Malik et al. Existing trends and applications of artificial intelligence in urothelial cancer: A scoping review

APPENDIX

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Appendix A. Search Strategy for Medline, Embase, Scopus and Web of Science

Database(s): **Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®** 1946-Present
Search Strategy:

#	Searches	Results
1	exp Artificial Intelligence/	143648
2	exp Diagnosis, Computer-Assisted/	86001
3	exp Pattern Recognition, Automated/	26206
4	exp Image Processing, Computer-Assisted/	252597
5	exp Machine Learning/	43312
6	exp Deep Learning/	10671
7	exp Natural Language Processing/	5418
8	artificial intelligen*.tw,kf.	21941
9	machine learn*.tw,kf.	61358
10	neural network*.tw,kf.	75043
11	deep learn*.tw,kf.	29505
12	computer vision.tw,kf.	5942
13	natural language process*.tw,kf.	5646
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	512550
15	exp Carcinoma, Transitional Cell/	20154
16	exp Urinary Bladder Neoplasms/	59458
17	exp Ureteral Neoplasms/	4966
18	exp Urethral Neoplasms/	2618
19	exp Kidney Neoplasms/	80716
20	((urothelial or transitional cell* or transition cell*) adj3 (carcinoma or neoplasm or cancer)).tw,kf.	22913
21	(bladder adj3 (carcinoma or neoplasm or cancer)).tw,kf.	49513
22	(ureteral adj3 (carcinoma or neoplasm or cancer)).tw,kf.	681
23	(urethral adj3 (carcinoma or neoplasm or cancer)).tw,kf.	622

24	((renal pelvis or ureteropelvic junction) adj3 (carcinoma or neoplasm or cancer)).tw,kf.	1004
25	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24	161234
26	14 and 25	3111

Database(s): **Embase Classic+Embase** 1947 to 2022 April 21
Search Strategy:

#	Searches	Results
1	exp artificial intelligence/	59984
2	exp machine learning/	304969
3	exp deep learning/	23792
4	exp natural language processing/	7663
5	artificial intelligen*.tw,kf.	26495
6	neural network*.tw,kf.	91346
7	machine learn*.tw,kf.	72556
8	deep learn*.tw,kf.	34090
9	computer vision.tw,kf.	6476
10	natural language process*.tw,kf.	6781
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	376840
12	exp transitional cell carcinoma/	33081
13	exp bladder cancer/	81081
14	exp ureter cancer/	2183
15	exp urethra cancer/	1389
16	((urothelial or transitional cell* or transition cell*) adj3 (carcinoma or neoplasm or cancer)).tw,kf.	35254
17	(bladder adj3 (carcinoma or neoplasm or cancer)).tw,kf.	72479
18	(ureteral adj3 (carcinoma or neoplasm or cancer)).tw,kf.	1006
19	(urethral adj3 (carcinoma or neoplasm or cancer)).tw,kf.	932
20	((renal pelvis or ureteropelvic junction) adj3 (carcinoma or neoplasm or cancer)).tw,kf.	1410
21	12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20	122440
22	11 and 21	1097

Database: Scopus
TITLE-ABS-KEY ("artificial intelligence" OR "artificial intelligent" OR "machine learning" OR "deep learning" OR "neural network" OR "computer vision" OR "computer-assisted diagnosis" OR "forecast" OR "natural language processing") AND TITLE-ABS-KEY ("urothelial cancer" OR "urothelial neoplasm" OR "urothelial carcinoma" OR "transitional cell carcinoma" OR "bladder cancer" OR "bladder neoplasm" OR "bladder carcinoma" OR "urethral cancer" OR "urethral neoplasm" OR "urethral carcinoma" OR "ureteral cancer" OR "ureteral neoplasm" OR "ureteral carcinoma" OR "renal pelvis cancer" OR "renal pelvis neoplasm" OR "renal pelvis carcinoma")
Results: 706 document results

Database: Web of Science
https://www.webofscience.com/wos/woscc/summary/78b17508-ac8f-4077-987f-8b00e52f23d0-32eaf9d2/relevance/1
((artificial intelligen*) OR (machine learn*) OR (deep learn*) OR (neural network*) OR (computer vision) OR (computer-assisted diagnosis) OR (natural language process*)) AND ((urothelial cancer) OR (urothelial neoplasm) OR (urothelial carcinoma) OR (transition* cell carcinoma) OR (bladder cancer) OR (bladder neoplasm) OR (bladder carcinoma) OR (urethral cancer) OR (urethral neoplasm) OR (urethral carcinoma) OR (ureteral cancer) OR (ureteral neoplasm) OR (ureteral carcinoma) OR (renal pelvis cancer) OR (renal pelvis neoplasm) OR (renal pelvis carcinoma))
Results: 779 results

Appendix B. Studies that applied artificial intelligence in urothelial cancer using radiomics

1st Author *	**Disease State**	**Specific Application**	**Type of Diagnosis/ Prognosis**	**AI Model(s) Used**	**Features**	**Accuracy**	**Sensitivity**	**Specificity**	**Area under the curve (AUC)**	**Comparison with non-AI Models**
Studies using AI for diagnosis										
Nguyen [5]	NMIBC	using tumour ADC to differentiate between malignant vs. benign tumours/wall-thickening	Detection	k-means clustering analysis	uniformity and irregularity of voxel ADC values within a tumour, MICD, LICD	N/A	N/A	N/A	N/A	No
Xu [36]	Other/ multiple disease states	to investigate the value of radiomics features from diffusion weighted imaging (DWI) in differentiating MIBC from NMIBC. comparing an RF model to an AR model in terms of performance	Staging	random forest (RF), all-relevant (AR) methods	11 DWI features + TUR results	89.7%	96.4%	78.1%	N/A	No
Garapati [38]	Other/ multipl	to classify bladder cancer into two staging	Staging	ML methods: linear	26 morphologi	N/A	N/A	N/A	N/A	No

	e disease states	categories: greater than or equal to stage 2 (T2, MIBC) and below stage T2 (NMIBC)		discriminant analysis (LDA), neural network, SVM, RF classifier	-cal features + 65 texture features					
Wang[66]	NMIBC	to build an MRI-based multiparametric radiomics model to grade BCa tumors noninvasively	Grading	LASSO, multivariable logistic regression	14 shape-based features, 220 GLCM features, 160 GLRLM features, 160, GLSZM features, 50 NGTDM features, 140 GLDM features, 180 first-order statistics features	83.33%	76.92%	88.24%	0.9276	No
Zheng[69]	Other/ multiple disease states	to create a nomogram to predict the grade of BCa: noninvasive vs invasive	Grading	SVM, RF, LASSO	2436 radiomics features + age, sex, tumour number, tumour size, hydronephr	89.9%	86.0%	94.9%	0.952	No

					osis and VI-RADS scoring					
Wang[73]	Other/ multipl e disease states	to create a nomogram to predict the muscle invasive status of BCa	Grading	SVM, LASSO	Histogram Features, CM Features, RLM Features, NGTDM Features	N/A	N/A	N/A	0.810 0.877 with addition of 2 independent predictors	No
Cui[99]	Bladder cancer	To develop a radiomics-model to predict the muscle-invasive status of bladder cancer	Staging	AdaBoost (final prediction is produced through a weighted majority vote (or sum) that combined the predictions from all the weak learners)	Shape-based, Grey-level run length matrix, Grey-level dependence matrix, grey-level size zone matrix	82.4%	79.4%	85.3%	0.824	Yes
Li[129]	Bladder cancer	estimate grade of bladder cancer and probability of recurrence	Segmentation	neural networks	36 features from morphologi cal and textural nuclear features	82.3%	N/A	N/A	N/A	No
Zheng[146]	Other/ multipl	To use radiomics-based predictive models on	Staging	DL-CNN	Selected radiomics	N/A	50.0%	81%	0.73	No

	e disease states	pre and post treatment CT scans to determine the response to treatment			features extracted from largest lesion on mpMRI					
Hammouda[154]	Bladder cancer	To establish a preoperative prediction model of myometrial invasion of bladder cancer based on CT images	Segmentation, Staging	SVM	Shape, grey-level co-occurrence matrix, gray size region matrix, gray run-length matrix, adjacent gray difference matrix and gray correlation matrix	70.0%	69.23%	66.67%	0.702	No
Zhang[160]	Bladder cancer	Using a SVM-RFE to discriminate between MIBC and NMIBC using MRI radiomic features	Grading	SVM-RFE	Radiomic features from MRI	96.30%	92.60%	100%	0.9857	No
Xu[162]	Other/ multiple disease states	To predict staging of bladder cancer from CT images	Staging	DCNN	features of tumor regions or bladder wall	N/A	N/A	N/A	N/A	Yes

					regions					
Li[166]	Other/ multiple disease states	To conduct automatic multiregion segmentation on bladder cancer walls and tumors from MRI images	Segmentation	Dilated CNN	Delineated images of MRI images of the bladder,	N/A	N/A	N/A	N/A	No
Evrimler[203]	mUC, UC	To predict treatment outcome for immunotherapy from CT images	Detection	3D-DCNN	CT scan images of bladder and hematochemical indicators	92.2%	92.9%	91.6%	N/A	No
Zhang[215]	Bladder cancer	distinguishing between low and high grade bladder cancer	Grading	SVM-RFE	102 features from both DWI and ADC maps	82.9%	78.5%	87.1%	0.861	Yes
Yang[220]	Other/ multiple disease states	distinguish NMIBC from MIBC through preop CT images	Staging	DL-CNN (VGG16, VGG19, Xception, InceptionV3, InceptionResNetV2, DenseNet121, DenseNet169, and DenseNet201)	demographic and CT image features	93.9%	88.9%	98.9%	0.997	No
Zhang[225]	Other/ multipl	preoperative prediction of muscle-invasive	Staging	CNN, t-distributed	imaging features on	74.7%	71.0%	77.3%	0.791	Yes

