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Artificial intelligence facilitates clinical management of epithelial dysplasia in multiple organs

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Abstract

Epithelial dysplasia is a condition characterized by a spectrum of architectural and cytological alterations to the epithelium, resulting from the accumulation of genetic alterations. It is associated with an increased risk of cancer progression in a variety of organs. However, the variability of different grading systems, as well as inter- and intra-examiner variability, gives rise to concerns regarding the reliability of the results. Histopathology represents the gold standard for the diagnosis of epithelial dysplasia. The combination of big data in pathology and artificial intelligence (AI) will facilitate the achievement of accurate diagnoses and treatments, providing objective and efficient methods to integrate and refine diverse morphological, molecular, and multi-omics information. This perspective provides a summary of the existing research and prospects for the application of AI to epithelial dysplasia in multiple organs. A number of studies have been conducted with the aim of developing a grading system and prognostic identification method for epithelial dysplasia in the oral cavity, larynx, esophagus, and stomach. Digital pathology-based AI may prove useful in facilitating the clinical management of epithelial dysplasia in multiple organs. In summary, digital pathology images obtained by scanning hematoxylin & eosin-stained slides, identifying image features, and building AI models using deep learning combined with machine learning algorithms, validated with real-world data from multicenter cohorts could provide AI as a promising clinical application in the future.

Keywords

Artificial intelligence, epithelial dysplasia, digital pathology, deep learning

Epithelial dysplasia is a disorder that is characterized by the differentiation and maturation of a lesion that is produced by the proliferation of abnormal or atypical epithelial cells. These epithelia frequently exhibit architectural and cytological changes, with the majority occurring in squamous cells such as keratinocytes.

The accumulation of genetic alterations represents a pivotal factor in the pathogenesis of epithelial dysplasia [1]. The term encompasses lesions in which part or all of the thickness of the epithelium is replaced by cells exhibiting varying degrees of cellular atypia. It is associated with an elevated risk of cancer progression in a range of organs [2–7]. Nevertheless, epithelial dysplasia is a histological phenomenon with no clinical morphological equivalent [1]. In the context of body sites such as the cervix, the term "intraepithelial neoplasia" is used with a similar meaning [8]. This is a histological diagnosis of considerable clinical significance. In studies of oral potentially malignant disorders, Barrett's esophagus and other pre-cancerous lesions, different grades of epithelial dysplasia demonstrate varying potential for cancer development [3, 5, 6, 9, 10]. There are extensive scientific reports on the clinical management and bench research of epithelial dysplasia. However, the evidence base is weak due to the variation in published studies, particularly in the variability of different grading systems, as well as the inter- and intra-examiner variability, which leads to reliability issues.

Histopathology represents the "gold standard" for the diagnosis of epithelial dysplasia. The interpretation of traditional histomorphology is dependent on the experience of the pathologist, and therefore, more objective and efficient methods are required to integrate and refine diverse morphological, molecular, and multi-omics information. The integration of pathology big data (comprising hundreds of thousands or more pathology images and records) with artificial intelligence (AI) has the potential to facilitate more accurate diagnoses and treatments, reduce the repetitive workload of pathologists, and enable the sharing of pathology diagnostic resources across regions. The advent of digital pathology and the concomitant advancement of computer algorithms have facilitated the application of AI technology in the field of pathology. At present, digital pathology-based AI has demonstrated considerable potential for use in the diagnosis of diseases, the guidance of treatment strategies, the evaluation of therapeutic efficacy, and the prediction of prognosis. This is achieved by the identification of image features, which are automatically learned from digital images and analyzed in relation to labels, such as diagnostic or prognostic purposes [3, 6, 9, 11–13]. These applications of AI in pathology assist in improving the objectivity and accuracy of pathological diagnosis, effectively reducing the workload of pathologists, and laying a solid foundation for the accurate diagnosis and treatment of diseases and the individualized management of patients.

Recent studies conducted comprehensive reviews of the use of AI in managing oral potentially malignant disorders and oral epithelial dysplasia [6, 14]. These findings indicated that AI could serve as a reliable, precise, and personalized medical decision-assisted tool to overcome the limitations of the epithelial dysplasia grading system and contribute to identifying stratified malignant transformation risk and guiding patient treatment strategies [6, 14]. The researches also described the dawn of the application of AI in the field of oral mucosa and explored future implementation pathways and possible challenges. In fact, AI is not only useful for grading management and prognostic assessment of epithelial dysplasia in the oral mucosa but also has promising applications for the clinical management of epithelial dysplasia in multiple organs.

