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ONCOLOGY: BRIEF REPORT

General cancer screening practices among adult survivors of retinoblastoma: Results from the Retinoblastoma Survivor Study

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Abstract

We assessed breast, cervical, and colorectal cancer screening practices in adult retinoblastoma (Rb) survivors and non-Rb controls. We found that most Rb survivors adhered to general population cancer screening recommendations. Rates did not differ among Rb survivors and non-Rb controls, or among survivors by laterality, even though bilateral survivors reported higher levels of concern about future health and cancer risk. Older age, being overweight/obese, and lack of recent contact with medical personnel were independently associated with decreased utilization of Pap smear among female Rb survivors. Future studies are warranted to determine whether these associations might provide an opportunity for intervention.

KEYWORDS
cancer screening, retinoblastoma, survivors, survivorship

Retinoblastoma (Rb) is the most common primary intraocular tumor of childhood with survival rates exceeding 95% in the United States.[1] Rb survivors with a germline *RB1* mutation have a markedly increased lifelong risk of subsequent malignant neoplasms (SMN).[2,3] Given the lack of data on how adult Rb survivors' early life experiences and risk of SMN might impact their patterns of breast, cervical, and colorectal cancer (CRC) screening, we sought to understand whether Rb survivors adhere to existing cancer screening guidelines during adulthood.[4–6] We hypothesized that those with bilateral disease, assumed to have a germline *RB1* mutation, would be more adherent to these guidelines than individuals with unilateral disease or unaffected peers.

We performed a cross-sectional, survey-based study of breast, cervical, and CRC screening practices in a large cohort of adult Rb survivors and a non-Rb comparison cohort as part of the Retinoblastoma Survivor Study, which has been previously described in detail.[7,8] Written informed consent was obtained from eligible participants treated for Rb between 1932 and 1994 who were ≥18 years old and alive at the time of study. Participants completed comprehensive questionnaires adapted from the Childhood Cancer Survivor Study (CCSS) between

Abbreviations: CCSS, Childhood Cancer Survivor Study; CI, confidence interval; CRC, colorectal cancer; Rb, retinoblastoma; RR, relative risk; SMN, subsequent malignant neoplasms

TABLE 1 Characteristics of adult Rb survivors and non-Rb control group in the Retinoblastoma Survivor Study

Characteristic	All Rb survivors (n = 470)	Unilateral Rb survivors (n = 218)	Bilateral Rb survivors (n = 252)	Non-Rb controls (n = 2271)	P1[a]	P2[b]
Age at study, median (range)	43 (18, 77)	44 (19, 77)	42 (18, 69)	37 (16, 62)	.09	<.001
Female	245 (52.1)	120 (55.0)	125 (49.6)	1215 (53.5)	.24	.59
Race/ethnicity					.37	<.001
White, non-Hispanic	406 (86.8)	185 (85.2)	221 (88.0)	2016 (92.0)		
Others	63 (13.2)	32 (14.8)	30 (12.0)	175 (8.0)		
Body mass index (mg/m^2)					.001	.60
<18.5	6 (1.3)	3 (1.4)	3 (1.2)	43 (1.9)		
18.5-24.99	189 (40.8)	103 (47.3)	86 (34.1)	911 (40.1)		
25.0-29.99	142 (30.7)	67 (30.7)	75 (30.0)	718 (31.6)		
≥30.0	126 (27.2)	41 (18.8)	85 (33.7)	557 (24.5)		
Health insurance					.10	.07
Yes, or Canadian	416 (88.9)	188 (86.6)	228 (90.8)	2064 (91.5)		
Household income					<.001	<.001
<$20 000	45 (10.3)	13 (6.5)	32 (13.5)	115 (5.4)		
≥$20 000	59 (13.5)	187 (93.5)	205 (86.5)	2000 (94.5)		
Highest education					.63	.21
High school or lower	64 (10.3)	28 (12.8)	36 (14.3)	263 (11.6)		
Post-high school or college	394 (86.0)	185 (84.9)	209 (82.9)	1961 (86.3)		
Contact with physician/nurse in past 2 years					.006	.54
Yes	408 (86.8)	179 (82.2)	229 (90.9)	1995 (87.9)		
Concerned about future health						
Not very/not at all concerned	138 (30.1)	92 (43.6)	46 (18.6)	914 (40.7)	<.001	<.001
Concerned/very concerned	320 (69.9)	119 (56.4)	201 (81.4)	1331 (59.3)		
Level of concern about developing SMN					<.001	<.001
Not very/not at all concerned	135 (29.5)	94 (44.5)	41 (16.6)	942 (42.0)		
Concerned/very concerned	323 (70.5)	117 (55.4)	206 (83.4)	1301 (58.0)		
Rb-directed therapy					<.001	
Chemotherapy or radiation	282 (60.7)	48 (22.4)	234 (93.2)	NA		
None	183 (39.3)	166 (77.6)	17 (6.8)			

Note. Column percentages are presented in parenthesis for categorical variables.
Abbreviations: Rb, retinoblastoma; SMN, subsequent malignant neoplasm.
[a]P1: comparison between survivors of unilateral versus bilateral Rb.
[b]P2: comparison between all Rb survivors versus non-Rb controls.

