Multidisciplinary Respiratory Medicine 2026; volume 21: 1089 - doi: 10.5826/mrm.2026.1089 Mattioli 1885

REVIEW

Imaging and AI in tertiary prevention of lung cancer: Narrative review and clinical perspectives

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ABSTRACT

Objective: To provide a structured narrative review of current evidence and future directions for artificial intelligence (AI) applications in the tertiary prevention of lung cancer, with a focus on radiology-driven recurrence surveillance, treatment response assessment, prognostic stratification, and real-world clinical implementation.

Methods: A narrative review was conducted using PubMed, Embase, Web of Science, and IEEE Xplore databases, covering studies published between January 2019 and March 2024. Search terms included lung cancer, tertiary prevention, radiomics, deep learning, recurrence, treatment response, and survival prediction. Studies were selected based on relevance to post-diagnosis clinical management, availability of quantitative performance metrics, and clarity of validation strategy. AI methodologies evaluated included radiomics, convolutional neural networks (CNNs), transformer-based temporal models, ensemble learning, and multimodal data integration. Evidence was critically appraised with respect to study design, cohort size, validation approach, and clinical applicability.

Results: Across tertiary-prevention tasks—particularly recurrence detection, treatment response monitoring, and survival prediction—AI-assisted models demonstrate performance improvements over conventional radiological assessment in selected, well-defined scenarios, especially when multimodal imaging and external validation are employed. Reported AUC values for recurrence and response prediction generally range from 0.75 to 0.92, though results remain heterogeneous. Radiomics–deep learning integration and ensemble models show the most consistent gains, while evidence for immunotherapy response prediction and long-term survival modeling remains limited by small cohorts and lack of prospective validation. Key barriers include data heterogeneity, limited interpretability, regulatory constraints, and integration into clinical workflows.

Conclusions: AI has the potential to meaningfully support tertiary prevention of lung cancer by enhancing surveillance accuracy, treatment monitoring, and prognostic assessment. However, clinical adoption requires rigorous external validation, standardized imaging and data pipelines, transparent model behavior, and alignment with evolving regulatory frameworks. With continued multidisciplinary collaboration and quality assurance, AI is likely to become an integral adjunct to radiological practice in personalized lung cancer management.

Key words: Artificial intelligence, radiology, lung, cancer, tertiary prevention, oncology

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Authors' contributions: C. Molfini Curci wrote the main manuscript text and provided the table and figures. C. Picone helped in the writing of the manuscript. A. Morabito, F. Perrotta and R. Mormile helped evaluating the current status of AI. in Radiology and Medicine. R. Pagliaro, A. Bianco, A. Ottaiano and A. Gallipoli D'Errico contributed providing relatable and on-point references and resources. All authors reviewed the manuscript.

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and material: Not applicable.

Conflict of interest: None of the authors have any conflict of interest to declare with the present manuscript. AB is Section Editor of *Multidisciplinary Respiratory Medicine*.

Funding: The research has been conducted thanks to support of LILT - “Lega Italiana per la lotta contro i Tumori”, Naples, Italy.

Acknowledgements: None.

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with a substantial proportion of patients experiencing recurrence, progression, or treatment-related complications even after initial therapy [1,2]. In this context, tertiary prevention — defined as strategies aimed at minimizing disease progression, detecting recurrence early, optimizing treatment response, and improving long-term outcomes — represents a critical yet challenging phase of lung cancer care [3]. Radiological imaging plays a central role in tertiary prevention, underpinning post-treatment surveillance, response evaluation, and prognostic assessment [4]. However, conventional image interpretation is constrained by inter-observer variability, limited sensitivity to subtle temporal changes, and the inability to fully integrate high-dimensional clinical and biological data [5–8]. Artificial intelligence (AI), particularly machine learning and deep learning approaches, has emerged as a promising tool to address these limitations by enabling quantitative, reproducible, and scalable image analysis [9]. While AI has been extensively explored in lung cancer screening and primary diagnosis, its specific role in tertiary prevention remains less clearly defined. Many reviews conflate early detection with post-treatment management, obscuring the distinct clinical requirements of recurrence surveillance, treatment monitoring, and long-term follow-up. AI-driven tools, such as deep learning-based image analysis and predictive modeling, enhance tumor surveillance by detecting subtle changes in imaging that may indicate recurrence or resistance to therapy [10](Figure 1). These technologies also enable real-time treatment response monitoring, allowing clinicians to adjust therapeutic strategies—such as immunotherapy or targeted treatments—based on dynamic, data-driven insights [11,12]. Beyond imaging, AI integrates multi-omics and clinical data to refine prognostic assessments, identifying high-risk patients who may benefit from more aggressive or personalized interventions [13,14]. For example, machine learning algorithms can analyze patterns in radiomics, genomics, and electronic health records to predict treatment outcomes or potential complications. While these advancements hold immense promise, challenges like data privacy, algorithmic bias, and seamless integration into clinical workflows must be addressed to ensure equitable and effective implementation. This review therefore focuses explicitly on AI applications relevant to tertiary prevention, critically evaluating their evidence base, clinical utility, and implementation challenges.

