BRAIN. Broad Research in Artificial Intelligence and Neuroscience

e-ISSN: 2067-3957 | p-ISSN: 2068-0473

Covered in: Web of Science (ESCI); EBSCO; JERIH PLUS (hkdir.no); IndexCopernicus; Google Scholar; SHERPA/RoMEO; ArticleReach Direct; WorldCat; CrossRef; Peeref; Bridge of Knowledge (mostwiedzy.pl); abcdindex.com; Editage; Ingenta Connect Publication; OALib; scite.ai; Scholar9; Scientific and Technical Information Portal; FID Move; ADVANCED SCIENCES INDEX (European Science Evaluation Center, neredataltics.org); ivySCI; exaly.com; Journal Selector Tool (letpub.com); Citefactor.org; fatcat!; ZDB catalogue; Catalogue SUDOC (abes.fr); OpenAlex; Wikidata; The ISSN Portal; Socolar; KVK-Volltitel (kit.edu)

2024, Volume 15, Issue 3, pages: 167-179.

Submitted: June 15th, 2024| *Accepted for publication:* October 28th, 2024

Artificial Intelligence Revolutionizes Esophageal Squamous Cell Carcinoma Management

Ana Fulga [1]
Doriana Iancu [2]
Oana-Maria Dragostin [3]
Iuliu Fulga [4]
Bogdan Alexandru Ciubara [5]
Carmina Liana Musat [6]
Ionut Dragostin [7]
Anamaria Ciubara [8]

[1] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, ana.fulgaa@gmail.com, https://orcid.org/0000-0002-7360-2796
[2] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, c_doriana@yahoo.com, https://orcid.org/0000-0002- 9469-2866
[3] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, oana.dragostin@ugal.ro
[4] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, fulgaiuliu@yahoo.com, https://orcid.org/0000-0002-7414-9348
[5] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, bogdan.ciubara@ugal.ro, https://orcid.org/0000-0002-8037-6002
[6] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, carmina.musat@ugal.ro, https://orcid.org/0000-0002-2383-6455
[7] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, ionut.dragostin@yahoo.com
[8] Dunarea de Jos University of Galati, Faculty of Medicine and Pharmacy, 35 AI Cuza st., 800010 Galati, Romania, anamburlea@yahoo.com, https://orcid.org/0000-0003-0740-3702

Abstract: *The application of artificial intelligence in esophageal tumor pathology highlights the ongoing and significant transformative impact AI has in medicine. This article provides a comprehensive overview of AI technologies' current use in diagnosing and treating esophageal squamous cell carcinoma (ESCC). Through our research, we identified and meticulously analyzed 33 relevant academic papers and studies that contribute to this field. These papers encompass a broad spectrum of AI applications related to the management of esophageal squamous cell carcinoma. AI integration and deployment in both the diagnosis process and therapeutic interventions for tumors offer highly promising prospects, for example, in endoscopic procedures AI algorithm can process endoscopic images in real-time to identify abnormalities that may be missed by the human eye, it can highlight subtle changes such as color variations, small growths or tissue anomalies, which might go unnoticed due to fatigue, distraction or human limitations in perceiving fine details. AI technologies enhance medical practice precision and effectiveness by significantly reducing the likelihood of human errors and offering practical, innovative solutions. Consequently, AI confluence with medical practice not only increases diagnosis accuracy but also improves the overall efficiency of treating esophageal squamous cell carcinoma.*

Keywords: *artificial intelligence; esophagus; squamous cell carcinoma; diagnosis.*

How to cite: Fulga, A., Iancu, D., Dragostin, O.-M., Fulga, I., Ciubara, B. A., Musat, C. L., Dragostin, I., & Ciubara, A. (2024). Artificial intelligence revolutionizes esophageal squamous cell carcinoma management. *BRAIN: Broad Research in Artificial Intelligence and Neuroscience*, 15(3), 167-179. https://doi.org/10.70594/brain/15.3/12

1. Introduction

Artificial intelligence (AI) management of esophageal squamous cell carcinoma (ESCC) has illustrated highly encouraging results in both the treatment and diagnosis of this type of cancer. AI technologies, with a particular focus on convolutional neural networks (CNN) and deep learning (DL) algorithms, have proven to be exceptionally effective in the identification and classification of esophagus lesions. Numerous preclinical studies have underscored the significant utility that AI systems bring to the diagnosis of ESCC (Tani, Y., et al. 2023; Piraianu, A.I., et al, 2023; Fulga, I., et al. 2008; Patrascanu, O.S., et al. 2024). One notable multicenter study demonstrated that computer-aided diagnosis systems, grounded in artificial intelligence, effectively support the diagnosis of lymph node metastasis in ESCC (Zhang, S.T., et al. 2023). This finding underscores the potential of AI to augment traditional diagnosis frameworks.

In a more recent and innovative research approach, deep learning techniques were applied specifically for the early detection of esophageal squamous cell carcinoma (Liao, J., et al., 2023). The challenge in early esophageal cancer detection often lies in the ability to accurately diagnose subtle macroscopic lesions using endoscopy. The interpretation of endoscopic images relies heavily on the experience and diagnostic proficiency of the endoscopist, making it vulnerable to human error. Herein lies the growing relevance of AI-assisted endoscopy which plays a pivotal role in reducing these discrepancies and enhancing diagnosis accuracy.

AI endoscopy has the potential to significantly minimize the variability and errors associated with human interpretation, thereby improving diagnosis outcomes. A recent systematic review and meta-analysis bolstered the evidence for AI effectiveness in the endoscopic diagnosis of esophageal cancer (Guidozzi, N. et al., 2023). This body of evidence collectively suggests that AI, when integrated into endoscopic procedures, can greatly enhance early detection capabilities and offer a robust, reliable support system for medical professionals in diagnosing esophageal squamous cell carcinoma. As such, the continued development and implementation of AI technologies in this domain promises to elevate the standards of medical practice, potentially leading to better patient outcomes and more efficient management of esophageal cancer.

