Chapter 28
Non-Hodgkin Lymphoma

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INTRODUCTION

Lymphomas are malignancies of the lymphoid cells and can be divided on the basis of pathologic features into Hodgkin and non-Hodgkin lymphomas (NHL), the latter an umbrella designation for at least 30 types of distinct B- and T-cell neoplasms. Although it was recently determined to be a B-cell lymphoma, Hodgkin lymphoma or Hodgkin's disease differs substantially from other lymphomas with respect to epidemiologic and survival characteristics, and so it is discussed in a separate chapter. Altogether, NHLs are substantially more common and, when grouped together as a single entity, represent one of the top five sources of cancer morbidity and mortality in the US population.

NHLs are also a growing component of the cancer burden; incidence rates increased over 80% between 1973 and 1999, one of the most rapid increases observed among all cancers. Some of the rapid increase in NHL incidence can be attributed to improvements in diagnostic practice and disease classifications, as well as to the HIV epidemic, as NHL is at least 100-times more likely to occur in the context of HIV-related immunosuppression. However, other reasons for the increasing incidence remain unclear. The extraordinary heterogeneity of NHLs has hindered our progress in its description and study. We took advantage of this unique opportunity to use the large, population-based SEER registry to examine survival patterns for NHLs considered together as a single entity as well as by separate histologic subtypes.

MATERIALS AND METHODS

Patients

Analyses included all patients aged 20 or over diagnosed with NHL (ICD-O-2 codes 9590-9595, 9670-9717) between 1988 and 2001 and reported to the SEER program. Patients were followed for vital status until 2002. Table 28.1 details exclusions from the case series, which resulted in a final series of 65,932 patients. Patients without histologic confirmation of lymphoma diagnosis were excluded from analysis.

Presence of HIV/AIDS

Persons with HIV infection have substantially elevated risks of developing and dying from NHL. In addition to its poorer prognosis, HIV/AIDS-related NHL differs from unrelated NHL with respect to epidemiologic, histologic, and clinical characteristics to be elucidated below. Although the SEER program has formally collected information regarding HIV/AIDS as part of the extent of disease information for lymphoma cases diagnosed in 1990 and beyond, this information tends to be somewhat incomplete in the SEER database. Therefore, all cases with evidence of positive HIV/AIDS status based on the extent of disease information or underlying cause of death (ICD-9 codes 0420-0449 or ICD-10 codes B020-B024) were separated from cases without any evidence of HIV for stratified analyses (1).

Table 28.1: Non-Hodgkin Lymphoma: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001

Number Selected/Remaining	Number Excluded	Reason for Exclusion/Selection
81,867	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
70,531	11,336	Select first primary only
69,699	832	Exclude death certificate only or at autopsy
69,020	679	Exclude unknown race
68,920	100	Active follow-up and exclude alive with no survival time
67,568	1,352	Exclude children (Ages 0-19)
67,568	0	Exclude in situ cancers for all except breast & bladder cancer
65,932	1,636	Exclude no or unknown microscopic confirmation
65,932	0	Exclude sarcomas

Stage classification

NHL tumors usually begin in lymph nodes or other lymphoid tissue but spread to extranodal sites, including organs. In the SEER database, classification of stage of disease at diagnosis for all lymphomas follows guidelines set forth at the 1971 Ann Arbor conference (2). In brief, it provides four stages of tumor spread relative to the diaphragm: I--involvement of a single lymph node region, II--involvement of two or more lymph node regions on one side of the diaphragm, III--involvement of lymph node regions on both sides of the diaphragm, IV--disseminated disease. Each stage can be subclassified as A or B type according to the absence or presence, respectively, of symptoms such as fever, night sweats, pruritus or weight loss of greater than 10 percent of total body mass. In the analyses below, stage information was complete for 90% and B-symptom information for 46% of the cohort without evidence of HIV/AIDS (Table 28.2).