Methods: Literature search and study selection

A structured literature search was performed in PubMed, Embase, and Web of Science. The search covered publications from January 2019 to March 2024 to capture recent methodological and clinical advances. Key search terms included combinations of: “lung cancer”, “non-small cell lung cancer”, “tertiary prevention radiomics”, “deep learning”, “convolutional neural networks”, “transformer models recurrence prediction”, “treatment response”, “survival modeling”, “follow-up”. Inclusion criteria were: studies addressing

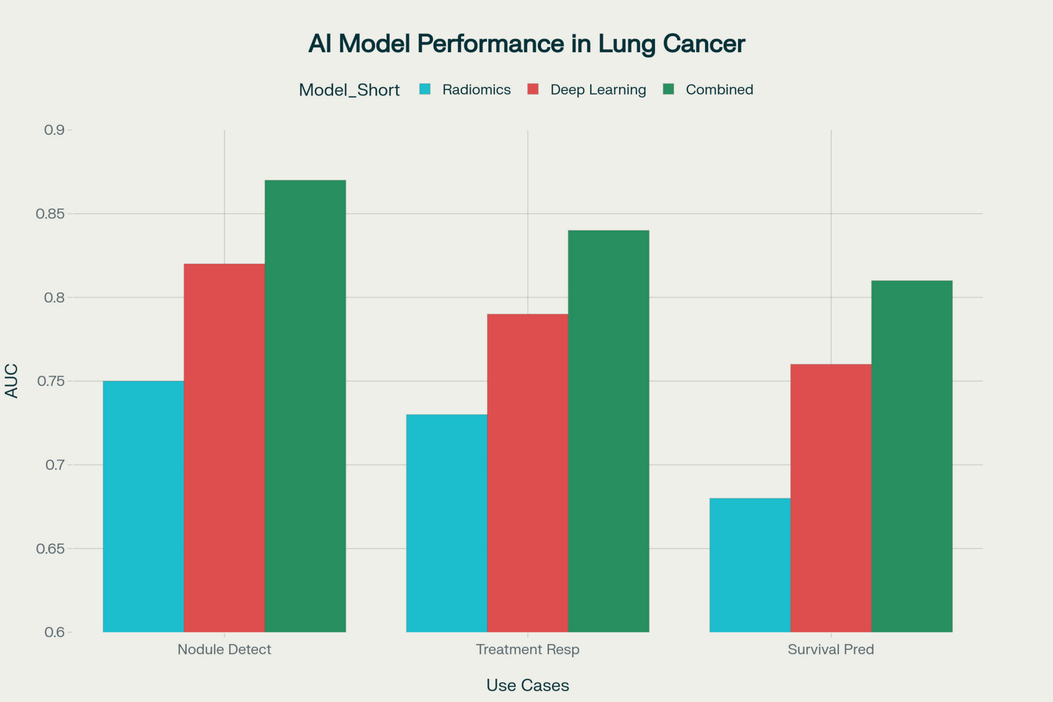

Figure 1. Performance comparison of AI model types in lung cancer tertiary prevention applications, showing superior performance of combined approaches.

post-diagnosis or post-treatment clinical endpoints (recurrence, progression, response, survival); use of AI-based imaging or multimodal models; reporting of quantitative performance metrics; clear description of cohort size and validation strategy. Screening-only studies, purely technical simulations without clinical endpoints, and studies lacking sufficient methodological detail were excluded. Representative studies were selected to illustrate key clinical tasks rather than to provide exhaustive coverage. We present a narrative review of the systematic research above described.

