RESEARCH COMMUNICATION

Reasons for Lower Survival from Non-Hodgkin's Lymphoma Among Older Patients

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Summary

Cancer-registry data for 710 patients, treated for non-Hodgkin's lymphoma (NHL) at a South Australian teaching hospital between 1977 and 2000, gave a five-year disease-specific survival of 53%, which was similar to population-based estimates for Australia, the USA, and Europe. This figure reduced with age at diagnosis from 69% for patients less than 40 years at diagnosis to 30% for those aged 80 years or more. Multivariable analysis indicated that older age was predictive of lower survival (p<0.001), after adjusting for grade (Working Formulation), Ann Arbor stage, bulk disease, B symptoms (weight loss, unexplained fever, night sweats), extra-lymphatic site involvement, and diagnostic period. No other clinical variable, when included in the model, affected the risk coefficient for age. Even among patients gaining complete remission following chemotherapy, the relative risk of death from NHL was 2.11 (95% CL: 1.24, 3.57) for patients aged 70 years or more at diagnosis when compared with younger patients. We conclude that older patients have lower survivals not explained by established risk factors and that this also applies to patients who achieve complete remission following chemotherapy.

Key Words: NHL - survival - age - prognosis - treatment

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Older patients with invasive cancer are less likely to survive their disease than younger patients, irrespective of the primary site (SACR, 2000). Australian data for 1992-97 indicate that five-year survivals decreased progressively for all sites combined from 81% for patients under 40 years at diagnosis to 42% for those aged 80 years or more (AIHW, 2001). Similar trends have been reported in Europe and North America (Berrino et al, 1999; Ries et al, 2002).

Reasons postulated for poorer outcomes in older patients have included more advanced stages and other disease-related risk factors, higher levels of frailty and co-morbidity, and a reduced capacity to withstand effects of cancer and its treatment (SACR, 2000). In addition, some older patients may receive less-effective treatments that have been "customized" to reduce side effects, or they may respond less favourably to standard treatments.

Survivals from non-Hodgkin's lymphomas (NHL) show a relatively steep decline with increasing age at diagnosis. Five-year survivals in Australia during 1992-97 decreased from 68% for patients less than 40 years of age to 30% for those aged 80 years or more (AIHW, 2001).

Recent studies have pointed to improved outcomes of therapy for older patients with diffuse large B-cell lymphomas, following the use of a 14-day (versus day 21) CHOP protocol (Pfreundschuh et al, 2002) or by adding the monoclonal antibody Rituximab to conventional CHOP treatment (Mounier et al, 2003). This indicates a potential for improvements in therapy to reduce age-related disparities in treatment outcome. The former study in particular suggests that poorer outcome in older patients may be overcome by optimising the dose intensity of chemotherapy.

In this study, we used 1977-2000 data from a cancer registry at a South Australian teaching hospital to investigate reasons for lower survivals from NHL in older patients. In particular, we investigated associations of age with: grade, stage and other prognostic indicators; type of care and intermediary outcomes; and survival, both unadjusted and adjusted for other risk factors. The hospital registry was preferred to the State's population registry as the data source because it included more clinical details (SACR, 2000).

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Patients and Methods

Data Collection and Definitions

Data items collected by the registry included: ICD-O (3rd edition) histological codes; grade (Working Formulation); Ann Arbor stage; presence of bulk disease (lesion size >10cm); presence of B symptoms (weight loss, unexplained fever, night sweats); involvement of lymphatic and extra-lymphatic sites; serum level of lactate dehydrogenase (> 230 International Units or less); and ECOG performance status (Fritz et al, 2000; NCCI, 2002; UICC, 1987; Oken et al, 1982). ROADS criteria were used to classify patients according to whether chemotherapy, radiotherapy or surgery was provided as part of the first course of treatment, and whether complete remission was achieved (Hahn Johnston & Richards, 1998). The registry obtained death details from the State Cancer Registry, which retrieved this information from official State death records, the National Death Index at the Australian Institute of Health and Welfare, and from interstate cancer registries. Under-reporting was checked periodically through active follow-up, and with deaths reported independently, and was found to be minimal, with little effect on calculated survivals (Bonett A et al, 1988; SACR, 2000). Further procedural details have been reported previously (SACR, 2000). The collection of State Cancer Registry data was mandated by State law, whereas the hospital-registry collection was authorized through State legislation and established with approval of the hospital's ethics committee.

