Incidence of Basal Cell and Squamous Cell Carcinomas in a Population Younger Than 40 Years

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Context The incidence of nonmelanoma skin cancer is increasing rapidly among elderly persons, but little is known about its incidence in the population younger than 40 years.

Objectives To estimate the sex- and age-specific incidences of basal cell carcinoma and squamous cell carcinoma in persons younger than 40 years in Olmsted County, Minnesota, and to evaluate change in incidence over time; to describe the clinical presentation, rate of recurrence and metastasis, and histologic characteristics of these tumors in this population-based sample.

Design Population-based retrospective incidence case review.

Setting Residents of Olmsted County, Minnesota, a population with comprehensive medical records captured through the Rochester Epidemiology Project.

Participants Patients younger than 40 years with basal cell carcinoma or squamous cell carcinoma diagnosed between 1976 and 2003.

Main Outcome Measures Incident basal cell carcinomas and squamous cell carcinomas and change in incidence of these tumors over time.

Results During the study period, 451 incident basal cell carcinomas were diagnosed in 417 patients and 70 incident squamous cell carcinomas were diagnosed in 68 patients. Of these tumors, 328 were histologically confirmed basal cell carcinomas and 51 were histologically confirmed squamous cell carcinomas. Overall, the age-adjusted incidence of basal cell carcinoma per 100 000 persons was 25.9 (95% confidence interval [CI], 22.6-29.2) for women and 20.9 (95% CI, 17.8-23.9) for men. The incidence of basal cell carcinoma increased significantly during the study period among women ($P<.001$) but not men ($P=.19$). Nodular basal cell carcinoma was the most common histologic subtype; 43.0% of tumors were solely nodular basal cell carcinoma and 11.0% had a mixed composition, including the nodular subtype. The incidence of squamous cell carcinoma was similar in men and women, with an average age- and sex-adjusted incidence per 100 000 persons of 3.9 (95% CI, 3.0-4.8); the incidence of squamous cell carcinoma increased significantly over the study period among both women ($P=.01$) and men ($P=.04$).

Conclusions This population-based study demonstrated an increase in the incidence of nonmelanoma skin cancer among young women and men residing in Olmsted County, Minnesota. There was a disproportionate increase in basal cell carcinoma in young women. This increase may lead to an exponential increase in the overall occurrence of nonmelanoma skin cancers over time as this population ages, which emphasizes the need to focus on skin cancer prevention in young adults.

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THE OVERALL INCIDENCE OF NONmelanoma skin cancer, consisting of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC), is increasing.[1-16] In the United States, approximately 800 000 new cases of BCC and 200 000 new cases of SCC were diagnosed in 2000.[1] Nonmelanoma skin cancer generally occurs in persons older than 50 years, and in this age group, its incidence is increasing rapidly.[2,7,8,12] However, little is known about its incidence in persons younger than 40 years. Survey, cancer registry, and population-based studies have sporadically investigated BCC and SCC in the young, but the numbers of cases in these studies have been too small to determine trends.[4,8-10,12-14] A report on the incidence of BCC and SCC in persons younger than 25 years in the north of England showed no significant change in incidence rates from the period 1968-1981 to the period 1982-1995; however, the number of participants in this study was too small to assess trends accurately over time.[17]

The natural history of nonmelanoma skin cancer in young persons is

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also in question. The histologic characteristics and clinical course of the tumors have been debated.[18-20] Some have reported that these tumors have a more aggressive behavior than nonmelanoma skin cancers in older populations,[18,19] and others have reported no difference in the behavior or histologic characteristics of these tumors based on age.[20]

The incidence trends, histologic characteristics, and overall natural history of nonmelanoma skin cancer, including cure rates, recurrence rates, and rates of metastasis, need to be defined more clearly in the young population. This would assist in risk stratification, prevention, education, and treatment as well as in health policy planning. The total annual cost of treating nonmelanoma skin cancer in the current Medicare population in the United States has been $426 million.[21] A potential increase in the incidence of this skin cancer in the young could mean an exponential increase in its occurrence in the future elderly population because those who have BCC or SCC are likely to develop more of these tumors. This increased incidence will result in sizeable increased medical costs.

The specific aim of our study was to estimate the sex- and age-specific incidence of BCC and SCC in Olmsted County, Minnesota, in a young population (<40 years old) from the beginning of 1976 through 2003. Another objective was to describe the clinical presentation (ie, age at diagnosis and location and size of lesion), rate of recurrence and metastasis, and histologic characteristics of these tumors in this population-based sample.

METHODS

Trends of SCC and BCC in the young were examined within the population of Olmsted County, Minnesota. Olmsted County is a population served primarily by 2 medical care facilities that have kept comprehensive clinical records for several decades. Olmsted County (with a 1990 population of 106 470) is 90 miles southeast of Minneapolis and St Paul, Minn, at latitude 43°55′ north. Approximately 70% of the county population resides within the city limits of Rochester, Minn, the county seat. The population is primarily white (96% in 1990) and largely middle class, with approximately 82% of the adult population being high school graduates. Except for a larger proportion of the working class being employed in health care–related occupations, the characteristics of the Olmsted County population are similar to those of the US white population.[22] Thus, the data from our study can be generalized to the white population of the United States.

