XXXIX CONGRESSO
DELL'ASSOCIAZIONE
ITALIANA DI EPIDEMIOLOGIA

Indici di infiammazione sistemici e mortalità per tutte le cause in soggetti HIV

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Inflammation and Cancer

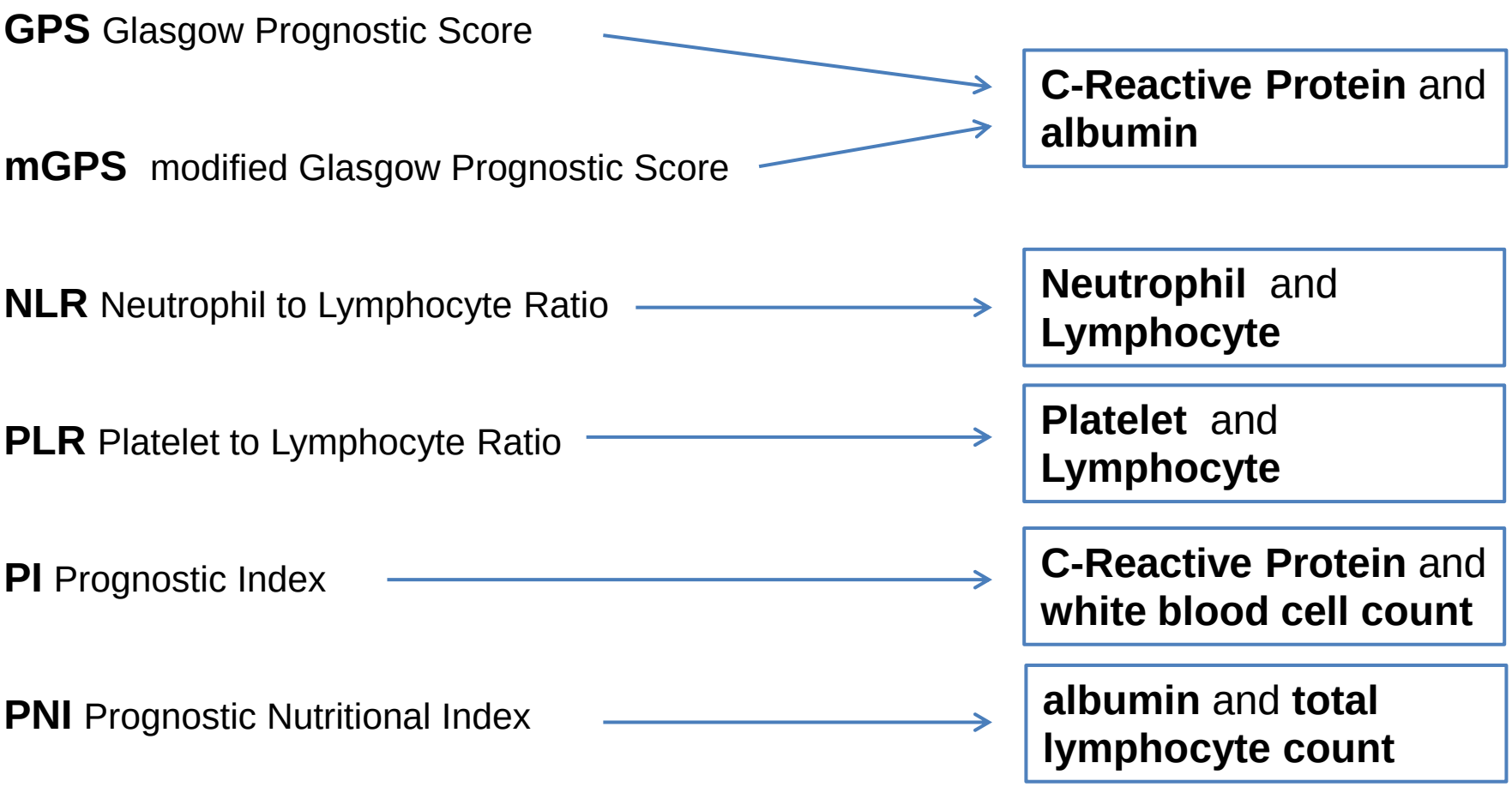
- Inflammation is a hallmark of cancer inside a complex host–tumor relationship, with most tumors having inflammatory cells and mediators in their microenvironment, which seem to play an important role in cancer development and progression.

- Inflammation and cancer development are connected by 2 pathways, consisting in an extrinsic (pre-existing inflammation) and intrinsic (oncogene activation) pathway.

- The activation of these pathways determines mobilization of transcription factors and inflammatory mediators, giving rise to recruitment of inflammatory cells, including neutrophils and megakaryocytes, and therefore leading to neutrophilia and thrombocytosis.

The resulting cascade of inflammatory mediators leads to tumor promotion, invasion, and metastasis.