Statistical Methods

STATA 6.0 software was used (STATA, 1999) to analyse the following:

A. Associations of Age with Prognostic Characteristics, Treatment and Intermediary Outcomes

We investigated the potential for age effects to be mediated through other prognostic indicators by analysing associations of age with grade, stage, B symptoms, bulk disease, involvement of specified organ sites, level of serum lactate dehydrogenase, and performance status. Associations of age with treatment modality and the achievement of a complete remission also were analysed. The Mann-Whitney U test was used for binary prognostic and treatment characteristics, whereas the Spearman rank correlation was performed when these characteristics were distributed on an ordinal or continuous scale (Armitage & Berry, 1987; STATA, 1999).

Multiple logistic regression also was used to explore associations of age and other prognostic characteristics with treatment modality (Armitage & Berry, 1987). Three separate analyses were undertaken, the dependent variables being chemotherapy, radiotherapy and surgery, respectively. All patient and clinical prognostic variables were entered into the regression analyses, with backwards elimination of those where: the fit of the model was not reduced ($p>0.050$ for change in chi-square goodness of fit); and the risk coefficient for age was not affected. Interaction terms (grade X age in years) were entered to test whether associations between age and treatment modalities varied by grade. Assumptions underlying the models, such as a lack of colinearity, were checked and found to be met. Model calibration was checked by comparing observed and expected values of the dependent variable across quantiles of estimated probabilities (Hosmer & Lemeshow, 1989).

B. Associations of Age and Other Prognostic Characteristics with Survival

Disease-specific survivals were calculated for each indicator, using Kaplan-Meier product-limit estimates (Armitage & Berry, 1987). This method was preferred to relative survival (Ederer et al, 1961), due to uncertainty whether the risk of death from non-cancer causes among these hospital patients would have equated with population norms (a required assumption for relative survival). Previous analyses have confirmed that the Kaplan-Meier method produces population-based survivals in South Australia that are equivalent to relative survivals (SACR, 1997). Censoring in the present study was at death from other causes (other than NHL) or on December 31st, 2000, whichever came first.

Associations of age with survival, after adjusting for other prognostic indicators, were investigated. All variables were entered into a multivariable Cox proportional hazards regression (Armitage & Berry, 1987), employing the same censoring criteria as for the Kaplan-Meier analyses. A backwards elimination of these variables was undertaken, as described for the multiple logistic regression. An interaction term (grade X age in years) was entered to test whether associations between age and survival varied by grade. Assumptions underlying the analyses, such as proportionality and an absence of colinearity, were tested and found to be met.

Results

Patient Characteristics

Seven hundred and ten patients with NHL were recorded on the registry during 1977-2000. They were classified by grade as low (27.5%), intermediate (60.8%), high (9.0%) or unknown (2.7%). Ascertainment of data items for these patients ranged from 100% for age and sex, to 95.8% for B symptoms and 87.5% for bulk disease. Serum lactate dehydrogenase was an exception, in that it only had been recorded from 1990 when readings were available for 82.9% of patients.

Associations of Diagnostic Age with Prognostic Indicators, Treatment and Intermediary Outcomes

A. Prognostic Indicators

Age was not associated with grade ($p=0.120$), stage ($p=0.502$), bulk disease ($p=0.832$) or B symptoms ($p=0.771$). Older patients were more likely to have poorer ECOG performance scores at diagnosis ($p=0.004$), with the percentage needing assistance with daily living increasing

from 9.3% for patients under 50 years to 14.7% for 50-69 year olds and 22.5% for older patients.

