Mizzou

Outcomes and monitoring of estrogen-related cancers Missouri women

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Presenter Disclosures

Iris Zachary

(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

Background

- Breast, ovarian, uterine and thyroid cancers occur primarily in women; all four of these cancers are estrogen-receptor positive cancers.
- About 80% of breast cancers are ER positive; over 50% of ovarian and uterine cancers and over 40% of papillary thyroid cancers are estrogen-receptor positive.
- Estrogen-receptor positive cancers have better short-term outcomes but also have increased recurrence rates.

Background cont.

- Li, *et al*. **Risk of Second Primary Female Genital Malignancies in Women with Breast Cancer: a SEER Analysis.** Hormones & cancer (2018). 9:197–204.
- Curtis RE, Freedman M, Sherman M, Fraumeni JF Jr. **Uterine corpus cancer following tamoxifen therapy for breast cancer: difference in risk by histologic subtype.** J Natl Cancer Inst 2003 (In Press).
- Ho SM. **Estrogen, Progesterone and Epithelial Ovarian Cancer.** Reprod Biol Endocrinol. 2003; 1: 73.

Background cont.

- Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). **New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000.** National Cancer Institute, NIH Publ. No. 05-5302. Bethesda, MD, 2006.
- American Cancer Society. **Cancer Facts & Figures 2009.** Atlanta: American Cancer Society; 2009.
  - Special Section: Multiple Primary Cancers, Cancer Facts and Figures 2009

Purpose

- Evaluate the risk of developing secondary cancer(s)
  - after being diagnosed with female breast cancer, ovarian cancer, uterine cancer or thyroid cancer
- Evaluate outcomes of secondary cancers.

Methods

- We examined demographic and tumor-related characteristics of women with ER+ breast, ovarian, uterine and thyroid cancer in the Missouri Cancer Registry and Research Center (MCR-ARC) central cancer registry database from 2005-2014 and their survival.
  - age at diagnosis of first cancer, race, residence (rural v. urban)
  - stage, time between diagnoses
- All female patients with breast cancer, ovarian cancer, uterine cancer and thyroid cancer from 2005-2014 were included.
- Survival analysis was used to compare the outcomes of women after being diagnosed with an estrogen-receptor positive cancer developing a secondary cancer.

Methods – SIRs

- Standardized Incidence Ratios (SIRs) calculated via SEER*Stat
- Case selection:
  - Female
  - Breast, ovarian, uterine, or thyroid
  - Malignant
  - Diagnosed 2005-2014
  - Known age, county, race
  - Exclude DCO/autopsy
- Follow-up through 2015, excluding 1st 2 months

Methods – SIRs

- Expected counts based on rates by
  - Age (20 groups in 5-year spans)
  - Sex (female only)
  - Race (WBO)
  - ACS 2008-2012 county % persons below poverty (<10, 10-<20, 20+)
  - Rural-Urban Continuum Code 2013 (Metro, Urban non-metro, completely rural or small urban)
  - Year of diagnosis (2005-2009, 2010-2014)

Methods – survival

- Cox proportional hazards (all-cause)
- 5 analyses (in principle):
  - Survival of *subsequent* X cancer (after an initial X cancer) vs X cancer in general
    - Where X is breast, thyroid, ovarian, uterine, or “non-estrogen-related”
  - (breast → breast) vs breast
  - (thyroid → thyroid) vs thyroid
  - (ovarian → ovarian) vs ovarian
  - (uterine → uterine) vs uterine
  - (non-estrogen → non-estrogen) vs non-estrogen
- Some analyses were skipped due to small case counts

Methods – survival (fixed covariates)

- Controlling for (based on *subsequent* tumor for the group of interest):
  - Year of diagnosis
  - Age at diagnosis (5-year spans, but <39 & 85+)
  - Race (WBO)
  - Stage at diagnosis (LRDU)
  - County % persons in poverty / MUR2013 in 7 groups:
    - <10% / Metro
    - 10 - <20% / Metro
    - ≥20% / Metro
    - 10 - <20% / Urban, non-metro
    - ≥20% / Urban, non-metro
    - 10 - <20% / Rural or small urban
    - ≥20% / Rural or small urban
  - ER/PR status (only for breast cancer survival)

Results – SIRs, **breast**

	Cohort	Subsequent breast SIR	Any 4 SIR
	All breast	**1.09**	**1.08**
Race	White	1.00	1.02
	Black	**1.82**	**1.56**
Year of dx	2005-2009	**1.19**	**1.13**
	2010-2014	0.88	0.97
Age at dx	00-39	**4.57**	**3.92**
	40-49	**1.40**	**1.43**
	50-69	1.01	0.99
	70+	1.00	1.0
Stage	Localized	1.05	1.06
	Regional	**1.15**	1.1
	Distant	1.29	1.25

Results – SIRs, **breast**

	Cohort	Subsequent breast SIR	Any 4 SIR
Latency	<1 year	**1.20**	**1.21**
	1 - <5 years	**0.82**	**0.88**
	5 - <10 years	**1.58**	**1.39**
Poverty %	<10	1.16	**1.18**
	10 - <20	1.05	1.04
	20+	**1.23**	**1.22**
RUCC2013	Metro	**1.06**	**1.09**
	Urban, non-metro	1.06	1.04
	Rural or small urban	1.11	0.98

