Evaluation of the risk of relapse in classical Hodgkin lymphoma (cHL) at event-free time points and survival comparison to the general population in British Columbia (BC)

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INTRODUCTION

- Studies in classical Hodgkin lymphoma (cHL) measure the time to event from the date of diagnosis (dx)
- Estimates of risk of relapse at subsequent time points would aid in patient counselling, surveillance and clinical trial design
- We evaluated the risk of relapse at defined event-free survival (EFS) time points and compared the risk of death to an age- and gender-matched population in British Columbia (BC)

METHODS

- The BC Cancer Agency Lymphoid Cancer Database was screened to identify all pts aged ≥16-69 y with cHL diagnosed May 1989-Dec 2012 treated with an ABVD/ABVD-like regimen
- Limited stage (LIM) = IA/B or IIA; advanced stage (ADV) = III/IV or stage IIB +/- bulky disease (≥10cm)
- Radiotherapy (RT) eras: extended-field (EF) May 1989 – Dec 1996; involved field (IF) Jan 1997 – Jan 2001; involved-nodal (IN) – Feb 2001 to present
- Event-free survival (EFS): Time from dx to relapse/progression, unplanned treatment or death from any cause
- Risk of relapse in the subsequent 5 y was measured from the time of dx (Year0) and at event-free time points: 1 y (Year1), 2 y (Year2), 3 y (Year3) and 5 y (Year5)
- Event decomposition was performed using a competing risk analysis. Expected (E) survival was determined from BC life tables, matching for age and gender. Relative survival was calculated using a conditional approach and expressed as a standardized mortality ratio of observed (O):E deaths

RESULTS

- 1402 pts with cHL were identified (Table1), median follow-up was 7.8 y (0.1 – 25.4 y); median age 32; 5 y OS 91.5%; DSS 93.6%
- The risk of HL relapse was similar across age categories (Figure 1; P=0.42)
- For LIM pts, 5 y risk of relapse from Year0 was 6.5% and < 2% from Year2 (Table 2)
- For ADV pts, 5 y risk of relapse from Year0 was 23.7% but was 3.85% by Year3 and at this time point comparable to LIM pts (P=.07)(Figure 2)
- For ADV pts the risk of relapse was inferior in high risk IPS (n=141) pts at Year0 (P=.002) but those remaining event free at 1 y had a similar risk of relapse to low risk pts (P=0.42)
- Although the 5 y OS improved as pts remained free of relapse, the relative survival did not normalize regardless of age, stage, RT era or IPS (Table3/Figure 3)

Table 1. Summary of cHL patient characteristics at diagnosis and causes of death.

Characteristic		Number (n=1402)	%
Gender	Male	749	53
	Female	653	47
Age y	16-24	360	26
	25-44	684	49
	45-60	246	17
	61-70	112	8
Radiotherapy era			
EF May 1989 – Dec 1996		370	26
IF Jan 1997 – Jan 2001		238	17
IN Feb 2001 – Dec 2014		794	57
Bulky disease ≥10cm		387	29
B symptoms		617	44
ECOG†	0-2	1323	96
	3-4	677	4
IPS^	Low 0-3	719	76
	High ≥4	141	15
	Incomplete data	89	9
Histology			
Nodular Sclerosis		1074	76
Mixed cellularity		139	10
Lymphocyte rich		39	3
Lymphocyte deplete		12	<1
Classic HL NOS		137	10
Treatment intention by stage			
Limited		453	32
Advanced		949	68
Cause of Death (n=199)			
Hodgkin Lymphoma		85	6
Treatment + cardiac deaths		38	3
Secondary cancer		33	2
Other		30	2
Unknown		13	<1

*Tumour dimensions available for 1325/1402 patients. †PS data available for 1377/1402 patients.

Table 2. 5 y risk of relapse in cHL pts at diagnosis (Year 0) and subsequent EFS time points. Risk of cHL relapse is expressed as a percentage (95% CI).

	5-y Risk of cHL relapse % Calculated from Time Point				
Group	Year 0	Year 1	Year 2	Year 3	Year 5
All patients (n=1402)	18.1 (16.1 - 20.2)	10.0 (8.4 - 11.7)	5.6 (4.3 - 7.1)	3.5 (2.4 - 4.9)	2.5 (1.5 - 3.9)
LIM stage (n=453)	6.5 (4.4 - 9.0)	4.5 (2.7 - 6.8)	1.9 (0.8 - 3.9)	2.3 (1.0 - 4.5)	1.6 (0.5 - 3.9)
ADV stage* (n=949)	23.7 (21.0 - 26.5)	12.9 (10.7 - 15.4)	7.6 (5.7 - 9.8)	4.1 (2.7 - 6.1)	3.0 (1.6 - 4.9)
IPS LOW (n=719)	21.4 (18.4 - 24.5)	11.9 (9.5 - 14.6)	7.1 (5.0 - 9.5)	4.1 (2.5 - 6.4)	3.2 (1.7 - 5.6)
IPS HIGH (n=141)	34.0 (26.2 - 42.0)	16.8 (10.2 - 24.8)	8.3 (3.6 - 15.5)	4.0 (1.0 - 10.4)	1.6 (0.1 - 7.5)
Age 16-24	16.4 (12.7 - 20.5)	7.7 (5.0 - 11.0)	3.7 (1.8 - 6.4)	2.5 (1.0 - 5.2)	2.9 (1.0 - 6.3)
Age 25-44	18.3 (15.5 - 21.3)	10.4 (8.1 - 13.1)	4.9 (3.3 - 7.1)	2.6 (1.3 - 4.5)	1.4 (0.5 - 3.1)
Age 45-60	17.8 (13.2 - 22.9)	11.4 (7.5 - 16.1)	7.0 (3.9 - 11.3)	5.5 (2.6 - 9.9)	3.8 (1.4 - 8.2)
Age 61-69	23.3 (15.7 - 31.8)	11.5 (5.8 - 19.4)	12.8 (6.0 - 22.2)	7.4 (2.3 - 16.8)	4.9 (0.8 - 14.8)

