

EFFECTS OF INFLAMMATORY MARKERS ON OVERALL SURVIVAL OF CERVICAL CANCER STRATIFIED BY STAGING

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INTRODUCTION

this study aims to investigate the effects of inflammatory markers on overall survival of cervical cancer (CC) stratified by staging.

METHODOLOGY

this cohort study had a sample of 1325 women over the age of 18, diagnosed and treated in a single reference center for CC in Brazil, during the years 2006-2009. The following indexes were analyzed: neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), derivation of neutrophil-lymphocyte ratio (dNLR), absolute neutrophils count (ANC). Descriptive analysis was performed using median and absolute and relative frequency for categorical variables. ANOVA was used for continuous variables and chi-square for categorical variables, to compare groups. Exploratory survival evaluation was performed using the Kaplan–Meier method. The comparison between survival curves was performed using the log-rank test, assuming statistical significance level of 5%. The variables with $p < 0.20$ were selected for inclusion in a multivariate Cox regression model, considering as statistical significance $p < 0.05$. Missing data were not considered in the analysis.

RESULTS

All markers with higher values showed worse survival. NLR > 5 had an average survival of 3.5 years, half when compared to those with NLR ≤ 5 (7.1 years). PLR > 300 had an average survival of 2.9 years, while ≤ 300 had a mean survival of 6.9 years. dNLR ≤ 3 had an average survival of 7.2 years, while > 3 had a mean survival of 3.6. ANC > 7500 presented survival of 4.3 years while those with ≤ 7500 had a mean survival of 7.1 years. When separated by staging, PLR, NLR and dNLR were significant for both early and advanced staging, whereas ANC was relevant only in advanced staging. Those without staging showed behavior similar to those in advanced staging. The biomarkers associated with the worst overall survival after adjusting for clinical variables were NLR > 5 (HR=2.14 CI 1.72 – 2.65; $p < 0.001$); PLR > 300 (HR=2.44 CI 1.92 – 3.11; $p < 0.001$); dNLR > 3 (HR=1.97 CI 1.58 – 2.47; $p < 0.001$); and ANC > 7500 (HR=1.81 CI 1.48 – 2.21; $p < 0.001$).

Table 1. Distribution of patients and overall survival according to markers of cancer related inflammation (n=1325)

Variables	N° total (% in column)	N° deaths (% in line)	Overall survival		
			Mean (SD)	95%CI	Log rank
NLR					
≤ 5	1107 (83.5)	372 (33.6)	7.1 (0.12)	6.8 – 7.3	p<0.001
> 5	218 (16.5)	149 (68.3)	3.5 (0.28)	2.9 – 4.0	
PLR					
≤ 300	1181 (89.1)	415 (35.1)	6.9 (0.12)	6.7 – 7.2	p<0.001
> 300	144 (10.9)	106 (73.11)	2.9 (0.32)	2.3 – 3.5	
dNLR					
≤ 3	1129 (84.3)	391 (33.6)	7.2 (0.12)	6.7 – 7.6	p<0.001
> 3	196 (15.7)	130 (66.4)	3.6 (0.30)	3.0 – 4.2	
ANC					
≤7500	1045 (78.9)	354 (33.9)	7.1 (0.12)	6.8 – 7.3	p<0.001
>7500	280 (21.1)	167 (59.6)	4.3 (0.26)	3.8 – 4.9	

NLR: neutrophil to lymphocyte ratio; ANC: absolute neutrophil count; dNLR: derived neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; CI: confidence interval; SD: Standard derivation. Mean in years. Statistically significant associations are in bold.

