

Review

Imaging of Immune Checkpoint Inhibitor–Related Pulmonary Toxicity: A Narrative Review of Current Evidence and Emerging Roles of Radiomics and Machine Learning

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Abstract: The advent of immune checkpoint inhibitors (ICIs) has revolutionized cancer treatment, offering an effective therapeutic option for advanced cancers. However, their widespread use has led to the occurrence of immune-related adverse events (irAEs), including pulmonary toxicity. ICI-induced pulmonary toxicity represents one of the most relevant irAEs because of its heterogeneous clinical and radiological presentation and its potential life-threatening course. Computed tomography (CT) is the imaging modality of choice for evaluating lung irAEs and the specific patterns associated with ICI-induced pneumonitis. A literature search of the PubMed and Scopus databases was conducted to identify studies published over the past decade investigating pulmonary adverse effects associated with ICI therapy. Relevant studies were reviewed with particular attention to the clinical and radiological features of ICI-induced pulmonary toxicity, including the main CT patterns of pneumonitis and the emerging applications of radiomics and machine learning. This narrative review aims to provide a comprehensive overview of the current evidence on the radiological manifestations of lung irAEs, with particular emphasis on CT findings and radiomics and its potential role in the prediction and diagnosis of lung irAEs. Ultimately, this research highlights the importance of a multidisciplinary approach in the diagnosis and management of ICI-induced pulmonary toxicity, with radiologists playing a critical role in identifying and monitoring these potentially life-threatening events.

Keywords: Immunotherapy; Immune-Related Adverse Events; Immune-Checkpoint Inhibitors; Lung Toxicity; Pneumonitis; Computed Tomography (CT); Radiomics; Machine Learning

1. Introduction

Immune checkpoint inhibitors (ICIs) are a class of immunotherapy drugs that induce an anti-tumoral response by modulating the immune system against tumor cells [1].

ICIs targeting PD-1 (Programmed Death-1), PD-L1 (Programmed Death Ligand-1), and CTLA-4 (Cytotoxic T-Lymphocyte Antigen-4) are standard therapies for advanced cancers and have demonstrated significant improvements in clinical outcomes compared with conventional chemotherapy and radiotherapy.

However, despite their efficacy, ICIs mechanism of activation of the immune system results in a peculiar toxicity profile, inducing immune-related adverse events (irAEs). Suspicion for irAEs arises from the temporal relationship between ICI exposure and the onset of clinical and/or radiologic presentations [2].

The clinical manifestations of these adverse events can be highly variable, reflecting the involvement of various organs and the different ways in which immune activation may affect them. Their recognition therefore requires careful evaluation of the patient's clinical history and the ICI treatment timing.

The progressively expanding indications of these agents across tumor types have steadily increased the number of patients exposed to ICIs and, consequently, the population potentially at risk of developing irAEs.

A recent meta-analysis of ICI safety showed that irAE incidence ranges from 54% to 76% and varies by ICI class [3]. Any organ can be involved, including the skin, endocrine glands, gastrointestinal tract, liver, lungs, and, less commonly, the cardiovascular and central nervous systems; in some cases, patients experience multiple irAEs simultaneously [2].

Among the spectrum of irAEs, pulmonary toxicity represents a particularly concerning condition. Although lung irAEs are generally mild to moderate and reversible, in some cases they can be severe and/or fatal, especially if not properly identified and treated [4].

The variable severity and presentation of pulmonary involvement can make diagnosis challenging, particularly when clinical findings overlap with other conditions. Consequently, timely recognition of lung toxicity remains essential for appropriate clinical management and patient outcomes.

Pulmonary toxicity was first described as checkpoint inhibitor pneumonitis (CIP) by Nishino et al. in 2015 [5]; its distinct features are defined by radiological and clinical presentation, which can mimic other lung inflammatory conditions [6].

Although some evidence suggests that the onset of irAEs may be associated with improved clinical outcomes [7], CIP occurrence is an unfavorable prognostic factor that negatively affects patients' survival, demonstrating the potential gravity of these adverse events [8].

The incidence of pulmonary toxicity in ICI-treated patients varies across studies, with rates ranging from 3%–19%; moreover, its severity appears to be higher in certain patients, particularly in those with lung cancer, pre-existing lung diseases or in patients previously treated with thoracic radiotherapy [9–11].