	e disease states	status using CT images		stochastic neighborhood embedding (t-SNE)	CT					
Studies using AI for prognosis										
Park[23]	mUC, UC	to predict the response and survival outcomes of patients with BCa treated with PD-1/PD-L1 immunotherapy	Survival, Treatment response	LASSO for feature selection, radiomics based model	total of 49 radiomic features	N/A	N/A	N/A	0.88	No
Choi[24]	MIBC	to predict response to neoadjuvant chemotherapy in patients with MIBC	Treatment response	RF classifier, multivariate logistic regression	3 Semantic Features + 11 Clinical Features	66.7%	75.0%	60.0%	0.75	No
Ye[25]	NMIBC	to predict treatment response to (Bacillus Calmette-Guerin) immunotherapy in pts with NMBIC	Treatment response	non-negative matrix factorization	107 CT-based radiomic features including 14 shape features, 18 histogram features, and 68 texture features	N/A	0.73	0.69	0.68	No
Tang[39]	Bladder cancer	looking at radiomics features (pelvic contrast enhanced computed tomography images) to predict the	Progression, Survival	unsupervised hierarchical clustering analysis, LASSO,	4 GLCM Features + 2 GLSZM Features	N/A	N/A	N/A	0.853	No

		tumor mutation burden status of BCa patients -> develop a TMB-predicting model based on radiomic data		logistic regression						
Cha[43]	MIBC	using pre- and post-treatment CT scans to distinguish between bladder cancers with and without complete chemotherapy responses	Treatment response	3 models - DL-CNN, RF-SL, and RF-ROI	Segmented bladder lesions on pre and post-treatment CT images	N/A	N/A	N/A	0.73	Yes
Wu[44]	Bladder cancer	using pre- and post-treatment CT scans for bladder cancer treatment response based on transfer learning by freezing different DL-CNN layers and varying DL-CNN structure	Treatment response	DL-CNN-1, -2, and -3	ROIs of pre- and post-chemo CT scans of the bladder	78.9%	75%	80%	0.86	No
Zheng[52]	Bladder cancer	preoperative prediction of Ki67 expression status, which is associated with survival outcomes	Survival	LASSO, SMOTE-LASSO, SVM-RFE, SMOTE-SVM, SVM	shape and size, first-order features, textural features, and wavelet features of segmented bladder tumours	81.5%	79.5%	86.7%	N/A	No

Rundo[61]	mBC	to predict treatment (immunotherapy) response	Treatment response	dense CNN	Visual features of chest-abdomen CT scans	92.5%	96%	87%	N/A	No
Sun[89]	MIBC	estimate likelihood of response to neoadjuvant chemotherapy	Treatment response	CDSS combined DL-CNN and radiomics model (random forest classifier)	pre- and post-chemo CT scans	N/A	N/A	N/A	0.8	Yes
Zhang[93]	MIBC	predict progression-free survival (clinicopathologic + radiomics nomogram vs. radiomics only vs. clinicopathologic only)	Survival	LASSO	intensity, shape, texture, Laplacian of Gaussian, and wavelet features from DWI/ADC images	N/A	N/A	N/A	N/A	No
Rundo[112]	mBC	accurate segmentation of bladder and bladder tumours	Treatment response	mRMR, random forest, linear regression, decision tree	optimal features from MR segmentation images from 2 groups of ROIs (tumour and normal	N/A	N/A	N/A	N/A	No

					bladder wall tissue)					
Xu[139]	Other/ multiple disease states	to predict response to neoadjuvant chemotherapy in MIBC patients	Recurrence	radial basis function SVM	13 Haralick features from the gray level co-occurrence matrix 5 features from the neighborhood gray tone difference matrix 10 features from the gray level run length matrix 10 features from the gray level size zone matrix.	62.10%	52.90%	69.40%	0.63	No
Parmar[143]	MIBC	to differentiate MIBC vs NMIBC pre-operatively	Treatment response	LASSO, RF, SVM	shape and size-based features, image	N/A	N/A	N/A	N/A	No

					intensity (first-order features), textural features and wavelet features + age, sex, MRI-determined number of tumors, MRI-determined tumor size and VI-RADS score					
Cha[152]	Bladder cancer	A multiparametric computer-aided diagnostic system developed to differentiate between BCa staging	Treatment response	CNN	13 Histogram Features, 25 GLCM Features, 16 GLRLM Features, 3 Morphological Features	95.24%	95.24%	95.24%	0.9864	Yes
Zhou[156]	MIBC	To build a CT-based radiomics model to predict the pathological grade of bladder cancer (BCa) preliminarily	Progression	Logistic Regression Model	First-order statistics, shape-based features, texture features,	83.8%	88.5%	72.7%	0.860	Yes

					gray-level run-length matrix, gray-level size zone matrix, gray-level dependence matrix					
Mi[209]	MIBC	The prediction accuracy of ML based CT radiomics of UC for Histological variance	Treatment response	Table 3. discusses the various ML algorithms that were used (Total of 15) the best two models were evaluated on the test set and ensembled by Voting Classifier	Image texture, nucleus morphology, clustering, and spatial correlations from single cell and regions of bladder tissue	79-90%	N/A	N/A	0.000-0.9667	No
Trebeschi[219]	mUC, UC	identify morphological changes in chest and abdomen CT scans to predict overall survival	Survival	own model (PAM, using VGG-like convolutional network, 2 other convolutional networks with VGG-like convnet and U-net)	Morphological changes in chest and abdo CT scans during follow-up	N/A	60%	74%	0.73	Yes

Studies using AI for diagnosis and prognosis										
Spyridonos[131]	Other/ multiple disease states	To develop and validate a nomogram based on radiomics and clinical predictors for personalized prediction of the recurrence risk in the first 2 yrs.	Grading, Recurrence	support vector machine (SVM)-based recursive feature elimination (SVM-RFE), LASSO	Histogram features, Haralick features extracted from co-occurrence matrix (CM), features extracted from run-length matrix (RLM), neighborhood gray-tone difference matrix (NGTDM) gray level size zone matrix (GLSZM)	80.95%	N/A	N/A	0.838	No
Studies using AI for other reasons										
Xu[85]	MIBC	support vector machine (SVM)-based feature selection and classification strategy were proposed to first		SVM	63 radiomic features from T2 weighted MRI	N/A	N/A	N/A	N/A	No

		rebalance the imbalanced sample size and then further select the most predictive and compact signature subset to verify its differentiation capability								

NMIBC = non-muscle invasive bladder cancer
MIBC = muscle invasive bladder cancer
mUC = metastatic urothelial carcinoma
UC = urothelial carcinoma

*Citations included can be found in Appendix G

Appendix C. Studies that applied artificial intelligence in urothelial cancer using genomics

1st Author	Disease State	Specific Application	Type of Diagnosis/ Prognosis	AI Model(s) Used	Features	Accuracy	Sensitivity	Specificity	Area under the curve (AUC)	Comparison with non-AI Models
Studies using AI for diagnosis										
Rosser[7]	Bladder cancer	gene expression profiling of urothelial cells to identify genes that might be used as diagnostic classifiers for BCa (it may be possible to detect BCa based on gene expression analysis alone), the hope is for this to eventually act as a non-invasive way to diagnose BCa instead of cystoscopy	Detection	hierarchical clustering and supervised ML algorithms	gene expression profiles of exfoliated urothelia from bladder washes	76%	N/A	N/A	N/A	No
Wang[76]	Bladder cancer	creating a gene signature to detect bladder cancer	Detection	SVM	70 gene expression profiles from	90%	83%	95%	0.93	No

		from controls			urine specimens					
Moisoiu[90]	Bladder cancer	synergy between miRNA and SERS profiling of urine for point-of-care diagnosis and molecular stratification of BC	Detection, Grading	logistic regression, naive Bayes, random forest	miRNA and SERS from urine samples				0.92	No
Velmahos[95]	Bladder cancer	identifying tumour-infiltrating lymphocytes to predict FGFR activation status (correlated to sensitivity of BLCA to targeted drugs)	Other	CNN, logistic regression	Tumour-infiltrating lymphocyte percentage from whole slide images of diagnostic bladder tumour biopsies	N/A	89%	42%	0.76	No
Angeletti[104]	Bladder cancer	to differentiate malignant vs benign cells in urothelial cell cytology specimens, also on cases diagnosed as "atypical", to predict follow up by biopsy	Detection	GENIE: GENetic Imagery Exploitation package	number of chromosomes per generation (60), maximum number of genes in each algorithm (20), backend discrimination (Fisher), crossover mechanism (Singlepoint), crossover rate	N/A	85%	95%	N/A	Yes

					(0.9), mutation parameter rate (0.25), gene mutation rate (0.6), fitness metric (Hamming), thresholding (Intelligent), selection rate (Tournament 3), elite fraction (0.1) and end-point fitness (1000)					
Lopez de Matura na[107]	Bladder cancer	to identify inflammatory genes associated with BCa risk	Detection	LASSO, RF	886 single-nucleotide polymorphism s	N/A	N/A	N/A	N/A	No
Pan[114]	Other/m ultiple disease states	To assess the association of pathway (set of genes) and phenotype in bladder cancer from a population based genetic study	Detection	synthetic feature RF	Genotyping data (sets of single nucleotide polymorphism s were converted into synthetic features)	N/A	N/A	N/A	N/A	No