Older patients also were more likely to have NHL lung involvement (p=0.007), the proportion affected increasing from 3.4% for patients under 50 years to 5.6% for 50-69 year olds, and 9.3% for those aged 70 years or more. By comparison, involvement of other organ sites was not age-related (p>=0.102).

A larger proportion of older patients had elevated levels of serum lactase dehydrogenase (>230 IU) (p=0.011). The proportion affected increased from 21.4% for patients under 50 years to 33.1% for 50-69 year olds and 42.4% for those aged 70 years or more.

B. Treatment

Of the 699 patients where details of the first course of treatment were available, 71.5% had chemotherapy, 14.9 % had surgery, and 8.3% had radiotherapy. Overall, 88.6% had one or more of these treatments. Fewer older patients were treated at diagnosis (p<0.001). The proportion not treated was 20.2% for patients aged 70 years or more, compared with 6.9% for 50-69 year olds and 6.1% for patients younger than 50 years.

After excluding low-grade cases, which generally are regarded as incurable, 49.7% of all patients were treated with curative intent. This proportion decreased with age from 73.2% for patients under 40 years of age to 63.8% for 40-49 year olds, 56.5% for 50-59 year olds, 46.9% for 60-69 year olds, 38.4% for 70-79 year olds, and 30.6 % for patients aged 80 years or more (p<0.001).

Multiple logistic regression indicated that after adjusting for diagnostic period, grade, stage, and involvement of one or more extra-lymphatic organ sites, the relative odds of chemotherapy was 0.49 (95% CL: 0.29, 0.72) for 70-79 year olds, and 0.17 (95% CL: 0.09, 0.32) for patients aged 80 years or more, when compared with younger cases as the reference category. Similar results applied when ECOG performance status was included in the model. The interaction term for age and grade indicated that the trend for a lower exposure to chemotherapy among older than younger patients varied by grade (p=0.010), with this trend being more pronounced for intermediate and high-grade than low-grade disease.

Multiple logistic regression did not show an association of age with treatment by radiotherapy (p=0.698) or surgery (p=0.321), when adjusting for the other variables retained in these models (i.e., grade, stage, and diagnostic period, both for the radiotherapy and surgery models, plus B symptoms and spleen involvement for the radiotherapy model). Similar results applied when ECOG performance status was included in these models.

C. Intermediary Outcomes

Among treated patients, the proportion gaining complete remission reduced with age (p<0.001) from 63.4% for patients under 50 years, to 55.3% for 50-69 year olds, and 37 4% for older patients (p<0.001). This trend persisted after adjusting for grade in a stratified analysis.

Survivals by Age and Prognostic Indicators

A. Univariate Analyses (Table 1)

Overall survivals from NHL ranged from 52.5% five years after diagnosis to 40.4% at 10 years and 33.5% at 15 years. While a difference was not found by sex (p=0.310), a pronounced difference was evident by age (p<0.001), with five-year survivals decreasing from 68.9% for patients less

Table 1. Survival (± standard error) from Non-Hodgkin's Lymphoma: South Australia Hospital-registry Data, 1977-2000*

Characteristic		Period from diagnosis (yrs.) 1	2	3	4	5	10	15	P value **
All (n=710)	100%	78.1% ±1.6	67.6% ±1.8	61.8% ±1.9	57.3% ±2.0	52.5% ±2.1	40.4% ±2.4	33.5% ±2.7	---
Age at diagnosis (yrs.):									
Under 40 (n=68)	100%	87.9% ±4.0	74.9% ±5.4	71.3% ±5.8	71.3% ±5.8	68.9% ±6.0	63.9% ±6.6	63.9% ±6.6	
40-49 (n=81)	100%	92.4% ±3.0	84.3% ±4.2	75.8% ±5.0	71.0% ±5.4	67.6% ±5.6	57.4% ±6.8	41.0% ±10.0	
50-59 (n=135)	100%	84.0% ±3.2	73.0% ±3.9	68.7% ±4.1	66.0% ±4.3	61.8% ±4.5	46.2% ±5.4	33.8% ±5.9	p<0.001
60-69 (n=176)	100%	80.4% ±3.1	68.6% ±3.7	64.3% ±3.8	58.1% ±4.0	51.3% ±4.2	37.2% ±5.0	35.1% ±5.1	
70-79 (n=179)	100%	68.2% ±3.6	58.4% ±3.8	50.5% ±4.0	46.7% ±4.0	41.3% ±4.1	27.9% ±4.7	23.2% ±5.8	
80+ (n=71)	100%	60.1% ±6.0	50.2% ±6.2	44.1% ±6.4	33.1% ±6.4	29.7% ±6.6	17.8% ±7.6	---	
ECOG performance status:									
0 (n=242)	100%	90.9% ±1.9	86.2% ±2.3	78.3% ±2.9	71.1% ±3.2	67.8% ±3.4	54.2% ±4.6	51.3% ±5.1	
1 (symptoms) (n=329)	100%	78.1% ±2.3	64.1% ±2.7	59.3% ±2.8	56.5% ±2.9	50.6% ±3.0	39.1% ±3.2	30.8% ±3.6	p<0.001

