

ORAL COMMUNICATION

What is left to say on COVID-19 today?

OC 59 Clinical features and impact on mortality of COVID-19 epidemics in patients with Non-Hodgkin lymphoma: long-term results from a tertiary center in Italy

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ABSTRACT

Introduction: Due to the heterogeneity of the monitoring strategies and scant reliability of available data, quantifying the magnitude of the COVID-19 pandemic in terms of excess mortality and disease progression in hematologic populations is still an open challenge. We aimed to determine whether patients with Non-Hodgkin lymphoma (NHL) experiencing COVID-19 have an increased risk of mortality and are prone to more severe outcomes according to ongoing treatments and disease activity.

Materials and Methods: An ambivalent study was conducted recruiting patients with NHL followed at the Haematology Unit of the “Federico II” University hospital of Naples, Italy, from March 2020 to January 2023.

Results: During a median follow up of 35 months [IQR:20-71], a total of 206 patients were enrolled and observed; more than half of the patients experienced COVID-19(57%). Comparisons between main demographical features, lymphoma subtype, and immunosuppressive treatments in patients with or without SARS-CoV-2 infection are resumed in Table 1.

Overall median age was 68 years in our cohort; comorbidities were observed in 86% of patients; DLBCL and follicular were the more represented NHL subtypes (33% and 29%, respectively). Most patients had received rituximab-based regimens (85%); 44% were administered bendamustine, 20% were on obinutuzumab.

Primary disease, treatments or baseline demographical parameters did not differ between the two groups. Nevertheless, a significant increase in overall mortality was recorded in patients experiencing SARS-CoV2 infection (34% vs 18%, $p=0.012$). In detail, when evaluating risk factors for mortality at multivariate Cox regression analysis (Table 2), male sex (aHR: 1.876, $p=0.045$), active NHL (aHR: 6.075, $p=0.009$), and occurrence of SARS-CoV2 infection (aHR: 3.776, $p=0.029$) showed to significantly worsen all-cause fatality rate. Notably, the mean survival time in patients with COVID-19 was reduced of a little less than a year (329 days, 1231 vs 1408 days, $p=0.011$ log rank test)(Fig. 1).

Looking at COVID-19 clinical features, approximately 15% of patients experienced severe-critical disease (30/118): examining predictors of severity, only refractory hematologic disease resulted as significant determinant of critical illness (aHR: 3.991, p=0.023) while infections occurring in Omicron era were associated with better outcomes (aHR: 0.09, p=0.005) (Table 3). No impact of sex, age, comorbidity burden, NHL subtype, hypogammaglobulinemia, vaccinal status, or immunochemotherapy was observed.

Conclusions: Patients with NHL and COVID-19 have an increased overall mortality compared to uninfected peers, independently from undergoing treatments, comorbidities, and baseline demographical features. Refractory disease emerges as significant determinant of severe-critical COVID-19. Our findings underscore the urgent need to mitigate the pandemic's impacts on this setting of patients who have been uniquely vulnerable to SARS-CoV2 threat.

Table 1. Laboratory features and clinical outcomes of patients with NHL who experienced or not SARS-CoV2 infection.

