PRE-ART PLATELET-TO-LYMPHOCYTE RATIO AND THE RISK OF SERIOUS NON-AIDS-EVENTS, AIDS-EVENTS AND MORTALITY IN PLWH STARTING FIRST-LINE ART

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BACKGROUND

- People living with HIV (PLWH) are at higher risk of serious non-AIDS events (SNAEs), like non-AIDS-defining malignancies and cardiovascular, renal, and hepatic diseases.
- SNAEs have been associated to different mechanisms, including HIV-related immune activation and inflammation.
- Neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) are new inflammatory biomarkers and prognostic factors for many conditions in general population, but they have been poorly analysed in PLWH.

AIM

The aim of our study was to assess the relationship between baseline PLR, NLR and LMR and the incidence of SNAEs, AIDS events and mortality.

STUDY DESIGN AND METHODS

- We conducted a restrospective observational cohort study nested with the ICONA Foundation Study cohort.
- We enrolled PLWH starting first line ART (baseline) between 1997 and 2021.
- PLR, NLR and LMR baseline values were divided in three subgroups (T1, T2, T3) based on the tertiles of their distribution.
- The primary outcome of our study was the incidence of SNAEs or death. Secondary outcomes were the incidence of AIDS events or death, and the all-cause mortality.
- The association between baseline PLR, NLR and LMR and the 15 years-risk of SNAEs, AIDS events and all-cause mortality were tested using Kaplan-Meier (KM) and Cox proportional hazard models, adjusting for age, CD4+ count, viral load, HCV-status, and year of starting ART.

RESULTS

We included 9,248 patients in the PLR analysis, 8,727 for NLR analysis and 1,090 for LMR analysis. Participants were mainly males, aged 38 years, with a median baseline CD4 count of 330/mmc.

PLR

Table 1 – Tertiles distribution of PLR, NLR and LMR

PLR	Min	Max	Mean	Number
T1	0,909	93,200	66.680	3083
T2	93,203	142,857	115,577	3085
T3	142,916	187179,5	565,117	3080
All	0,909	187179,5	248,993	9248

NLR	Min	Max	Mean	Number
T1	0,0007	1,246	0,871	2909
T2	1,246	2,045	1,612	2909
T3	2,045	2100,000	5,655	2909
All	0,0007	2100,000	2,712	8727

LMR	Min	Max	Mean	Number
T1	0,1425	3,000	2,0051	365
T2	3,003	4,593	3,767	362
T3	4,594	570,000	19,081	363
All	0,142	570,000	8,277	1090

Table 2 – Baseline characteristics by PLR tertiles

Baseline characteristics	PLR T1	PLR T2	PLR T3	p-value
Female	463 (15%)	681 (22,1%)	978 (31,8%)	< 0,001
Age (median)	38 (31, 46)	37 (31, 45)	39 (33, 47)	< 0,001
IDU	597 (19,4%)	436 (14,1%)	387 (12,6%)	< 0,001
MSM	1388 (45,0%)	1390 (45,1%)	1039 (33,7%)	< 0,001
Not Italian	763 (24,7%)	934 (30,3%)	1150 (37,3%)	< 0,001
AIDS diagnosis	150 (4,8%)	165 (5,3%)	668 (21,7%)	< 0,001
CD4+ count	404 (276, 579)	370 (254, 505)	195 (54, 337)	< 0,001
CD8+ count	1270 (920, 1706)	899 (703, 1153)	559 (376, 766)	< 0,001
CD4+ count < 200	436 (14,2%)	530 (17,2%)	1552 (51,1%)	< 0,001
HCV Ab positivity	642 (20,8%)	441 (14,3%)	400 (13,0%)	< 0,001
HBsAg positivity	28 (0,9%)	25 (0,8%)	8 (0,3%)	0,009
CVD diagnosis	23 (0,7%)	19 (0,6%)	29 (0,9%)	0,337
Diabetes	71 (2,3%)	55 (1,8%)	62 (2,0%)	0,349
Smoking	1003 (32,5%)	1000 (32,4%)	890 (28,9%)	0,002
Total cholesterol (median)	158 (133, 183)	160 (137, 185)	158 (132, 185)	0,021
eGFR (median)	105 (92, 115)	106 (93, 116)	106 (94, 116)	0,002

The cumulative rate of SNAEs or death in T1 (23%) was significantly higher compared to T2 (18%) and T3 (19%); this result was also confirmed at the standard Cox regression model and adjusting for the confounding factors. The prognostic role of PLR was also evaluated for the secondary outcomes: PLR less than 93 (T1) and higher than 142,9 (T3) was strongly associated with a higher risk of AIDS, and lower level of PLR (T1) was strongly associated with the all-cause mortality, also in the adjusted analysis.