In terms of treatment, AI could play an important role in planning surgery and adjuvant treatments such as chemotherapy and radiotherapy. A notable example is the use of AI for the assessment of intrapapillary capillary invasion, which helps to determine tumor invasion depth and, implicitly, to select the most appropriate therapeutic strategy. Thus, a group of researchers focused on the tools that AI offers in addressing this disease and tried to provide an upgraded vision to maximize present uses and identify future directions of this technology (Zhang, Y.H., et al., 2020).

Esophageal cancer is a major diagnosis, economic, and therapeutical challenge in high-endangered regions. Its major risk factors include tobacco and alcohol consumption, both carcinogens can cause direct damage to the DNA of esophageal cells, leading to mutations and neoplasm development; dietary factors such as hot beverages consumption which causes chronic inflammation and increases ESCC risk; nutritional deficiencies, as well as preserved and processed foods; socio-economical factors and genetic predispositions.

AI use has advanced outcome prediction and diagnosis by integrating various features such as clinical, pathological, radiological, and genetic variables to achieve promising results. Big data AI can discover hidden patterns, meaningful information, and deep knowledge from huge masses of data.

For example, deep learning and machine learning technologies can be used to extract deep understanding in areas such as genomics, transcriptomics, proteomics, radio mics, and digital pathological image analysis as so: analyzing large-scale genomic data and DNA sequences to help identify mutations, structural variations, and genetic variants associated with different diseases, ML models can predict the functional impact of genetic mutations, for example, whether a variant is benign or pathogenic, also improves the understanding of genotype-phenotype relationships.

In transcriptomics, the models are applied to analyze RNA sequencing data to understand gene expression patterns across different conditions or tissues. These models can uncover differential gene expression, leading to insights into cell behavior, development, and disease progression. It also helps with dimensionality reduction and clustering in scRNA-seq data, identifying cell types and states in complex tissues, for example identifying rare cell populations and providing insight into cell differentiation in developmental biology or cancer.

This approach can assist physicians in a comprehensive and synthetic understanding of tumoral pathology. In addition, AI can identify recently developed biomarkers from available data, helping to improve the process of screening, detection, diagnosis, treatment, and prognosis of tumors. By doing so, personalized treatment can be provided and clinical outcomes can be optimized for each patient (Kawamura, M. et al., 2024).

DL, particularly CNNs is applied to digitized pathology slides to identify and classify disease states such as cancerous tissues, they can also assess the tumoral grade and severity by analyzing patterns in tissue images, providing more consistent and objective grading.

AI and the learning methods vary in complexity and applicability: Deep Learning (DL) and Machine Learning (ML) are general frameworks that incorporate multiple specific techniques, including neural networks (Lee, S.I. et al., 2018; LeCun, Y., et al., 2015) and Convolutional Neural Networks (CNN) represent neural networks that apply in specific scenarios (images for CNN) (Piraianu, A.I., 2023).

2. Literature Review

The authors performed an extensive current literature review, that included original articles studying various clinical AI applications in ESCC. The authors have also conducted comprehensive searches of Google Scholar, Science Direct, PubMed, and Web of Science databases for identifying relevant manuscripts. 2 sets of keywords were used to recognize the title terms, studies abstract, and keywords: (i) the first set included „artificial intelligence" combined with „esophageal squamous cell carcinoma" and „diagnosis"; (ii) the second set, the term „artificial intelligence" combined with „esophageal squamous cell carcinoma" and „treatment". We limited our search to papers published in English within the previous 6 years; in addition, AI and ESCC publications were consulted and we found more than 33 relevant ones.

The selection criteria for our review were meticulously focused on studies that examined the application of artificial intelligence in the context of esophageal squamous cell carcinoma. Throughout our research, we diligently and consistently applied these selection criteria to assess the relevance and quality of the studies included. To ensure thorough evaluation, the studies were critically analyzed based on several key criteria: (1) the journal in which the study was published, (2) the publication date to ensure the latest advancements were considered, (3) the overall study design to analyze the robustness of the search framework, (4) the methods of analysis employed in each study to gauge their appropriateness and precision, (5) the results presented, and (6) the conclusions drawn by the authors.

During the initial screening process, the abstracts of the identified studies were carefully reviewed and any studies that were not written in English were excluded to maintain linguistic consistency and comprehensive understanding. To further assure the quality and reliability of the data, particular attention was given to several specific characteristics in the comprehensive review of studies that met all the criteria. This included evaluating the rational design of methods, the clarity and accuracy of the results, the depth of the discussion, the soundness of the conclusions, and identifying any signs of methodological bias or issues in data interpretation that might influence or negatively impact the results of the reviewed studies.

Additionally, we scrutinized potential sources of bias that could arise from various factors such as sample size, selection process, and data analysis methods. By doing so, we aimed to identify any methodological flaws or interpretational errors that could undermine the validity and reliability of the findings. This rigorous approach allowed us to curate a selection of studies that not only aligned with our initial criteria but also upheld high standards of scientific integrity. Such thorough vetting ensures that the conclusions drawn from our review are founded on high-quality evidence, providing a reliable foundation for understanding the application of AI in the diagnosis and treatment of ESCC.

The inclusion criteria were the following: studies examining the AI application in otorhinolaryngology, the treatment and diagnosis of ESCC; English publications; published in the last 6 years, studies in the structure of an academic journal article.

Exclusion criteria were the following: non-English articles; withdrawn studies (the removal is essential to maintain the integrity and credibility); posters, short papers or abstracts only; duplicate studies; and studies with an abstract or title that does not match the topic. Research limitations included methodology variations between included studies and potential publication bias. The rapid evolution of AI technologies in healthcare restricts capturing the latest research.

3. Results

After a thorough assessment and review of the 356 articles, the authors identified and included a subset of 33 directly relevant papers to our research. These selected studies provided valuable insights into the AI use and impact in Otorhinolaryngology, forming the basis of our review. The 33 scientific articles reviewing the present applications of AI in the management of ESCC have been schematically summarized in Table 1.

Table 1. Scientific articles analyzing AI management in ESCC.

