Long-Term Health Outcomes of Surgical Menopause

Vanessa Jacoby, MD, MAS
Associate Professor
Obstetrics, Gynecology, and Reproductive Sciences
University of California, San Francisco
Disclosures

None
Overview

• Overview of surgical menopause for women with HBOC

• Impact of surgical menopause on...

  Heart health
  Bone health and risk of fractures
  Cognitive ability/memory
What is natural menopause?

“Natural” menopause....

--No menstrual period for 1 year

--Average age is 51 years
Slow and Gradual Hormone Changes

Changes in estradiol and FSH during MT (SWAN)

*The y axis is unitless. The units of hormone are noted in the corresponding curves. Harlow SD Menopause 2012;19:387-95 (reproduced with permission from Randolph JF JCEM 2011;96:746-54)
What is surgical menopause?
Ovarian Hormones in Menopause

561 women, age 50-90

Laughlin et al, 2000, Jo Clin Endo and Metab
Surgical menopause: Hysterectomy

**Total Hysterectomy:**
No periods, but not menopause by hormones
Supracerical (subtotal) Hysterectomy: No periods, but not menopause by hormones
Surgical menopause: Oophorectomy

Bilateral Salpingo-oophorectomy (BSO): Removal of both fallopian tubes and ovaries
Surgical menopause: Oophorectomy

Bilateral Salpingo-oophorectomy (BSO): No periods and menopause by hormones
Bilateral Salpingo-oophorectomy (BSO) for women with HBOC is...

Risk Reducing Salpingo-oophorectomy (RRSO)
Surgical menopause: Hysterectomy

- Fallopian tube
- Ovary
- Ovary
Surgical menopause: RRSO

Questions?
## RRSO versus Natural Menopause

<table>
<thead>
<tr>
<th></th>
<th>Natural Menopause</th>
<th>RRSO</th>
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</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>51</td>
<td>35-45</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>gradual</td>
<td>sudden</td>
</tr>
<tr>
<td><strong>Hormone level</strong></td>
<td>Low</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Treatment for symptoms</strong></td>
<td>Hormones common</td>
<td>Many seek nonhormonal treatment</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td>May have other surgery, diagnosis of cancer</td>
</tr>
</tbody>
</table>
RRSO Benefits

Significant decrease in risk of cancer…

- Ovarian (90%)
- Fallopian tube
- Peritoneal
- Breast (up to 75%)
National Guidelines: Age at RRSO

BRCA 1: 35-40 years
BRCA 2: 40-45 years
Lynch Syndrome: 35-40 years
BRIP1, RAD51C, RAD51D: Consider 45-50 years
Risk Reduction: With or Without Hysterectomy?

Hysterectomy with RRSO…

1. Increased risk of uterine cancer (e.g. Lynch Syndrome)

2. Other gynecologic reason for hysterectomy

3. Plan to take tamoxifen

4. Plan to take estrogen after surgery, hope to avoid progesterone
Risk Reduction: With or Without Hysterectomy?

If using hormones to help with menopause symptoms...

- Estrogen AND Progestin to avoid uterine cancer
- Estrogen only is OK
Salpingectomy

Removal of Fallopian Tubes only
Salpingectomy

- Evidence that some ovarian cancer may begin in fallopian tube but...

NCCN Guidelines:
“salpingectomy alone is not the standard of care and is discouraged outside a clinical trial”
Who undergoes RRSO?

- 50% of women with known BRCA mutations
- More likely if...
  - Have had breast cancer
  - Family history of cancer
  - Age >45 years
National Guidelines for Non-Cancer Outcomes after RRSO

Society for Gynecologic Oncology:

“limited information is available regarding management of women following RRSO”

National Comprehensive Cancer Network (NCCN):

Discuss “medical issues” during RRSO counseling, but what health issues or risks should be addressed?
Surgical menopause: RRSO

Questions?
Noncancerous Consequences of RRSO
Noncancerous Consequences of RRSO

Challenges: A lot of studies...

---use data from LOW RISK population undergoing hysterectomy

---evaluate health many years AFTER RRSO

---do not account for use of hormone therapy

Very difficult to be certain about health after RRSO. More studies needed!
Impact of Premature Menopause

Spontaneous menopause occurs <40 years
Impact of Premature Menopause

Increased risk of:
• Heart disease and death from heart disease
• Osteoporosis (thin bones) and fractures
• Impaired cognitive function
Impact of Premature Menopause

BUT.....

Is this really similar to RRSO for HBOC?
Oophorectomy in LOW risk women

Definite risks of BSO
NONE

Possible risk of BSO
• Coronary heart disease:
• Osteoporosis/fracture:
• Sexual functioning/ QOL:
• Dementia:
• Death:
Oophorectomy in LOW risk women

Definite risks of BSO
NONE

Possible risk of BSO
• Coronal heart disease: Inconclusive data
• Osteoporosis/fracture: Inconclusive data
• Sexual functioning/ qol: Inconclusive data
• Dementia: Inconclusive data
• Death: Inconclusive data
Oophorectomy with Hysterectomy in LOW risk women

Different population because…..

