Journal of Geriatric Oncology 16 (2025) 102160

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

journal homepage: www.elsevier.com/locate/jgo

Research Paper

# Real-world data on the clinical features, therapy patterns, and outcomes of older adults with diffuse large B-cell lymphoma in Latin America: A study from the *Grupo de Estudio Latinoamericano de Linfoproliferativos* (GELL)

Myrna Candelaria [a,*], Luis Villela [b], Luis F. Oñate-Ocana [a], Brady Beltran [c,d], Maria Torres-Viera [e], Ana Oliver [f], Henry Idrobo [g], Fernando Perez-Jacobo [h], Guilherme Perini [i], Camila Peña [j], Laura Korin [k], Denisse Castro [l], Victoria Irigoyen [m], Sally Paredes [l], Jose A. Hernandez-Hernandez [n], Perla Colunga [o], David Gomez-Almaguer [p], Guillermo Ruiz-Argüelles [q], Melani Otañez [r], Jorge J. Castillo [s], Luis Malpica [t]

[a] *Instituto Nacional de Cancerología México, Mexico*
[b] *Universidad Autonoma de Sinaloa, Hospital Fernando Ocaranza ISSSTE, Mexico*
[c] *Instituto de Investigaciones Biomédicas, Universidad Ricardo Pala, Lima, Peru*
[d] *Hostpial Edgardo Rebagliati Martins, Lima, Peru*
[e] *Clínica Santa Sofía, Instituto de Oncologia y Hematología de la Universidad Central de Venezuela, Caracas, Venezuela*
[f] *Hospital Británico, Uruguay*
[g] *Junta Directiva Grupo de Estudios de Linfoproliferativos & Scientific Director in Pereira, Colombia*
[h] *Hospital Central Norte PEMEX, Mexico*
[i] *Hospital Israelita Albert Einstein, Sao Paolo. Brazil*
[j] *Hospital del Salvador, Santiago de Chile. Chile*
[k] *Instituto Alexander Fleming, Argentina*
[l] *Hospital Nacional Edgardo Rabagliati Martíns, Centro de Investigación de Medicina de Precisión, Universidad de San Martin de Porras, Lima, Peru*
[m] *Hospital Casmu y Hospital Cosem, Uruguay*
[n] *Escuela de Medicina y Ciencias de la Salud, TEC de Monterrey, Mexico*
[o] *Hospital Universitario de Neuvo León, Universidad Autónoma de Nuevo León. Mexico*
[p] *Hospital Universitario de Nuevo León, Mexico*
[q] *Clínica Ruiz, Puebla, Mexico*
[r] *Hospital de Alta Especialidad de Sonora, Mexico*
[s] *Division of Hematological Malignancies, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA*
[t] *Department of Lymphoma and Myeloma, The University of Texas, MD Anderson Cancer Center, Houston, TX, USA*

ARTICLE INFO

*Keywords:*
Prognosis
Lymphoma
Older adults
B-cell malignancies

ABSTRACT

*Introduction:* Diffuse large B-cell lymphoma (DLBCL) is the most common type of B-cell lymphoma, predominantly afflicting older adults. There remains a notable absence of data regarding DLBCL in older adults in Latin America.

*Materials and Methods:* We conducted a retrospective analysis of 608 newly diagnosed Latin American patients with DLBCL aged ≥65 years.

*Results:* The median age at diagnosis was 74 years (range: 65–96 years), 51 % were female, 36 % had an Eastern Cooperative Oncology Group (ECOG) performance status (PS) ≥2, and 65 % had advanced disease. The most common regimens used were standard-dose R-CHOP ($n$ = 420, 69 %), R-CVP ($n$ = 77, 12 %), R-mini-CHOP ($n$ = 74, 12 %), and CHOP/CVP ($n$ = 30, 5 %). With a median follow-up of 60 months (95 % confidence interval [CI]: 38.7–75.2 months), the five-year overall survival (OS) rate was 50 % (95 % CI, 43–58). An ECOG PS ≥2 (hazard ratio [HR] 1.93; 95 % CI 1.51–2.46; $p < 0.01$), advanced clinical stage (HR 1.46; 95 % CI 1.12–1.91; $p < 0.01$), increased serum lactic dehydrogenase level (HR 1.48; 95 % CI 1.16–1.87; p < 0.01), and albumin level < 3.5 mg/dL (HR 1.64; 95 % CI 1.29–2.10; p < 0.01) were associated with an inferior OS. Using anthracyclines (HR 0.50;

* Corresponding author at: Av San Fernando 22, sección XVI, Tlalpan, 14080 Mexico City, Mexico.
*E-mail addresses:* candelariahmgloria@gmail.com (M. Candelaria), guilherme.perini@eisntein.br (G. Perini), j.a.hernandez@tec.mx (J.A. Hernandez-Hernandez), jruiz1@hsctmexico.com (G. Ruiz-Argüelles), jorgej_castillo@dfci.harvard.edu (J.J. Castillo), lemalpica@mdanderson.org (L. Malpica).

https://doi.org/10.1016/j.jgo.2024.102160
Received 18 June 2024; Received in revised form 11 November 2024; Accepted 21 November 2024
Available online 30 November 2024
1879-4068/

95 % CI 0.38–0.66; $p < 0.01$) and using rituximab (HR 0.51; 95 % CI 0.36–0.73; $p < 0.01$) were independently associated with a superior OS.

