# Take It or Leave It Updates on Opportunistic Salpingectomy

Kimberly Walhof, MD

January 4, 2018

## Why this topic?

- The department remains split on this topic
- There are new data
- Guidelines are available
- There are answers to some of our common questions

## Disclosures

- No financial conflicts of interest
- I am a Canadian citizen

## Outline

- The fallopian tube and "ovarian" cancer
- What we know now
- What we hope to know someday
- Professional Guidelines

## The problem

### Estimated Deaths, 2016

Female	\$		
	Lung & bronchus	72,160	26%
	Breast	40,450	14%
X	Colon & rectum	23,170	8%
	Pancreas	20,330	7%
	Ovary	14,240	5%
	Uterine corpus	10,470	4%
	Leukemia	10,270	4%
	Liver & intrahepatic bile duct	8,890	3%
	Non-Hodgkin lymphoma	8,630	3%
	Brain & other nervous system	6,610	2%
	All Sites	281,400	100%

Siegel RL et al. Cancer Statistics, 2016. <u>CA Cancer J Clin.</u> 2016 Jan-Feb;66(1):7-30.

## The solution?

- Protective factors:
  - Oral Contraceptive Pills

Duration of Use	Relative Risk (compared to non-user)
<5 years	0.8
5-10 years	0.7
>10 years	0.6

- Parity
- Breastfeeding
- Tubal ligation

Fallopian tube as the "gateway" for spread of cancer

Table 3	ORs for epithelial ovarian cancer associated with tubal ligation by
cell type:	WHO Collaborative Study of Steroid Contraceptives and Neoplasia.
	1979-1988

Historical college	Tubal ligation		Not sterilized		OR"	95% CI	
Histological cell type	Cases	Controls	Cases	Controls	OK-	93% CI	
Serous	17	141	154	893	0.98	0.53-1.80	
Mucinous	15	139	91	578	0.88	0.46-1.69	
Clear cell	1	61	34	167	$0.33^{b}$	0.007-2.68	
Endometrioid	1	7.3	48	273	$0.21^{b}$	0.048 - 1.49	
Other	0	12	24	148	0,	0-3.44	

<sup>&</sup>quot; Adjusted for parity and oral contraceptive use.

Estimated by exact methods.

Table 2						
Pathologic	findings	in	seven	PO	specimens	

Case no. mutation	Age at PO	Ovary	Fallopian Tube	Uterine Serosa	Peritoneal/Omental	Staging
1* BRCA1	48	Rt: Two microscopic foci of serous carcinoma	5 cm tumor attached to Rt tubal fimbria- serous carcinoma	Negative	Metastatic carcinoma present in peritoneal biopsy	Fallopian tube IIb
2* BRCA1	40	Focal microscopic serous carcinoma on surface of one ovary	Negative	Negative	Peritoneal washings positive for serous primary	Ovary Ia
3* BRCA1	59	Multiple foci of serous carcinoma on surface of both ovaries	Microscopic carcinoma of tubal fimbria	Micro-scopic carcinoma	Peritoneal washings positive for adenocarcinoma	Ovary IIc
4* BRCA1	64	Negative	Fimbrial focus of adenocarcinoma-in-situ	Negative	Negative	Fallopian tube Stage 0
5 BRCA1	42	Negative	Serous carcinoma of tubal fimbria	Negative	Negative	Fallopian tube Ib
6 BRCA2	53	Negative	Microscopic adnexal carcinoma	Negative	Primary peritoneal origin favored	Peritoneal No staging
7 BRCA1	44	Serous LMP tumor with micropapillary features; microscopic carcinoma on surface of both ovaries	Fimbrial serous carcinoma	Negative	Negative	Fallopian tube IIa

LMP: low malignant potential.

<sup>\*</sup> Described previously in [8].

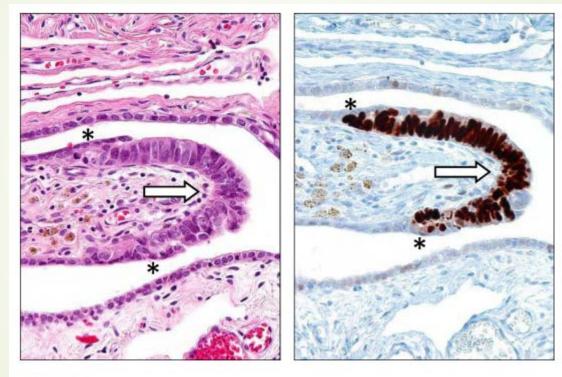
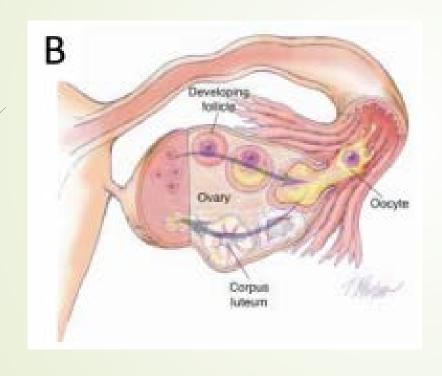
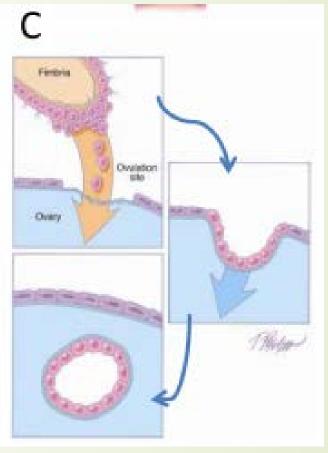