• Reason for hysterectomy may cause health risks

• Hysterectomy alone may have health risks

• Hormone use very common
Oophorectomy with Hysterectomy in LOW risk women

Different population because.....
BRCA mutation may be a risk factor for noncancerous conditions

No DNA repair

Heart disease
Diabetes
High cholesterol
Surgical menopause: RRSO

Questions?
Health Outcomes after RRSO: Heart disease
Menopause and Heart Disease

Menopause is a risk factor for heart attacks…

MAYBE!

Incidence of myocardial infarction in men and women

- Men
- Women

Two-year event rate per 1000

Age at examination

- 35-44
- 45-54
- 55-64
- 65-74
- 75-84
Menopause and Heart Disease

Maintains endothelial function (lining of blood vessels)

Suppresses cholesterol levels

Increase in insulin cell response
## Heart Health

<table>
<thead>
<tr>
<th>Disease</th>
<th>Number of deaths/year</th>
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<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>459,096</td>
</tr>
<tr>
<td>Lung Ca</td>
<td>70,880</td>
</tr>
<tr>
<td>Breast</td>
<td>40,460</td>
</tr>
<tr>
<td>Colorectal</td>
<td>26,180</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>16,530</td>
</tr>
<tr>
<td>Ovary</td>
<td>15,280</td>
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Heart Health: RRSO

The study we WISH we had……

Before RRSO: Check heart health

1, 2, 3, 5, 10 years:
Check heart health
Heart Health: RRSO

The studies we actually have……

Check heart health many years AFTER RRSO

Maybe heart disease or protective factors occurred prior to RRSO
Heart Health: RRSO

The study we actually have…….

Women in Norway who had RRSO compared to NO RRSO, more likely to:
--have Metabolic Syndrome (high blood pressure, high cholesterol, high blood sugar)
--increased risk of heart disease and diabetes

But…
No RRSO group was not with BRCA mutations!

Michelsen, et al, Int J Gynecol Ca 2010
Heart Health: RRSO Summary

- Premature natural menopause increases risk
- Oophorectomy at time of hysterectomy *may* increase risk
- No completed, well-designed studies of women with BRCA mutations to assess RRSO heart risks
Surgical menopause: RRSO

Questions?
Bone Health

Estrogen keeps bones strong!
Bone Health

Rapid decrease in bone density at menopause
Bone Health: RRSO

The studies we actually have……

Check bone density many years AFTER RRSO

Maybe poor density occurred *prior* to RRSO….but probably not!
Bone Health after RRSO

- RRSO generally found to decrease bone density
  - Osteopenia (bone thinning) 30-72% in studies
  - Osteoporosis (low bone mass/skeletal fragility) and fracture risk
- RRSO <50 years=higher risks for osteopenia
- Estrogen use may decrease risk of osteopenia, but some studies have found persistent osteopenia even with use
Bone Health after RRSO

Questions remain…

• Should I get a DEXA (bone density scan) and if so, when?

• How can I prevent bone thinning?
Bone Health after RRSO

Recommendations for post-menopausal women:

• Vitamin D 800 IU + 1,200mg elemental Calcium daily

• Weight-bearing exercise three times/week
  -- Jogging is not better than walking. Do what you enjoy!

• Smoking cessation
  -- Smoking increases fracture risk and decreases bone density
Surgical menopause: RRSO

Questions?
Cognitive function and Estrogen

Strong biologic evidence that estrogen supports cognitive function:

-- estrogen receptors in the brain
-- stimulates nerve cells to communicate
-- protects nerve cells from toxins
Cognitive function and Estrogen

Oral estrogen + progesterone INCREASE risk for cognitive impairment (age 65-79 years)

Cumulative Hazard of Probable Dementia and Any Impairment From Time of WHI Enrollment

- Probable Dementia
  - Mean Duration of Trials:
    - CEE+MPA: 4.2 yrs; CEE-Alone: 5.4 yrs
  - HT
  - Placebo

- Any Impairment
  - Mean Duration of Trials:
    - CEE+MPA: 4.2 yrs; CEE-Alone: 5.4 yrs
  - HT
  - Placebo

P=0.003
P=0.008

RRSO: Cognitive function

No studies of RRSO
Memory and Oophorectomy

Small studies on memory….none in U.S. population

• Some memory tests worse in women with surgical versus natural menopause who did NOT take hormone therapy (100 women in Italy, average age 51)

• Memory declined 3-6 months after hysterectomy/BSO compared with “control” group (50 women in Egypt, average age 41)

Nappi et al, Gynecol Obstet Invest 1999
Farrag et al, dement Geriatr Cogn Disord 2002
# BSO and Dementia

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk of impaired cognitive function or dementia with BSO?</th>
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<tbody>
<tr>
<td><strong>Mayo Cohort</strong></td>
<td>NO for BSO overall</td>
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<tr>
<td>Rocca WA et al</td>
<td>YES for some groups</td>
</tr>
<tr>
<td><em>Neurology 2007</em></td>
<td>age 43-48 BSO</td>
</tr>
<tr>
<td></td>
<td>no Estrogen to age 50</td>
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<tr>
<td><strong>Rancho Bernardo</strong></td>
<td>NO</td>
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<tr>
<td>Kritz-Silverstein</td>
<td></td>
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<td><em>J Am Geriatr 2002</em></td>
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Next Steps for Non-Cancerous Outcomes

1. Conduct better studies!

2. Change guidelines on post-RRSO management
   • When to order DEXA?
   • When to check lipids?

3. Aim is to support long-term survival and inform decision-making for RRSO