*Discussion:* In a large cohort of Latin American older patients with DLBCL, therapy and outcome patterns are similar to those reported internationally. The lack of standardized geriatric assessments in Latin America represents an essential area for research to better stratify older patients with DLBCL deemed to be at higher risk for toxicity.

## 1. Background

Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma [1]. The incidence of DLBCL increases from 45 cases to 112 per 100,000 people in patients aged 60–64 and 80–84, respectively [2]. Life expectancy has increased over the last decades and will be 83 years for women and 80 for men by 2030; thus, a larger number of older patients with DLBCL is expected to be diagnosed and treated [3].

DLBCL in older adults (i.e., ≥65 years of age) is heterogeneous due to a high frequency of functional limitations and comorbidities and may have different biological profiles and clinical behavior [4]. Data on the management and outcomes of older patients with DLBCL in Latin America are limited. Previous publications [5] documented 525,425 new cases of non-Hodgkin lymphoma (NHL) in patients over 15 years of age and it was more prevalent in males (56 %). The five-year prevalence of NHL cases in Latin America was 1,498,914. Additionally, the Hemato-Oncology Latin American (HOLA) observational study of 5140 patients with various hematological malignancies found that 57 % ($n$ = 2967) had NHL. This study included seven countries: Argentina, Brazil, Chile, Colombia, Mexico, Panama, and Guatemala [6]. As has been described in other populations, the most frequent NHL was DLBCL (49 %). Another report on the epidemiology of the types of NHL in Central and South America, in which Argentina, Brazil, Chile, Guatemala and Peru participated, [7] also documented that DLBC was the most frequent subtype (40 %), followed by follicular lymphoma and other B-cell lymphomas. It is also noteworthy that there is no published data from other Latin American countries, including Cuba, Ecuador, Dominican Republic, Costa Rica, Bolivia, Paraguay, and Uruguay.

To date, chemoimmunotherapy remains the standard of care for older adults with DLBCL, with some authors proposing a reduction in the dose intensity of the treatment regimen to improve tolerability (e.g., R-mini-CHOP) [8,9,11–15]. However, such changes may also compromise therapy responses and survival rates.

We conducted a retrospective review using the *Grupo de Estudio Latinoamericano de Linfoproliferativos* (GELL) real-world database on patients with DLBCL aged ≥65 years managed in Latin American countries. We describe clinical characteristics, therapy, and outcome patterns, with a focus on the effect of treatment type on survival.

## 2. Methods

### 2.1. Study Design

We conducted a muti-institutional retrospective analysis of patients diagnosed and managed for DLBCL in reference hospitals in the following countries: Mexico, Peru, Venezuela, Uruguay, Colombia, Brazil, Chile, and Argentina. The Institutional Review Board of each participating institution approved this study. The inclusion criteria were patients aged ≥65 years, newly diagnosed with DLBCL, and who received therapy with curative intent. Patients with incomplete medical records, human immunodeficiency virus (HIV) infection, primary or secondary central nervous system involvement, and those admitted for best-supportive care were excluded.

#### 2.1.1. Clinical and Laboratory Study Variables

We evaluated the following clinical characteristics: age, sex, the presence of B symptoms, number of extranodal sites, and performance status defined by the Eastern Cooperative Oncology Group (ECOG) scale [16], clinical stage, and prognosis group according with International Prognostic Index (IPI) score. The following laboratory parameters at diagnosis were included: serum albumin, white blood cell count, and serum lactic dehydrogenase (LDH) levels.

#### 2.1.2. Treatment and Response Evaluation

Therapy regimens and dose modification were recorded. For analysis purposes, the therapy regimens were classified as follows: [1] standard R-CHOP (rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, doxorubicin 50 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days); [2] R-mini-CHOP (rituximab 375 mg/m$^2$, cyclophosphamide 400 mg/m$^2$, doxorubicin 25 mg/m$^2$, 1 mg vincristine, and prednisone 40 mg/m$^2$ for 5 days); and [3] physician's preference of regimen (e.g., R-EPOCH) or dose-adjustments including different doses to R-CHOP, and omission of doxorubicin (R-CHP), rituximab (CHOP), or both (CVP). Prophylactic granulocyte colony-stimulating factor (G-CSF) was used per the investigator's criteria or hospital policy. Therapy responses were evaluated using standard international criteria. For computed tomography (CT) studies, we used the International Working Group criteria [17] and the Lugano criteria for positron emission tomography (PET)/CT evaluation [18]. There was no central review for either pathology or imaging response evaluation.

