Cutaneous Lymphoma Incidence Patterns in the United States: A Population-based study of 3,884 Cases

Short Title: Cutaneous Lymphoma Incidence Patterns in the US

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ABSTRACT

There have been no prior large population-based studies focusing on cutaneous lymphomas (CL) in the United States. Using the Surveillance, Epidemiology and End Results (SEER) program, we analyzed age-adjusted CL incidence rates (IR) and survival rates by gender and race/ethnicity. There were 3,884 CLs diagnosed during 2001-2005. Cutaneous T-cell lymphomas (CTCLs) accounted for 71% (IR=7.7/1,000,000 person-years), while cutaneous B-cell lymphomas (CBCLs) accounted for 29% (IR=3.1/1,000,000 person-years). Males had a statistically significant higher IR of CL than females [14.0 vs. 8.2/1,000,000 person-years, respectively; M:F IRR 1.72; p<0.0001]. The M:F IRR ranged between 1.28-2.55 for the various CTCLs and CBCLs. Age-adjusted CL IRs were highest among Non-Hispanic Whites and Blacks (both 11.5/1,000,000 person-years), followed by Hispanic Whites (7.9) and Asian/Pacific Islanders (7.1). The CTCL IR was highest among Blacks (10.0/1,000,000 person-years), while the CBCL IR was highest among Non-Hispanic Whites (3.5). Over the last 25 years, the CL IR increased from 5.0/1,000,000 person-years during 1980-1982 to 14.3 during 2001-2003. During 2004-2005 the CL IR was 12.7. Part of this recent apparent change could be related to incomplete case ascertainment, or potential leveling off of IRs. CLs rates vary markedly by race, gender supporting the notion that they represent distinct disease entities.
INTRODUCTION

Primary cutaneous lymphomas (CL) represent 19% of extranodal non-Hodgkin lymphoma (NHL) and are a diverse group of lymphoid neoplasms manifesting heterogeneous clinical, histologic, immunophenotypic, cytogenetic, and molecular features. Given their rarity and heterogeneity, CLs present substantial diagnostic and therapeutic challenges. CLs present with unique clinical features. Some lymphomas such as mycosis fungoides (MF) present only in the skin and are never primary in the lymph nodes or other extranodal sites. In contrast, some primary CLs histologically resemble their counterparts in the lymph nodes, but differ in terms of phenotype, clinical behavior and prognosis, suggesting that they represent distinct entities. Because of their unique features and fundamental differences with non-cutaneous sites, it is important to study the epidemiology of CLs. Although the epidemiology of MF has been reported in multiple case series, only a few population-based studies have been conducted to date. Furthermore, the epidemiology of other cutaneous Natural Killer (NK)/T-cell and B-cell lymphomas overall has been very limited or unknown.

The classification of primary CLs has evolved over the past 50 years, and currently they are categorized according to the 2005 World Health Organization (WHO)-European Organization for Research and Treatment of Cancer (EORTC) joint classification. The emphasis of this classification is on the definition of disease entities and cell lineage is the starting point in the classification. This
consensus classification takes into account clinical behavior as well as the distinct histological and molecular genetic features compared to nodal counterparts, and it includes three main categories based on the cell of origin: cutaneous mature T-cell and/or NK-cell lymphoma (CTCL), cutaneous B-cell lymphoma (CBCL), and immature hematologic malignancies.

CTCLs are the most common CL, and they include mycosis fungoides (MF), Sézary syndrome (SS), cutaneous CD30+ T-cell lymphoproliferative disorders, and primary cutaneous peripheral T-cell lymphoma. MF is the most common type and is characterized by a proliferation of small- to medium-sized T lymphocytes with cerebriform nuclei. Risk factors for MF include advanced age, black race, and male gender. Although infectious agents, and environmental exposures have been studied, the etiology of MF remains unknown. The CD30+ lymphoproliferative disorders are characterized by expression of the cell surface receptor CD30+, which is a marker of activated T-cells and a member of the tumor necrosis factor superfamily. Cutaneous CD30+ lymphoproliferative disorders include both lymphomatoid papulosis, which is a chronic recurrent lymphoproliferative skin disease, and primary cutaneous anaplastic large-cell lymphoma, which is a low-grade malignancy. Cutaneous peripheral T-cell lymphoma represents a heterogeneous group of lymphomas that do not fit into any of the better defined CTCL subtypes.
CBCLs are much rarer than CTCLs. In the 2005 WHO-EORTC classification, there are three main subtypes of primary cutaneous B-cell lymphomas: marginal zone B-cell lymphoma, follicle center lymphoma, and diffuse large B-cell lymphoma. Primary cutaneous DLBCL-leg type typically present with tumors mostly restricted to the legs and have a poorer prognosis (5 year survival rate of 70%) compared with patients with other types of CBCL.

Literature on the CLs has been limited because of the rarity and inability to study large numbers of patients. Therefore, the overall epidemiology of CL subtypes has not been well investigated using population-based data. Since the etiology of CLs subtypes remain largely unknown, comparison of incidence rates and patterns for specific subtypes may elucidate important clues for future studies. In this study, we conducted a comprehensive analysis of CL incidence rates and relative survival rates in the US population-based Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute (NCI) according to patient demographic characteristics and histologic types, using the 2005 WHO-EORTC classification.

METHODS

Population-based age distribution at diagnosis (density plots), incidence, and survival data were evaluated for cutaneous lymphoma cases diagnosed among residents of 16 SEER program registries during 2001-2005. The 16 registries include 8 states (Connecticut, Hawaii, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, and Utah), Greater California, rural Georgia, and 6 metropolitan...
areas (Atlanta, Detroit, Los Angeles, San Francisco-Oakland, San Jose-
Monterrey, and Seattle-Puget Sound). These registries represent approximately
23% of the US population, including 23% of Whites/Caucasians, 23% of African
Americans, 53% of Asians, and 70% of Hawaiian/Pacific Islanders. Data for
American Indians/Alaska Natives, the Alaska registry, and cases with race coded
as “unknown” were excluded.

The SEER cancer registry personnel include highly-trained abstractors
and coders who review medical records, including pathology reports. Quality
control efforts include review of case-finding, re-abstracting, and re-coding.
Registry data are submitted electronically without personal identifiers to the NCI
twice per year. SEER records the primary site of the tumor and does not collect
data regarding metastatic sites.

