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Neutrophil-to-Lymphocyte Ratio and Mean Platelet Volume in Relation to Pressure Ulcer Stages in a Palliative Care Unit: A Retrospective Single-Center Study

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Research Article

Keywords: pressure ulcer, palliative care, neutrophil-to-lymphocyte ratio, mean platelet volume, Braden scale, retrospective study, Karnofsky performance status, wound origin, pressure injury prevention

Posted Date: July 3rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9978541/v1

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Additional Declarations: No competing interests reported.

Abstract

Background.

Pressure ulcers (PUs) cause significant morbidity in palliative inpatients, yet their epidemiology in non-oncological palliative populations remains poorly described. The neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume (MPV) are inexpensive markers of systemic inflammation examined in relation to PU development and staging in intensive-care cohorts, but have not been evaluated in non-oncological palliative populations.

Objective.

To examine whether admission NLR and MPV relate to pressure ulcer presence and stage in non-oncological palliative inpatients, and to characterize the epidemiology, wound origin and clinical correlates of pressure ulcers in this under-described population.

Methods.

Retrospective single-center study reported per STROBE. Of 348 screened patients, 99 with any active malignancy were excluded to remove malignancy-related hematological confounding, leaving 249. PUs were staged by the attending palliative care physician using EPUAP/NPIAP criteria. The primary analysis related NLR and MPV to PU stage using the Kruskal–Wallis test and Spearman correlation with 95% confidence intervals; factors associated with PU presence were examined secondarily by multivariable logistic regression.

Results.

PU point prevalence was 40.2% (100/249); of staged PUs (n = 100) the distribution was Stage I 19.0%, II 61.0%, III 17.0%, IV 3.0%. Neither NLR nor MPV differed across PU stages I–IV (NLR: medians 4.3, 3.6, 4.1, 2.2; Kruskal–Wallis p = 0.521; Spearman r = − 0.109, 95% CI − 0.299 to 0.089. MPV: medians 9.9, 10.1, 10.0, 9.6 fL; p = 0.878; r = − 0.068, − 0.261 to 0.131). PLR and SII showed no stage gradient. Neither NLR nor MPV discriminated deep (Stages III–IV) from superficial (Stages I–II) wounds, but with only 20 deep-stage wounds these estimates were uninformative (AUC 0.43 for NLR and 0.44 for MPV, 95% CI 0.29–0.57 and 0.30–0.59; both intervals include the no-discrimination value of 0.50). Of note, 94.1% of Stage III wounds and all Stage IV wounds had been present on admission, versus only 5.3% of Stage I wounds (p < 0.001), a pattern predictable in referral-based units receiving patients with pre-existing chronic wounds. Secondarily, lower Braden score (OR 0.677) and lower Karnofsky score (OR 0.960) were independently associated with PU presence, as was longer length of stay (OR 1.045; subject to potential reverse causation). After adjustment, neither NLR nor MPV was independently associated with PU

presence (p = 0.48 and p = 0.14). Thirty-day mortality (14.1%) was associated with older age and lower functional status, not with the markers or PU presence.

Conclusions.

In this non-oncological palliative cohort, the marker–stage question could not be reliably answered: advanced-stage ulcers were almost entirely present on admission, so admission markers reflected pre-referral systemic state rather than the staged wound, and only 20 deep-stage wounds were available. The null marker–stage result should therefore be read as inconclusive rather than as evidence of no association. Neither inflammatory marker was independently associated with PU presence after adjustment; the actionable correlates were clinical risk measures, lower Braden and Karnofsky scores, and stroke for hospital-acquired ulcers. A notable finding is a high PU prevalence of 40.2% in a non-oncological palliative population, with prevalent and incident wounds reported separately. A major methodological issue identified is the wound-origin/stage confound that renders cross-sectional admission-marker studies uninterpretable in referral-based palliative units. Whether NLR or MPV track PU severity remains open and can be addressed only by prospective studies restricted to hospital-acquired ulcers.

1. INTRODUCTION

Pressure ulcers (PUs) are localised injuries to the skin and underlying soft tissue, usually over a bony prominence, resulting from sustained pressure or pressure combined with shear [1]. In palliative care, patients present with advanced end-stage disease, profound immobility, malnutrition and impaired functional reserve, conferring among the highest PU risk of any clinical setting. Reported PU prevalence in palliative inpatients ranges from 6.9% to 47%, with incidence from 6.7% to 22.4% [2, 3, 4], the range reflecting case-mix and whether wounds present on admission are counted.