Batista da Costa[123]	MIBC	To predict if bladder cancer is NE-like, a high risk subgroup, from transcriptome wide gene expression data		RF	Transcriptome-wide expression profiles	TCGA: 45% LUND: 45.8%	N/A	N/A	N/A	No
Rosser[130]	Bladder cancer	gene expression profiling from shed urothelium to detect bladder cancer	Detection	feature selection algorithm they derived	gene expression profiling from exfoliated urothelia	76%	90%	65%	N/A	Yes
Tang[168]	Other/multiple disease states	To classify bladder cancer into subtypes based on stem cell gene sets, and test how different subtypes respond to chemotherapy/immunotherapy	Other	K-means clustering	4876 differential genes	N/A	N/A	N/A	N/A	No
Kouznetsova[183]	Other/multiple disease states	To identify metabolites and biomarkers associated with early or late stage bladder cancer from urine samples	Staging	Multilayer Perceptron (MLP) and Stochastic Gradient Descent (SGD)	Early/Late Stage Metabolite Profile from Urine Samples	82.54%	N/A	N/A	N/A	No
Batista da Costa[190]	MIBC	To identify patients with NEBC, a subgroup within MIBC, from	Other	Unsupervised Hierarchical Clustering, Random Forest	Whole-transcriptome RNA sequencing	100%	N/A	N/A	N/A	No

		finding predictive biomarkers in transcriptome wide expression profiles on MIBC tumors			from microarray data, which was normalized					
Alanee[191]	Other/multiple disease states	To predict the presence of Bladder Cancer from applying genetic analysis on single-cell flow cytometry on urine samples	Detection	Advanced Genetic Algorithm (uses RF)	50 high grade, cystoscopy confirmed, superficial bladder cancer patients + 15 healthy donor early morning urine samples	N/A	98%	80%	0.9	No
Loeffler[204]	MIBC	Predict the mutations of the FGFR3 gene	Other	Deep learning network (DeepHistology)	digitized slides of muscle-invasive bladder cancers stained with hematoxylin and eosin	N/A	N/A	N/A	0.625	Yes
Studies using AI for prognosis										
Kim[1]	NMIBC	whether genetic signature expressed by specific molecular subtypes of NMIBC can predict prognosis	Treatment response, Survival, Progression, Recurrenc	novel prediction model (based on DBN algorithm)	genetic profile of subtypes of NMIBC (ex. DP.BCG+, REC.BCG+, EP)	N/A	N/A	N/A	N/A	No

		and response to CBG treatment	e							
Urbanowicz[8]	Bladder cancer	investigate relationship b/w DNA repair gene SNPs, smoking and BCa susceptibility in 355 cases and 559 controls enrolled in a population-based study of BCa	Recurrence, Survival	attribute-feedback supervised classifier system (AF-UCS)	seven SNPs that were previously related to BCa, age, gender, smoking hx, tumor stage and grade, age at diagnosis (yrs), survival time in years (survivorship), time to first recurrence in years	69.68%	N/A	N/A	N/A	No
Chen[9]	Bladder cancer	role of KDM6A in BCa tumor progression and outcome, role of KDM6A in regulating the anti-tumor response	Other	CIBERSORT algorithm	412 samples from BC patients in the United States + 101 samples from BC patients in China	N/A	N/A	N/A	N/A	No
Zhang[19]	Bladder cancer	trying to understand the role of the tumor microenvironment in the progression of BC to develop	Survival	CIBERSORT algorithm (a deconvolution algorithm, also uses support vector	Relative abundance of 22 immune cell types and differentially expressed	N/A	N/A	N/A	N/A	No

		targeted immunotherapies for patients and improve survival		regression), ESTIMATE algorithm	genes within tumour microenvironment of bladder tumour					
Tang[20]	Bladder cancer	identify metabolic genes involved in bladder cancer that can act as biomarkers and metabolic targets for therapies	Survival	cluster analysis, K means clustering (Unsupervised), CIBERSORT algorithm, ESTIMATE algorithm	1734 metabolism-related genes in bladder cancer samples	N/A	N/A	N/A	>0.63	No
Mitra[29]	MIBC	genomic classifiers to predict patients with MIBC who are at risk of recurrence post cystectomy, created a 15-marker genomic signature that identifies patients at greatest risk of recurrence	Recurrence	RF model	Transcriptome-wide expression profiles from 1.4 million feature-arrays on archival tumours	N/A	N/A	N/A	0.86	Yes
Poirion[32]	Bladder cancer	to identify the survival subtype (gene signature) of patients with bladder cancer	Survival	DeepProg is a deep learning (autoencoder) pipeline: unsupervised learning	used the training dataset obtained from TCGA with three types of omics: mRNA, miRNA and	NA	N/A	N/A	N/A	No

					methylation. For each omic, they constructed an individual autoencoder to produce new features linked to survival					
Yates[40]	Bladder cancer	epigenetic predictive models that look at gene promoter methylation to predict tumor progression in BCa pts	Progression	neuro fuzzy models (NFM)	Loci on 17 gene promoters suspected to be associated with tumour progression	90%	75%	97%	N/A	No
Mitra[50]	mBC	predicting nodal metastasis	Progression	genetic programming (supervised learning)	quantitative gene expression profiles of primary tumour tissue	81%	60%	90%	N/A	No
Chu[68]	mUC, UC	to determine tumour microenvironment signatures associated with poor overall survival and response to immunotherapy	Survival, Treatment response	ConsensusClusterPlus (unsupervised clustering)	tumour microenvironment patterns	N/A	N/A	N/A	1 year survival: 0.747 2 year survival: 0.805 Immunotherapy: 0.687 - 0.826	No

Xu[70]	Bladder cancer	to design a prediction model combining TME-related gene signatures and patient clinical characteristics and develop a nomogram to forecast the prognosis of BCa patients at 1, 3, and 5 years.	Survival	LASSO, non-negative matrix factorization (NMF) algorithm	tumour microenvironment genes	N/A	N/A	N/A	Training set: 1 year: 0.818 3 years: 0.776 5 years 0.771	No
Yin[71]	Other/multiple disease states	developed a 13-mRNA gene signature to predict disease progression from NMIBC to MIBC	Progression, Survival	LASSO	73 differentially expressed genes	N/A	N/A	N/A	Validation Dataset: 0.858, 0,761 (grade)	No
Kang[72]	Other/multiple disease states	to create a prognostic nomogram to predict overall survival at 3,5,8 years	Survival	logistic regression ML, LASSO	RNA sequencing data of 411 primary BLCA samples and 19 normal solid tissue samples	N/A	N/A	N/A	0.699	No
Dai[74]	Bladder cancer	to predict overall survival in pts with BCa	Survival	logistic regression, LASSO	5 differentially expressed genes	N/A	N/A	N/A	0.664	No
Mao[77]	Bladder cancer	to distinguish high vs low risk BCa patients with	Survival	random survival forest variable	49 long noncoding RNA	N/A	N/A	N/A	0.871	No

		different disease specific survival or overall survival outcomes		hunting algorithm, k means clustering	expression profiles					
Lopez de Maturana[86]	NMIBC	To investigate the predictive ability of common SNPs for the progression of NMIBC to MIBC	Recurrence, Progression	Bayesian LASSO	clinico-pathological prognosticators + SNP data	N/A	N/A	N/A	N/A	No
Wang[91]	Bladder cancer	generated risk score that correlates with OS and DFS	Survival	LASSO	genes associated with survival	N/A	N/A	N/A	0.75	No
Fan[97]	mUC, UC	identify alternative splicing clusters associated with overall survival and disease-free survival	Survival	ConsensusClusterPlus (unsupervised clustering)	10 alternative splicing events	N/A	N/A	N/A	0.8965976	No
Zhu[98]	Bladder cancer	To identify possible immune-related genes as prognostic factors and build a prognostic model	Progression	Lasso-penalized COX Regression	Transcriptome RNA-sequencing and clinical data	N/A	N/A	N/A	0.784	No
Chai[100]	Bladder cancer	to identify genes that affect survival of BCa patients	Survival	deep neural net: transfer learning-based Cox proportional hazards	336 patients from The Cancer Genome Atlas	N/A	N/A	N/A	N/A	Yes

				network						
Chen[103]	mBC	to create a nomogram based on prognostic genes to predict survival of metastatic bladder cancer patients	Survival, Treatment response	LASSO	gene expression data	N/A	N/A	N/A	Training Cohort: 0.815 Testing Cohort: 0.752 Combined Cohort: 0.805	No
Wessolly[109]	MIBC	to identify predictive biomarkers of therapeutic efficacy of platinum-based treatment	Survival	CNN	145 epitopes	N/A	N/A	N/A	N/A	No
Xu[117]	MIBC	To predict and stratify patients on overall survival of MIBC from DNA methylation signatures and clinicopathological data	Survival	Lasso cox regression	DNA Methylation data and clinicopathological data (age, smoking status, Tumor (T) stage, and Lymph node metastasis (N) stage.)	N/A	N/A	N/A	0.65	No
Guo[118]	Other/multiple disease states	To predict survival and progression risk from CpG methylation	Survival, Progression	Lasso Cox Regression, SVM-RFE	CpG methylation data	N/A	N/A	N/A	0.864	No

		biomarkers and uses LASSO and SVM-RFE to select them								
Khan[120]	MIBC	To predict the benefit of hypoxia-modifying therapy to radiation treatment for bladder cancer from miRNA biomarkers	Treatment response	Boruta Algorithm (RF)	miRNA expression data induced with a fold change > 1.0	N/A	N/A	N/A	N/A	No
Li[125]	Bladder cancer	predicting survival outcome, TME cell infiltration, identify molecular subtypes, and efficacy of immunotherapy	Survival, Treatment response	LASSO, random survival forest, cox regression model	46 TNF family genes	12 months: 79.0% 36 months: 81.0% 60 months: 80.0%	N/A	N/A	N/A	No
He[126]	Bladder cancer	predicting overall survival, relapse-free survival, and recurrence of BLCA based on lncRNA	Recurrence, Survival	LASSO cox regression	14 lncRNA for OS, 12 lncRNA for RFS	N/A	N/A	N/A	0.780	No
Jung[167]	NMIBC	To identify genetic biomarkers related to basal and luminal keratin expression to classify NMIBC into UROMOL	Progression	distance-based gene-expression classifier	RNA sequencing data	0.94	N/A	N/A	N/A	No

		classes								
Wang[173]	mUC, UC	To predict treatment response to immunotherapy from differential gene expression analysis	Treatment response	SVM for feature selection	RNA sequencing data	N/A	N/A	N/A	N/A	No
Chen[176]	Other/multiple disease states	To identify relevant genetic biomarkers that predict survival from RNA expression analysis	Survival	Random Forest	RNA gene expression results	N/A	N/A	N/A	0.665	No
Catto[182]	Other/multiple disease states	To predict the presence and timing of relapse using different machine learning models from experimental molecular biomarkers	Recurrence	Neuro-fuzzy Modeling, ANN, LR	Experimental biomarkers like p53, mismatch repair proteins, conventional clinicopathological data	88-95%	N/A	N/A	N/A	Yes
Bartsch[195]	mUC, UC	To predict recurrence risk within 5 years after transurethral resection from analyzing gene expression using whole genome profiling and qPCR	Recurrence	NFM	PCR generated normalized gene expression values	N/A	68.6%	61.5%	N/A	No