Cutaneous lymphoma cases were identified using the World Health
Organization’s International Classification of Diseases for Oncology, 3rd edition
(ICD-O-3) codes for primary cutaneous (anatomic site codes: C44.0-44.9) non-
Hodgkin lymphomas (morphology codes 9670-9728 and 9827, excluding 9675).16
Since several lymphoma codes were added to the ICD-O in the 3rd edition, which
SEER first used for cases diagnosed during 2001, we included cases diagnosed
during 2001-2005. We categorized individual 4-digit histology codes into major
histologic groups according to the criteria specified in the latest 2005 WHO-
EORTC Classification of cutaneous lymphomas.1,6 The specific morphology
codes that were used are shown in Table 1. Tumors classified as malignant lymphoma not otherwise specified (NOS) ICD-O-3 (9590), non-Hodgkin NOS (9591), mixed small and large cell, diffuse lymphoma (9675), and precursor T-cell lymphoblastic lymphoma (9729) were excluded (n=237, 5.5% of cases). CTCLs classified as B-cell immunophenotype, CBCLs classified as T-cell immunophenotype, and all tumors classified as null cell immunophenotype were also excluded (n=180, 4.2% of cases). Anatomic sites were tabulated according to ICD-O-3 topography codes: head and neck [skin of the lip (C44.0), eyelid (C44.1), external ear (C44.2), unspecified parts of the face (C44.3), and scalp and neck (44.4)]; trunk (C44.5); upper limb and shoulder (C44.6); lower limb and hip (C44.7); multi-site tumors (C44.8); and tumors classified as “not otherwise specified” (C44.9). The category primary cutaneous diffuse large B-cell lymphoma, leg (pcDLBCL-leg) was based on the specific histologic codes (9680, 9684) and the topography code for skin of the lower limbs (C44.7).

Age-adjusted (2000 US standard) incidence rates (IR) were calculated using the SEER*Stat software public use program version 6.4.4. Incidence rates were expressed as new cases per 1,000,000 person-years and were analyzed by age, gender, race, ethnicity, and year of diagnosis. Long-term temporal trend analyses were based on 1980-2005 data from the SEER 9 registries, and short-term trends are based on 1992-2005 data from the SEER 12 registries. Temporal trends and age-specific rates were plotted using a semilog scale, with a y:x axis ratio of one log cycle = 40 years such that an angle of 10
degrees portrayed a change of 1% per year. We aggregated over years to derive more stable rate estimates. Our study represents a descriptive exploratory analysis. Should the reader wish to compare rates, the variance of an incidence rate can be approximated by dividing the rate (number of cases/1,000,000 person-years) squared by the number of cases on which the rate was based. Differences in rates and ratios of rates can be tested by calculating approximate confidence intervals according to Miettinen and Nurminen.

Probability age distributions at diagnosis in single years (or density plots) were stratified by cutaneous lymphoma subtype and gender, as previously described. Density plots showed smoothed age distributions at diagnosis using a non-parametric (model-free) approach. The area under each density plot represented 100% of cutaneous lymphoma cases, where density X 100 = percent relative frequency distribution.

Five-year relative survival rates for cases diagnosed during 1992-1999 in the 12 SEER registries and during 2000 in the 16 SEER registries combined were calculated using the actuarial method in SEER*Stat 6.4.4. Relative survival is defined as the ratio of the proportion of observed survivors in a cohort of patients to the proportion of expected survivors in a comparable cohort of the general population (http://srab.cancer.gov/survival/measures.html), thus representing survival in the absence of other causes of death. Only cases with a
cutaneous lymphoma as the first primary cancer were included in the survival analysis. Patients with CL as a second cancer as well as cases with a subsequent cancer were excluded. Relative survival rates were only available for Whites and Blacks and were not yet available for Hispanics and Asian/Pacific Islanders. The period of survival was from the date of diagnosis to the date of last contact, death, or December 31, 2005.

RESULTS

The number of cases, percent distribution, and IR of CLs are shown according to histologic type in Table 1. In total, 3,884 cases (IR 10.7/1,000,000 person-years) of CLs were diagnosed among residents of the 16 SEER registries during 2001-2005. Examination of extranodal lymphomas by primary site revealed that CLs accounted for 6% of cases and were the second most common form of extranodal NHL, following the GI lymphomas (27%). This trend was observed during the last three decades 1976-1985 through 1996-2005 in the SEER 9 registries (data not shown).

CTCL was the most common CL subtype accounting for 2,769 or 71% of cases (IR 7.7/1,000,000 person-years) (Table 1). MF was the most common CTCL subtype, comprising 54% of the CTCLs (IR 4.1/1,000,000 person-years), followed by cutaneous peripheral T-cell lymphoma (29%) and Cutaneous CD30+ T-cell lymphoproliferative disorders (14%). Together, these three histologic types represented 97% of all CTCL cases. Other CTCL included 23 cases of subcutaneous panniculitis-like T-cell lymphoma and 12 cases of NK/T cell
lymphoma-nasal type, both new disease entities included in the 2001 WHO classification. In contrast to CTCL, CBCL accounted for 1,105 cases or 29% of all CLs (IR 3.1/1,000,000 person-years). The most common CBCL subtypes were (40%) primary cutaneous diffuse large-B cell lymphoma (pcDLBCL) (IR 1.2/1,000,000 person-years) and cutaneous follicle center lymphoma (30%) (IR 0.9/1,000,000 person-years), followed by cutaneous marginal zone B-cell lymphoma (25%) (IR 0.8/1,000,000 person-years).

Overall, males had a statistically significant higher IR of CLs than females (14.0 versus 8.2/1,000,000 person-years, respectively; M:F IRR 1.72 p<0.0001) (Table 1). The M:F IRRs ranged between 1.28-2.55 among the various T-cell and B-cell lymphoma subtypes and were significantly elevated except for Sézary Syndrome (M:F IRR=2.11, p=0.05, based on small numbers) and pcDLBCL-leg type (M:F IRR=1.19, p=0.44).

Non-Hispanic Whites and Blacks had the highest IR for CL overall (11.5/1,000,000 person-years), followed by Hispanic Whites (7.9), and Asian/Pacific Islanders (7.1) (Table 2). The latter two IRs were statistically significantly lower than the rate among Non-Hispanic Whites. CL IR among Asian/Pacific Islanders was lower than the other racial groups across all SEER registries, ranging from 4.8/1,000,000 person-years (95% CI 2.2-9.0; N=12) in New Jersey to 10.0 (95% CI 7.2-13.4; N=23) in San Francisco-Oakland.
The highest CTCL IR was among Blacks (IR 10.0 /1,000,000 person-years) followed by Non-Hispanic Whites (8.1), and Asian/Pacific Islanders and Hispanic Whites (both 5.1) (Table 2). The M:F rate among Blacks was 1.44 times the IR among Non-Hispanic Whites (p<0.0001), whereas the cutaneous peripheral T-cell lymphoma IRs among Non-Hispanic Whites and Blacks were similar (2.5 and 2.8/1,000,000 person-years, respectively). In contrast to other CTCL subtypes, the IR for cutaneous CD30+ T-cell lymphoproliferative disorders was highest among Non-Hispanic Whites (1.3/1,000,000 person-years). The IRs of MF, cutaneous CD30+ T-cell lymphoproliferative disorders, and cutaneous peripheral T-cell lymphoma were each significantly lower among Hispanic Whites and Asian/Pacific Islanders than Non-Hispanic Whites.

