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# Urinary volatile metabolomic biomarkers for detection of bladder cancer

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## Abstract

**Background:** Early detection of bladder cancer (BC) is necessary for improved outcomes, but current diagnostic methods may lack the necessary sensitivity. Metabolomics, particularly the analysis of urinary volatile organic compounds (VOCs), offers a promising, non-invasive approach to BC detection [1,2]. **Objective:** The study aimed to investigate potential urinary biomarkers for the detection and staging of BC using metabolomics approaches, in particular gas chromatography-mass spectrometry (GC-MS), and to apply machine learning algorithms to establish a biomarker panel for the accurate detection and staging of BC. **Methods:** Our study collected urine samples from 196 participants, including 98 BC patients (67 non-muscle invasive bladder cancer, and 31 muscle-invasive bladder cancer) and 98 cancer-free controls. Ethical approval was obtained, and informed consent was signed by all participants. Headspace solid-phase microextraction coupled with gas chromatography-mass spectrometry (HS-SPME-GC-MS) was used for volatile profiling in urine. Statistical analyses included principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA), receiver operating characteristic (ROC) analysis, and univariate tests to identify biomarkers for BC detection and staging. **Results:** Our study found 19 urinary volatile metabolites that effectively discriminate BC patients from cancer-free controls. A panel of ten potential biomarkers was identified for the detection of BC with a sensitivity of 81%, specificity of 90% and accuracy of 85%. This biomarker panel consisted of two aromatic compounds, three ketones, three alcohols, one pyran-like compound, and one fatty acid. Compared to controls, the panel achieved 83% sensitivity, 87% specificity, and 84% accuracy for NMIBC, and 90% sensitivity, 77% specificity, and 87% accuracy for MIBC. No significant differences in urinary volatile profiles were observed between NMIBC and MIBC patients. **Conclusions:** The identified panel of 10 biomarkers showed significant potential to discriminate between BC patients and controls. While further research is warranted to differentiate NMIBC from MIBC cases, our findings highlight the value of urinary volatile biomarkers in advancing diagnostic approaches for improved patient care.

**Keywords:** bladder cancer; metabolomics; volatile organic compounds; gas chromatography – mass spectrometry; urinary biomarkers

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