Characteristic		Period from diagnosis (yrs.) 1	2	3	4	5	10	15	P value **
2-4 (needs assistance) (n=112)	100%	47.0% ±4.9	32.8% ±4.7	28.3% ±4.5	23.5% ±4.4	19.4% ±4.2	12.5% ±3.9	10.0% ±3.9	
Unknown (n=27)	(100%)	(88.9%) (±6.0)	(84.4%) (±7.2)	(80.0%) (±8.1)	(80.0%) (±8.1)	(80.0%) (±8.1)	(40.0%) (±28.6)	(—)	
Grade (Working Formulation):									
Low (n=195)	100%	95.7% ±1.5	88.6% ±2.4	82.5% ±3.0	76.9% ±3.4	70.0% ±3.8	51.6% ±4.8	38.4% ±5.4	
Intermediate (n=432)	100%	72.6% ±2.2	61.4% ±2.4	55.5% ±2.5	51.3% ±2.6	47.7% ±2.6	36.5% ±3.1	33.9% ±3.4	p<0.001
High (n=64)	100%	69.0% ±5.9	53.2% ±6.5	47.7% ±6.6	43.8% ±6.6	39.9% ±6.6	36.8% ±6.7	32.2% ±7.3	
Unknown (n=19)	(100%)	(57.4%) (±11.5)	(45.2)% (±11.9)	(45.2)% (±11.9)	(45.2)% (±11.9)	(22.6%) (±17.0)	(—)	(—)	
Ann Arbor stage:									
I (n=172)	100%	94.1% ±1.8	90.2% ±2.3	86.7% ±2.7	83.0% ±3.1	80.3% ±3.3	69.0% ±4.6	64.2% ±5.4	
II (n=104)	100%	77.7% ±4.2	65.6% ±4.9	59.6% ±5.1	56.1% ±5.2	50.7% ±5.4	44.7% ±5.8	36.4% ±6.4	p<0.001
III (n=111)	100%	75.7% ±4.2	67.7% ±4.6	61.6% ±4.9	56.4% ±5.1	55.1% ±5.2	40.6% ±6.5	10.5% ±8.5	
IV (n=306)	100%	71.3% ±2.6	55.9% ±3.0	48.6% ±3.0	43.8% ±3.1	36.8% ±3.1	22.0% ±3.2	19.8% ±3.2	
Unknown (n=17)	(100%)	(55.7%) (±12.7)	(55.7%) (±12.7)	(55.7%) (±12.7)	(46.5%) (±13.5)	(46.5%) (±13.5)	(—)	(—)	
Bulk disease (> 10cm):									
No (n=475)	100%	85.4% ±1.7	77.4% ±2.0	71.5% ±2.2	66.4% ±2.3	60.5% ±2.5	46.5% ±2.9	39.1% ±3.3	p<0.001
Yes (n=146)	100%	60.6% ±4.1	40.6% ±4.2	34.5% ±4.2	30.2% ±4.1	27.2% ±4.0	20.9% ±4.6	15.7% ±5.7	