### 2.2. Statistical Analysis

Demographics, clinical features, and therapies received were summarized using descriptive statistics. The primary study outcomes were response to treatment and overall survival (OS). Depending on the setting, Chi-square or U-Mann Whitney tests were used to compare categorical variables. Survival curves were plotted using the Kaplan-Meier method, and differences between subgroups were estimated using the log-rank test. OS was measured from the date of diagnosis until death from any cause or last follow-up. Univariate Cox proportional-hazard regression models were fitted to identify OS predictors, and variables with $p$-value <0.05 were included in the multivariate analysis. The selected variables were then fitted in a multivariate Cox proportional-hazard regression model. Variables with a p-value <0.05 were considered independent OS predictors. STATA version 17.0 and SPSS version 25 software (IBM, Corp., Armonk, NY) were used for computations and graphs.

## 3. Results

### 3.1. Demographic and Clinical Features

A total of 651 patients were submitted for inclusion, of whom 43 did not receive chemotherapy for their lymphoma and were excluded from the study. Six hundred and eight patients had sufficient data for analysis and were included from: Mexico ($n$ = 435), Peru ($n$ = 76), Argentina ($n$ = 31), Venezuela ($n$ = 24), Brazil ($n$ = 20), Colombia ($n$ = 9), Chile (n = 7), and Uruguay ($n$ = 6).

Table 1 summarizes the data based on age at diagnosis (i.e., 65–79 vs. ≥80 years). There were no statistical differences in baseline clinical characteristics between patients aged <80 or ≥ 80.

**Table 1**
Comparison of clinical characteristics, treatment, and outcome by age group.

| Age group | 65–79 years $N = 493$ (%) | ≥80 years $N = 115$ (%) | *p*-value |
|---|---|---|---|
| Sex: | | | |
| Female | 243 (49) | 58 (51) | 0.89 |
| Male | 250 (51) | 57 (49) | |
| ECOG*: | | | |
| 0–1 | **324 (66)** | **64 (56)** | **0.03** |
| ≥2 | **169 (44)** | **51 (44)** | |
| Extranodal sites: | | | |
| 0–1 site | 379 (77) | 96 (83) | 0.16 |
| ≥2 sites | 114 (23) | 19 (17) | |
| Clinical Stage: | | | |
| I-II | 166 (34) | 44 (38) | 0.06 |
| III-IV | 327 (66) | 71 (62) | |
| LDH levels: | | | |
| Normal | 251 (51) | 70 (61) | 0.06 |
| Elevated | 242 (49) | 45 (39) | |
| Albumin level | | | |
| ≥3.5 g/dL | 280 (57) | 58 (51) | 0.14 |
| <3.5 g/dl | 213 (43) | 57 (49) | |
| IPI ** | | | |
| | 94 (19) | 21 (18) | 0.85 |
| - Low | 132 (27) | 34 (29) | |
| - Intermediate-low | | | |
| - Intermediate-high | 160 (32) | 40 (35) | |
| - High | | | |
| | 107 (22) | 20 (18) | |
| **Treatment:** | | | |
| **R-CHOP**[a] | **356 (72)** | **64 (56)** | **0.004** |
| **CHOP/R-CVP/CVP**[b] | **72 (15)** | **35 (30)** | |
| **R-miniCHOP**[c] | **58 (12)** | **16 14)** | |
| **R-EPOCH**[d] | **7 (1)** | **0 (0)** | |
| **Anthracycline use** | | | |
| **Yes** | **427 (87)** | **84 (73)** | **0.001** |
| **No** | **66 (13)** | **31 27)** | |
| Rituximab use | | | |
| Yes | 460 (93) | 103 (89) | 0.17 |
| No | 33 7) | 12 (11) | |
| **Response** | | | |
| **Complete** | **304 (62)** | **55 (48)** | **0.02** |
| **Partial** | **45 (9)** | **14 (12)** | |
| **No response** | **144 (29)** | **46 (40)** | |
| Median OS (95 % CI) | 34.9 (32.5–37.4) | 26.5 (21.7–31.3) | 0.003 |
| Cause of death: | | | |
| Lymphoma | 135 (27) | 45 (39) | 0.055 |
| Infection-treatment related | 58 (12) | 14 (12) | |
| Comorbidities | | | |
| Unknown | 17 (3) | 8 (7) | |
| | 30 (6) | 11 (10) | |

* ECOG: Eastern Cooperative Oncology Group.
** IPI: International Prognostic Index.
[a] RCHOP: rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, doxorubicin 50 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days.
[b] CHOP/RCVP/CVP: CHOP rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, doxorubicin 50 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days/ RCVP: rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days/ CVP: cyclophosphamide 750 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days.
[c] RminiCHOP: rituximab 375 mg/m$^2$, cyclophosphamide 400 mg/m$^2$, doxorubicin 25 mg/m$^2$, 1 mg vincristine, and prednisone 40 mg/m$^2$ for 5 days.
[d] REPOCH: rituximab 375 mg/m$^2$; etoposide 50 mg/m$^2$, daily in 96 h continuous infusion; doxorrubicine 10 mg/m$^2$, daily in 96 h continuous infusion; vincristine 0.4 mg/m$^2$, daily in 96 h continuous infusion and cyclophosphamide750 mg/m$^2$, on day 5.