The initiation of the Rochester Epidemiology Project in 1966 and its continuation through the present affords the opportunity to perform accurate incidence studies.[22] The complex array of medical record data, medical and surgical indexing systems, tumor registry data, and non–Mayo Clinic sources have been combined to provide incidence data for almost any disease diagnosed in Olmsted County. Comprehensive medical diagnostic information that spans several decades is available for a defined population. The sources of data that constitute the Rochester Epidemiology Project include residents treated at Mayo Clinic, Olmsted Medical Group, Olmsted Community Hospital, regional hospitals, and nursing homes and by private practitioners. Thus, the information is essentially complete and is an excellent source for examining trends in disease over time.

This study was approved by the institutional review boards of the Mayo Foundation and Olmsted Medical Center. Informed consent was not required. Only records authorized for research use were used. Potential cases of SCC and BCC were identified through the resources of the Rochester Epidemiology Project described above. The study included patients younger than 40 years who were residents of Olmsted County at the time that BCC or SCC of the skin was first diagnosed. Only incident cases from the beginning of 1976 through 2003 were included. Patients were excluded if they had a genetic disease that predisposed to accelerated development of BCC and/or SCC (ie, basal cell nevus syndrome or xeroderma pigmentosum), congenital lesions such as nevus sebaceus that predispose to development of BCC, or previous treatment with radiation at the site of tumor occurrence. These cases were excluded from the study because the conditions are characterized by inherent etiologic factors that place these patients at high risk of nonmelanoma skin cancer at an early age by mechanisms different from those of the general population. Within the small population included in our study, a few patients with these diagnoses and inherent etiologic risk factors potentially could change the incidence patterns observed in the general population of Olmsted County younger than 40 years. One person with basal cell nevus syndrome and 2 with BCC arising in nevus sebaceus were excluded from the study. The exclusion of these 3 cases for these reasons does not negatively or positively alter the overall outcome of incidental trends. Also, cases of SCC or BCC that were not confirmed by an official pathology report were excluded. Cases of SCC of the anogenital region were excluded because these tumors are caused by a different set of predisposing risk factors than nonmelanoma skin cancers at other anatomical sites. Using these criteria, we identified 70 potential SCCs in 68 patients and 451 BCCs in 417 patients.

The medical records for all patients with BCC or SCC were reviewed and the following relevant information was abstracted: residence (Olmsted County resident or nonresident), date of birth, sex, race (white, Hispanic, black, Asian, American Indian, Middle Eastern descent, or other), transplantation with long-term immunosuppression, date of diagnosis, histologic diagnosis of tumor (confirmed in all cases by an official pathology report), location and size of tumor, method of

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treatment (none, liquid nitrogen, electrodessication and curettage], excision, Mohs surgery, or other), date of recurrence, and evidence of metastasis (at the time of diagnosis or follow-up). Race/ethnicity was determined by patients in their personal medical records. Because the different skin types of different races and ethnicities place individuals at varying risks of nonmelanoma skin cancer, this was an important study variable. Of the 521 incident tumors, archived histologic slides of 398 were available for histologic examination and review by a board-certified dermatopathologist (T.A.B.) for the purposes of this study. The dermatopathologist was blinded to the original diagnosis. Basal cell carcinomas were classified by subtype (nodular, micronodular, superficial, infiltrating or sclerosing, or metatypical) and SCCs by the degree of differentiation (well, moderately, or poorly differentiated). The criteria for the diagnoses of BCC and SCC and the determination of subtype and differentiation were in accordance with those published elsewhere.[23]

Basal cell carcinomas and SCCs were analyzed separately. Age- and sex-specific incidence rates in Olmsted County during 1976-2003 were calculated overall and for 5-year intervals. The incidence rates were calculated with the assumption that the entire population of Olmsted County younger than 40 years was at risk. The numerator was the number of persons with a first occurrence of either BCC or SCC within this period, and the denominator was obtained from the decennial census data for 1976-2003, with linear interpolation between census years. Rates were age- and sex-adjusted to the population structure of US whites in 2000. The 95% confidence intervals for the rates were calculated assuming a Poisson error distribution. The relation of BCC or SCC incidence rates to sex, age, and time period (5-year intervals) of diagnosis were assessed by fitting generalized linear models assuming a Poisson error structure using the SAS procedure GENMOD (SAS version 8.2; SAS Institute Inc, Cary, NC). The observations used for the regression analysis were the crude incidence counts for all combinations of sex, 5-year age groupings, and 5-year time periods, which were offset by the natural logarithm of the number of persons. The significance of linear trends across age groupings and time periods were each assessed with likelihood ratio statistics with 1 degree of freedom. The significance of interaction terms and higher-order polynomials was also examined. Overdispersion was accounted for by estimating a dispersion parameter (ie, deviance divided by its degrees of freedom), which was then used to adjust the variance of the parameter estimates.[24]

Recurrence-free survival was estimated on a per-patient basis using the Kaplan-Meier method. The duration of follow-up was calculated from the date of diagnosis to the date of the documented recurrence or the last clinical follow-up.

Tumor size (based on the maximal tumor dimension of the largest tumor per patient) was compared between men and women using the Wilcoxon rank sum test. The correlation between tumor size and either the year of diagnosis or the age at diagnosis was assessed using the Spearman rank correlation coefficient. Associations between tumor location (torso vs nontorso) and sex, year of diagnosis, or BCC subtype (with indicator variables to define the different types) were assessed by fitting separate logistic regression models. In these models, generalized estimating equation methods (SAS procedure GENMOD) were used to model the correlation among the multiple tumors per patient. All calculated P values were 2-sided, and $P<.05$ was considered statistically significant.