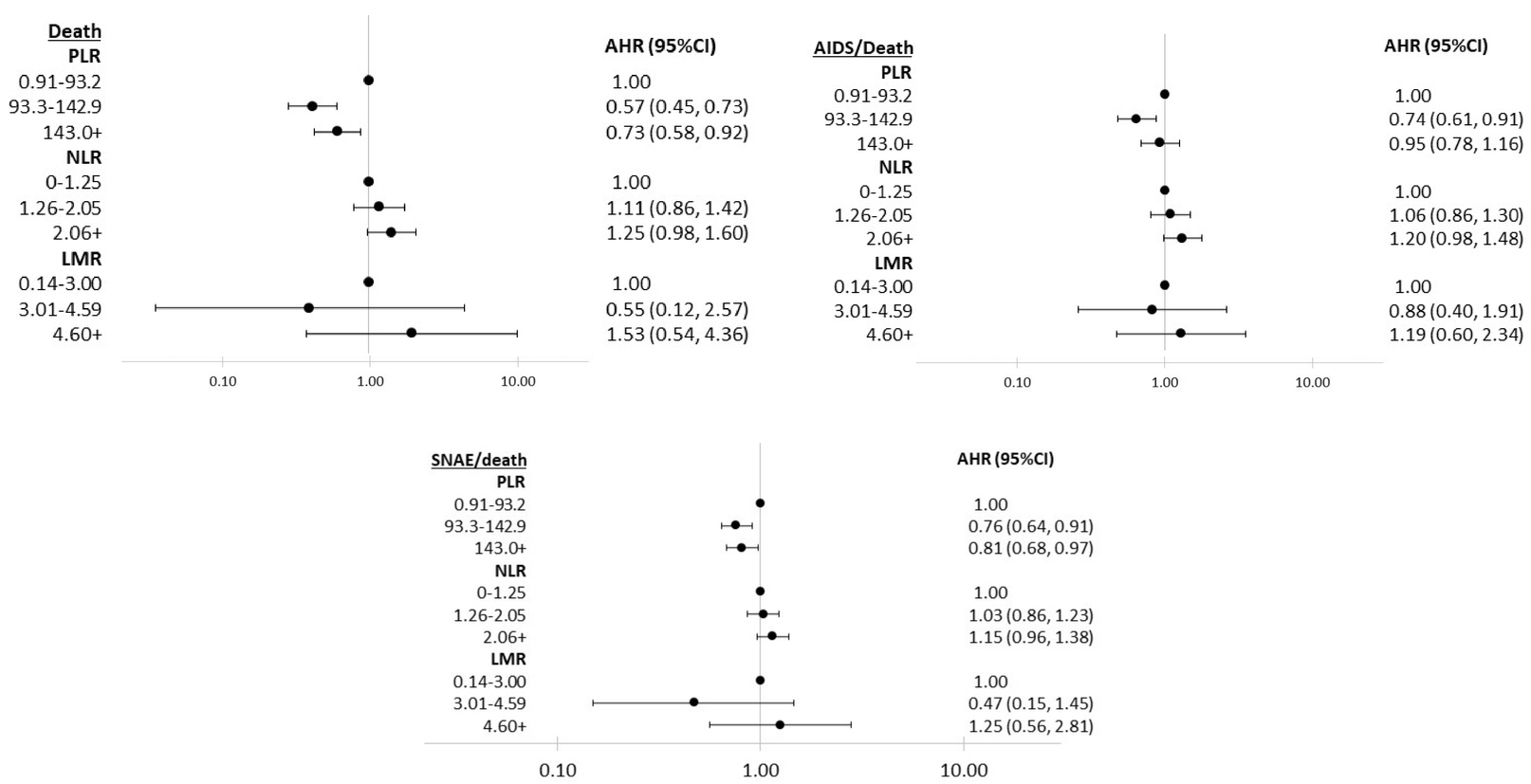
NLR

For higher values of NLR T3 (T3, NLR > 2,04) there were significantly more SNAEs compared to both T1 and T2 subgroups; moreover, as expected, in this subgroup there was a higher incidence of AIDS events and a higher mortality for all-cause. However, all these results have not been confirmed at the Cox regression model adjusting for CD4+ T cells count and the other a priori identified confounding factors.

LMR

For LMR T1 subgroup (LMR < 3,00) there were significantly more SNAEs compared to T2 and T3. However, using a standard Cox regression model and adjusting for confounding factors, no significant difference was observed between LMR subgroups. Moreover, in LMR T1 group there was a higher risk of AIDS events and a higher all-cause mortality, but these results were not confirmed at the adjusted analysis.

Figure 1 – Risk of SNAEs, AIDS events and mortality



CONCLUSIONS

Our data show that in PLWH starting a first-line ART, baseline PLR is a strong predictor of the risk of SNAEs, AIDS events and mortality, independently of key confounding factors. Because the biomarker is derived from common blood parameters routinely collected in the clinics, its use should be encouraged to identify and carefully manage PLWH who are at increased risk of poor long-term clinical outcomes.

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