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Review article

Tumor pathology

The Paris System for Reporting Urinary Cytology – a critical review of its role in advancing precision diagnostics with insights into artificial intelligence integration

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Urinary cytology serves as a vital diagnostic tool for urothelial carcinoma, offering a non-invasive screening method and guiding treatment decisions. The Paris System for Reporting Urinary Cytology (TPS) addresses historical challenges, providing a structured framework and enhancing diagnostic precision. The review explores the integration of artificial intelligence (AI) into urinary cytology, emphasizing its collaborative potential with TPS. A systematic literature review analyzes AI applications, revealing promising advancements but highlighting concerns about generalizability and over-reliance on deep learning. The study underscores the importance of collaborative efforts for successful AI implementation, addressing challenges and ensuring seamless integration into clinical practice. While the synergy between TPS and AI shows promise, cautious consideration is necessary for widespread and reliable adoption, emphasizing ongoing refinement and validation.

Key words: urinary cytology, urothelial carcinoma, The Paris System for Reporting Urinary Cytology, precision diagnostics, standardized reporting, diagnostic challenges, clinical implications

Introduction

Urinary cytology plays an important role in the diagnosis of urothelial carcinoma, a type of cancer that primarily affects the urinary tract, including the bladder, ureters, and renal pelvis [1]. The significance of urinary cytology lies in its ability to detect abnormal cells shed from the lining of the urinary tract into the urine. These cells, when carefully examined under a microscope, can provide valuable information about the presence of urothelial carcinoma and its potential aggressiveness.

Urinary cytology emerges as a pivotal diagnostic modality in urothelial carcinoma, providing a multifaceted approach to enhance patient care. The non-invasive screening capability of urinary cytology offers a straightforward and repeatable method, making it an invaluable tool for routine monitoring, especially in high-risk populations with a history of bladder cancer. Complementary to advanced imaging studies such as cystoscopy, urinary cytology contributes unique insights at the cellular level, confirming the presence of cancerous cells and guiding subsequent diagnostic and treatment decisions [1].

One of the distinctive strengths of urinary cytology lies in its capacity to reduce the necessity for invasive procedures. The non-invasive nature of urine sample collection minimizes patient discomfort and contributes to a more patient-friendly

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diagnostic approach. In cases where urinary cytology indicates a low likelihood of urothelial carcinoma, unnecessary invasive interventions may be avoided, aligning with the principles of personalized and targeted medicine.

The Paris System for Reporting Urinary Cytology (TPS) is a standardized classification system designed to improve the consistency and precision of reporting urinary cytology, providing distinct categories with defined clinical implications [2, 3]. Before TPS, interpreting results faced challenges, including subjective interpretations, lack of standardized criteria, and inconsistencies [2, 4]. Pathologists used varied terminology, leading to confusion, while different classification systems hindered result comparison. Limited interobserver agreement and unclear clinical implications posed further issues, risking overdiagnosis or underdiagnosis. TPS addressed these challenges, offering a structured framework, improving consistency, and enhancing clinical utility in urinary cytology reporting [5].

This review aims to analyze TPS's effectiveness in overcoming historical challenges. Additionally, the research explores artificial intelligence (AI) and image processing integration in urinary cytology, emphasizing image analysis, pattern recognition, and potential contributions to personalized treatment strategies. Anticipated findings aim to enhance understanding of the synergistic relationship between TPS and AI, illuminating their potential to revolutionize urinary cytology reporting for improved diagnostic precision in oncology.

Overview of TPS

The TPS introduces a structured classification system comprising categories with distinct clinical implications [2, 3]. TPS categorizes specimens as non-diagnostic, negative for high-grade urothelial carcinoma, atypical urothelial cells, suspicious for high-grade urothelial carcinoma, high-grade urothelial carcinoma, and other malignancies. This standardized approach addresses the historical lack of uniformity, providing clear criteria for each category. TPS significantly improves communication between pathologists and clinicians, ensuring a consistent understanding of findings, and facilitating informed decision-making in patient management.

The TPS demonstrates notable strengths in enhancing diagnostic precision. Its standardized categories provide a clear and consistent framework, reducing the subjectivity that previously characterized urinary cytology reporting. The structured approach, including categories like "atypical urothelial cells" and "suspicious for high-grade urothelial carcinoma," facilitates more accurate and reliable interpretations [6]. By offering well-defined criteria for each category, TPS minimizes variability among pathologists, resulting in improved diagnostic precision [7, 8]. This standardization is particularly crucial in the context of urothelial carcinoma, where early and precise diagnosis is paramount for effective clinical management.