Cai[212]	NMIBC	predicting recurrence-free probability in patients with NMIBC	Recurrence	ANN	age, gender, number of lesions, diameter of lesions, LOH on Chr 18, stage, grade	N/A	N/A	N/A	N/A	Yes
Catto[213]	mUC, UC	predicting disease progression in NMIBC	Progression	NFM + ANN	panel of 200 progression-related genes, pick ~11/200	N/A	N/A	N/A	N/A	Yes
Bulashevska[214]	mUC, UC	To use Bayesian Networks to identify gene changes associated with UC tumourigenesis	Progression	Bayesian Network	Papillary UC Tumours and DNA extractions from tissue samples	90.1%	N/A	N/A	N/A	No
Hepburn[223]	MIBC	predict treatment response to neoadjuvant chemotherapy in MIBC pts	Treatment response	RGIFE (ranked guided iterative feature elimination), which uses random forest	microarray gene expression data (9 gene signature)	100%	N/A	N/A	N/A	No
Studies using AI for diagnosis and prognosis										
Grivas[28]	MIBC	genomic classifier to identify tumors with NE-like transcriptomic profile, also did survival analysis of	Detection, Survival, Treatment response	RF model	Formalin-fixed, paraffin-embedded tumor tissue was used for whole	N/A	N/A	N/A	N/A	No

		patients with NE-like tumors that saw they had very poor outcomes compared to non-NE-like patients, also looked at patient's response to therapy			transcriptome analysis with GeneChip1 Human Exon 1.0 ST Array (Affymetrix) in a Clinical Laboratory Improvement Amendments certified laboratory (Decipher Biosciences [15]). Microarray data were normalized and genes summarized using single-channel array normalization. the model generates molecular subtypes using MIBC tumor transcriptomes					
Sathipati[57]	Bladder cancer	developed a survival time estimator called BLC-SVR to estimate the survival in BLC	Detection, Survival	support vector regression (SVR), an optimal feature selection algorithm	106 miRNA expression profiles of patients with BLC from The Cancer	75.60%	N/A	N/A	N/A	No

		patients using miRNA expression profiles. also wanted to see if an miRNA signature identified by their model was useful at diagnosing BCa		called IBCGA	Genome Atlas (TCGA) database. Each miRNA profile consisted of 485 miRNAs which were the variables for survival estimation					
Modlich[58]	Other/multiple disease states	to identify genes involved in BCa progression (NMIBC->MIBC->metastatic disease)	Detection, Progression	two-way clustering algorithm (unsupervised)	gene expression profiles	N/A	N/A	N/A	N/A	No
Sapre[113]	Other/multiple disease states	To predict the presence of bladder cancer for diagnosis and recurrence from miRNA biomarkers in urine	Detection, Recurrence	SVM, using miRanda, miRDB, miRWalk, RNA22 and TargetScan	RNA sequencing data from urine	N/A	88%	48%	0.74	No
Hecker[119]	Other/multiple disease states	To classify tumor staging and progression from miRNA-mRNA interactions using RNA analysis	Staging, progression	k nearest shrunken centroid classifier	Normalized miRNA and mRNA expression data	N/A	83-93%	94-99%	N/A	No
Lauss[142]	mUC, UC	to predict urothelial cancer stage, grade, and survival in	Staging, Grading, Survival	SVM and nearest centroid	28 gene expression profiles	Stage: 72-89% Grade: 75-86% Survival: 51-	N/A	N/A	N/A	No

		independent gene expression data sets.		classifier		63%				
Abbod[189]	Other/multiple disease states	To predict progression, staging, and grading through identifying relevant genetic changes from gene expression profiles	Staging, Grading, Progression, Recurrence	NFM, ANN, Logistic Regression	Gene Expression Profiles, of RNA expression results from tissue microarray analysis	100%	45-100%	0-30%	N/A	Yes
Alkanhal[196]	Bladder cancer	predicting grade, stage, progression, relapse, and time to progression	Staging, Grading, Progression	ANN	gene expression profile of 6117 genes	N/A	N/A	N/A	N/A	No

NMIBC = non-muscle invasive bladder cancer
MIBC = muscle invasive bladder cancer
mUC = metastatic urothelial carcinoma
UC = urothelial carcinoma

*Citations included can be found in Appendix G

Appendix D. Studies that applied artificial intelligence in urothelial cancer using clinicopathological data

1st Author	Disease State	Specific Application	Type of Diagnosis/ Prognosis	AI Model(s) Used	Features	Accuracy	Sensitivity	Specificity	Area under the curve (AUC)	Comparison with non-AI Models
Studies using AI for diagnosis										
Tokmakci[82]	MIBC	To estimate muscle invasive disease in transitional cell carcinomas	Staging	ANN	1. age; 2. sex; 3. pelvicalyceal dilatation (detected in excretory urography); 4. maximum size of the tumor detected on ultrasound, regardless of tumor asymmetry and multiplicity, and; 5. location of tumor base	N/A	100%	96.10%	N/A	No
Lo[157]	Bladder cancer	To apply AI to predict potential variables that lead	Detection	C4.5, Random Forest, SVM, MLP, Logistic	Select features based on patient	85.9%	84.3%	85.8%	0.871	No

		to delayed diagnosis of BCa with patients dealing with hematuria		Regression	characteristics, cysto after hematuria, hospital characteristics, visiting behavior, and physician characteristics					
Yu[165]	MIBC	To propose a DL based model to improve segmentation accuracy of IW, OW, and BT	Segmentation	Cascade augmentation U-Net (CNN)	T2-Weighted MRI scans	N/A	N/A	N/A	N/A	No
Bhambhvani[200]	Bladder cancer	Comparing the performance of ANN, a type of machine learning algorithm, with that of multivariable Cox proportional hazards models in the prediction of 5-year disease-specific survival (DSS) and overall survival (OS) in patients with bladder cancer	Survival	Cox Proportional Hazards, ANN	age, sex, race, grade, SEER stage, tumor size, lymph node involvement, degree of extension, and surgery received	N/A	N/A	N/A	0.81	No
Tsai[210]	Bladder cancer	Machine Learning used to analyze	Detection	Decision Tree, SVM, Random	31 different clinical data	87.6%	89.5%	85.5%	0.932	No

		Clinical Lab Data and Predict bladder cancer		Forest, XGBoost, Light Gradient Boosting Machine	points					
Studies using AI for prognosis										
Ji[2]	Bladder cancer	identify significant prognostic marker sets for predicting death from BLCA, compare ANFIS to logistic regression and MLP neural networks	Survival	ANFIS (adaptive network-based fuzzy inference system), uses fuzzy c-means; MLP (multi-layer perception) neural network	histological type, tumour grade, lymph nodes, bilharziasis history, tumour stage, DNA ploidy, gender, age	N/A	89.5%	80.7%	N/A	Yes
Ji[3]	Bladder cancer	identify significant prognostic marker sets (clinical and pathological features) for predicting disease-free survival and death within 5 years of diagnosis	Survival	RBF network (radial basis function)	histological type, tumour grade, lymph nodes, bilharziasis history, tumour stage, DNA ploidy, gender, age interval	62.7%	67.1%	57.9%	N/A	No
Kirk[4]	MIBC	identify differences in postop lab values between readmitted vs. nonreadmitted patients following	Recurrenc e	SVM (support vector machine), random forest regression algorithm	age, BMI, Charlson comorbidity score, marital status, gender, race,	N/A	N/A	N/A	0.68	Yes

		radical cystectomy			insurance, CBC, basic metabolic panel (Na, K, Cl, bicarbonate, BUN, creatinine, glucose), coagulation studies (PT, PTT, INR), postop complications					
Vukicevic[17]	Bladder cancer	try to make reliable ANNs to predict advanced BC in pts undergoing radical cystectomy	Progression	ANN	parameters: a type of ANN objective function, # of neurons in hidden layer, type of activation functions in layers, portion of data used for training, testing and validation, learning algorithm and learning momentum	86.8%	87.5%	84.6%	90.8%	No
Fujikawa[47]	mUC, UC	to predict disease progression and	Progression,	ANN	tumour stage, grade, number,	N/A	100%	67%	N/A	No

		tumour recurrence within 15 years	Recurrenc e		age, gender, tumour architecture, estimates of mean nuclear volume					
Catto[49]	mUC, UC	predicting tumour progression	Progressio n	NFM, ANN, LR	tumour stage and grade, age, gender, smoking status, immunohistoc hemical expression of p53, methylation of 11 loci	100%	100%	100%	1.00	No
Klen[53]	MIBC	predict risk of early death after radical cystectomy from baseline variables (preop)	Survival	logistic regression with lasso regularization	24 Clinical Features	N/A	N/A	N/A	0.73	No
Yao[55]	mBC	predict overall survival in BCa patients with brain mets, evaluate suitable therapeutic modalities	Survival	LASSO	grade, primary surgery, chemotherapy, radiotherapy, palliative care, confined brain mets, CDCC score	N/A	N/A	N/A	0.823	No
Hasna in[56]	MIBC	predict recurrence and survival 1,3,	Recurrenc e, Survival	support vector machines	Select cluster of features	N/A	N/A	N/A	N/A	Yes

		and 5 years post-radical cystectomy to help inform patient monitoring and post-cystectomy treatment		(SVM), bagged SVM, K-nearest neighbor (KNN), adaptive boosted trees (AdaBoost), random forest (RF), and gradient boosted trees (GBT)	based on preoperative and operative (radical cystectomy) assessments, demographics, clinical diagnostic info preop, tumour marks, and pathologic and surgical data at time of cystectomy including adjuvant therapy treatment info					
Catto[67]	mUC, UC	To determine the recurrence risk of Nonmetastatic Urothelial Cancer after Radical Cysectomy	Treatment response	Neurofuzzy model	Gender, Pathologic Stage, Pathologic Grade, Carcinoma in situ , Lymphovascular Invasion	84%	81%	85%	N/A	No
Kolasa[81]	MIBC	to predict if patients with bladder cancer post cystectomy would survive the time period of 5 years	Survival	software neural network	sex, age, T, G, # of removed lymphnodes, # of positive lymphnodes	N/A	N/A	N/A	N/A	No

