

## Integrating inflammation and nutritional status: Monocyte-to-albumin ratio as a novel prognostic marker in nasopharyngeal cancer

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Nasopharyngeal cancer (NPC) is a prominent head and neck cancer, with a multifactorial aetiology that includes Epstein-Barr virus (EBV) infection, genetic susceptibility, and environmental exposures. Notably, the incidence of NPC is expected to show an approximately 35% increase in new cases (from 133,354 cases to 179,476 cases) and an approximately 42% increase in NPC-related deaths (from 80,008 deaths to 113,851 deaths) from 2020 to 2040.<sup>1</sup> NPC has a striking geographic predilection, with the highest number of NPC cases and deaths occurring in East Asia and Southeast Asia.<sup>1</sup> Interestingly, the American Association for Cancer Research has designated April as the Head and Neck Cancer Awareness Month, although NPC, which belongs to this group of cancers, is not as prevalent in the West. The high proportion of NPC cases presenting at a locally advanced stage, estimated at approximately 70%,<sup>2</sup> underscores the need to identify strategies that can enhance the therapeutic effectiveness of contemporary treatments, such as concurrent chemoradiotherapy (CCRT). For recurrent and metastatic diseases, the treatment modalities include induction chemotherapy with gemcitabine-cisplatin, and immunotherapy with immune-checkpoint inhibitors (specifically toripalimab and camrelizumab), with plasma EBV-DNA levels guiding the monitoring of treatment response and recurrence.<sup>3</sup> One effective approach to risk stratification and treatment optimisation is the use of prognostic biomarkers.

The study by Ni et al.,<sup>4</sup> which highlights the monocyte-to-albumin ratio (MAR) for prognostication in NPC patients, is thus timely. In this study, the authors reported that pretreatment MAR was an independent prognostic marker in NPC patients who had undergone CCRT. This retrospective cohort study included 860 eligible patients treated between 2010 and 2014, who met the inclusion criteria of having newly diagnosed non-metastatic NPC with no history of other cancers or inflammatory conditions. All patients received CCRT (comprising radical intensity-modulated radiation therapy and platinum-based chemotherapy either weekly or every 3 weeks), and

had pretreatment EBV-DNA assessment. The cohort was categorised into 2 groups, a high-MAR group and a low-MAR group, based on a maximum selection log-rank statistic-derived cut-off. NPC patients in the low-MAR group had a significantly higher overall survival rate than those in the high-MAR group. Additionally, multivariate analysis identified tumour stage, age, nodal stage, body mass index, and MAR as independent prognostic factors for overall survival in NPC patients. They subsequently developed a new nomogram-based prognostic model that incorporated MAR, along with the other identified independent prognostic variables, to predict overall survival in NPC patients. It is worth noting that the prognostic performance of MAR in immunotherapy-treated NPC remains unknown because the study predated the use of immunotherapy.

Considering that the study by Ni et al.<sup>4</sup> evaluated the prognostic value of integrating inflammation and nutritional markers, what is the underlying rationale for these factors in influencing the outcomes of NPC patients following CCRT? Since Stephen Paget's seminal paper on the cooperation between tumour cells (which he called "seed") and the organ microenvironment (which he named "soil"),<sup>5</sup> known as the "seed and soil" hypothesis, the tumour microenvironment (TME) has gained much attention for its role in tumour progression and metastasis.<sup>6</sup> The TME in NPC is a dynamic and complex network of tumour-associated cells, including tumour-infiltrating immune cells, cancer-associated fibroblasts, and tumour endothelial cells, as well as non-cellular components such as the extracellular matrix, chemokines, cytokines, and metabolites, which interact closely to shape tumour development and progression.<sup>6</sup> The immune landscape of NPC, which is generally closely associated with EBV infection, contains both anti-tumour immune cells (including cytotoxic T lymphocytes, natural killer cells, and M1-like macrophages) and immunosuppressive cells that facilitate tumourigenesis (including regulatory T lymphocytes, myeloid-derived suppressor cells, and M2-like macrophages).<sup>6,7</sup> Tumour-associated

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macrophages (TAMs) are abundant in the TME, and undifferentiated M0 macrophages can differentiate into anti-tumour cytotoxic M1-like macrophages or immunosuppressive M2-like macrophages.<sup>6,7</sup> As TAMs are recruited from circulating monocytes that infiltrate tumour tissue through chemotactic factors,<sup>7</sup> peripheral blood monocytes may serve as an easily accessible surrogate marker for TAMs within the TME.