RESULTS

Basal Cell Carcinomas

During the study period, 451 incident BCCs were diagnosed in 417 Olmsted County residents. Of these 451 tumors, histologic slides of 341 (75.6%) were reviewed by a board-certified dermatopathologist to confirm the diagnosis and subtype of BCC; histologic slides were not available for 110 tumors (24.4%). Of the 341 tumors reviewed histologically, 328 were confirmed to be BCCs and 13 were interpreted as trichoepitheliomas or desmoplastic trichoepitheliomas despite a previous official pathology report of BCC.

Of the 417 patients, 397 (95.2%) were white, 1 was Asian, and 2 were of Middle Eastern descent. The race/ethnicity of 17 patients was not known or not recorded. The large percentage of whites is consistent with the racial composition of the population of Olmsted County. The mean (SD) age at diagnosis was 33.3 (4.8) years, and 56.6% of the patients were women. The group included 2 transplant recipients who were immunosuppressed, 1 patient who had human immunodeficiency virus infection, and 1 who was receiving long-term prednisone therapy for inflammatory bowel disease. The highest educational level attained was recorded for 364 patients: 66 (18.1%) had a high school education or less, 72 (19.8%) had some postsecondary education, 149 (40.9%) had a college education, and 77 (21.2%) had completed graduate school. Smoking status was known for 397 patients: 61 (15.4%) were using tobacco at the time of diagnosis, 81 (20.4%) were past smokers, and 255 (64.2%) reported never smoking. Of the 417 patients, 393 (94.2%) had 1 incident tumor, 17 (4.1%) had 2 incident tumors, 4 (1.0%) had 3 incident tumors, and 3 (0.7%) had 4 incident tumors.

Incidence trends based on the subset of 304 patients with 328 histologically confirmed BCC tumors were similar to those based on all 417 patients (FIGURE 1). Thus, we present incidence data based on all 417 patients, with 451 incident BCCs identified by official pathology report, and subset analyses of BCC subtypes based on the 328 histologically confirmed tumors. As shown in TABLE 1, incidence of BCC in the young population generally in-

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creased during the 1976-2003 period ($P<.001$). This was driven by the increase in tumors in women ($P<.001$) but not in men ($P=.19$). Also, there was a linear increase in incidence with age among both men and women ($P<.001$; Table 1). The incidence over time by sex and age is shown in FIGURE 2. In particular, the incidence has increased steadily over time among women 36 to 39 years old.

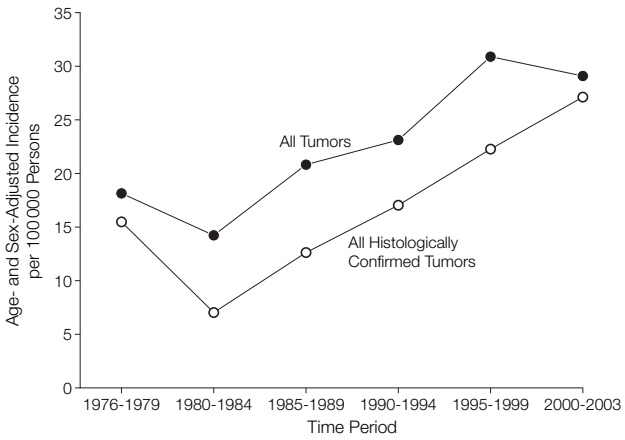
Men were more likely to have larger BCC tumors than women (median, 7 mm vs 6 mm; $P<.001$). There was no significant correlation between maximum tumor size and either year of diagnosis ($r=0.09$; $P=.08$) or age at diagnosis ($r=0.03$; $P=.58$). There was also no significant change in maximum tumor size of incident BCCs during the study period (median, 6, 6, 6, 6, 6, and 7 mm for 1976-1979, 1980-1984, 1985-1989, 1990-1994, 1995-1999, and 2000-2003, respectively).

The most common location of BCCs was the head and neck region, with most tumors occurring on the central face in both men and women (TABLE 2). Tumors on the torso were more common among women than men ($P=.02$). The distribution of tumor location changed over time ($P<.001$). In particular, the proportion of all tumors located on the torso increased steadily from 18.9% in 1976-1979 to 50.0% in 2000-2003 (16.7%, 33.3%, 38.6%, and 39.7% for 1980-1984, 1985-1989, 1990-1994, and 1995-1999, respectively).

The majority (54.6%) of BCCs were treated by excision. Also, 20.6% of the tumors were treated by electrodessication and curettage and 20.6% by Mohs surgery; 12 (2.7%) were presumedly removed with biopsy and received no further treatment; 3 (0.7%) were treated with liquid nitrogen; and 4 (0.9%) had other treatment (the tumor was treated with a carbon dioxide laser and fluorouracil in 1 patient each and with imiquimod in 2 patients).

Seven tumors recurred in 7 patients: 3 tumors recurred less than 2 years

Figure 1. Age- and Sex-Adjusted Incidence of Basal Cell Carcinoma per 100 000 Persons by 5-Year Intervals in Olmsted County, Minnesota, 1976-2003



Results are shown separately based on all 417 patients with incident tumors and the subset of 304 patients with histologically confirmed tumors.