Unknown (n=89)	(100%)	(68.5%) (±5.0)	(58.9%) (±5.5)	(54.1%) (±5.7)	(54.1%) (±5.7)	(54.1%) (±5.7)	(41.2%) (±7.2)	(34.3%) (±8.7)	
B symptoms:									
No (n=451)	100%	86.7% ±1.6	77.8% ±2.0	71.1% ±2.3	66.3% ±2.4	60.9% ±2.5	46.8% ±3.0	41.9% ±3.4	p<0.001
Yes (n=229)	100%	63.9% ±3.2	48.4% ±3.5	44.2% ±3.5	39.6% ±3.5	35.9% ±3.6	27.8% ±3.9	19.2% ±4.0	
Unknown (n=30)	(100%)	(56.5%) (±9.5)	(56.5%) (±9.5)	(52.5%) (±9.7)	(52.5%) (±9.7)	(52.5%) (±9.7)	(—)	(—)	
Serum lactate dehydrogenase:									
Up to 230 IU (n=232)	100%	90.7% ±2.0	82.5% ±2.7	76.0% ±3.1	68.9% ±3.5	64.3% ±3.7	55.1% ±4.4	—-	p<0.001
Over 230 IU (n=121)	100%	55.0% ±4.6	35.1% ±4.6	30.7% ±4.5	28.5% ±4.4	24.0% ±4.4	20.2% ±4.5	—-	
Unknown (n=357)	(100%)	(78.6%) (±2.2)	(69.0%) (±2.5)	(63.2%) (±2.6)	(59.4%) (±2.7)	(54.5%) (±2.8)	(41.4%) (±3.0)	(35.1%) (±3.2)	
Spleen involvement:									
No (n=549)	100%	80.5% ±1.7	71.7% ±2.0	65.7% ±2.1	61.5% ±2.2	56.8% ±2.3	45.4% ±2.7	37.6% ±3.2	p<0.001
Yes (n=158)	100%	69.6% ±3.8	51.9% ±4.2	46.6% ±4.3	41.0% ±4.4	36.1% ±4.3	21.4% ±4.4	17.6% ±4.4	
Unknown (n=3)	(100%)	(—)	(—)	(—)	(—)	(—)	(—)	(—)	
Extra-lymph. site(s) involvement:									
No (n=188)	100%	88.6% ±2.4	84.5% ±2.7	80.6% ±3.0	77.9% ±3.2	74.9% ±3.4	60.3% ±4.5	43.3% ±5.9	
Yes (n=503)	100%	74.7% ±2.0	61.5% ±2.3	54.9% ±2.3	49.6% ±2.4	44.0% ±2.5	32.0% ±2.8	29.7% ±2.9	p<0.001
Unknown (n=19)	(100%)	(63.8%) (±12.2)	(55.8%) (±13.0)	(55.8%) (±13.0)	(55.8%) (±13.0)	(55.8%) (±13.0)	(55.8%) (±13.0)	(55.8%) (±13.0)	