Histologic classification

NHL has long been recognized as a heterogeneous group of lymphoid malignancies, and multiple classification schemes have been developed over the past several decades. In 1994 an international group of expert hemato-

Table 28.2: Non-Hodgkin Lymphoma: Number of Cases, Distribution and 5-Year Relative Survival Rates (RSR) (%) by Sex, Race, Age (20+), Ann Arbor Stage, and HIV/AIDS Status, Ages 20+12 SEER Areas, 1988-2001

	Total			non-HIV/AIDS			HIV/AIDS		
Characteristics	Cases	Percent	5-Year RSR (%)	Cases	Percent	5-Year RSR (%)	Cases	Percent	5-Year RSR (%)
Total	65,932	100.0	56.3	61,214	100.0	60.0	4,718	100.0	14.8
Sex									
Male	36,354	55.1	52.5	31,982	52.2	58.7	4,372	92.7	13.8
Female	29,578	44.9	60.9	29,232	47.8	61.3	346	7.3	27.2
Race									
White	56,851	86.2	57.1	53,040	86.6	60.6	3,811	80.8	15.0
Black	4,502	6.8	48.2	3,724	6.1	56.2	778	16.5	13.2
Race/sex									
White male	31,232	47.4	53.4	27,620	45.1	59.4	3,612	76.6	14.3
White female	25,619	38.9	61.5	25,420	41.5	61.8	199	4.2	29.7
Black male	2,605	4.0	43.4	1,955	3.2	55.0	650	13.8	11.6
Black female	1,897	2.9	54.8	1,769	2.9	57.5	128	2.7	20.5
Age (20+)									
20-34	4,522	6.9	53.6	3,246	5.3	69.8	1,276	27.0	12.8
35-49	11,646	17.7	59.7	9,090	14.8	72.4	2,556	54.2	14.1
50-64	16,925	25.7	63.6	16,196	26.5	65.7	729	15.5	17.4
65-79	23,591	35.8	53.7	23,453	38.3	53.8	138	2.9	35.2
80+	9,248	14.0	37.9	9,229	15.1	37.9	19	0.4	~
Ann Arbor Stage									
I	19,971	30.3	69.4	18,463	30.2	74.5	1,508	32.0	15.7
IA	7,238	11.0	77.5	6,781	11.1	81.6	457	9.7	24.5
IB	1,926	2.9	50.7	1,592	2.6	60.4	334	7.1	10.6
II	9,098	13.8	61.1	8,685	14.2	63.0	413	8.8	25.4
IIA	3,357	5.1	68.1	3,256	5.3	69.2	101	2.1	34.6
IIB	2,018	3.1	50.5	1,858	3.0	53.4	160	3.4	20.9
III	7,910	12.0	49.7	7,407	12.1	51.9	503	10.7	21.6
IIIA	2,573	3.9	59.5	2,452	4.0	61.2	121	2.6	28.1
IIIB	2,240	3.4	38.3	2,001	3.3	41.5	239	5.1	15.0
IV	22,558	34.2	42.4	20,610	33.7	46.0	1,948	41.3	9.5
IVA	5,119	7.8	51.2	4,781	7.8	53.8	338	7.2	17.9
IVB	6,203	9.4	30.0	5,328	8.7	34.1	875	18.5	7.9
Unstaged	6,395	9.7	65.7	6,049	9.9	68.9	346	7.3	17.8