Results – SIRs, **thyroid**

	Cohort	Subsequent thyroid SIR	Any 4 SIR
	All thyroid	1.67	1.16
Race	White	1.69	1.19
	Black	^	0.96
Year of dx	2005-2009	1.32	1.15
	2010-2014	2.41	1.19
Age at dx	00-39	^	0.79
	40-49	1.8	**1.52**
	50-69	^	1.03
	70+	**^**	1.39
Stage	Localized	1.68	1.17
	Regional	^	1.13
	Distant	^	^

Results – SIRs, **thyroid**

	Cohort	Subsequent thyroid SIR	All 4 SIR
Latency	<1 year	**6.64**	1.45
	1 - <5 years	^	1.14
	5 - <10 years	^	1.07
Poverty %	<10	^	1.56
	10 - <20	1.8	1.05
	20+	^	1.31
RUCC2013	Metro	1.33	1.14
	Urban, non-metro	^	1.31
	Rural or small urban	^	^

Results – SIRs, **ovarian**

	Cohort	Subsequent ovarian SIR	Any 4 SIR
	All ovarian	^	1.11
Race	White	^	1.08
	Black	^	^
Year of dx	2005-2009	^	0.73
	2010-2014	^	**1.83**
Age at dx	00-39	^	^
	40-49	^	^
	50-69	^	1.17
	70+	^	0.66
Stage	Localized	^	**1.79**
	Regional	^	**0.42**
	Distant	^	1.19

Results – SIRs, **ovarian**

	Cohort	Subsequent ovarian SIR	All 4 SIR
Latency	<1 year	^	**1.85**
	1 - <5 years	^	0.9
	5 - <10 years	^	0.93
Poverty %	<10	^	^
	10 - <20	^	1.09
	20+	^	1.99
RUCC2013	Metro	^	**1.79**
	Urban, non-metro	^	^
	Rural or small urban	^	1.19

Results – SIRs, **uterine**

	Cohort	Subsequent uterine SIR	Any 4 SIR
	All uterine	**0.29**	**1.15**
Race	White	**0.32**	1.14
	Black	^	1.25
Year of dx	2005-2009	**0.29**	1.09
	2010-2014	^	**1.27**
Age at dx	00-39	^	^
	40-49	^	1.25
	50-69	^	1.1
	70+	^	1.22
Stage	Localized	^	1.13
	Regional	^	1.31
	Distant	^	^

Results – SIRs, **uterine**

	Cohort	Subsequent uterine SIR	All 4 SIR
Latency	<1 year	^	**1.39**
	1 - <5 years	^	1.15
	5 - <10 years	^	0.97
Poverty %	<10	^	**1.60**
	10 - <20	**0.30**	1.04
	20+	^	1.35
RUCC2013	Metro	**0.30**	1.14
	Urban, non-metro	^	1.15
	Rural or small urban	^	1.26

Results – SIRs, **non-estrogen**

	Cohort	Subsequent non-estrogen SIR	Any 4 SIR
	All non-estrogen	**1.93**	1.04
Race	White	**1.94**	1.04
	Black	**1.87**	1.02
Year of dx	2005-2009	**1.87**	1.02
	2010-2014	**2.07**	1.06
Age at dx	00-39	**5.42**	**2.03**
	40-49	**3.46**	**1.26**
	50-69	**2.31**	1.04
	70+	**1.53**	0.95
Stage	Localized	**2.08**	**1.18**
	Regional	**2.04**	0.94
	Distant	**1.53**	**0.84**

Results – SIRs, **non-estrogen**

	Cohort	Subsequent non-estrogen SIR	All 4 SIR
Latency	<1 year	**2.06**	1.03
	1 - <5 years	**1.90**	1.02
	5 - <10 years	**1.88**	1.09
Poverty %	<10	**1.92**	0.96
	10 - <20	**1.96**	1.06
	20+	**1.79**	1.02
RUCC2013	Metro	**1.94**	1.01
	Urban, non-metro	**1.90**	**1.15**
	Rural or small urban	**2.07**	0.95

Results – survival

- (breast → breast) vs breast
  - **HR 1.57 (p-val < .0001); 605 cases in group of interest**
- (thyroid → thyroid) vs thyroid
  - HR 0.73 (p-val = .6650); 13 cases in group of interest
- (ovarian → ovarian) vs ovarian
  - *(too few cases)*
- (uterine → uterine) vs uterine
  - *(too few cases)*
- (non-estrogen → non-estrogen) vs non-estrogen
  - **HR 1.41 (p-val < .0001)**; 2937 cases in group of interest

Conclusion

- With the increase in survival of cancer patients, there is an increased need to look at outcomes for patients diagnosed with estrogen-related cancers.

- Increased risk of developing either breast or thyroid cancer as a second malignancy after a diagnosis with one of the cancers
- *Decreased* risk of developing subsequent uterine cancer

- For breast→breast cancer, the risk begins to increase after about the first 5 years after diagnosis
- Targeted follow up of patients with either breast or thyroid cancer can be beneficial for outcomes

Conclusion, cont.

- Follow up of patients for this cancer survivor group is important and monitoring can be beneficial for outcomes.
- Survival for subsequent breast tumors is worse; not statistically significantly different for thyroid (small number of cases)

Questions?

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