Engineered Science

Advancements in Bladder Cancer Management: A Comprehensive Review of Artificial Intelligence and Machine Learning Applications

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Abstract

Artificial intelligence (AI) and machine learning (ML) have emerged as powerful tools in the diagnosis and treatment of bladder cancer, offering significant advancements in accuracy and speed. AI algorithms have enabled precise segmentation of the bladder wall and accurate detection of bladder tumors using non-invasive 3D image-based features from CT and MRI scans. Decision support systems based on AI have improved the assessment of treatment efficacy for muscle-invasive bladder cancer. AI-assisted cystoscopy has demonstrated higher sensitivity and specificity in identifying and categorizing bladder lesions, potentially outperforming human urologists. ML algorithms, including artificial neural networks, have shown superior predictive capabilities in prognosis and outcome prediction compared to conventional models. Radiomics and ML techniques have enhanced bladder cancer staging and treatment response assessment through accurate analysis of imaging data. AI-driven biomarker discovery, including metabolomics, has the potential to revolutionize non-invasive bladder cancer diagnosis and monitoring. Automated histologic grading and molecular typing facilitated by AI have led to faster and more precise diagnoses, enabling personalized treatment plans. The integration of AI and ML in bladder cancer diagnosis has the potential to improve patient outcomes significantly. By providing faster and more precise diagnoses, AI-driven approaches can enhance treatment planning and response evaluation. Additionally, AI-assisted cystoscopy and improved biomarkers can lead to less invasive and more effective diagnostic techniques. Furthermore, AI-driven prognostic models offer a more accurate prediction of patient outcomes, enabling personalized treatment strategies. These contributions collectively indicate a promising future for AI and ML in bladder cancer management, enhancing diagnostic accuracy, treatment efficacy, and patient care.

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1. Introduction

Bladder cancer is a significant global health concern, with approximately 573,278 new cases and 212,536 new deaths reported worldwide(1) Prevalence and death rates are highest in industrialized countries such as the United States, Germany, and Taiwan.[1,2] Bladder cancer is more common in males than women and has a death rate four times greater in men than women worldwide.[1] The current gold standard for non-invasively identifying bladder cancer is urinary cytology, which has a high degree of specificity but low sensitivity.[2] The diagnostic procedure of choice for bladder cancer is cystoscopy.[2] Although cystectomy is a common part of standard treatment for bladder cancer, it is associated with severe morbidity and a drop in quality of life.[1,2] As a result, the strategy of preserving the bladder has gained popularity. However, there is an urgent need to enhance patient outcomes through the creation of accurate predictive models with high sensitivity and specificity for the efficacy of a given medicine. The use of AI has the potential to dramatically improve the detection and treatment of bladder cancer. AI makes use of computational methods that imitate the underlying mechanisms of human intelligence, such as cognition, deep learning, adaptation, engagement, and sensory

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comprehension.[3] In recent years, AI algorithms have been used to perform a variety of clinical tasks associated with the diagnosis and prognosis of bladder cancer, including bladder wall segmentation, automatic tumour detection, staging, and grading, and the prediction of recurrence, treatment response, and overall survival.[4,5]

In order to accurately detect the distribution of heterogeneous tumours,[6] AI can be combined with the 3D image-based features of non-invasive computed tomography and magnetic resonance imaging. In addition, AI based decision support systems have been created to assess therapeutic response in muscle-invasive bladder cancer.[6] In addition, AI has improved cystoscopy, leading to more precise diagnoses by highlighting anomalies that could otherwise go undetected by a human's unaided eye.[5,6] Predictions of recurrence and survival rates for bladder cancer patients can also be made with the help of ML algorithms.[7]

As a result of these shortcomings, accurate predictive models with high sensitivity and specificity are needed00001000 to determine whether or not a certain medicine would be effective in treating bladder cancer (BCa). Automatic tumour detection, staging, grading, recurrence, treatment response, and overall survival prediction are just few examples of the many supervised learning difficulties that modern ML applications in Bladder cancer diagnosis and outcome prediction address. In this scenario, CT urograms from two groups of controls and patients with Bladder cancer are employed as input, and the presence or absence of malignant lesions in each picture is indicated by binary labels as output.[7]

The advent of deep learning (DL) has additionally accelerated up AI progress in recent years. Artificial neural networks (ANN) and deep convolutional neural networks (DCNN), two types of ANN with a lot of popularity due to their accuracy, are trained as part of DL. DCNN can be used to classify and anticipate cystoscopic findings. To aid urologists in the course of cystoscopic examinations, a DL model such as this one could be incorporated into an AI-assisted image diagnostic tool.[8] As the big data era gets underway, more complicated healthcare data will become available. These data frequently contain redundant information, are noisy, and exhibit high fluctuation. AI, with

ML algorithms and ANN processes, can provide an accurate and comprehensive view of a clinical scenario.[9] Thus, this review aims to examine the research and application potential of AI, ML, and DL in BCa.