Qureshi[83]	Other/multiple disease states	to predict cancer recurrence (within 6mo of diagnosis) and stage progression in patients with Ta/T1 BCa (NMIBC) and to predict 12 mo survival in patients with T2-T4 BCa (MIBC)	Recurrence, Progression, Survival	ANN	progression: tumor stage, grade, size, number, EGFR status. recurrence and survival: smoking habit (Y/N), histology of mucosal biopsies, presence of concomitant cis (Y/N), tumor metaplasia (Y/N), tumor architecture, tumor site, c-erbB2 and p53 status	82%	100%	78%	N/A	No
Lam[84]	Bladder cancer	To use ANN to predict the 5-year mortality of radical cystectomies	Survival	ANN	Age, Tumor Stage, Albumin level, Surgical Approach	72.64%	N/A	N/A	N/A	No
Lee[94]	NMIBC	predicting tumour recurrence, progression, and survival (RFS and PFS)	Recurrence, Progression, Survival	SVM	age, smoking history, urine cytology, prostate volume, intravesical prostate	N/A	N/A	N/A	0.749	No

					protrusion, tumor stage, tumour grade, tumour size, number of tumours, CIS, BCG					
Ji[102]	Bladder cancer	to predict survival: is a patient alive and free of disease or is the patient dead within 5 years of diagnosis	Survival	ANN: radial basis function neural nets	histological type, grade, lymph node status, Bilharziasis history, stage, DNA Ploidy, gender, age interval	85%	N/A	N/A	N/A	No
Kolasa[108]	Bladder cancer	to determine prognostic factors for overall survival in bladder cancer	Survival	self-organizing Kohonen neural networks (unsupervised clustering)	sex, age, tumour stage, tumour grade, nonclassic differentiation number, positive lymph nodes, surgically removed lymph nodes	N/A	N/A	N/A	N/A	No
Buchner[127]	Other/multiple disease states	predicting tumour recurrence, cancer-specific mortality, and all-cause death following RC with pelvic lymph node	Recurrence, Survival	ANN	age, gender, tumour stage and grade, CIS, pathological lymph node	75.9%	37.9%	90.7%	N/A	Yes

		dissection			status, and lymphovascular invasion					
Ji[135]	Bladder cancer	predict disease recurrence + mortality within 5 yrs of diagnosis based on best feature subset and based on bilharziasis history	Recurrence, Survival	RBF network	histology, tumour grade, lymph nodes, bilharziasis history, stage, DNA ploidy, sex, age interval	70.37%	75%	69.57%	N/A	No
Obajemu[140]	Bladder cancer	to predict survival and risk (high vs low risk of mortality) of patients with BCa to help guide tx decisions and management.. model should be able to provide recommendations for risk management	Survival	fuzzy logic systems (FLS)	2918 patients from BCa patients at the Royal Hallamshire Hospital in Sheffield	N/A	N/A	N/A	0.91	Yes
el-Mekresh[141]	MIBC	to predict 5 yr survival post radical cystectomy	Survival	ANN	age, sex, bilharziasis, histology, tumour grade, tumour stage, lymph nodes, lymphovascular invasion, type of urinary	N/A	N/A	N/A	0.86	Yes

					diversion					
Bassi[197]	MIBC	estimating overall 5-year survival in patients undergoing radical cystectomy for bladder cancer	Survival	Netcyst (feed-forward multilayer ANN)	age at sugery, previous BLCA, vascular invasion, lymphatic invasion, perineural invasion, prostate infiltration, concomitant prostate adenocarcinoma, neoplasm of upper urinary tract, pT stage, pathological N stage, WHO grade	76.4%	62.7%	86.1%	N/A	Yes
Abbod[201]	mUC, UC	Using both ANNs and NFMs to predict the behaviour of bladder cancer in patients	Recurrence	ANN and NFM	Analysis A & B: Stage, Age, Grade, Sex, Smoking exposures, Previous Cancers (non-TCC) B only: p53, hMLH1, hMSH2	95%	94%	96%	N/A	Yes
Abbod[202]	mUC, UC	Comparing the predictive	Progression	ANN, NFM	Analysis A: Stage, Grade,	94%-100%	88%-100%	97%-100%	N/A	Yes

		accuracies of NFM, ANN and traditional statistical methods for prediction of bladder cancer using Experimental molecular biomarkers, including p53 expression and gene methylation, and conventional clinicopathological data after treatment			Age, Sex, Smoking exposure, Previous Cancers; Analysis B-D: p53, Methylation, RARB					
Jobczyk[205]	NMIBC	Predict recurrence and progression of early-stage bladder cancer	Recurrence	Deep Neural Networks	gender, age, T stage, histopathological grading, tumor burden and diameter, EORTC and CUETO scores, and type of intravesical treatment	N/A	N/A	N/A	N/A	No
Song[217]	Bladder cancer	predict 10-year BLCA survival based on clinical factors	Survival	logistic regression model	age and sex, risk factors (cigarette smoke, high risk occupation, BMI, FHx),	76%	65%	79%	0.77	No

					muscle invasiveness, tumour histology, molecular features (p53 mutation, p53 IHC positivity, p53 IHC staining intensity)					
Abuhelwa[226]	mUC, UC	Predicting survival outcome with immunotherapy in urothelial cancer, compare expert preselected features vs. all-in list (uncurated)	Survival	GBM, random forest, Cox-boosted model, penalised generalised linear models	5 demographic factors + 9 laboratory factors + 9 disease/treatment factors	N/A	N/A	N/A	N/A	No
Studies using AI for diagnosis and prognosis										
Mengual[116]	Other/multiple disease states	To assess the diagnostic performance of published BC biomarkers (BC-116 for detection, BC-106 for recurrence) from urine samples, and compared to urine cytology	Detection, Recurrence	nomogram, SVM	Peptide extracts from urine samples	N/A	90.4%	29.1%	0.67	No

NMIBC = non-muscle invasive bladder cancer
MIBC = muscle invasive bladder cancer

mUC = metastatic urothelial carcinoma
UC = urothelial carcinoma

*Citations can be found in Appendix G

Appendix E. Studies that applied artificial intelligence in urothelial cancer using image analysis

1st Author	Disease State	Specific Application	Type of Diagnosis/ Prognosis	AI Model(s) Used	Features	Accuracy	Sensitivity	Specificity	Area under the curve (AUC)	Comparison with non-AI Models
Studies using AI for diagnosis										
Hadjiiski[6]	Bladder cancer	bladder segmentation package to identify characteristics in CTU images for bladder segmentation purposes and compare to radiologist's work	Segmentation	CLASS (Conjoint Level set Analysis and Segmentation System): computer aided detection system, 3D bladder segmentation	regions of interest on CTU slices	N/A	N/A	N/A	N/A	Yes
Lingley-Papadopoulos[10]	Bladder cancer	algorithm to classify images as noncancerous, dysplasia, carcinoma in situ, or papillary lesions, and to determine tumor invasion -> algorithm to	Detection, Staging	textural analysis, decision tree	(1) the correlation of the cooccurrence matrix with “neighbor” defined as the pixel immediately to the right, (2)	N/A	92%	62%	N/A	No

		classify tissue as cancerous vs noncancerous			the mean of the histogram, (3) the second moment of the histogram, and (4) the range of intensities in the image.					
Chai[11]	Bladder cancer	to segment the bladder for plans of a multiple-plan adaptive radiotherapy approach	Segmentation	created their own model	Training: 95 bladder contours from 8 patients Validation: 233 CBCT scans from the remaining 22 patients	N/A	N/A	N/A	N/A	No
Spyridonos[12]	Bladder cancer	algorithm to classify BCa tumors as low or high risk based on H&E stain images	Grading	Bayesian classifier	nucleus area, roundess, concavity, mean value, variance, skewness, kurtosis, the other ffeatures were computed from the co-occurence matrix (2D histogram describing the frequency with	88%	N/A	N/A	N/A	No

					which 2 adjacent pixels occur in the nucleus's image)					
Gordon [13]	Bladder cancer	DL-CNN to distinguish bladder wall from the inside and outside of the bladder -> used as a segmentation tool to segment the inner and outer wall of the bladder using CTU (CT urography) images	Segmentation	DL-CNN called Cuda Convnet	ROIs extracted from 2D slices of the training cases and labelled as within or not within the bladder wall	N/A	N/A	N/A	N/A	Yes
Cha[14]	Bladder cancer	computerized system for bladder segmentation of CT urography images to help improve computer-aided detection of BCa -> seeing how this new LCR method can improve the segmentation of bladders by CLASS (a system the researchers originally designed a few years ago)	Segmentation	conjoint level set analysis and segmentation system (CLASS)	radiologist provided manual outlines on the CT slices for all cases	N/A	N/A	N/A	N/A	Yes