PUs intensify suffering, predispose to infection, reduce quality of life and have been associated with reduced survival in advanced disease [3, 5]. Because prevention strategies reduce the substantial clinical and resource burden of established PUs [1, 2], inexpensive markers that could refine assessment of PU severity are of clinical interest. The neutrophil-to-lymphocyte ratio (NLR), derived from the routine complete blood count, reflects the balance between innate inflammatory activity and adaptive immunity and has been associated with impaired wound healing and, in intensive-care cohorts, with PU development [6]; examination across PU stages found no NLR or PLR gradient and only an isolated MPV elevation at intermediate stages [7], indicating inconsistent overall evidence; whether NLR relates to PU stage in non-oncological palliative populations is unestablished. The mean platelet volume (MPV) reflects platelet size and activation and has been proposed as an accessible marker of inflammation across diverse conditions [8]. Both rise or fall with systemic inflammatory and infective states and are obtainable at no additional cost from tests performed routinely on admission.

Advanced-stage PUs (Stages III–IV) involve deeper tissue destruction and might be expected to provoke a more pronounced local and systemic inflammatory response than superficial injuries, potentially detectable in these hematological indices. In oncological palliative cohorts, NLR has been shown to track infection and systemic deterioration [9], but whether NLR or MPV relate specifically to PU stage in non-oncological palliative populations has not been examined. To address this question while minimizing the hematological confounding intrinsic to malignancy, we studied a cohort from which all active malignancy was excluded. We therefore set two objectives: to examine whether admission NLR and MPV relate to pressure ulcer presence and stage in a non-oncological palliative inpatient cohort, and to characterize the epidemiology, wound origin and clinical correlates of pressure ulcers in this population. The marker–stage comparison was the pre-specified primary analysis and the clinical-correlate analysis a pre-specified secondary analysis. It should be noted that in referral-based palliative units, which regularly receive patients with pre-existing chronic wounds, admission hematological markers may reflect cumulative pre-referral systemic burden rather than the stage of the wound at assessment; as described in the Results, this structural feature rendered the marker–stage comparison uninterpretable in the present dataset, a finding that is itself reported as a design lesson for future studies in this setting.

2. METHODS

2.1 Study design and reporting

This retrospective single-center study was conducted in the palliative care unit of a secondary hospital between 1 January 2022 and 1 January 2025 and is reported in accordance with the STROBE statement. The study was conducted in accordance with the Declaration of Helsinki. Approval was granted by the Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee (approval no. 2026/02–11). As this was a retrospective study, the Ethics Committee approved a waiver of informed consent. Participant flow is shown in Fig. 1.

2.2 Participants

Medical records of adult patients (≥ 18 years) admitted for > 24 hours were reviewed. Patients with any active malignancy, whether solid or hematological, were excluded, both to remove the hematological confounding intrinsic to malignancy and its treatment (lymphopenia, myelosuppression, cytokine dysregulation), which would otherwise alter NLR and MPV independently of wound status, and to study a defined, non-oncological population in which hematological indices would not be distorted by malignancy-related pathophysiology. Patients with a history of active chemotherapy or radiotherapy and those with bone marrow failure were thereby also excluded. Of 348 screened patients, 99 with malignancy were excluded, leaving an analytic cohort of 249.

2.3 Variables and PU assessment

Age, sex, length of stay, comorbidities, Karnofsky Performance Status (KPS) and Braden Risk Assessment Scale score at admission, discharge destination and 30-day mortality were extracted. The admission complete blood count provided neutrophil count, lymphocyte count, MPV, platelet count and haemoglobin. NLR was calculated as the neutrophil-to-lymphocyte ratio; the platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII = neutrophil × platelet / lymphocyte) were computed as secondary inflammatory markers. All patients were assessed for skin integrity and pressure ulcers by the attending palliative care physician at admission and during their stay. PUs were staged according to EPUAP/NPIAP criteria [1]: Stage I (non-blanchable erythema of intact skin), Stage II (partial-thickness skin loss), Stage III (full-thickness skin loss) and Stage IV (full-thickness tissue loss with exposed bone, tendon or muscle). The date of first PU identification was recorded; wounds identified at the admission (day 0) assessment were classified as present on admission and those first identified subsequently as hospital-acquired.