### 3.2. Therapy Regimens and Responses

The most common therapy regimens were standard-dose R-CHOP ($n = 420$, 69 %), R-CVP ($n = 77$, 12 %), R-mini-CHOP ($n = 74$, 12 %), and CHOP/CVP ($n = 30$, 5 %). Seven patients (1 %) received R-EPOCH

**Table 2**
Response by chemotherapy regimen.

| Response | R-CHOP[a] $N = 420$ | R-miniCHOP[b] $N = 74$ | CHOP/CVP/R-CVP[c] $N = 107$ | R-EPOCH[d] N = 7 |
|---|---|---|---|---|
| Complete | 283 (68 %) | 43 (57 %) | 48 (44 %) | 3 (43 %) |
| Partial | 32 (8 %) | 5 (8 %) | 14 (13 %) | 1 (13 %) |
| No response | 105 (25 %) | 26 (35 %) | 45 (42 %) | 3 (43 %) |

[a] RCHOP: rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, doxorubicin 50 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days.
[b] RminiCHOP: rituximab 375 mg/m$^2$, cyclophosphamide 400 mg/m$^2$, doxorubicin 25 mg/m$^2$, 1 mg vincristine, and prednisone 40 mg/m$^2$ for 5 days.
[c] CHOP/CVP/RCVP: CHOP/RCVP/CVP: CHOP rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, doxorubicin 50 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days/ RCVP: rituximab 375 mg/m$^2$, cyclophosphamide 750 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days/ CVP: cyclophosphamide 750 mg/m$^2$, vincristine 1.4 mg/m$^2$ [maximum dose 2 mg] and prednisone 100 mg/day for 5 days.
[d] REPOCH: rituximab 375 mg/m$^2$; etoposide 50 mg/m$^2$, daily in 96 h continuous infusion; doxorrubicine 10 mg/m$^2$, daily in 96 h continuous infusion; vincristine 0.4 mg/m$^2$, daily in 96 h continuous infusion and cyclophosphamide750 mg/m$^2$, on day 5.

(Table 2). The overall response rate was 69 %, with a complete response rate of 59 % and a partial response rate of 10 %. Categorical responses by treatment regimen are shown in Table 2.

With a median follow-up of 60 months (95 % CI: 39–75 months), the median OS in the entire cohort was 56 months (95 % CI: 39–73) with a five-year OS rate of 50 % (95 % confidence interval [CI] 43–58; Fig. 1). During the follow-up period, 318 patients died. The causes of death were lymphoma ($n = 180$, 30 %), infection ($n = 72$,12 %), ischemic cardiomyopathy (n = 7, 1 %), non-infectious therapy-emergent toxicity ($n = 6$, 1 %), heart failure (n = 6, 1 %), and cerebrovascular event (n = 6, 1 %). The cause of death was unknown in 41 cases (7 %).

No differences were found between countries in terms of response rate or survival.

In the univariate analysis, factors associated with an increased risk of mortality were ECOG ≥2 (5-year OS rate 34 %, 95 % CI 27–40 % vs. 62 %, 95 % CI 56–67 %; Fig. 2A), advanced clinical stage (5-year OS rate 45 %, 95 % CI 39–50 % vs. 63 %, 95 % CI 56–70 %; $p < 0.01$; Fig. 2B), high serum LDH level (5-year OS rate 43 %, 95 % CI 36–49 % vs. 59 %, 95 % CI 53–65 %; $p < 0.01$; Fig. 2C), albumin <3.5 mg/dL (5-year OS rate 37 %, 95 % CI 31–43 % vs. 63 %, 95 % CI 57–68 %; $p < 0.01$; Fig. 2D), and age ≥ 75 (5-year OS rate 46 %, 95 % CI 40–53 % vs. 56 %, 95 % CI 50–61 %; $p = 0.03$). Conversely, administering anthracyclines (5-year OS rate 56 %, 95 % CI 52–61 % vs. 24 %, 95 % CI 16–34 %; p < 0.01;