Hashemi[15]	Bladder cancer	computer-aided system to diagnose blood in urine, benign and malignant masses in cystoscopy images	Detection	CNNs (VGG16, ResNet50), multi layer perceptron network (supervised learning)	local binary patterns used for feature extraction of images: input images divided into 8x8 cells with 32x32 dimensions and LBP was calculated for each cell independently, then these features are linked together to form 1 feature vector. since there was such a high number of extracted features from the medical images, the researchers used principal component analysis (PCA) for feature reduction	54.37%	N/A	N/A	N/A	No
Lazo[16]	UTUC	using 4 CNNs in parallel to segment the ureter's lumen	Segmentation	CNN	11 videos from 6 patients undergoing ureteroscopy	N/A	N/A	N/A	N/A	Yes

					procedures were used, all models were trained at minimizing the loss of function based on the dice similarity coefficient where TP is the # of pixels that are in the lumen, FN is the # of pixels miss-classified as lumen, and FN is the # of pixels classified as part of lumen but actually they were not					
Gosnell[21]	Bladder cancer	creating a triage system to analyze cystoscopy images to determine if further assessment is needed (assign priority to diff patients based on if malignant disease is present or not)	Detection	unsupervised segmentation system	cystoscopy images with biopsy pathology report	N/A	N/A	N/A	N/A	No
Emina	Bladder	diagnostic	Detection	neural network	digital atlas for	99.52%	N/A	N/A	N/A	No

ga[22]	cancer	classification of cystoscopic images using DL models: these models were able to distinguish carcinoma in situ from cystitis or interstitial cystitis		models: ResNet50, VGG-19, VGG-16, Inception V3, Xception; also developed 2 deep CNNs	cystoscopy which has 44 different cystoscopic findings					
Xu[27]	Bladder cancer	noninvasive tumor staging using MRI images of patients already diagnosed with BCa	Staging	SVM, RF classifier	To further characterize visual perceptive pattern of bladder tumors, six 3D Tamura features that reflect the coarseness, contrast, directionality, line-likeness, regularity and roughness of a region were also extracted from the intensity map of each VOI. In summary, a total of 58 3D texture features of four groups, including 26 GLCM	89%	90%	88%	0.94	No

					features (f1-f13 and Rf1-Rf13 represent the mean and range values of 13 Haralick features, respectively), 13 GLGCM features (Gf1-Gf13), 13 GLCCM features (Cf1-Cf13) and 6 Tamura features (Ta1-Ta6), were extracted from each VOI					
Pantazopoulos[31]	mUC, UC	using NNs to distinguish benign from malignant cells and lesions of the lower urinary tract. compares performance of 2 different neural networks	Detection	Two NNs: back propagation and learning vector quantization (LVQ)	25 features extracted by the measurement system	97%	N/A	N/A	N/A	No
Freitas[34]	Bladder cancer	see how well CapsNet could classify BCa in white light cystoscopy images when compared to	Detection	DL model that may be more appropriate for small datasets: capsule neural networks	Histogram of oriented gradients (HOG) to capture info about edges	96.9%	N/A	N/A	N/A	No

		other deep learning approaches			and corners, local binary patterns (LBP) to extract rotation invariant texture features, wavelet transform (WT) plays a role in compression of medical images, image denoising, image enhancement, tomographic reconstruction, and feature extraction. inputs are the HOG features (for color and local shape info, more specificially fine texture encoding), LBP features (for texture encoding) and wavelet features (for color and					

					texture encoding) which all feed into the final classifier					
Spyridonos[35]	Bladder cancer	to classify urinary bladder carcinomas as high or low-risk based on the WHO grading system	Grading	support vector machines (SVM), probabilistic neural nets (PNN)	morphological features (nuclear sizae and shape distribution), textural features (nuclear chromatin organization), PNN: 3 morphological features (nuclear concavity, range of roundness, SD of area) and 1 textural feature (the cluster shade for inter-pixel distance d=1). SVM: 2 morphological features describing nuclear shape distribution (range of area and SD of	85.3%	N/A	N/A	N/A	No

					area) and 2 textural features (cluster shade for inter-pixel distance d=1 and d=3)					
Li[45]	Other/multiple disease states	classifying invasive and noninvasive bladder cancers based on cystoscopic images	Staging	CNN and SVM	Cystoscopic image	88.24%	N/A	N/A	N/A	No
Zhou[46]	Other/multiple disease states	classify medical images of bladder tumours to measure degree of tumour infiltrating bladder wall	Staging	ResNet, EvidentialNet, DenseNet, RuleNet (all DCNN)	MR images of bladder cancer	72.14	N/A	N/A	N/A	No
Eminaga[51]	Bladder cancer	Computer-aided diagnosis of bladder cancer on cystoscopic images	Detection	DCNN models (ResNet50, VGG-19, VGG-16, InceptionV3, and Xception)	Cystoscopic Images	99.52%	99.52%	N/A	N/A	No
Sokolov[54]	Bladder cancer	evaluates cells from urine to detect bladder cancer, compared with cystoscopy	Detection	random forest, extremely randomized forest, gradient boosting trees	Surface parameters of urine cells, found in SI Appendix 6	94%	81%	98%	0.91	Yes
Liu[62]	Bladder	to segment the	Segmentat	SVM	intensity and	99.99%	99.98%	100%	1.00	No

	cancer	cancer region and then measure the invasion depth of bladder cancer	ion, Staging		texture features					
Ge[63]	Bladder cancer	to segment the bladder to detect tumors	Segmentat ion	MD-Unet: CNN	MRI images	N/A	N/A	N/A	N/A	No
Cha[65]	Bladder cancer	to achieve better bladder segmentation compared to the researchers previous models	Segmentat ion	DL-CNN	input regions of interest on CT images. edge features, line features, 4 rectangel features	N/A	N/A	N/A	N/A	No
Kaneko[87]	mUC, UC	Using a CNN that classifies urine cell images as negative or positive for urothelial cancer	Detection	CNN	Urine cell images	95%	96.70%	95%	0.99	Yes
Niazi[92]	NMIBC	automated image analysis to recognize major anatomical structures from bladder biopsy images	Segmentat ion	modified U-net (CNN)	whole slide H&E images of T1 bladder biopsies	89.3%	N/A	N/A	N/A	No
Freitas[96]	NMIBC	classifying bladder cancers (staging)	Detection, Staging	RBF networks, VGG16, ResNet-34, CapsNet	cystoscopic image features (ex. color, gradient, texture)	96.9%	N/A	N/A	N/A	No

Cha[101]	Bladder cancer	to detect bladder masses fully or partially within the contrast enhanced region of the bladder	Detection	linear discriminant classifier	normalized radial length area, rectangularity, area, average gray level, and two contrast features	N/A	84.9%	N/A	N/A	No
Chai[105]	MIBC	to segment the bladder and test the model's ability to pick the appropriate plan from a library of plans for a multiple plan adaptive radiotherapy	Segmentation	developed own model	cone-beam CT scans	N/A	N/A	N/A	N/A	No
Awan[106]	mUC, UC	to identify malignant and atypical cells in urine cytology to help determine high vs low risk of malignancy and thus predict risk of diagnosis	Detection	CNN: Xception model, RetinaNet	398 cytology slides	N/A	N/A	N/A	N/A	Yes
Papageorgiou[110]	Other/multiple disease states	creating a model for tumor grading	Grading	fuzzy cognitive map grading tool (FCM-GT)	8 Histological Features	95.55%	N/A	N/A	N/A	No
Lebret[121]	Other/multiple	To predict the presence of bladder	Detection	VisioCyt (uses resnet based	Fluorescence contrast urine	N/A	84.9%	81.2%	N/A	No

	disease states	cancer for diagnosis from urine cytology (fluorescent slide images), compared with experts		network (CNN))	slides					
Vriesema[124]	Other/multiple disease states	To predict the presence of Bladder Carcinoma from bladder wash samples (Papanicolaou stained image slides)	Detection	Scanner that uses Neural Network	Selected Digitized Cell Images from Bladder Wash	92%	N/A	N/A	N/A	No
Hu[132]	Bladder cancer	to distinguish between cancer and non cancer cells via bladder cell images	Detection	single hidden layer feed-forward NN with error back-propagation, c-means (fuzzy and non-fuzzy)	cellular area, average intensity, texture, and shape factor	N/A	N/A	N/A	N/A	No
Wettel and[133]	NMIBC	create a novel pipeline for tissue segmentation and accurate grading of NMIBC tissue via whole-slide images	Segmentation, Grading	CNN	ROIs following segmentation of whole-slide images of bladder + cancer tissue	90%	85%	100%	N/A	No
Muralidaran[136]	mUC, UC	ANN to diagnosis and grade UC based on urine	Detection, Grading	ANN	nuclear area, nuclear perimeter,	100%	N/A	N/A	N/A	No

		cytology features			nuclear diameter, SD of nuclear area, integrated gray value					
Cao[138]	Other/multiple disease states	to predict bladder tumor stage and grade using MRI images	Staging, Grading	SVM	morphological features, texture features	82%	N/A	N/A	N/A	No
Ikeda[145]	Bladder cancer	to detect bladder tumors from cystoscopic images with an accuracy comparable to that of a urologist	Detection	CNN	2102 cystoscopic images	97.20%	95.40%	97.60%	0.98	No
Gavriel[150]	MIBC	to improve the accuracy of 5 year prognosis for MIBC patients compared to the gold standard, TNM staging	Staging	linear SVM, decisions tree (DT), linear regression (LR), RF, k nearest neighbours (KNN)	126 imaging features, 60 spatial features, 15 clinical features	80.0%	100%	71.4%	N/A	Yes
Yang[153]	Bladder cancer	Study uses 4 different convolutional neural networks to recognize bladder tumours based on cystoscopic images	Detection	CNN (LeNet, AlexNet, GooLeNet and EasyDL)	Cystoscopic Images	96.9%	N/A	N/A	N/A	Yes

Garcia[155]	MIBC	A Deep Convolutional Embedded Attention Clustering that classifies histological patches into different levels of disease	Grading	Deep Convolutional Clustering Algorithm	Histological Patches - More detail not given	90.34%	85.51%	92.75%	0.8775	No
Du[158]	Bladder cancer	To create a DL network that can recognize bladder cancer based on cystoscopy images	Segmentation	AlexNet Model (CNN)	Cystoscopy Images	96.90%	96.80%	N/A	N/A	No
Lilli[159]	mUC, UC	Proposing a DL-NN to detect BCa from urinary cytopathology images	Detection	Neural Network	Urinary Cytopathology screening images	89.90%	N/A	N/A	N/A	No
Ma[164]	Bladder cancer	To develop a U -Net based deep learning approach (U -DL) for bladder segmentation in computed tomography urography (CTU) as a part of a computer -assisted bladder cancer detection and	Segmentation	U-net Deep Learning Model	CT Images	N/A	N/A	N/A	N/A	No

		treatment response assessment pipeline								
Woerl[170]	MIBC	To predict if MIBC is a molecular subtype from images of histopathology HE stained whole slides	Other	RNN	Digitized augmented histopathology slides of tumor tissue	N/A	N/A	N/A	N/A	No
Lorencin[171]	Other/multiple disease states	To diagnose bladder cancer from bladder flexible cystoscopy images	Detection	MLP	Images of flexible cystoscopy bladder images, with diagnosis confirmed by biopsy	N/A	N/A	N/A	0.99	No
Yin[172]	Other/multiple disease states	To differentiate NMIBC and MIBC (superficially invasive Ta) from histopathological slides stained by hematoxylin and eosin	Staging	PNN, SVM, LR, MLP	Images of Histopathological slides stained by hematoxylin and eosin, with features of desmoplastic reaction, retraction artifact, and abundant pinker cytoplasm	91-96%	N/A	N/A	N/A	No