AI Technologies relevant to tertiary prevention

Radiomics and deep learning architectures

The foundation of AI applications in lung cancer tertiary prevention rests upon sophisticated machine learning architectures that have demonstrated remarkable capabilities in medical image analysis and clinical decision support [15]. Convolutional Neural Networks (CNNs) represent the cornerstone technology, exhibiting superior performance in extracting hierarchical features from medical imaging data through automated pattern recognition processes that surpass human visual detection capabilities [16]. These deep learning architectures excel at identifying subtle morphological changes, textural variations, and spatial relationships within CT, PET, and multimodal imaging datasets that correlate directly with disease progression and treatment response indicators [17,18]. Radiomics methodologies complement deep learning approaches by extracting quantitative features from medical images, including first-order statistics describing pixel intensity distributions, shape descriptors characterizing tumor geometry, and textural features capturing spatial heterogeneity patterns [19,20]. The integration of radiomic signatures with clinical variables consistently demonstrates superior predictive accuracy compared to traditional imaging assessment methods, with area under the curve (AUC) values ranging from 0.65 to 0.85 across different clinical endpoints [21,22] (Figure 2). Advanced feature selection techniques, including Least Absolute Shrinkage and Selection Operator (LASSO) regression and correlation-based filtering, enable

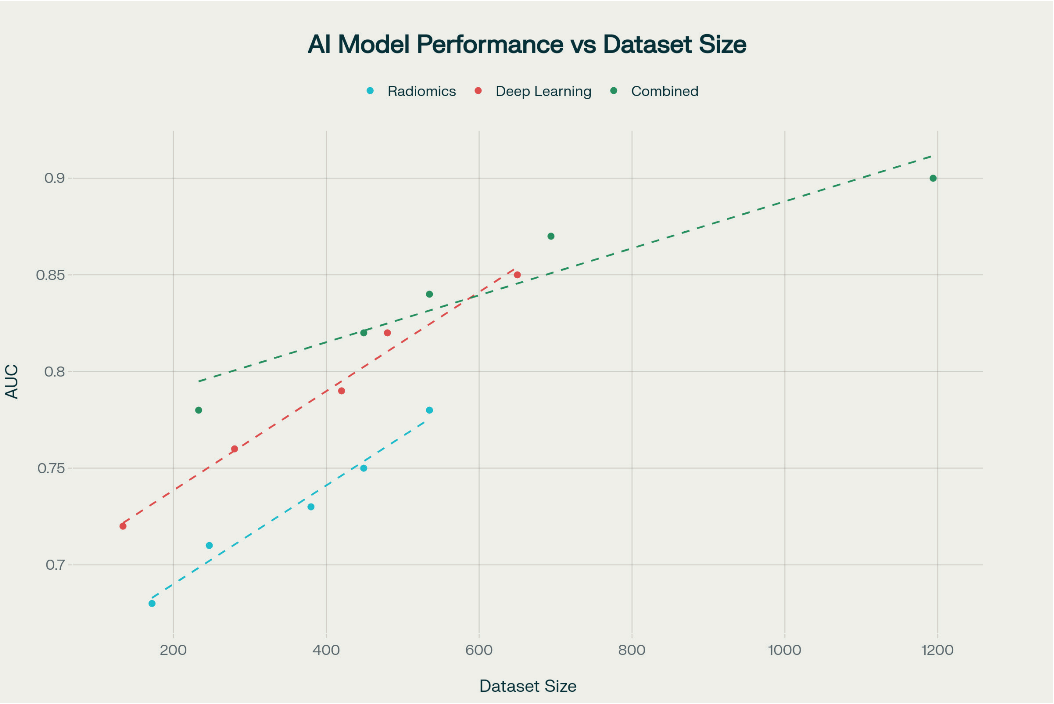

Figure 2. Relationship between dataset size and AI model performance in lung cancer applications, showing improved performance with larger datasets across all model types.

identification of the most informative radiomic features while reducing dimensionality and preventing overfitting [20,23,24].