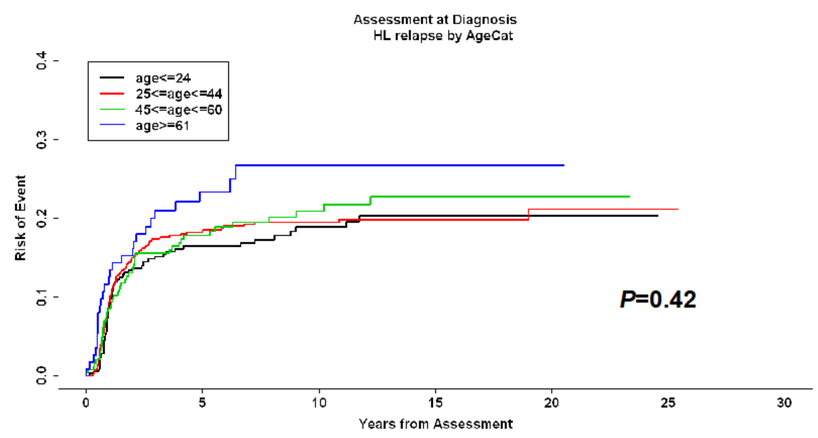

Figure 1. The risk of relapse among age groups for patients with cHL at diagnosis

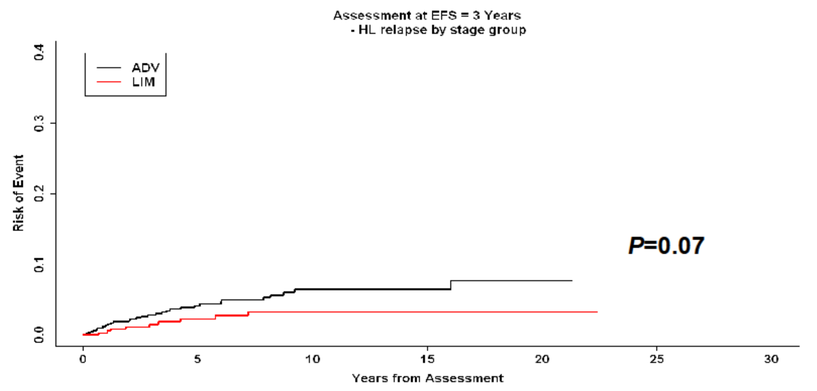

Figure 2. The risk of subsequent HL relapse in advanced versus limited stage patients event-free at 3 y

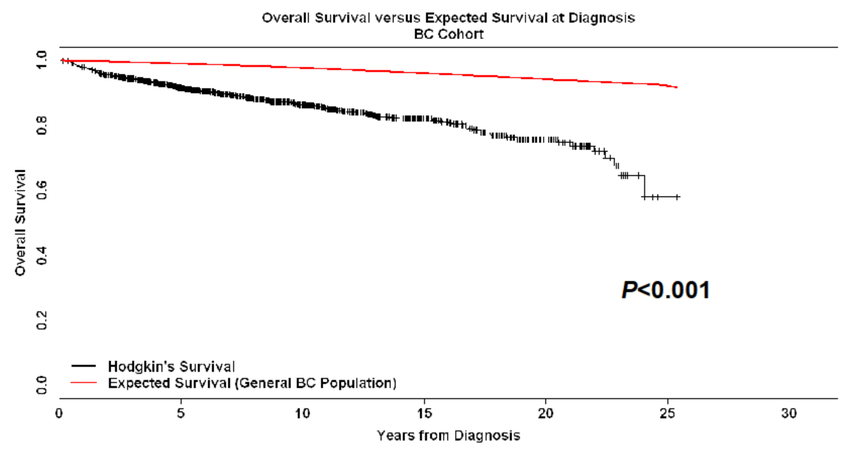

Figure 3. The relative survival of all cHL patients compared to the general population in BC at diagnosis

Table 3. Standardized mortality rates (SMR) for cHL patients at diagnosis and at event-free survival (EFS) time points

Variable	*Diagnosis*	*EFS 1 y*	*EFS 2 y*	*EFS 3 y*	*EFS 5 y*
All	6.05 P<0.001	4.21 P<0.001	3.67 P<0.001	3.41 P<0.001	3.45 P<0.001
Stage LIM	3.02 P<0.001	2.97 P<0.001	2.54 P<0.001	2.65 P<0.001	2.58 P<0.001
Stage ADV	7.59 P<0.001	4.68 P<0.001	4.25 P<0.001	3.85 P<0.001	3.96 P<0.001
IPS LOW 0-3	7.59 P<0.001	4.95 P<0.001	4.41 P<0.001	4.15 P<0.001	4.23 P<0.001
IPS HIGH ≥4	8.50 P<0.001	4.81 P<0.001	3.43 P<0.001	3.21 P<0.001	3.73 P<0.001

*89/1402 ADV pts unable to be assigned to low or high groups.

CONCLUSIONS

- The 5 y risk of relapse for ADV cHL is < 5% for pts remaining event free at 3 y
- Age did not emerge as a predictor of relapse and, thus, robust older pts should be treated considered for curative intent treatment
- Although the relative survival improves with duration of EFS, it remains inferior to the general population

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