* Disease-specific survivals (see text). Date of censoring: December 31st, 2000. Data source: cancer registry at a teaching hospital.
** P values derived from Cox proportional hazards regression (data in brackets excluded).

than 40 years to 29.7% for those aged 80 years or more.

Grade also was predictive (p<0.001), the five-year survival ranging from 70.0% for low-grade to 39.9% for high-grade disease. Stage was an additional predictor (p<0.001), with the five-year survival decreasing from 80.3% for stage I to 36.8% for stage IV. Other determinants of lower survivals were bulk disease (p<0.001), B symptoms (p<0.001), elevated serum lactate dehydrogenase (p<0.001), and poorer ECOG performance status (p<0.001). Survivals also were lower when there was involvement of the spleen (p<0.001) and one or more extra-lymphatic sites (p<0.001), and in particular, the liver (p<0.001), lung (p<0.001), mediastinum (p=0.002), marrow (p=0.002), and potentially the central nervous system (p=0.074).

Higher survivals occurred when complete remission was achieved after the first course of treatment (p<0.001). The five-year survival was 78.2% for patients who gained complete remission, compared with 22.2% when this outcome was not achieved.

B. Multivariable Analyses

All Patients (Table 2)

Older age was predictive of death from NHL, after adjusting for grade, stage, B symptoms, bulk disease, diagnostic period, and involvement of one or more extra-lymphatic sites. The relative risk of fatality increased progressively with age to 6.35 (95% CL: 3.52, 11.46) for patients aged 80 years or more when compared with the reference category of less than 40 years of age.

Including other correlates of age in the model (i.e., ECOG performance, level of serum lactate dehydrogenase, and lung involvement) had little effect on the risk coefficient for age. Moreover, age remained a significant predictor of case fatality (p<0.001) after including treatment variables in the model (expressed as the provision or non-provision of chemotherapy, radiotherapy and surgery, respectively), and when stratifying by treatment intent. The interaction term for age and grade did not suggest a difference in age-related trends in fatality between grades (p=0.963). Separate analyses confirmed that regression coefficients for age were similar, irrespective of grade.

Patients Receiving Chemotherapy (Table 3)

Older age was a determinant of fatality, when adjusting for grade, stage, B symptoms, bulk disease, and diagnostic period. The relative risk of fatality increased progressively with age to 5.93 (95% CL: 3.00, 11.71) for patients aged 80 years or more, when compared with the reference age range of less than 40 years. The interaction term for age and grade suggested that age-related fatality trends varied by grade (p=0.062), there being a less pronounced trend for higher-grade cancers.

When the multivariable analysis was restricted to cases achieving complete remission following chemotherapy, and adjustment was made for grade, stage, and diagnostic period, the relative risk of fatality was 2.11 (95% CL: 1.24, 3.57) for patients aged 70 years or more as opposed to younger patients. Meanwhile, the interaction term for age and grade did not suggest a difference in age-related fatality trend between grades (p=0.254).

Table 2. Relative risk (95% confidence limits) of Fatality from Non-Hodgkin's Lymphoma: South Australian Hospital-registry Data, 1977-2000*

Multivariable proportional hazards regression Predictors	Relative risk
Age at diagnosis (yrs.):	
Under 40 (reference) (n=57)	1.00
40-49 (n=68)	1.71 (0.93, 3.15)
50-59 (n=113)	2.15 (1.24, 3.71)
60-69 (n=147)	2.58 (1.52, 4.40)
70-79 (n=134)	3.87 (2.26, 6.64)
80+ (n=57)	6.35 (3.52, 11.46)
Grade (Working Formulation):	
Low (reference) (n=163)	1.00
Intermediate (n=358)	1.80 (1.34, 2.42)
High (n=55)	2.18 (1.40, 3.39)
Ann Arbor stage:	
I (reference) (n=147)	1.00
II (n=92)	2.32 (1.48, 3.63)
III (n=92)	3.17 (2.02, 4.96)
IV (n=245)	3.43 (2.42, 4.86)
Bulk disease (>10cm):	
No (n=439)	1.00
Yes (n=137)	1.65 (1.26, 2.16)
B symptoms:	
No (n=395)	1.00
Yes (n=181)	1.61 (1.25, 2.08)
Extra-lymphatic site(s) involvement:	
No (n=162)	1.00
Yes (n=414)	1.36 (0.96, 1.92)
Diagnostic period:	
1977-82 (n=115)	1.00
1983-88 (n=114)	0.87 (0.62, 1.22)
1989-94 (n=172)	0.86 (0.62, 1.19)
1995-2000 (n=175)	0.67 (0.46, 0.98)

* Cox proportional hazards regression (see text).
Date of censoring: December 31st, 2000.
Data source: cancer registry at a teaching hospital.
Includes cases with complete data on these predictor variables.

Discussion

Although these data were not population-based, the 53% five-year survival was similar to population-based figures, such as the 54% for South Australia in 1977-98 (SACR, 2000), the 55% for Australia in 1992-97 (AIHW, 2000) and the USA in 1992-98 (Ries et al, 2002), and the 49% for Europe in 1985-89 (Berrino et al, 1999).