Figure 1.

Serous tubal intraepithelial carcinoma (STIC). A. High magnification. Hematoxylin and eosin stain. B. Immunohistochemical stain for p53. An asterisk defines the boundary of the lesion.

Kurman and Shih. The Origin and Pathogenesis of Epithelial Ovarian Cancer – A Proposed Unifying Theory Am J Surg Pathol. 2010 March;34(3):433-443.





Kurman and Shih. The Origin and Pathogenesis of Epithelial Ovarian Cancer – A Proposed Unifying Theory Am J Surg Pathol. 2010 March; 34(3):433-443.

- Intraoperative complications
- Cost
- Effect on ovarian function
- Risk of regret

- Intraoperative complications
  - No significant difference in retrospective studies

	e measures of risk			.,				
Variable	Hysterectomy only (n = 8362)	Hysterectomy with bilateral salpingectomy (n = 3670)	P value <sup>a</sup>	Hysterectomy with bilateral salpingo- oophorectomy (n = 8904)	P value <sup>a</sup>	Tubal ligation (n = 13719)	Salpingectomy for sterilization (n = 1569)	P value <sup>a</sup>
Age, y <sup>b</sup>	$48.6 \pm 12.7$	$43.5\pm7.6$	< .001	$54.2 \pm 11.9$	< .001	$34.8 \pm 5.7$	$36.0 \pm 5.4$	< .001
Operating room time, min <sup>b</sup>	117.3 ± 47.7	133.6 ± 50.1	< .001	139.7 ± 54.2	< .001	61.0 ± 25.1	71.2 ± 23.5	< .001
Missing data on operating room time	2967	279	_	2173	_	4965	221	_
Length of hospital stay, d <sup>b</sup>	2.52 ± 3.0	2.37 ± 1.9	.010	2.93 ± 4.3	< .001	1.31 ± 3.1	1.23 ± 4.5	.117
Readmission, n (%)	379 (4.5)	159 (4.3)	.632	506 (5.7)	.001	309 (2.3)	28 (1.8)	.233
Readmission, adjusted odds ratio <sup>c</sup>	1.00 (Reference)	0.91 (0.75, 1.10)	.347	1.34 (1.16, 1.53)	< .001	1.00 (Reference)	0.83 (0.56, 1.23)	.547
Blood transfusion, n (%)	219 (2.6)	89 (2.4)	.54	225 (2.5)	.704	74 (0.5)	6 (0.4)	.415
Blood transfusion, adjusted odds ratio <sup>c</sup>	1.00 (Reference)	0.86 (0.67, 1.10)	.183	1.09 (0.90, 1.33)	.353	1.00 (Reference)	0.77 (0.56, 1.23)	.36

There were 67 women who underwent hysterectomy with cophorectomy who are not included in this Table.

McAlpine. Uptake and risks of opportunistic salpingectomy. Am J Obstet Gynecol 2014.

Compared with the reference hysterectomy-alone procedure for hysterectomy with bilateral salpingectomy or bilateral salpinge-coophorectomy and as compared with the reference tubal ligation for a salpingectomy procedure; Data are given as mean ± SD; Odds ratios for hospital readmission and blood transfusion were adjusted for patient age. Regressions that compared salpingectomy with tubal ligation also were controlled for delivery by cesarean section during the hospitalization stay.