2. Search strategy and keywords

To systematically gather relevant literature for this review, a comprehensive search strategy was employed across multiple electronic databases. The search aimed to identify studies and articles related to the application of AI and ML in bladder cancer diagnosis and treatment. The following databases were explored:

PubMed
Scopus
Web of Science
IEEE Xplore
Google Scholar

The search for relevant publications was carried out comprehensively, encompassing articles from the inception of each database up to [mention your specific end date or year]. To ensure a thorough exploration of the literature, a combination of pertinent keywords and Medical Subject Headings (MeSH terms) was employed in various Boolean combinations. These keywords and terms included "Bladder cancer," "Bladder carcinoma," "Artificial intelligence," "Machine learning," "Deep learning," "Neural networks," "Histopathological grading," "Molecular typing," "Diagnosis," "Prognosis," "Treatment," "Radiomics," "Image analysis," "Gene expression analysis," "Biomarkers," "Treatment response," "Personalized medicine," "Clinical data," and "Electronic health records." This comprehensive approach allowed for the identification of a wide range of relevant studies and publications across various databases.

The search was limited to articles published in English and focused on human subjects. The reference lists of selected articles were also reviewed for additional relevant publications. The initial search yielded a substantial number of articles, which were then screened for relevance. Abstracts and full texts were assessed, and studies that met the inclusion criteria were included in this review. The search strategy aimed to encompass a wide range of studies to provide a comprehensive overview of the topic.

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3. AI aided Cystoscopy

Bladder cancer (BC) is a malignancy that is common around the world, with a high rate of recurrence, with considerable morbidity, and mortality. Cystoscopy (BC) is currently the gold standard for identifying and keeping track of bladder cancer. However, there are drawbacks to manual cystoscopy, such as subjectivity and inter-observer variability. Therefore, a precise and consistent method for diagnosing bladder cancer is urgently needed. This need may be met by AI, which makes it possible to create precise predictive models with high sensitivity and specificity.

AI-assisted cystoscopy is one of the most exciting uses of AI in bladder cancer treatment. The viability and promise of AI-aided cystoscopy in identifying and categorizing bladder lesions have been established in a number of studies. A deep learning algorithm called CystoNet, created by Shkolyar *et al.*,[15] can recognise bladder tumors in white light imaging (WLI) cystoscopic recordings. A convolutional neural network (CNN) trained using 2335 frames of a healthy or benign bladder and 417 labelled frames of urothelial carcinoma with histological confirmation was used to create CystoNet. When tested on 54 full-length cystoscopy recordings, the system has a sensitivity of 95.5% and a specificity of 98.6%.

Transfer learning was used in a work by Ikeda *et al.*[24] to create a bladder tumour classifier using a pre-trained CNN (GoogLeNet). The system identified bladder cancer with a sensitivity of 90% and a specificity of 94%, highlighting the promise of transfer learning in AI-assisted cystoscopy. In addition, Lucas *et al.*[20] used pre-trained CNNs to extract and classify characteristics from 72 movies of Trans urethral resection of bladder tumor (TURBT) taken using a probe-based confocal laser endomicroscopy (pCLE). The CNN was taught to distinguish between low-grade and high-grade tumors as well as between benign and malignant lesions. The accuracy of the technique was 79% for separating benign from malignant urothelium and 82% for differentiating high-grade from low-grade urothelial tumors.

AI has emerged as a transformative technology in the field of cystoscopy, a widely used procedure for diagnosing bladder cancer. Cystoscopy involves inserting a thin, flexible tube with a camera (cystoscope) into the bladder to visualize its interior and detect abnormalities, including tumors. AI-driven advancements in cystoscopy have significantly improved accuracy by addressing some of the inherent limitations of traditional cystoscopy, such as subjectivity, inter-observer variability, and the potential for missed lesions. Let's delve deeper into the use of AI in cystoscopy and its role in improving accuracy:

AI algorithms, trained on extensive datasets of cystoscopy images, demonstrate the potential to automatically identify and classify bladder lesions. CNNs prove particularly effective in this realm, exhibiting high sensitivity and specificity in detecting bladder tumors. By highlighting suspicious regions in real-time, the AI system can alert urologists to potential lesions that might have been overlooked during traditional cystoscopy, addressing a critical challenge. False negatives, often an issue due to human visual perception limitations, can be mitigated through AI-enhanced cystoscopy, augmenting the urologist's ability to detect subtle lesions and thereby improving early cancer detection. Furthermore, AI algorithms can function as computer-aided diagnostic tools, offering immediate feedback during cystoscopy and assisting urologists in making more accurate assessments. AI's role extends to objective documentation by recording and analyzing the entire cystoscopy procedure, generating comprehensive reports that include crucial details for follow-up and treatment planning. Integration with enhanced imaging techniques, such as narrow-band imaging (NBI) and fluorescence cystoscopy, further amplifies AI's impact. AI's continuous learning and improvement through model refinement based on new data is pivotal, enabling enhanced accuracy and performance over time. By acting as a clinical decision support tool, AI-driven cystoscopy collaborates with urologists, providing evidence-based recommendations and second opinions, fostering confident and informed decision-making. As AI-assisted cystoscopy continues to advance, ensuring its robustness and generalizability across diverse datasets through external validation is imperative. To enhance patient outcomes, future research should emphasize the verification of these algorithms on larger and more varied datasets, as well as their practical implementation in clinical settings.

4. Radiomics for staging and treatment response assessment

Radiomics and ML have demonstrated potential for bladder cancer staging and grading that is correct, which is essential for choosing the most effective treatment plan and follow-up therapy. Preoperative bladder cancer tumour grading has been devised using multiparametric MRI-based radiomic analysis models. With an AUC of 0.9233 for the training cohort and 0.9276 for the validation cohort, Wang *et al.*'s study found that a joint model combining T2-weighted imaging, DWI, ADC, and Max-out performed better than the other four single-modality models in terms of accuracy, sensitivity, and specificity.[31] A radiology department implemented AI-driven radiomics analysis for bladder cancer staging based on multiparametric MRI scans. The AI algorithm extracted and analyzed a wide range of quantitative imaging features, such as texture, shape, and intensity, from the MRI images to create a radiomic signature for each patient. This shows promise for reducing subjectivity and encouraging increased use in the future for grading bladder cancers prior to surgery. For the assessment of the efficacy of muscle-invasive bladder cancer treatments, computerised decision-support systems (CDSS) incorporating deep learning convolutional neural network and radiomic features have been established. With mean AUCs of 0.80 for CDSS-T alone, 0.74 for clinicians who did not use CDSS-T, and 0.77 for clinicians who did use CDSS-T, Cha *et al.*'s study found that CDSS-T enhanced the performance of attending abdominal radiologists, diagnostic radiology residents, attending oncologists, and attending urologists in assessing pathologic T0 disease.[32]

The validity of a "concurrent approach," in which AI predictions may be displayed from the outset and it is up to the clinician to use them in their decision-making process, must be further investigated. The FDA currently permits physicians to utilize computer-aided detection (CAD) tools as "second readers," revisiting their initial diagnosis with the computer's prediction as additional data.[33] Predicting disease-specific

survival and overall survival in bladder cancer treatment is essential for choosing the most effective course of action. In a comparison of ANN and multivariable CPH models, Bhambhvani *et al*. found that their ANN model predicted overall survival more accurately (AUC 0.81 vs 0.70 vs CPH models) and disease-specific survival with comparable accuracy (AUC 0.80 vs 0.81) in bladder cancer patients.[31] In order to create a predictive model with clinicopathological variables from a primary bladder cancer dataset of 3503 BC patients, Hasnain *et al*. combined a variety of ML techniques,[28] the model predicted patient recurrence and survival with better than 70% sensitivity and specificity 1, 3, and 5 years after radical cystectomy. These studies show the capability of radiomics and ML to predict bladder cancer patient prognosis and treatment response with accuracy.

5. Improving biomarkers

With a high specificity of 99%, urinary cytology has long been regarded as a desirable non-invasive screening test for bladder cancer, although its sensitivity for high-grade malignancies is only 0-50% and lower for low-grade cancers. This can be improved upon by using additional urine markers, such as Fluorescent in Situ Hybridization (FISH), Immunocyte, Nuclear Matrix Protein (NMP)-22, and Bladder Tumour Antigen (BTA stat). These markers all have higher sensitivity than urinary cytology, but they have not yet completely replaced it.[34]

Using ML techniques is one promising way to increase the precision of biomarkers for BC diagnosis. In a recent study, the ability to predict 5-year disease-specific survival (DSS) and overall survival (OS) in BC patients using multivariable CPH models and artificial neural networks (ANN) was assessed.[35] In comparison to the CPH models, which had an AUC of 0.70 for OS and 0.81 for DSS, the ANN models demonstrated more accuracy, with an area under the curve (AUC) of 0.81 for OS and 0.80 for DSS. The ANN OS model's calibration slope and intercept were 1.03 and 0.04, respectively, whereas the ANN DSS model's values were 0.99 and 0.04, respectively. These findings imply that ANN models might be more useful in predicting BC patients' survival outcomes.