2.4 Statistical analysis

Continuous variables are reported as median [IQR] and categorical variables as n (%). The primary analysis related NLR and MPV to PU stage: medians were compared across the four stages using the Kruskal–Wallis test, and the monotonic relationship between marker and stage was quantified by the Spearman correlation coefficient with 95% confidence intervals. Post-hoc pairwise stage comparisons used the Mann–Whitney U test with Bonferroni correction. The ability of NLR, MPV and the Braden score to discriminate (deep versus superficial PU, and PU presence, respectively) was summarized by the area under the receiver-operating-characteristic curve (AUC), with 95% confidence intervals calculated by the DeLong method. As a secondary analysis, factors associated with PU presence were examined by multivariable logistic regression. Clinical covariates with $p < 0.10$ on univariate logistic screening (length of stay, Karnofsky score, Braden score, stroke and COPD) were entered together with the two inflammatory markers of primary interest (NLR and MPV), which were included irrespective of univariate significance because they are the study's exposures of interest; age was not retained (univariate $p = 0.46$). Multicollinearity was assessed by variance inflation factors; a time-to-event sensitivity analysis was also performed, restricting the outcome to hospital-acquired PU. In this analysis, time from admission to first PU identification was the outcome; patients discharged or who died without a hospital-acquired PU were censored at that point. The same clinical covariates as the logistic model, including length of stay, were entered into a Cox proportional hazards regression; because the directionality problem affecting length of stay is partially mitigated in the time-to-event framework (hospital-acquired PU can only follow, not precede, admission), the Cox estimate for this covariate is preferred for clinical inference, though the reverse-causation caveat is not fully resolved. The proportional hazards assumption was assessed by Schoenfeld residuals. Comparisons in the descriptive Table 1 are exploratory and uncorrected; they should not be interpreted as confirmatory. No a priori power calculation was performed, as this was an analysis of all consecutive eligible admissions. Instead, the minimum detectable effect was computed to aid interpretation of null findings. With $n = 100$ staged patients the study had 80% power (two-tailed $\alpha = 0.05$) to detect a marker–stage Spearman correlation of $|r| \geq 0.28$; the observed correlations ($|r| \leq 0.12$) lay well below this threshold. For the binary outcome (n

= 249, 100 events) the minimum detectable odds ratio was approximately 1.4 per standard-deviation increment. The study could therefore exclude moderate-to-large associations but not small ones. Analyses used SPSS v26; $p < 0.05$ (two-tailed) was considered significant. Missing data were not imputed and complete cases were analyzed; within the analytic cohort all variables, including pressure-ulcer stage, were complete (all 100 ulcers were staged).

3. RESULTS

3.1 Cohort characteristics

The analytic cohort comprised 249 patients (147 female [59.0%]; median age 82 years [IQR 74–89]). The comorbidity profile reflected a non-oncological palliative population: hypertension (70.7%), stroke (46.6%), diabetes mellitus (37.3%) and Alzheimer's disease (35.3%). Median Karnofsky score was 30 [IQR 30–40] and median Braden score 13 [IQR 12–14]. PU point prevalence was 40.2% (n = 100); of these, 38 (38.0%) were present on admission and 62 (62.0%) were hospital-acquired. Thirty-day mortality was 14.1%. Cohort characteristics are presented in Table 1.

Table 1
Cohort characteristics stratified by pressure ulcer presence (n = 249).

Variable	Total (n = 249)	PU Absent (n = 149)	PU Present (n = 100)	p
Demographic				
Age, years, median [IQR]	82 [74–89]	82 [73–89]	82 [75–89]	0.625
Female sex, n (%)	147 (59.0)	88 (59.1)	59 (59.0)	1.000
Length of stay, days, median [IQR]	11 [6–20]	8 [5–14]	16 [10–32]	< 0.001
Karnofsky score, median [IQR]	30 [30–40]	30 [30–40]	30 [30–30]	0.001
Braden score, median [IQR]	13 [12–14]	13 [13–15]	12 [11–13]	< 0.001
Comorbidities, n (%)				
Hypertension	176 (70.7)	106 (71.1)	70 (70.0)	0.888
Diabetes mellitus	93 (37.3)	58 (38.9)	35 (35.0)	0.594
Stroke	116 (46.6)	61 (40.9)	55 (55.0)	0.038
Alzheimer's disease	88 (35.3)	50 (33.6)	38 (38.0)	0.501
COPD	61 (24.5)	43 (28.9)	18 (18.0)	0.053
Coronary artery disease	72 (28.9)	37 (24.8)	35 (35.0)	0.089
Chronic kidney disease	55 (22.1)	35 (23.5)	20 (20.0)	0.538
Laboratory parameters, median [IQR]				
NLR	4.5 [2.7–7.4]	5.1 [3.0–7.7]	3.8 [2.4–6.1]	0.029
MPV, fL	10.3 [9.7–11.0]	10.5 [9.8–11.2]	10.0 [9.4–10.5]	**< 0.001**
PLR	167.4 [126.0–256.8]	173.3 [117.9–260.9]	163.7 [126.9–242.6]	0.579
SII	1090 [626–2127]	1182 [666–2453]	1042 [625–1722]	0.160
Haemoglobin, g/dL	10.2 [9.0–11.7]	10.3 [8.9–11.9]	10.0 [9.2–11.2]	0.427
Neutrophil, $\times 10^3/\mu L$	6.3 [4.7–9.4]	6.6 [4.7–10.2]	6.3 [4.7–8.0]	0.194
Lymphocyte, $\times 10^3/\mu L$	1.4 [1.0–2.0]	1.4 [1.0–1.9]	1.5 [1.1–2.2]	0.196
Platelet, $\times 10^3/\mu L$	251 [191–335]	240 [189–336]	262 [199–331]	0.410