Xu[174]	Other/multiple disease states	To predict staging of bladder cancer from CT images	Staging	DCNN	features of tumor regions or bladder wall regions	N/A	N/A	N/A	N/A	No
Lucas[175]	Other/multiple disease states	To predicting bladder cancer grading and presence from probe based confocal laser endomicroscopy frames	Grading, Detection	LSTM RNN	Frames of probe based confocal laser endomicroscopy	82%	N/A	N/A	N/A	No
Sanghvi[177]	Other/multiple disease states	To diagnose bladder cancer from urine cytology slides	Detection	CNN	TPSRUC cytomorphological features (N/C ratio, hyperchromasia, chromatin coarseness, and nuclear membrane irregularity), cell degradation and overall malignancy	84.2%	79.5%	84.5%	0.88	No
Dolz[178]	Other/multiple disease states	To conduct automatic multiregion segmentation on bladder cancer walls and tumors from MRI images	Segmentation	Dilated CNN	Delineated images of MRI images of the bladder, done by experts	N/A	N/A	N/A	N/A	No

Spyridonos[181]	Other/multiple disease states	To predict grading of bladder cancer from stained tissue sections	Grading	ANN	36 nuclei features from stained bladder tissue sections	95%	N/A	N/A	N/A	No
Wu[184]	Other/multiple disease states	To detect Bladder Cancer with short latency from bladder cystoscopy images	Detection	CAIDS parsing network	Bladder Cystoscopy Images	93.9%	95.4%	N/A	N/A	No
Nojima[188]	mUC, UC	To identify malignant potential and diagnose urothelial carcinoma cells as invasive/non-invasive, high/low grade from Papanicolaou-stained urinary cytology glass slides	Grading, Staging	VGG (CNN)	Papanicolaou-stained urinary cytology glass slides	95.36%	90.51%	96.82%	0.8953	No
Jansen[192]	NMIBC	To predict the grade of NMIBC using ML from digitized transurethral resection specimens	Grading	U Net Based Segmentation Network, VGG	Digitized transurethral resection specimens of the urothelium (annotated by experts)	76%	71%	76%	N/A	No
Harmon[193]	MIBC	To identify patients with lymph node metastasis from cystectomy tumor	Staging	CNN	digital pathology images, only regions	71.1%	N/A	82.6%	0.755	No

		sample images			containing tumor from the bladder cystectomy specimens					
Segota[198]	Bladder cancer	Using CNN and a Transfer Learning approach to the semantic segmentation of CT images	Segmentation	CNN	CT images captured in frontal, axial and sagittal frames	N/A	N/A	N/A	0.9999	No
Zhang[216]	mUC, UC	Evaluate Morphogo (digital scanning instrument) for urine cytological diagnosis of UC	Detection	CNN	morphological features of abnormal urothelial cells (N:C ratio>0.7, hyperchromasia)	N/A	N/A	N/A	N/A	No
Lorencin[218]	Bladder cancer	GAN-based image data augmentation for urinary bladder cancer diagnosis	Detection	deep convolutional generative adversarial networks (DCGAN), CNN (AlexNet and VGG16)	cystoscopic images	N/A	N/A	N/A	0.99	No
Liu[227]	NMIBC	To improve image resolution and support prediction of bladder tumour stage from CT urograms	Staging	Deep learning (Bicubic, SRCNN, FSR CNN, VDSR, DRCN, LapSRN, and	CT data of 75 bladder patients	N/A	94.74%	N/A	N/A	No

				DRRN)						
Studies using AI for prognosis										
Cha[37]	Bladder cancer	to calculate change in tumor size of BCa patients in response to neoadjuvant chemotherapy	Treatment response	DL-CNN	region of interest on CT	N/A	N/A	N/A	0.73	Yes
Harmon[41]	MIBC	to identify MIBC patients with lymph node metastases based on the evaluation of primary tumors (histologic appearance and features of digital pathology slides)	Progression	Four different models using ResNet-101 architecture, AdaBoost	For multivariable analysis, a final model was constructed by using the following input variables: age, disease stage, presence of high-risk histology, lymphovascular invasion (LVI), and number of LNs excised (Table 2). After backward Akaike information criterion	71.1%	N/A	84.5%	N/A	Yes

					selection, the final multivariable model included age, T stage, and the presence of LVI.					
Kimura [59]	MIBC	to use texture features to predict chemoradiotherapy response of MIBC patients	Treatment response	Random forest (RF) and support vector machine (SVM)	five conventional indexes (mean, first quartile (Q1), second quartile (Q2), third quartile, and standard deviation of gray levels); six first-order histogram indexes (skewness, kurtosis, excess kurtosis, entropy log10, entropy log2, and energy); three first-order shape indexes (compacity, volume in mL, and volume in voxels); and 32	89%	86%	91%	0.96	No

					second-order features from the gray-level co-occurrence matrix (GLCM), the neighborhood gray-level different matrix (NGLDM), the gray-level run-length matrix (GLRLM), and the gray-level zone length matrix (GLZLM).					
Shao[60]	NMIBC	to see if BCa patients recover better from surgery using normal health monitoring (controls) vs extended health monitoring (cases)	Other	deep CNN	3D Ultrasound Images from 60 patients	N/A	N/A	N/A	N/A	No
Nguyen[79]	MIBC	to predict response to chemo in MIBC patients	Treatment response	K means clustering	3T dynamic contrast enhanced magnetic resonance imaging of 30 patients	97%	96%	100%	0.96	No

Lin[115]	Other/multiple disease states	To predict survival for bladder urothelial carcinoma from transcriptome data, CECT images, and clinical data	Survival	nomogram, wgcna, lasso cox regression (ML)	CECT scan images of bladder, Transcriptome Data, Clinicopathological Data (age over 65 or under, gender, race, ajcc stage, tumor stage, lymph node metastasis)	N/A	92.8%	89.6%	0.956	No
Wu[144]	MIBC	DL-CNN to look at bladder CT images to monitor BCa tx response (predict the effectiveness of various BCa tx options)	Treatment response	DL-CNN	6209 region of interests from pre- and post-chemo CT	64.1% - 78.9%	41.7% - 75%	80%	0.86	No
Tasoulis[148]	Other/multiple disease states	to predict recurrence of superficial bladder cancer	Recurrence	Feed forward NNs, unsupervised K-windows, fuzzy c-means clustering	morphological and textural nuclear features (morphological: nuclear area, roundness, concavity)	91.77%	92.83%	90.43%	0.936	No
Ying[149]	MIBC	to predict overall survival of patients post-radical cystectomy	Survival	CNN	299 CT studies	N/A	N/A	N/A	N/A	No

Cai[151]	NMIBC	to predict recurrence post TUR-BT	Recurrence	ANN	sex (male or female), age (<65 or ≥65 years), previous histopathological data (pTaG1, pTaG2 or pTaG3), previous recurrence rate (1 recurrence/year, 2 recurrence/year, 3 or more/year), response to previous Bacille Calmette-Guérin adjuvant therapy (yes or no), number of lesions (single or multiple), size of lesions (1,2,3,4,5 or more), presence of tumor associated inflammatory reaction (yes	83.63%	81.67%	95.87%	0.816	No

					or no) and adjuvant therapy after TUR-BT (yes or no).					
Cha[163]	MIBC	To evaluate whether a CT-based decision system for MIBC can improve identification of patients who have responded completely to neoadjuvant chemotherapy	Treatment response	CDSS-T(Combination of DL-CNN and Radiomic features)	ROI from CT scans (both complete response and incomplete response as well as from before and after treatment)	N/A	N/A	N/A	0.8	Yes
Hadjiiski[169]	Other/multiple disease states	To predict treatment outcome of chemotherapy from pre and post chemotherapy CT scans	Treatment response	DL-CNN	91 radiomics features	N/A	N/A	N/A	0.855	No
Rundo[179]	mUC, UC	To predict treatment outcome for immunotherapy from CT images	Treatment response	3D-DCNN	CT scan images of bladder and hematochemical indicators	92.22%	92.9%	91.6%	N/A	No
Lucas[185]	NMIBC	To predict recurrence and recurrence free survival from digitized formalin-	Recurrence, Survival	VGG16 (CNN)	Digitized formalin-fixed paraffin-embedded histopathology	75%	89%	57%	0.76	No

		fixed paraffin-embedded histopathology slides			slides					
Tokuyama[187]	NMIBC	To predict recurrence of NMIBC after transurethral resection from nuclear morphological features	Recurrence	SVM, RF	Nuclear Morphologic and Textural Features	90%	N/A	N/A	N/A	No
Brieu[194]	MIBC	To predict survival from tumor budding, and to identify and quantify tumor budding from immunofluorescence labelled whole slide tissue images	Survival	CNN, Semantic Segmentation NN	TNM stage, pT stage, Lymph node status, Metastasis Grade, Growth Pattern, Treatment, Gender, Age, Number of TB in core, Number of TB in invasive front, Density of TB in core, Density of TB in invasive front, Number of TB in a single 0.785mm2 field of view, Number of TB	N/A	N/A	N/A	N/A	No

					in ten 0.785mm2 fields of view, Number of TB in ten 0.238mm2 fields of view					
Studies using AI for diagnosis and prognosis										
Chen[147]	Other/multiple disease states	to diagnose BCa using H&E slides, also to predict tumor stage (high vs low risk) and overall survival at 1,3,5 years	Detection, Staging, Survival	LASSO	nuclear pleomorphism, mitosis, carcinoma infiltration, cancer invasion, tumor cell differentiation, and pathological grading. Quantitative image features of object shape, size, texture, and pixel intensity distribution were further extracted via multiple modules, including measure	N/A	N/A	N/A	0.941	No

					models of 'Object Intensity Distribution', 'Object Intensity', 'Texture', and 'Object Size Shape'.					
Ali[199]	Bladder cancer	Four pre-trained convolution neural networks were utilized to predict image malignancy, invasiveness, and grading	Detection, Staging, Grading, Progression	CNN	216 BL images, that were acquired in four diferent urological departments and pathologically identifed with respect to cancer malignancy, invasiveness, and grading.	N/A	95.77%	87.84%	N/A	No