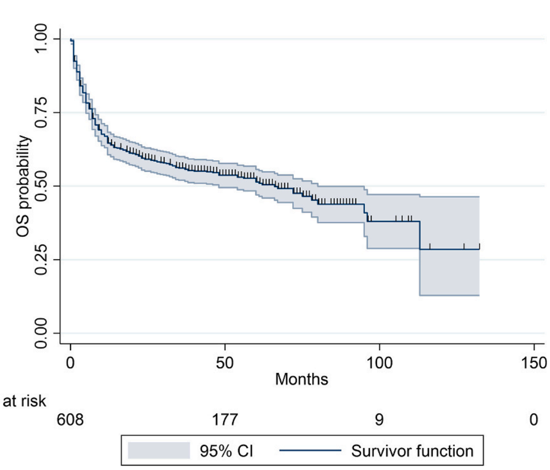


**Fig. 1.** Overall survival for the entire cohort.

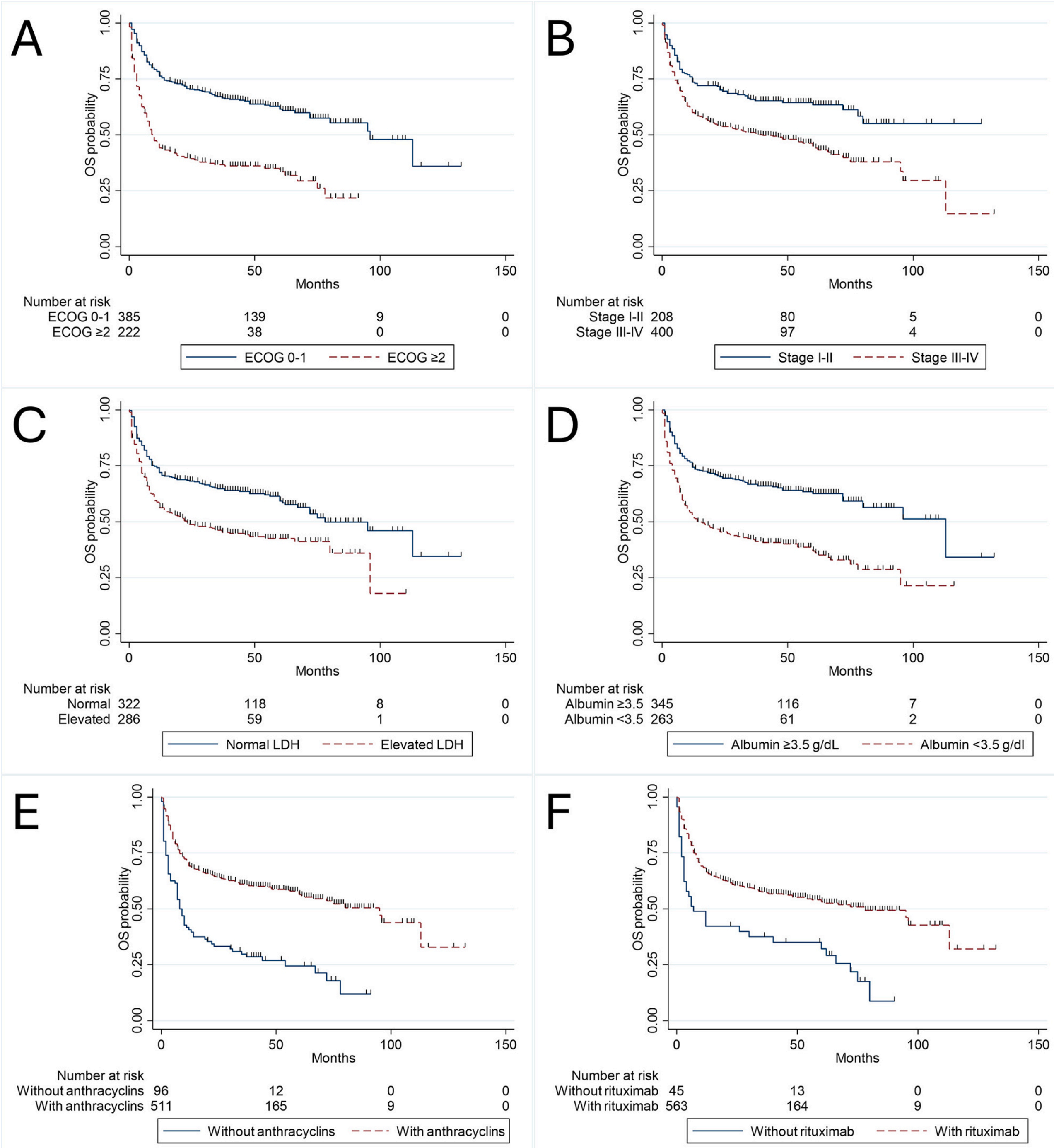


**Fig. 2.** Overall survival estimates according to ECOG (2 A), clinical stage (2B), LDH levels (2C), albumin levels (2D), anthracycline use (2E), and rituximab administration (2F).

Fig. 2E) and using rituximab (5-year OS rate 53 %, 95 % CI 48–57 % vs. 32 %, 95 % CI 19–46 %; $p < 0.01$; Fig. 2F) were associated with a decreased risk of death.