Variable	Total (n = 249)	PU Absent (n = 149)	PU Present (n = 100)	p
Demographic				
Outcomes				
30-day mortality, n (%)	35 (14.1)	19 (12.8)	16 (16.0)	0.465
PU present on admission (of PU), n (%)	38 (38.0)	—	38 (38.0)	—
PU hospital-acquired (of PU), n (%)	62 (62.0)	—	62 (62.0)	—

Data are median [IQR] or n (%). Mann–Whitney U for continuous, Fisher exact for categorical variables; comparisons are exploratory and uncorrected. NLR: neutrophil-to-lymphocyte ratio; MPV: mean platelet volume; PLR: platelet-to-lymphocyte ratio; SII: systemic immune-inflammation index.

3.2 NLR and MPV in relation to PU stage (primary analysis)

Among the 100 patients with complete PU staging, the stage distribution was Stage I 19 (19.0%), Stage II 61 (61.0%), Stage III 17 (17.0%) and Stage IV 3 (3.0%). Neither NLR nor MPV differed significantly across PU stages. Median NLR values were 4.3, 3.6, 4.1 and 2.2 for Stages I–IV (Kruskal–Wallis p = 0.521), with a negligible and non-significant Spearman correlation between stage and NLR (r = − 0.109, 95% CI − 0.299 to 0.089, p = 0.280). Median MPV values were 9.9, 10.1, 10.0 and 9.6 fL (Kruskal–Wallis p = 0.878; Spearman r = − 0.068, 95% CI − 0.261 to 0.131, p = 0.504). All post-hoc pairwise comparisons were non-significant after Bonferroni correction. The secondary inflammatory markers PLR and SII likewise showed no stage gradient (p = 0.625 and p = 0.734). Areas under the curve for distinguishing deep (III–IV) from superficial (I–II) PUs were 0.43 for NLR (95% CI 0.29–0.57) and 0.44 for MPV (95% CI 0.30–0.59). With only 20 deep-stage wounds these estimates are imprecise and their confidence intervals include the no-discrimination value of 0.50; the markers therefore showed no useful capacity to discriminate wound depth; the AUC point estimates slightly below 0.50 likely reflect statistical noise around the no-discrimination value rather than a true inverse association. These results are presented in Table 2.

Table 2
Primary analysis: NLR, MPV and other hematological markers in relation to pressure ulcer stage (n = 100 with complete staging).

Variable	Stage I (n = 19)	Stage II (n = 61)	Stage III (n = 17)†	Stage IV (n = 3)†	p
Primary markers					
NLR, median [IQR]	4.3 [2.3–10.4]	3.6 [2.7–6.1]	4.1 [2.2–5.8]	2.2 [2.1–3.0]	0.521
MPV, fL	9.9 [9.7–10.6]	10.1 [9.4–10.5]	10.0 [9.3–10.6]	9.6 [9.4–10.0]	0.878
NLR Spearman r = − 0.109 (95% CI − 0.299 to 0.089), p = 0.280					
MPV Spearman r = − 0.068 (95% CI − 0.261 to 0.131), p = 0.504					
Other hematological markers					
PLR	161.8 [118–232]	165.6 [135–267]	182.1 [124–234]	149.6 [89–173]	0.625
SII	892 [660–1932]	1085 [581–1854]	1167 [626–1461]	681 [425–926]	0.734
Haemoglobin, g/dL	10.9 [9.5–11.7]	10.0 [9.0–11.4]	9.8 [9.6–10.6]	9.4 [8.9–9.4]	0.273
Neutrophil, ×10³/μL	6.3 [5.1–10.3]	6.3 [4.1–8.0]	6.3 [5.3–7.4]	6.0 [5.3–6.0]	0.820
Lymphocyte, ×10³/μL	1.7 [1.0–2.4]	1.4 [1.1–2.0]	1.6 [1.2–2.3]	2.2 [1.9–2.5]	0.490
Wound origin (interpretive confound)					
Present on admission, n (%)	1 (5.3)	18 (29.5)	16 (94.1)	3 (100)	**< 0.001**
Hospital-acquired, n (%)	18 (94.7)	43 (70.5)	1 (5.9)	0 (0)	—

Data are median [IQR] or n (%); Kruskal–Wallis p-values are for the overall four-group comparison; chi-squared for wound-origin rows. †Stage III (n = 17) and Stage IV (n = 3) are presented descriptively only; these subgroups are too small for valid inference, and p-values reported in this table reflect the overall Kruskal–Wallis test across all four stages they should not be interpreted as reflecting differences attributable to the individual small subgroups. The wound-origin rows show that advanced stages were almost entirely present on admission, confounding any stage-wise marker comparison.

