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Review article

Radiomics and quantitative imaging modalities in pediatric cystic fibrosis: A narrative review

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Abstract: Cystic fibrosis is a progressive multisystem disease with pulmonary complications being the main cause of morbidity and mortality, especially in pediatric patients. Structural lung changes may be present early and cannot be detected by conventional tools such as spirometry or visual computed tomography scoring. This narrative review summarizes the current evidence on advanced imaging methods, especially radiomics-based approaches, for assessing the severity, progression, and therapeutic response of lung disease in cystic fibrosis. We searched PubMed Central for studies published from 2014 to 2025 using terms related to cystic fibrosis, radiomics, computed tomography, and pulmonary density. Initially, six articles were selected, and additional relevant studies were included for methodological context. The reviewed literature shows that radiomics and quantitative imaging can be correlated with pulmonary function and clinical outcomes, whereas ultra-low-dose CT, MRI and automated image analysis may improve objective and radiation-sparing monitoring of bronchiectasis, air trapping and other lung abnormalities. However, challenges remain with variability in imaging protocols, limited reproducibility, and insufficient external validation. Radiomics and quantitative imaging show promise for the personalized monitoring of cystic fibrosis lung disease, but larger multicenter pediatric studies with standardized protocols are needed before clinical implementation.

Keywords: cystic fibrosis; radiomics; computed tomography; pediatric; quantitative imaging; magnetic resonance imaging; ultra-low-dose CT

1. Introduction

Anterior cruciate ligament (ACL) injuries are among the most common knee lig

1.1 Cystic Fibrosis

Cystic fibrosis (mucoviscidosis) is one of the most common life-limiting autosomal recessive disorders among Caucasian populations, with an incidence often reported at approximately 1 in 3,200 live births(1,2). It is a multisystem disorder caused by pathogenic variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on chromosome 7q31.2, which alter the CFTR protein and epithelial ion transport(2,3).

CFTR is a transmembrane protein involved in chloride and bicarbonate transport across epithelial surfaces. Dysfunctional CFTR affects multiple organs, but pulmonary disease remains the main driver of morbidity and mortality in patients with cystic fibrosis (2,3).

CF follows an autosomal recessive inheritance pattern and affects individuals who inherit two disease-causing CFTR variants. More than 2,000 CFTR variants have been described, although not all are disease-causing(2,3).

Survival has improved substantially over time. In the United States, survival projections for patients diagnosed in 2010 estimated survival into the early 40s, with potential extension into the 50s if advances in care continued (4).

Because CF remains a progressive lung disease, life expectancy is still reduced. Nevertheless, newborn screening, earlier diagnosis, and therapeutic improvements have increased survival, so many patients now reach adulthood(1,4).

1.2 The promise of advanced imaging

Spirometry, particularly forced expiratory volume in 1 second (FEV1), has historically served as a principal benchmark for CF severity(5). However, FEV1 can be insensitive to early structural changes that commonly arise in childhood before major spirometric decline. Therefore, imaging has become central in CF care because it enables direct visualization and quantification of structural lung damage(6,7).

Chest X-rays (CXRs) remain common because they are inexpensive and low dose, but they have limited sensitivity for mild or early lung damage and show interobserver variability when scored visually (7–10). Computed tomography (CT) provides detailed anatomical information on bronchiectasis, mucus plugging, airway wall thickening, and air trapping, and is increasingly used in CF assessment(6,7). Because repeated radiation exposure is a concern in pediatric patients, low-dose and ultra-low-dose CT protocols have been explored (11–13). Magnetic resonance imaging (MRI), including ultrashort echo-time (UTE) techniques, has gained attention as a radiation-free alternative for selected applications (5,14).

1.3 Radiomics

Radiomics is the extraction of high-dimensional quantitative features from medical images, potentially revealing texture, intensity, and shape patterns that are not apparent on visual inspection (15–17). The workflow usually includes image acquisition, segmentation, feature extraction, feature selection, and predictive modeling, and it requires standardization to improve reproducibility (18,19). In CF, radiomics-based CT scores have been investigated as objective biomarkers of disease severity and exacerbation risk (20).