	Year of Study	**Author**	**ML/DL/CNN Method**	**Application**
AI endoscopy	2020	Tokai Y. (2020)	CNN	Early diagnosis
	2023	Mohan A. (2023)	ML DL	Diagnosis, treatment, and prognosis
	2019	Horie Y. (2019)	CNN	Early screening
	2023	Huang J. (2023)	ML DL	Early screening
	2022	Gong EJ. (2022)	DL	Diagnosis
	2020	Hussein M. (2020)	DL	Screening and early diagnosis
	2023	Pan Y (2023)	CNN	Diagnosis
	2023	Zhang J.Q. (2023)	CNN	Screening, early diagnosis, and favorable prognosis
	2021	Shiroma S. (2021)	DL	Diagnosis
	2018	di Pietro M. (2018)	CNN	Screening, diagnosis, and therapy
	2021	Bang C.S. (2021)	ML	Diagnosis
	2020	Huang L.M. (2020)	CNN	Early screening
	2021	Liu Y. (2021)	CNN	Early screening
	2021	Li J.C. (2021)	CNN	Early screening
	2022	Tsai T.J. (2022)	CNN	Early screening
	2022	Shimamoto. Y. (2022)	ML DL	Depth invasion screening
	2021	Berbís M.A. (2021)	ML	Diagnosis
	2023	Yuan X.L. (2023)	CNN	Early screening
	2022	Liu W. (2023)	CNN	Early screening
Advanced imaging diagnosis with AI	2023	Hosseini F. (2023)	CNN	Early screening CT
	2024	Wu X (2024)	DL	Prediction CT
	2023	Yue Y. (2023)	CNN GloD LoATUNet	Segmentation PET-CT

	2023	Zhong H. (2023)	CNN 3D Res-UNet	Segmentation CT
	2021	Yeh J.C. (2021)	CNN 3D-CNN	Prognosis PET-CT
Molecular and genomic diagnosis with AI	2022	Sasagawa S. (2022)	ML	Immuno-genomic profile
AI radiotherapy	2024	Kawamura M. (2024)	ML	Revolutionizing AI radiotherapy
	2021	Jin D. (2021)	ML	Tumor size measurement
	2021	Liu R. (2021)	ML	Radiotherapy efficiency evaluation
	2023	Xie Y. (2023)	ML	Radiotherapy response prediction

4. Discussions

Esophageal cancer (EC) is one of the most common malignant tumors of the digestive tract. Early EC lesion treatment by endoscopic therapy can lead to a cure, the curative effect being similar to surgery. Currently, the upper gastrointestinal endoscopy remains the standard method for diagnosing CE, with its accuracy partly dependent on the clinicians' professional experience. Artificial intelligence use in screening for early detection of CE is especially helpful for less experienced endoscopists. Tokai at al., reviewed the advances in applied artificial intelligence technology in the early clinical diagnosis of EC by endoscopy, which proved useful for those interested in this field (Tokai, Y., et al. 2020).

Combining artificial intelligence technologies with endoscopic methods is a promising direction for improving the management and diagnosis of esophageal cancer. This integration has the potential to improve patient outcomes and minimise the mortality rate associated with this serious form of cancer. A recent study aimed to analyze and understand the application of artificial intelligence in the diagnosis, treatment, and prognosis of esophageal cancer, highlighting the crucial role of computer-assisted diagnosis and computer-aided detection as essential tools for medical practitioners in the near future (Mohan, A., et al., 2023).

The CNN system developed for esophageal cancer detection can quickly examine stored endoscopic images with elevated sensitivity. However, intensive training could improve diagnosis accuracy. The use of this system could facilitate early identification in practice, with the potential to improve short-term prognosis (Horie, Y., et al., 2019).

Another study pursues to highlight the applications and perspectives of artificial intelligence-assisted endoscopic ultrasound (EUS-AI) in the digestive diseases field in the last decade. It complements recent studies, which have revealed that EUS-AI has proven superiority or at least equivalence compared to conventional methods in the diagnosis, prognosis, and quality monitoring of under epithelial lesions, early esophageal and gastric, also pancreatic diseases, including cysts, autoimmune pancreatitis, and cancer. EUS-AI implementation has opened new perspectives for individualized precise medicine and introduced new approaches in the diagnosis and treatment of digestive diseases (Huang, J., et al., 2023).

A deep learning model has recently been developed that can accurately classify esophageal cancers, precancerous lesions, and non-neoplasms. This model validation was carried out by multicenter external tests, and the explanations for its decisions are supported by attention map analysis (Gong, E.J., et al., 2022). Computer-aided diagnosis can play a crucial role in the near future in supporting endoscopists for the early detection and diagnosis of esophageal cancers, thereby facilitating the administration of curative endoscopic therapy. This technology promises to support doctors' efforts in identifying and treating esophageal cancer in its early stages (Hussein, M., et al., 2020).

A 2023 study investigated the use of artificial intelligence to diagnose early-stage ESCC and estimate the depth of tumor invasion through various imaging techniques. The remarkable ability of AI to recognize images is essential for the identification and diagnosis of ESCC, having the potential to reduce diagnosis errors and support endoscopists in their evaluations (Pan, Y., et al.

2023). Advances in diagnostic technologies have facilitated screening implementation, early detection, and improved prognosis. The use of CNN for image analysis promises to revolutionize esophageal cancer diagnosis and prognosis, offering promising perspectives in the early detection of early stages and dysplasia (Zhang, J.Q., et al. 2023). In recent years, artificial intelligence potential built on deep learning has been explored for the diagnosis of superficial ESCC in video images obtained during esogastroduodenoscopy (EGD) (Shiroma, S., et al., 2021). Since the esophagus can be easily accessed by endoscopy, early identification, and curative treatment is feasible (DiPietro, M., et al., 2018). Esophageal cancer diagnosis or precancerous lesions by endoscopic imaging depends on the clinician's level of expertise and is inevitably affected by the variability of observations between different operators.

The need for more effective methods to detect and characterize early esophageal neoplasm has led to an AI research intensification. Thus, AI techniques in the endoscopic detection of early EC are intensively reviewed. Research is also being done on the morphopathological and genetic diagnosis of early EC, as well as risk assessment (Huang, L.M, et al., 2020).