Table 1. Incidence of Basal Cell Carcinoma per 100 000 Persons by 5-Year Intervals and Age in Olmsted County, Minnesota, 1976-2003*

	Women		Men		Both Sexes	
	No. of Cases (n = 236)	Rate per 100 000	No. of Cases (n = 181)	Rate per 100 000	No. of Cases (n = 417)	Rate per 100 000
Period†						
1976-1979	13	13.4	22	22.9	35	18.2‡
1980-1984	22	14.3	19	14.0	41	14.1‡
1985-1989	34	20.3	33	21.2	67	20.7‡
1990-1994	46	26.4	32	19.7	78	23.0‡
1995-1999	74	41.6	36	20.4	110	31.0‡
2000-2003	47	31.6	39	26.7	86	29.1‡
Age group, y						
0-20	8	1.7	2	0.4	10	1.0
21-25	15	12.6	3	2.9	18	8.1
26-30	47	34.5	30	23.6	77	29.2
31-35	70	55.7	66	53.2	136	54.5
36-39	96	99.6	80	86.1	176	93.0
Age-adjusted (95% CI)†		25.9 (22.6-29.2)		20.9 (17.8-23.9)		23.4 (21.1-25.6)‡

Abbreviation: CI, confidence interval.
*There was a linear increase in the incidence of basal cell carcinoma across study periods ($P<.001$). However, this trend was driven by an increase in tumors in women ($P<.001$) but not in men ($P = .19$). There was a linear increase in the incidence of basal cell carcinoma with age among both men and women ($P<.001$).
†Adjusted to the population structure of the US white population younger than 40 years in 2000.
‡Rate is sex- and age-adjusted.

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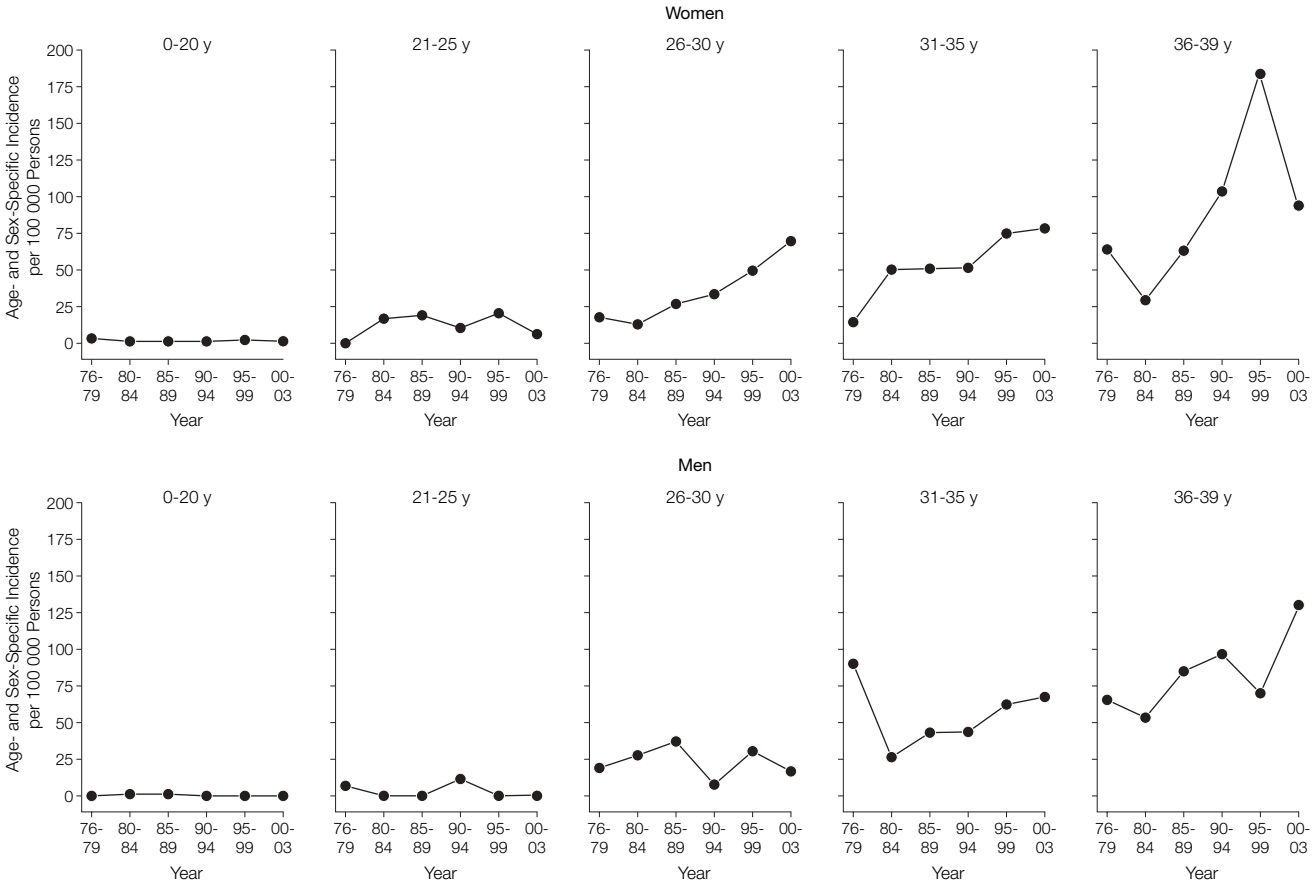
Figure 2. Age- and Sex-Specific Incidence of Basal Cell Carcinoma per 100 000 Persons by 5-Year Intervals in Olmsted County, Minnesota, 1976-2003



after the initial diagnosis, 3 occurred 2 to 3 years later, and 1 occurred 13.7 years after diagnosis. Among patients without recurrence, the median follow-up was 3.7 years (interquartile range, 1.6-8.6 years). Recurrence rates were 0%, 0.8%, 1.8%, and 1.8% at 1, 2, 3, and 5 years, respectively, after the initial diagnosis. No metastases were documented.