pathologists proposed the first international consensus classification system, now known as the WHO classification. The WHO system has been incorporated into the newest (third) edition of the coding system used by all cancer registries: the International Classification of Diseases—Oncology (ICD-O). However, data available for analysis were collecting using the more obsolete ICD-O, second edition (ICD-O-2) system. We used the ICD-O-2 to ICD-O-3 conversion tables to create histologic groupings base on ICD-O-2 that are more reflective of the WHO concepts. These groupings, with their associated ICD-O-2 codes, are as follows: small B-lymphocytic lymphoma (9670,9823), lymphoplasmacytic lymphoma (9671), mantle cell lymphoma (9673, 9674, 9677), mixed small/large cell diffuse lymphoma (9675-76), large B-cell diffuse lymphoma (9680-81, 9683-84, 9688, 9712), Burkitt's lymphoma (9687), follicular grade 2 (9691), follicular grade 1 (9695, 9696), follicular grade 3 (9697-9698, 9693), all follicular combined (9690-9693, 9695-9698), marginal zone (9710-9711, 9715), mycosis fungoides/Sezary's syndrome (9700-9701), other mature T-cell lymphomas (9702-04, 9706-08, 9716), angioblastic T-cell (9705), cutaneous T-cell (9709), anaplastic T-cell (9714), other T-cell (9708, 9716-9718,9827), NK/null cell (9713), precursor B-cell lymphoma/leukemias (9685,9821), and unspecified lymphomas (9590-9592, 9672,9682,9694).

RESULTS

Patients with evidence of HIV/AIDS

Of the 65,932 adult patients with NHL in this analysis, 4,718 (over 7%) had some evidence of HIV/AIDS on the basis of the medical record or cause of death information. These patients were more likely than patients without evidence of HIV/AIDS to be male (93% vs. 52%), aged 20-50 at diagnosis (81% vs. 20%) and black (17% vs. 6%). Survival was very poor for these patients, with relative survival rate of 15% at five years (Table 28.2). Figure 28.1 shows the relative survival curves for black and white male patients with and without evidence of HIV/AIDS.

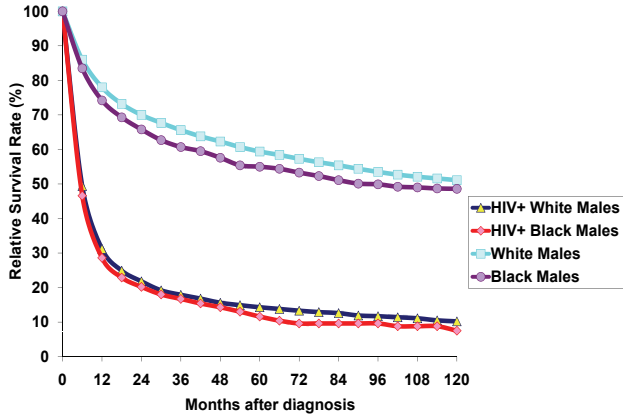
Patients without evidence of HIV/AIDS

Patients without evidence of HIV/AIDS numbered 61,214; 80% were aged 50 years or older at diagnosis, 52% were male, and 87% were of white race. Overall, survival rates for these patients were moderate, with 78% surviving one year after diagnosis relative to the general population, but this rate declined to 60% at five years and 51% at ten years. Relative survival after NHL is influenced by age, sex, race/ethnicity, stage of disease, and histologic type and the relative survival curves for NHL patients continue to decline as years since diagnosis increases irrespective of these factors.

Age, sex and race

Table 28.2 shows survival by age, sex, and race. Overall, females had somewhat higher five-year relative survival rates (61%) than males (59%), and whites (61%) had slightly higher rates than blacks (56%). Assessing survival jointly by sex and race shows that these factors influence survival subtly but independently. Relative survival rates for white females (62%) were slightly higher than those for white males (59%), black females (58%), and black males (55%). Without consideration of factors possibly associated with race and sex like stage at diagnosis, whites

Figure 28.1: Non-Hodgkin Lymphoma: Relative Survival Rates (%) for Males by Race and HIV Status, Ages 20+, 12 SEER Areas, 1988-2001



demonstrated better survival rates than blacks, and females survived better than males.

Patient age at diagnosis strongly influences survival patterns after NHL diagnosis. Figure 28.2 shows survival curves by sex for detailed age groups over time, showing generally linear associations of increasing age with poorer survival, particularly as regards survival in the first 5 years after diagnosis.