2008 and 2011. The study was approved by the Memorial Sloan Kettering and National Cancer Institute Institutional Review Boards.

Four hundred seventy survivors consented and completed the survey (response rate 72.2%). Non-Rb controls were a random sample of CCSS survivors' nearest age, living siblings (n = 2271).[9] Cancer screening outcomes included: mammogram within the previous 2 years among women aged ≥40 years; Pap smear within the past 2 years among women ≥21 years; and screening colonoscopy/sigmoidoscopy in the past 10 years for individuals ≥50 years, which were based on US surveillance guidelines available at the time of survey.[4–6]

Sociodemographic data were compared among Rb survivors, by disease laterality, and between Rb survivors versus non-Rb controls using Fisher's exact and the Wilcoxon rank-sum tests. Log-binomial regression with robust variance estimate was used to directly estimate relative risk (RR),[10] compare cancer screening outcomes between groups, and evaluate factors associated with screening outcomes among survivors. A multivariable model was constructed, including factors associated with each cancer screening outcome at $P < .1$ levels. Body mass index was categorized as underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obese (≥30 kg/m^2). Household income was categorized using previously established cutoffs.[8]

All analyses were performed with SAS Version 9.3 (SAS Institute Inc., Cary, NC). Two-sided *P*-values < .05 indicate statistical significance.

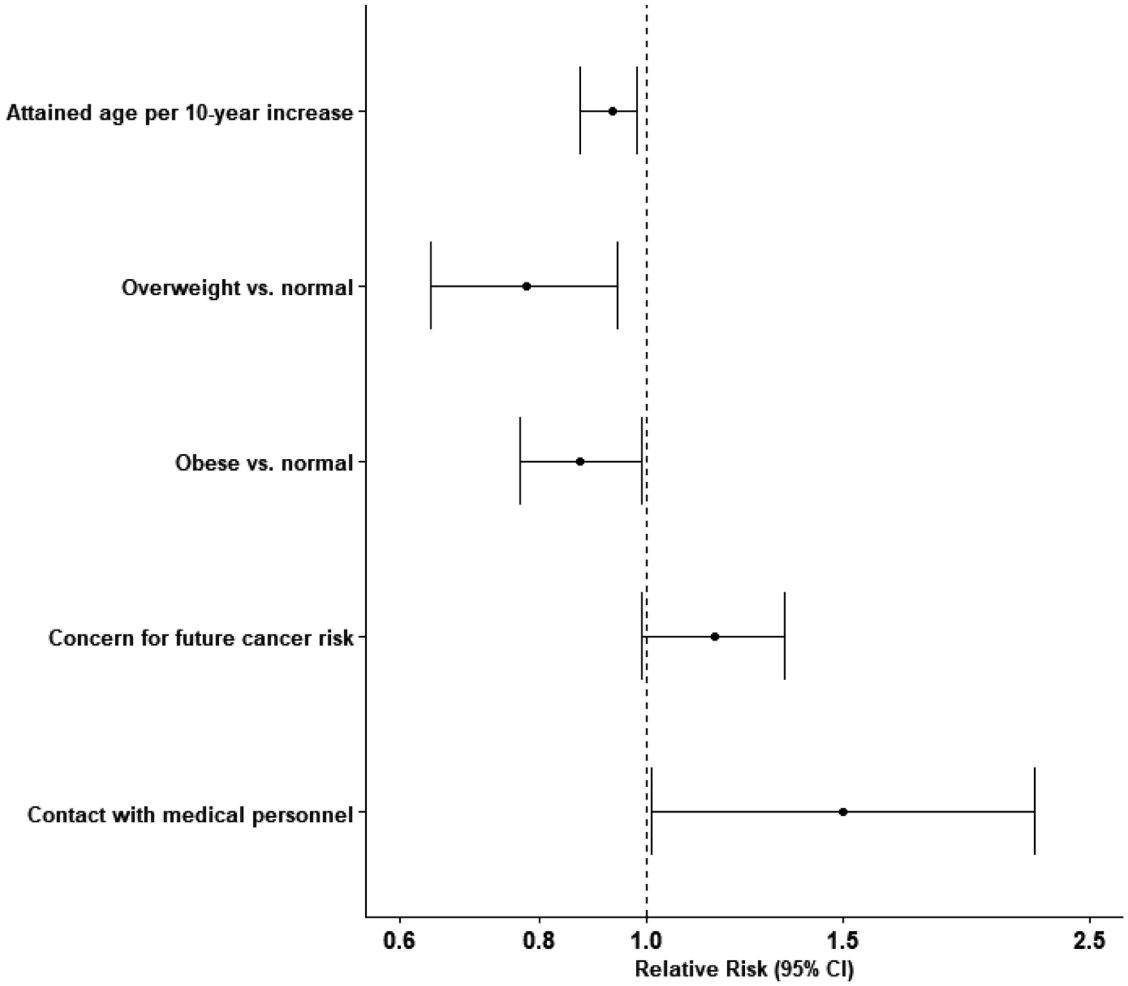

FIGURE 1 Multivariable analysis of factors associated with cervical cancer screening utilization among female retinoblastoma survivors. This forest plot depicts the factors independently associated with cervical cancer screening utilization among female retinoblastoma survivors. Relative risks and 95% confidence intervals were estimated using a multivariable log-binomial regression model with a robust variance estimate

