POD24 AND SEROUS EFFUSION INVOLVEMENT IMPACT ON OVERALL SURVIVAL IN FOLLICULAR LYMPHOMA ATTENDED AT THE NATIONAL CANCER INSTITUTE IN MEXICO: A SURVEY OF 370 PATIENTS

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Introduction

Follicular lymphoma (FL) is the most common indolent non-Hodgkin's lymphoma,[1] and the median overall survival (OS) may exceed 20 years. However, in a minority of patients, the course is characterized by progression and frequent relapses, with an aggressive behaviour and ultimately, refractoriness.[2]

Multiple clinic-biological prognostic models have been developed in an attempet to stratify the risk of FL patients, nonetheless, these have limited representativeness for LATAM patients, since they were not included in those studies.[3,4,5]

Additionally, POD-24 as a marker of high-risk disease was developed arbitrarily and have not been thoroughly tested for LATAM patients.[6]

Objectives

- Describe the clinical and epidemiological characteristics of FL in our institution.
- Identify the factors associated with overall survival in patients with FL.

Methods

Retrospective analysis, to identify factors influencing on overall survival (OS) in patients with FL. Patients ≥ 18 years of age, with histological diagnosis of FL, without previous treatment, attended at the Instituto Nacional de Cancerología (Mexico City, Mexico) from Jan-2010 to December 2020. Clinical, biochemical and histological variables were included. Descriptive analysis was done for demographic and clinical characteristics. Median and standard deviation (SD) was used, as a measure of dispersion. Overall survival (OS) was defined since diagnosis until the date of the last follow-up or death. Survival curves were calculated by the Kaplan-Meier method, and differences between subgroups were compared with the Log-Rank test. Cox-regression analysis was used to identify the variables associated with overall survival.

Finally, to investigate if progression of disease at different timepoints had differential impact on overall survival, a landmark analysis was performed at 6-month intervals following first line therapy. HRs and confidence intervals were calculated using a Cox proportional Hazard model. All statisticals tests were considered significant with a p value ≤ 0.05. GraphPad Prism 9.3 and R studio were employed for graphs and statistical testing.

Results

370 patients were included (female: 216, 58.4%), with a median age of 54.99±12.67 years. Most of them had advanced disease III/IV (n=311, 84%) and low grade (n=263, 71%). Bulky disease was documented in 42.2%, bone marrow involvement in 31%, extranodal disease in 28.9%, and serous involvement in 18.6%. Only 329 cases received treatment, and the most frequent schema was CHOP-rituximab (n=315, 95%). Response rates in the first line of treatment were as follows: complete response (CR) 73.5%, partial response (PR), 9.7%, stable disease (SD) 2.4%, progressive disease (PD) 6.2% and undetermined in 8.2%.

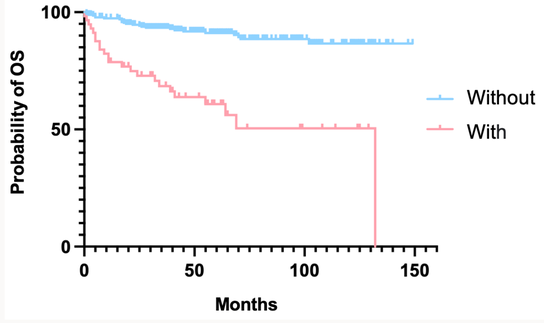
66% of patients received rituximab maintenance. 101/329 patients had progression of disease within 2 years (POD24). Transformation to DLBCL was documented in 3.9%.

OS was 80.69% at 10 years. In our proportional hazards model, serous involvement (p=0.0284, HR: 2.649, 95%CI: 1.11-6.38) and POD24 (p<0.0001, HR: 19.74, 95%CI: 8.59-50.21) were significantly associated with OS.

Results of the Cox regression analysis in 329 patients with FL

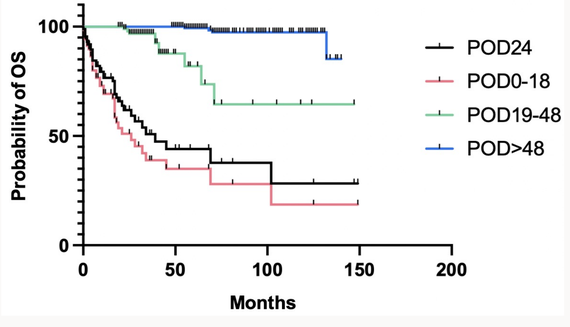
PARAMETERS	ADVERSE FACTOR	HR (CI 95%)	p Value
Sex	Male	1.20 (0.586-2.520)	0.6260
Age	≥60 years	1.17 (0.546-2.531)	0.6801
B – symptoms	Present	1.72 (0.743-4.196)	0.2181
Extranodal disease	Present	1.35 (0.616-2.923)	0.4434
Serous involvement	Present	2.649 (1.113-6.382)	0.0284
Bone marrow infiltration	Present	1.16 (0.599-2.224)	0.6620
Clinical stage	III/IV	2.20 (0.3917-41.57)	0.4637
ECOG	≥2	0.94 (0.373-2.347)	0.9037
DHL	Elevated	1.24 (0.553-2.769)	0.5998
Serum B2-microglobulin	Elevated	1.91 (0.793-5.102)	0.1691
POD24	Yes	19.74 (8.599-50.21)	<0.0001

OS in patients with serous involvement



Additionally, the HRs were calculated for patients with POD at 0 – 6 months (HR: 8.05, 95%CI: 4.12-14.44), 7 – 12m (HR: 2.75, 95%CI: 1.54-4.61), 13 – 18m (HR: 8.52, 95%CI: 3.5-17.67), 19 – 24m (HR: 3.9, 95%CI: 2.16-6.61), 25 – 48m (HR: 5.34, 95%CI: 3.83-7.43) & 49 – 72m (HR: 2.95, 95%CI: 2.07-4.17), suggesting a cut-off point at 18 could better represent high-risk population in our cohort.

OS of all cases grouped by PODs



Discussion

To our knowledge, this is the first study that demonstrates the relevance of serous involvement at diagnostic and its impact in OS. It was previously suggested as an important prognostic factor in the study by Brice et al in 1997[7], however this was not thoroughly discussed in their work. Other models, including FLIPI, FLIPI-2 and PRIMA-PI, did not analyzed specifically serous involvement.[3,4,5] In our study, factors included in the final score of these models like serum B2-microglobulin, were not significant in the multiparametric model, when accounting for serous involvement, further supporting its clinical relevance.

The other key factor affecting OS was POD24. In the study by Casulo et al, POD12, POD24, and POD36 correlated with worse OS. There was no comparison between the choice of the different periods, and the selection of POD24 was arbitrary.[6] In our study, POD18 better identifies a high-risk population, since the time period including 13-18 months was associated with the highest HR. These suggests that a landmark analysis of Casulo et al, data could clarify the best time point for POD.

Conclusion

In a LATAM reference cancer center, serous involvement at diagnosis and POD24 were significantly associated with worse OS in patients with FL.

References

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