In CF, quantitative imaging can support clinical phenotyping, treatment monitoring, and trial endpoints(6,20–22). In pediatric CF, advanced imaging may permit earlier intervention by detecting structural disease before overt spirometry decline(13,23). This narrative review evaluates how modern radiomics-based and quantitative imaging methods are applied in pediatric CF, comparing them with established methods and highlighting challenges and future directions for clinical translation. Where adult or mixed-age cohorts are discussed, their findings are considered in terms of methodological relevance to pediatric practice.

2. Materials and Methods

We performed a literature review using the PubMed Central database that focused on the diagnosis and evaluation of progression of cystic fibrosis in pediatric patients using radiomics techniques. Our goal was to evaluate the efficacy of these imaging methods in this specific context, with particular emphasis on the use of quantitative imaging biomarkers for disease characterization, severity assessment, and monitoring of therapeutic response.

The study also examines the link between these biomarkers and the severity of lung disease, the predictive and prognostic value of imaging patterns in cystic fibrosis, and the implications for patients who could benefit from personalized treatments.

Initially, we conducted a general, preliminary search to find the terms commonly used in searches about cystic fibrosis, computed tomography, radiomics, and pulmonary density.

The database search was conducted in 2025 and covered publications from 2014 to 2025. Two independent reviewers applied the following Boolean search string: “cystic fibrosis" AND "computed tomography" AND "radiomics" AND "lungs" AND "pulmonary density". Filters applied: English language, human studies, full free text, publication date 2014-2025. We have examined the most relevant articles for information about CT radiomics and pulmonary densities in cystic fibrosis in pediatric patients. During the initial stage of the selection process, we analyzed the titles and abstracts of the articles found. Duplicates were removed before screening. If the abstract was relevant to our study, we then analyzed the full text.

We retrieved 43 articles discussing “cystic fibrosis CT pulmonary density” and 4 items labeled “Cystic Fibrosis CT Radiomics,” screening titles and abstracts for relevance.

Articles were included if they:

1. Addressed CF diagnosis or disease monitoring.
2. Explored quantitative or radiomics-based imaging approaches (CT, MRI, or CXR).
3. Involved pediatric patients, or presented methodologies generalizable to pediatric cohorts.

We excluded articles focusing solely on non-pulmonary aspects of CF, published before 2014, not in English, without available or inaccessible full-texts, or not reporting quantitative pulmonary imaging methods. Of 47 records retrieved, 12 duplicates were removed, leaving 35 records for title and abstract screening. After screening, 14 full texts were assessed for eligibility, 8 were excluded (5 for non-quantitative methods, 2 for exclusively non-pulmonary focus, 1 inaccessible full text). Ultimately, 6 studies meeting core inclusion criteria were selected, as shown in Figure 1. To enrich the review and contextualize findings, additional references were incorporated on radiomics theory, low-dose imaging protocols, reproducibility standards, and pediatric CF imaging guidelines, these are cited narratively and not part of the six core studies (e.g., PRAGMA-CF).