The subtypes of the 328 histologically confirmed BCCs are summarized in TABLE 3. Nodular BCC was the most common form, with 177 tumors (54.0%) being either solely nodular BCC (n=141) or having a mixed composition (n=36). Seventy-nine tumors (24.1%) were solely superficial BCC. Eighty-nine tumors (27.1%) were classified as an aggressive subtype. These included tumors composed predominantly of either the infiltrating or sclerosing subtypes or the micronodular subtype (n=53) and tumors with at least roughly one third of their volume consisting of 1 of these subtypes (n=36). Of the 328 histologically confirmed BCCs, 179 (54.5%) were located on the head and neck, 135 (41.2%) on the torso, and 14 (4.3%) on the extremities. The frequency distribution of the BCC subtypes was significantly different according to tumor location ($P<.001$). Of the 135 tumors located on the torso, 65 (48.1%) were superficial, 48 (35.6%) were nodular, 10 (7.4%) were aggressive, 8 (5.9%) consisted of 2 subtypes, and 4 (3.0%) were other subtypes. In contrast, of the 179 tumors on the head and neck, 7 (3.9%) were superficial, 88 (49.2%) were nodular, 42 (23.5%) were aggressive, 28 (15.6%) consisted of 2 subtypes, and 14 (7.8%) were other sub-

Table 2. Anatomical Sites of 451 Incident Basal Cell Carcinomas in 417 Patients

Site	No. (%) Women (n = 257 Tumors)	No. (%) Men (n = 194 Tumors)
Head and neck	137 (53.3)	124 (63.9)
Scalp	5	7
Forehead	15	25
Nose/eyelid/chin*	54	32
Temple	11	20
Cheek	27	20
Lip	12	1
Ear	0	1
Neck	13	18
Torso	108 (42.0)	58 (29.9)
Shoulder	32	14
Chest	33	13
Abdomen	9	2
Back	34	29
Extremities	12 (4.7)	12 (6.2)
Arm	8	4
Forearm	0	3
Wrist/hand	0	0
Thigh	3	0
Leg	1	5
Foot/ankle	0	0

*Of the 86 basal cell carcinomas, 60 were on the nose, 24 on the eyelids, and 2 on the chin.

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types. The frequency distribution of BCC subtypes was similar for men and women (among men, 21.9% superficial, 46.7% nodular, and 16.1% aggressive; among women, 25.7% superficial, 40.3% nodular, and 16.2% aggressive). No obvious trend in change of BCC subtypes was detected over time (nodular, 67.7%, 36.8%, 41.5%, 43.6%, 42.5%, and 36.4%; superficial, 9.7%, 15.8%, 24.4%, 16.1%, 26.4%, and 34.1% for 1976-1979, 1980-1984, 1985-1989, 1990-1994, 1995-1999, and 2000-2003, respectively).

Table 3. Summary of BCC Subtypes in 328 Lesions From 304 Incident Cases Based on Review of Pathology Slides*

BCC Subtype	Tumors, No. (%)
Nodular	141 (43.0)
Superficial multifocal	79 (24.1)
Aggressive	53 (16.2)
Infiltrative/sclerosing	24
Micronodular	20
Metatypical	9
Fibroepithelioma of Pinkus	3 (0.9)
Other†	16 (4.9)
Mixed composition	36 (11.0)
Nodular and infiltrative	13
Nodular and micronodular	22
Infiltrative and micronodular	1

*Three hundred forty-one basal cell carcinoma (BCC) cases were reviewed; of these, 13 tumors were interpreted as trichoepithelioma or desmoplastic trichoepithelioma. Another 110 cases of BCCs were not available for review.
†Includes cases in which the biopsy was so superficial that the subtype could not be determined, even though BCC could be diagnosed.

Squamous Cell Carcinomas

During the study period, 70 incident SCCs were diagnosed in 68 patients. Fifty-one (72.8%) of these tumors were confirmed histologically. Two specimens (2.9%) were interpreted as actinic keratosis despite the previous official pathology report of SCC and 1 (1.4%) as an inverted follicular keratosis; 2 specimens (2.9%) had nondiagnostic features and 1 (1.4%) was classified as BCC on subsequent review; 13 specimens (18.6%) were not available for histologic examination.

Of the 68 patients, 63 (92.6%) were white, 2 were Asian, and 1 was Hispanic. The race/ethnicity of 2 patients was not known or not recorded. The mean (SD) age at diagnosis was 33.4 (5.4) years, and 47% of the patients were women. The group included 4 transplant recipients who were immunosuppressed and another patient who was receiving long-term prednisone therapy for Crohn disease. The highest educational level attained was recorded for 64 patients: 17 (26.6%) had a high school education or less, 12 (18.8%) had some postsecondary education, 28 (43.8%) had a college education, and 7 (10.9%) had completed graduate school. Smoking status was known for 66 patients: 21 (31.8%) were using tobacco at the time of diagnosis, 13 (19.7%) were past smokers, and 32 (48.5%) reported never smoking. All 68 patients had a single incident tumor except for 1 immunosuppressed transplant recipient, who had 3 incident tumors.