- Intraoperative complications
- Cost
  - Time Is Money

#### TABLE 2

#### Operative/perioperative measures of risk of opportunistic salpingectomy

Variable	Hysterectomy only (n = 8362)	Hysterectomy with bilateral salpingectomy (n = 3670)	<i>P</i> value <sup>a</sup>	Hysterectomy with bilateral salpingo- oophorectomy (n = 8904)	P value <sup>a</sup>	Tubal ligation (n = 13719)	Salpingectomy for sterilization (n = 1569)	<i>P</i> value <sup>a</sup>
Age, y <sup>b</sup>	48.6 ± 12.7	$43.5 \pm 7.6$	< .001	$54.2 \pm 11.9$	< .001	$34.8 \pm 5.7$	$36.0 \pm 5.4$	< .001
Operating room time, min <sup>b</sup>	117.3 ± 47.7	133.6 ± 50.1	< .001	139.7 ± 54.2	< .001	61.0 ± 25.1	71.2 ± 23.5	< .001

- Intraoperative complications
- Cost

Item	Filshie	Ligasure	Harmonic	Postpartum
Clips (2)	161.24	-	-	-
Ports	45.26	58.20	58.20	-
Applier or Handpiece	-	470.25 / 483.55	384.33	-
Cords	-	32.81	-	-
Suture	-	-	+	1.39-2.88 per tie
Total Method Associated Cost	206.50	561.26	442.53	Variable (\$2-500)

- Intraoperative complications
- Cost
- Effect on ovarian function

Table 2 Primary outcomes measures.

Parameters	TLH plus salpingectomy Group A (n.79)	Standard TLH Group B (N.79)	p
$\Delta$ AMH (ng/mL)	$-0.06 \pm 0.1$	$-0.08 \pm 0.1$	0.35
$\Delta$ FSH (mIU/ml)	$1.3 \pm 1.1$	$1.0 \pm 0.8$	0.15
Δ AFC (n)	$-0.27 \pm 0.6$	$-0.14 \pm 0.3$	0.09
<ul> <li>Δ Mean ovarian diameters (mm)</li> <li>Δ PSV (cm/s)</li> </ul>	$-0.25 \pm 0.8$	$-0.19 \pm 0.6$	0.57
	$-0.31 \pm 1.9$	$-0.19 \pm 1.0$	0.61

Mortili Met al. Prophylactic salpinglectemy in premenogacy low-risk women for ovarian cancer: primum non nocere. Gynecol Oncol. 2013 Jun. 129(3)44-8-51.

- Intraoperative complications
- Cost
- Effect on ovarian function
- Risk of regret

Table 4. Rate Ratios of Regret After Tubal Sterilization According to Characteristics at Sterilization*					
Characteristic	Unadjusted	95% Confidence interval	Adjusted o	95% Confidence interval	
	1000 1000	201001700	Time Time		
Age (y)					
18-30	2.3	2.0, 2.7	1.9	1.6, 2.3	
>30	Referent				
Race	4.77	15.20	4.0	44.45	
Nonwhite White	1.7 Referent	1.5, 2.0	1.3	1.1, 1.5	
	Keterent				
Married at time of sterilization					
No	1.4	1.2, 1.6	1.3	1.1, 1.6	
Yes	Referent				
History of abortion					
No	Referent				
Yes	1.3	1.1, 1.5	1.2	1.0,† 1.4	
Reason for sterilization					
Contraceptive	1.4	0.65, 2.2			
Medical	Referent				
Time between					
sterilization and					
birth of youngest					
child					
Postpartum					
After vaginal	2.5	2.0, 3.1	1.6	1.2, 2.1	
delivery					
After cesarean	3.0	2.3, 4.1	2.0	1.5, 2.8	
Interval <sup>5</sup>					
15 d-1 y	1.8	1.5, 2.3	1.3	1.0,‡ 1.7	
2 y-3 y	1.8	1.4, 2.3	1.4	1.1, 1.8	
4 y-7 y	1.5	1.1, 1.9	1.2	0.9, 1.6	
≥8 y or no	Referent				
previous birth					

<sup>\*</sup> Each variable was adjusted simultaneously for all variables that were significant in unadjusted analyses and for cohort of entry (1979, 1980, 1982, 1985, 1986, 1987).

Hillis SD et al. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol. 1999 Jun;93(6):889-95.

Rock J et al. Tubal anastomosis: pregnancy success following reversal of Falope ring or monopolar cautery sterilization. Fertil Steril. 1987 Jul;48(1):13-7.

<sup>†</sup> Lower confidence limit = 0.997.

<sup>\*</sup>Lower confidence limit = 1.02.

<sup>5</sup> Time was coded as per Table 1.

# What we hope to know someday (current research)

The Canadians!
British Columbia Ovarian Cancer Prevention Project



# What we hope to know someday (current research)

- ► HOPPSA (Sweden)
  - Register based randomized controlled trial
  - Salpingectomy vs no salpingectomy
  - Short-term outcome: complication rate
  - Intermediate term outcome: menopause symptoms
  - Long term outcome: Epithelial ovarian cancer
  - 4400 participants
- Mirena IUD (Memorial Sloan Kettering)

## Professional guidelines around the world

- American College of Obstetricians and Gynecologists Committee Opinion
  - "Prophylactic salpingectomy may offer clinicians the opportunity to prevent ovarian cancer in their patients."
- Society of Gynecologic Oncology Clinical Practice Statement
  - "Risk-reducing salpingectomy should also be discussed and considered with patients at the time of abdominal or pelvic surgery, hysterectomy or in lieu of tubal ligation."