The decrease in five-year survival with increasing diagnostic age (from 69% for patients under 40 years to 30% for those aged 80 years or more) also was similar to age-related trends elsewhere (AIHW, 2002; Berrino et al, 1999; Ries et al, 2002). It is apparent from these findings that our patient group had outcomes typical of those observed in other western populations.

Table 3. Relative Risk (95% confidence limits) of Fatality from Non-Hodgkin's Lymphoma in Patients Receiving Chemotherapy as Part of the First Course of Treatment: South Australian Hospital-registry Data, 1977-2000*

Multivariable proportional hazards regression Predictors	Relative risk
Age at diagnosis (yrs.):	
Under 40 (reference) (n=47)	1.00
40-49 (n=57)	1.46 (0.78, 2.76)
50-59 (n=87)	2.00 (1.11, 3.59)
60-69 (n=111)	2.31 (1.31, 4.09)
70-79 (n=92)	3.68 (2.07, 6.54)
80+ (n=26)	5.93 (3.00, 11.71)
Grade (Working Formulation):	
Low (reference) (n=110)	1.00
Intermediate (n=274)	1.63 (1.17, 2.26)
High (n=36)	2.35 (1.41, 3.92)
Ann Arbor stage:	
I (reference) (n=64)	1.00
II (n=79)	1.89 (1.07, 3.34)
III (n=79)	2.48 (1.41, 4.38)
IV (n=198)	2.78 (1.64, 4.69)
Bulk disease (>10cm):	
No (n=310)	1.00
Yes (n=110)	1.79 (1.33, 2.41)
B symptoms:	
No (n=271)	1.00
Yes (n=149)	1.34 (1.01, 1.79)
Diagnostic period:	
1977-82 (n=87)	1.00
1983-88 (n=79)	0.97 (0.67, 1.42)
1989-94 (n=121)	0.91 (0.63, 1.31)
1995-2000 (n=133)	0.76 (0.50, 1.15)

* Cox proportional hazards regression (see text).
Date of censoring: December 31st, 2000.
Data source: cancer registry at a teaching hospital.
Includes cases with complete data on predictor and treatment variables.

Older cases were not found to have NHLs with higher-risk profiles than younger cases, as indicated by grade, stage, B symptoms, bulk disease, spleen involvement, or involvement of one or more extra-lymphatic organ sites. It is not surprising, therefore, that an age-related survival gradient remained after adjusting for these characteristics. Moreover, adjustment for other prognostic indicators that were age-related (i.e., NHL lung involvement, level of serum lactate dehydrogenase, and performance status) had little effect on the age-related survival gradient. It seems from these results that older patients had poorer outcomes that were not explained by generally accepted disease-related prognostic markers.

Older patients were less likely than younger patients to be treated at diagnosis, and specifically, to have chemotherapy, which likely contributed to poorer disease control. It is not clear from our study how the suitability of older cases for chemotherapy was determined. While older patients did have a poorer performance-status, this measure did not account for their lower exposure to chemotherapy. Unfortunately, co-morbidity data were not collected by the registry, preventing investigation of the impact of this characteristic on treatment decisions.

When analyses were restricted to patients treated with chemotherapy who achieved a complete remission, older patients were still more likely to die from their NHL, after adjusting for disease-related prognostic markers. We suspect that these poorer outcomes may have been affected by a lower intensity of therapy, but the data collected by the cancer registry lacked the detail necessary to test this hypothesis. We propose to collect more detailed data on treatment regimens, both planned and actually administered, and on co-morbidity, to investigate the extent to which these factors explain the poorer outcomes in older patients.

Our results indicate that poorer outcomes in elderly patients are not explained by differences in characteristics of the primary disease. We suspect that better outcomes may be achieved by optimising therapy, both with regard to the regimens used and dose intensity. Formal objective assessments of co-morbidity may be necessary to minimise the exclusion from optimal therapy of elderly patients who would benefit from this care.

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