The incidence trends based on the subset of 51 patients with 51 histologically confirmed SCCs were similar to those based on all 68 patients (FIGURE 3). Thus, we present the incidence data based on the 68 patients with 70 incident SCCs as identified by official pathology report and present subset analyses of SCCs based on the 51 tumors for which the diagnosis was confirmed histologically. As shown in TABLE 4, the incidence of SCC increased slightly over time in our young population during the study period ($P=.001$); this trend was significant for both women ($P=.01$) and men ($P=.04$). The incidence has increased at a similar rate with age for both men and women ($P<.001$). However, men aged 36 to 39 years had twice the incidence as women in the same age group (Table 4).

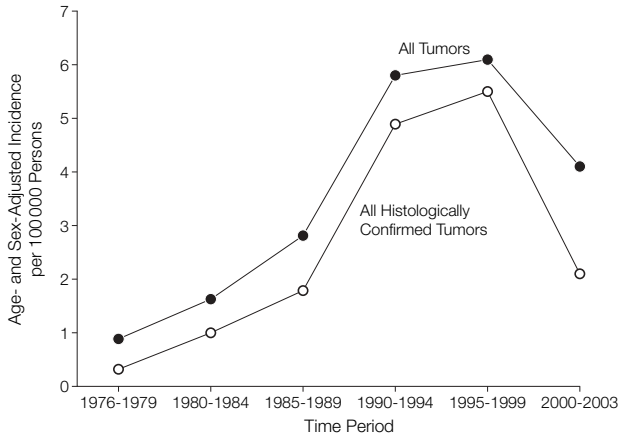
Maximum tumor size was not significantly different between men and women (median, 5.5 mm vs 5 mm; $P=.71$). The correlation between tumor size and either year of diagnosis ($r=-0.09$; $P=.52$) or age at diagnosis ($r=-0.04$; $P=.79$) was not significant.

The most common location of SCCs was the head and neck, with most tumors occurring on the central face in both men and women (TABLE 5). The location of the tumors was similar for men and women. According to the pathology review of the 51 tumors, 28 were well differentiated, 3 were moderately differentiated, 2 were poorly differentiated, 15 were in situ lesions, and 3 were indeterminate because of sectioning.

The majority (53%) of the SCCs were treated by excision. Also, 14% were treated by electrodessication and curettage, 21% by Mohs surgery, and 9% with a carbon dioxide laser; 3% were presumed removed with biopsy and received no further treatment.

There were 2 recurrences: 1 well-differentiated tumor recurred 2.8

Figure 3. Age- and Sex-Adjusted Incidence of Squamous Cell Carcinoma per 100 000 Persons by 5-Year Intervals in Olmsted County, Minnesota, 1976-2003



Results are shown separately based on all 68 patients with incident tumors and the subset of 51 patients with histologically confirmed tumors.

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months after diagnosis and 1 moderately differentiated tumor recurred 7.1 months after diagnosis. Among patients without recurrence, the median follow-up was 4.9 years (interquartile range, 2.5-7.3 years). The recurrence rate at 1 year after the initial diagnosis was 3.2% (95% confidence interval, 0-7.4). No metastases were documented.

The degree of differentiation was not different between men and women. Also, there did not appear to be any difference in differentiation across the 1976-2003 period; however, the overall number of cases was too small to assess for a trend.

Table 4. Incidence of Squamous Cell Carcinoma per 100 000 Persons by 5-Year Intervals and Age in Olmsted County, Minnesota, 1976-2003*

	Women		Men		Both Sexes	
	No. of Cases (n = 32)	Rate per 100 000	No. of Cases (n = 36)	Rate per 100 000	No. of Cases (n = 68)	Rate per 100 000
Period†						
1976-1979	1	0.6	1	1.3	2	0.9‡
1980-1984	1	0.7	4	2.5	5	1.6‡
1985-1989	4	2.3	5	3.2	9	2.8‡
1990-1994	10	5.9	9	5.8	19	5.8‡
1995-1999	10	5.6	11	6.5	21	6.1‡
2000-2003	6	4.1	6	4.2	12	4.1‡
Age group, y						
0-20	1	0.2	1	0.2	2	0.2
21-25	2	1.7	2	2.0	4	1.8
26-30	5	3.7	5	3.9	10	3.8
31-35	12	9.5	7	5.6	19	7.6
36-39	12	12.5	21	22.6	33	17.4
Age-adjusted (95% CI)†		3.5 (2.3-4.7)		4.3 (2.9-5.7)		3.9 (3.0-4.8)‡

Abbreviation: CI, confidence interval.
*There was a linear increase in the incidence of squamous cell carcinoma across the study period ($P = .001$). This trend was significant for both women ($P = .012$) and men ($P = .039$). There was also a linear increase in the incidence of squamous cell carcinoma with age among both men and women ($P < .001$).
†Adjusted to the population structure of the US white population younger than 40 y in 2000.
‡Rate is sex- and age-adjusted.

