

Effectiveness of four inflammatory markers in predicting prognosis in 2374 women with breast cancer

Bárbara Reis Wariss (master student)^a, Karen de Souza Abrahão^a, Suzana Sales de Aguiar^a, Anke Bergmann (co-advisor)^a, Luiz Claudio Santos Thuler (advisor)^{a,b}
 a. Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil
 b. Federal University of Rio de Janeiro State (UNIRIO), Rio de Janeiro, Brazil

OBJECTIVE

To analyze the association between four biomarkers and overall survival in patients with breast cancer (BC).

METHODOLOGY

This cohort study had a sample of 2374 women over the age of 18, diagnosed and treated in a single reference center for BC in Brazil, during the year 2008–2009. The following pretreatment indices were analyzed: neutrophil–lymphocyte ratio (NLR), a derived neutrophil–lymphocyte ratio (dNLR), absolute neutrophil count (ANC) and platelet–lymphocyte ratio (PLR). A descriptive analysis was performed using median (range) and absolute and relative frequency as categorical variables. Exploratory survival evaluation was performed using the Kaplan-Meier method and the log-rank test for comparison between survival curves, with a statistical significance level of 5%. The variables with $p < 0.20$ were selected for inclusion in a multivariate Cox regression model, considering as statistically significant $p < 0.05$.

Table 1. Distribution of patients and overall survival according to markers of cancer related inflammation (n=2288)

Variables	N total (% in column)	N deaths (% in line)	Overall survival		
			Mean (SD)	95%CI	Log-rank
NLR					
< 4	2160 (94.4)	437 (20.2)	5.2 (0.03)	5.1–5.3	
4–5	51 (2.2)	14 (27.4)	4.4 (0.29)	3.9–5.0	p<0.001
> 5	77 (3.4)	43 (55.8)	3.0 (0.27)	2.5–3.5	
PLR					
< 150	1767 (77.2)	324 (18.3)	5.3 (0.03)	5.2–5.4	
150–300	473 (20.7)	140 (29.6)	4.6 (0.09)	4.4–4.8	p<0.001
> 300	48 (2.1)	30 (62.5)	2.8 (0.34)	2.1–3.5	
dNLR					
< 2	1926 (84.2)	382 (19.8)	5.2 (0.03)	5.2–5.3	
2–3	278 (12.1)	71 (25.5)	4.7 (0.12)	4.4–4.9	p<0.001
> 3	84 (3.7)	41 (48.8)	3.4 (0.03)	2.9–3.9	
ANC					
≤ 7500	2121 (92.7)	424 (20.0)	5.2 (0.37)	5.2–5.3	
> 7500	167 (7.3)	70 (41.9)	3.8 (0.18)	3.4–4.2	p<0.001

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

RESULTS

After adjusting for clinical variables, the biomarkers associated with worse overall survival were NLR > 5 (HR = 1.66 95%CI 1.08–2.55; $p = 0.021$) and PLR > 300 (HR = 1.82 95%CI 1.10–2.99; $p = 0.019$). When stratified by molecular subtype, the independent markers related to death were PLR > 300 for triple negative (HR 3.27 95%CI 1.38–7.76; $p = 0.007$); NLR > 5 (HR 2.47 95%CI 1.16–5.28; $p = 0.019$), ANC > 7500 (HR 1.84 95%CI 1.17–2.90; $p = 0.008$) and dNLR > 3 (HR 2.45 95%CI 1.29–4.66; $p = 0.006$) for luminal.

CONCLUSION

NLR and PLR are independent markers of prognosis in BC. Further studies are needed in patients with overexpression of HER 2.