Ensemble and foundational models

Ensemble learning approaches combine multiple models or data sources to mitigate individual algorithmic biases [25]. Multi-center validation studies demonstrate that ensemble models integrating radiomics, deep learning, and clinical data can achieve accuracy rates exceeding 0.78 with F1-scores of 0.57 for complex classification tasks such as metastatic disease prediction and treatment response assessment [26]. The synergistic combination of different AI approaches addresses individual algorithmic limitations while enhancing overall predictive capabilities through diverse analytical perspectives [27,28]. Foundational AI models represent a paradigmatic shift from task-specific algorithms to generalizable frameworks that can be adapted for multiple clinical applications while maintaining robust performance across diverse patient populations [29]. The foundational model developed by Pan et al., trained on 11,467 radiographic cancers, demonstrates exceptional versatility in oncological imaging applications, achieving AUC values of 0.67 for 2-year overall survival prediction when combined with clinical variables [30]. These pre-trained systems leverage transfer learning principles to adapt knowledge gained from large-scale datasets to specific clinical tasks, reducing training requirements while maintaining high performance standards [16,22,31].

Multimodal and temporal modeling

Multimodal integration—combining CT and PET imaging with clinical data and molecular features—has revolutionized lung cancer care by linking imaging phenotypes with genomic, proteomic, and clinical characteristics to provide a more comprehensive assessment of disease and patient outcomes [32,33]. Machine learning algorithms can identify complex patterns within multi-omics datasets that correlate with specific cancer subtypes, treatment responses, and prognostic indicators, enabling truly personalized therapeutic strategies [34]. The integration of radiogenomics approaches, combining imaging features with molecular characteristics, provides unprecedented insights into tumor biology and treatment mechanisms that traditional single-modality approaches cannot achieve [15,17,35].

Temporal analysis capabilities of modern AI systems enable sophisticated longitudinal monitoring through advanced architectures such as transformer-based models and recurrent neural networks[16]. These systems excel at analyzing time-series imaging data to identify subtle progression patterns that precede clinically apparent disease advancement, providing early warning indicators for treatment failure or disease recurrence [34,36]. The Multimodal Transformer-based Simple Temporal Attention (MMTSimTA) networks demonstrate exceptional performance with AUC values of 0.84 for 3-month survival prediction, indicating particular strength in short-term prognostic assessment (Figure 3) [37–39].

Clinical applications in tertiary prevention

Clinical data validation and AI performance in lung cancer application

Clinical validation studies across multiple institutional settings have confirmed the generalizability and clinical utility of AI systems in real-world practice environments [17,40]. Analysis of large cooperative group trials such as NRG/RTOG 0617 provides robust validation platforms demonstrating AI system capabilities to identify prognostic signatures that complement traditional clinical variables while maintaining consistent performance across diverse patient populations [19,41]. These comprehensive validation efforts establish confidence in AI system reliability across different institutional settings, imaging protocols, and patient demographics [21,42].