Table 1 presents a review of published reports on the grading and prognostic management of epithelial dysplasia by AI models in various organs, including the oral cavity, larynx, esophagus, stomach, colorectum, and cervix [2–5, 8, 9, 11, 12, 15, 16]. The studies predominantly employed Aperio or Nanozoomer scanning systems with 20× or 40× magnification to obtain digital whole slide images (WSIs). A range of deep learning algorithms, including visual geometry group (VGG) and residual neural network (ResNet), were employed in the construction of AI models. The performance of the models was evaluated using a number of metrics, including the area under the receiver operating characteristic (ROC) curve (AUC), accuracy, sensitivity, and specificity. The dimensions of a WSI exceed the capacity for training and constructing a deep learning model. To address this issue, multi-instance learning (MIL) methods are employed, whereby it is assumed that at least one small region of the image contains the requisite morphological information for image analysis [17]. Consequently, the entire slide is divided into identical patches of the same size and resolution (224 × 224 pixels or 512 × 512 pixels, etc.) for the creation of deep learning AI. While the size of the patch is reduced, the number of images increases exponentially, resulting in the creation of vast datasets comprising millions or even more patches. The AUC was moderate at the patch level, but integrating pathomics features generated by patch-level models through machine learning or deep learning algorithms could improve WSI-level predictive performance [3, 4]. The results of AI for histological grading assessment and prognostic identification of epithelial dysplasia in all reported organs are promising. This suggests that digital pathology-based AI can facilitate the clinical management of epithelial dysplasia in multiple organs.

Table 1. Artificial intelligence (AI) model for histological grading and prognostic identification of various epithelial dysplasia

Organ	Purpose	WSI scanning system	Magnification	Patches	AI model	Model performance	Reference
Oral cavity	Histological grading	Aperio	20×	299 × 299 pixels	VGG16	Testing AUC: 0.65	Araújo et al. [16], Brazil (2023)
	Prognostic identification	Nanozoomer	20×	512 × 512 pixels	ResNet50 and lightGBM	Testing AUC: 0.81 (95% CI, 0.73–0.90)	Cai et al. [3], China (2023)
		Aperio, Nanozoomer	20×, 40×	512 × 512 pixels	IDaRS	Testing AUC: 0.78	Bashir et al. [12], UK (2023)
		Aperio, Nanozoomer	10×	NA	NuClick (for cell detection)	Testing AUC: 0.76 (95% CI, 0.68–0.85)	Mahmood et al. [11], UK (2023)
Larynx	Histological grading	Nanozoomer	20×	224 × 224 pixels	DenseNet121	Testing AUC: 0.89 (95% CI, 0.81–0.95)	Lubrano et al. [2], France (2024)
Esophagus	Histological grading	Mirax Desk	20×	224 × 224 pixels	ResNet50	Testing AUC: 0.80	Beuque et al. [9], Netherlands (2021)
		Aperio	40×	1,280 × 1,280 pixels	YOLOv5 and ResNet101	0.89 accuracy for 3-class, 0.96 accuracy for 2-class	Faghani et al. [5], USA (2022)
Stomach	Histological grading	Iscan Coreo	20×	320 × 320 pixels	ResNet50 and domain adaption	Testing AUC: 0.82	Shi et al. [4], China (2022)
Colorectum	Histological grading	AT2	20×	224 × 224 pixels	ResNet18	Testing AUC: 0.97 (95% CI, 0.95–0.99)	Kim et al. [15], USA (2023)
Cervix	Histological grading	PloidyScanner	20×	224 × 224 pixels	VGG16	Testing AUC: 0.76 (95% CI, 0.73–0.78)	Bao et al. [8], China (2020)

WSI: whole slide image; lightGBM: light gradient boosting machine; IDaRS: iterative draw-and-rank sampling; AUC: area under the receiver operating characteristic curve; 95% CI: lower and upper values of the 95% confidence interval; NA: not applicable; VGG16: visual geometry group 16; ResNet50: residual neural network 50; DenseNet121: dense convolutional network 121; YOLOv5: You Only Look Once version 5

It would seem that there is a growing tendency towards the use of computer-assisted digital pathology in place of conventional pathology techniques. The advent of multi-omics and bioinformatics has enabled pathologists to utilize a greater array of molecular and imaging data as diagnostic references. The advent of high-throughput big data has introduced novel professional demands for pathologists. It is becoming increasingly apparent that histopathology slides contain a wealth of information that extends beyond their diagnostic utility. These include molecular alterations, cellular interactions, and prognostic identification. Nevertheless, there is a growing concern regarding the shortage of histopathologists and the increasing workload. In order to address these challenges, it is essential to develop robust, sensitive, and efficient computational tools that can assist in medical decision-making. Such tools may assist pathologists in performing routine diagnostic tasks and alleviating the considerable workloads they currently face. Moreover, they may provide new insights for precision medicine in further research. It seems reasonable to posit that research and translation based on digital pathology AI will prove to be a key strategy for addressing these challenges in the future.

Abbreviations

AI: artificial intelligence

WSIs: whole slide images

Declarations

Author contributions

XJC: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. The author read and approved the submitted version.

