Dear Editor,

We recently read and discussed with interest the article by Du et al titled “Induction chemotherapy followed by radiotherapy for N3 head and neck squamous cell carcinoma”. This retrospective analysis is particularly important in its approach to guide management in head and neck squamous cell carcinoma (HNSCC) with N3 nodes and adds to the existing knowledge on treating this subset of patients. The main strength of the study is that it not only highlights the role of induction chemotherapy (ICT) in N3 nodal disease in HNSCC patients but also tells how the treatment can be further tailored based on the response to the ICT. The management options of N3 neck nodes in patients with HNSCC may predominantly be nonsurgical. This however might depend on the site and T-stage of primary disease and the resectability apart from the response to chemotherapy. Also whether the disease would be suitable for organ preservation is another factor that should be considered while deciding further treatment.

Randomized trials in the past have attempted to study the role of ICT in patients with N2/N3 nodes. The main drawback is that patients with N3 nodes constituted only between 11% and 23% at best, which has been pointed out by the authors themselves. It is in this background that series such as this by Du et al and previous publications would help us to decide the management of HNSCC patients with N3 node. However, the ICT regimens used across the previously published studies, including the randomized trials and the present study, have not been uniform; however, the available evidence suggests that the Taxanes, Cisplatin and 5-fluorouracil (TPF) regimen offers the best response rate, time to progression, and overall survival as mentioned by the authors.

One of the conclusions by Du et al has been that patients who respond to ICT do not benefit from upfront neck dissection (UFND) before radiotherapy. This statement may not apply to all HNSCC, it may well depend on the site of the primary and the T-stage as well and not only on the response to ICT. Patients with the primary from the oral cavity will mandate surgery and appropriate adjuvant treatment. Even for primary arising from larynx and hypopharynx, the subsequent choice of treatment (surgery vs chemoradiotherapy) following ICT would be based on the T-stage and resectability of the neck node. So the conclusion of UFND not offering any benefit before radiotherapy might hold true to patients who would mandate nonsurgical treatment options as per their disease. But for primaries necessitating surgery as the treatment (eg, oral cavity, T4 larynx/hypopharynx), this conclusion might not be applicable. In this study, the nodal disease has primarily been classified as per the size of the node (>7 or <7 cm); however, if the patient is being considered for surgical treatment (depending upon the above-mentioned points), then factors which may affect resectability, for example, fixity to surrounding structures, proximity to vessel, would matter in the decision making.

Malik et al from our institute has published an article on the utility of ICT in unresectable neck nodes in which other than the size of the node, certain clinicoradiological factors were taken as indications to give ICT. These included gross extracapsular spread, extensive soft tissue involvement, encasement of the carotid artery (>180°). The study cohort primarily included oral cavity cancers (n = 32, 62.7%) followed by cancer of unknown primary (n = 7, 13.7%), oropharyngeal cancers (n = 7, 13.7%), and laryngeal (n = 3, 5.9%), hypopharyngeal cancers (n = 1, 2%), paranasal sinus malignancies (n = 1, 2%). The favorable nodal response was seen 64.7% (n = 33/55) patients. Among the ones with a favorable nodal response, 87.9% were amenable to treatment with curative intent. The patients who were treated with surgery showed the highest overall survival of 24 months in the series by Malik et al.4 Du et al consider only the RECIST criteria for response assessment. In the study by Malik et al, both radiological and clinical response was noted before planning further treatment. It has been observed that the response noted in the RECIST criteria may not help in the clinical decisions and there is discordance between radiological response rates and surgical decision making, and there was no linear correlation between radiological size decrement and tumor response.
The analysis and treatment guidelines in N3 nodal disease of head neck squamous cell carcinoma is of vital importance as there is still no consensus on a definite treatment protocol, though the treatment for these group of patients is predominantly nonsurgical. However, after highlighting the various issues mentioned above, we believe that certain factors need to be taken into consideration following ICT for an N3 nodal disease apart from the response rate. These include site and stage of primary and resectability of the nodal disease.

To conclude, surgery should also be part of the treatment algorithm and its role would be based on the site of primary, T-stage of the disease, and resectability in addition to the response of ICT. Also, the response to ICT should include both the radiological response as well as the clinical response of the disease. A prospective study, if not a randomized trial, with response assessment based on clinical as well radiological response, taking into consideration the surgical management of the nodal disease, based on the above-mentioned factors, can further help to refine the treatment protocols for patients with HNSCC with N3 nodes.

CONFLICT OF INTEREST
The authors declare no potential conflict of interest.

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REFERENCES