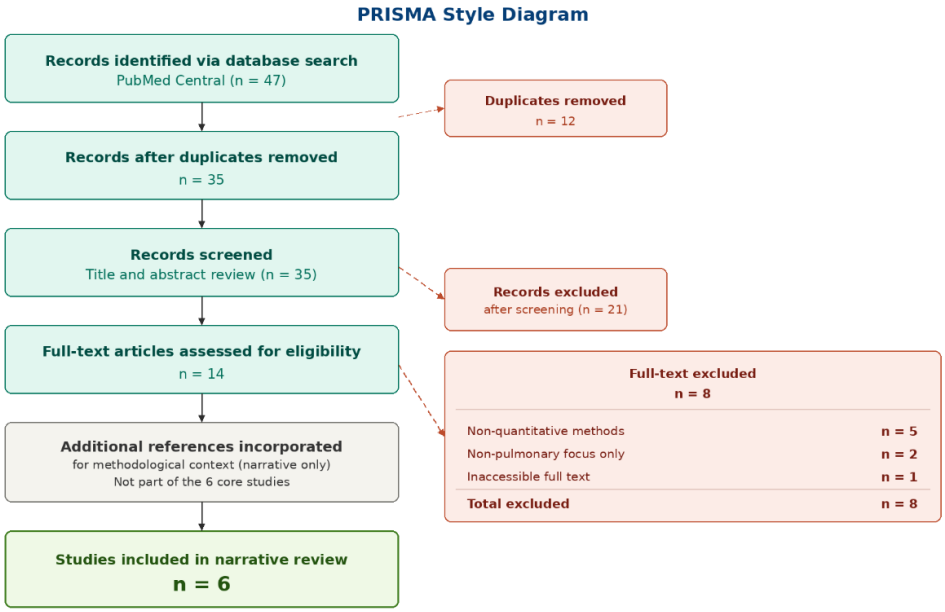


Figure 1 (PRISMA style flow diagram) provides a summary of the selection process.

3. Results

We extracted key data from each included study, including cohort size, age group (pediatric, adult, or mixed), imaging modality used (CT or MRI), segmentation modality, radiomic features or software employed, validation strategy, clinical endpoints, and main conclusions regarding the efficacy or limitations of quantitative imaging. This narrative synthesis was complemented by a broader discussion of methodological considerations in CF radiomics research, highlighting reproducibility, standardization, and pediatric-specific challenges.

We also surveyed specialized lung analysis tools used in CF imaging and radiomics workflows, including YACTA, PRAGMA-CF, PyRadiomics, and Chest Imaging Platform-related segmentation approaches(20,22–25).

Overall findings were synthesized to propose recommendations and identify gaps for future investigations, especially around pediatric CF imaging.

In Table 1, we provide an overview of the six original articles that employed advanced quantitative or radiomics-oriented methods to assess CF lung disease. We highlight study objectives, design, key imaging modalities, software used, and main outcomes.

Table 1. Key Studies Employing Advanced Imaging Analysis in Cystic Fibrosis

Author	Objective	Cohort	Methods	Software / Key Score	Conclusions
Dettmer et al.(22)	Assess CT changes before/after elexacaftor-tezacaftor-ivacaftor	Adult cohort	Retrospective; 22 adult CF patients; CT before and after ETI	YACTA for airway and parenchymal analysis; Brody score	Quantitative CT changes correlated with clinical outcomes and were reproducible; adult data require pediatric validation.
Zeimpekis et al. (14)	Compare lung signal intensity on UTE MRI versus fast spin-echo MRI	Pediatric cohort	Retrospective pediatric MRI cohort; lung segmentations	OsiriX MD; pyOsiriX	UTE MRI produced higher lung signal and feasible quantitative lung measurements in children.
Chassagnon et al. (20)	Develop radiomics-based CT scores for CF severity and exacerbation risk	Adult cohort	Retrospective; 215 adult CF patients; 38 CT radiomic features	Myrian XP-Lung; Matlab	Radiomics-based CT scores were associated with disease severity and acute exacerbation risk.
Bayfield et al.(13)	Implement and compare ultra-low-dose CT with low-dose CT in early CF lung disease	Pediatric cohort	Prospective pediatric CF population; visual and quantitative comparisons	YACTA v2.9.1.12	Ultra-low-dose CT provided comparable quantitative bronchiectasis information with lower radiation dose.
Campredon et al.(21)	Evaluate CT response to lumacaftor-ivacaftor	Mixed cohort	Multicenter pre/post CT study; unsupervised machine learning	Python; PyRadiomics; Bhalla score	Radiomics clustering showed bronchial disease improvement after therapy and association with clinical response.
Weinheimer et al.(26)	Quantify longitudinal airway dimensions and air trapping in mild pediatric CF	Pediatric cohort	36 school-age children; 144 serial spirometer-controlled CT scans	Fully automated CT airway and air-trapping analysis	Quantitative CT captured subtle regional and temporal interdependence between air trapping and bronchiectasis.

