Estimating the survival of children and young adults with Hodgkin and Non-Hodgkin lymphoma at Johns Hopkins

Lola Charles
Mentored by Dr. Patrick Brown

Introduction

Hodgkin Lymphoma (HL) refers to the presence of large cancerous lymphocytes known as Reed-Sternberg cells in the lymph nodes. To combat disease progression, Johns Hopkins Hospital (JHH) uses a novel regimen of chemotherapy called Bv-AVEPC which consists of five cycles where each cycle has a duration of 21 days (Friedman et al., 2014). Non-Hodgkin Lymphoma (NHL) refers to the rapid growth of large cancerous lymphocytes found in the lymph tissue, neck, abdomen, or bones (Minard-Colin et al., 2015). For this study, the experimental chemotherapy consists of six injections of rituximab in addition to standard chemotherapy. After the rounds of treatment are given, patients are observed for many years to calculate the period in which they do not experience an event. This period is known as the event-free survival (EFS) rate where the patient does not have any relapses nor complications associated with the treatment. The EFS will be used to determine the efficacy of the novel treatment as compared to the national average of existing treatments. The EFS will also be used to determine if there is a significant difference in the treatment efficacy between the subtypes of HL and NHL.

Materials and Methods

To determine the EFS of the lymphoma patients in the JHH electronic database, the patients were first categorized under nine different subtypes (Table 1) and compiled in a spreadsheet. The spreadsheet also included the patient's disease subset, whether an event occurred, event date, date of diagnosis, and date of last follow up. The EFS was calculated using one of two different equations depending on whether or not the patient experienced an event. If the patient had experienced an event, the EFS was calculated using the time frame between the date of diagnosis and the date of event occurrence. If the patient had not experienced an event, the timeframe between their date of diagnosis and the date of last follow up is recorded instead. This process was completed using the program GraphPad Prism®. EFS rates were calculated for each subtype along with the overall survival rate. The overall EFS was used to compare the treatment success of JHH and national averages.

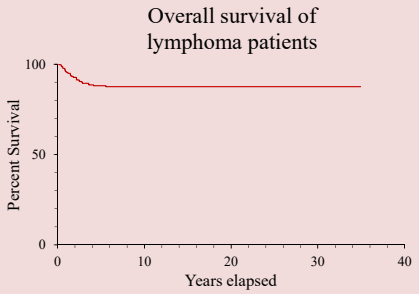
Lymphoma Classifications				
Hodgkin	Non-Hodgkin			
Classical	ALCL	PMBCL	DLBCL	Other
NLP	Burkitt	T-Lly	B-lly	

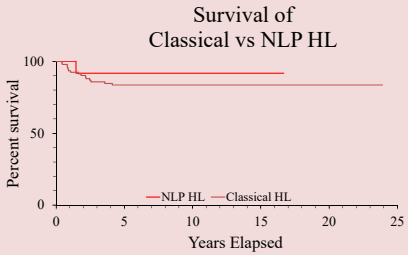
Table 1 (left): This table displays the two classifications of HL and the nine classifications of NHL found in the JHH database.

Results

To analyze the event-free survival of patients with HL and NHL, a Kaplan-Meier survival curve (Graphs 1–3) was generated for all the patients ($N = 219$) within their respective cancer subtypes. In the experiment, it was determined by a log-rank statistical test that pediatric NHL patients at JHH in the seven subtypes did not experience significantly different EFS rates from each other ($p > 0.05$) at the median time to patient follow-up (six years). The same result was true about the HL patients within their respective categories. The EFS rates for each category were also compared to approximate national standards for EFS rates to find that JHH patients experienced better rates than expected in some categories, and worse rates in others (Table 2).

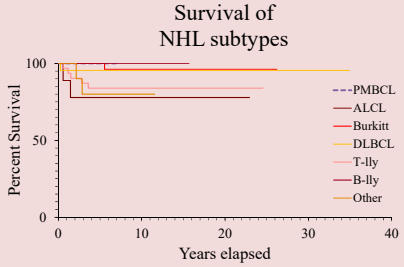
Graph 1 (right): This graph displays the Kaplan-Meir survival curve for all the lymphoma pediatric lymphoma patients in the JHH database, NHL and HL included. The calculated overall survival rate with a six year follow up is 88 percent. No log rank test was calculated in this group since there is no group to compare it to.





Graph 2 (left): This image displays the Kaplan-Meier survival curve for the two Hodgkin lymphomas in the database. Results from the log-rank statistical test produced values of χ^2 (1, $n = 103$) = 0.3886, $p = 0.5331$. This indicates that there is no statistically significant difference between the event-free survival rates of the two lymphomas.

Graph 3 (right): This graph displays the survival of NHL patients within the varying subtypes over time. The log-rank statistical test produced values of χ^2 (6, $n = 111$) = 7.123, $p = 0.3096$. This indicates that there is no statistically significant difference between the survival of the NHL subtypes.



Results (cont.)

EFS rates of pediatric lymphoma patients			
Classification	Patients (*n*)	JHH (%)	National (%)
PMBCL	4	100	93
DLBCL	20	95	91
NLP	9	89	90
cHL	77	80	86
B-Lly	8	100	85
Burkitt	18	94	80
T-Lly	24	83	72
ALCL	8	75	70
other	8	n/a	n/a

Table 2 (left): This table displays the EFS rates calculated for pediatric lymphoma patients at six years follow-up. EFS rates in each category were compared to national rates from five to ten years follow-up for the same category. The "other" category did not have national EFS rates for comparison. The cells shaded in grey display the only subtypes in which JHH had a lower EFS rate.

Conclusion

The purpose of this project was to evaluate the quality of treatment for pediatric lymphoma patients by examining the difference between EFS rates of patients at JHH and other hospitals nationally. The EFS rates at JHH were greater or less than national averages depending on the disease classification. The hypothesis that JHH's pediatric lymphoma patients have greater EFS rates than national averages is supported by six of the eight classifications that could be compared to national rates. For the groups that experienced lower EFS rates (cHL and NLP), this suggests an inferiority of treatment methods compared to the national standard. Furthermore, treatment efficacy between the subtypes within HL and NHL are insignificant based on the calculated *p*-values greater than 0.05. Possible errors include the skewing of data by a small number of patients in a classification. Further research can be conducted to find whether there is a significant difference in the efficacy of treatment between patients in different stages.

References

Friedman, D. L., Chen, L., Wolden, S., Buxton, A., McCarten, K., Fitzgerald, T. J., . . . Schwartz, C. L. (2014). Dose-intensive response-based chemotherapy and radiation therapy for children and adolescents with newly diagnosed intermediate-risk Hodgkin lymphoma: a report from the children's oncology group study ahod0031. *Journal of Clinical Oncology, 32*(32), 3651-3658.

Minard-Colin, V., Brugieres, L., Reiter, A., Cairo, M. S., Gross, T. G., Woessmann, W., . . . Patte, C. (2015). Non-Hodgkin Lymphoma in children and adolescents: progress through effective collaboration, current knowledge, and challenges ahead. *Journal of Clinical Oncology, 33*(27), 2963-2974.