Remarkable technological progress is currently being observed in the AI field applications for the early clinical detection of CE by endoscopy, being useful for those interested in this development (Liu, Y., 2021). Non-magnifying endoscopy with narrow-band imaging (NM-NBI) has been often used in routine ESCC screening. NBI performance for early ESCC screening is, however, notably affected by operator experience. Artificial intelligence can be a unique approach to compensate for operator inexperience (Li, J.C., et al., 2021).

Another update is represented by esophageal cancer early diagnosis by band-selective hyperspectral imaging. Thus, the integration of hyperspectral imaging (HSI) with spectral selection for color reproduction was explored. White light imaging (WLI) was simulated to mimic NBI (Tsai, T.J., et al., 2022). Shimamoto Y.'s 2020 study explores artificial intelligence use for real-time evaluation of video images in determining the invasion depth of esophageal squamous cell carcinoma (Shimamoto, Y., et al, 2020).

Generally, AI and ML have considerable potential to assist physicians in the evaluation of cancerous diseases and other gastrointestinal tract conditions. Their use in radiology interpretation and endoscopic pathologic images can have extensive applications in various clinical scenarios. They include automatic tumoral detection, classification and segmentation, assessment of tumor staging, patient stratification, and treatment response prediction (Berbis, M.A., et al., 2021).

Although NBI is a useful way for the detection and delineation of ESCC, there is a risk of incorrectly determining some lesions' edges even with NBI. Yuan et al., aimed to develop an AI system for detecting superficial ESCC and precursor lesions, also delineating lesions extent under NBI. This AI system could accurately detect superficial ESCCs and precursor lesions and delineate the extent of lesions under NBI (Yuan, X.L., et al, 2023).

Another study mentions that endoscopy with WLI is the most used technique used for ESCC screening, but it can be difficult to precisely detect and delineate early ESCC margins using this method. The authors developed an AI model that improves this detection and delineation capability under WLI endoscopy, thereby providing a more accurate and efficient method for the early diagnosis of ESCC. It is remarkable that by using AI, the study demonstrated a favourable approach to improve efficiency and accuracy in the diagnosis of early ESCC, a condition where rapid and accurate detection can significantly influence patient prognosis and treatment (Liu, W., et al, 2022).

AI and integrated endoscopic technologies offer new insights and solutions for esophageal cancer diagnosis and treatment. These advances could significantly improve diagnosis accuracy, disease management, and patient prognosis, particularly in the early identification of malignant tumors. The use of AI is particularly beneficial for less experienced practitioners, helping to reduce error rates and improve outcomes.

This review results highlight machine learning-based potential methodologies in esophageal cancer early detection. The average analyzed methodologies accuracy in endoscopic computed tomography (CTE) was over 89%, highlighting a significant impact in the early CE identification.

Furthermore, the greatest success in using clinical imaging for early detection has been seen in WLI. Among all machine learning techniques, CNNs have demonstrated superior accuracy and sensitivity in early CE identification compared to other methods. The use of these machine learning methods can significantly contribute to improving the accuracy in the early detection of CE, providing essential support to radiologists, endoscopists, and pathologists in diagnosis and therapeutic planning (Hosseini, F., et al, 2023).

Obtaining an accurate prediction of the depth invasion of ESCC is crucial for optimizing treatment and reducing invasive procedures, thereby minimizing complications and associated costs. Currently, available methods, which are often invasive and expensive, have difficulty achieving the required level of precision. This situation underlines the urgent need for more effective and non-invasive alternatives (Wu, X., et al, 2024).

Radiotherapy plays a crucial role in esophageal squamous cell carcinoma primary treatment. In the pre-radiotherapy planning stage, a major challenge is the precise delineation of gross esophageal tumor (GTV) volume on images. In the current clinical practice, manual delineation is affected by high integrated variability and even between assessments by the same oncologist and is an exhausting task. There is an urgent requirement for efficient computer-aided automatic segmentation methods. For this purpose, there was developed a new deep neural network named GloD-LoATUNet (Yue, Y., et al., 2023).

Another innovative method was implemented to evaluate the 3D Res-UNet model effectiveness in the fully automated segmentation of esophageal cancer (EC) and to compare segmentation accuracy between traditional images (CI) and 40 keV virtual monoenergy images (Zhong, H., et al., 2023).

The existence of lymphovascular invasion (LVI) and perineural invasion (PNI) is of great importance in the prognosis of esophageal squamous cell carcinoma. At present, positron emission tomography (PET) is the only means of functional assessment before treatment. In this regard, a method was proposed to predict LVI and PNI presence in esophageal squamous cell carcinoma using pet imaging data by teaching a three-dimensional convolutional neural network (3D-CNN) (Yeh, J.C., et al, 2021).

Recent advances in radiomic technologies signify the advent of a groundbreaking era in biomarker discovery, heralding the potential for much deeper and more detailed tumor characterization. This new frontier is made possible by the availability of massive volumes of medical data and the sophisticated use of computerized image analysis, significantly augmented by the capabilities of artificial intelligence. These advancements open up promising new perspectives for the identification of more accurate and robust biomarkers, which are crucial in the precise understanding and treatment of various cancers, including esophageal cancer.

AI-assisted medical imaging and machine learning represent a significant leap forward, holding immense potential to transform clinical outcomes by enhancing early detection capabilities, facilitating precise tumor segmentation, and predicting the patterns of tumor invasion in esophageal cancer. These technologies are not only valuable in increasing the accuracy and efficiency of initial diagnosis but also play a critical role in ongoing therapeutic monitoring and planning.

Implementing these cutting-edge technologies into clinical practice promises to revolutionize the way practitioners approach cancer diagnosis and treatment. By reducing interrater variability, AI can ensure more consistent and reliable assessments across different medical professionals. Moreover, these technologies can substantially decrease the manual effort required for image analysis, freeing up valuable time for healthcare providers to focus on patient care and other critical tasks. Additionally, the reduction in associated complications with manual image interpretation leads to improved patient outcomes and a better overall healthcare experience.

Furthermore, AI and machine learning algorithms offer the capability to continuously learn and improve from new data, enhancing their accuracy and utility over time. This continuous improvement can facilitate the development of personalized treatment plans, tailored to the specific characteristics of the patient’s tumor, thereby optimizing therapeutic efficacy and minimizing adverse effects.