Table 1 summarizes characteristics of Rb survivors, by disease laterality, and non-Rb controls; there were 164 Rb survivors eligible for the mammography analysis; 241 for Pap smear; and 130 for CRC screening. Survivors of bilateral disease were more likely than those with unilateral disease to: be obese (33.7% vs 18.8%, $P = .001$); report household income <$20 000 (13.5% vs 6.5%, $P < .001$); have received systemic chemotherapy/radiation (93.2% vs 22.2%, $P < .001$); and have contact with a medical provider ≤2 years prior to survey completion (90.9% vs 82.8%, $P = .006$). Survivors of bilateral disease were more concerned about future health (81.4%) and developing SMN (83.4%) than those with unilateral disease (56.4% and 55.4%, both $P < .001$).

There was no difference in frequency of screening mammogram or Pap test during the recommended interval (mammogram: 76.2% vs 73.7%, $P = .53$; Pap test: 82.9% vs 84.4%, $P = .66$) between all Rb survivors and non-Rb controls. Eligible Rb survivors reported higher rates of CRC screening than non-Rb controls (70.0% vs 54.9%, $P \leq .006$), but after adjusting for age, the difference was not significant. There was no difference in utilization of mammography (80.0% vs 72.4%, $P = .24$); Pap smear (83.7% vs 82.3%, $P = .75$); or colonoscopy/sigmoidoscopy (68.6% vs 71.4%, $P = .73$) among Rb survivors with unilateral versus bilateral disease.

In multivariable analysis, older age (RR 0.96, 95% confidence interval [CI]: 0.93-0.99), being overweight (RR 0.78, 95% CI: 0.64-0.94), or obese (RR 0.87, 95% CI: 0.77-0.99) were significantly associated with decreased utilization of Pap smear during the designated interval; survivors who reported contact with medical personnel ≤2 years were more likely to have had cervical cancer screening (RR 1.50, 95% CI: 1.01-2.23) (Figure 1).

Among this large cohort of adult Rb survivors, we found that most survivors adhered to general population recommendations for breast, cervical, and CRC screening, and rates were not different from non-Rb controls. Interestingly, we did not observe different patterns of utilization among Rb survivors by disease laterality. This is surprising because survivors of bilateral Rb reported greater concern about future health, including risk of developing SMN, and contact with medical personnel within the past 2 years, which we would have expected to lead to greater adherence with cancer screening. However, it is also possible that the lack of difference in screening rates between survivors of uni-

lateral versus bilateral disease suggests that all Rb survivors, regardless of disease laterality, are well monitored and informed about their future health risks.

Over three quarters of eligible Rb female participants reported a mammogram or Pap smear (76.2% and 83.0%, respectively), while 70.0% observed CRC surveillance recommendations. These screening rates are similar to previously published results in Rb survivors[11] and other non-Rb childhood cancer survivors.[12] A prior analysis of average-risk female childhood cancer survivors demonstrated that 67% had a mammogram and 81% had a Pap smear within the recommended period.[12] Both Rb and non-Rb survivors adhered to screening guidelines more closely than the general population, where crude screening prevalence was 67.4% for mammogram,[13] 72.8% for Pap smear,[14] and 64.5% for CRC screening[15] during this time.

Several factors were independently associated with decreased utilization of Pap smear, including older age and overweight/obesity. Prior studies have suggested that obese women are less likely to adhere to breast and cervical cancer screening recommendations due to fear or embarrassment about their bodies.[16,17] A Swiss population-based study found a significant association between overweight/obesity, lack of physical activity, and poor dietary behaviors and suboptimal cervical screening adherence.[18] It is unclear if a similar phenomenon underlies the association between weight status and Pap smear utilization in Rb survivors; future studies are needed as this may provide an opportunity for intervention to increase adherence in female Rb survivors, and perhaps in the general population as well.

Several limitations must be considered. All screening practices were self-reported. General population-recommended screening intervals were defined using guidelines in place at the time of survey, which have since changed. All study participants were alive at the time of study; it is possible that screening practices differed among individuals who predeceased the study.

This report provides updated data on the general cancer screening practices of a large cohort of adult Rb survivors compared to non-Rb controls. Our data suggest that adult Rb survivors adhere to general cancer screening guidelines, but there remains room for improvement. Clinicians should continue promoting adherence to general population cancer screening guidelines. Associations between weight status and decreased cervical cancer screening utilization warrant further investigation.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest related to the current work. However, they do report the following disclosures: Ira Dunkel reports consulting for Apexigen, Bayer, Bristol-Myers Squibb, Celgene, Eisai, Pfizer in the past 36 months, as well as contracts with MSKCC to support clinical research studies: Bristol-Myers Squibb, Genentech, Novartis. Danielle Novetsky Friedman held an advisory role for Fennec in the past 36 months. Charles Sklar received honoraria from Novo Nordisk.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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