Salpingectomy for Ovarian Cancer Prevention. Committee Opinion No. 620. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:279-81.

SGO Clinical Practice Statement: Salpingectomy for Ovarian Cancer Prevention. Nov 2013. Available online: <a href="www.sgo.org">www.sgo.org</a> Salvador S et al. No. 344-Opportunistic Salpingectomy and Other Methods of Risk Reduction for Ovarian/Fallopian Tube/Peritoneal Cancer in the General Population. J Obstet Gynaecol Can. 2017 Jun;39(6):480-493.

## Conclusions

- New paradigm for ovarian cancer
- Our patients may be encouraged to ask about salpingectomy
- All guidelines recommend a conversation about salpingectomy

### References

Committee Opinion No. 620. Salpingectomy for Ovarian Cancer Prevention. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:279-81.

Dilley SE, Straughn JM, Leath CA. The evolution of and evidence for opportunistic salpingectomy. <u>Obstet Gynecol</u>. 2017 Oct; 130(4): 814-824.

Finch et al. Clinical and pathologic findings of prophylactic salpingo-oophorectomy in 159 BRCA1 and BRCA2 carriers. <u>Gyn Onc.</u> 2006 100(1) 58-64.

GOC Statement Regarding Salpingectomy and Ovarian Cancer Prevention. 15 Sep 2011. The Society of Gynecologic Oncology of Canada.

Hillis SD et al. Poststerilization regret: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol. 1999 Jun; 93(6):889-95.

Kindelberger et al. Intraepithelial Carcinoma of the Fimbria and Pelvic Serous Carcinoma: Evidence for a causal relationship. <u>Am</u> <u>J Surg Pathol.</u> 2007;31:161-169

Kurman RJ and LM Shih. The origin and pathogenesis of epithelial ovarian cancer - a proposed unifying theory. <u>Am J Surg Pathol</u>. 2010 March;34(3):433-443.

McAlpine JN et al. Opportunistic salpingectomy: uptake, risks, and complications of a regional initiative for ovarian cancer prevention. <u>Am J Ostet Gynecol</u>. 2014 May;210(5):471.e1-11.

Morelli M et al. Prophylactic salpingectomy in premenopausal low-risk women for ovarian cancer: primum non nocere. <u>Gynecol Oncol</u>. 2013 Jun;129(3)448-51.

Powell CB et al. Salpingectomy for Sterilization: Change in Practice in a Large Integrated Health Care System, 2011-2016. Ostet Gynecol. 2017 Nov;130(5):961-967.

### References

Rock J et al. Tubal anastomosis: pregnancy success following reversal of Falope ring or monopolar cautery sterilization. Fertil Steril. 1987 Jul;48(1):13-17.

Rosenblatt KA, Thomas DB. Reduced risk of ovarian cancer in women with a tubal ligation or hysterectomy. The World Health Organization Collaborative Study of Neoplasia and Steroid Contraceptives. <u>Cancer Epidemiol Biomarkers Prev</u> 1996;5:933-5.

Royal College of Obstetricians & Gynaecologists. The Distal Fallopian Tube as the Origin of Non-Uterine Pelvic High-Grade Serous Carcinomas. Scientific Impact Paper No. 44. Nov 2014. Available Online: <a href="https://www.rcog.org.uk">www.rcog.org.uk</a>.

Salvador S et al. No. 344-Opportunistic Salpingectomy and Other Methods of Risk Reduction for Ovarian/Fallopian Tube/Peritoneal Cancer in the General Population. <u>J Obstet Gynaecol</u> Can. 2017 Jun;39(6):480-493.

SGO Clinical Practice Statement: Salpingectomy for Ovarian Cancer Prevention. Nov 2013. Available online: <a href="https://www.sgo.org">www.sgo.org</a>

Siegel RL et al. Cancer Statistics, 2016. CA Cancer J Clin. 2016 Jan-Feb;66(1):7-30.

Sieh W et al. Tubal ligation and the risk of ovarian cancer subtypes: a pooled analysis of case-control studies. Int J Epidemiol. 2013 Apr;42(2):579-589.

Sopik V et al. Why have ovarian cancer mortality rates declined? Part I. Incidence. Gynecol Oncol. 2015 Sep;138(3):741-9.

Walhof, Kimberly A. Email correspondence with Todd Bruin, Select Health. 5 Dec 2017.

www.clinicaltrials.org

www.ovcare.ca

## Questions?