In contrast to CTCL, Non-Hispanic Whites had the highest IR for CBCL (3.5/1,000,000 person-years), followed by Hispanic Whites (2.8), Asian/Pacific Islanders (1.9) and Blacks, who had the lowest IR (1.5) (Table 2). Hispanic and Non-Hispanic Whites had similar IRs of cutaneous marginal B-cell lymphoma (0.7 and 0.9/1,000,000 person-years, respectively, p=0.38). The IRs for CBCL and most subtypes among Blacks were half those among Non-Hispanic Whites.

We found the IR of CL in metropolitan counties (11.5/1,000,000 person-years) was higher than non-metropolitan counties (8.9/1,000,000 person-years, P<0.0001) (data not shown). The IR of CTCL was also higher in metropolitan counties (8.3/1,000,000 person-years) than non-metropolitan counties.
(6.1/1,000,000 person-years; P<0.0001). However, IRs of CBCL were similar in metropolitan (3.2/1,000,000 person-years) and non-metropolitan counties (2.8/1,000,000 person-years; P=0.2224).

Age-Specific Incidence and Age Distribution at Diagnosis

CTCL rates overall increased exponentially with age peaking around age 80 (Figure 1a); this pattern was generally apparent for MF, cutaneous peripheral T-cell lymphoma, and cutaneous CD30$^+$ T-cell lymphoproliferative disorders (Figures 1b-1d). Rates for CTCL overall, MF, cutaneous CD30$^+$ T-cell lymphoproliferative disorders, and cutaneous peripheral T-cell lymphoma were similar among males and females at ages <30 years but notably higher among males than females at older ages; and by age 60, the IR among males was double that among females (Figure 1a-1d). In addition, M:F incidence rate ratios (IRRs) increased from 0.95 in CTCL patients <20 years old to 2.66 in those >85 years (data not shown). Age-specific rates for CTCL reflected non-parametric age distributions at diagnosis (Figure 1e-1h), with early- and late-onset peak frequencies near ages 50-60 years and 70-80 years, respectively. With the exception of cutaneous peripheral T-cell lymphoma, women demonstrated predominant early-onset cancer populations, whereas men had more prominent late-onset disease. In cutaneous peripheral T-cell lymphoma, men demonstrated predominant early-onset cancer populations and women had prominent late-onset disease.
Age-specific rates for CBCL overall and the subtypes increased exponentially among both males and females, with males consistently having higher IR than females (Figure 2a-d). The male predominance decreased with age for CBCL overall and for pcDLBCL, in contrast to increasing male to female differences for the CTCLs (Figures 1a-d). Male:female IRRs decreased from 1.66 in CBCL patients 20-29 years to 1.39 in patients >85 years old (data not shown). Indeed, in contrast to CTCLs, CBCL density plots among women generally demonstrated dominant late-onset cutaneous lymphomas, whereas men had prominent early-onset disease (Figure 2e-h).

Temporal trends

During 1980-2005 in the original 9 SEER areas, 5,908 cases of CL were diagnosed. Over the last 25 years, CL IRs increased from 5.0/1,000,000 person-years during 1980-1982 to 14.3 during 2001-2003. However, during the period of 2004-2005 the IR of CL was 12.7/1,000,000 (Figure 3). This finding was inconsistent with the previous trend. The IRs for CTCL and CBCL rose before peaking during 2001-2003. In contrast, IRs for the major subtypes did not change greatly.

Generally, IRs for CL rose in each racial/ethnic group but IRs were lower among Hispanic Whites and Asian/Pacific Islanders than among Non-Hispanic Whites (Figure 4a-e). During 1992-96, Blacks had the highest IR for CL but during 2001-2005, it was highest among Non-Hispanic Whites (Figure 4a).
CTCL rates among Hispanic Whites declined in the most recent time period (Figure 4b). IRs were clearly higher among Blacks than Whites for CTCL overall and MF (Figure 4b-c), but highest among Non-Hispanic Whites for cutaneous peripheral T-cell lymphoma (Figure 4d). During 1992-96 to 2001-2005 IRs increased more rapid for CBCL than CTCL (Figures 4b, 4e). CBCL IRs were highest among Non-Hispanic Whites and recent IRs were lowest among Blacks (Figure 4e).

Anatomic distribution

The anatomic distribution of 39% of CTCL was classified as "not otherwise specified" (NOS), especially MF (46%) (Table 3). In contrast to CTCL, the head and neck was the most common anatomic site (50%) for CBCL, and only 10% were NOS. Most (70%) cutaneous follicle center lymphomas arose on the head and neck. The most frequently affected anatomic site of pcDLBCL and cutaneous marginal B-cell lymphoma was also the head and neck.

Survival rates

Overall 5-year relative survival rates for patients with CTCL and CBCL were high (85% and 87%, respectively) (Table 4). CTCL survival rates ranged from 91% for patients with MF to 40% for patients with Sézary syndrome. CBCL survival rates ranged from 96%-93% for patients with cutaneous follicle center lymphoma or cutaneous marginal B-cell lymphoma. Survival rates were much lower among patients with pcDLBCL-leg (45%) than pcDLBCL-other (81%).
Five-year relative survival rates were similar among males and females with CTCL (84% and 88%, respectively) and CBCL (both 86%). Overall CTCL and CBCL survival rates were highest among Whites (both 87%) and lowest in Blacks (82% and 83 %, respectively).

We analyzed the CL overall survival rates in patients diagnosed before age 40 years. We found that the overall 5-year relative survival rate of patients with CTCL and CBCL were 91.8% and 85.6% respectively, with males and females having similar rates. There were 18 patients with cutaneous lymphoma diagnosed before age 15 years (17 of which had CTCL), and their overall 5-year relative survival rate was 93.9%.

**DISCUSSION**

In this study, we calculated population-based IR and survival rates of CLs diagnosed among residents of 16 SEER registries from 2001-2005, accounting for approximately 23% of the U.S. population. This report includes 3,884 cases of CLs. Unique and important findings include variation in incidence patterns of cutaneous T-cell and B-cell lymphomas by gender, race and histologic types suggesting that these lymphomas are etiologically distinct. In addition, we report new findings regarding CL incidence and survival patterns in Hispanic Whites and Asian/Pacific Islanders.