In multivariate analysis, ECOG ≥2 (hazard ratio [HR] 1.92, 95 % CI 1.50–2.46; $p < 0.01$), advanced clinical stage (HR 1.47, 95 % CI 1.12–1.92; $p < 0.01$), high serum LDH level (HR 1.47, 95 % CI 1.16–1.87; $p < 0.01$), and albumin <3.5 mg/dL (HR 1.66, 95 % CI 1.30–2.11; $p < 0.01$) were independently associated with an inferior OS, while administering anthracyclines (HR 0.50, 95 % CI 0.38–0.72; $p < 0.01$) and using rituximab (HR 0.50, 95 % CI 0.35–0.72; $p < 0.01$) were independently associated with a superior OS. Univariate and multivariate models are shown in Table 3.

## 4. Discussion

We report on a large retrospective study describing the clinical features, treatment patterns, and outcomes of patients aged ≥65 years with DLBCL from participating institutions in eight Latin American countries. Because of the retrospective design, we are not able to report the total number of patients with DLBCL treated in that period, but we were able to review the outcomes of patients who did receive treatment.

In Latin America, most older patients with DLBCL who receive

**Table 3**
Cox proportional-hazard regression analysis for overall survival.

| Variable | Group | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|---|
| | | HR | 95 % CI | P | HR | 95 % CI | P |
| Age | 65–74<br>≥75 | 1.28 | 1.02–1.62 | 0.03 | 1.09 | 0.85–1.37 | 0.51 |
| ECOG performance | 0–1<br>≥2 | 2.56 | 2.02–3.23 | <0.01 | 1.93 | 1.51–2.46 | <0.01 |
| Clinical stage | I-II<br>III-IV | 1.74 | 1.34–2.27 | <0.01 | 1.46 | 1.12–1.91 | <0.01 |
| LDH level | Normal<br>High | 1.70 | 1.34–2.14 | <0.01 | 1.48 | 1.16–1.87 | <0.01 |
| Extranodal sites | 0–1<br>≥2 | 1.21 | 0.95–1.54 | 0.13 | | | |
| Albumin level | ≥3.5 g/dL<br><3.5 g/dL | 2.18 | 1.72–2.75 | <0.01 | 1.64 | 1.29–2.10 | <0.01 |
| Anthracycline use | Yes<br>No | 0.39 | 0.30–0.51 | <0.01 | 0.50 | 0.38–0.66 | <0.01 |
| Rituximab use | Yes<br>No | 0.46 | 0.32–0.65 | <0.01 | 0.50 | 0.35–0.72 | <0.01 |

HR: Hazard ratio; CI: Confidence interval; ECOG: Eastern Cooperative Oncology Group; LDH: lactate dehydrogenase.

treatment have an ECOG performance status of 0–1, almost half are older than 75 years, and most are treated with standard R-CHOP. Poor performance status, advanced clinical stage, low serum albumin, increased LDH level, and the omission of anthracyclines or rituximab were all associated with poor outcomes.

Although DLBCL is curable in approximately 60 % of patients, the standard treatment with R-CHOP may present some challenges in older adults, requiring therapy modifications or dose adjustments. In a retrospective study from Argentina [19], patients who had a geriatric evaluation were shown to have a higher OS (1-year OS: 82 % vs. 64 %). This may be because the geriatric evaluation allowed a better decision on treatment. Similarly, in a study from the Italian Lymphoma Onco-hematological Group [20], a geriatric assessment helped classify patients into "fit," "unfit," and "frail," allowing for dose adjustments based on the patient's fitness evaluation. This tool reported the OS as 89 % at five years. Similarly, a prospective simplified assessment in older patients done by the Fondazione Italiana Linfomi [21], including 1163 patients with DLBCL used the simplified version of the GA (sGA) and classified patients as fit (55 %), unfit (28 %), and frail (18 %) with significantly different three-year OS: 87 % (95 % CI, 81 to 91) in fit patients, 69 % (95 % CI, 63 to 73) in unfit patients, and 42 % (95 % CI, 36 to 49) in frail patients. In our study, we did not perform a geriatric assessment, and clinicians used ECOG performance status for therapy decision-making, representing a weakness of this report.

Nonetheless, we found poor performance status, as well as low serum albumin levels, to be an adverse prognostic factor for OS. A previous report found ECOG performance status and serum albumin levels as independent prognostic factors for OS and progression-free survival in DLBCL [22], although the study included a younger population.

Different reduced-dose therapy regimens have been proposed for managing older patients with DLBCL [12–15]. However, no standard or specific chemoimmunotherapy regimen has been accepted worldwide. Some guidelines recommend a risk comorbidity stratification before indicating a reduced-dose chemoimmunotherapy regimen [23]. In patients with hematological malignancies, frailty has been proposed as a marker of biological age [24]. An algorithm for treatment decisions based on geriatric assessment has been proposed for older patients to be considered fit or frail [15,21], recommending R-CHOP for the former group and R-mini-CHOP or palliative care for the latter. In our retrospective study, every clinician determined the most optimal therapy option for their patients based on clinical judgment and the patient's ECOG performance status. We found that most patients aged ≥80 received R-mini-CHOP compared to their younger counterparts, who primarily received R-CHOP. Our findings correlate with previously published reports that included predominantly non-Hispanic populations [25–28].