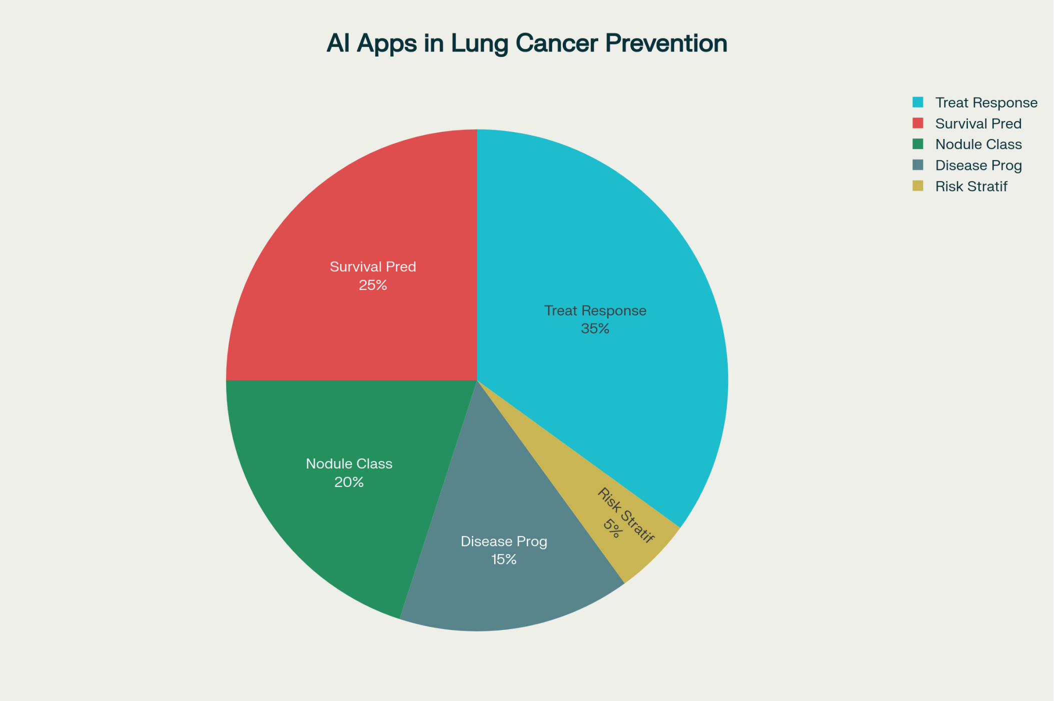

Figure 3. Distribution of AI applications across different clinical tasks in lung cancer tertiary prevention.

Treatment response assessment

The integration of AI technologies into established response evaluation frameworks represents a significant advancement in clinical lung cancer management, transcending limitations of traditional assessment methods[43,44]. Response Evaluation Criteria in Solid Tumors (RECIST) enhancement through AI applications enables comprehensive three-dimensional tumor analysis that captures morphological changes, heterogeneity patterns, and temporal dynamics beyond conventional one-dimensional measurements [45,46]. Deep learning models integrated with RECIST frameworks demonstrate remarkable predictive accuracy for treatment response, achieving AUC values exceeding 0.90 in validation cohorts while providing early indicators of therapeutic efficacy that enable proactive treatment modification [32,47,48] (Figure 4).

Multi-modal imaging integration combining CT morphological analysis with PET metabolic assessment has demonstrated superior performance compared to single-modality approaches across multiple clinical endpoints [49]. Studies utilizing combined imaging datasets achieve sensitivity rates above 85% and specificity above 90% for treatment response prediction, while automated lesion tracking systems provide quantitative monitoring of multiple pulmonary nodules simultaneously (Table 1) [16,34]. These capabilities are particularly valuable for patients with multiple metastatic lesions where manual assessment