Lung irAEs have been reported less frequently with CTLA-4 inhibitors than PD-1 and PD-L1 inhibitors, but combination therapies involving both anti-CTLA-4 and anti-PD-1 inhibitors tend to be associated with higher rates of adverse pulmonary events [2,12].

Although there is considerable variability, the median time to onset of lung irAE is around 2–3 months after starting ICI treatment; because most adverse events occur within the first months of therapy, the early post-treatment period represents a critical window for clinical and radiological surveillance [10].

Imaging plays a crucial role in managing patients receiving ICIs; its main objective is to evaluate response to therapy while accurately diagnosing complications such as irAEs or infections.

In this context, radiological assessment is particularly important because clinical manifestations may be non-specific, and imaging findings can provide essential information regarding the presence and characteristics of pulmonary involvement. The interpretation of these findings is therefore required to recognize possible lung toxicity.

CT is the modality of choice and allows early detection and accurate evaluation of the pattern, distribution and extent of lung irAEs. Its ability to provide detailed morphological information makes CT particularly valuable in characterizing CIP heterogeneous manifestations, while assessment of the distribution and extent of abnormalities contributes to a more complete evaluation of pulmonary involvement in affected patients.

The most common lung CT patterns in patients treated with ICIs, described using the American Thoracic Society/European Respiratory Society (ATS/ERS) classification of idiopathic interstitial pneumonias [13], include organizing pneumonia (OP), non-specific interstitial pneumonia (NSIP), hypersensitivity pneumonia (HP), acute interstitial pneumonia/acute respiratory distress syndrome/diffuse alveolar damage (AIP/ARDS/DAD), obliterative bronchiolitis (OB), eosinophilic pneumonia (EP) and sarcoid-like reaction (SLR) [10,14,15] (Table 1).

Table 1. CT imaging features of the most common radiologic patterns of ICI-related pulmonary toxicity.

CT Patterns of ICI-Related Lung Toxicity	
Organizing pneumonia (OP)	Multiple patchy consolidations and GGOs with peribronchovascular and subpleural distribution; sometimes perilobular pattern and reversed halo sign are visible.
Non-specific interstitial pneumonia (NSIP)	Bilateral GGOs, irregular reticular opacities and traction bronchiectasis with architectural distortion; bilateral with predominant lower-lung involvement and sparing of subpleural parenchyma.

Table 1. Cont.

CT Patterns of ICI-Related Lung Toxicity	
Hypersensitivity Pneumonitis (HP)	Bilateral centrilobular nodules predominant in upper lobes, lobular areas of air trapping and patchy GGOs.
Acute Interstitial Pneumonia/Acute Respiratory Distress Syndrome/Diffuse Alveolar Damage (AIP/ARDS/DAD)	Diffuse and confluent bilateral areas of GGO and/or consolidation, especially in the dependent parenchyma in the exudative phase; reticular pattern with traction bronchiectasis in the organizing and fibrotic phase.
Obliterative bronchiolitis (OB)	Bilateral mosaic attenuation pattern and bronchial wall thickening; occasionally bronchiectasis and centrilobular nodules are present.
Eosinophilic pneumonia (EP)	Bilateral/ unilateral areas of GGO or consolidation, generally transient and migratory.
Sarcoid-like reaction (SLR)	Bilateral and symmetrical hilar and mediastinal lymphadenopathies, sometimes associated with peribronchovascular micronodules and peribronchial interstitial thickening.

OP is the most frequent lung irAE imaging pattern. HRCT in OP is characterized by patchy, diffuse and bilateral consolidations and ground-glass opacities (GGO), which are often migratory. These findings typically have a predominant subpleural and peribronchovascular distribution [13–15]. Additional features of OP include perilobular opacities and the “reversed halo sign”, which consists of a focal area of GGO surrounded by a ring of denser air-space consolidation. When the surrounding ring is incomplete, this finding is referred to as the “atoll sign” [15,16].

