinic Oophorectomy Study)\(^1\)

- Osteoporosis and bone fx 50%
- Coronary Heart Disease 33%
- Stroke 62%
- Cognitive impairment 60%

All-cause mortality: 28%

\(^1\) Faubion SS, Kubilie CL, et al. long-term health consequences of premature menopause or early Menopause and considerations for management. Climacteric 2015;18:483-491
ET and HT Reduce Mortality After Surgical Menopause


- BSO <45 not treated with ET HR = 1.67
- BSO <45 treated with ET HR = 0.65

HT- Cochrane Database Syst Rev. 2015: reduction = 39%
(Women under 60 or < 10 yrs post menopause)

Savolainen-Peltonen. JCEM 2016;101:2794-2801: "The sooner after the onset of menopause an estradiol-based HT is initiated, the better it protects against cardiac death risk. ET reduction = 47%"

BSO (Cont.)

- In women age 45 and younger, estrogen therapy controls symptoms and reduces disease risk and mortality when it is initiated close to the time of BSO, continued at least until the average age of natural menopause, and is prescribed at higher doses than usual.

WHI 2011: Clinical Outcomes HR by Age Groups: CEE vs. Placebo

<table>
<thead>
<tr>
<th>Age</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>0.94</td>
<td>1.00</td>
<td>1.06</td>
</tr>
<tr>
<td>Total MI</td>
<td>0.54</td>
<td>1.05</td>
<td>1.23</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.27</td>
<td>1.27</td>
<td>1.13</td>
</tr>
<tr>
<td>DVT</td>
<td>0.71</td>
<td>1.20</td>
<td>1.26</td>
</tr>
<tr>
<td>PE</td>
<td>1.20</td>
<td>1.57</td>
<td>0.74</td>
</tr>
<tr>
<td>Inv Breast Ca</td>
<td>0.80</td>
<td>0.73</td>
<td>0.81</td>
</tr>
<tr>
<td>Colo Rectal Ca</td>
<td>0.80</td>
<td>0.90</td>
<td>1.83</td>
</tr>
<tr>
<td>Hip fx</td>
<td>1.55</td>
<td>0.87</td>
<td>0.90</td>
</tr>
<tr>
<td>DEATH</td>
<td>0.73</td>
<td>1.04</td>
<td>1.12</td>
</tr>
</tbody>
</table>

BSO= 39%. Hyst <age 40+ 40%; age 40-49= 44%. In age 50-59 Xs mortality = 13/10,000/yr

LaCroix A et al. JAMA 2011;305: pg. 1311

Hormone replacement in young women with surgical ovarian insufficiency

- Women with oophorectomy at age 45 or younger need higher dose estrogen replacement therapy
- Treatment should be at least until age of natural menopause
- Best results are seen in women who start at time of oophorectomy and continue for 10 years or longer
- Progesterone in women with retained uterus

Oophorectomy: Key Points

• Despite ACOG recommendations to conserve ovaries at the time of hysterectomy, BSO continues to be the major cause of estrogen deficiency in premenopausal women.

• The steep decline in estrogen use after surgical menopause has resulted in more than a million younger women who are at increased risk for osteoporosis, atherosclerosis, dementia, sexual dysfunction and other conditions due to estrogen deficiency.

• Although the WHI-estrogen Study findings only apply tangentially to these women, major cohort studies indicate the disease and mortality consequences of estrogen deficiency can be overcome by estrogen therapy initiated as close as possible to the time of surgery and continued for 10 years or more (at least until the age of natural menopause).

• A major public health education campaign is called for to help women and health care providers understand the risks of not using estrogen after BSO and the benefits and safety of its use.