In our study CTCL constituted the majority (71%) of CLs similar to previous studies (75-85%).\(^2,^4,^6,^{21,22}\) We found that the CTCL IR was
7.7/1,000,000 person-years, similar to that (6.4/1,000,000 person-years) reported by a recent SEER-based study using data from the original 9 registries analyzing 4,783 cases of CTCL from 1973-2002.\textsuperscript{4} We found that CBCLs were much less common than CTCL, accounting for 29% of CLs overall. This finding is consistent with two previous studies in which CBCL constituted 24% of CLs.\textsuperscript{2,6} For the first time to our knowledge, we report comprehensive IRs for CBCL overall (3.1/1,000,000 person-years) and subtypes in the United States. The CTCL IR was more than twice that of CBCL. A population-based study conducted in Florence, Italy reported a CBCL IR of 7/1,000,000 person-years.\textsuperscript{5} We found distinct differences in the anatomic distribution among CLs. Most CTCL (39%) did not have a skin site specified, whereas CBCL were classified mostly distributed on the head and neck (50%), similar to previous reports.\textsuperscript{23,24} We found cutaneous follicle center lymphoma had the highest frequency (70%) of head and neck tumors consistent with an earlier study (75%).\textsuperscript{25}

Our study revealed major racial differences in IRs among CL subtypes. Blacks had statistically higher IR of CTCL and MF than other races, consistent with previous studies.\textsuperscript{4,26} To our knowledge, for the first time we reported that the CTCL IRs among Asian/Pacific Islanders and Hispanic Whites were lower than among Blacks and Non-Hispanic Whites. In contrast to MF, IRs for primary cutaneous peripheral T-cell lymphoma and cutaneous CD30\textsuperscript{+} T-cell lymphoproliferative disease were similar among Non-Hispanic Whites and Blacks. In addition, we found that during 1992-2000, the IR of primary cutaneous
peripheral T-cell lymphoma among Non-Hispanic Whites was higher than Blacks, and in recent years the IRs of Non-Hispanic Whites and Blacks converged.

In contrast to CTCL, our study showed that CBCL was almost exclusively a disease of Whites with higher IRs for CBCL overall, cutaneous marginal zone B-cell lymphoma and follicle center lymphoma among Non-Hispanic Whites compared with other races. Cutaneous marginal zone B-cell lymphoma consisted of 7% of all CL similar to the Dutch and Austrian Cutaneous Lymphoma Group (7%).6 Borrelia burgdorferi infection has been reported to be associated with a subgroup of primary cutaneous marginal zone B-cell lymphoma in European27 but not in Asian28 or US cases.29,30

Our study revealed some unique findings in Asian/Pacific Islanders. Asian/Pacific Islanders compared to Non-Hispanic Whites had significantly lower IRs for CTCL and CBCL subtypes, except for pcDLBCL in which IRs were similar and higher, respectively. CL IRs among Asian/Pacific Islanders were lower than other racial groups across US SEER registries and not restricted to just Hawaii (data not shown). pcDLBCL has been reported as the most frequent (89%) CBCL subtype in Japanese patients.31 Epidemiologic investigations have shown similar incidence patterns of lymphomas among foreign-born and United States-born Asians, supporting the role of host susceptibility in etiology.32
We found a consistent male predominance for all CL subtypes. The predominance of males with CTCL overall is consistent with previous reports.\textsuperscript{4,7,33} We also showed a male predominance across two other CTCL subtypes: cutaneous peripheral T-cell lymphoma and cutaneous CD30\textsuperscript{+} T-cell lymphoproliferative disorders. The IRRs were statistically significantly higher for all CL subtypes with few exceptions (e.g. Sézary syndrome).

We observed that age-specific IR of CBCL increased exponentially with age. This finding is consistent with a previous case report where the median age at diagnosis was 68 years.\textsuperscript{34} A similar age-specific trend has been reported for extra-cutaneous DLBCL.\textsuperscript{32} Aging and age-related effects such as immune senescence may be particularly important for CLs in which IRs increase steeply with age. In addition, chronic inflammation, DNA damage, and diminished immune surveillance that occur with older age\textsuperscript{35} may also contribute to lymphoma development. We also found that the age-specific IRs as well as the M:F IRRs of CTCL increased with age, in contrast to CBCL in which the M:F IRRs decreased with age.

The 5-year relative survival rate for patients with CTCL was 85%. Patients with MF had the highest 5-year survival rate (91%) among patients with CTCL, similar to a study by the Dutch and Austrian Cutaneous Lymphoma Group (88%).\textsuperscript{6} A recent population-based study of 821 patients at the Thames Cancer Registry in Southeast England showed significant improved survival among MF patients.
over the past 20 years.\textsuperscript{36} Nevertheless, it is not clear whether this increase is primarily due to increased diagnosis at early stages of disease or to other factors, such as improved treatments.\textsuperscript{37} Our study showed that patients with Sézary syndrome had the lowest 5-year survival rate among patients with CTCL. This survival rate is higher than a previous report (24\%).\textsuperscript{6} We found a higher 5-year relative survival rate (79\%) for pcPTL patients compared to those reported (20-50\%) by the French Study Group on Cutaneous Lymphomas\textsuperscript{38} and the Dutch and Austrian Cancer Registries.\textsuperscript{6,39,40} The differences in survival among studies may be secondary to the populations studied and histologic subtypes constituting cutaneous peripheral T-cell lymphoma. Many of the studies reported disease-specific and observed survival rates,\textsuperscript{6,39,40} which also may contribute to the differences in survival. We also observed a high 5-year relative survival rate (87\%) for patients with CBCL. Patients with cutaneous marginal zone B-cell lymphoma and cutaneous follicular center lymphoma had the highest 5-year relative survival rates (93\% and 96\%, respectively), similar to previous studies (99\% and 95\%, respectively).\textsuperscript{6} Our study revealed that patients with pcDLBCL-leg (46\%) had decreased survival consistent with previous reports\textsuperscript{6,38,41,42} and similar survival rates to patients pcDLBCL-leg type in the Dutch Cutaneous Lymphoma Working Group (55-58\%)\textsuperscript{41} and the French Study Group on Cutaneous Lymphomas (41\%).\textsuperscript{42}

Examination of the temporal trends of CL showed that from 1980-1982 to 2001-2003 the IR of CL overall and CTCL and CBCL have increased (Figure 3) similar
to a previous study using the original 9 SEER registry areas that reported an increased in IR of CTCL\textsuperscript{4} This pattern was also observed in NHL overall in which there was an estimated 50% increase in US age-adjusted IR from 1970 to 1990, then a stabilization of rates after 1990.\textsuperscript{32} Changes in diagnostic practice over time and the emergence of acquired immunodeficiency syndrome pandemic in the early 1980s contributed to the rise in NHL, but were not sufficient to explain entirely the dramatic increases.\textsuperscript{32} There are other possible explanations for the overall long term increase in IRs. Population-based studies and cancer registries have used three different editions of ICD-O and two Field Trial editions to classify CL since 1978.\textsuperscript{43} Each new ICD-O edition had additional histologic classifications or revisions (1986,\textsuperscript{44} 1988,\textsuperscript{45} 1990,\textsuperscript{46} and 2000\textsuperscript{47}). New lymphoma classifications resulted in new additions and redistributions of broadly defined cases of CL among the more specific subclassifications.\textsuperscript{6} Hence, these changes have created inconsistencies over time in classification.

Most recently from 2001-2003 to 2004-2005, the CL IRs (including CTCL and CBCL) apparently decreased. The CL IR during 2004-2005 is inconsistent with the previous observed trend. There are possible explanations for this finding. Delayed identification and reporting of CL cases may have contributed to the recent change. To correct for this, in recent years SEER has been computing “delay-adjusted” rates.\textsuperscript{48} This has been shown to be particularly important for cutaneous melanomas, with a recent approximate 5% increase in “delay-adjusted” rates compared with rates initially reported. We compared the rates for
CL during 2001-2003 as initially reported and “delayed-adjusted” two years later and found a 5% increased in rates between submissions. Similarly, Dores et al. recently reported a non-significant 6% increased between submissions for MF-SS during 1990 thorough 1994.\textsuperscript{49} Thus, if we adjust the most recent (2004-2005) CL rate by 5%, this would account for perhaps half the observed apparent change. Alternatively, our findings could indicate that recent IRs are leveling off. Future studies should examine recent IRs for CLs over time carefully when additional data are available before conclusions are made on the recent trends for CLs.