On HRCT, NSIP typically reveals peripheral GGOs associated with irregular reticulations and traction bronchiectasis and bronchiolectasis. NSIP pattern is generally bilateral, with predominant lower-lung involvement and often sparing of subpleural parenchyma. Honeycombing is rarely present [13].

HRCT findings in HP include multiple and bilateral centrilobular nodules with upper lobe predominance. Additionally, areas of reduced attenuation and vascularity, indicative of “air trapping” and patchy or diffuse GGOs, are commonly seen [13–15].

The typical HRCT findings in ARDS vary according to the disease phase. In the acute phase, GGOs and pulmonary opacities (predominant in the dependent parenchyma) are usually present. In the later stages, CT may show either complete resolution or progression to a reticular pattern with traction bronchiectasis. Pleural effusion may also be observed [13,16].

On HRCT, OB often demonstrates sharply defined areas of reduced lung attenuation with associated narrowed vessels, resulting in a “mosaic pattern” which becomes more evident on expiratory scans. Bronchial wall thickening is frequently observed, while centrilobular nodules and bronchiectasis are less common findings [13,17].

In HRCT of EP the pattern is typically characterized by consolidations or GGOs, which can be either unilateral or bilateral; these pulmonary abnormalities are generally transient and migratory [15,18].

On HRCT, SRL presents with bilateral and symmetrical hilar and mediastinal lymphadenopathy. These findings may be accompanied by peribronchovascular micronodules, peribronchial interstitial thickening and, less commonly, coalescence of micronodules forming pseudo-masses with a predominantly dependent lung distribution [19].

The present review aims to explore the radiological features associated with lung irAEs and emerging developments in radiomics for their assessment.

2. Methods

A literature search was conducted in PubMed and Scopus databases to identify pertinent publications on lung irAEs with particular focus on imaging findings and radiomics.

The literature search covered the period between January 2015 and June 2026 and was last performed on 30 June 2026.

The search was performed using combinations of the following keywords and Boolean operators: (“lung irAE” OR “pulmonary irAE” OR “immune checkpoint inhibitors”) AND (“pneumonitis”) AND (“imaging” OR “CT” OR “radiomics”).

In addition to original research articles, case reports and reviews were also included to ensure a comprehensive overview of ICI-associated pneumonitis.

Only English-language publications were considered.

Titles and abstracts were screened for relevance, followed by full-text review to confirm eligibility.

The literature selection was not intended to be systematic; rather, studies were selected primarily to provide an illustrative overview of the clinical, radiological and radiomics aspects of lung irAEs.

Articles were preferentially selected based on their focus on imaging patterns and on the potential role of radiomics in the assessment of lung irAEs in patients receiving ICIs.

Finally, data extraction was carried out considering study type, patient population, type of ICI used, radiological patterns observed, CT imaging features, timing of pneumonitis onset, clinical severity, management strategies and patient outcomes.

Particular attention was given to imaging characteristics and, where available, the application of radiomics for the characterization or assessment of ICI lung irAEs.

3. Results

3.1. Incidence and Risk Factors

The incidence of pulmonary irAEs across the included studies varied significantly, ranging from 3% to 19% [10,11]. This heterogeneity may be explained by different diagnostic criteria, imaging protocols and assessment methods, as well as variations in the timing and frequency of imaging evaluations. Moreover, irAEs incidence may be influenced by the clinical characteristics of the study populations, including cancer type and stage and the specific administered ICI.

Notably, pneumonitis occurred more frequently in patients treated with combination therapy involving anti-PD-1/PD-L1 and anti-CTLA-4 agents, with a reported incidence of 6.5–10% compared to monotherapy with anti-PD-1 or anti-PD-L1 inhibitors, where the incidence is 3–4% [10]. This increased risk observed with combination therapy may reflect the broader immune activation resulting from simultaneous blockade of distinct inhibitory pathways.

Additionally, some studies have demonstrated that PD-1/PD-L1 inhibitors exhibit a greater incidence and severity of pulmonary toxicity compared with anti-CTLA-4 agents [20,21].

Moreover, PD-1 inhibitors have a higher occurrence and severity of pulmonary toxicity than PD-L1 inhibitors [20].

The incidence of ICI-related pneumonitis tends to be higher in lung cancer (1–6%) compared with other tumor types (0.1–4%) [12].