One finding substantially constrains interpretation of the marker results, and is worth anticipating in any similar referral-based unit: the distribution of wound origin differed sharply by stage. Whereas 94.7% of Stage I and 71.7% of Stage II PUs were hospital-acquired, 94.1% of Stage III and all Stage IV PUs were present on admission ($p < 0.001$). Advanced-stage PUs were therefore predominantly wounds that had developed before referral, so the admission NLR and MPV of these patients reflect their pre-admission systemic state rather than a response to the staged wound. When the comparison was restricted to hospital-acquired PUs, only a single deep-stage wound remained, precluding any valid stage-wise analysis. The Stage III ($n = 17$) and Stage IV ($n = 3$) groups are too small for reliable inference; they are retained in Table 2 for descriptive completeness and transparency, not as a basis for statistical conclusions.

On uncorrected univariate comparison (Table 1; exploratory only), both NLR and MPV were nominally lower in PU-present than PU-absent patients (NLR 3.8 vs 5.1, $p = 0.029$; MPV 10.0 vs 10.5 fL, $p < 0.001$). The absolute MPV difference of 0.5 fL is small and of negligible clinical relevance. The NLR difference ran counter to what an inflammatory hypothesis would predict, patients with pressure ulcers had lower, not higher, NLR values; this inverse direction is discussed below.

3.3 Factors associated with PU presence (secondary analysis)

In multivariable logistic regression ($n = 249$, McFadden pseudo-R^2=0.225), lower Braden score (OR 0.677 per point, 95% CI 0.558–0.822, $p < 0.001$), longer length of stay (OR 1.045 per day, 95% CI 1.020–1.072, $p < 0.001$) and lower Karnofsky score (OR 0.960 per point, 95% CI 0.926–0.996, $p = 0.032$) were independently associated with PU presence. After adjustment, however, neither inflammatory marker was independently associated with PU presence (NLR OR 1.004, 95% CI 0.992–1.017, $p = 0.479$; MPV OR 0.810, 95% CI 0.615–1.068, $p = 0.135$); the univariate MPV association ($p = 0.008$) did not persist after adjustment, indicating confounding by functional status rather than an independent link to pressure ulceration. Stroke (OR 1.594, $p = 0.129$) and COPD (OR 0.805, $p = 0.566$) were not independently significant; the univariate protective association of COPD likewise attenuated, consistent with a confounded signal. All variance inflation factors were < 1.2 (Table 3). The length-of-stay association is vulnerable to reverse causation: patients with PUs may remain hospitalised longer as a consequence of the wound, rather than solely as a pre-existing exposure. A time-to-event sensitivity analysis, which treats PU development as the outcome and thereby avoids this directionality problem, confirmed lower Braden score (hazard ratio 0.749, $p < 0.001$) and stroke (hazard ratio 1.975, $p = 0.010$) as the factors most consistently associated with hospital-acquired PU (62 events, 7 covariates; events-per-variable ratio 8.86); given this EPV, all associations from this model, including the stroke finding, should be treated as hypothesis-generating rather than confirmatory. Karnofsky score was not independently significant in this model after adjustment. The proportional hazards assumption was not materially violated on Schoenfeld residual assessment. The Braden scale discriminated PU presence with an AUC of 0.733 (95% CI 0.671–0.796); this is an in-sample, unvalidated estimate subject to optimistic bias and should not be used as a clinical recalibration threshold without external prospective validation.

Table 3
Secondary analysis: multivariable logistic regression of factors associated with pressure ulcer presence (n = 249).

Variable	OR	95% CI	p	VIF
Braden score (per + 1 point)	0.677	0.558–0.822	**< 0.001 ****	1.15
Length of stay (per day)	1.045	1.020–1.072	**< 0.001 ****	1.09
Karnofsky (per + 1 point)	0.960	0.926–0.996	**0.032 ***	1.07
Stroke	1.594	0.873–2.909	0.129 ns	1.04
COPD	0.805	0.384–1.687	0.566 ns	1.08
NLR (per + 1 unit)	1.004	0.992–1.017	0.479 ns	1.01
MPV (per + 1 fL)	0.810	0.615–1.068	0.135 ns	1.04
McFadden pseudo-R^2 = 0.225 | n = 249 | all VIF < 1.2				

*Adjusted for length of stay, Karnofsky score, Braden score, stroke, COPD, NLR and MPV. McFadden pseudo-R^2=0.225 (values of 0.2–0.4 indicate good model fit and are not comparable to ordinary-least-squares R^2). ** p < 0.01; * p < 0.05; ns: not significant. OR: odds ratio; CI: confidence interval; VIF: variance inflation factor.*

3.4 Thirty-day mortality (exploratory secondary analysis)

Thirty-day mortality in the analytic cohort was 14.1% (35/249) and did not differ by pressure-ulcer presence (16.0% [16/100] with a pressure ulcer versus 12.8% [19/149] without; p = 0.465). Neither inflammatory marker distinguished survivors from non-survivors (NLR p = 0.22; MPV p = 0.25). In an exploratory logistic model relating 30-day mortality to pressure-ulcer presence, age, Karnofsky score and Braden score (35 events, 4 predictors; events-per-variable ratio 8.75, below the conventional threshold of 10, results should be treated as hypothesis-generating only), the independent predictors were older age (OR 1.06 per year, 95% CI 1.02–1.11, p = 0.003) and lower Karnofsky score (OR 0.89 per point, 95% CI 0.84–0.94, p < 0.001); pressure-ulcer presence was not associated with mortality (OR 1.10, 95% CI 0.48–2.50, p = 0.82). Mortality was not analyzed by individual stage owing to the small number of advanced-stage wounds.