In addition, a potential limitation of the study is complete inclusion of all patients diagnosed at dermatologist’s offices into SEER. However, this may not be a main limitation since most CL cases are referred to specialty clinics at university hospitals for further work-up and treatment, and thus would be identified by SEER. In addition, any pathological specimen sent from a dermatologists’ office to a hospital for diagnosis would be identified by SEER staff and included if a resident of the SEER catchment area. Lastly, SEER has mounted considerable effort to identify those cases diagnosed at a dermatologist’s office and not identified otherwise.

We found that pcDLBCL accounted for 44% of CBCLs similar to a recent report\textsuperscript{2} but in contrast to a previous study.\textsuperscript{50} Distinguishing between pcDLBCL and primary cutaneous follicular center lymphoma is challenging. Classification on
the basis of morphology is difficult and associated with high intra observer variation. Various studies have shown that some primary cutaneous follicular center lymphomas in which the majority of tumor cells are centroblasts previously have been categorized as DLBCL by most observers.\textsuperscript{1,34,51-53} Despite the predominance of centroblasts, clinical studies have suggested that these lymphomas have a benign clinical course. A recent study in The Netherlands by Senff et al. found that of 167 patients with primary CL classified as DLBCL using the WHO classification, 109 (65\%) were reclassified as primary cutaneous follicular center lymphoma after histologic examination.\textsuperscript{50} It is possible that some cases in our study coded as pcDLBCL would probably be classified today by an expert hematopathologist as primary cutaneous follicular center lymphoma.

In conclusion, our result of primary cutaneous follicular center lymphoma and pcDLCL should be interpreted with caution until a future population-based study conducts a detailed histologic review of CBCL in the US and our findings are confirmed.

In comparing CLs with NHL overall, we found several differences and similarities. While B-cell lymphomas comprised the majority (90.4\%) of NHL overall,\textsuperscript{54} we found that CTCL accounted for the majority of primary CLs (71\%). Interestingly, both cutaneous B cell lymphomas and NHL overall shared similar distribution of histologic subtypes. The most common nodal B-cell lymphoma subtypes are DLBCL (30-40\%), and follicle center lymphoma (20-30\%).\textsuperscript{31,53} Similarly, we also found that pcDLBCL and primary cutaneous follicular center
lymphoma accounted for 40% and 30% of cases, respectively. In contrast to T-cell lymphomas overall in which peripheral T-cell lymphoma is the most common type (33%), followed by MF/Sézary syndrome (28.5%), we found MF to be the most common CTCL subtype (54%), followed by primary cutaneous peripheral T-cell lymphoma (29%). Both cutaneous and overall B-cell lymphomas, IR were higher in Whites, while Blacks had higher rates of cutaneous and overall T-cell lymphomas.

We conducted a population-based study which avoids the biases associated with hospital and clinical series, and provided us with enough statistical power to calculate incidence and survival rates. The strengths of this study were the large sample size of rare lymphomas and unbiased ascertainment and assessment of cases. This study has shown variation in incidence patterns by race, gender, age, and histologic type, supporting the notion that CL represent distinct disease entities. Our study showed previously unrecognized epidemiological features that may ultimately be characteristic findings of the various CL subtypes. While Blacks had statistically higher IR of CTCL, Non-Hispanic Whites had statistically higher rates of CBCL. A consistent male predominance was observed in the majority of CL subtypes. We also found that CTCL M:F IRRs increased with age, as opposed to CBCL in which M:F IRRs decreased with age. CBCL cases were mostly anatomically distributed on the head and neck, in contrast to CTCL. Overall, patients with CL had relatively high survival rates, with the exception of
Sézary syndrome. Further investigations using large populations and molecular tools are warranted to elucidate the etiology of the diverse spectrum of CLs.

ACKNOWLEDGEMENTS

The authors thank the SEER program staff at NCI and the registries for their invaluable work and Mr. John Lahey of IMS, Inc. for figure preparation. This research was supported in parts by the Intramural Program of DCEG, National Cancer Institute, National Institutes of Health, Bethesda, Maryland;

AUTHORSHIP

Conception and design: Jorge R. Toro
Administrative support: Porcia Bradford and Jorge R. Toro
Provision of study materials or patients: Porcia Bradford, Susan Devesa and Jorge R. Toro,
Collection and assembly of data: Porcia Bradford, Susan Devesa and Jorge R. Toro
Statistical analyses: Porcia Bradford, Susan S. Devesa, William F. Anderson
Interpretation: Porcia Bradford, Susan S. Devesa, William F. Anderson, and Jorge R. Toro

Manuscript writing: Porcia Bradford, Susan Devesa, Jorge R. Toro
Final approval of manuscript: Porcia Bradford, Susan S. Devesa, William F. Anderson, and Jorge R. Toro

The authors have no relevant financial conflict of interest.
REFERENCES


Figure Legend

**Figure 1.** Age-specific cutaneous lymphoma incidence rates and age distributions at diagnosis by gender for all cutaneous T-cell lymphomas (CTCLs) combined, mycosis fungoides (MF), primary cutaneous peripheral T-cell lymphoma (pcPTL), and cutaneous CD30+ lymphoproliferative disorders (CD30+ LPD).

**Figure 2.** Age-specific cutaneous lymphoma incidence rates and age distributions at diagnosis by gender for all cutaneous B-cell lymphomas (CBCLs) combined, primary cutaneous marginal zone lymphoma (pcMZL), primary cutaneous follicular center lymphoma (pcFCL), and primary cutaneous diffuse large B-cell lymphoma (pcDLBCL).

**Figure 3.** Cutaneous lymphoma temporal trends during 1980-1982 to 2004-2005 by year of diagnosis for all cutaneous lymphomas (CL), cutaneous T-cell lymphomas (CTCLs), mycosis fungoides (MF), primary cutaneous peripheral T-cell lymphoma (pcPTL), and CD30+ lymphoproliferative disorders (CD30+ LPD).