Risk factors associated with an increased possibility of developing lung irAE include pre-existing lung conditions such as chronic obstructive pulmonary disease (COPD), interstitial lung disease, asthma and lung cancer; an increased incidence of lung irAEs is also observed among individuals aged 65 years or older and in patients with a history of thoracic radiotherapy [9].

These risk factors do not necessarily preclude ICI use, but they highlight the need for careful baseline assessment and close monitoring during treatment. Baseline chest CT and respiratory symptoms evaluation can be particularly useful for distinguishing newly developed pneumonitis from pre-existing pulmonary abnormalities, infection, tumor progression or radiation-induced lung injury.

The severity of ICI pneumonitis is assessed using classification systems such as the Common Terminology Criteria for Adverse Events (CTCAE) to standardize adverse event grading. It uses a five-point scale based on symptom severity; in July 2025, the National Cancer Institute (NCI) released the updated 6th CTCAE version (**Table 2**) [22]. The use of a standardized grading system is particularly important for ICI pneumonitis because clinical presentation can vary considerably, ranging from incidental radiographic abnormalities in asymptomatic patients to rapidly progressive respiratory failure. Moreover, the CTCAE grade has important therapeutic implications, as it can guide decisions regarding continuation or interruption of immunotherapy, the initiation and intensity of corticosteroid therapy, hospitalization, and, in severe cases, permanent discontinuation of ICI treatment.

A meta-analysis reported pneumonitis incidence with anti-PD-1 agents ranging from 1.9% to 3.6% for all grades and from 0.4% to 1.2% for grade ≥ 3 [23]. For anti-PD-L1 the incidence of pneumonitis was reported to be approximately 2–3% across all grades [24]. In contrast, pneumonitis associated with anti-CTLA-4 monotherapy was rare, with an incidence of less than 1% [25]. These findings suggest that although most cases of ICI-related pneumonitis are low grade, a clinically relevant proportion can progress to severe or life-threatening respiratory

toxicity, particularly in susceptible patients.

Table 2. NCI CTCAE version 6.0 pneumonitis grading system.

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric)	Severe symptoms; oxygen indicated; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric)	Life-threatening respiratory compromise; urgent intervention indicated (e.g., tracheotomy or intubation)	Death

3.2. Imaging

Imaging plays a critical role in managing patients undergoing ICI therapy. Its primary objective is to assess therapeutic response while enabling accurate diagnosis of potential complications, including irAEs and infections.

The combination of radiologic and clinical data is crucial for accurate diagnosis, especially to differentiate lung irAEs from other causes of lung injury (infections, radiation pneumonitis, underlying interstitial lung disease).

In some cases, pulmonary irAEs may be incidentally detected on follow-up CT before the onset of clinical symptoms. Moreover, the absence of respiratory symptoms does not necessarily exclude pulmonary involvement, highlighting the relevance of radiological assessment in patients undergoing treatment. Conversely, symptomatic patients may present with relatively nonspecific imaging abnormalities, further supporting the need for correlation between clinical and radiological findings.

CT is the imaging modality of choice, offering early detection and precise characterization of lung abnormalities; in particular, chest CT allows the evaluation of the lung irAEs prevalent pattern, distribution and extension.

Another role of CT is the close monitoring of patients who experienced CIP and are re-challenged with ICI therapy, as well as those who are not re-exposed, because of the risk of recurrent pneumonitis that can occur even after complete resolution of symptoms [26]. Comparison with previous examinations is particularly useful in this setting, as it allows evaluation of changes in the extent and morphology of pulmonary abnormalities.

The question of whether immunotherapy can be safely resumed after pneumonitis has recently attracted growing attention, and dedicated cohort studies are now investigating the clinical characteristics and prognostic factors associated with the feasibility of ICI continuation, given the potential loss of antitumor efficacy associated with prolonged treatment interruption [27].

In a recent study conducted on patients with non-small cell lung cancer (NSCLC), the most common chest CT features found in CIP are illustrated and include GGOs (96% of cases), consolidations (54%), interlobular septal thickening (48%), and reticular opacities (40%); less frequently observed features are traction bronchiectasis, nodular opacities and pleural effusion [28].