Systemic inflammation-based biomarkers



Systemic inflammation-based biomarkers

Variables	Criteria	Score
GPS	C-Reactive Protein ≤1.0 mg/dl and albumin ≥3.5 g/dl	0
	C-Reactive Protein >1.0 mg/dl and albumin ≥3.5 g/dl	1
	C-Reactive Protein ≤1.0 mg/dl and albumin <3.5 g/dl	
	C-Reactive Protein >1.0 mg/dl and albumin <3.5 g/dl	2
mGPS	C-Reactive Protein ≤1.0 mg/dl	0
	C-Reactive Protein >1.0 mg/dl and albumin ≥3.5 g/dl	1
	C-Reactive Protein >1.0 mg/dl and albumin <3.5 g/dl	2
PI	C-Reactive Protein ≤1 mg/dl and white blood cell count ≤11,000/μl	0
	C-Reactive Protein ≤1 mg/dl and white blood cell count >11,000/μl	1
	C-Reactive Protein >1 mg/dl and white blood cell count ≤11,000/μl	
	C-Reactive Protein >1 mg/dl and white blood cell count >11,000/μl	2
PNI	albumin (g/dl) × 10 + 0.005 × total lymphocyte count (/μl) ≥45	0
	albumin (g/dl) × 10 + 0.005 × total lymphocyte count (/μl) <45	1

GPS Glasgow Prognostic Score, **mGPS** modified Glasgow Prognostic Score, **PI** Prognostic Index, **PNI** Prognostic Nutritional Index

Systemic inflammation-based biomarkers

PubMed ▾ "neutrophil to lymphocyte ratio" and cancer **Search**

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1. Pre-treatment **neutrophil-to-lymphocyte ratio** is associated with neutrophil and T-cell infiltration and predicts clinical outcome in patients with glioblastoma.

   Han S, Liu Y, Li Q, Li Z, Hou H, Wu A.
   BMC **Cancer**. 2015 Sep 4;15(1):617.
   PMID: 26341881
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2. Neutrophil and Lymphocyte Counts as Clinical Markers for Stratifying Low-Risk Prostate **Cancer**.

   Kwon YS, Han CS, Yu JW, Kim S, Modi P, Davis R, Park JH, Lee P, Ha YS, Kim WJ, Kim IY.
   Clin Genitourin **Cancer**. 2015 Aug 6. pii: S1558-7673(15)00191-3. doi: 10.1016/j.clgc.2015.07.018. [Epub ahead of print]
   PMID: 26341038
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HIV and Survival

Systemic inflammation-based biomarkers and survival in subject with solid cancer

573 subjects (76.3% males, mean age = 46.2 years)