By using metabolomics, BC biomarkers can be improved yet another way. A recent study,[36] using urine metabolomics, identified promising indicators for the diagnosis of BC. The expression of 19 metabolites from different metabolic pathways was observed to differ between BC patients and healthy controls. A logistic regression model was used to further filter a subset of 11 of these metabolites, producing a ROC curve with an AUC value of 0.983, a sensitivity of 95.3%, and a specificity of 100%. These findings highlight the need for additional study into the discovery of biomarkers for different diseases and show the promise of metabolomics as a non-invasive tool for diagnosing BC.

Study by Tsai et al leveraged clinical laboratory data and machine learning techniques to develop predictive models for bladder cancer among 1336 patients with various urological conditions. Utilizing features such as calcium, alkaline phosphatase, albumin, urine ketone, urine occult blood, creatinine, alanine aminotransferase, and diabetes, the lightGBM model demonstrated robust accuracy, sensitivity, and specificity in discriminating bladder cancer from cystitis and other cancers, offering a promising approach for enhanced diagnostic precision.[10]

Finally, non-invasive biomarkers for BC detection and monitoring are being investigated and developed constantly. The improvement of the precision and dependability of BC biomarkers has shown encouraging outcomes when using ML approaches like metabolomics and artificial neural networks.

6. Automated histologic grading and molecular typing

Algorithms are now able to recognize and categorize tumors based on their histological characteristics and molecular markers because to advancements in AI and ML. For instance, datasets generated from PSA, MRI-guided biopsies, genetic biomarkers, and Gleason grading are frequently employed in the diagnosis of prostate cancer for patient risk assessment, follow-up, and treatment planning.[37] Similar to this, radiomics and AI from multiparametric magnetic resonance imaging (MRI) have been employed for the evaluation of molecular subtypes in breast cancer using multi-layer perceptron feed-forward artificial neural networks (MLP-ANN) for pairwise comparisons.[38] Additionally, several experimental setups and post-experiment analytical methods for tumour classification have been compared using AI-based systems. For instance, a study compared three PCA-based classification methods—linear discriminant analysis (LDA), support vector machine (SVM), and artificial neural network (ANN)—under various experimental circumstances and found that SVM had the highest classification accuracy.[39] APTw) MRI has been employed in the diagnosis of bladder cancer to establish the stage and histologic grade of the disease. Combining APTw and ADC improved diagnostic performance for differentiating between low- and high-grade bladder cancer, according to the study.[40,41]

Automated histopathological grading and molecular typing are pivotal in the effective management of bladder cancer. Histopathological grading, a crucial step in gauging cancer aggressiveness, has traditionally relied on manual examination by pathologists, which is time-consuming and subjective due to inter-observer variability. AI, especially employing deep learning techniques like CNNs, has emerged as a powerful tool for analyzing histopathological images. CNNs can extract intricate features from these images, aiding in the identification of subtle cellular and tissue patterns associated with different grades of bladder cancer. Transfer learning, involving fine-tuning pre-trained CNN models on histopathological images, enhances grading accuracy by leveraging learned representations. AI algorithms can further segment Regions of Interest (ROIs) within histopathological slides, focusing on tumor areas and improving grading

accuracy by excluding non-cancerous tissues. Integrating clinical data, encompassing patient demographics, medical history, and genetic information, enhances AI models for a comprehensive and personalized assessment of cancer aggressiveness.

6. Prognostic algorithms

In a study by Bhambhvani *et al.*[30] using traditional clinicopathological data from 161,227 bladder cancer patients in The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) 18 database, they compared the performance of multivariable CPH models and artificial neural networks (ANN) in predicting 5-year disease-specific survival (DSS) and overall survival (OS) in bladder cancer patients.

When compared to the CPH model's AUC of 0.70, the ANN model more accurately predicted OS with an AUC of 0.81, while the AUCs for the DSS were comparable (0.80 and 0.81, respectively). From a substantial perspective primary bladder cancer dataset of 3503 BC patients, Hasnain *et al.*[28] integrated a number of ML approaches to produce a predictive model including clinicopathological characteristics. After a radical cystectomy (RC), the patient's recurrence and survival were predicted with greater than 70% sensitivity and specificity at 1, 3, and 5 years. These findings imply that AI and ML algorithms can assist prognostic models for bladder cancer to be more accurate and precise, which would enhance treatment planning and patient outcomes.

Table 1. Summary of recent AI studies and machine learning applications from the literature on bladder cancer management.

