

Supplementary materials

Appendix 1. Search strategy.

Medline (Ovid)

(Exp metabolomics or metabolom*.mp or lipid*.mp or exp Nucleotides or (nucleotide*).mp or exp Amino Acids or (amino acid*).mp or exp Mass Spectrometry or (mass adj2 spectrometry).mp or (mass adj2 spectroscopy).mp or (mass spectrum analysis).mp or exp Magnetic Resonance Spectroscopy or (magnetic resonance spectroscop*).mp or (MR spectroscop*).mp or (NMR spectroscop*).mp or (nuclear magnetic resonance).mp) AND (exp Urinary Bladder Neoplasms or (Urinary Bladder Neoplasm*).mp or (bladder adj2 neoplasm*).mp or (bladder adj2 tumor*).mp or (bladder adj2 tumour*).mp or (bladder adj2 cancer*).mp or (Urinary Bladder cancer*).mp or (Urinary Bladder malignant tumor*).mp) AND (randomized controlled trial.pt or controlled clinical trial.pt or randomized.ab or placebo.ab or randomly.ab or trial.ab or (clinical adj2 trial).mp or (randomi*ed adj2 controlled adj2 trial).mp or exp double-blind method or Exp cohort studies or (cohort adj2 stud*).mp or exp case-control studies or (case-control adj2 stud*).mp or exp Cross-sectional studies or (cross-sectional adj2 stud*).mp or (descriptive adj2 stud*).mp or (observational adj2 stud*).mp).

Central

(Exp metabolomics or metabolom*.mp or lipid*.mp or exp Nucleotides or (nucleotide*).mp or exp Amino Acids or (amino acid*).mp or exp Mass Spectrometry or (mass adj2 spectrometry).mp or (mass adj2 spectroscopy).mp or (mass spectrum analysis).mp or exp Magnetic Resonance Spectroscopy or (magnetic resonance spectroscop*).mp or (MR spectroscop*).mp or (NMR spectroscop*).mp or (nuclear magnetic resonance).mp) AND (exp Urinary Bladder Neoplasms or (Urinary Bladder Neoplasm*).mp or (bladder adj2 neoplasm*).mp or (bladder adj2 tumor*).mp or (bladder adj2 tumour*).mp or (bladder adj2 cancer*).mp or (Urinary Bladder cancer*).mp or (Urinary Bladder malignant tumor*).mp).

Embase

((('metabolomics'/exp or 'metabolom*':ti,ab or 'lipid*':ti,ab or 'nucleotide'/exp or 'nucleotide*':ti,ab or 'amino acid'/exp or 'amino acid*':ti,ab or 'mass spectrometry'/exp or 'mass next/2 spectrometry':ti,ab or 'mass next/2 spectroscopy':ti,ab or 'mass spectrum analysis':ti,ab or 'nuclear magnetic resonance spectroscopy'/exp or 'magnetic resonance spectroscop*':ti,ab or 'MR spectroscop*':ti,ab or 'NMR spectroscop*':ti,ab or 'nuclear magnetic resonance':ti,ab) AND ('bladder tumor'/exp or 'Urinary Bladder Neoplasm*':ti,ab or 'bladder next/2 neoplasm*':ti,ab or 'bladder next/2 tumor*':ti,ab or 'bladder next/2 tumour*':ti,ab or 'bladder next/2 cancer*':ti,ab or 'Urinary Bladder cancer*':ti,ab or 'Urinary Bladder malignant tumor*':ti,ab) AND ('randomized controlled trial'/exp or 'randomi*ed NEXT/2 controlled NEXT/2 trial':ti,ab or 'clinical trial'/exp or 'clinical NEXT/2 trial':ti,ab or 'double blind procedure'/exp or 'cohort analysis'/exp or 'cohort*':ti,ab or 'case control study'/exp or 'case-control next/2 stud*':ti,ab or 'cross-sectional study'/exp or 'cross-sectional next/2 stud*':ti,ab or 'descriptive next/2 stud*':ti,ab or 'observational next/2 stud*':ti,ab)) AND [embase]/lim.

Supplementary Table 1. Metabolic profiling of lipid pathway in bladder cancer.

Study	Sample type	Analytical platform	Choline-containing compounds			Additional lipid compounds					
			Choline	Phospho-choline	Glycerophosphocholine	Inositol	Acetoacetate	TG	Glycerol	Ethanolamine	Carnitine
Pasikanti et al., 2010 [22]	Urine	GC-TOFMS							↓		
Putluri et al., 2011 [24]	Urine	LC-MS									↑
Huang et al., 2011 [25]	Urine	LC-MS									↓
Cao et al., 2012 [27]	Serum	H-NMR	↓				↑				
Pasikanti et al., 2013 [29]	Urine	GC×GC-TOFMS							↓		
Tripathi et al., 2013 [35]	Tissue	HR-MAS-NMR GC-MS	↑	↑	↑	↑		↑			
Jin et al., 2014 [33]	Urine	HPLC-QTOFMS									↑
Wittmann et al., 2014 [36]	Urine	UHPLC-MS/MS GC-MS	↑	↑						↓	↑
Loras et al., 2019 [45]	Tissue and urine	H-NMR	↑ ↓	↑ ↓	↑ ↓						
Luczykowski et al., 2021 [47]	Urine	LC-MS		↑							
Li et al., 2022 [49]	Urine	LC-MS	↑								

TG, triglycerides; GC, gas chromatography; MS, mass spectrometry; TOFMS, time-of-flight MS; LC, liquid chromatography; NMR, nuclear magnetic resonance; H-NMR, proton NMR; HR-MAS-NMR, high resolution-magic angle spinning NMR; HPLC-QTOFMS, high-performance liquid chromatography-quadrupole time-of-flight MS; GC×GC-TOFMS, two-dimensional GC-TOFMS; UHPLC-MS/MS, ultra-high performance liquid chromatography/tandem MS. ↓, down-regulated; ↑, up-regulated; ↓↑, undetermined trend.

Supplementary Table 2. Metabolic profiling of aldehyde pathway in bladder cancer.

Study	Sample type	Analytical platform	Methanal	Ethanal	Propanal	Butanal	Pentanal	Hexanal	Heptanal	Nonenal	Dodecanal
Jobu et al., 2012 [32]	Urine	GC-MS								↑	↑
Wei et al., 2019 [44]	Blood	HS-GC-MS	↑	↑	↑	↑	↑	↑	↑		
Pinto et al., 2021 [48]	Urine	HS-SPME-GC-MS	↓					↓			

MS, mass spectrometry; GC, gas chromatography; HS-GC-MS, chromatography-MS coupled with a headspace generator sampler; HS-SPME-GC-MS, headspace solid-phase microextraction GC MS. ↓, down-regulated; ↑, up-regulated; ↓↑, undetermined trend.