

## To the Editor: How Do We Solve This Confusion?

Dear Editor,

We read with great interest the article titled “Neoadjuvant Therapy for Rectal Cancer Affects Lymph Node Yield and Status Without Clear Implications on Outcome: The Case for Eliminating a Metric and Using Preoperative Staging to Guide Therapy” by Abdel-Misih et al.<sup>1</sup> We came across another article on a similar topic,<sup>2</sup> but with conflicting conclusions.

In their study, based on the National Cancer Database (NCDB), Abdel-Misih et al concluded that nodal yield in rectal cancer is multifactorial, and that node yield and status were not significant predictors of overall survival (OS). Thus, nodal metric may not be clinically relevant in the era of neoadjuvant therapy. Conversely, the other article<sup>2</sup> stated that their study, also based on the NCDB, clearly demonstrated that lymph node yield is associated with OS in stage I–III rectal cancer, independent of neoadjuvant therapy.

In rectal cancer, neoadjuvant therapy combinations are considered the standard of care, with variations in approach depending on the center.<sup>3,4</sup> But these 2 different results based on the same database are confusing. Can the authors clarify these 2 contradictory results?

Sincerely,

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Baris Yildiz, MD  
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## Authors' Reply to Letter to Editor: Confusion Solved; Sort Of

We appreciate Dr. Tez et al's inquiry regarding contrasting results between similar studies published in *JNCCN*<sup>1</sup> and the *Journal of Clinical Pathology*<sup>2</sup> using an identical data set. These studies examined the impact of lymph node yield and status on outcomes in rectal cancer in the era of neoadjuvant therapy.

First, it is prudent to clarify that these 2 studies used 2 different data sources. Xu et al used the NCDB, which yielded a robust 25,447 patients who met inclusion criteria. Our study<sup>1</sup> used the NCCN database. The NCDB is a hospital-based cancer registry collected from >1,500 Commission on Cancer (CoC)-accredited facilities. In contrast, the NCCN database was a prospective database abstracted from 8 of NCCN's 27 Member Institutions, yielding 1,680 patients with similar inclusion criteria.

The conclusions drawn using these different retrospective datasets are conflicting. In the Xu et al study, a suboptimal node yield was associated with decreased OS independent of neoadjuvant treatment. This contradicts our findings, in which neither nodal yield nor status predicted for OS. Additionally, administration of neoadjuvant therapy was one of several independent predictors of survival.

These disparate results highlight the positives and negatives of using retrospective “big data.” Such data sets allow for extensive data analysis, providing well-powered sta-

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tistics and the associated interpreted conclusions. However, we must also remember that these big data sets often merge dissimilar patient populations and potentially different types of care. The NCDB, due to its nature, introduces a lot of variability in both patients and level of cancer care. Likewise, a data set limited to 8 NCCN Member Institutions has potential for biases given the cancer-centric care offered, with a referral bias that may impact the data and results.

Hence, disparate results are explained, but confusion remains as to the implications and impact of lymph nodes remain. This again highlights the limitations of retrospective data and the need for high-quality prospective studies to answer complex questions.

Sincerely,

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## References

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