COMMENT

Nonmelanoma skin cancer is the most common form of cancer worldwide, and its incidence is increasing. This increasing incidence is most likely due to a combination of multiple factors, including increased exposure to UV light, ozone depletion, and increased surveillance. Long-term exposure to the sun resulting in photodamage is perhaps the biggest risk factor for nonmelanoma skin cancer. Also, genetic defects, as in basal cell nevus syndrome and xeroderma pigmentosum, are risk factors for the accelerated development of nonmelanoma skin cancer. Understanding of these genetic factors is in its infancy. According to a recent study, a decrease in DNA repair capacity is greater in healthy young patients without other predisposing genetic abnormalities who have a history of nonmelanoma skin cancer than in age-matched controls, suggesting that to-be-determined genetic susceptibility may be the key factor in the early onset of nonmelanoma skin cancer.[25]

Because the incidence of nonmelanoma skin cancer increases with age, increased longevity of the general population is thought to be a major cause of the increasing incidence of this cancer.[4,8,9,13] The increasing incidence with age possibly reflects cumulative sun exposure and damage over time. Our results show that the incidence of BCC and SCC increased with the age of the patients during the study period. This is in agreement with the general trend. However, our study also shows that the incidence is increasing over time in the young. This increase is not related to advanced age with associated cumulative sun exposure.

Our study has shown that the age-adjusted incidence of BCC for 1976-2003 increased significantly among women. This incidence is significantly higher for women than for men. A trend toward higher incidence of BCC in young women than in men has been reported by others.[18,19] This is a different male-female ratio of incidence than that found in studies that included all ages. In those studies, nonmelanoma skin cancer was more frequent in men.[4,8,9,13] A previous study[13] that used the Rochester Epidemiology Project (1976-1984) and included all ages found that the age-adjusted annual incidence of BCC for women (124/100 000 persons) was significantly less than that for men (175/100 000 persons), an expected difference based on general trends from that seen in the young population of our study.

Table 5. Anatomical Sites of 70 Incident Squamous Cell Carcinomas in 68 Patients

Site	No. (%)	
	Women (n = 34 Tumors)	Men (n = 36 Tumors)
Head and neck	21 (61.8)	24 (66.7)
Scalp	0	2
Forehead	2	0
Nose/eyelid/chin	6	6
Temple	2	5
Cheek	5	4
Lip	3	5
Ear	1	1
Neck	2	1
Torso	7 (20.6)	6 (16.7)
Shoulder	2	1
Chest	5	0
Abdomen	0	3
Back	0	2
Extremities	6 (17.6)	6 (16.7)
Arm	1	0
Forearm	0	1
Wrist/hand	2	4
Thigh/hip	1	0
Leg	1	1
Foot/ankle	1	0

Our study also showed that the incidence of SCC has increased significantly over time for both men and women. Previous studies that included all age groups and used the Rochester Epidemiology Project (1976-1984[4] and 1984-1992[9]) reported that the

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age-adjusted annual incidence of SCC among women (22.5/100 000 persons and 71.2/100 000 persons, respectively) was lower than that among men (63.1/100 000 persons and 155.5/100 000 persons). In our data from the period 1976-2003, the age-adjusted SCC incidence was higher in men than in women (4.3 per 100 000 vs 3.5 per 100 000), but this was not statistically significant. It could be that the volume of cases was not sufficient to detect significant differences because of the small number of SCC cases in young persons.

The increased incidence of BCC and SCC in our young patient population could be related to increased public awareness of nonmelanoma skin cancer and increased surveillance. However, if these were the principal factors for this increase, it would be expected that these skin cancers would be detected at an earlier stage, resulting in a decrease in the size of the incident tumors over time. Interestingly, we did not find this expected decrease; the size of BCCs and SCCs was stable over the study period. The median size of the BCCs of men was significantly higher than that of women. The median size of SCCs was not significantly different between the sexes.

Women are assumed to pay closer attention to their appearance and the health of the skin and, thus, seek medical attention sooner than men do. This may contribute to the differences we noted between men and women in the size and incidence of nonmelanoma skin cancers, marked in this study by differences observed with regard to BCC.

Women between 20 and 40 years old who have a history of BCC have been found to be more likely to have past or current smoking than those without a history of BCC.[26] In Olmsted County, 23% and 31% of students in 12th grade reported weekly cigarette use in 1992 and 1999, respectively. In 1992 and 1999, 23% and 21%, respectively, of the adults in Olmsted County reported weekly use of tobacco. Access to tobacco by age in Olmsted County is not available for more direct comparisons. In our study population, 15.4% of those with BCC and 31.8% of those with SCC reported use of tobacco at the time of diagnosis. Thus, the use of tobacco products by our patients with BCC does not appear to be higher than that of the general population of Olmsted County. However, there is some suggestion that the use of tobacco by our patients with SCC may have been slightly higher than that of the general population of Olmsted County. The risk of SCC in smokers has been documented.[27,28]

The use of a tanning bed has been shown to be a risk factor for nonmelanoma skin cancer in young women.[26] This risk may contribute importantly to the increasing incidence of this cancer; however, we do not have access to information about use of tanning beds by our study population. A previous study that examined use of commercial tanning facilities by Minnesota adolescents in suburban St Paul, 78 miles north of Olmsted County, showed that 34% of study respondents had used commercial tanning facilities, with a lifetime prevalence of indoor tanning of 51% for women and 15% for men.[29] This is a high use of indoor tanning, especially by young women, among whom the incidence of nonmelanoma skin cancer is increasing. A national survey conducted in collaboration with the American Academy of Dermatology in 1986, with follow-up in 1996, showed that regular use of a tanning bed had increased from 2% to 6% among those older than 18 years.[30] In the 1996 survey, this use was shown to be higher for younger age groups, women, and whites. These studies support the possibility that increased use of indoor tanning contributes to the increasing incidence of nonmelanoma skin cancer seen in young populations, especially women.

