

The impact of positive surgical margins after cystectomy on oncological outcomes: a nationwide study

Authors:

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Background:

Localized muscle-invasive bladder cancer (MIBC) only yields five-year survival rates of approximately 50% after treatment with curative intent. Radical cystectomy (RC) is recommended as the preferred curative treatment option for MIBC, with trimodality treatment as bladder-sparing alternative. The European Association of Urology (EAU) guidelines provide clear recommendations for the use of neoadjuvant treatment for patients undergoing RC. Neoadjuvant chemotherapy (NAC) is recommended for cisplatin-eligible patients, providing a 8% survival benefit. Nevertheless, survival rates after RC are still poor.

Adjuvant treatment provides another opportunity to improve survival outcomes. Postoperative risk indicators, pT3-4 and/or pN+, are currently used to classify patients at high risk of disease recurrence. The current era with emergence of new therapeutic agents warrants reevaluation of identifying patients who might benefit from adjuvant treatment. Pending availability of accurate biomarkers, pathological features remain crucial.

Abstract

Objective: To evaluate if surgical margin status alongside existing postoperative risk indicators improves identification of bladder cancer patients who may benefit from adjuvant therapy following radical cystectomy.

Methods: In this nationwide cohort study, patients aged 18 years and older diagnosed with muscle-invasive bladder cancer (MIBC) without nodal or distant metastasis (cT2-4aN0/xM0) between November 2017 and December 2020 who underwent radical cystectomy (RC) were selected from the Netherlands Cancer Registry. Detailed information on surgical margin status was obtained through linkage with the Dutch central pathology database Palga. Overall survival (OS) and progression-free survival (PFS) were assessed using the Kaplan-Meier method. Multivariable Cox regression analysis was performed to assess the independent prognostic effect of positive surgical margins (CIS only or invasive carcinoma) on PFS and OS.

Results: We identified 1,445 MIBC patients treated by RC (53% open, 47% robot-assisted), of whom 135 (9.3%) had positive surgical margins (10.7% in open and 7.7% in robot-assisted). In the entire cohort, OS was 79% and 60% at 12 and 48 months after RC, respectively. PFS was 70% and 61% at 12 and 24 months. Multivariable Cox regression showed a worse PFS (HR 2.13, 95%CI 1.67-2.72) and OS (HR 2.02, 95%CI 1.58-2.58) in patients with surgical margins with invasive carcinoma versus patients with negative margins. Patients with only CIS in the margins appeared to have worse PFS as well (HR 1.60, 95%CI 1.00-2.58) but results were not statistically significant. No difference was found for OS (HR 1.30, 95%CI 0.80-2.12).

Conclusion: Positive margins should be considered a 'high risk feature', as they result in increased risk of disease progression and impaired survival outcomes. These findings support further investigation of the potential efficacy of adjuvant therapy (i.e., radiotherapy and systemic therapy) among patients with positive surgical margins.