The spectrum of ICI-pneumonitis CT patterns includes OP (most common), followed by NSIP, HP, SLR, EP, OB and in severe cases AIP/ARDS. Distribution is often bilateral (unilateral or lobar patterns are also reported), multifocal and localized in the lower and peripheral lung zones [10,29–31].

AIP/ARDS pattern is associated with more severe disease and worse outcome, while other radiological patterns are generally linked to a milder disease course [32–34].

Patients with mild pneumonitis typically have a favorable prognosis, and most can resume ICI therapy once symptoms resolve. In contrast, those with severe, refractory pulmonary toxicity often experience greater difficulty in continuing immunotherapy, with a substantial proportion requiring permanent discontinuation of treatment [34,35].

In some cases, pneumonitis does not resolve despite adequate corticosteroid therapy. Naidoo et al. have described this phenomenon as chronic pneumonitis, defined by clinical and radiologic evidence of pneumonitis that persists or worsens after steroid tapering and requires immunosuppressive treatment for more than 12 weeks. Their research suggests that approximately 2% of patients with NSCLC and melanoma treated with anti-PD-L1 agents develop ICI-related chronic pneumonitis, which shows a chest CT pattern consistent with the findings observed during the initial episode [36].

Furthermore, chronic and severe CIP may result in protracted pulmonary injury, which can lead to lung fibrosis, a rare but potentially serious complication. Nevertheless, the precise incidence of this progression is not clearly defined in the current literature [37].

Fibrotic changes typically manifest as reticulations, traction bronchiectasis and honeycombing on follow-up chest CT and are usually associated with impaired pulmonary function [38,39].

These findings represent structural changes that may remain after the acute inflammatory phase and can be evaluated through comparison with earlier CT examinations. Their identification is therefore relevant to document the evolution of pulmonary toxicity and its potential relationship with lung functional impairment [40].

3.3. Radiomics

The CT-based lung radiomic models have demonstrated promising results in predicting the development of lung irAEs, particularly when these models are associated with clinical data.

These findings highlight the potential of machine learning models that combine clinical parameters and radiomic features extracted from baseline lung CT scans to improve the identification of patients with an increased risk of developing adverse respiratory events following ICI treatment.

Radiomics therefore provides a non-invasive complement to traditional diagnostic methods, with potential applications in patient risk stratification and individualized clinical management [41,42].

A recent systematic review and meta-analysis confirmed that machine learning models integrating radiomics with clinical characteristics achieve excellent predictive performance for CIP; hybrid models combining imaging-derived and clinical features thus appear to provide the greatest predictive value for CIP [43].

However, the current evidence should be interpreted thoughtfully, because most of the studies currently available are based predominantly on retrospective cohorts and differences in patient populations, feature extraction and selection methods may limit the reproducibility of the proposed models.

For example, Colen et al. highlighted the potential of radiomics to predict the risk of developing CIP in patients undergoing ICI therapy, demonstrating its potential as an early risk-assessment tool [44].

Similarly, Zhang et al. developed a prediction model for patients with NSCLC, combining radiomic features from baseline CT scans with clinical information. This integrated model significantly improved the accuracy of predicting CIP risk, reflecting an important advancement in personalized cancer care [45]. The model's ability to account for both imaging and clinical factors is a step forward in precision medicine, enabling clinicians to identify adverse events before they manifest clinically; however, these findings would need to be validated in larger, prospectively recruited cohorts before these models can be considered sufficiently reliable for routine clinical use.

Tan et al. further expanded this approach by developing a multimodal deep learning model that incorporates both clinical data and pre-treatment chest CT scans. This model offers an innovative way to assess CIP risk in lung cancer patients, emphasizing the power of deep learning techniques to handle complex, multi-source datasets and provide highly specific predictions [46]. Such advancements in predictive modelling not only enable early intervention but also reduce unnecessary treatments or surveillance, enhancing the overall efficiency of cancer care.