The female survival advantage was also apparent across age groups. Figure 28.2 shows that females generally have better survival than males over time. Some of the differences by sex observed in persons aged 20-49 years may relate to HIV/AIDS-related lymphoma that could not be identified in the SEER database. In addition, all age groups individually demonstrated consistently declining relative survival with time since diagnosis. As described below, age at diagnosis additionally impacted relative survival regardless of stage of disease spread and symptomatology.

Stage of disease at diagnosis

Like most other cancers, outcome after NHL is impacted largely by the extent of disease spread at time of diagnosis. Figure 28.3 shows relative survival curves for younger (ages 20-64 years) and older (ages 65+) patients by Ann Arbor stage of disease. Younger and older patients had essentially similar distributions of stage at diagnosis (Stage I: 30% vs. 30%, Stage II: 14% vs. 14%, Stage III: 12% vs. 12%, Stage IV: 34 % vs. 34%, unknown: 10% vs. 10%). Relative survival rates decreased incrementally with increasing stage, with the exception of older patients, for whom survival patterns were similar in stages III and IV, with equivalent survival in the long-term (10 years after diagnosis). Additionally important to outcome was the presence or absence of B-symptoms. Although B-symptom status was unknown for a large proportion of patients, we examined stage and B-symptom specific survival curves for the patients with complete information (Figure 28.4). Stage for stage, patients with B-symptoms had substantially poorer survival than patients without symptoms. For example, the 5-year relative survival rate for patients with stage IA was 82%, compared to the 60% for patients with stage IB (Table 28.2).

Table 28.3: Non-Hodgkin Lymphoma: Number of Cases and 5-Year Relative Survival Rates (RSR) (%) by Age (20+) and Ann Arbor Stage, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS: 28,049 Cases)

Age Group (Years)	Ann Arbor Stage									
	Total		IA		IB		IIA		IIB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
All Ages (20+)	28,049	58.6	6,781	81.6	1,592	60.4	3,256	69.2	1,858	53.4
20-34	1,758	69.0	368	86.7	141	70.5	222	83.3	183	68.9
35-49	4,617	70.4	1,142	87.1	264	75.0	487	81.5	323	61.5
50-64	7,632	63.8	1,821	86.2	350	68.7	908	74.0	474	57.8
65-79	10,243	51.3	2,479	78.6	589	50.0	1,173	63.8	648	44.4
80+	3,799	36.7	971	62.9	248	38.1	466	41.0	230	31.5

Table 28.3 (continued)

Age Group (Years)	Ann Arbor Stage									
	Total		IIIA		IIIB		IVA		IVB	
	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)	Cases	5-Yr RSR (%)
All Ages (20+)	28,049	58.6	2,452	61.2	2,001	41.5	4,781	53.8	5,328	34.1
20-34	1,758	69.0	116	78.3	137	67.8	242	58.5	349	45.5
35-49	4,617	70.4	407	79.2	326	63.1	740	68.1	928	46.2
50-64	7,632	63.8	712	67.3	532	41.4	1,377	60.7	1,458	38.9
65-79	10,243	51.3	874	48.8	716	31.2	1,795	45.7	1,969	25.2
80+	3,799	36.7	343	35.7	290	14.5	627	28.0	624	13.7

Stage, age, and B-symptom status

Table 28.3 shows the relationship of age to NHL survival, within stage and B-symptom strata. For patients diagnosed at age 50 or older, survival decreased with age within each stage/ B-symptom category. The poorer survival of patients with B-symptoms is observed across all age groups and stages. Sex did not appear to appreciably modify these differences (data not shown).

