Age Conditional Probability of Ocular and Ocular Adnexal Malignancies

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Keywords

Cancer risk · Cumulative probability · Lacrimal gland carcinoma · Ocular adnexal cancer · Risk assessment · Uveal melanoma · Retinoblastoma

Abstract

Aim: The aim of this study was to discuss and illustrate the role age-conditional probability has in communicating risk of developing ocular and ocular adnexal malignancies.

Methods: Cross-sectional incidence for retinoblastoma, uveal melanoma, conjunctival melanoma, and lacrimal gland carcinomas from 2000 to 2017 were obtained from the Surveillance, Epidemiology and End Results (SEER) database. Incidence rates were age-adjusted to the 2000 United States population. Age-adjusted incidence was converted to age-interval and cumulative risks. Outcomes were examined in 20-year intervals and cumulatively for adult cancers and yearly for retinoblastoma. **Results:** The risk of each malignancy displayed age-dependent variation. For adult malignancies, men were at higher risk at most age intervals. Uveal melanoma had the greatest cumulative lifetime risk. The probability of developing retinoblastoma declines precipitously after age 3 years. **Conclusions:** Age-conditional probability of developing cancer is a conceptually friendly means of understanding and communicating risk. It is particularly useful in comparing the risks of uncommon or rare

cancers, such as those found in and around the eye. The assessment of risk in terms of age-conditional probability is a versatile and an underutilized pedagogical tool.

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Introduction

The risk of developing cancer plays an important role in describing its epidemiology and in gaining insights into pathobiology. For ocular and ocular adnexal malignancies, the discussion of risk is confounded by the relative rarity of tumors in and around the eye. Several metrics such as mean age-adjusted incidence are usually used to communicate the risk of acquiring cancer. Age-conditional probability is one method that is conceptually accessible and takes into account the strong association of developing different types of cancer during different periods of age [1–4]. Broadly speaking, age-conditional probability can be thought of as the risk of developing a first-time cancer in a susceptible population during a specified time interval. Frequently, this estimate is expressed as a cumulative risk from birth. This type of probability calculation has been underutilized in the study of ocular and ocular adnexal malignancies in part because uncommon tumors depend upon large population-based databases.

This paper describes the age-conditional probabilities of 4 ocular and ocular adnexal cancers using incidence data and vital statistics from the Surveillance, Epidemiology, and End Results (SEER) program. We discuss how age-conditional probability complements other risk metrics and its role in assessing the relative public health burden of cancer.

Methods

Datasets from SEER 18 State Registry were extracted using SEER*Stat version 8.3.6.1 [5]. All ocular and ocular adnexal malignancies except of eyelid skin from 2000 to 2017 were included in the analysis, based on the November 2019 SEER update [6]. The software and database are available from the NCI website without charge. The downloaded datasets from SEER contain incidence data for specific tumors by 5-year age groups and gender. The denominator population for rate calculations were the susceptible populations in the 18 SEER geographic areas.

Within SEER*Stat, the Site and Morphology of Collaborative Stage Data Collection System version 02.04+ was used to extract incidence on 4 eye cancers: uveal melanoma, conjunctival melanoma, lacrimal gland carcinoma, and retinoblastoma. Uveal melanoma included iris, ciliary body, and choroid [7]. Lacrimal gland malignancies did not include lymphoma. For the overall category of “Eye and Orbit,” topography codes C69.1 through 69.9 were linked to behavior code 3 for malignant neoplasm [8]. Malignancies of eyelid skin were excluded.

Incidence rates were age-adjusted to the 2000 United States (US) population [9, 10]. Age-conditional and cumulative risks were calculated from the integral (calculus)-derived relationship of rate to probability using the life table method described by Schouten et al. [11]. Life tables for the study population were obtained from National Vital Statistics reports released annually by the Center for Disease Control (CDC) [12]. Outcomes were gender-specific and divided into 4 age groups and 5 cumulative age intervals (i.e., length of observation) for adult cancers: 0–19 years; 20–39 years; 40–59 years; 60–79 years; and lifetime. The age-interval and cumulative risks for retinoblastoma was annual through 5 years, then 5–10 years, and lifetime. Risks were expressed as single person occurrence per susceptible population with proportional rounding to 3 places. As a means of confirming the general validity of our analyses, we examined the lifetime risks of 3 common cancers (lung-bronchus, breast, and prostate) for comparison with previously published cumulative risks from SEER [13, 14].

Results

Age-interval and cumulative probabilities of uveal and conjunctival melanoma are shown in Table 1, and lacrimal gland carcinoma and all ocular and ocular adnexal cancers in Table 2. Women throughout life are less likely to have these 3 malignancies or cumulative ocular/ocular adnexal cancer overall compared to men. Uveal melano-

ma was the most common malignancy among them, having a lifetime probability of 1 in 1,720 and 1 in 1,980 in men and women, respectively. The lifetime risk of cancer of the lacrimal gland was 1 in 45,600 for men and 1 in 63,900 for women. Conjunctival melanoma fell between these extremes. By comparison, the lifetime risk of uveal melanoma in men is roughly 200 times less than developing prostate cancer and in women nearly 250 times less than developing breast cancer (Tables 1, 3).

Table 4 displays the annual interval and cumulative risk of retinoblastoma to age 5, risk between 5 and 10 years of age, and lifetime risk. The differences in gender risk at these age intervals were small enough to warrant combining genders. As Table 4 illustrates, there was a considerable decline in risk of retinoblastoma after age 3, and negligible lifetime risk after age 5. During the first year of life, the probability of retinoblastoma is 1 in 34,800.