Several studies and real-world examples have highlighted the effectiveness of TPS in providing a standardized and comprehensive system for urinary cytology reporting [9]. However, like any diagnostic system, TPS has areas for improvement. Challenges may arise in cases with borderline or atypical features, where the interpretation may still rely on the pathologist's expertise. Ongoing research and feedback from clinical practice are essential for refining TPS and addressing any limitations, ensuring its continuous evolution to meet the dynamic demands of urinary cytology diagnostics.

Despite its strengths, the implementation of TPS in clinical practice is not without challenges. One notable controversy surrounds the concern of potential over-reliance on urinary cytology alone for the diagnosis of urothelial carcinoma, highlighting the need for a multimodal approach. Additionally, challenges persist in standardizing reporting across diverse clinical settings, laboratories, and pathologists. Ensuring consistent adherence to TPS criteria and overcoming interobserver variability remain ongoing challenges. Ongoing efforts are directed toward addressing these controversies and challenges, with a focus on refining TPS guidelines and fostering broader acceptance within the medical community [3].

The role of AI in urinary cytology

Currently, urine cytology is assessed through manual examination by skilled cytopathologists, who visually identify and interpret cellular abnormalities. However, the increasing volume of samples and the need for precision make automated analysis crucial. Automation ensures consistent and efficient evaluation, reducing the potential for human error and enabling faster turnaround times. Implementing automated tools, especially with the integration of AI, not only enhances diagnostic accuracy but also addresses the growing demand for streamlined and standardized urinary cytology reporting in clinical settings.

In medical diagnostics, AI emerges as a transformative force, promising heightened precision and efficiency [10]. Within urinary cytology, its applications, notably in image analysis and pattern recognition, offer enhanced capabilities for accurate diagnosis. Recent studies showcase the integration of AI tools with the TPS, underscoring their collaborative potential to refine diagnostic accuracy [11]. This synergy between AI and TPS represents a significant stride towards advancing urinary cytology as a more effective and reliable diagnostic tool.

AI advancements in urinary cytology

In this study, a systematic literature review was performed by searching PubMed until January 8, 2024, utilizing the query ("Urine"[Mesh]) AND (("Artificial Intelligence"[Mesh]) OR ("Diagnosis, Computer-Assisted"[Mesh])). While the study protocol was not registered, deviating from the PRISMA guidelines, it was a deliberate choice as the systematic review served as a supportive tool rather than the primary focus. The aim was to offer insights into the current landscape of artificial intelligence applications in automated urine cytology analysis, providing

a comprehensive understanding of the state of the field as of the specified date.

The inclusion criteria for the literature review were meticulously defined: eligible papers had to focus on urine cytology testing for potential urothelial diagnosis, employ artificial intelligence or image processing for automated image analysis, involve human materials, be published in English, and have a publication date of 2014 or later. Conversely, exclusion criteria were clearly outlined, excluding papers on urine testing for non-oncological purposes, those not assessing image analysis method performance, studies where the model only described cellular features without offering a provisional diagnosis, and those based on animal studies. This stringent criteria framework ensured a focused and relevant selection of literature aligning with the study's objectives.

The search process in PubMed initially yielded 81 titles, which were subjected to title screening, resulting in the selection of 12 abstracts for further evaluation (fig. 1). After thorough abstract screening, 7 articles were chosen for full-text reading. To ensure a comprehensive review, 4 additional references were manually added. In total, 11 articles underwent full-text examination. Following a meticulous review, 8 articles were deemed relevant and included in the comprehensive analysis, ensuring the synthesis of the most pertinent information for the study's objectives (tab. I).

The studies included in the review exhibited diverse aims and employed varied study designs. Dataset sizes ranged widely, from 49 to 2405 cytology slides, with some studies adopting the conventional division into subsets for model development, validation, and testing. Notably, the imaging methods used varied, with one study utilizing digital still camera images and others employing whole-slide images obtained through digital pathology scanners. Despite these differences, a consistent benchmark for evaluating model performance across the majority of the studies was maintained; the comparison to previous assessments conducted by experienced cytopathologists served as the universally recognized golden standard in all instances.