Histology

As described above, NHL is a category blanketing more than 30 different B and T-cell malignancies, many of which are still being distinguished and described as new molecular diagnostic tools become available. Table 28.4 shows counts and five-year relative survival rates for distinct NHL subtypes as recorded by the SEER database. Seventeen percent of patients were reported as having lymphoma, not otherwise specified (NOS) and were not assigned a histologic subtype, which limits the interpretability of the distribution of other specified subtypes. Regardless, large B-cell lymphoma (36.6%) and follicular lymphoma (19.3%) were the two most common subtypes. Five-year relative survival rates for follicular lymphomas, particularly grades 1 (80%) and 2 (76%) were substantially higher than that for large B-cell lymphomas (50%). In general, lymphoma subtypes can be grouped into indolent subtypes with more favorable survival features, or as aggressive lymphomas with poorer outcomes.

Figure 28.2: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Age Group (20+) and Sex, 12 SEER Areas, 1988-2001 (Patients with No Evidence of HIV/AIDS: 61,214)

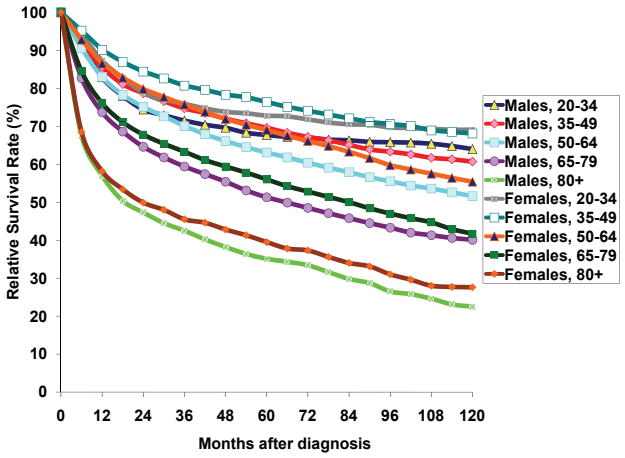


Figure 28.3: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Stage and Age Group (20+), 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS)

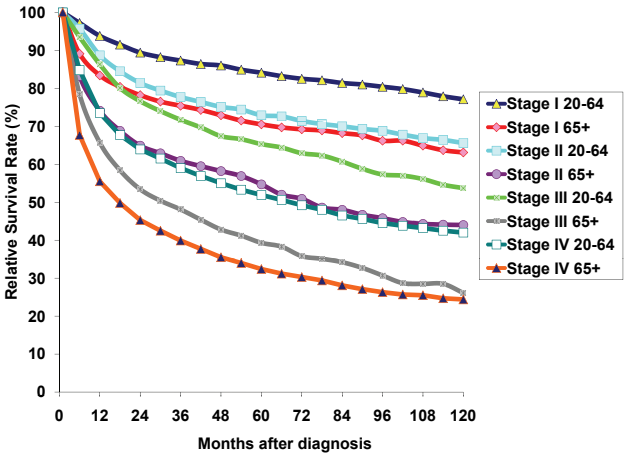


Figure 28.4: Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Stage and B-Symptoms, Ages 20+, 12 SEER Areas, 1988-2001 (Patients with Complete Stage Information and No Evidence of HIV/AIDS)

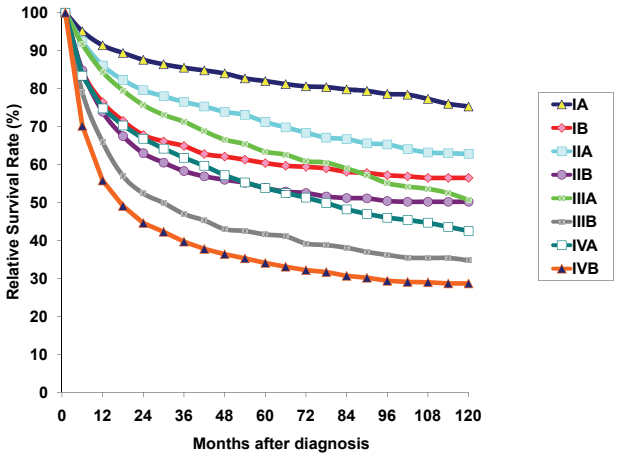


Table 28.4: Non-Hodgkin Lymphoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Histologic Subtype, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214 Cases)

