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Hormonal contraception and therapy use in breast cancer survivors: Do recurrence and mortality risks increase?

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INTRODUCTION

- Breast cancer survivors are advised to avoid hormone use for contraception and menopausal symptoms, given the lack of adequate research and standardized recommendations.
- Limited non-hormonal options are available for preventing pregnancy or treating menopausal symptoms.
- This leads to a high risk of unintended pregnancies and/or inadequately treated menopausal symptoms.
- Determining the risk of recurrence and mortality may guide clinicians in recommending options for both safe and effective hormone use.

STUDY AIM

- To assess the recurrence and mortality risks of contraceptive and non-contraceptive hormone use in breast cancer survivors.

METHODS

- Retrospective study of women 18-55 years who were diagnosed with stage 0-III breast cancer during 2006-2015 and entered remission following first-course Rx.
- Hormonal therapies included:
 - Hormonal contraception (pill, patch, ring, injection, subcutaneous device, intrauterine device).
 - Non-contraceptive hormonal therapies (e.g., those for menopausal symptoms).
- Multivariable extended proportional hazards models were used to estimate adjusted hazard ratios (HR), as well as overall survival and combined local-regional and distant recurrence probabilities.
- Models incorporated the time-dependent effects of hormone therapy, while adjusting for time-invariant patient, tumor, and treatment effects.

RESULTS

- Following the diagnosis of cancer in 3,437 total patients, 3,134 (91.2%) used no hormones, 171 (4.98%) used hormonal contraceptives, 129 (3.75%) used non-contraceptive hormones, and 3 (0.09%) used both.
- Versus other groups, patients who used hormones, whether for contraception or control of postmenopausal symptoms, were more often White; hormonal contraceptive users were younger; and non-contraceptive hormone users had longer follow-up times (Table 1).
- Models including patients who used hormonal contraceptives versus no hormones revealed no difference between the groups in terms of overall survival or recurrence (Table 2, Figure).
- Models including patients who used non-contraceptive hormones versus no hormones revealed no difference in recurrence but greater risk of non-cancer related death in patients who used hormones (Table 2, Figure).

Table 2. Relative hazard of recurrence and death for patients who used contraceptive or non-contraceptive hormones vs. no hormones, with estimated 5 and 10-year probabilities of recurrence and survival.

Patient group by receipt of hormone therapy and Outcome	Risk of recurrence or death, HR (95% CI)	5-year probability (95% CI)	10-year probability (95% CI)
Outcome: Disease Recurrence			
None	Reference	0.072 (0.062-0.084)	0.123 (0.094-0.160)
Contraceptives	0.78 (0.34-1.80)	0.052 (0.024-0.113)	0.242 (0.055-0.743)
Non-contraceptives	1.52 (0.77-2.99)	0.117 (0.071-0.190)	0.139 (0.087-0.217)
Outcome: Overall Survival			
None	Reference	0.954 (0.944-0.963)	0.877 (0.832-0.911)
Contraceptives	0.52 (0.13-2.15)	0.975 (0.903-0.994)	0.975 (0.903-0.994)
Non-contraceptives	2.95 (1.70-5.09)	0.915 (0.847-0.953)	0.673 (0.348-0.862)

CONCLUSIONS

- Breast cancer survivors who use hormonal contraceptives are not at increased risk of recurrence or mortality relative to women who do not use hormones. However, those who use hormones for control of menopausal symptoms have a higher overall mortality risk.
- Limitations of our study included: (1) Identification and duration of medication use were based on medication reconciliation and prescription history, which could underestimate hormone exposure, and (2) Permanent methods of sterilization were not considered.

Table 1. Patient, tumor, and treatment characteristics for patients who used no hormones, contraceptive hormones (CH), and non-contraceptive hormones (NCH).

Characteristic	Overall	None	CH ^a	NCH ^a
Age (yr), mean (SD)	47.7 (6.04)	47.9 (5.89)	42.8 (7.02)	48.2 (5.41)
White race/ethnicity, n (%)	2960 (86.1)	2684 (85.6)	156 (91.2)	117 (90.7)
Obese, n (%)	856 (24.9)	781 (24.9)	45 (26.3)	29 (22.5)
Stage of disease, n (%)				
0	823 (24.0)	753 (24.0)	39 (22.8)	31 (24.0)
I-II	2247 (65.4)	2042 (65.2)	120 (70.2)	83 (64.3)
III	367 (10.7)	339 (10.8)	12 (7.02)	15 (11.6)
ER/PR positive, n (%) ^b	2562 (78.8)	2343 (79.3)	126 (75.5)	91 (73.4)
HER2/neu positive, n (%) ^b	394 (15.4)	369 (15.8)	15 (11.5)	10 (10.4)
Surgery performed, n (%)	3419 (99.5)	3119 (99.5)	169 (98.8)	128 (99.2)
Hormone therapy received, n (%)	2305 (67.1)	2105 (67.2)	116 (67.8)	82 (63.6)
Length of follow-up (yr), mean (SD)	4.34 (2.73)	4.31 (2.72)	3.44 (2.57)	6.18 (2.25)

^a Three patients who used both CH and NCH are excluded from subgroup statistics.

^b For ER/PR and HER2/neu, respectively, 187 (5.4%) and 874 (25.4%) patients were missing test results.

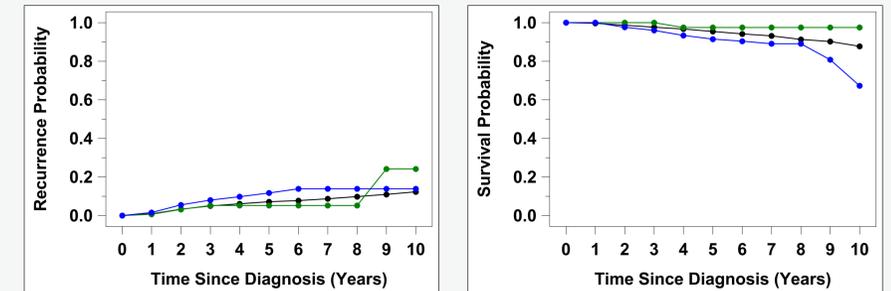


Figure. Probability curves for disease recurrence (left) and overall survival (right) in patients who used no hormones (black) vs. contraceptive hormones (green) vs. non-contraceptive hormones (blue) during the 10 years following cancer diagnosis.

REFERENCES

- Breast Cancer in Young Women. Centers for Disease Control and Prevention Website. http://www.cdc.gov/cancer/breast/young_women/index.htm Published May 8, 2014. Accessed November 2, 2015.
- Quinn MM, Letourneau JM, Rosen MP. Contraception after cancer treatment: describing methods, counseling, and unintended pregnancy risk. *Contraception* 2014; 89 (5): 466-471.
- U.S. Medical Eligibility Criteria for Contraceptive Use. Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. June 18, 2010.
- Petra CM, Faubion SS, MacLaughlin KL, Long ME, Pruthi S. Caring for the breast cancer survivor's health and well-being. *World Journal of Clinical Oncology* 2014; 5 (4): 693-704.
- Xuan TB, Wiebren TA, Makar AP, Buytaert G, Weyler J, Van Dam PA. Use of the levonorgestrel-releasing intrauterine system in breast cancer patients. *Fertility and Sterility* 2008; 90 (1): 17-22.