As these technologies continue to evolve, they will likely become integral components of a comprehensive cancer care strategy, seamlessly integrating with existing diagnostic tools and therapeutic approaches. AI’s potential to provide real-time, data-driven insights can assist clinicians in making more informed decisions, ultimately leading to better prognosis and higher survival rates for patients with esophageal cancer. The convergence of AI with radio mics and medical imaging thus holds the promise of a future where cancer care is more precise, personalized, and effective, paving the way for significant advancements in the early detection, diagnosis, and treatment of esophageal cancer, and possibly other types of cancer as well.

Biopsy specimen immunogenomic profiling predicts response to neoadjuvant chemotherapy in ESCC. Esophageal squamous cell carcinoma is one of the most aggressive types of cancer and is mainly treated with platinum-based NAC. Some of these react well to NAC. Still, biomarkers predict NAC sensitivity and their response mechanism in esophageal squamous cell carcinoma remains unclear. Genome and RNA sequencing examination of 141 ESCC biopsy specimens before NAC treatment to result in a machine learning-based diagnosis model was performed to predict NAC reactivity in ESCC and analysis of the association between immunogenomic features and NAC response. Neutrophil infiltration may play an important role in ESCC's response to NAC. Specific copy number alterations and copy number signatures in the ESCC genome have also been shown to be significantly associated with NAC response. Interactions between tumor genome and immune characteristics of ESCC are probably a good indicator of a therapeutic target for ESCC, and machine learning prediction for NAC response is useful (Testa, U., et al, 2017).

Major somatic genetic abnormalities presented a different genetic landscape in esophageal adenocarcinoma (EAC) compared to ESCC. EAC is a heterogenous cancer, that is dominated by copy number alterations, a high mutational burden, receptor tyrosine-kinase co-amplification, and frequent TP53 mutations. The cellular origins of EAC are still not well understood: animal models have supported a cellular origin either from stem cells located in the basal layer of the esophageal epithelium or from progenitors present in the cardia region. Many studies support the cancer stem cells (CSCs) existence and their capability of initiating and maintaining EAC or ESCC. The exact CSCs identification as well as their purpose in EAC and ESCC pathogenesis remain to be demonstrated. The reviewed studies suggest that the current molecular and cellular characterization of EAC and ESCC should serve as a background for the development of up-to-date treatment strategies (Merchan Gomez, B., et al, 2023).

AI systems, particularly CNNs and deep learning methods, have significantly improved the accuracy of diagnosing ESCC, with some methodologies achieving over 89% accuracy in early detection via endoscopic computed tomography (CTE). AI algorithms, such as deep learning models, are used to analyze MRI or CT scans of the brain, detecting early signs of tumors or abnormal growths. This can be crucial for identifying brain metastasis from neoplasms like pharyngo-esophageal cancer. CNNs excel in pattern recognition, helping in the identification of small lesions that might indicate early-stage neurological deterioration, potentially linked to cancer-related effects. Some patients suffer from neurodegenerative conditions, such as cognitive decline due to cancer-related factors. AI can help detect these changes early through imaging biomarkers, improving treatment outcomes. Studies have highlighted AI's role in reducing human error rates and variability in interpretation during endoscopic procedures, providing substantial support for medical professionals, and improving early detection capabilities.

AI use in genomic analysis represents a significant advance in cancer diagnosis and treatment. Biopsy specimens immunogenomic offers a promising method for personalizing treatment, while genomic and molecular characterization of esophageal cancer opens new avenues for innovative therapies. Integrating these approaches into clinical practice can transform cancer management by providing patients with more effective and personalized treatments.

From a radiation-oncology specialist’s point of view, broad perspectives are emerging on the application of artificial intelligence in radiotherapy. Thus, the use of AI in the context of self-segmentation is explored and current trends in planning, optimization, evaluation, and prognosis prediction in radiation treatments are analyzed, focusing on the benefits that AI can bring to both patients and medical staff, highlighting future perspectives for this technology in the field (Jin, D., et al., 2021). Extensive studies have addressed the following AI-assisted ESCC treatment perspectives:

-DeepTarget, with whole tumor assessment and clinical target volume segmentation in esophageal cancer radiotherapy (Dong, Y., et al, 2015);

-Clinical target volume precise delineation for cross-segmented ESCC based on the lymph node metastases model (Liu, Z., et al., 2021);

-Evaluating local and regional failure and its impact on survival by comparing involved field irradiation (IFI) with elective lymph node irradiation (ELN) for patients with esophageal squamous cell carcinoma who underwent postoperative radiotherapy (Moding, E.J., et al. 2013);

-Advances in understanding the hallmarks of cancer and the discovery of specific pathways by which cells react to radiation have opened new perspectives for the development of targeted molecular therapies, intending to expand the therapeutic efficacy of radiotherapy with the development of strategies that could improve the results of radiation therapy, either by increasing the chances of tumor healing or by reducing toxicity on healthy tissues (Xie, Y., et al., 2023);

-Establishment and validation of an artificial neural network-based radiomics model for pretreatment prediction of radiotherapy reaction of advanced ESCC, by using integrated data combined with the feasible baseline features of computed tomography (Turing, A.M.I., et al., 1950).

Integrating artificial intelligence into esophageal squamous cell carcinoma treatment offers numerous benefits, from non-invasive and accurate diagnosis to optimizing and personalizing radiation therapy. Continued advances in the field promise to significantly improve treatment outcomes and patients' quality of life, while reducing the risks and side effects associated with traditional procedures.

AI has facilitated more precise treatment planning and execution in radiotherapy, with advancements such as automatic segmentation methods – like the newly developed deep neural network GloD-LoATUNet – enhancing the accuracy of tumor volume delineation.

Integration of AI into molecular and genomic diagnosis has allowed for the prediction of treatment responses, opening doors for personalized therapeutic strategies.

Research in the field of artificial intelligence (AI), particularly when applied to medical diagnosis and treatment, often faces a variety of limitations. One of the primary challenges is data quality and availability, as most AI models require large volumes of high-quality data to learn effectively. In many instances, the necessary data may be incomplete, inconsistent, or difficult to access, which can hinder the development and accuracy of these models.