Histology (ICD-O Code)	Cases	Percent	Relative Survival Rate (%) 1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	61,214	100.0	77.5	69.9	65.8	60.0	53.5	50.8
Small B Lymphocytic (9670,9823)	4,586	7.5	87.8	82.1	77.2	67.9	55.4	49.5
Lymphoplasmacytic (9671)	802	1.3	86.0	80.5	74.9	64.6	50.6	45.5
Mantle cell (9673)	1,558	2.5	83.9	72.6	65.2	51.1	37.4	34.3
Mixed small/large diffuse (9675)	2,219	3.6	77.5	68.1	62.4	55.5	49.4	47.7
Large B-cell diffuse, NOS* (9679,9680,9684)	22,390	36.6	67.0	57.1	53.8	50.4	47.3	45.9
Burkitts (9687)	508	0.8	53.5	47.8	47.4	45.4	45.1	45.1
Follicular grade 2 (9691)	3,701	6.0	94.6	88.5	83.2	75.7	67.1	61.6
Follicular grade 1 (9695)	4,649	7.6	95.9	92.2	88.1	79.8	68.4	63.8
Follicular grade 3 (9698)	2,170	3.5	88.5	81.5	76.2	69.2	61.9	60.8
All follicular combined (9690-9691, 9695-9698)	11,784	19.3	93.6	88.2	83.6	75.8	66.3	61.6
Marginal zone (9689,9699)	2,646	4.3	93.8	91.6	88.7	83.7	80.6	64.2
Mycosis fungoides, Sezary (9700-9701)	1,815	3.0	97.1	95.1	92.4	88.4	84.5	82.6
Mature T-cell, NOS* or other (9702)	725	1.2	61.9	48.8	43.6	38.1	34.3	32.5
Angioblastic T (9705)	144	0.2	61.1	55.4	49.0	38.3	28.4	28.4
Cutaneous T (9709)	738	1.2	92.7	88.8	86.6	84.4	79.8	77.8
Anaplastic T (9714)	605	1.0	69.0	59.8	56.6	53.9	52.7	43.9
Other specified T (9708,9716-9718,9827)	66	0.1	67.7	64.2	56.1	42.5	33.4	0.0
NK/null T (9719)	75	0.1	53.1	48.1	47.3	40.6	32.2	32.2
Precursor cells (9727-9729)	394	0.6	66.8	49.6	45.6	40.3	38.5	38.0
Lymphoma, NOS* (9590-9591,9596)	10,159	16.6	70.6	62.9	58.3	51.6	44.7	42.5

* NOS: Not Otherwise Specified
~ Statistic not displayed due to less than 25 cases.
! Not enough intervals to produce rate.

Table 28.5: Non-Hodgkin Lymphoma: Number and Distribution of Cases and 1-, 2-, 3-, 5-, 8-, & 10-Year Relative Survival Rates (%) by Predominant Extranodal NHL Sites, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214 Cases)