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Cystoscopy								
Atsushi Ikeda *et al.* (2020) [11]	Support System of Cystoscopic Diagnosis for Bladder Cancer Based on AI	ImageNet18 dataset (1000-class classification)	Cystoscopic images	Classification of bladder cancer lesions vs normal tissue	NA	CNN based on GoogLeNet17 with transfer learning	Area under the ROC curve=0.98, Youden index=0.837, Sensitivity=89.7%, Specificity=94.0%	AI system capable of classifying tumor-lesions and normality with high accuracy
Negassi *et al.* (2020) [12]	ML/DL/CNN applications in cystoscopic image recognition	177 images of histologically confirmed bladder tumors, 133 images of healthy urothelium	Cystoscopic images		N/A	ImageNet-Convolutional Neural Network	Sensitivity-93.0%, Specificity-83.7%	Differentiate between tumor and healthy urothelium
Ikeda *et al.* (2020) [13]	Cystoscopic diagnosis of bladder cancer using AI	431 images of tumors, 1671 normal images	Cystoscopic images			GoogleNet architecture and fine-tuned with Adam algorithm	Sensitivity-89.7%, Specificity-94.0%, Area under the ROC curve-0.98	Classify cystoscopic images, including tumor lesions and normality
Ikeda *et al.* (2021) [14]	Improve bladder tumor detection using transfer learning	1-1.2 million general images, 8,728 gastroscopic images, 2,102 cystoscopic images				Convolutional neural network (CNN)	Sensitivity: 95.4%, Specificity: 97.6%	Value of transfer learning in limited datasets for bladder tumor detection

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Shkolyar *et al.* (2019) [15]	Augmented bladder tumor detection using deep learning	Development dataset: 95 patients for training and 5 patients for testing	141 videos from 100 patients who underwent TURBT			CystoNet (CNN-based image analysis platform)	Per-frame sensitivity: 90.9%, Per-frame specificity: 98.6%, Per-tumor sensitivity: 90.9%	Improvement in cystoscopy quality and availability using CystoNet for bladder tumor detection
Ikeda *et al.* (2020) [16]	Support system of cystoscopic diagnosis for bladder cancer	2,102 cystoscopic images: 1,671 normal tissue, 431 tumor lesions	TIFF files of 1350×1080 pixels by white light			CNN model based on GoogLeNet with transfer learning		

Imaging

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Soheila Borhani *et al.* (2022) [17]	Bladder cancer diagnosis and outcome prediction	N/A	Pelvic CT images with and without bladder malignancies	Automated bladder tumor detection using CNN-based model named CystoNe	N/A	Non-linear supervised classification CNN-based model	Sensitivity=0.91, Specificity=0.99	AI based BCa diagnostics and prognostics has the potential to improve patients' quality of life and reduce the financial burden
Sebastian Marscher e *et al.* (2022) [18]	Organ segmentation algorithm for radiation treatment planning	N/A	Thoracic CT images (n=237) Pelvic CT images (n=102)	Automatic contouring of organs at risk in radiation treatment planning	N/A	DI2IN based on a Convolutional Encoder-Decoder architecture with a multi-level feature concatenation auto segmentation algorithm	Dice Similarity Coefficient (DSC)=0.88, Hausdorff Distance (HD95) bladder=6.7 mm	A deep image-to-image network (DI2IN) algorithm for automatic contouring of organs at risk in radiation treatment planning.
Ge *et al.* (2019) [19]	Progress of radiomics with ML in bladder cancer management	84 bladder cancer lesions from 76 CT urography (CTU) cases				LDA, NN, SVM, RAF	Accuracy: 82.9%, Sensitivity: 78.4%, Specificity: 87.1%, AUC: 86.1%	Application of radiomics and ML for precision medicine in bladder cancer management

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Lucas *et al.* (2019) [20]	Towards automated in vivo bladder tumor stratification using Confocal Laser Endomicroscopy	pCLE data acquired using Cellvizio 100 series with topical administration of fluorescein	Field of view: 240 µm, lateral resolution: 1 µm, depth of field: 10 µm	Patients with high-grade UCB and high-grade papillary UCB lesions		Long Short Term Memory (LSTM) in Recurrent Neural Network (RNN)	Differentiation of healthy/benign vs. malignant urothelium (Accuracy: 79%) and low-grade vs. high-grade papillary UCB (Accuracy: 82%)	Lucas *et al.* (2019) Proper stratification of pCLE videos of in vivo bladder lesions
Timothy C. Chang *et al.* (2021) [21]	Endourology and Robotic Surgery	479 images representing 44 different benign and malignant bladder lesions; dataset of 100 RARPs surgeries	Deep learning systems and robotic video/image-based data	Classification of bladder lesions and key steps in robotic surgery		Deep Learning systems including RP-Net based on InceptionV3	> 95% accuracy for classification;	Potential for improved patient outcomes