355 solid non-AIDS defining cancer

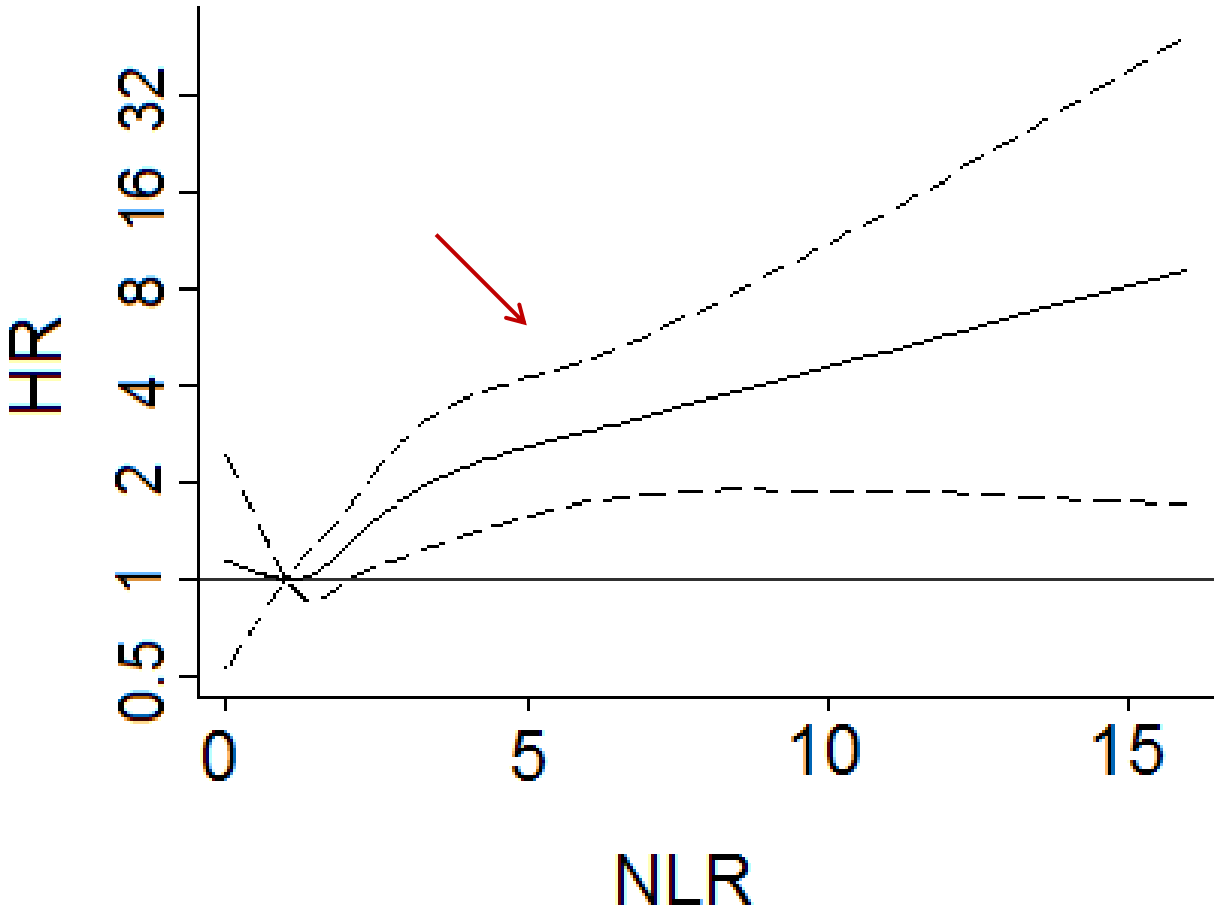
218 solid AIDS defining cancer

Raffetti E et al. Systemic inflammation-based biomarkers and survival in HIVpositive subject with solid cancer in an Italian multicenter study. J Acquir Immune Defic Syndr. 2015 Aug 15;69(5):585-92.

Systemic inflammation-based biomarkers and survival in subject with solid cancer

		HR (95% CI)	P value
GPS	0	Ref.	
	1	1.24 (0.44-3.51)	NS
	2	7.45 (2.16-25.77)	**0.001**
mGPS	0	Ref.	
	1	1.10 (0.42-2.90)	NS
	2	6.50 (2.3-20.83)	**0.002**
NLR	<3	Ref.	
	3-5	1.76 (1.08-2.88)	**0.025**
	≥ 5	2.81 (1.34-5.73)	**0.005**
PLR	<150	Ref.	
	150 – 300	1.30 (0.84-2.00)	NS
	≥ 300	2.84 (1.34-6.02)	**0.006**
PNI	0	Ref.	
	1	2.86 (1.68-4.91)	**<0.001**

Systemic inflammation-based biomarkers and survival in subject with solid cancer



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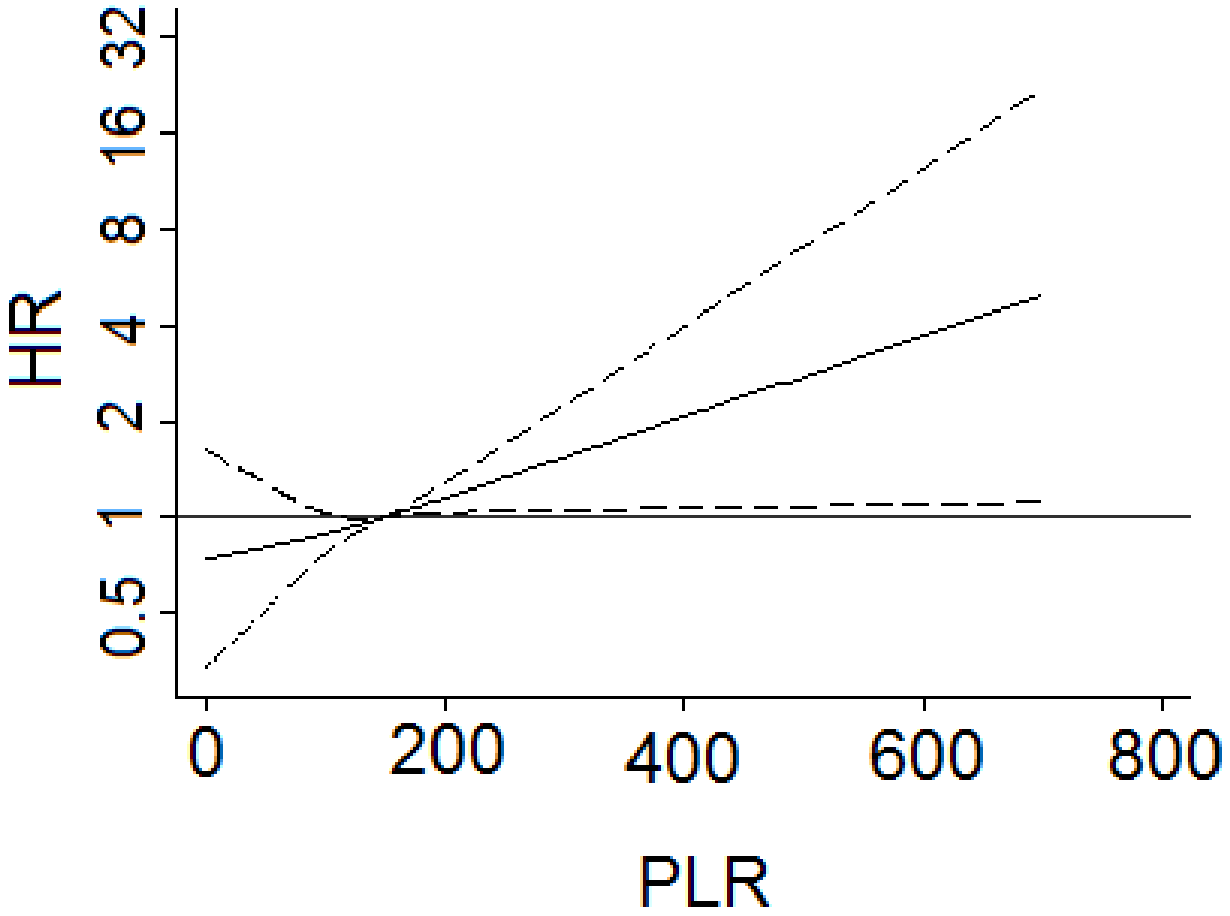