Among the eight studies included, three specifically focused on AI-assisted methods for the detection of high-grade urothelial carcinoma cells or atypical cells. The predominant trend observed in most of the published research involved the utilization of deep learning models to automate predicted diagnoses. Notably, only one of the studies employed classical image processing methods, indicating a prevalent reliance on advanced deep learning approaches for the development and implementation of AI in automated urine cytology analysis.

The evaluation of model performance in the study encompassed various metrics, with most studies reporting the area under the curve (AUC). The AUC is a metric used in binary classification models, representing the ability of the model to distinguish between positive and negative instances. It ranges from 0 to 1, with a higher AUC indicating better discriminatory

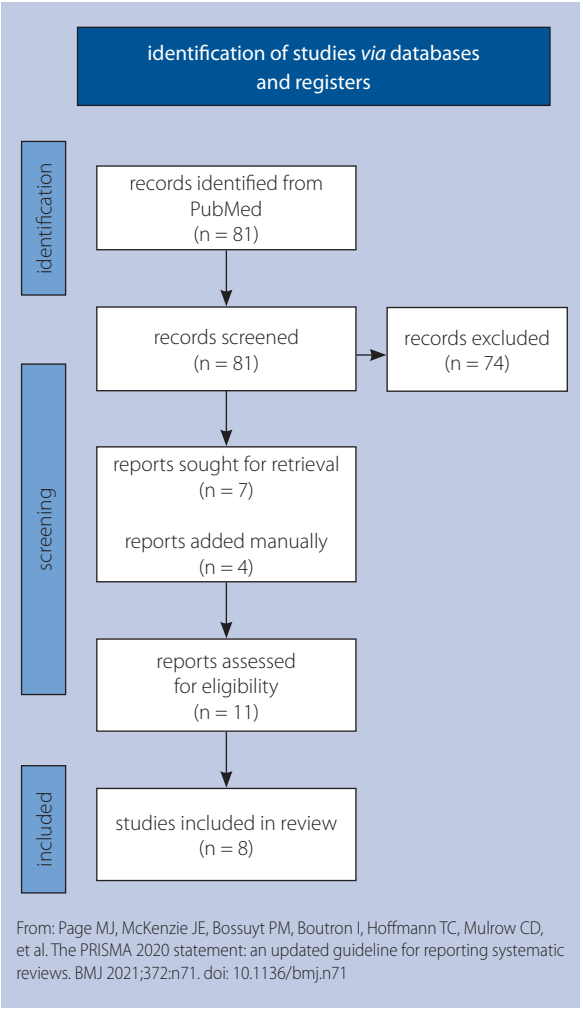

Figure 1. PRISMA 2020 flow diagram

power. In the presented studies, the AUC values of the developed models ranged from 0.78 to 0.99, suggesting a high level of accuracy. Additionally, specificity, indicating the model's ability to correctly identify negative instances, varied between 83% and 85%, while sensitivity, reflecting the model's capability to identify positive instances, ranged from 63% to 97%. These metrics collectively provided a comprehensive assessment of the models' discriminatory performance and diagnostic accuracy in automated urine cytology analysis.

While AI advancements in urinary cytology exhibit promise, the heterogeneity in study methodologies and dataset sizes raises concerns about generalizability. The reliance on deep learning without classical image processing warrants scrutiny, as the field may benefit from a more balanced exploration of diverse methodologies. Additionally, the high AUC values suggest robust discriminatory power, yet skepticism lingers over potential overfitting to specific datasets. Despite these reservations, the transformative potential of AI in urothelial carcinoma diagnostics is evident, but careful consideration and validation are crucial in ensuring the reliability and applicability of these models in diverse clinical scenarios.

Table I. Overview of AI-/image-processing-assisted diagnostic approaches in urinary cytology: a comparative analysis of image analysis methods and model performance