4. DISCUSSION

This study evaluated admission NLR and MPV in relation to pressure ulcer presence and stage in non-oncological palliative inpatients and characterized the clinical correlates of PU in this population. Neither marker was associated with PU stage, and neither showed useful discrimination of deep from superficial wounds (AUC 0.43 and 0.44; estimates imprecise, confidence intervals including 0.50). Before drawing any conclusion from this, the result needs to be set against the structure of the data: inconclusive is a more accurate description than negative.

The core interpretive problem is the confounding of wound origin with stage, a pattern predictable for a referral-based palliative unit that receives patients with pre-existing chronic wounds. Almost all advanced-stage PUs in this cohort were present on admission, having developed in other settings before referral, whereas almost all superficial PUs were hospital-acquired. The admission NLR and MPV of patients with deep wounds therefore index the cumulative systemic burden accrued before transfer, prolonged immobility, chronic infection, nutritional depletion, rather than an inflammatory response to the wound at its current stage. A cross-sectional comparison of admission markers across stages thus compares biologically non-equivalent groups. Restricting the analysis to hospital-acquired wounds, which would align marker timing with wound development, left a single deep-stage case; the dataset is therefore structurally unable to answer whether NLR or MPV track PU severity. Only a prospective study enrolling enough hospital-acquired deep wounds and timing marker measurement to wound onset could answer this question.

The biology of these markers in advanced illness raises a further complication. NLR was lower, not higher in PU-present patients, and showed a non-significant trend toward lower values at higher stages; this inverse direction is unexplained by the present data. NLR in this population is likely dominated by systemic factors, infection burden, immune dysregulation and metabolic derangements common in advanced non-oncological disease [9, 10] rather than by local wound events; none of these confounders was measured and their relative contribution cannot be quantified. This finding should be acknowledged as an unresolved directional signal requiring prospective investigation rather than attributed post hoc to unmeasured mechanisms. The lower MPV in PU-present patients, a difference of only 0.5 fL, is of a magnitude unlikely to be clinically meaningful. These observations are consistent with prior palliative data: Yildirim Polat et al. found individual leucocyte counts, albumin and prealbumin, but not NLR related to PU stage [11], and Uzan et al. showed that in palliative patients NLR indexes systemic infection rather than localised wound events [9]. In intensive-care cohorts admission NLR and MPV have predicted pressure-ulcer development [6]; yet a study examining these markers across pressure-ulcer stages, as we did, likewise found no NLR, PLR or lymphocyte-to-monocyte gradient and only an isolated higher MPV at intermediate stages [7] consistent with the interpretation that these markers may reflect pre-referral systemic state rather than wound stage, though this cannot be confirmed from the present data. Both the prior literature and the present data point toward NLR and MPV reflecting global systemic condition rather than wound stage in this population.

The secondary analysis confirmed clinically expected correlates of PU presence. Lower Braden score and lower Karnofsky score were independently associated with PU presence in the logistic model; although these two measures are conceptually related (both capture functional capacity), they were retained together because they index distinct constructs, Braden quantifies skin-specific risk factors including moisture, activity and sensory perception, whereas Karnofsky indexes overall performance status and VIFs remained below 1.2, indicating no material multicollinearity. Critically, when the inflammatory markers were entered into this adjusted model, neither NLR nor MPV was independently associated with PU presence, and the crude univariate MPV association disappeared on adjustment, suggesting the unadjusted signal reflected confounding by functional status rather than any direct