**Figure 4.** Age-adjusted cutaneous lymphoma incidence rates during 1992-1996 to 2001-2005 by year of diagnosis and race for: a) all cutaneous lymphomas; b) all cutaneous T-cell lymphomas (CTCLs); c) mycosis fungoides (MF); d) primary
cutaneous peripheral T-cell lymphoma (pcPTL); and e) cutaneous B-cell lymphomas (CBCL).
<table>
<thead>
<tr>
<th>ICD-O-3 Codes</th>
<th>Total Cases</th>
<th>Frequency by Cell type</th>
<th>Male Cases</th>
<th>Female Cases</th>
<th>M:F IRR</th>
<th>PVALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3,884</td>
<td>100.0%</td>
<td>2285</td>
<td>14.0</td>
<td>1,599</td>
<td>8.2</td>
</tr>
<tr>
<td>Mature T-Cell and NK-Cell Neoplasms (CTCLs)</td>
<td>2,769</td>
<td>71.3%</td>
<td>1,626</td>
<td>10.0</td>
<td>1,143</td>
<td>5.9</td>
</tr>
<tr>
<td>Mycosis fungoides (MF)</td>
<td>1,487</td>
<td>38.3%</td>
<td>868</td>
<td>5.3</td>
<td>619</td>
<td>3.2</td>
</tr>
<tr>
<td>Sézary syndrome (SS)</td>
<td>33</td>
<td>0.8%</td>
<td>20</td>
<td>0.1</td>
<td>13</td>
<td>0.1</td>
</tr>
<tr>
<td>Cutaneous CD30+ T-cell lymphoproliferative disorders (CD30+ LPD)</td>
<td>396</td>
<td>10.2%</td>
<td>333</td>
<td>1.5</td>
<td>163</td>
<td>0.8</td>
</tr>
<tr>
<td>Subcutaneous panniculitis-like T-cell lymphoma (SPTCL)</td>
<td>23</td>
<td>0.6%</td>
<td>17</td>
<td>0.1</td>
<td>~</td>
<td>~</td>
</tr>
<tr>
<td>Primary cutaneous peripheral T-cell Lymphoma (pcPTL)</td>
<td>809</td>
<td>20.8%</td>
<td>485</td>
<td>3.0</td>
<td>324</td>
<td>1.7</td>
</tr>
<tr>
<td>Extramedullary NK/T-cell lymphoma, nasal type</td>
<td>12</td>
<td>0.3%</td>
<td>9</td>
<td>0.1</td>
<td>3</td>
<td>0.1</td>
</tr>
<tr>
<td>Adult T-cell leukemia/lymphoma (HTLV-1 pos)</td>
<td>2</td>
<td>0.0%</td>
<td>2</td>
<td>0.1</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Angioimmunoblastic T-cell lymphoma</td>
<td>7</td>
<td>0.2%</td>
<td>4</td>
<td>0.1</td>
<td>~</td>
<td>~</td>
</tr>
<tr>
<td>Mature B-cell Neoplasms</td>
<td>1,105</td>
<td>28.5%</td>
<td>651</td>
<td>4.0</td>
<td>454</td>
<td>2.3</td>
</tr>
<tr>
<td>Cutaneous marginal zone B-cell lymphoma (pcMZL)</td>
<td>274</td>
<td>7.1%</td>
<td>161</td>
<td>1.0</td>
<td>113</td>
<td>0.6</td>
</tr>
<tr>
<td>Cutaneous follicle center lymphoma (pcFCL)</td>
<td>331</td>
<td>8.5%</td>
<td>200</td>
<td>1.2</td>
<td>131</td>
<td>0.7</td>
</tr>
<tr>
<td>Cutaneous diffuse large B-cell lymphoma (pcDLBCL)</td>
<td>443</td>
<td>11.4%</td>
<td>252</td>
<td>1.6</td>
<td>191</td>
<td>0.9</td>
</tr>
<tr>
<td>Leg (pcDLBCL-leg)</td>
<td>101</td>
<td>2.6%</td>
<td>45</td>
<td>0.3</td>
<td>56</td>
<td>0.3</td>
</tr>
<tr>
<td>Other than leg (pcDLBCL-other)</td>
<td>342</td>
<td>8.8%</td>
<td>197</td>
<td>1.3</td>
<td>145</td>
<td>0.7</td>
</tr>
<tr>
<td>Extracutaneous lymphomas involving the skin</td>
<td>57</td>
<td>1.5%</td>
<td>38</td>
<td>0.2</td>
<td>19</td>
<td>0.1</td>
</tr>
<tr>
<td>Lymphoplasmacytic lymphoma</td>
<td>9</td>
<td>0.2%</td>
<td>4</td>
<td>0.1</td>
<td>5</td>
<td>0.1</td>
</tr>
<tr>
<td>Mantle cell lymphoma</td>
<td>12</td>
<td>0.3%</td>
<td>10</td>
<td>0.1</td>
<td>2</td>
<td>0.1</td>
</tr>
<tr>
<td>Burkitt lymphoma</td>
<td>4</td>
<td>0.1%</td>
<td>3</td>
<td>0.1</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Immature Hematologic Neoplasms</td>
<td>9727, 9728</td>
<td>0.3%</td>
<td>8</td>
<td>0.1</td>
<td>2</td>
<td>0.1</td>
</tr>
<tr>
<td>Blastic NK-cell lymphoma</td>
<td>9727</td>
<td>0.2%</td>
<td>6</td>
<td>0.1</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Precursor B-cell lymphoblastic lymphoma</td>
<td>9728</td>
<td>0.1%</td>
<td>4</td>
<td>0.1</td>
<td>2</td>
<td>0.1</td>
</tr>
</tbody>
</table>

1ICD-O-3 CODES 9699, 9708, 9718, 9719, 9727, 9728 are new and were not included in ICD-O-2

†Rates are per 1,000,000 person-years and age-adjusted to the 2000 US Standard Population (19 age groups - Census P25-1130).