Reference	Year	Country	Cytology / cytoblock	Automation of diagnosis	Image analysis method	Size of dataset	Golden standard	Time required for analysis	Performance of the model (best model if multiple models)
Gelwan E. et al. [12]	2019	USA	cytology slides scanned (whole-slide images)	AI-assisted	image processing (SurePath and BCCS software)	53 slides	–	–	–
Lebret T. et al. [13]	2022	France	cytology slides scanned (whole-slide images)	automated	machine learning (VisioCyt software)	1,360 slides: 598 training 762 validation	cytology result by pathologist	–	sensitivity – 85% specificity – 81%
Lilli L. et al. [14]	2021	Italy	cytology slides images made using digital still camera	automated	deep learning	60 slides (690 images performed, and data augmentation procedure conducted to multiply the dataset): 2,616 training 872 validation 872 testing	–	–	–
Nojima S. et al. [15]	2021	Japan	cytology slides scanned (whole-slide images)	automated	deep learning	232 slides (divided into 61,512 images): 64% training 16% validation 20% testing	cytology result by pathologist	–	AUC – 0.99 F1 score – 0.90 sensitivity AI – 91% specificity AI – 97% accuracy AI – 95% precision AI – 90%
Ou Y.C. et al. [16]	2022	Taiwan	cytology slides scanned (whole-slide images)	AI-assisted	deep learning	150 slides: 7 training 12 validation 131 testing	–	–	–
Sanghvi A.B. et al. [17]	2019	USA	cytology slides scanned (whole-slide images)	automated	deep learning	2,405 cytology slides: 1615 training 790 validation	cytology result by pathologist	–	AUC – 0.88 sensitivity – 80% specificity – 85%
Tsuji K. et al. [11]	2023	Japan	cytology slides scanned (whole-slide images)	AI-assisted	deep learning	535 slides: 181 development 39 testing cell level 315 testing slide level 117 histological slides from the same patients	cytology result by pathologist + comparison with subsequent histopathology results	139 s	AUC – 0.78 accuracy – 86% prediction of HGUC in histopathology based on cytology analysis: sensitivity: model – 63% pathologist – 46% p = 0.0037 specificity: AI – 83% pathologist – 89% p = 0.13

Table I cont. Overview of AI-/image-processing-assisted diagnostic approaches in urinary cytology: a comparative analysis of image analysis methods and model performance

Reference	Year	Country	Cytology / cytoblock	Automation of diagnosis	Image analysis method	Size of dataset	Golden standard	Time required for analysis	Performance of the model (best model if multiple models)
									accuracy: AI – 74% pathologist – 68% p = 0.08
Zhang Z. et al. [18]	2020	China	cytology slides scanned (whole-slide images)	automated	deep learning	49 slides: 37 training 12 testing	cytology result by pathologist	–	–

Challenges, considerations, and future directions

The integration of AI tools in urinary cytology reporting brings forth potential challenges. One significant hurdle is the need for robust datasets that encompass the diverse spectrum of urinary cytology specimens. Limited datasets may hinder the AI's ability to accurately identify nuanced patterns or rare abnormalities. Additionally, the interpretability of AI-generated results poses a challenge, as understanding the underlying decision-making process of complex algorithms is crucial to gain trust in their clinical application. Ensuring the seamless integration of AI into existing laboratory workflows and addressing issues related to standardization and validation are key challenges that must be overcome to realize the full potential of AI in urinary cytology reporting.

Successful implementation of AI tools in urinary cytology reporting hinges on collaborative efforts between pathologists, clinicians, and AI developers. Establishing a strong synergy among these stakeholders is essential for tailoring AI algorithms to meet the specific needs of urinary cytology diagnostics. Collaborative endeavors foster a mutual understanding of the clinical context and intricacies of pathology, enabling AI developers to design algorithms that align with the nuanced decision-making processes of pathologists. Continuous communication and feedback loops ensure that AI tools are refined based on real-world clinical experiences, optimizing their performance over time. This collaborative approach not only accelerates the development and validation of AI algorithms but also enhances their acceptance and integration into routine clinical practice, ultimately improving diagnostic accuracy and patient outcomes.

Conclusions

In summary, the critical review underscores the transformative impact of the TPS in addressing historical challenges and providing a standardized framework. TPS enhances diagnostic precision, reduces subjectivity, and improves communication between pathologists and clinicians [19]. The integration of AI introduces exciting prospects, but the prevailing reliance on advanced algorithms raises concerns about potential overfitting and limited exploration of alternative methodologies. The collaboration between TPS and AI shows promise, but a cautious approach is essential to ensure the reliability and applicability of these advancements across diverse clinical scenarios.

Article information and declarations

Author contributions

Irmina M. Michałek – conceptualization, literature analysis, writing – original draft, writing – review and editing.
Monika Durzyńska – writing – review and editing.
Florentino L. Caetano dos Santos – literature analysis, writing – review and editing.

Conflict of interest

None declared

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