Histopathology

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Harmon *et al.* (2020) [22]	Predict positive lymph nodes from primary tumors in bladder cancer using digital pathology	Training and validation: 219 patients, Testing: 89 patients	307 patients were identified TCGA (n = 294) in-house (n = 13)			Multivariable Logistic Regression models	AUC of clinicopathological model-0.755, AUC of AI score-0.866	Identify patients at higher risk of having positive LNs during cystectomy
Woerl *et al* (2020) [23]	Predicting molecular subtype of MIBC samples from histomorphology using deep learning	Two cohorts: (1) The Cancer Genome Atlas Urothelial Bladder Carcinoma dataset (407 patients) and (2) cohort with 16 treatment-naïve patients	Image tiles generated from annotations	Molecular subtype prediction from hematoxylin and eosin (HE) slides		ResNet (CNN)	Combined AUC of ROC curve: 0.89 (micro averaging), 0.87 (macro averaging), AUC: 0.85 (micro- or macro averaging), Accuracy: 75.00%	Deep learning-based prediction of molecular features in MIBC from HE slides, potentially improving clinical management

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Biomarkers, Molecular and Genetics								
Loeffler *et al.* (2022) [24]	Predict mutations of the Fibroblast Growth Factor Receptor (FGFR) gene		Digitized slides stained with hematoxylin and eosin from the Cancer Genome Atlas (TCGA) cohort	FGFR3 mutations detected with an AUROC of 0.701 (p < 0.0001) in the TCGA cohort and 0.725 (p < 0.0001) in the "Aachen" cohort	Deep Learning Network			Detect genetic alterations of the FGFR3 gene of bladder cancer patients directly from histological slides.
Treatment and prognostication								
Okyaz Eminaga *et al.* (2022) [25]	AI-Based Prognostic Model for Urologic Cancers: A SEER-Based Study	N/A	Survival probabilities	Risk stabilization based on the risk velocity	N/A		Harrell's Concordance Index	Feasible data-driven AI solution for cancer-specific survival estimation and potential follow-up management of urologic cancers
Kong *et al.* (2022) [26]	Predict immunotherapy response in cancer patients	IMvigor210, The Auslander dataset, Riaz dataset	Cohorts with at least 30 samples and 10 responders/non-responders	N/A		Support Vector Classifier (SVC), Random Forest (RF), and Deep Neural Network (DNN) models	NA	Network-based method to select immunotherapy response associated biomarkers; robust ML-based predictions for precision oncology

Author	Objective	Dataset	Input	Output	Training Features	Algorithms	Performance Index	Outcomes
Lee *et al.* (2021) [27]	Prognosis of non-muscle invasive bladder cancer based on intravesical prostatic protrusion (IPP)	Newly diagnosed primary NMIBC patients with CT scans and minimum 5-year follow-up				Support Vector Machine (SVM)	Accuracy: 0.803, AUC: 0.749	Prognostic significance of intravesical prostatic protrusion in NMIBC recurrence risk
Zaki Hasnain *et al.* (2019) [28]	ML models for predicting post-cystectomy recurrence and survival in bladder cancer patients	Data pruned to 3499 patients after removing cases with missing survival data from a cohort of 3503 patients	Preoperative and operative data	Recurrence and survival prediction		Support Vector Machines (SVM), bagged SVM, K-Nearest Neighbors (KNN), Adaptive Boosted Trees (AdaBoost), Random Forest (RF), Gradient Boosted Trees (GBT)		Benchmark for predicting oncologic outcomes and opportunities for improving care
Nicolas Brieu *et al.* (2019) [29]	Automated tumor budding quantification by ML augments TNM staging in muscle-invasive Bladder Cancer Prognosis	Patients who underwent radical cystectomy for muscle-invasive bladder cancer (n=163)	IHC images of bladder carcinoma	Tumor budding quantification		CNN, color deconvolution, K-Means clustering, heuristic post-processing rules	High TB correlated with higher TNM stage and pT stage	improved model fit compared to TNM staging

Table 1 presents a comprehensive list of the articles that were meticulously reviewed in the preparation of this manuscript.

The comparative analysis in Table 2 underscores the significance of AI-enhanced diagnosis, demonstrating its superior efficacy in accuracy, efficiency, and overall diagnostic precision compared to traditional methods, thereby highlighting its potential to revolutionize clinical decision-making and patient care.

7. Challenges and solutions

The integration of AI in bladder cancer care presents both opportunities and challenges. One of the significant challenges is the need for robust and diverse datasets that encompass various patient demographics, disease stages, and treatment responses. Limited or biased data can result in AI models that do not generalize well across different populations. Addressing this challenge involves collaboration among healthcare institutions and researchers to compile comprehensive and representative datasets, ensuring the inclusivity of diverse patient profiles. Additionally,

Table 2. Comparison between AI enhanced diagnosis and traditional diagnosis.