Data heterogeneity is another significant limitation, as data sourced from different institutions, machines, or patient populations can vary widely, leading to inconsistency that can affect the model's performance. This variability necessitates extensive preprocessing and normalization efforts to ensure that the AI systems can generalize across diverse datasets.

Population diversity further complicates the generalizability of AI models. Many models are trained on specific populations or demographics, which can limit their effectiveness when applied to different groups. For instance, a model trained on a predominantly caucasian population may not perform as well on a diverse, multi-ethnic cohort. This limitation underscores the need for training datasets to be representative of the broader population to avoid biases and ensure equitable performance across all patient groups.

The cost associated with developing, implementing, and maintaining AI systems is another major consideration. The financial investment required for these technologies includes not only the initial development and acquisition of data, but also ongoing expenses related to system updates, maintenance, and integration with existing healthcare infrastructure. Small or under-resourced medical facilities may find it challenging to allocate the necessary funds for these advanced systems, potentially leading to disparities in access to cutting-edge diagnostic and treatment tools.

Despite these limitations, ongoing research and technological advancements continue to address these challenges, bringing AI closer to realizing its full potential in enhancing medical diagnosis and treatment.

5. Conclusions

The field of AI in the diagnosis and treatment of esophageal cancer is solidly positioned at the forefront of medical innovation, offering promising prospects for further advancements. Continuous research and development, coupled with efforts to address existing limitations, are likely to enhance AI's role in personalized medicine, improving diagnosis accuracy and therapeutic efficacy. As AI technologies continue to mature, they hold the potential to revolutionize cancer care, promoting more precise, personalised, and effective treatment paradigms. These solid foundations position AI as a critical tool in transforming clinical practice and improving patient outcomes in esophageal squamous cell carcinoma.

Latest advances in artificial intelligence use and integrated endoscopic technologies have transformed approaches in esophageal cancer treatment and diagnosis. The implementation of these technologies offers significant opportunities to enhance diagnosis accuracy, disease treatment, and prognosis. Artificial intelligence plays an important role in malignant lesions early detection, reducing errors and inter-rater variability, which can revolutionize clinical practice and lead to more personalized and effective treatments. Also, advances in genomic and molecular analysis increase the prospect of developing innovative therapies tailored specifically to each patient, which could radically transform the management of esophageal cancer.

References

Bang, C. S., Lee, J. J., & Baik, G. H. (2021). Computer-aided diagnosis of esophageal cancer and neoplasms in endoscopic images: A systematic review and meta-analysis of diagnostic test accuracy. *Gastrointestinal Endoscopy, 93*(5), 1006-1015.e13. https://doi.org/10.1016/j.gie.2020.11.025

Berbís, M. A., Aneiros-Fernández, J., Mendoza Olivares, F. J., Nava, E., & Luna, A. (2021). Role of artificial intelligence in multidisciplinary imaging diagnosis of gastrointestinal diseases. *World Journal of Gastroenterology, 27*(27), 4395-4412.

Di Pietro, M., Canto, M. I., & Fitzgerald, R. C. (2018). Endoscopic management of early adenocarcinoma and squamous cell carcinoma of the esophagus: Screening, diagnosis, and therapy. *Gastroenterology, 154*(2), 421-436. https://doi.org/10.1053/j.gastro.2017.07.041

Dong, Y., Guan, H., Huang, W., Zhang, Z., Zhao, D., Liu, Y., Zhou, T., & Li, B. (2015). Precise delineation of clinical target volume for crossing-segments thoracic esophageal squamous cell carcinoma based on the pattern of lymph node metastases. *Journal of Thoracic Disease, 7*(12), 2313-2320. https://doi.org/10.3978/j.issn.2072-1439.2015.12.10

Fulga, I., Musat, C. L., Crassas, R., & Ceavdari, N. (2008). Child sexual abuse: Offender's modus operandi aspects in intra-aggressional period. *Romanian Journal of Legal Medicine, 16*(1), 31–36.

Gong, E. J., Bang, C. S., Jung, K., Kim, S. J., Kim, J. W., Seo, S. I., Lee, U., Maeng, Y. B., Lee, Y. J., Lee, J. I., Baik, G. H., & Lee, J. J. (2022). Deep-learning for the diagnosis of esophageal cancers and precursor lesions in endoscopic images: A model establishment and nationwide multicenter performance verification study. *Journal of Personalized Medicine, 12*(7), 1052. https://doi.org/10.3390/jpm12071052

Guidozzi, N., Menon, N., Chidambaram, S., & Markar, S. R. (2023). The role of artificial intelligence in the endoscopic diagnosis of esophageal cancer: A systematic review and meta-analysis. *Diseases of the Esophagus, 36*(12), doad048. https://doi.org/10.1093/dote/doad048

Horie, Y., Yoshio, T., Aoyama, K., Yoshimizu, S., Horiuchi, Y., Ishiyama, A., Hirasawa, T., Tsuchida, T., Ozawa, T., Ishihara, S., Kumagai, Y., Fujishiro, M., Maetani, I., Fujisaki, J., &

Tada, T. (2019). Diagnostic outcomes of esophageal cancer by artificial intelligence using convolutional neural networks. *Gastrointestinal Endoscopy, 89*(1), 25-32. https://doi.org/10.1016/j.gie.2018.07.037

Hosseini, F., Asadi, F., Emami, H., & Ebnali, M. (2023). Machine learning applications for early detection of esophageal cancer: A systematic review. *BMC Medical Informatics and Decision Making, 23*(1), 124.