Conflicts of interest

The author declares that there are no conflicts of interest.

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Not applicable.

Consent to participate

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References

1. Tilakaratne WM, Jayasooriya PR, Jayasuriya NS, De Silva RK. Oral epithelial dysplasia: Causes, quantification, prognosis, and management challenges. Periodontol 2000. 2019;80:126–47. [DOI] [PubMed]
2. Lubrano M, Bellahsen-Harrar Y, Berlemont S, Atallah S, Vaz E, Walter T, et al. Diagnosis with confidence: deep learning for reliable classification of laryngeal dysplasia. Histopathology. 2024;84: 343–55. [DOI] [PubMed]
3. Cai X, Li L, Yu F, Guo R, Zhou X, Zhang F, et al. Development of a Pathomics-Based Model for the Prediction of Malignant Transformation in Oral Leukoplakia. Lab Invest. 2023;103:100173. [DOI] [PubMed]
4. Shi Z, Zhu C, Zhang Y, Wang Y, Hou W, Li X, et al. Deep learning for automatic diagnosis of gastric dysplasia using whole-slide histopathology images in endoscopic specimens. Gastric Cancer. 2022;25: 751–60. [DOI] [PubMed]
5. Faghani S, Codipilly DC, Vogelsang D, Moassefi M, Rouzrokh P, Khosravi B, et al. Development of a deep learning model for the histologic diagnosis of dysplasia in Barrett's esophagus. Gastrointest Endosc. 2022;96:918–25.e3. [DOI] [PubMed]
6. Adeoye J, Su YX. Leveraging artificial intelligence for perioperative cancer risk assessment of oral potentially malignant disorders. Int J Surg. 2024;110:1677–86. [DOI] [PubMed] [PMC]
7. Cai X, Zhang J, Zhang H, Zhou X, Zhou Z, Jing F, et al. Architectural and cytological features of epithelial dysplasia associated with transformation risk. Oral Dis. 2023;[Epub ahead of print]. [DOI] [PubMed]
8. Bao H, Bi H, Zhang X, Zhao Y, Dong Y, Luo X, et al. Artificial intelligence-assisted cytology for detection of cervical intraepithelial neoplasia or invasive cancer: A multicenter, clinical-based, observational study. Gynecol Oncol. 2020;159:171–8. [DOI] [PubMed]

9. Beuque M, Martin-Lorenzo M, Balluff B, Woodruff HC, Lucas M, de Bruin DM, et al. Machine learning for grading and prognosis of esophageal dysplasia using mass spectrometry and histological imaging. Comput Biol Med. 2021;138:104918. [DOI] [PubMed]
10. Cai X, Zhang J, Han Y, Tang Q, Zhang H, Li T. Development and validation of a nomogram prediction model for malignant transformation of oral potentially malignant disorders. Oral Oncol. 2021;123: 105619. [DOI] [PubMed]
11. Mahmood H, Shephard A, Hankinson P, Bradburn M, Araujo ALD, Santos-Silva AR, et al. Development and validation of a multivariable model for prediction of malignant transformation and recurrence of oral epithelial dysplasia. Br J Cancer. 2023;129:1599–607. [DOI] [PubMed] [PMC]
12. Bashir RMS, Shephard AJ, Mahmood H, Azarmehr N, Raza SEA, Khurram SA, et al. A digital score of peri-epithelial lymphocytic activity predicts malignant transformation in oral epithelial dysplasia. J Pathol. 2023;260:431–42. [DOI] [PubMed] [PMC]
13. Cai X, Zhang H, Wang Y, Zhang J, Li T. Digital pathology-based artificial intelligence models for differential diagnosis and prognosis of sporadic odontogenic keratocysts. Int J Oral Sci. 2024;16:16. [DOI] [PubMed] [PMC]
14. Alajaji SA, Khoury ZH, Jessri M, Sciubba JJ, Sultan AS. An Update on the Use of Artificial Intelligence in Digital Pathology for Oral Epithelial Dysplasia Research. Head Neck Pathol. 2024;18:38. [DOI] [PubMed] [PMC]
15. Kim J, Tomita N, Suriawinata AA, Hassanpour S. Detection of Colorectal Adenocarcinoma and Grading Dysplasia on Histopathologic Slides Using Deep Learning. Am J Pathol. 2023;193:332–40. [DOI] [PubMed] [PMC]
16. Araújo ALD, Silva VMD, Moraes MC, de Amorim HA, Fonseca FP, Sant'Ana MSP, et al. The use of deep learning state-of-the-art architectures for oral epithelial dysplasia grading: A comparative appraisal. J Oral Pathol Med. 2023;52:980–7. [DOI] [PubMed]
17. van der Laak J, Litjens G, Ciompi F. Deep learning in histopathology: the path to the clinic. Nat Med. 2021;27:775–84. [DOI] [PubMed]