Additionally, radiomics is supportive in distinguishing CIP from other forms of pneumonitis, which is crucial for tailoring the most appropriate treatment strategies. Cheng et al. proposed a novel study that explored the use of radiomics to differentiate CIP from radiation pneumonitis (RP), a common form of lung injury in cancer patients undergoing both ICIs and radiotherapy (RT) [47]. This differentiation is essential, as the management strategies for CIP and RP differ significantly and misdiagnosis could lead to inappropriate interventions. Although these findings suggest that quantitative imaging analysis could provide useful diagnostic information, this application remains at an early stage and requires validation in larger, multicenter cohorts with standardized imaging protocols.

Overall, the available evidence [41–45] supports the potential of radiomics and artificial intelligence as complementary tools for the prediction and characterization of pulmonary irAEs [46–49]. Nevertheless, their current application remains limited by the retrospective nature of most studies, relatively small and heterogeneous cohorts, limited external validation, and variability in CT acquisition and radiomic analysis.

Multimodal approaches may improve the integration of imaging and clinical data; however, deep learning models also have important limitations, including the need for large and representative datasets and reduced performance across different populations and imaging protocols. Therefore, despite their potential to support early identification of patients at risk of pulmonary toxicity, further validation is needed before their routine clinical use.

Future prospective and multicenter studies with standardized CT acquisition and radiomic feature extraction protocols will be essential to determine whether radiomics can provide reproducible and clinically relevant information and then support their use in routine clinical practice.

While this review provides valuable insights, it is important to consider the limitations. The incidence of pulmonary toxicity may be underestimated or overestimated depending on the methodologies employed in each study; in fact, the heterogeneity of the included studies, particularly concerning patient characteristics, cancer types, treatment regimens, imaging protocols, and machine learning approaches, should be considered when interpreting the findings.

Moreover, although we included studies published between January 2015 and June 2026, considering the rapidly evolving field of immunotherapy, some recent findings may not have been captured in the included studies. Advances in ICI treatment strategies, radiomic methodologies, artificial intelligence, and imaging techniques are continuously emerging, and studies published after the search period could provide additional evidence.

4. Discussion

This narrative review synthesizes the current evidence on ICI-related pulmonary toxicity imaging, with particular attention to the radiological features of CIP and the potential role of radiomics in its prediction. Three main findings emerge. First, CIP is a relatively frequent and possibly severe irAE, with an incidence ranging from 3% to 19% across studies [11]; rates are higher in patients with lung cancer, pre-existing lung disease and prior thoracic radiotherapy [9], and in those receiving combination immunotherapy (6.5–10%) compared with anti-PD-1/PD-L1 monotherapy (3–4%) [12]. Second, CT remains the reference imaging modality. In the cited NSCLC cohort [28], the most frequent CT findings are GGOs (96% of cases), consolidations (54%), interlobular septal thickening (48%) and reticular opacities (40%). Third, quantitative imaging has emerged as a promising complement to clinical assessment: radiomic information extracted from baseline chest CT, particularly when combined with clinical data, can help predict pneumonitis before treatment starts [41,42,46].

The heterogeneity of CT appearances is clinically relevant because CIP imaging manifestations may overlap with infectious pneumonia, pulmonary edema, tumor progression, radiation pneumonitis and other inflammatory lung diseases. This overlap can make diagnosis particularly challenging in patients with advanced malignancy, in whom several potential causes of respiratory deterioration may coexist. Consequently, recognition of CT patterns should be integrated with clinical presentation, treatment history, laboratory findings and, when appropriate, microbiological investigations. Radiological assessment should therefore be considered within a multidisciplinary diagnostic framework rather than as an isolated determinant of diagnosis [50].

CT examinations may provide additional information by demonstrating the evolution or resolution of pulmonary abnormalities following ICI interruption and corticosteroid treatment, although radiological improvement alone cannot establish a causal relationship with immunotherapy.

The temporal relationship between ICI exposure and pulmonary toxicity is another important consideration. Although CIP can develop at different stages of treatment, the first few months after ICI initiation represent an important period for clinical surveillance. Baseline CT consequently has a dual role: it documents the patient's pre-treatment pulmonary condition and provides a baseline against which subsequent changes can be assessed. This is particularly relevant in patients with pre-existing interstitial abnormalities, emphysema, fibrosis or previous radiation-induced changes, where distinguishing newly developed inflammatory abnormalities from pre-existing disease may be difficult.

