LETTER TO THE EDITOR

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Comment on "The prognostic impact of tumor necrosis in non-muscle invasive bladder cancer"

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Dear Editor,

We read with great interest the article entitled "The prognostic impact of tumor necrosis in non-muscle invasive bladder cancer[1]." The study[1] aimed to investigate the predictive value of tumor necrosis in patients with non-muscle-invasive bladder cancer and its impact on disease progression and recurrence. The conclusion of this study stated that the presence of tumor necrosis is a significant predictor of disease progression (p=0.00) in patients with non-muscle-invasive bladder cancer, which highlights the importance of considering tumor necrosis as a prognostic factor in patients with non-muscle-invasive bladder cancer. While we found the study to be informative and valuable, we would like to raise some potential limitations that should be considered.

First, as body mass index (BMI) is a well-established risk factor for bladder cancer, with obesity being linked to a higher incidence of this type of cancer, it is crucial to understand the impact of BMI on the prognostic value of tumor necrosis in patients with non-muscle-invasive bladder cancer. A previous study[2] revealed that patients with T1G3 non-muscle-invasive bladder cancer with an increase in BMI had a significantly higher likelihood of experiencing disease progression and a higher risk of bladder cancer-related death, emphasizing the importance of considering BMI in prognostic assessments for patients with non-muscle-invasive bladder cancer. Furthermore, another study[3] conducted on a cohort of survivors with bladder cancer demonstrated that adiposity may play a role in the recurrence of bladder cancer, particularly among smokers. The study[3] demonstrated that individuals with a high BMI and a history of smoking had a significantly higher risk of bladder cancer recurrence compared to those with a low BMI and no history of smoking. The potential mechanisms underlying this association include the impact of adipose tissue on inflammation, insulin resistance, and hormone production, which can create a favorable environment for tumor growth and progression. These findings suggest that BMI should be taken into account when assessing the risk of bladder cancer recurrence and developing personalized treatment plans for survivors with bladder cancer. Therefore, the absence of BMI data in this study[1] limits the ability to draw comprehensive conclusions about the prognostic impact of tumor necrosis in patients with non-muscle-invasive bladder cancer.

Second, the conclusion of this study cannot be considered definitive regarding the impact of tumor necrosis on the prognosis of non-muscle-invasive bladder cancer. While this study suggests that tumor necrosis was associated with cancer progression (p<0.001), as shown in Table 1, a subsequently more rigorous analysis using multivariate Cox regression has shown that there is no association between tumor necrosis and the recurrence (p>0.05) and progression (p>0.05) in patients with non-muscle-invasive bladder cancer, as described in Table 2 of this study[1]. Statistically, the evidence level of multivariate Cox regression analysis is higher than that of Kaplan-Meier analysis, because Cox regression analysis takes into account the influence of all confounding factors (such as age, gender, tumor number, and tumor size) while Kaplan-Meier analysis does not. Therefore, the conclusion that tumor necrosis is related to tumor progression may not be entirely appropriate. It is crucial to acknowledge the study's limitations and the need for further research to achieve a clear and definitive conclusion regarding the prognostic impact of tumor necrosis in non-muscle-invasive bladder cancer. Further research may need to focus on identifying other factors that may be more closely associated with cancer progression in patients with non-muscle-invasive bladder cancer. Additionally, future studies may need to incorporate more rigorous analyses, such as multivariate Cox regression analysis, to provide a more accurate understanding of the

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prognostic impact of tumor necrosis. Until then, the current study's results should be interpreted with caution, and further investigation is required to clarify the prognostic significance of tumor necrosis in non-muscle-invasive bladder cancer.

AUTHORS' CONTRIBUTIONS

DW: Conceptualization, Investigation, Writing – original draft, Writing – review & editing. **YL:** Conceptualization, Writing – original draft.

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