Our study is inherently limited by its retrospective design. There were no standardized tools to assess fitness in our patient population other than clinicians' judgment, and there was no central pathology or imaging review to confirm pathological diagnosis and therapy responses. In addition, we did not include data on the use of granulocyte-colony stimulating factor in this patient population, despite its broad indication, due to the heterogeneous application of this agent in our resource-limited setting study. Additionally, the limited access to all diagnostic tools and therapeutic options could not be analyzed since we included patients receiving lymphoma- directed treatment, but did not have access to the whole population with DLBCL in Latin America. Despite these limitations, our study offers valuable real-world insights into the treatment practices for DLBCL across Latin American countries, reflecting the realities of management within similar contexts. One of our major strengths lies in our substantial sample size and the diversity of Hispanic populations across eight Latin American nations.

In conclusion, in a large cohort of Latin American older adults with DLBCL, therapy and outcome patterns were similar to those reported internationally. ECOG performance status ≥2, advanced clinical stage, hypoalbuminemia, increased LDH levels, and the omission of anthracyclines or rituximab impacted OS. The lack of standardized geriatric assessments in Latin America represents an essential area for research to better stratify patients with DLBCL ≥65 years deemed to be at higher risk for toxicity. Prospective, collaborative, multi-institutional clinical trials are required to define the optimal therapeutic strategy in older adults living in resource-limited settings.

## Author Contributions

Study concepts: MC/LV; Study design: MC/LV; Data acquisition: MC/LV/LFO/MTV/BB/AO/HI/PFJ/GP/CP/LK/DC/VI/SP/JAH/PC/DGG/GRA/MO; Quality control of data and algorithms: LV/JC/LMData analysis and interpretation: MC/JC; Statistical analysis: MC/JC; Manuscript preparation: MC/JC/LM/LV; Manuscript editing: MD/JC; Manuscript review: MC/LV/LFO/MTV/BB/AO/HI/PFJ/GP/CP/LK/DC/VI/SP/JAH/PC/DGG/GRA/MO/LM/JC.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References


[1] Christensen K, Doblhammer G, Rau R, Vaupel J. Ageing populations: the challenges ahead. Lancet 2009;374:1196–208. https://doi.org/10.1016/S0140-6736(09)61460-4.

[2] Thieblemont C, Coiffer B. Lymphoma in older patients. J. Clin. Oncol. 2007;25:1916–23. https://doi.org/10.1200/JCO.2006.10.5957.

[3] Zheng Y, Canudas-Romo V. Global health inequality: analyses of life disparity and healthy life disparity. Eur. J. Pub. Health 2024;34:225–9. https://doi.org/10.1093/eurpub/ckae010.

[4] Rittberg R, Decker K, Lambert P, Bravo J, St. John P, Turner D, et al. Impact of age, comorbidity, and polypharmacy on receipt of systemic therapy in advanced cancers: a retrospective population – based study. J. Geriatr. Oncol. 2024;15:101689. https://doi.org/10.1016//j.jgo.2023.101689 [Epub 2024Jan 13].

[5] Globocan. Data Source from International Agency for Research on Cancer. Available from: http://gco.iarc.fr; 2020.

[6] de Moraes Tiesche, Hungria V, Chiattone C, Pavlovsky M, Abenoza LM, Agreda GP, et al. Epidemiology of hematological malignancies in real-world settings: findings from the Hemato-oncology Latin America observational registry study. J. Glob. Oncol. 2019;5:1–19.

[7] Laurini JA, Perry AM, Boilesen E, Diebold J, Maclenan KA, Müller-Hermenelink HJ, et al. Classification of non-Hodgkin lymphoma in central and South America: a review of 1028 cases. Blood 2012;120:4795–801.

[8] Pfreundschuh M, Trumper L, Osterborg A, Pettengell R, Trneny M, Imrie K, et al. CHOP-like chemotherapy plus rituximab versus CHOP-like chemotherapy alone in young patients with good-prognosis diffuse large B-cell lymphoma: a randomized controlled trial by the MabThera international trial (MInT) group. Lancet Oncol. 2006;7:379–91. https://doi.org/10.1016/S1470-2045(06)70664-7-.

[9] Pfreunschuh M, Schubert J, Ziepert M, et al. Six versus eight cycles of bi-weekly CHOP-14 with or without rituximab in elderly patients with aggressive CD20 + B-cell lymphomas: a randomised controlled trial (RICOVER-60). Lancet Oncol. 2008;9:105–16.

[11] Coiffier B, Thieblemont C, Van Den Neste E, Lepeu G, Plantier I, Castaigne S, et al. Long term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. Blood 2010;116:2045. https://doi.org/10.1182/blood-2010-03-276246.