Our calculations for lifetime risk of carcinoma of the lung-bronchus, breast, and prostate compared favorably to 2 previous SEER studies (Table 3) [13, 14].

Discussion

Ocular and ocular adnexal cancers are uncommon to rare, but verbal descriptors of occurrence are subjective and prone to differing interpretations by both lay persons and medical professionals [15]. A common surrogate for communicating risk is incidence, or the probability of developing cancer over a stated period of time. Cancer incidence can be reported in various ways from average age adjusted to age stratified [16]. Given the strong age-dependent profile of all cancers, age-conditional probability is a valuable method of communicating risk as it applies to specific clinical situations. The validity of the estimate, however, depends on accurate counts of new cancer cases and approximation of the denominator population at risk as it changes over time intervals. For this reason, we relied upon the SEER database for cross-sectional incidence and the CDC for vital statistics.

Our finding that men are at greater risk of the 3 adult cancers examined in this study compared to women is consistent with the overall heightened susceptibility of men to many common malignancies [17]. Analysis of the SEER 2004–2008 database, age-adjusted to the 2000 US standard population, had shown the incidence rate for all cancers for men was 553 per 100,000 compared to 416.4 for women [18]. Similarly, the lifetime risk of developing cancer was 44.8% for men compared to 38.1% for women [18]. The reasons are likely multifactorial, probably often

Table 1. Age interval and cumulative risks of uveal and conjunctival melanoma by gender

Age interval, years	Uveal melanoma				Conjunctival melanoma			
	male		female		male		female	
	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:
0–19	588,000	588,000	460,000	460,000	1,580,000	1,580,000	1,320,000	1,320,000
20–39	39,600	37,600	39,200	36,400	367,000	301,000	546,000	276,000
40–59	6,640	5,860	7,970	6,660	129,000	93,100	153,000	99,800
60–79	2,730	2,070	3,410	2,390	38,700	30,500	50,200	35,500
Lifetime		1,720		1,980		20,900		25,600

Table 2. Age interval and cumulative risks of lacrimal gland carcinoma and all ocular adnexal malignancies

Age interval, years	Lacrimal gland carcinoma				All ocular and ocular adnexal malignancies*			
	male		female		male		female	
	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:	interval 1 in:	cumulative 1 in:
0–19	3,670,000	3,670,000	2,600,000	2,600,000	12,300	12,300	12,700	12,700
20–39	367,000	484,000	669,000	536,000	25,000	8,320	27,800	8,730
40–59	152,000	120,000	288,000	190,268	4,890	3,170	6,340	3,720
60–79	77,100	51,400	119,000	77,283	1,800	1,270	2,640	1,630
Lifetime		45,600		63,900		1,020		1,330

* Includes all intraocular and ocular adnexal/orbital malignancies except eyelid skin. See Methods for corresponding ICD-O codes.

Table 3. Lifetime risk of developing common cancers (2017)

Tumor	Current study lifetime risk 2000–2017 USA 1 in:	Published lifetime risk 1 in:	
		1991–2016 USA*	1998–2000 USA†
Lung and bronchus (overall)	15.4	–	–
Men	14.7	15	13
Women	17.1	17	17
Prostate (men)	7.3	9.0	6.0
Breast (women)	8.2	8.0	7.0

* SEER data from Siegel et al. [13]. † SEER data from Gloeckler Ries et al. [14].

Table 4. Retinoblastoma age interval and cumulative risks

Age interval, years	Retinoblastoma*	
	age-interval risk 1 in:	cumulative risk 1 in:
0–1	34,800	34,800
1–2	60,500	22,100
2–3	74,900	17,100
3–4	226,000	15,900
4–5	421,000	15,300
5–10	462,000	14,700
Lifetime		14,600

* Gender risks not different at this level of rounding.

tumor specific, include genetic and environmental influences, and remain largely speculative and the focus of investigation [17].

Our results support the generally acknowledged low probability of developing an ocular or ocular adnexal cancer. Although none of the results are unexpected, the

display of information is edifying. Even for the most frequently studied ocular malignancy uveal melanoma, age-conditional risks complement what is known about its epidemiology [19–21]. Examining specific cancers using age interval and cumulative probabilities are not new. SEER has been reporting them for many common cancers

since the 1990s, but to our knowledge, ocular and ocular adnexal malignancies have not been described in this manner. Age-conditional cancer risk is a useful means of exploring the public health burden of cancers as it permits comparison across cancer types and age groups [3]. It also poses cancer risk in a format that is easy to assimilate and potentially instructive.

Conclusions

Age interval and cumulative probabilities of ocular and ocular adnexal cancer can be calculated using cross-sectional incidence and population vital statistics from sources such as SEER [13, 14]. Age-conditional probabilities can be examined at various age intervals and according to various patient characteristics (e.g., gender, race, ethnicity, etc.), iterations of which are limited by the interests of investigators and availability of collected data. Age-conditional risk is conceptually friendly and can be used as a pedagogical tool.

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Statement of Ethics

This study complied with guidelines of human research as it applies to protected health information in medical records. The study was exempted by the Institutional Review Board of the Morssani College of Medicine as the data used in analyses was collective, devoid of personal identifiers, and existed in public domain.

Conflict of Interest Statement

The authors have no ethical, proprietary, or commercial conflicts of interest.

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Author Contributions

C.E.M. concept/application; M.N. data collection; M.N. and C.E.M. data analysis; C.E.M. original draft of the manuscript; M.N. and C.E.M. revision of the manuscript; M.N. and C.E.M. creation of the tables.