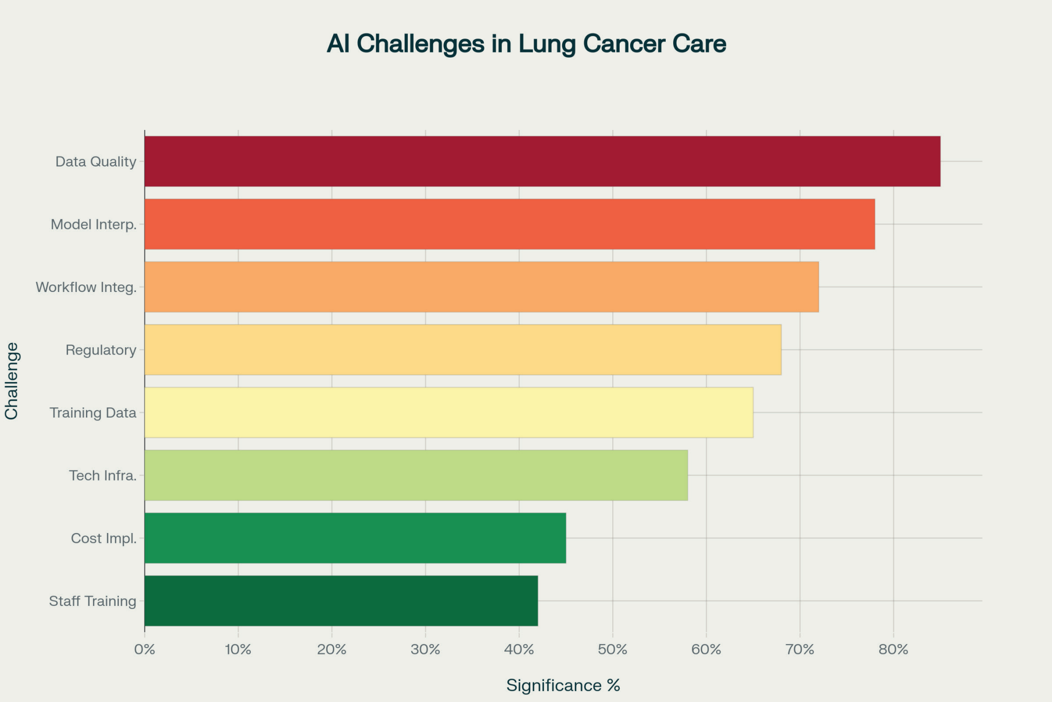

Figure 4. Major challenges in AI implementation for lung cancer care ranked by significance.

Table 1. Integration Strategy Performance Outcomes.

Approach	Accuracy	Sensitivity	Specificity	AUC	Clinical Utility
Traditional	0.65	0.58	0.72	0.65	Limited
AI-Enhanced	0.78	0.74	0.83	0.79	Moderate
Integrated Framework	0.87	0.85	0.89	0.87	High
Next-Gen Systems	0.92	0.89	0.94	0.92	Very High

becomes time-intensive and prone to observer variability [39,50].

Prognostic stratification and survival modeling

Comprehensive survival analysis applications represent among the most challenging and clinically relevant implementations of AI in lung cancer care, requiring integration of complex clinical, pathological, and imaging variables that exceed human analytical capabilities [25,26]. Machine learning-assisted recurrence prediction models achieve accuracy rates of 76% with AUC values of 0.81 for early-stage NSCLC patients, enabling identification of high-risk individuals who may benefit from intensified surveillance or adjuvant therapy [27]. These systems analyze multidimensional interactions between clinical variables, imaging phenotypes, and temporal patterns to provide personalized risk stratification that optimizes resource utilization while maintaining appropriate clinical oversight [47]. Advanced prognostic integration combining foundational AI architectures with clinical risk models demonstrates encouraging results in large-scale validation studies, with combined foundational AI and clinical features achieving AUC values of 0.67 for survival prediction. The integration of genomic-radiological signatures further enhances prognostic capabilities by incorporating molecular characteristics that correlate with treatment responses and resistance mechanisms [41]. Multi-omics approaches utilizing microRNA, mRNA, DNA methylation, and clinical data show enhanced survival prediction over single-modality models while employing sophisticated analytical techniques for data compression and integration [51]. Real-world clinical utility assessment demonstrates significant improvements in diagnostic accuracy when AI tools supplement routine radiological evaluation [52]. The integration of AI-based computer-aided diagnosis (CAD) tools with clinical risk models shows increased sensitivity from 38% to 56% at the 65% risk threshold while maintaining similar false positive rates, translating to standardized net benefit improvements from -3.3 to 18. These quantitative improvements in clinical decision-making demonstrate substantial practical value for patient care optimization and resource allocation efficiency [42].