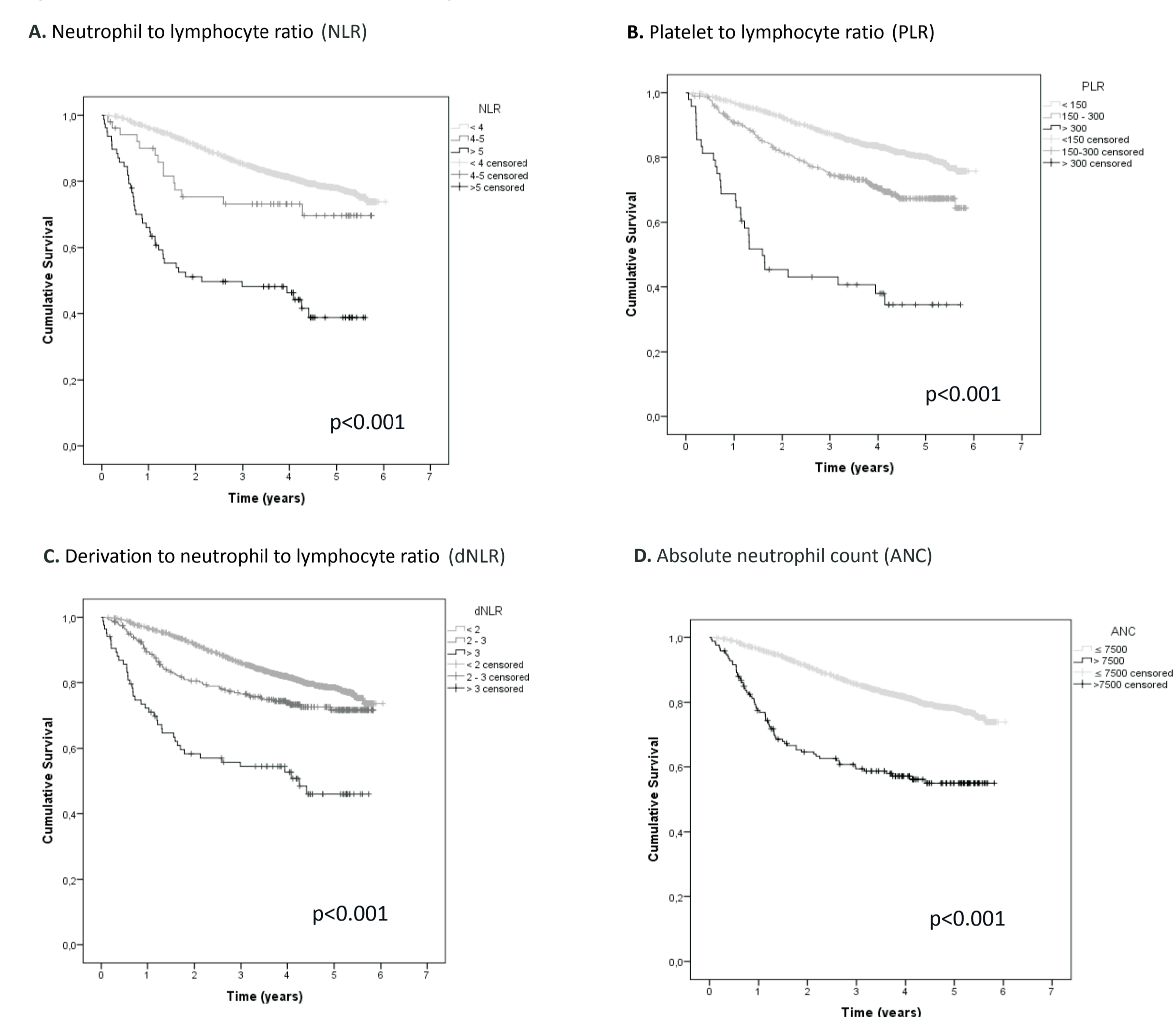


Fig. 1. Kaplan-Meier Curves for overall survival stratified by markers of cancer related inflammation.

Table 2. Risk of death according to the markers of cancer related inflammation and stratified by molecular subtype.

Variables	Overall		Triple negative		Her 2		Luminal A and B	
	Adjusted HR (95%CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
NLR*								
< 4	1.00		1.00		1.00		1.00	
4–5	1.03 (0.57–1.89)*	0.914	1.18 (0.48–2.92)*	0.715	0.71 (0.94–5.37)*	0.741	1.04 (0.43–2.52)*	0.937
> 5	1.66 (1.08–2.55)*	0.021	1.33 (0.71–2.50)*	0.374	2.39 (0.94–6.08)*	0.068	2.47 (1.16–5.28)*	0.019
PLR*								
< 150	1.00		1.00		1.00		1.00	
150–300	1.06 (0.84–1.33)*	0.624	1.11 (0.75–1.66)*	0.595	1.60 (0.91–2.82)*	0.102	0.92 (0.66–1.29)*	0.633
> 300	1.82 (1.10–2.99)*	0.019	3.27 (1.38–7.76)*	0.007	2.05 (0.71–5.93)*	0.182	1.48 (0.69–3.17)*	0.311
ANC*								
≤ 7500	1.00		1.00		1.00		1.00	
> 7500	1.26 (0.92–1.74)*	0.150	0.86 (0.51–1.45)*	0.583	2.07 (0.92–4.67)*	0.078	1.84 (1.17–2.90)*	0.008
dNLR								
< 2	1.00		1.00		1.00		1.00	
2–3	1.02 (0.76–1.38)*	0.869	0.93 (0.57–1.54)**	0.937	1.54 (0.69–3.45)**	0.293	1.02 (0.67–1.55)**	0.923
> 3	1.53 (0.99–2.38)*	0.053	1.00 (0.49–2.08)**	0.980	2.84 (0.98–8.16)**	0.053	2.45 (1.29–4.66)**	0.006

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

+ Adjusted for: molecular subtype, TNM staging and surgery (n=2288).

* Adjusted for: molecular subtype, TNM staging, education and surgery (n=2288).

** Adjusted for: TNM staging and surgery.

*** Adjusted for: TNM staging, education and surgery.

Statistically significant association are in bold.