Apart from monocyte counts, the other variable in the MAR index is albumin, a functional protein synthesised by the liver, an organ that is essential to the systemic inflammatory response. Albumin is a marker of nutrition and is a negative acute-phase reactant that decreases in inflammation. In the context of systemic inflammation, hepatic synthesis of albumin is downregulated and catabolic loss is increased through capillary leak. Therefore, albumin levels may reflect both malnutrition and persistent systemic inflammation driven by active malignancy.<sup>8</sup> A decline in albumin levels has also been shown in studies to confer a poorer survival prognosis in NPC patients,<sup>9</sup> thus aligning with the findings of Ni et al.<sup>4</sup> Furthermore, Fang et al.<sup>10</sup> identified albumin, monocyte count, and the systemic immune-inflammation index (platelet  $\times$  neutrophil / lymphocyte) as independent prognostic factors for overall survival in non-metastatic NPC, which, when combined into an Inflammation Nutrition Risk Score, had predictive value similar to that of established prognostic tools, including TNM staging and EBV-DNA levels.

Thus far, genetic mutations, including *TP53* mutations and microRNA expression levels, have been found to correlate with disease prognosis and progression in NPC patients.<sup>11</sup> However, to date, only the plasma EBV-DNA levels in NPC patients have been translated into clinical practice.<sup>12,13</sup> As reported by Ni et al.,<sup>4</sup> integrating inflammatory and nutritional indicators may have significant potential for predicting disease outcomes in NPC patients. Wider adoption of this composite index could lead to pretreatment optimisation of nutritional status to improve survival outcomes in NPC patients. It is also imperative that cross-laboratory and cross-population standardisation of MAR units and cut-offs, as is applicable to all other inflammation indices, be completed before clinical adoption.

Beyond NPC, the MAR, combined with neutrophil percentage-to-haemoglobin ratio and carcinoembryonic antigen, has also been reported to be effective in detecting non-small cell lung cancer (NSCLC).<sup>8</sup> Hence, MAR has also been explored as a diagnostic discriminator in NSCLC, suggesting biological relevance beyond NPC. Thus, prognostic validation in other cancers remains limited. In the future, the prognos-

tic utility of MAR should be further investigated across other cancer types.

### Ethics statement

*Not applicable, as no study participants were recruited.*

### Declaration

*The authors declare that they have no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.*

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### REFERENCES

1. Zhang Y, Rumgay H, Li M, et al. Nasopharyngeal cancer incidence and mortality in 185 countries in 2020 and the projected burden in 2040: Population-based global epidemiological profiling. *JMIR Public Health Surveill* 2023;9:e49968.
2. Cai M, Wang Y, Ma H, et al. Advances and challenges in immunotherapy for locally advanced nasopharyngeal carcinoma. *Cancer Treat Rev* 2024;131:102840.
3. Rueda Domínguez A, Cirauqui B, García Castaño A, et al. SEOM-TTCC clinical guideline for nasopharyngeal carcinoma (update 2025). *Clin Transl Oncol* 2026;28:1151-64.
4. Ni W, Xu F, Lin Y, et al. Prognostic value of the monocyte-to-albumin ratio in nasopharyngeal carcinoma: A retrospective cohort study. *Ann Acad Med Singap* 2026;55:231-9.
5. Langley RR, Fidler IJ. The seed and soil hypothesis revisited--the role of tumor-stroma interactions in metastasis to different organs. *Int J Cancer* 2011;128:2527-35.
6. Liu H, Tang L, Li Y, et al. Nasopharyngeal carcinoma: current views on the tumor microenvironment's impact on drug resistance and clinical outcomes. *Mol Cancer* 2024;23:20.
7. Wu H, Li J, Yao R, et al. Focusing on the interplay between tumor-associated macrophages and tumor microenvironment: from mechanism to intervention. *Theranostics* 2025;15:7378-408.
8. Zhao ST, Chen XX, Yang XM, et al. Application of monocyte-to-albumin ratio and neutrophil percentage-to-hemoglobin ratio on distinguishing non-small cell lung cancer patients from healthy subjects. *Int J Gen Med* 2023;16:2175-85.
9. Yang H, Wang K, Liang Z, et al. Prognostic role of pre-treatment serum albumin in patients with nasopharyngeal carcinoma: A meta-analysis and systematic review. *Clin Otolaryngol* 2020;45:167-76.
10. Fang WN, Wu HX, Wu ZP, et al. A scoring system based on inflammatory and nutritional indicators to predict the long-term survival of patients with non-metastatic nasopharyngeal carcinoma. *Sci Rep* 2024;14:20229.
11. Krishnan M, Babu S. Biomarkers in nasopharyngeal carcinoma (NPC): Clinical relevance and prognostic potential. *Oral Oncol Rep* 2024;11:100640.
12. Bossi P, Chan AT, Licita L, et al. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2021;32:452-65.
13. Tang LL, Chen YP, Chen CB, et al. The Chinese Society of Clinical Oncology (CSCO) clinical guidelines for the diagnosis and treatment of nasopharyngeal carcinoma. *Cancer Commun (Lond)* 2021;41:1195-227.