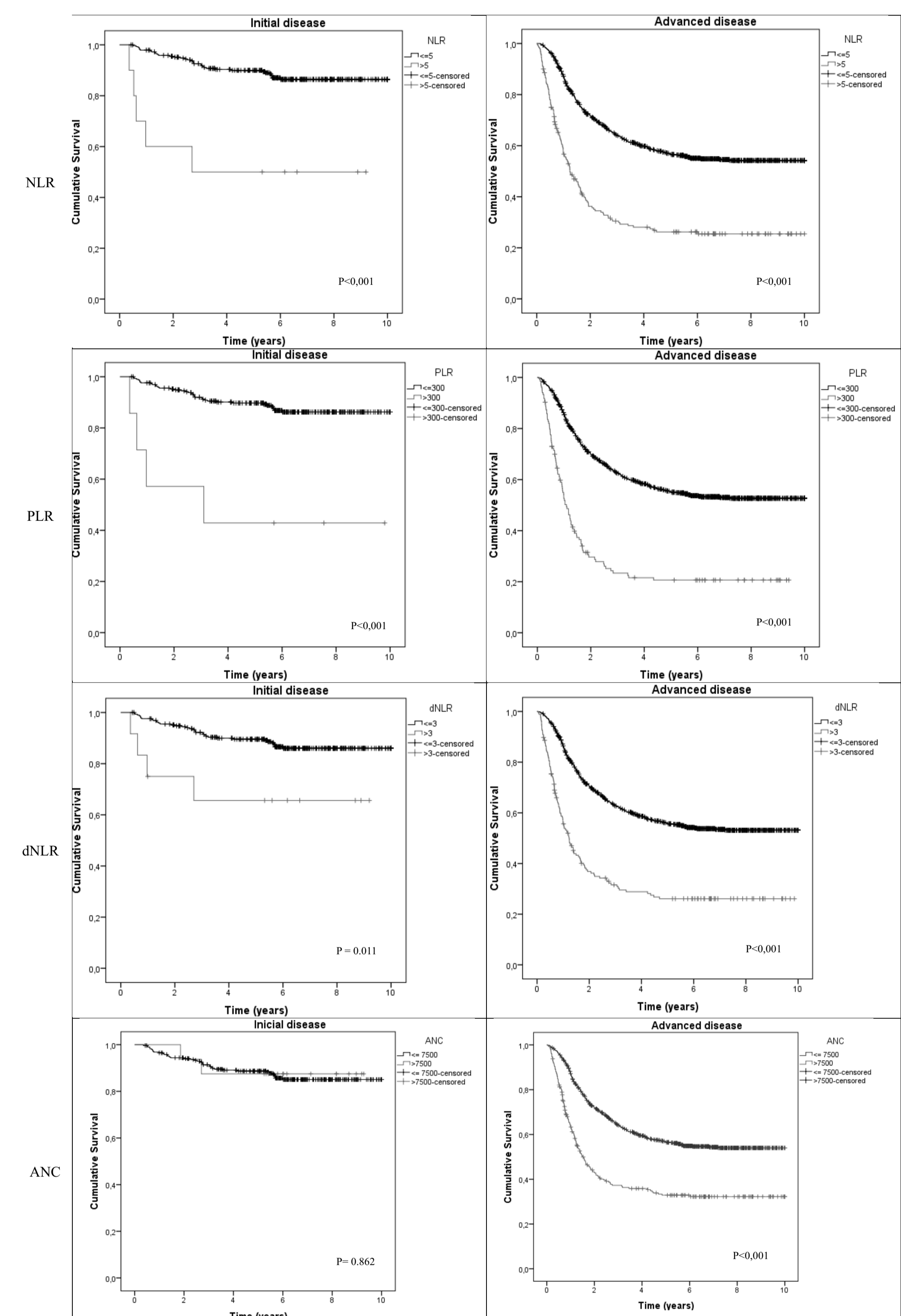


Figure 1. Kaplan Meier overall survival curve stratified by inflammatory marker and staging of the disease. NLR: neutrophil ratio and lymphocytes. PLR: ratio platelets and lymphocytes. dNLR: ratio between neutrophils and leukocytes minus neutrophils. ANC: absolute number of neutrophils.

Table 2. Risk of death according to the markers of cancer related inflammation

Variables	Crude		Adjusted	
	HR (95%CI)	P value	HR (95%CI)	P value
NLR				
≤ 5	1.00		1.00	
> 5	3.55 (2.93 – 4.30)	< 0.001	2.14 (1.72 – 2.65)*	< 0.001
PLR				
≤ 300	1.00		1.00	
> 300	3.98 (3.21 – 4.94)	< 0.001	2.44 (1.92 – 3.11)*	< 0.001
dNLR				
≤ 3	1.00		1.00	
> 3	3.24 (2.65 – 3.95)	< 0.001	1.97 (1.58 – 2.47)*	< 0.001
ANC				
≤ 7500	1.00		1.00	
>7500	2.65 (2.20 – 3.18)	< 0.001	1.81 (1.48 – 2.21)*	< 0.001

NLR: neutrophil to lymphocyte ratio; ANC: absolute neutrophil count; dNLR: derived neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; CI: confidence interval; HR: hazard ratio.

Statistically significant associations are in bold

* adjusted for staging, hemoglobin at the beginning of treatment, comorbidities and performance status.

CONCLUSION

PLR, dNLR and NLR had worse prognosis independent of staging, whereas ANC was only relevant in advanced staging.