Huang, J., Fan, X., & Liu, W. (2023). Applications and prospects of artificial intelligence-assisted endoscopic ultrasound in digestive system diseases. *Diagnostics, 13*(17), 2815. https://doi.org/10.3390/diagnostics13172815

Huang, L. M., Yang, W. J., Huang, Z. Y., Tang, C. W., & Li, J. (2020). Artificial intelligence technique in detection of early esophageal cancer. *World Journal of Gastroenterology, 26*(39), 5959-5969. https://doi.org/10.3748/wjg.v26.i39.5959

Hussein, M., González-Bueno Puyal, J., Mountney, P., Lovat, L. B., & Haidry, R. (2020). Role of artificial intelligence in the diagnosis of oesophageal neoplasia: 2020 an endoscopic odyssey. *World Journal of Gastroenterology, 26*(38), 5784-5796. https://doi.org/10.3748/wjg.v26.i38.5784

Jin, D., Guo, D., Ho, T. Y., Harrison, A. P., Xiao, J., Tseng, C. K., & Lu, L. (2021). DeepTarget: Gross tumor and clinical target volume segmentation in esophageal cancer radiotherapy. *Medical Image Analysis, 68*, 101909. https://doi.org/10.1016/j.media.2020.101909

Kawamura, M., Kamomae, T., Yanagawa, M., Kamagata, K., Fujita, S., Ueda, D., Matsui, Y., Fushimi, Y., Fujioka, T., Nozaki, T., Yamada, A., Hirata, K., Ito, R., Fujima, N., Tatsugami, F., Nakaura, T., Tsuboyama, T., & Naganawa, S. (2024). Revolutionizing radiation therapy: The role of AI in clinical practice. *Journal of Radiation Research, 65*(1), 1-9.

LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature, 521*(7553), 436–444. https://doi.org/10.1038/nature14539

Lee, S. I., Celik, S., Logsdon, B. A., Lundberg, S. M., Martins, T. J., & Oehler, V. G. (2018). A machine learning approach to integrate big data for precision medicine in acute myeloid leukemia. *Nature Communications, 9*(1), 42. https://doi.org/10.1038/s41467-017-02465-5

Li, J. C., Li, B., Cai, S. L., Tan, W. M., Alikong, A., Feng, X. S., Yu, H. H., Lu, P. X., Feng, Z., Yao, L. Q., Zhou, P. H., Yan, B., Zhong, Y. S., & Yuan, X. L. (2021). Comparative study on artificial intelligence systems for detecting early esophageal squamous cell carcinoma between narrow-band and white-light imaging. *World Journal of Gastroenterology, 27*(3), 281-293. https://doi.org/10.3748/wjg.v27.i3.281

Liao, J., Li, X., Gan, Y., Han, S., Rong, P., Wang, W., Li, W., & Zhou, L. (2023). Artificial intelligence assists precision medicine in cancer treatment. *Frontiers in Oncology, 12*, 998222. https://doi.org/10.3389/fonc.2022.998222

Liu, W., Yuan, X., Guo, L., Pan, F., Wu, C., Sun, Z., Tian, F., Yuan, C., Zhang, W., Bai, S., Feng, J., Hu, Y., & Hu, B. (2022). Artificial intelligence for detecting and delineating margins of early ESCC under WLI endoscopy. *Clinical and Translational Gastroenterology, 13*(1), e00433. https://doi.org/10.14309/ctg.0000000000000433

Liu, Y. (2021). Artificial intelligence-assisted endoscopic detection of esophageal neoplasia in early stage: The next step? *World Journal of Gastroenterology, 27*(14), 1392-1405. https://doi.org/10.3748/wjg.v27.i14.1392

Liu, Z., Li, Z., Tian, J., & Wang, X. (2021). Adjuvant radiotherapy of involved field versus elective lymph node in patients with operable esophageal squamous cell cancer: A single institution prospective randomized controlled study. *Journal of Cancer, 12*(11), 3180-3189.

Merchán Gómez, B., Milla Collado, L., & Rodríguez, M. (2023). Artificial intelligence in esophageal cancer diagnosis and treatment: Where are we now? A narrative review. *Annals of Translational Medicine, 11*(10), 353.

Moding, E. J., Kastan, M. B., & Kirsch, D. G. (2013). Strategies for optimizing the response of cancer and normal tissues to radiation. *Nature Reviews Drug Discovery, 12*(7), 526-542. https://doi.org/10.1038/nrd4003

Mohan, A., Asghar, Z., Abid, R., Subedi, R., Kumari, K., Kumar, S., Majumder, K., Bhurgri, A. I., Tejwaney, U., & Kumar, S. (2023). Revolutionizing healthcare by use of artificial intelligence in esophageal carcinoma: A narrative review. *Annals of Medicine and Surgery, 85*, 4920-4927. https://doi.org/10.1097/MS9.0000000000001175

Pan, Y., He, L., Chen, W., & Yang, Y. (2023). The current state of artificial intelligence in endoscopic diagnosis of early esophageal squamous cell carcinoma. *Frontiers in Oncology, 13*, 1198941. https://doi.org/10.3389/fonc.2023.1198941

Patrascanu, O. S., Tutunaru, D., Musat, C. L., Dragostin, O. M., Fulga, A., Nechita, L., Ciubara, A. B., Piraianu, A. I., Stamate, E., Poalelungi, D. G., Dragostin, I., Iancu, D., Ciubara, A., & Fulga, I. (2024). Future horizons: The potential role of artificial intelligence in cardiology. *Journal of Personalized Medicine, 14*(6), 656. https://doi.org/10.3390/jpm14060656

Piraianu, A. I., Fulga, A., Musat, C. L., Ciobotaru, O. R., Poalelungi, D. G., Stamate, E., Ciobotaru, O., & Fulga, I. (2023). Enhancing the evidence with algorithms: How artificial intelligence is transforming forensic medicine. *Diagnostics, 13*(18), 2992. https://doi.org/10.3390/diagnostics13182992

Sasagawa, S., Kato, H., Nagaoka, K., Sun, C., Imano, M., Sato, T., Johnson, T. A., Fujita, M., Maejima, K., Okawa, Y., Kakimi, K., Yasuda, T., & Nakagawa, H. (2022). Immuno-genomic profiling of biopsy specimens predicts neoadjuvant chemotherapy response in esophageal squamous cell carcinoma. *Cell Reports Medicine, 3*(8), 100705. https://doi.org/10.1016/j.xcrm.2022.100705

Shimamoto, Y., Ishihara, R., Kato, Y., Shoji, A., Inoue, T., Matsueda, K., Miyake, M., Waki, K., Kono, M., Fukuda, H., Matsuura, N., Nagaike, K., Aoi, K., Yamamoto, K., Inoue, T., Nakahara, M., Nishihara, A., & Tada, T. (2020). Real-time assessment of video images for esophageal squamous cell carcinoma invasion depth using artificial intelligence. *Journal of Gastroenterology, 55*(11), 1037-1045. https://doi.org/10.1007/s00535-020-01716-5