Although the head and neck region is the most common site for BCC and SCC, only about 60% of BCCs and SCCs were found in this location in our patients, lower than the expected 80% to 90% reported for the general adult population.[31] A trend toward a greater number of BCCs occurring on the torso in younger patients has been reported previously.[32,33] This change in location has also been thought to support the etiologic factor of excessive outdoor tanning, use of tanning parlors, or both.

According to earlier large studies of subtypes of BCCs in adult populations, 56.0% to 78.7% of BCCs are the nodular subtype, 9.0% to 17.5% are the superficial subtype, and 0.5% to 16.6% are the morpheaform subtype.[33-37] Although nodular BCC was the most common subtype in our study, the proportion of incident nodular BCCs in the young population of this study was lower than that of previous reports, resulting in the superficial, micronodular, or infiltrating or sclerosing subtypes combined contributing a larger proportion of incident cases than in previous reports. However, the comparison of studies of subtypes of BCC is difficult because of differences in definitions and histologic criteria; also, not all the studies included a classification of mixed tumors. Moreover, some studies grouped subtypes differently; for example, 1 study included micronodular tumors with nodular ones.[32]

Because we did not assess the incidence of subtypes of BCC in Olmsted County residents older than 40 years, we cannot compare subtypes in younger and older populations. The results of previous studies that evaluated the incidence of more aggressive forms of BCC in the young were mixed. Leffell et al[19] reported that the incidence of aggressive subtypes of BCC among those referred for Mohs surgery was higher for patients aged 35 years or younger (57% of BCCs) than for those older than 35 years (31% of BCCs). This difference was prominent among women and not significant among men. To control for referral bias for Mohs surgery, Leffell et al[19] also examined data from general pathology reports and found that the incidence of aggressive forms of BCC in women aged 35 years or younger was 23% (7/31) and 9% for those

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older than 35 years. There was no increase in the incidence of aggressive subtypes of BCC in men aged 35 years or younger. Roudier-Pujol et al[20] did not find a similar increase in the incidence of morphea-type BCC or aggressive BCCs in patients aged 35 years or younger compared with those older than 35 years. In our study, approximately 27% of BCCs were the aggressive subtype, which is a slightly higher percentage than that reported in young patients by Leffell et al[19] on the basis of general pathology reports. We did not find any difference in aggressive subtypes of BCC between men and women.

As shown previously, the mean age of patients with the superficial subtype of BCC is younger than that of patients with other subtypes of BCC.[32,33,38] This may explain why a relatively higher proportion of our patients had superficial rather than nodular BCCs compared with previous studies (Table 4). Studies that have shown an increased number of truncal lesions and a higher proportion of superficial BCCs in the young have led to the suggestion that intense intermittent sun exposure and damage may be more important in these cases, as suspected in melanoma, than accumulation of long-term sun exposure and damage.[33,38]

The increasing incidence of nonmelanoma skin cancer in the young population of Olmsted County may be due to increased sun exposure, increased use of tanning beds, use of tobacco (especially in the development of SCC), increased patient knowledge and surveillance, or a combination of these. Currently, none of these factors can be confirmed to be the direct cause with regard to this patient population; however, they are indirectly supported by existing knowledge of these risk factors.

The limitations of our study include missed incident cases of BCC or SCC that were diagnosed clinically and treated without biopsy or histologic confirmation. This would lead to a lower reported incidence than the true rate. Because the standard procedure of the health care systems in Olmsted County is to perform a biopsy before treating nonmelanoma skin cancer, it is unlikely that we missed many incident cases for this reason, especially in our young population. Our study relied on the complete and accurate reporting of medical diagnoses in the medical record. With the high quality of the pathology reports of SCC and BCC, the percentage of cases missed because of reporting error is believed to be minimal. Also, not all incident cases had pathology slides accessible for review to confirm the diagnosis and determine the subtype of the tumor. However, when the incidence trends in cases of histologically reviewed BCC and SCC were compared with those in cases of BCC and SCC documented by pathology report alone, no difference was found. The exclusion of cases of incident BCC arising in patients with basal cell nevus syndrome, xeroderma pigmentosum, nevus sebaceus, or in fields of previous radiation may be considered a limitation; however, this resulted in the exclusion of only 3 patients and would not affect the overall outcome. Another limitation is the limited ability to generalize our study data because the population in Olmsted County has a higher level of education than the entire population of the United States and is predominantly white.

Despite these inherent limitations, our study has demonstrated an increase in the incidence of nonmelanoma skin cancer in young adults, with a disproportionate increase of BCC in young women who resided in Olmsted County, Minnesota, in 1976-2003. This increase may lead to an exponential increase in the overall occurrence of nonmelanoma skin cancer over time as the population ages. This may mean even greater demands for health care related to nonmelanoma skin cancer. Our results also emphasize the need to focus on the prevention of skin cancer in the very young so that the increasing incidence of a potentially preventable cancer can be halted.

Author Contributions: Dr Christenson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Christenson, Vachon, Otley, Weaver, Roenigk.
Acquisition of data: Christenson, Borrowman, Tollefson.
Analysis and interpretation of data: Christenson, Vachon, Weaver, Roenigk.
Drafting of the manuscript: Christenson, Vachon, Tollefson, Weaver, Roenigk.
Critical revision of the manuscript for important intellectual content: Christenson, Borrowman, Vachon, Otley, Weaver, Roenigk.
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Woe to that nation whose literature is cut short by the intrusion of force. This is not merely interference with freedom of the press but the sealing up of a nation's heart, the excision of its memory.
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