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Early Detection of Metastatic Progression by Circulating Tumor DNA in Patients Undergoing Bladder-preserving Trimodality Therapy

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Abstract
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Abstract

Purpose: Radical cystectomy (RC) and trimodality therapy (TMT) are efficacious treatments for muscle invasive bladder cancer (MIBC). Novel methods for post-treatment surveillance are needed to detect recurrence. This study assesses the value of plasma circulating tumor DNA (ctDNA) for detection of post-TMT recurrence.

Methods: We performed a retrospective ctDNA analysis in 42 patients with MIBC treated with TMT. Patients were stratified as post-TMT ctDNA (+) or ctDNA (-) and assessed for metastasis-free survival (MFS) and recurrence-free survival (RFS) using Kaplan-Meier and Cox regression methods.

Results: At a post-TMT median follow-up of 448 days (range: 100-1555), 6 patients (14%) were ctDNA (+) and 36 (86%) were ctDNA (-); 5 of 6 (83%) ctDNA (+) patients developed radiographic evidence of metastasis. All 36 ctDNA (-) patients were without metastasis. ctDNA positivity correctly identified all metastatic progression with 100% sensitivity and 95% specificity at 1-year post-TMT surveillance. Further, ctDNA-based detection preceded clinical detection of metastasis with a median lead-time of 57 days and maximal lead-time of 139 days. ctDNA (+) status was associated with worse MFS ($p< 0.0001$) and RFS ($p=0.0005$). In univariable analysis, ctDNA (+) status was the only variable significantly associated with worse RFS (HR 6.36, 95% CI: 1.93-20.96, $p=0.0024$).

Conclusion: Plasma ctDNA is a potential biomarker for early detection of metastatic progression after TMT. Our hypothesis-generating findings provide a basis for larger studies to evaluate the utility of ctDNA-guided surveillance post-TMT.