‡Statistic could not be calculated due to less than 10 cases.
TABLE 2. Cutaneous lymphomas diagnosed during 2001-2005 in the 16 SEER program registries by histologic type and race/ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Non-Hispanic White</th>
<th>Hispanic White</th>
<th>Black</th>
<th>Asian/</th>
<th>Pacific/Islander</th>
<th>B:NHW</th>
<th>HW:NHW</th>
<th>A/PI:NHW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Rate</td>
<td>Cases</td>
<td>Rate</td>
<td>Cases</td>
<td>Rate</td>
<td>Cases</td>
<td>Rate</td>
</tr>
<tr>
<td>TOTAL</td>
<td>3,874</td>
<td>10.7</td>
<td>2,919</td>
<td>11.5</td>
<td>400</td>
<td>11.5</td>
<td>328</td>
<td>7.9</td>
</tr>
<tr>
<td>Mature T-Cell and NK-Cell Neoplasms (CTCLs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycosis fungoides (MF)</td>
<td>2,769</td>
<td>7.7</td>
<td>2,032</td>
<td>8.1</td>
<td>349</td>
<td>10.0</td>
<td>219</td>
<td>5.1</td>
</tr>
<tr>
<td>Sézary syndrome (SS)</td>
<td>1,487</td>
<td>4.1</td>
<td>1,033</td>
<td>4.1</td>
<td>212</td>
<td>5.9</td>
<td>132</td>
<td>2.9</td>
</tr>
<tr>
<td>Cutaneous CD30+ T-cell lymphoproliferative disorders (CD30+ LPD)</td>
<td>396</td>
<td>1.1</td>
<td>315</td>
<td>1.3</td>
<td>31</td>
<td>0.9</td>
<td>29</td>
<td>0.7</td>
</tr>
<tr>
<td>Subcutaneous panniculitis-like T-cell lymphoma (SCPTL)</td>
<td>23</td>
<td>0.1</td>
<td>11</td>
<td>0.0</td>
<td>6</td>
<td>~</td>
<td>0</td>
<td>~</td>
</tr>
<tr>
<td>Primary cutaneous peripheral T-cell Lymphoma (pcPTL)</td>
<td>809</td>
<td>2.2</td>
<td>634</td>
<td>2.5</td>
<td>96</td>
<td>2.8</td>
<td>50</td>
<td>1.3</td>
</tr>
<tr>
<td>Other</td>
<td>21</td>
<td>0.1</td>
<td>11</td>
<td>0.0</td>
<td>3</td>
<td>~</td>
<td>5</td>
<td>~</td>
</tr>
<tr>
<td>Mature B-cell Neoplasms (CBCLs)</td>
<td>1,105</td>
<td>3.1</td>
<td>887</td>
<td>3.5</td>
<td>51</td>
<td>1.5</td>
<td>109</td>
<td>2.8</td>
</tr>
<tr>
<td>Cutaneous marginal zone B-cell lymphoma (pcMZL)</td>
<td>274</td>
<td>0.8</td>
<td>219</td>
<td>0.9</td>
<td>12</td>
<td>0.3</td>
<td>31</td>
<td>0.7</td>
</tr>
<tr>
<td>Cutaneous follicle center lymphoma (pcFCL)</td>
<td>331</td>
<td>0.9</td>
<td>281</td>
<td>1.1</td>
<td>11</td>
<td>0.4</td>
<td>29</td>
<td>0.7</td>
</tr>
<tr>
<td>Cutaneous diffuse large B-cell lymphoma (pcDLBCL)</td>
<td>443</td>
<td>1.2</td>
<td>347</td>
<td>1.3</td>
<td>23</td>
<td>0.7</td>
<td>42</td>
<td>1.2</td>
</tr>
<tr>
<td>Leg (pcDLBCL-leg)</td>
<td>101</td>
<td>0.3</td>
<td>70</td>
<td>0.3</td>
<td>4</td>
<td>~</td>
<td>12</td>
<td>0.4</td>
</tr>
<tr>
<td>Other than leg (pcDLBCL-other)</td>
<td>342</td>
<td>1.0</td>
<td>277</td>
<td>1.1</td>
<td>19</td>
<td>0.5</td>
<td>30</td>
<td>0.8</td>
</tr>
<tr>
<td>Extracutaneous lymphomas involving the skin</td>
<td>57</td>
<td>0.2</td>
<td>40</td>
<td>0.2</td>
<td>5</td>
<td>~</td>
<td>7</td>
<td>~</td>
</tr>
</tbody>
</table>

Immature hematologic neoplasms were excluded (n=10) due to small numbers
IRR indicates incidence rate ratio
1Hispanic cases are not mutually exclusive from whites, blacks, Asian/Pacific Islanders, and American Indians/Alaska Natives.
Incidence data for Hispanics are based on NHIA and exclude cases from the Alaska Native Registry and Kentucky.
2Other includes Extranodal NK/T-cell lymphoma, Adult T-cell leukemia/lymphoma, Angioimmunoblastic T-cell lymphoma
3This group includes Small lymphocytic lymphoma, Lymphoplasmacytic lymphoma, Mantle cell lymphoma, and Burkitt lymphoma
4Rate not shown, based on <10 cases
TABLE 3. Cutaneous lymphomas diagnosed during 2001-2005 in the 16 SEER program registries by histologic type and anatomic location

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Head and neck</th>
<th>Trunk</th>
<th>Upper Limb</th>
<th>Lower Limb</th>
<th>Multi-site</th>
<th>NOS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Cases (%)</td>
<td>Cases</td>
<td>Cases (%)</td>
<td>Cases (%)</td>
<td>Cases (%)</td>
<td>Cases</td>
</tr>
<tr>
<td>Total</td>
<td>3,874</td>
<td>816 (21.1%)</td>
<td>803</td>
<td>20.7%</td>
<td>444 (11.5%)</td>
<td>567 (14.8%)</td>
<td>73</td>
</tr>
<tr>
<td>Mature T-Cell and NK-Cell Neoplasms (CTCLs)</td>
<td>2,769</td>
<td>269 (9.7%)</td>
<td>610</td>
<td>22.0%</td>
<td>313 (11.3%)</td>
<td>442 (16.0%)</td>
<td>69</td>
</tr>
<tr>
<td>Mycosis fungoides (MF)</td>
<td>1,487</td>
<td>42 (2.8%)</td>
<td>371</td>
<td>25.0%</td>
<td>126 (8.5%)</td>
<td>231 (15.5%)</td>
<td>40</td>
</tr>
<tr>
<td>Sézary syndrome (SS)</td>
<td>33</td>
<td>0 (0.0%)</td>
<td>2</td>
<td>6.1%</td>
<td>0 (0.0%)</td>
<td>1 (3.0%)</td>
<td>2</td>
</tr>
<tr>
<td>Cutaneous CD30+ T-cell lymphoproliferative disorders (CD30+ LPD)</td>
<td>396</td>
<td>73 (18.4%)</td>
<td>40</td>
<td>15.2%</td>
<td>81 (20.5%)</td>
<td>82 (20.7%)</td>
<td>5</td>
</tr>
<tr>
<td>Subcutaneous panniculitis-like T-cell lymphoma (SCPTL)</td>
<td>23</td>
<td>1 (4.4%)</td>
<td>1</td>
<td>4.4%</td>
<td>4 (17.4%)</td>
<td>3 (13.0%)</td>
<td>1</td>
</tr>
<tr>
<td>Primary cutaneous peripheral T-cell Lymphoma (pcPTL)</td>
<td>809</td>
<td>150 (18.5%)</td>
<td>172</td>
<td>21.3%</td>
<td>98 (12.1%)</td>
<td>121 (15.0%)</td>
<td>20</td>
</tr>
<tr>
<td>Extramedullary NK/T-cell lymphoma, nasal type</td>
<td>12</td>
<td>3 (25.0%)</td>
<td>3</td>
<td>25.0%</td>
<td>1 (8.3%)</td>
<td>2 (16.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Adult T-cell leukemia/lymphoma (HTLV-1 pos)</td>
<td>2</td>
<td>0 (0.0%)</td>
<td>0</td>
<td>0.0%</td>
<td>1 (50.0%)</td>
<td>1 (50.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Angioimmunoblastic T-cell lymphoma</td>
<td>7</td>
<td>0 (0.0%)</td>
<td>0</td>
<td>0.0%</td>
<td>1 (14.3%)</td>
<td>2 (28.6%)</td>
<td>1</td>
</tr>
<tr>
<td>Mature B-cell Neoplasms (CBCLs)</td>
<td>1,105</td>
<td>547 (49.5%)</td>
<td>193</td>
<td>17.5%</td>
<td>131 (11.9%)</td>
<td>125 (11.3%)</td>
<td>4</td>
</tr>
<tr>
<td>Cutaneous marginal zone B-cell lymphoma (pcMZL)</td>
<td>274</td>
<td>98 (35.8%)</td>
<td>62</td>
<td>22.6%</td>
<td>59</td>
<td>21.5%</td>
<td>14</td>
</tr>
<tr>
<td>Cutaneous follicle center lymphoma (pcFCL)</td>
<td>331</td>
<td>231 (69.8%)</td>
<td>45</td>
<td>13.6%</td>
<td>18</td>
<td>5.4%</td>
<td>4</td>
</tr>
<tr>
<td>Cutaneous diffuse large B-cell lymphoma (pcDLBCL)</td>
<td>443</td>
<td>188 (42.4%)</td>
<td>80</td>
<td>18.1%</td>
<td>44</td>
<td>9.9%</td>
<td>101</td>
</tr>
<tr>
<td>Extracutaneous lymphomas involving the skin§</td>
<td>57</td>
<td>30 (52.6%)</td>
<td>6</td>
<td>10.5%</td>
<td>10</td>
<td>17.5%</td>
<td>6</td>
</tr>
</tbody>
</table>