Ai enhanced diagnosis	Traditional diagnosis
Leverages multi-omics data, clinical records, and medical imaging.	Relies on fragmented data sources
Automated histopathological grading and molecular typing	Manual grading and typing by pathologist
High precision due to advanced algorithms and ML	Subject to inter-observer variability
Tailored treatment plans based on individual patient data	Limited personalization of treatment
Early detection through data analysis	May result in late stage diagnosis
Predicts treatment response based on genetic markers	Limited ability to predict treatment response
Streamlines diagnostic process	Time consuming and labor intensive

advancements in federated learning, a technique that allows models to be trained across multiple decentralized sources of data, offer a potential solution to data privacy concerns while promoting data sharing and model improvement.

Another obstacle is the interpretability and transparency of AI algorithms, particularly in complex medical decision-making processes. Building AI models that provide clear explanations for their predictions is crucial for gaining trust from clinicians and ensuring the safe integration of AI into clinical workflows. Research in explainable AI methods and model interpretability is essential to make AI more understandable and acceptable to healthcare professionals.

Moreover, ensuring regulatory compliance and adherence to healthcare standards is a critical challenge. AI algorithms need to meet stringent regulatory requirements to ensure patient safety and data security. Collaborative efforts between AI developers, healthcare institutions, and regulatory bodies are vital to establish guidelines and standards for AI implementation, validation, and monitoring within the healthcare sector.

Lastly, the integration of AI into routine clinical practice requires education and training of healthcare professionals. Understanding the capabilities and limitations of AI models is necessary for optimal utilization and interpretation of AI-generated insights. Continuous training programs, workshops, and educational initiatives can bridge the knowledge gap and facilitate seamless adoption of AI technologies in bladder cancer care.

In Table 3, we delineate the advantages and limitations of employing AI in bladder cancer management. It provides insights into the potential benefits and challenges associated with integrating AI into bladder cancer management, guiding clinicians and researchers in harnessing its strengths while addressing its limitations for more effective and informed decision-making.

Addressing these challenges collectively will pave the way for the effective implementation of AI in bladder cancer care, ultimately improving patient outcomes and revolutionizing the landscape of cancer diagnosis, treatment, and management.

8. Conclusion
The application of AI and ML in bladder cancer care has shown remarkable potential, revolutionizing various aspects of diagnosis and treatment. The key findings presented in this

Table 3. Advantages and limitations of AI in bladder cancer management.

Advantages	Limitation
1. Improved diagnostic accuracy	1. Data Dependence and Quality: AI models heavily rely on high-quality and diverse datasets for accurate predictions. Limited or biased data may lead to suboptimal results
2. Early detection and prognosis	2. Ethical Considerations: The use of AI in healthcare raises ethical concerns related to data privacy, patient consent, and potential biases in algorithmic decision-making.
3. Personalized treatment strategies	3. Interpretability and Transparency: Some AI models, particularly deep learning algorithms, are often considered "black boxes," making it challenging to interpret their decision-making process.
4. Improved treatment planning	4. Integration into Clinical Workflow: Incorporating AI into existing clinical workflows requires careful implementation and acceptance by healthcare professionals.
5. Reduced Healthcare costs	5. Expertise and Training: AI implementation demands skilled personnel with expertise in both medical and AI fields. Training healthcare professionals to use AI effectively can be time-consuming.
6. Empowering patients	6. Lack of Standardization: The lack of standardized AI algorithms and protocols may result in variations in diagnostic outcomes and treatment recommendations.
7. Advancement in Research	7. Regulatory and Legal Challenges: Regulatory approval and compliance with legal requirements can be complex and time-consuming for AI applications in healthcare.
	8. Data Security and Privacy: Storing and processing sensitive patient data requires robust security measures to prevent data breaches.

review demonstrate how AI-driven algorithms have enhanced diagnostic precision, treatment planning, and patient outcomes. As we look to the future, further developments in AI and ML hold the promise of even greater impact on bladder cancer care.

Figure 1 illustrates the workflow in the management of bladder cancer with integrated AI, providing a visually accessible representation that enhances comprehension of the process. This figure serves to elucidate key stages of the workflow and specifically highlights the strategic points where AI is incorporated, facilitating a clearer understanding of its role in the overall management approach.

8.1 Future directions

AI and ML have revolutionized the field of healthcare, particularly in the realm of bladder cancer care. These technologies can analyze extensive patient data, encompassing genetic profiles, imaging results, and treatment responses, to craft personalized treatment plans tailored to each individual. This approach has the potential to yield more effective therapies while mitigating side effects. Moreover, AI algorithms can detect subtle patterns in patient data, enabling early identification of bladder cancer and accurate prognosis. Timely intervention based on these insights significantly improves survival rates and reduces the necessity for aggressive treatments. Additionally, AI-assisted tumor boards, utilizing multidisciplinary teams of experts, can be pivotal in discussing individual patient cases. AI algorithms provide valuable insights and recommendations rooted in the latest research and patient data, enhancing informed decision-making. However, for AI to be seamlessly integrated into routine clinical practice, the development of user-friendly tools that seamlessly integrate with existing healthcare systems is imperative. Addressing ethical considerations, such as data privacy, bias, and transparency, is crucial to ensure fair and equitable healthcare delivery as AI and ML continue to play a prominent role in bladder cancer care.