Shiroma, S., Yoshio, T., Kato, Y., Horie, Y., Namikawa, K., Tokai, Y., Yoshimizu, S., Yoshizawa, N., Horiuchi, Y., Ishiyama, A., Hirasawa, T., Tsuchida, T., Akazawa, N., Akiyama, J., Tada, T., & Fujisaki, J. (2021). Ability of artificial intelligence to detect T1 esophageal squamous cell carcinoma from endoscopic videos and the effects of real-time assistance. *Scientific Reports, 11*(1), 7759. https://doi.org/10.1038/s41598-021-87405-6

Tani, Y., Ishihara, R., Inoue, T., Okubo, Y., Kawakami, Y., Matsueda, K., Miyake, M., Yoshii, S., Shichijo, S., Kanesaka, T., Yamamoto, S., Takeuchi, Y., Higashino, K., Uedo, N., Michida, T., Kato, Y., & Tada, T. (2023). A single-center prospective study evaluating the usefulness of artificial intelligence for the diagnosis of esophageal squamous cell carcinoma in a real-time setting. *BMC Gastroenterology, 23*(1), 184. https://doi.org/10.1186/s12876-023-02788-2

Testa, U., Castelli, G., & Pelosi, E. (2017). Esophageal cancer: Genomic and molecular characterization, stem cell compartment and clonal evolution. *Medicines, 4*(3), 67. https://doi.org/10.3390/medicines4030067

Tokai, Y., Yoshio, T., Aoyama, K., Horie, Y., Yoshimizu, S., Horiuchi, Y., Ishiyama, A., Tsuchida, T., Hirasawa, T., Sakakibara, Y., Yamada, T., Yamaguchi, S., Fujisaki, J., & Tada, T. (2020). Application of artificial intelligence using convolutional neural networks in determining the invasion depth of esophageal squamous cell carcinoma. *Esophagus, 17*(3), 250-256. https://doi.org/10.1007/s10388-020-00716-x

Tsai, T. J., Mukundan, A., Chi, Y. S., Tsao, Y. M., Wang, Y. K., Chen, T. H., Wu, I. C., Huang, C. W., & Wang, H. C. (2022). Intelligent identification of early esophageal cancer by band-selective hyperspectral imaging. *Cancers, 14*(17), 4292. https://doi.org/10.3390/cancers14174292

Turing, A. M. (1950). Computing machinery and intelligence. *Mind, 59*(236), 433–460. https://doi.org/10.1093/mind/lix.236.433

Wu, X., Wu, H., Miao, S., Cao, G., Su, H., Pan, J., & Xu, Y. (2024). Deep learning prediction of esophageal squamous cell carcinoma invasion depth from arterial phase enhanced CT images: A binary classification approach. *BMC Medical Informatics and Decision Making, 24*(1), 3.

Xie, Y., Liu, Q., Ji, C., Sun, Y., Zhang, S., Hua, M., Liu, X., Pan, S., Hu, W., Ma, Y., Wang, Y., & Zhang, X. (2023). An artificial neural network-based radiomics model for predicting the radiotherapy response of advanced esophageal squamous cell carcinoma patients: A multicenter study. *Scientific Reports, 13*(1), 8673. https://doi.org/10.1038/s41598-023-35556-z

Yeh, J. C., Yu, W. H., Yang, C. K., Chien, L. I., Lin, K. H., Huang, W. S., & Hsu, P. K. (2021). Predicting aggressive histopathological features in esophageal cancer with positron emission tomography using a deep convolutional neural network. *Annals of Translational Medicine, 9*(1), 37.

Yuan, X. L., Zeng, X. H., Liu, W., Mou, Y., Zhang, W. H., Zhou, Z. D., Chen, X., Hu, Y. X., & Hu, B. (2023). Artificial intelligence for detecting and delineating the extent of superficial esophageal squamous cell carcinoma and precancerous lesions under narrow-band imaging (with video). *Gastrointestinal Endoscopy, 97*(4), 664-672.e4. https://doi.org/10.1016/j.gie.2022.12.003

Yue, Y., Li, N., Zhang, G., Zhu, Z., Liu, X., Song, S., & Ta, D. (2023). Automatic segmentation of esophageal gross tumor volume in 18F-FDG PET/CT images via GloD-LoATUNet. *Computer Methods and Programs in Biomedicine, 229*, 107266. https://doi.org/10.1016/j.cmpb.2022.107266

Zhang, J. Q., Mi, J. J., & Wang, R. (2023). Application of convolutional neural network-based endoscopic imaging in esophageal cancer or high-grade dysplasia: A systematic review and meta-analysis. *World Journal of Gastrointestinal Oncology, 15*(11), 1998-2016. https://doi.org/10.4251/wjgo.v15.i11.1998

Zhang, S. T., Wang, S. Y., Zhang, J., Dong, D., Mu, W., Xia, X. E., Fu, F. F., Lu, Y. N., Wang, S., Tang, Z. C., Li, P., Qu, J. R., Wang, M. Y., Tian, J., & Liu, J. H. (2023). Artificial intelligence-based computer-aided diagnosis system supports diagnosis of lymph node metastasis in esophageal squamous cell carcinoma: A multicenter study. *Heliyon, 9*(3), e14030. https://doi.org/10.1016/j.heliyon.2023.e14030

Zhang, Y. H., Guo, L. J., Yuan, X. L., & Hu, B. (2020). Artificial intelligence-assisted esophageal cancer management: Now and future. *World Journal of Gastroenterology, 26*(35), 5256-5271. https://doi.org/10.3748/wjg.v26.i35.5256

Zhong, H., Li, A., Chen, Y., Huang, Q., Chen, X., Kang, J., & You, Y. (2023). Comparative analysis of automatic segmentation of esophageal cancer using 3D Res-UNet on conventional and 40-keV virtual mono-energetic CT images: A retrospective study. *PeerJ, 11*, e15707. https://doi.org/10.7717/peerj.15707