NMIBC = non-muscle invasive bladder cancer
MIBC = muscle invasive bladder cancer
mUC = metastatic urothelial carcinoma
UC = urothelial carcinoma

*Citations included can be found in Appendix G

Appendix F. Studies that applied artificial intelligence in urothelial cancer using other data types

1st Author	Disease State	Specific Application	Type of Diagnosis/ Prognosis	AI Model(s) Used	Features	Accuracy	Sensitivity	Specificity	Area under the curve (AUC)	Comparison with non-AI Models
Studies using AI for diagnosis										
Karemore[30]	Bladder cancer	prototype called LVQ to build a classifier that can differentiate between cancer and control patients with BCa	Detection	ANN, learning vector quantization (LVQ) is a prototype-based supervised classification algorithm	wavelengths from spectroscopy data	86.11%	N/A	N/A	N/A	No
Hu[33]	Bladder cancer	comparing the performance of using a neural network (supervised) vs fuzzy c means (unsupervised) for bladder cancer cell classification	Detection	neural network: backpropagation (supervised), fuzzy-c means clustering (unsupervised)	characteristics of cells, 4 features: area, average intensity, shape factor (roundness), and texture. also pgDNA value was used as a feature but this is not a	N/A	N/A	N/A	N/A	No

					visual property					
Parekattil[48]	Other/ multiple disease states	detection of bladder cancer	Detection	neural network	urine levels of nuclear matrix protein-22, monocyte chemoattractant protein-1, urinary intercellular adhesion molecule-1	N/A	100%	75.7%	N/A	Yes
Noone[64]	Bladder cancer	to develop an algorithm for cancer surveillance (ie, to detect unreported cases of bladder cancer) that is critical for estimating bladder cancer incidence in the United States.	Detection	classifier was built using: logistic regression, classification and regression trees (CART), random forest, support vector machines (SVM), and logic regression	age, sex, race, year of diagnosis, tumour stage, comorbidities, cancer treatment	95.4%	97.7%	99.9%	0.778	No
Pantazopoulos[75]	Other/ multiple disease states	to discriminate benign vs malignant lower urinary tract lesions	Detection	learning vector quantizer (LVQ)-type neural network (NN)	morphometric and texture features	97.57%	100%	96.6%	N/A	No
Mao[78]	Bladder cancer	to use urinary nucleosides as biomarkers for	Detection	Support vector machine based recursive	44 urinary nucleosides	95%	100%	90%	N/A	No

		BCa detection		feature elimination (SVM-RFE) and a new feature selection method called support vector machine based partial exhaustive search algorithm (SVM-PESA)						
Schroek[88]	Bladder cancer	NLP of bladder pathology reports to abstract data on histology, invasion, grade, presence of muscularis propria, and presence of CIS	Detection, Grading, Staging	NLP	text from bladder pathology reports	96%	No Cancer: 0.88 Urothelial Carcinoma: 0.98 PUNMLP:0.50 Other Histology: 0.67	N/A	N/A	Yes
Chen[111]	NMIBC	to identify tumors as high or low grade	Grading	ANN	262 spectra taken from 32 bladder specimens	93.1%	88.5%	95.1%	N/A	No
Pilchowski[122]	MIBC	To differentiate MIBC with and without metastasis from protein pattern analysis using protein chip	Detection	XLMiner using fuzzy c means clustering	Flight Mass Spectroscopy Q10 and CM10 protein expression data	N/A	63%	88%	N/A	No

		mass spectroscopy, and uses ML to select differentially expressed protein								
Ding[128]	Bladder cancer	use serum peptide profiles of BC patients and healthy volunteers for early diagnosis of BC	Detection	K-nearest neighbour	protein profile from preoperative serum samples	N/A	91.43%	90.91%	N/A	No
Murphy [137]	Bladder cancer	developed an algorithm to detect instances of delayed diagnostic evaluation in patients with hematuria and applied the algorithm to a large EHR database to identify patients at risk for bladder cancer	Detection	developed their own	100 patients clinical data within a Department of Veterans Affairs	N/A	64%	96%	N/A	No
Ikeda[161]	NMIBC	To use AI to support and improve cystoscopic diagnosis of bladder cancer	Detection	Convolutional Neural Network	Cystoscopic images (1671 images of normal tissues and 431 images of tumour lesions)	N/A	89.70%	94.00%	0.98	No
Yang[206]	Other/	predict NMIBC vs.	Detection,	NLP	patient notes					No

	multiple disease states	MIBC vs. no cancer vs. unknown based on notes	Staging		(pathology, surgical, urology)					
Wang[208]	Bladder cancer	To develop a machine learning model that classify Bladder cancer based on two-dimensional copper signatures	Detection	Random Forest	Copper isotopic composition and concentration in plasma and red blood cells	89.80%	87.80%	91.50%	0.920	No
Belugina[221]	Bladder cancer	predict "level of risk" in bladder cancer patients	Detection	CIBERSORTx, Lasso cox regression	mRNA, miRNA, lncRNA expression, DNA methylation, CNV	N/A	N/A	N/A	N/A	No
Studies using AI for prognosis										
Petalas[80]	mUC, UC	to predict cancer recurrence at different follow up times	Recurrence	probabilistic neural network	4 features: 2 describing nuclear texture, 2 related to shape distribution of nuclei in the sample were identified as important markers for	73%	N/A	N/A	N/A	No

					patients' outcome prediction					
Wang[180]	Other/ multiple disease states	To predict survival from clinicopathological datasets, comparing between different machine learning models	Survival	ELM (extreme learning machine)	Gender, Age, Albumin Level, Surgical Approach, Tumor Stage, Follow up period, type of diversion	80.0%	N/A	N/A	N/A	No
Jung[207]	mUC, UC	stratify risk in inverted urothelial papilloma	Other	Support Vector Machines	698 differentially expressed proteins	N/A	N/A	N/A	N/A	No
Weng[211]	Bladder cancer	A machine learning framework is developed to use biopsy pathology specimen to generate models of likelihood of neoadjuvant chemotherapy response	Other	SVM, Random Forest	No feature selection performed - just used clinco-pathological features	N/A	N/A	N/A	N/A	No
Zhang[222]	MIBC	potentiometric sensor response from urine sample to detect bladder cancer	Survival	random forest, extreme gradient boosting classifier, SVM, voting classifier,	24 sensor potentials in urine	73%	77%	70%	N/A	No

				logistic regression						
Chen[224]	Bladder cancer	stratify MIBC patients into subgroups at different risks of overall survival	Survival	random forest, Naive Bayes, k-Nearest Neighbor, Adaboost algorithms	gene-level CNV profile, mRNA and miRNA expression profile, DNA methylation data (total 100 features)	N/A	N/A	N/A	0.784	No
Studies using AI for diagnosis and prognosis										
Stomp-Agenant[18]	mUC, UC	urothelial carcinoma detection and grading using superficial problem measurements vs nonsuperficial probe measurements with a Raman system, seeing if a superficial vs nonsuperficial probe is better at discriminating benign from malignant tissue	Detection, Grading	data processing algorithms were developed in GNU octave version 6.1.0	biopsies that didn't contain inflammation, biopsies that could be classified by a pathologist, ~5-10 spectra were included per biopsy location. preprocessing steps: calibrate wavelengths, reject overexposed spectra, sum spectra at each tissue sample/biopsy,	N/A	90%	87%	0.95	No

					separate noise with Savitzky-Golay filter, normalize measurement by exposure time, subtract autofluorescence, divide by total autofluorescence, perform extended multiplicative scatter correction					
Frantzi[26]	Bladder cancer	two urine biomarker panels to detect presence of BCa in pts and to detect disease recurrence	Detection, Recurrence	SVM	Primary Disease: 721 patients clinical data Recurrent Disease: 636 patients clinical data	N/A	91%	68%	0.87	No
Glaser[134]	Other/ multiple disease states	NLP to auto extract stage, grade, and quality info from TURBT pathology reports	Grading, Staging	NLP	pathology reports for TURBT (date of procedure, age, sex, demographics, CIS, lamina propria, muscularis	88%	N/A	N/A	N/A	No

					propria, grade, invade, stage...)					
Schuett fort[186]	mUC, UC	To predict the survival, lymph node involvement, and upstaging after radical cystectomy from systemic inflammatory response biomarkers	Staging, Survival, Recurrenc e	LASSO least absolute shrinkage and selection operator regression	a panel of SIR biomarkers, including albumin–globulin ratio, neutrophil–lymphocyte ratio, De Ritis ratio, monocyte–lymphocyte ratio and modified Glasgow prognostic score	N/A	N/A	N/A	0.73	No
Studies using AI for other reasons										
Tan[42]	MIBC	using NLP and claims-based data to identify pts undergoing radical cystectomy for bladder cancer + characterize procedure based on surgical approach and diversion type		NLP	linguistic patterns in recorded text regarding preop diagnosis, postop diagnosis, performed procedures sections of surgeon's	N/A	98.8%	100%	100%	Yes

					operative note, professional billing records, and comments documented in OR log; combined with hospital discharge diagnosis and procedure ICD-9 codes					

NMIBC = non-muscle invasive bladder cancer
MIBC = muscle invasive bladder cancer
mUC = metastatic urothelial carcinoma
UC = urothelial carcinoma

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Appendix G. List of Included Studies

1. Kim SK, Park SH, Kim YU, et al. A Molecular Signature Determines the Prognostic and Therapeutic Subtype of Non-Muscle-Invasive Bladder Cancer Responsive to Intravesical Bacillus Calmette-Guérin Therapy. *International Journal of Molecular Sciences*. 2021;22(3):1450. doi:10.3390/ijms22031450
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