Primary Site (ICD-O Code)	Cases	Percent	Relative Survival Rate (%) 1-Year	2-Year	3-Year	5-Year	8-Year	10-Year
Total	61,214	100.0	77.5	69.9	65.8	60.0	53.5	50.8
Nodes (C770-C779)	40,797	66.6	76.1	67.3	62.6	56.0	49.0	46.0
Skin (C440-C449)	3,879	6.3	94.1	91.2	88.7	84.9	80.6	78.9
Stomach (C160-C169)	3,233	5.3	74.4	70.8	69.2	67.4	63.3	62.3
Small Intestine (C170-C179)	1,220	2.0	72.6	66.7	64.7	62.6	61.0	59.0
Brain (C710-C719)	1,014	1.7	50.6	38.0	30.8	21.2	13.5	10.4
Lung (C340-C349)	705	1.2	75.5	69.8	65.8	61.6	50.9	50.9
Colon (C180-C189, C260)	728	1.2	73.8	67.4	65.7	61.4	56.6	53.3
Bone Marrow (C421)	542	0.9	69.3	62.5	56.8	45.2	40.5	40.3
Spleen (C422)	610	1.0	81.8	74.7	71.8	67.5	60.8	57.7
Liver (C220)	224	0.4	49.7	45.3	43.6	40.0	33.9	33.4
Mediastinum (C380-C389)	211	0.3	75.2	67.2	63.4	59.6	57.5	57.5

Figure 28.5 shows relative survival curves for indolent lymphomas, including the cutaneous lymphomas like mycosis fungoides, while Figure 28.6 shows relative survival curves for aggressive lymphomas. Indolent lymphomas, particularly follicular, small B-lymphocytic, and lymphoplasmacytic lymphomas, were observed to have nearly linear declines in relative survival over time, while relative survival curves for aggressive lymphomas, particularly large –cell and most T cell lymphomas, were observed to level off with time.

Extranodal site of diagnosis for extranodal lymphoma

Nodal or extranodal site at primary diagnosis of lymphoma influences survival outcomes. More than 20% of NHL patients in this series were observed to have some extranodal presentation (n=12,366). Table 28.5 shows counts and five-year survival rates for nodal or common extranodal sites of presentation. Lymphoma present in the central nervous system (CNS) or brain had the worst five-year relative survival rate (21%) while skin, the most common site of extranodal presentation, had the most favorable (85%). About 5.3% of all lymphomas presented in the stomach and had a five-year relative survival rate of 67%.

DISCUSSION

Overall, more than half of the patients diagnosed with NHL survive five years after diagnosis. However, relative survival rates after most types of NHL declined consistently over time, rather than leveling off as do survival curves for some solid tumors. Decreasing relative survival over time reflects the ongoing risks of disease recurrence, treatment sequelae, and health outcomes noted to follow treatment for lymphoma.

Survival patterns after NHL are heterogeneous and vary enormously by HIV status, age at diagnosis, stage, presence of B-symptoms, histologic type, and to a lesser extent, sex and race. This substantial variation is demonstrated by five-year survival rates ranging from 82% with Stage IA disease to 8% in patients with HIV-associated NHL and Stage IVB.

Over 7% of the patients that were eligible for this survival analysis had some evidence of HIV-associated disease, which was shown to prognosticate extremely poor survival. This proportion is probably not reflective of the overall contribution of HIV/AIDS-associated lymphoma to the total burden of NHL, as many patients with evidence of HIV/AIDS were diagnosed without histologic confirmation and were excluded from analysis. In addition, there is an under ascertainment of the HIV/AIDS cases. HIV-associated NHL is considerably more aggressive than sporadic NHL, and treatment choices are constrained by the weakened immune system, causing poor survival. A further limitation of this analysis is the assessment of outcomes over a time period when highly active antiretroviral therapies were introduced for treatment of HIV/AIDS. These therapies have been shown to improve survival after HIV/AIDS related lymphoma substantially (3). While caution must be used in interpreting these results, the main point is that for total NHL survival is heavily influenced by HIV/AIDS.