relationship to pressure ulceration. A comparable Turkish single-center cohort (n = 339) published in 2025 reported a similar prevalence (33.6%) and identified cardiovascular and neurological comorbidity, alongside care dependency, as the main risk factors [12]. The 40.2% prevalence observed here is substantially higher than the 12.4% reported in a 2019 systematic review of palliative care patients drawn predominantly from oncological cohorts [13]; this disparity most likely reflects the profound functional impairment of this non-oncological referral population (median Karnofsky score 30) rather than a deficit in preventive care. A time-to-event sensitivity analysis identified lower Braden score and stroke as the factors most consistently associated with hospital-acquired PU. Length of stay, although statistically significant in the logistic model, should be interpreted cautiously given its susceptibility to reverse causation; the time-to-event analysis, which avoids this problem, is the more appropriate basis for clinical inference. The Braden scale AUC of 0.733 is an in-sample estimate subject to optimistic bias; without external cross-validation or an independent cohort, this value cannot be used as a recalibration benchmark. That Braden scores clustered at the lower end of the scale is unsurprising given the degree of functional impairment in this population [14], and underlines the value of routine Braden assessment at palliative care admission. The association of stroke with hospital-acquired PU, observed in the hypothesis-generating sensitivity analysis (HR 1.975, p = 0.010; EPV 8.86), is consistent with the immobility, sensory impairment and incontinence accompanying cerebrovascular disease, but requires prospective confirmation.

The PU point prevalence of 40.2%, with 62 hospital-acquired ulcers (24.9% of all 249 admissions), is reported with prevalent and incident cases separated, an approach that avoids the conflation common in this literature [3]. The hospital-acquired rate reflects the profound functional impairment of this cohort (median Karnofsky score 30, indicating severe disability and complete dependence) rather than a discrete lapse in preventive care, though this distinction cannot be formally confirmed without process data. The high prevalence reflects both the severe functional impairment of this cohort and the inclusion of pre-existing wounds in the prevalence denominator. Because most published palliative PU data derive from predominantly oncological cohorts, these figures should be compared across populations only with caution: the present cohort represents a distinct, under-characterized non-oncological palliative population in which immobilising neurological and cardiorespiratory disease; stroke, dementia, COPD rather than malignancy predominates. This population is clinically coherent and increasingly encountered as palliative care broadens beyond oncology, yet remains poorly described in the pressure ulcer literature.

Several limitations deserve emphasis. Most critically for the primary aim, the confounding of wound origin with stage together with the very small numbers of deep-stage wounds (Stage IV n = 3) means the study cannot determine whether NLR or MPV relate to PU severity; the null result should be read as uninformative rather than as evidence of no association. This confounding pattern was predictable for a referral-based palliative unit and constitutes a design limitation. No a priori power calculation was performed; retrospective minimum-detectable-effect estimates indicate the study could detect a Spearman correlation of $|r| \geq 0.28$ (80% power) but not the smaller associations observed ($|r| \leq 0.12$). Second, the exclusion of all malignancy, while appropriate for removing hematological confounding,

limits generalizability to oncological palliative patients. Third, the single-center retrospective design constrains causal inference and external validity. Fourth, the inclusion of length of stay in the logistic regression is vulnerable to reverse causation; the sensitivity analysis partially addresses this, but the primary length-of-stay estimate should be interpreted as an association of uncertain directionality. Fifth, several established PU risk factors were unavailable: serum albumin, prealbumin, body mass index, incontinence and the NRS-2002 nutritional score. Most critically from a biomarker perspective, C-reactive protein (CRP), the most directly relevant inflammatory comparator was not recorded; without concurrent CRP data, it cannot be determined whether the null NLR and MPV associations reflect a genuine absence of inflammatory signal or a methodological limitation of these indirect indices in this population. Future studies should include CRP alongside NLR and MPV. Sixth, hematological values were measured only at admission, precluding longitudinal correlation with wound development. Seventh, the Braden AUC is an unvalidated in-sample estimate subject to optimistic bias. Eighth, pressure ulcer staging was performed by a single palliative care physician; independent double-rating and formal inter-rater reliability assessment (κ) were not performed. Stage I classification is particularly susceptible to inter-rater variability in elderly patients with altered skin pigmentation or oedema. The absence of a κ estimate means that misclassification between Stage I and II cannot be excluded, which would affect both the stage distribution and the primary analysis. A sensitivity analysis excluding Stage I wounds (n = 19) to assess the robustness of the null marker–stage finding to potential misclassification was not performed and represents an unaddressed limitation. Ninth, data on pressure-injury prevention measures (repositioning schedules, support surfaces) were unavailable, limiting interpretation of the hospital-acquired component.

5. CONCLUSIONS

In this palliative care cohort, the relationship between NLR or MPV and PU stage could not be reliably evaluated, for a reason that is predictable in this setting: advanced-stage wounds were almost entirely present on admission, making admission hematological values reflective of patients' pre-referral systemic state rather than the staged wound. The observed null should therefore be interpreted as inconclusive rather than as evidence of no association. The study could detect only moderate-to-large associations (minimum detectable Spearman $|r| \approx 0.28$), and the very small number of deep-stage wounds further precludes inference. Among factors examined secondarily, lower Braden score and lower Karnofsky score were independently associated with PU presence; lower Braden score and stroke were the factors most consistently associated with hospital-acquired PU in the time-to-event analysis. The association of length of stay with PU presence may be partly attributable to reverse causation. The Braden AUC of 0.733 (95% CI 0.671–0.796) is an unvalidated, in-sample estimate subject to optimistic bias and should not be applied as a recalibration benchmark without external prospective validation. Viewed in this light, the study contributes primarily in two respects: a characterisation of pressure-ulcer epidemiology in a non-oncological palliative population in which prevalent and incident wounds are reported separately, and identification of the wound-origin/stage confound that makes cross-sectional admission-marker studies uninterpretable in referral-based units. Whether NLR or MPV carry actionable

information about PU severity is a question the present data cannot answer. Prospective studies restricted to hospital-acquired ulcers, with markers measured at wound onset, adequate enrolment of deep-stage wounds, and incorporation of nutritional status and C-reactive protein, are needed to resolve it.