Standardized baseline imaging and structured radiological reporting could therefore improve both clinical interpretation and the value of imaging data subsequently used for radiomic analysis.

From a methodological perspective, radiomics offers the possibility of extracting quantitative information that may not be readily appreciable through conventional visual assessment. Features describing texture, intensity, spatial distribution and tissue heterogeneity may capture subtle differences in lung parenchymal characteristics and potentially identify imaging signatures associated with the risk of pulmonary toxicity. The integration of radiomic features with clinical characteristics, treatment variables and laboratory biomarkers may therefore provide a more comprehensive assessment of individual risk than any single parameter alone.

Nevertheless, the biological and clinical significance of individual radiomic features is often difficult to establish. Furthermore, the high dimensionality of radiomic datasets relative to the number of clinical events creates a substantial risk of overfitting. Robust feature-selection procedures and rigorous validation are consequently essential to develop models that are reproducible and transferable across institutions.

These issues also emphasize the importance of model interpretability. Before radiomic or machine-learning

models can be incorporated into routine clinical decision-making, clinicians should be able to understand the estimated level of risk.

In clinical practice, validated pretreatment risk models could adapt imaging surveillance to the individual patient: those at high predicted risk could receive earlier or more frequent chest CT, while low-risk patients could avoid unnecessary radiation exposure and costs. Risk models could also guide decisions on combination regimens and monitoring during the first 2–3 months of treatment, when pneumonitis most commonly develops [51]. After recovery from pneumonitis, the same tools could support decisions on ICI re-challenge, where recurrent pneumonitis remains a concern even after complete resolution of symptoms [26]. These models support, but do not replace, standardized grading systems, such as the CTCAE.

Several limitations influence these results. No formal methodological quality or risk-of-bias assessment was performed for the included studies. Therefore, the strength and reliability of the available evidence should be interpreted with caution, particularly given the heterogeneous nature of the literature, which included original studies, case reports and review articles.

Most studies are retrospective, with relatively small and heterogeneous cohorts, variable outcome definitions (any-grade versus grade ≥ 2 pneumonitis) and limited external validation; CT-related variability can further reduce the reproducibility of radiomic information [52], and none of the models has yet been validated in a prospective trial.

Future prospective, multicenter studies with standardized CT acquisition and radiomic extraction protocols and predefined endpoints are therefore needed before these models can be used in routine practice. If these steps are achieved, radiomics and machine learning could become valuable decision-support tools for the early identification, surveillance and management of ICI-related pulmonary toxicity, within the multidisciplinary framework that remains essential for optimal patient outcomes.

5. Conclusions

The advent of ICIs has redesigned oncological care, but irAEs, particularly pulmonary toxicity, reveal a substantial clinical challenge. This review provides a comprehensive synthesis of current evidence regarding the clinical and imaging spectrum of ICI-induced pneumonitis, emphasizing the importance of close monitoring for pulmonary toxicity.

Lung irAE, if identified promptly, can often be managed successfully, resulting in favorable clinical outcomes and enabling the safe continuation or resumption of immunotherapy. Therefore, routine monitoring through clinical assessment and imaging is crucial for patients undergoing ICI therapy, particularly those at high risk due to factors such as pre-existing lung conditions, advanced age and combination treatment regimens.

Radiological imaging, particularly chest CT, remains essential for diagnosing and managing lung irAEs. However, optimizing patient outcomes requires moving beyond isolated image interpretation toward a unified multidisciplinary framework integrating oncologists, radiologists, pulmonologists and pathologists, guiding precise immunosuppressive interventions and reducing long-term pulmonary injury.

The growing recognition of radiomics and machine learning roles represents promising tools for the prediction, diagnosis and management of irAEs. By identifying high-risk patients early, these innovations could enable more personalized treatment strategies, and reduce the incidence of serious adverse events. Continuous updating of the literature and prospective validation remain the decisive steps before these models can fully enter routine clinical practice.

Author Contributions

Study conception, M.C.I.; data collection and analysis, M.C.I. and D.V.T.; interpretation of the results, M.C.I. and D.V.T.; draft manuscript preparation, M.C.I. and D.V.T. Both authors have read and agreed to the published version of the manuscript.

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