[12] Peyrade F, Jardin F, Thieblemont C, Thyss A, Emile JF, Castaigne S, et al. Attenuated immunochemotherapy regimen (R-miniCHOP) in older patients older than 80 years with diffuse large B-cell lymphoma: a multicentre, single-arm, phase 2 trial. Lancet Oncol. 2011;12:460–8. https://doi.org/10.1016/S1470-2045(11)70069-9.

[13] Nolasco-Medina D, Reynoso-Noveron N, Mohar-Betancourt A, Aviles-Salas A, García-Perez O, Candelaria M. Comparison of three chemotherapy regimens in older patients with diffuse large B cell lymphoma (DLBCL). Experience at a single National Reference Center in Mexico. Biomed. Res. Int. 2016;2016:9817606. https://doi.org/10.1155/2016/9817606.

[14] Candelaria M, Villela L, Torres-Viera MA, Peña C, Roa M, Zambrano D, et al. Real-world experience in older patients with diffuse large B-cell lymphoma treated in Latin America: a study by the Latin American study group of lymphoproliferative disorders (GELL). J. Geriatr. Oncol. 2023;14(7):101565. https://doi.org/10.1016/j.jgo.2023.101565.

[15] García-Baztán A, Oteiza-Olaso J, Gonzales-Montejo NJ, Ramón-Espinoza MF, Tamayo-Rodríguez I, Martínez-Velilla N, et al. Treatment individualization in diffuse large B cell lymphoma: is frailty enough for old adults? An original article. Clin. Lymphoma Myeloma Leuk. 2023;23:e348–59. https://doi.org/10.1016/j.clml.2023.06.010.

[16] Conill C, Verger E, Salamero M. Performance status assessment in cancer patients. Cancer 1990;65:1864–6.

[17] Cheson B Pfistner, Juweid ME, et al. Revised response criteria for malignant lymphoma. J. Clin. Oncol. 2007;25:579–86.

[18] Meignan M, Gallamini A, Haioun C, et al. Report on the 5th InternationalWorkshop on positron emission tomography in lymphoma held in Menton, France, 19-20 September 2014. Leuk. Lymphoma 2015;56:1229–32. https://doi.org/10.3109/10428194.2015.1029748.

[19] Warley F, Kalmus M, Cristaldo N, Otero V, Ismael IL, Boietti B, et al. Determination and Management of Risk for practices and procedures in the elderly (DRIPP): the impact of a comprehensive geriatric evaluation in elderly with diffuse large B-cell lymphoma. Hematol. Transfus. Cell Ther. 2023. https://doi.org/10.1016/j.htct.2023.09.2367.

[20] Spina M, Balzarotti M, Uziel L, Ferreri AJM, Fratino L, Magagnoli M, et al. Modulated chemotherapy according to modified comprehensive geriatric assessment in 100 consecutive elderly patients with diffuse large B-cell lymphoma. Oncologist 2012;17:838–46.

[21] Merli F, Luminari S, Tucci A, Arcari A, Rigacci L, Hawles E, et al. Simplified geriatric assessment in older patients with diffuse large B-cell Lymhoma: the prospective elderly project of the Fondazione Italiana Linfomi. J. Clin. Oncol. 2021;39:1214–22.

[22] Saglam B, Albayrak M, Yildiz A, Tighoglu P, Tighoglu M, Aras MR, et al. The prognostic impact of comorbidity, nutritional and performance status on patients with diffuse large B cell lymphoma. Niger. J. Clin. Pract. 2023. https://doi.org/10.4103/njcp.njcp_175_23.

[23] Wildiers H, Heeren P, Puts M, et. Al.. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. J. Clin. Oncol. 2014;32:2595–603. https://doi.org/10.1200/JCO.2013.54.8347.

[24] Fired LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J. Gerontol. Ser. A Biol. Sci. Med. Sci. 2001;56:M146–56. https://doi.org/10.1093/Gerona/56.3.m146.

[25] Marchesi F, Cenfra N, Altomare L, et al. A retrospective study of 73 elderly patients ($\geq$ 75 years) with aggressive B-cell-non-Hodgkin lymphoma: clinical significance of treatment intensity and comprehensive geriatric assessment. J. Geriatr. Oncol. 2013;4:242–8. https://doi.org/10.1016/j.jgo.2013.04.003.Epub2013May7.

[26] Kreher S, Lammer F, Augustin D, et al. R-splitCHOP chemotherapy for elderly patients with diffuse large B-cell lymphoma. Eur. J. Haematol. 2014;93:70–6. https://doi.org/10.1111/ejh.12304.Epub2014;ar28.

[27] Olivieiri A, Gini G, Bocci C, et al. Tailored therapy in an unselected population of 91 elderly patients with DLBCL prospectively evaluated using a simplified CGA. Oncologist 2012;17:663–72. https://doi.org/10.1634/theoncologist.2011-0355.

[28] Chichara D, Westin J, Oki Y, et al. Management strategies and outcomes for very elderly patients with diffuse large B-cell lymphoma. Cancer 2016;122:3145–51.