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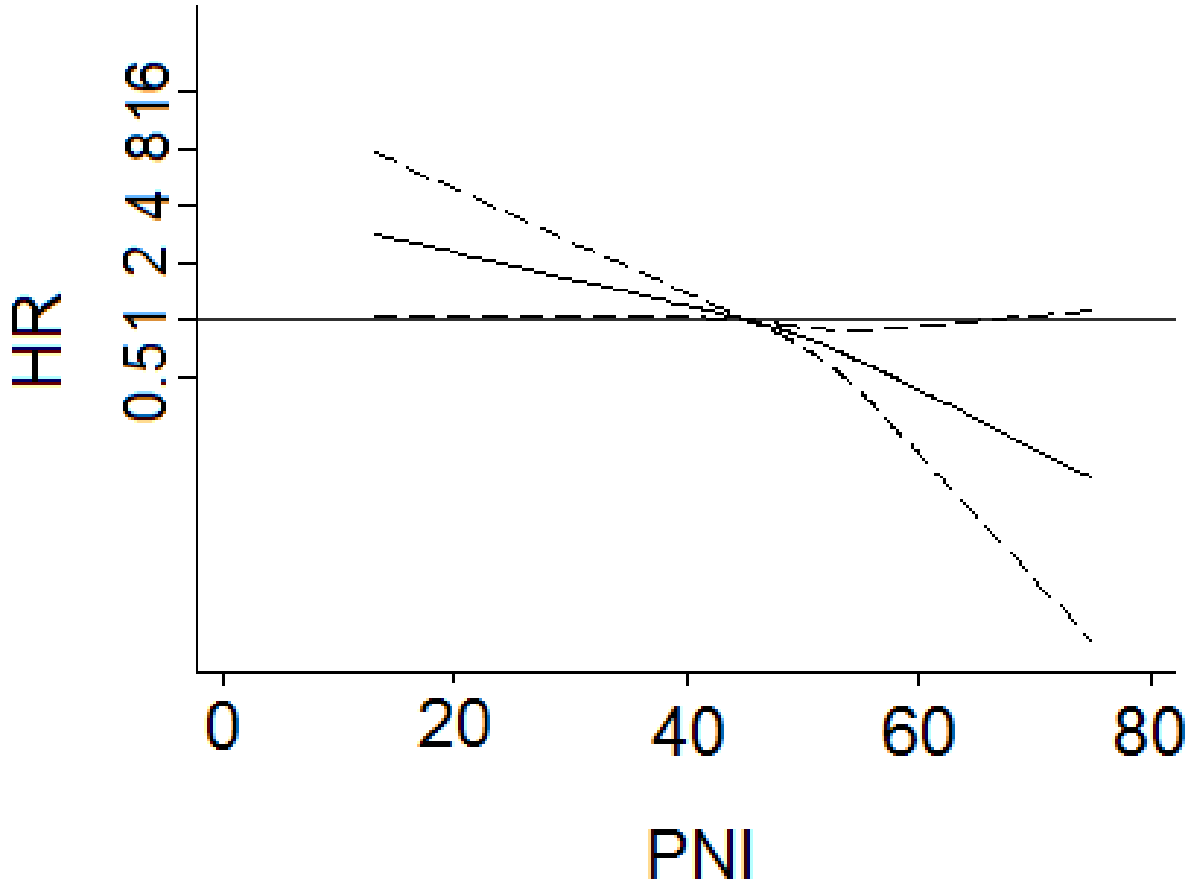