NOS indicates not otherwise specified

†Upper limb cases include all of upper extremity and shoulder

‡Lower limb cases include all of lower extremity and hip

§This group includes small lymphocytic lymphoma (n=32), lymphoplasmacytic lymphoma (n=9), mantle cell lymphoma (n=12), and Burkitt lymphoma (n=4).
Table 4. Five-year relative survival rates among patients diagnosed with cutaneous lymphoma during 1992-2000 in the 16 SEER program registries by histologic type, gender, and race

<table>
<thead>
<tr>
<th>Histologic Type</th>
<th>TOTAL</th>
<th>Males</th>
<th>Females</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>SR SE</td>
<td>N</td>
<td>SR SE</td>
<td>N</td>
</tr>
<tr>
<td>Mature T-Cell and NK-Cell Neoplasms (CTCLs)</td>
<td>2,270</td>
<td>85.4% 1.0%</td>
<td>1,331</td>
<td>84.5% 1.0%</td>
<td>939</td>
</tr>
<tr>
<td>Mycosis fungoides (MF)</td>
<td>1,403</td>
<td>90.9% 1.2%</td>
<td>793</td>
<td>91.9% 1.0%</td>
<td>610</td>
</tr>
<tr>
<td>Sézary syndrome (SS)</td>
<td>45</td>
<td>39.5% 8.6%</td>
<td>28</td>
<td>31.6% 10.6%</td>
<td>17</td>
</tr>
<tr>
<td>Cutaneous CD30+ lymphoproliferative disorders (CD30+ LPD)</td>
<td>100</td>
<td>73.1% 5.2%</td>
<td>72</td>
<td>67.3% 5.0%</td>
<td>28</td>
</tr>
<tr>
<td>Primary cutaneous peripheral T-cell lymphoma (pcPTL)</td>
<td>722</td>
<td>79.1% 2.0%</td>
<td>438</td>
<td>75.7% 2.0%</td>
<td>284</td>
</tr>
<tr>
<td>Mature B-cell Neoplasms (CBCLs)</td>
<td>610</td>
<td>86.5% 2.1%</td>
<td>348</td>
<td>86.2% 2.7%</td>
<td>262</td>
</tr>
<tr>
<td>Cutaneous marginal zone B-cell lymphoma (pcMZL)</td>
<td>99</td>
<td>93.1% 4.4%</td>
<td>56</td>
<td>91.5% 5.9%</td>
<td>42</td>
</tr>
<tr>
<td>Cutaneous follicle center lymphoma (pcFCL)</td>
<td>162</td>
<td>96.2% 3.5%</td>
<td>84</td>
<td>94.7% 4.5%</td>
<td>78</td>
</tr>
<tr>
<td>Cutaneous diffuse large B-cell lymphoma (pcDLBCL)</td>
<td>290</td>
<td>77.3% 3.4%</td>
<td>179</td>
<td>80.7% 4.0%</td>
<td>111</td>
</tr>
<tr>
<td>Leg (pcDLBCL-leg)</td>
<td>48</td>
<td>46.3% 9.4%</td>
<td>31</td>
<td>48.9% 11.7%</td>
<td>17</td>
</tr>
<tr>
<td>Other than leg (pcDLBCL-other)</td>
<td>242</td>
<td>81.2% 3.4%</td>
<td>148</td>
<td>85.9% 4.0%</td>
<td>94</td>
</tr>
<tr>
<td>Extracutaneous lymphomas involving the skin†</td>
<td>60</td>
<td>86.6% 5.9%</td>
<td>29</td>
<td>75.7% 9.8%</td>
<td>31</td>
</tr>
</tbody>
</table>

The period of survival was from the date of diagnosis to the date of last contact, death, or December 31, 2005. Includes 2,318 cases diagnosed 1992-1999 in the SEER 12 and 562 cases diagnosed during 2000 in the SEER 16 registries. Relative survival rates were only available for Whites and Blacks and were not yet available for Hispanics and Asian/Pacific Islanders, thus Hispanics and Asian/Pacific Islanders were excluded from race-specific survival analyses (n=415). N indicates number; SR, survival rate; and SE, standard error

†This group includes small lymphocytic lymphoma, lymphoplasmacytic lymphoma, mantle cell lymphoma, and Burkitt lymphoma

‡Rate not shown, based on <10 cases

§There were 100 cases of CD30+ LPD and 98 cases of pcMZL diagnosed during 1992-2000.
Figure 1. Age-specific cutaneous lymphoma incidence rates and age distributions at diagnosis by gender for all cutaneous T-cell lymphomas (CTCLs) combined, mycosis fungoides (MF), primary cutaneous peripheral T-cell lymphoma (pcPTL), and cutaneous CD30+ lymphoproliferative disorders (CD30+ LPD).
Figure 2. Age-specific cutaneous lymphoma incidence rates and age distributions at diagnosis by gender for all cutaneous B-cell lymphomas (CBCLs) combined, primary cutaneous marginal zone lymphoma (pcMZL), primary cutaneous follicular center lymphoma (pcFCL), and primary cutaneous diffuse large B-cell lymphoma (pcDLBCL).
Figure 3. Cutaneous lymphoma temporal trends during 1980-1982 to 2004-2005 by year of diagnosis.
Figure 4. Age-adjusted cutaneous lymphoma incidence rates during 1992-1996 to 2001-2005 by year of diagnosis and race for a) all cutaneous lymphomas; b) all cutaneous T-cell lymphomas (CTCLs); c) mycosis fungoides (MF); d) cutaneous peripheral T-cell lymphoma (pcPTL) and e) cutaneous B-cell lymphomas (CBCL).
Cutaneous lymphoma incidence patterns in the United States: a population-based study of 3,884 cases

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