8.2 Potential Impact

The integration of AI and ML in bladder cancer care holds significant promise, offering a transformative impact on both patients and healthcare providers. AI-powered algorithms have the potential to significantly enhance diagnostic accuracy by aiding clinicians in identifying bladder lesions more precisely during cystoscopy and analyzing imaging data for accurate tumor staging. Moreover, AI can predict patient responses to specific treatments, enabling personalized treatment planning tailored to individual patient characteristics, thereby improving treatment outcomes. This tailored approach not only enhances patient care but also has the potential to reduce healthcare costs by optimizing resource utilization through early detection and personalized treatment strategies, mitigating expenses associated with aggressive treatments and disease management. Furthermore, AI-driven diagnostic tools can empower patients by providing them with access to comprehensive information, facilitating informed discussions with healthcare providers regarding treatment options and potential outcomes. Additionally, AI and ML can accelerate research efforts through large-scale analysis of patient data, potentially leading to the discovery of novel biomarkers and therapeutic targets. In conclusion, responsible and ethical integration of AI and ML in bladder cancer care holds the key to realizing their full potential, ultimately
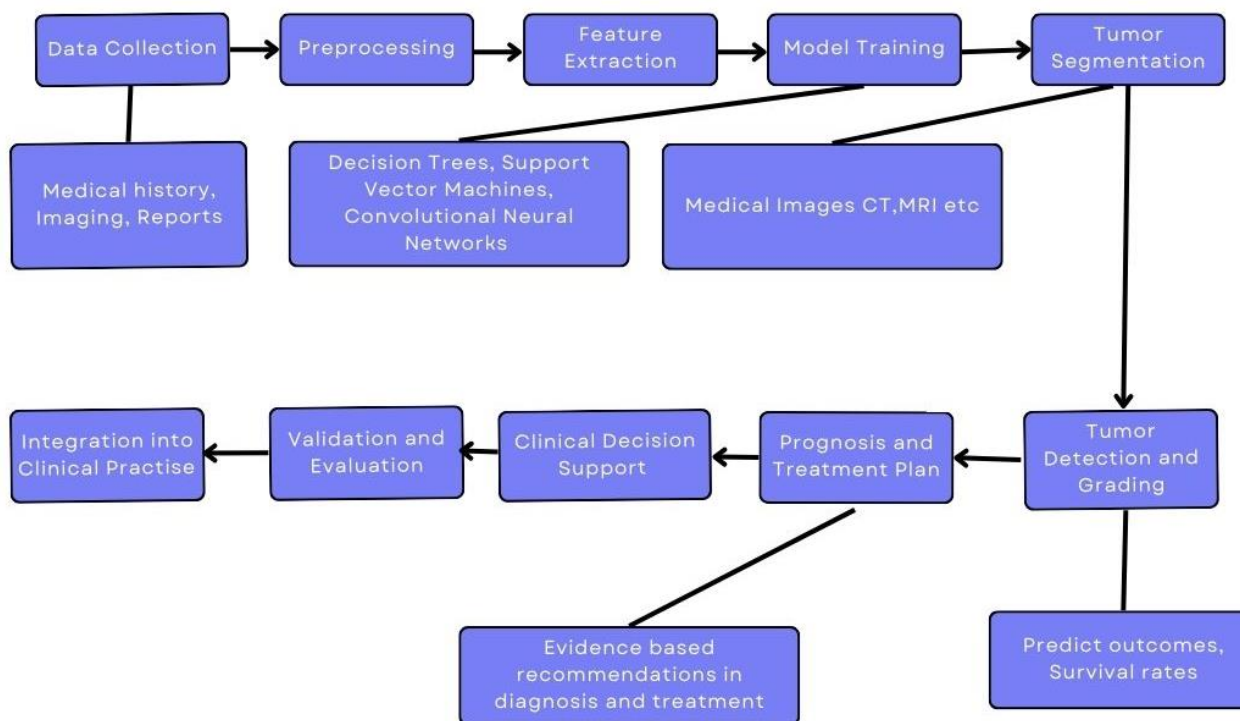

Fig. 1 Workflow in management of bladder cancer with AI integration.

revolutionizing bladder cancer management, improving diagnostic precision, treatment efficacy, and overall patient well-being.

Conflict of Interest

There is no conflict of interest.

Supporting Information

Not applicable.

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