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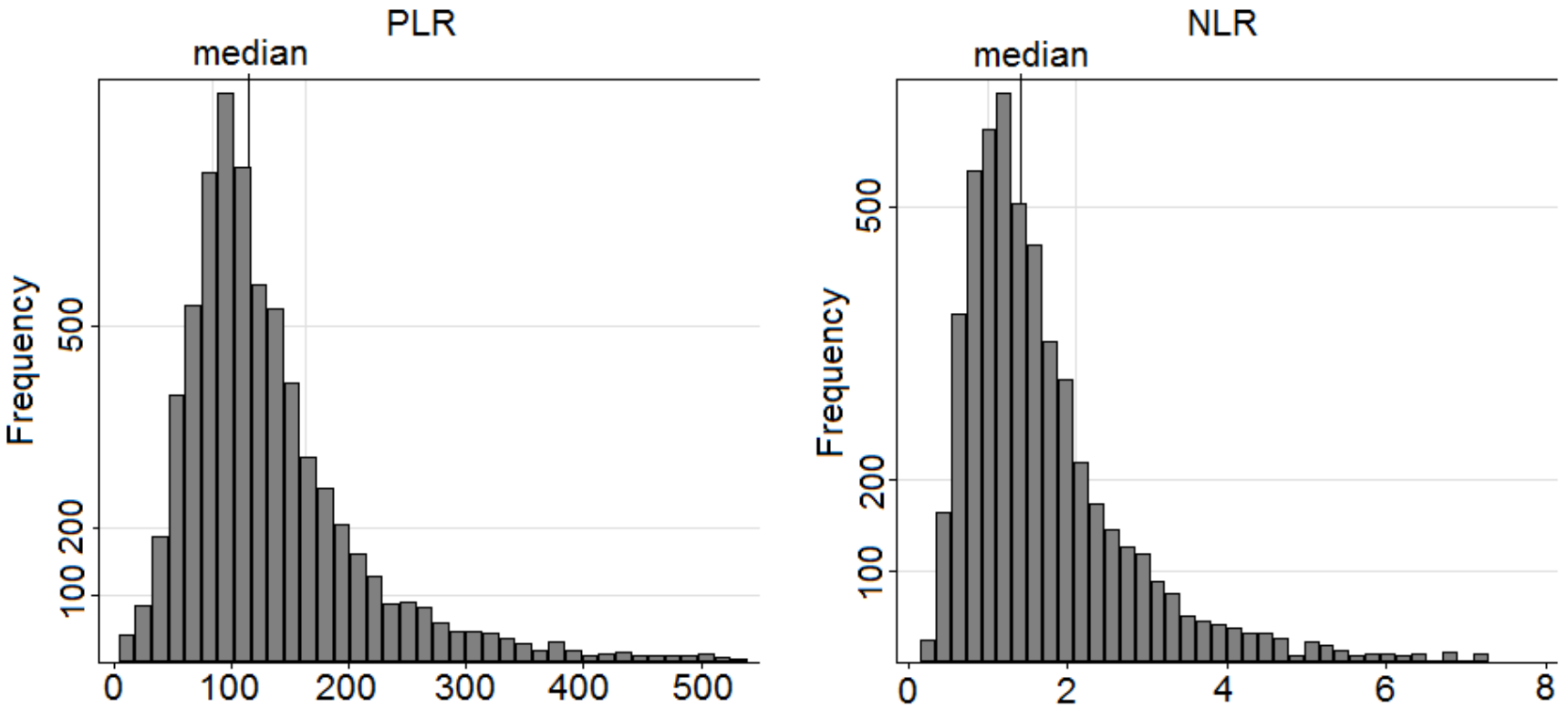
Inflammation and Mortality

- High circulating levels of markers of inflammation and coagulation (C-Reactive protein, IL-6, and D-dimer) are predictors of mortality in healthy subjects.
- HIV-infected persons even with long-term, effective antiretroviral therapy have persistent, low grade inflammation and immune activation.
- Elevated levels of inflammation biomarkers (IL-6, TNF, D-dimer and C-reactive protein) are predictors of non-AIDS events and all-cause mortality