Declarations

Competing Interests:

The authors declare that they have no competing interests.

Ethics Approval and Consent to Participate:

This study was conducted in accordance with the Declaration of Helsinki. Approval was granted by the Zonguldak Bülent Ecevit University Non-Interventional Clinical Research Ethics Committee (approval no. 2026/02–11). As this was a retrospective study, the Ethics Committee approved a waiver of informed consent.

Consent for Publication:

Not applicable.

Funding:

The authors received no specific funding for this work.

Author Contribution

Author Contributions: M.G.B.: Conceptualisation, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review and editing. D.F.Ş.: Conceptualisation, Supervision, Validation, Writing – review and editing. All authors have read and approved the final manuscript.

Data Availability

The dataset used and analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

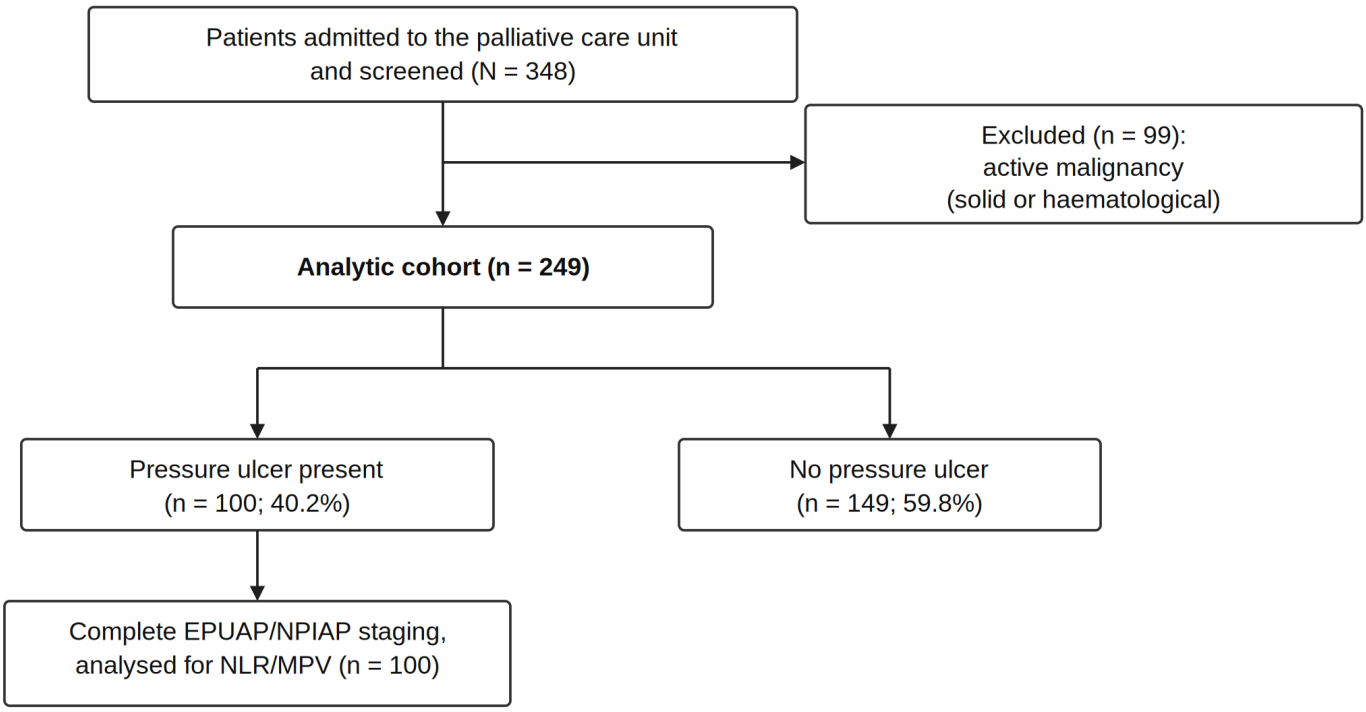


Figure 1

Participant flow (STROBE). PU: pressure ulcer; NLR: neutrophil-to-lymphocyte ratio; MPV: mean platelet volume.

Supplementary Files

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- STROBEChecklist.docx