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Comment/Perspective

RE "The associations between pretreatment neutrophil-to-lymphocyte ratio, sarcopenia and frailty in older patients with head and neck cancer"

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Dear Editor,

We congratulate Meerkerk and colleagues on their investigation of the relationships between pretreatment neutrophil-to-lymphocyte ratio (NLR), sarcopenia, and frailty in older patients with head and neck cancer (HNC)[1]. The authors deserve commendation for defining sarcopenia in accordance with the European Working Group on Sarcopenia in Older People criteria[2], requiring concurrent reductions in skeletal muscle strength and mass—an approach that remains uncommon in oncologic research, where imaging-only surrogates are frequently employed. Notwithstanding this definitional rigor, two aspects warrant further consideration, as they may influence the study's clinical applicability and interpretation.

First, although the authors report significant associations between elevated NLR and frailty[1], the discriminatory performance of NLR is inadequate for screening purposes; with a specificity of only 47 % and an overall accuracy of 61 %, nearly half of non-frail patients would be misclassified as potentially frail[3]. Such performance would substantially increase unnecessary referrals for comprehensive geriatric assessment (GA) in real-world practice, contradicting the stated objective of improving efficiency in resource-limited settings. Screening instruments should therefore be evaluated primarily on clinical utility and operational performance, rather than on statistical association alone. Established tools, such as the G8, demonstrate a more favorable balance of sensitivity and specificity and have undergone prospective validation across diverse oncologic populations[4]. When evaluated against this benchmark, NLR does not confer meaningful incremental value.

Second, the study underscores a persistent conceptual issue in the frailty literature: the tendency to conflate frailty with biological surrogates of inflammation or muscle mass. As demonstrated in the multivariable analyses by Meerkerk and colleagues, comorbidity burden and nutritional impairment largely account for the observed association between NLR and frailty[1]. This finding suggests that NLR may function primarily as a nonspecific marker of global disease severity or catabolic stress, rather than reflecting a frailty-specific biological mechanism. Frailty is a multidimensional functional syndrome characterized by impaired physiologic reserve across multiple systems[5]. Reducing this construct to an inflammatory ratio risks biological oversimplification and interpretive overstatement. This concern is particularly salient given that structured GA domains already capture vulnerability more directly and demonstrate greater prognostic relevance.

In conclusion, although the available data do not support the use of NLR as a reliable frailty screening tool, Meerkerk and colleagues demonstrated that systemic inflammation, sarcopenia, and frailty frequently coexist in older patients with HNC[1]. Future investigations would benefit from moving beyond isolated biomarkers toward integrative, prospectively validated models that preserve the functional and multidimensional nature of frailty.

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