Systemic inflammation-based scores in HIV Cohort

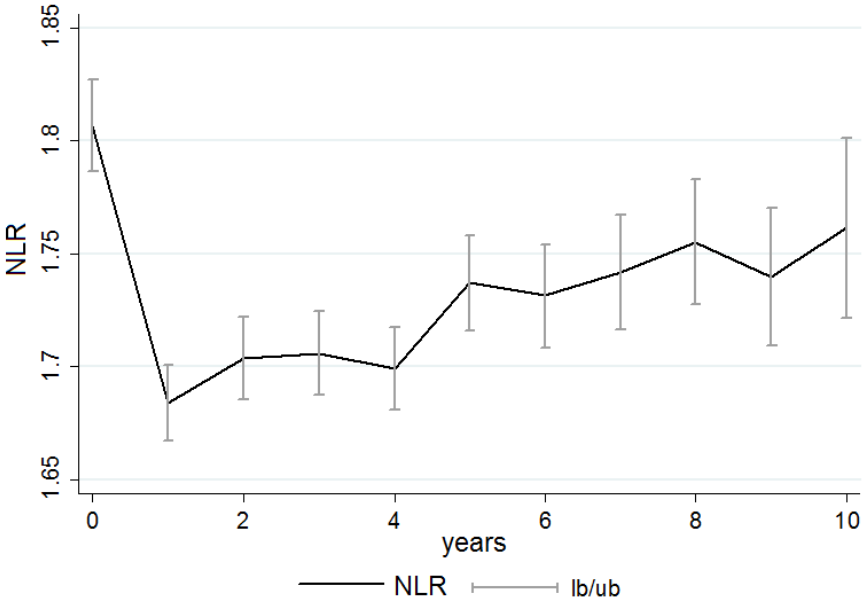
8230 patients naïve at antiretroviral treatment enrolled in period 2000-2012

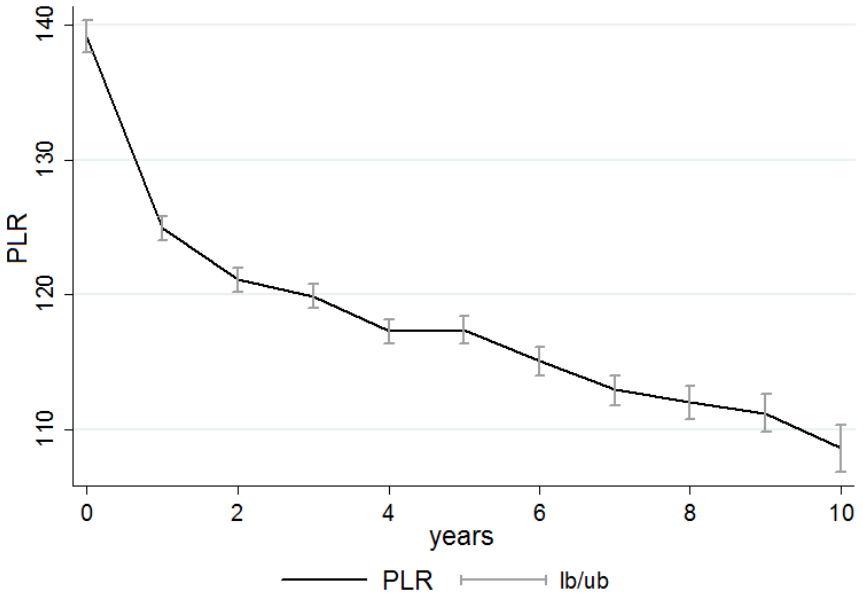


Raffetti E et al. Systemic inflammation-based scores and mortality for all causes in HIV-Infected patients: a multicenter cohort study. (under revision)

Systemic inflammation-based scores in HIV Cohort

Variations of NLR and PLR values during follow-up.