Implementation challenges and limitations

Data standardization, interpretability and regulations

Data quality, heterogeneity, and standardization are ongoing obstacles. AI models are sensitive to differences in imaging protocols, device calibration, and annotation practices, restricting their generalizability. Many radiomics studies rely on retrospective, single-center cohorts with limited patient diversity, further constraining external validity and reproducibility. Moreover, the lack of standardized image acquisition and feature extraction protocols remains a substantial barrier for multicenter collaborations and for building robust, transportable algorithms [31,34]. Harmonization and next-generation solutions converge through advanced preprocessing pipelines that address institutional variations while enabling sophisticated multi-modal data integration. ComBat harmonization methods combined with transformer-based architectures create robust frameworks for standardizing imaging protocols across diverse clinical environments while facilitating radiogenomics integration [17]. Federated inference represents a promising solution for multi-institutional collaboration while preserving data privacy. This approach enables model development across multiple healthcare institutions without sharing raw patient data, thereby improving model generalization while maintaining strict privacy protections [16]. Model interpretability and transparency present additional hurdles. Deep learning architectures, which currently deliver state-of-the-art performance, often function as "black boxes," making their decision-making processes opaque to clinicians. This lack of explainability reduces trust in AI systems and makes their integration into clinical decision-making difficult, particularly when patient safety and legal liability are at stake [41,53]. Furthermore, most research focuses on internal validation, with few studies achieving robust prospective or multicenter external validation, raising concerns about true clinical effectiveness. Explainable AI integration with foundational models represents a convergence of interpretability requirements and advanced deep learning capabilities. Explainable AI XAI) techniques such as SHAP (SHapley

Additive exPlanations) and gradient-weighted class activation mapping (Grad-CAM) have emerged as essential tools [54–56]. These approaches enable clinicians to understand feature importance and visualize decision-making processes, fostering greater acceptance of AI systems in clinical practice [57]. These integrated approaches address clinical trust concerns while leveraging pre-trained model capabilities for enhanced generalization [18]. Real-time monitoring and continuous learning systems utilize ensemble methods combining traditional radiomics with advanced deep learning for dynamic performance optimization. IoT-enabled monitoring systems will revolutionize patient care through continuous health parameter tracking using AI-integrated wearables and telemedicine platforms. These systems can provide early warning signals for disease recurrence or treatment complications, enabling timely interventions and reducing hospital readmissions [41]. Furthermore, the integration of circulating tumor DNA (ctDNA) monitoring with AI-driven analysis will enable more precise disease surveillance and treatment response assessment, moving beyond traditional imaging-based approaches [31].

Synthesis and future perspectives

The integration of artificial intelligence into lung cancer tertiary prevention represents a paradigm shift that transcends traditional approaches to radiological assessment and clinical decision-making. Current evidence establishes that AI systems, particularly ensemble approaches combining radiomics and deep learning methodologies, consistently outperform traditional analytical methods across multiple clinical endpoints while providing quantitative, reproducible, and objective assessment capabilities. The development of foundational AI models, multi-modal integration strategies, and sophisticated ensemble approaches has created a robust technical foundation for clinical implementation that addresses both current clinical needs and future therapeutic developments [58–60]. However, successful translation of these technological advances into routine clinical practice requires addressing substantial challenges related to data standardization, system interpretability, regulatory compliance, and workflow integration.

The future trajectory of AI in lung cancer tertiary prevention lies in comprehensive, multimodal systems that integrate imaging, genomic, and clinical data to provide personalized treatment recommendations supported by robust validation frameworks and quality assurance protocols. As these technologies mature through continued validation studies and regulatory approval processes, AI systems will become increasingly integral to lung cancer management, offering improved patient outcomes through more precise, personalized, and timely interventions. The continued collaboration between AI researchers, clinical oncologists, radiologists, and regulatory bodies will be crucial for advancing this field and ultimately benefiting patients through enhanced diagnostic accuracy, improved prognostic assessment, and optimized therapeutic strategies. The establishment of comprehensive validation protocols, ethical guidelines, and quality assurance frameworks will ensure safe and effective clinical deployment while maximizing the transformative potential of AI technologies in lung cancer care.

Conclusions

AI applications in lung cancer tertiary prevention show measurable potential to enhance recurrence surveillance, treatment response assessment, and prognostic stratification when applied within clearly defined clinical contexts. While ensemble and multimodal approaches provide the most consistent benefits, current evidence is heterogeneous and often limited by retrospective design and lack of external validation. Continued methodological rigor, transparency, and multidisciplinary collaboration are essential to translate AI innovations into safe, effective, and equitable clinical practice.

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Received for publication: 2 February 2026 - Accepted for publication: 26 March 2026.

Licensee Mattioli 1885, Italy
Multidisciplinary Respiratory Medicine 2026; 21: 1089
doi: 10.5826/mrm.2026.1089