	Total (n=206) n (%)	Infected with SARS-CoV2 (n=118) n (%)	Not infected with SARS-CoV2 (n=88) n (%)	P (log test)
Sex/male	111 (54)	64 (54)	47 (54)	0.506
Age > 70 years old	141 (68)	79 (66)	62 (70)	0.287
Median age (years, IQR)	68 (55-74)	66.5 (59-72)	69 (60-77)	0.008
Comorbidities				
Presence of comorbidities	178 (86)	100 (84)	78 (88)	0.511
Chronic kidney disease	25 (12)	13 (11)	12 (14)	0.565
Cardiovascular disease	95 (45)	49 (42)	42 (48)	0.192
Diabetes	27 (13)	12 (10)	15 (17)	0.122
COPD	19 (9)	14 (12)	5 (6)	0.126
Obesity	38 (19)	12 (10)	6 (7)	0.192
HL Lymphoma				
DLCL	68 (33)	35 (30)	33 (38)	0.400
T-cellular	60 (29)	32 (26)	28 (32)	0.038
Marginal	33 (16)	15 (12)	18 (21)	0.142
Other	68 (33)	34 (29)	34 (39)	0.702
Overall treatment				
Rituximab	174 (84)	98 (83)	76 (86)	0.536
Obinutuzumab	48 (23)	28 (23)	19 (21)	0.561
Bendamustine	92 (44)	50 (42)	42 (48)	0.248
Lenalidomide	38 (18)	18 (15)	20 (23)	0.181
Gemtuzumab	20 (10)	9 (8)	11 (12)	0.220
Radiotherapy	23 (11)	11 (9)	12 (14)	0.993
Prior HDCT/autot-SCT	22 (10)	8 (7)	4 (5)	0.483
Primary disease features				
Length of last < 12 months	21 (10)	11 (9)	6 (7)	0.718
Length of last > 12 months	166 (80)	107 (91)	41 (47)	0.147
Active NHL	138 (67)	74 (62)	64 (73)	0.094
None diagnosis	62 (30)	38 (32)	24 (28)	0.181
Refractory disease	20 (10)	11 (9)	7 (8)	0.485
Disease remission	78 (38)	40 (34)	38 (44)	0.483
Vaccination	177 (86)	101 (84)	76 (86)	0.974
Overall mortality	56 (27)	31 (26)	25 (28)	0.023
Median overall follow-up (months, IQR)	35 (20-71)	34.5 (20-58)	36.5 (21-76.5)	0.551

Table 2. Risk factors for mortality in patients with NHL (n= 27).

	Lymphocyte			Multiorgan		
	HR	95% CI	p	aHR	95% CI	p
Male sex	1.815	1.030 - 3.136	0.039	1.870	1.023 - 3.468	0.045
Age > 70 years	1.881	1.101 - 3.2	0.021	2.260	1.259 - 4.056	0.006
Obinutuzumab	2.000	1.177 - 3.371	0.012	2.446	1.380 - 4.312	0.007
treatment						
Active disease	3.653	1.720 - 7.761	<0.001	3.803	1.969 - 6.915	0.000
Sars-CoV2 infection	2.165	1.178 - 3.980	0.011	2.012	1.075 - 3.766	0.029

Figure 1. Survival estimates in patients with NHL, with and without Sars-Cov2 infection.

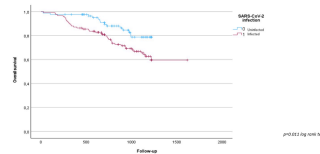


Table 3. Predictive factors of severe COVID-19 disease according to WHO clinical classification in patients with NHL (n = 118).

	Mild-to-moderate disease (n=88) n (%)	Severe-to-critical disease (n=30) n (%)	HR	95% CI	p	aHR	95% CI	p
Obinutuzumab treatment	15 (18)	13 (43)	2.431	1.153 - 5.125	0.020	0.810	0.220 - 3.007	0.783
Bendamustine treatment	34 (39)	22 (73)	2.404	1.063 - 5.415	0.031	0.568	1.051 - 3.221	0.058
Combined Anti-CD20 agents + Bendamustine	17 (20)	11 (37)	2.201	1.007 - 4.894	0.048	1.540	0.495 - 5.005	0.442
Disease remission	27 (31)	3 (10)	0.300	0.054 - 0.964	0.005	0.225	0.028 - 1.922	0.079
Refractory disease	5 (6)	8 (26)	5.129	2.105 - 12.540	<0.001	3.991	1.234 - 12.120	0.023
Chemotherapy 90 days before SARS-CoV-2 infection	25 (28)	18 (60)	3.804	1.408 - 10.270	0.008	1.375	0.448 - 4.227	0.578
Vaccination	80 (92)	21 (70)	0.173	0.077 - 0.390	<0.001	0.321	0.073 - 1.408	0.132
Omicron waves	3 (3)	5 (17)	0.093	0.010 - 0.214	<0.001	0.090	0.019 - 0.506	0.005