# Regarding "Endoscopic surgery versus conservative treatment in nasopharyngeal carcinoma patients with nasopharyngeal necrosis": the potential confounding role of nutritional support

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**Rhinology 64: 3,** 0 - 0, 2026
https://doi.org/10.4193/Rhin25.622

**Received for publication:**
October 29, 2025
**Accepted:** February 2, 2026

**Associate Editor:**
Basile Landis

**Dear Editor:**

We read with great interest the article by Ouyang et al. in a recent issue of Rhinology, which compares the effectiveness of endoscopic surgery and conservative therapy for nasopharyngeal necrosis (NN) in patients with nasopharyngeal carcinoma (NPC) [1]. The authors are to be commended for their rigorous work on a large cohort, employing propensity score matching (PSM) and inverse probability of treatment weighting (IPTW) to balance baseline characteristics. Their conclusion that endoscopic surgery offers superior overall survival (OS) compared to conservative treatment, particularly for middle necrosis, provides a crucial benchmark for managing this severe complication.

However, we believe the interpretation of these findings warrants caution, considering the potential confounding role of nutritional support, which may not have been fully accounted for in the analysis. The authors astutely identified that a baseline albumin (ALB) level ≤ 35 g/L and a C-reactive protein/albumin (CRP/ALB) ratio ≥ 0.31 were independent adverse prognostic factors for OS [1]. This highlights the profound impact of patients' underlying nutritional and inflammatory status on survival. Poor nutritional status is a well-established negative prognosticator in NPC patients undergoing radiotherapy, directly correlating with treatment tolerance and outcomes [2,3].

The study categorizes treatments into a dichotomy of "endoscopic surgery" versus "conservative therapy." A critical point is that "conservative therapy" is a heterogeneous group, explicitly including "nutritional support" as one of its components [1]. Similarly, patients undergoing major endoscopic surgery, especially with extensive necrectomy and flap reconstruction, almost invariably receive intensive perioperative and postoperative nutritional interventions, which can range from enteral feeding via nasogastric or gastrostomy tubes to total parenteral nutrition. The intensity and modality of this nutritional support are likely to differ substantially from that offered to patients in the conservative arm, who may have received more varied or less aggressive nutritional counseling and supplementation [4].

Therefore, the superior outcomes observed in the surgical group might be attributable not only to the surgical procedure itself but also to the more aggressive and standardized nutritional support that typically accompanies such major interventions. This co-intervention acts as a significant potential confounder. The current analysis, while adjusting for baseline nutritional status (ALB, CRP/ALB), does not appear to adjust for the therapeutic variable of nutritional support intensity. Importantly, malnutrition itself has been linked to adverse clinical outcomes in nasopharyngeal carcinoma. In a recent multicenter cohort study, Wang et al. reported that malnutrition indicates poorer clinical outcomes in patients with NPC [5]. This evidence supports the clinical plausibility that differences in nutritional management—beyond baseline laboratory markers—may influence prognosis. Therefore, imbalance in the intensity and modality of nutritional support between surgical and conservative strategies could contribute to the observed survival differences and potentially inflate the apparent independent effect of surgery.

To further strengthen their significant findings, I constructively suggest that the authors consider a post-hoc analysis based on their existing data. If records permit, stratifying both the

conservative and surgical cohorts by the intensity of nutritional support received (e.g., no formal support vs. oral nutritional supplements vs. mandatory enteral/parenteral nutrition) could help disentangle the effects of the primary treatment from the nutritional co-intervention. Such an analysis would provide a more nuanced understanding of whether surgery remains superior across all levels of nutritional support and would be invaluable for designing future prospective trials, including the ongoing NCT05228093 trial mentioned by the authors.

In conclusion, Ouyang et al. have provided a landmark study in a challenging clinical area. Clarifying the independent contribution of nutritional management would refine our therapeutic strategies and enhance the already profound impact of their research.

## Authorship contribution

WZH drafted and revised the letter.

## Conflict of interest

The author declares that he has no conflict of interest.

## Funding

None.

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