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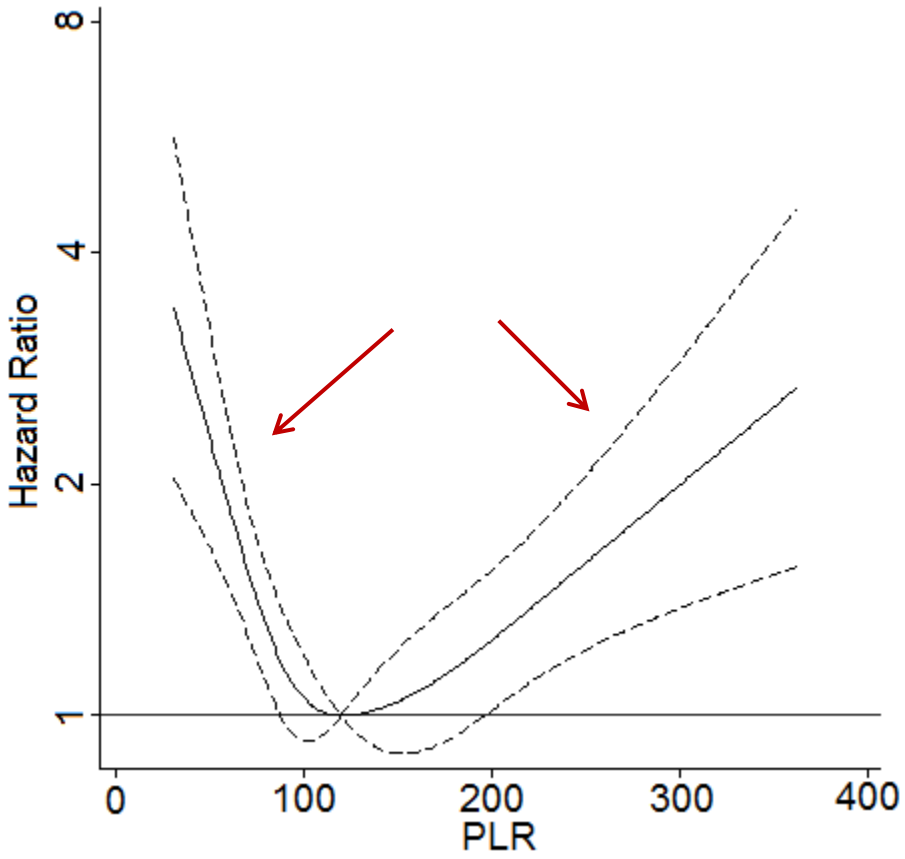
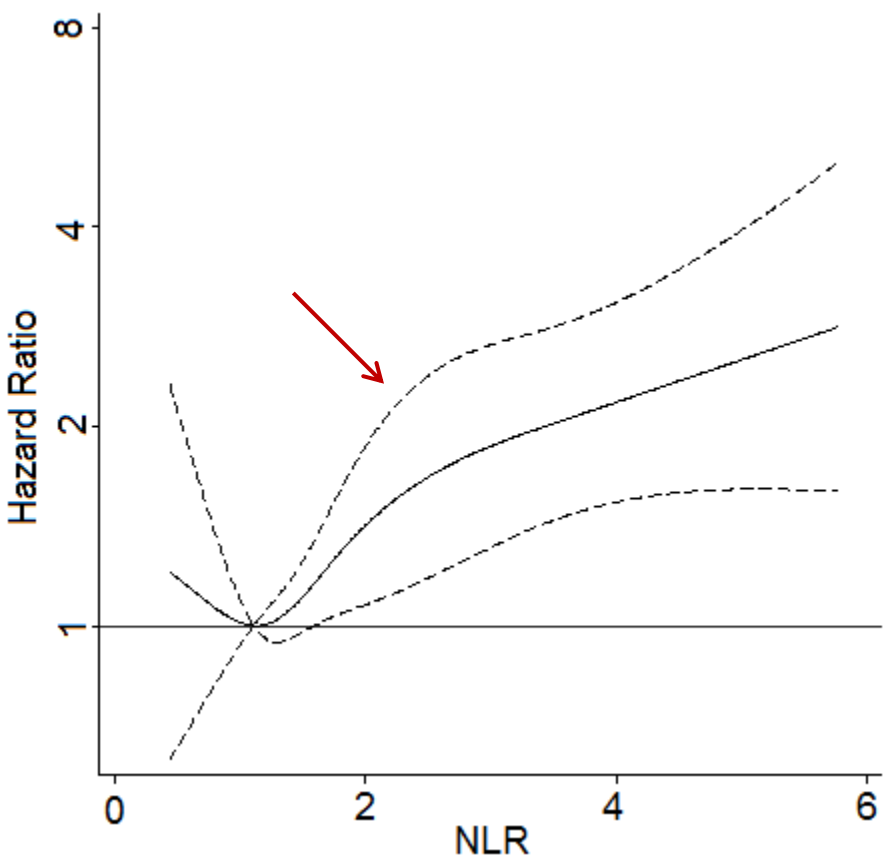
Systemic inflammation-based scores and mortality for all causes

		Time independent models		Time-dependent models	
		HR (95% CI)	**P value**	**HR (95% CI)**	**P value**
PLR	**<100**	1.57 (1.23-1.99)	**<0.001**	1.47 (1.14-1.90)	**0.003**
	100-200	Ref		Ref	
	≥200	1.34 (1.02-1.75)	**0.034**	1.42 (1.06-1.89)	**0.017**
NLR	**<2**	Ref		Ref	
	2-4	1.17 (0.90-1.53)	NS	1.47 (1.12-1.92)	**0.005**
	≥4	1.82 (1.28-2.60)	**0.001**	2.78 (1.97-3.91)	**<0.001**

Raffetti E et al. Systemic inflammation-based scores and mortality for all causes in HIV-Infected patients: a multicenter cohort study. (under revision)