Figure 28.5: Indolent Non-Hodgkin Lymphoma: Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214)

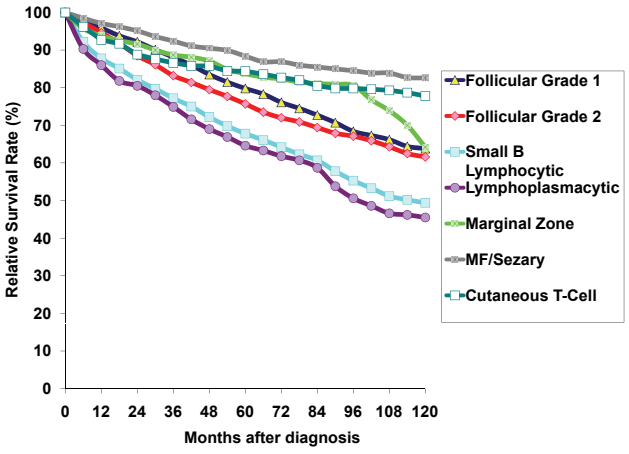
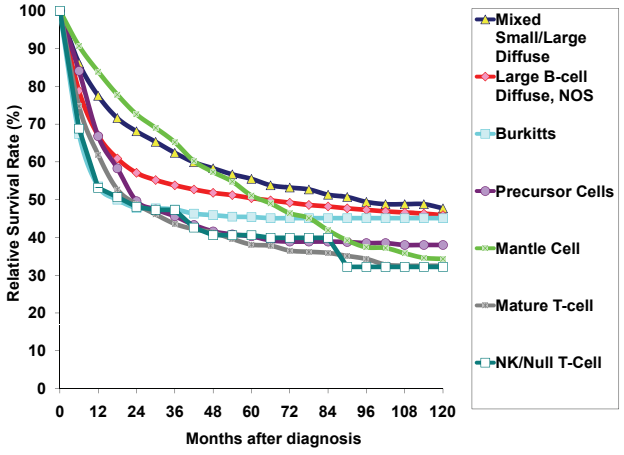


Figure 28.6: Aggressive Non-Hodgkin Lymphoma Relative Survival Rates (%) by Histology, Ages 20+, 12 SEER Areas, 1988-2001
(Patients with No Evidence of HIV/AIDS: 61,214)



Age strongly influenced survival as older persons typically experienced poorer survival, and even within stage, older persons had lower survival rates. NHL incidence rates were higher in males than females across the age spectrum, but females had slightly higher survival rates. As with most cancers, stage at diagnosis exerted considerable impact on survival. The presence of B-symptoms dramatically lowered survival within all stage and age groups.

The heterogeneity of NHL is particularly evident when considering the different patterns of survival by histologic subtypes. The survival curves of aggressive NHLs declined rapidly in the early months following diagnosis, but leveled off over time, a pattern similar to that of many solid tumors. This pattern contrasted dramatically with that of the indolent lymphomas, where a gradual steady decline was observed over the entire period of follow-up. While rarely cured, patients with indolent lymphomas typically have long periods of remission (4). The site of extranodal involvement was also observed to strongly influence survival.

Standard treatment choices for NHL are determined primarily by histologic subtype and stage and generally include both chemotherapy and radiation therapy. While treatment has improved survival after diagnosis with lymphoma, it may cause additional health problems. A significantly increased risk of second primary cancers has been noted in persons surviving 15 years or more after diagnosis with NHL (5), and cardiac toxicity has been reported (6). The monoclonal antibody rituximab has been shown to be helpful in assisting immune responses against lymphoma cells, thereby providing a treatment choice with fewer side effects than other therapies for a subset of NHLs expressing the CD20 antigen (7). Other treatment innovations include novel chemotherapy agents and regimens including bone marrow or peripheral blood stem cell transplantation. The high and increasing incidence of NHLs underscores the importance of continuing efforts to develop therapies that will improve survival and reduce adverse treatment effects.

These population-based data are based on nearly 66,000 patients diagnosed between 1988 and 2001. While the SEER data provide a large representative sample to examine numerous clinical and demographic predictors of survival after diagnosis with NHL, especially for rare subtypes, data were not available on treatment differences and comorbidity, two additional factors which impact survival and could explain some of the observed patterns. These analyses do, however, provide evidence of the considerable variation in survival patterns for NHL patients, reflecting the incredible heterogeneity of this disease entity.

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