Systemic inflammation-based scores and mortality for all causes





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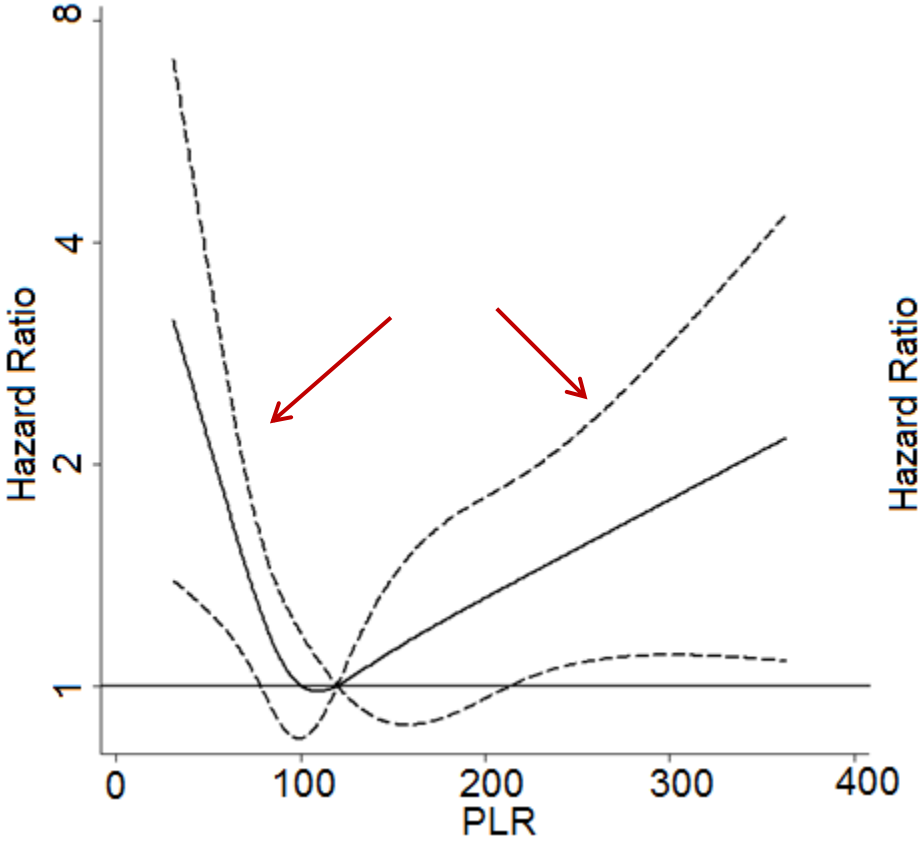
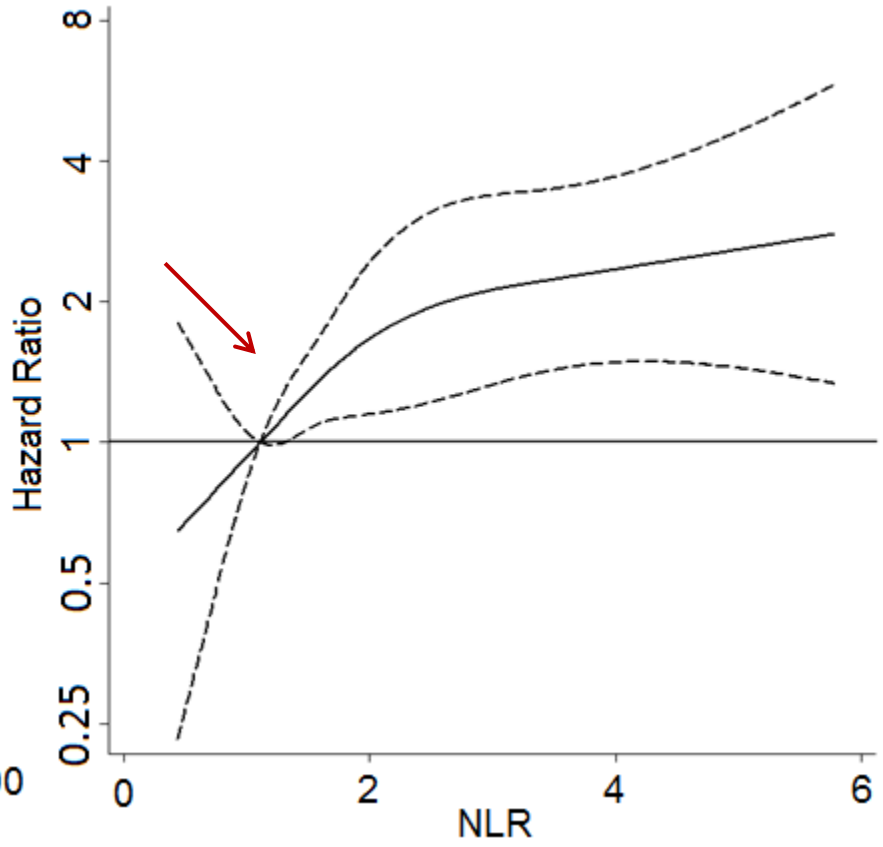
Systemic inflammation-based scores and mortality for all causes

Analysis restricted to non-HCV and HBV-coinfected subjects





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Conclusion

- In HIV positive subjects, systemic inflammatory biomarkers have been shown to be predictor of:

  1) **survival of patients with solid NADC** (GPS, mGPS, NLR, PLR and PNI) and **NHL** (GPS, mGPS, PI and PNI);

  2) **mortality for all causes** in all patients (NLR and PLR).

The authors declare no conflict of interest