Dettmer et al.(22) enrolled exclusively adult patients, whereas Chassagnon et al. (20) and Campredon et al.(21) included adult or mixed-age CF cohorts. These studies are included because their radiomics methodologies are directly applicable to pediatric imaging workflows. Findings should not be generalized to children without dedicated validation. Bayfield et al. (13) and Weinheimer et al.(26) provide pediatric or school-age quantitative CT evidence, supporting the feasibility of radiation-sparing or longitudinal imaging approaches in children with CF.

Radiomics-based CT scores: Chassagnon et al. (20) and Campredon et al.(21) highlighted the potential of machine learning and cluster analysis for capturing CF disease severity or therapy response. These approaches can complement visual scores and may correlate with clinical indices such as FEV1, BMI, exacerbation risk, or modulator response.

Zeimpekis et al.(14) tested UTE MRI in children and demonstrated feasible quantitative lung signal and density measurements. This technique may partly substitute CT in specialized centers, although further validation and standardization remain necessary.

Software tools such as YACTA, PyRadiomics, OsiriX MD, and Myrian XP-Lung featured prominently, reflecting a growing reliance on automated or semi-automated approaches for airway and parenchymal measurements in CF. Differences in segmentation algorithms and feature definitions underscore the need for standardization(18,19,24,25).

A structured comparison of the six core studies reveals important methodological heterogeneity. Imaging modalities ranged from CT radiomics (Chassagnon et al.(20)) to ultra-low-dose CT (Bayfield et al.(13)), UTE MRI (Zeimpekis et al.(14)), and longitudinal automated CT analysis in school-age children (Weinheimer et al. (26)). Segmentation approaches included automated software (YACTA, Myrian XP-Lung) and semi-automated or open-source tools (OsiriX MD, PyRadiomics). Validation strategies varied substantially: Chassagnon et al. (20) performed internal validation, Campredon et al.(21) used unsupervised clustering, and none of the six core studies provided robust multicenter pediatric external validation. Sample sizes ranged from 22 adults in Dettmer et al.(22) to 215 patients in Chassagnon et al. (20). Primary endpoints included FEV1, BMI, exacerbation risk, therapy response, airway dimensions, and air trapping. This heterogeneity limits direct comparisons and underlines the need for standardized protocols. Although CF is predominantly a pediatric disease, dedicated pediatric radiomics studies remain relatively scarce. PRAGMA-CF, a quantitative CT scoring method validated in young CF patients, exemplifies the type of systematic quantification that radiomics and AI-based automation aim to accelerate (23,27).

Ultra-low-dose CT implementation in children, as reported by Bayfield et al. (13), and automated longitudinal CT analysis in school-age children, as reported by Weinheimer et al.(26), indicate that serial quantitative imaging is becoming more feasible. Future pediatric studies could combine ULD protocols with robust radiomic data to detect subclinical disease progression or to monitor early treatment effects.

3.1 Multi-Modality Approaches

Chest X-ray is common in CF care, yet it is relatively insensitive for mild or early lung pathology(7–10). Recent deep learning work has demonstrated automated CF chest radiograph scoring with performance approaching that of pediatric radiologists (28). Although CXR radiomics is less explored because of lower resolution, these proof-of-concept data support broader AI adoption.

CT imaging remains the reference standard for structural lung assessment, revealing bronchiectasis, mucus plugging, airway wall thickening, and air trapping with high spatial resolution(6,7). Conventional scoring systems such as Bhalla, Brody, CF-CT, and PRAGMA-CF are semi-quantitative and time-intensive. Radiomics offers deeper pixel-level quantification of lung parenchyma and airway changes, potentially improving sensitivity to early disease(20,23).

However, reproducibility across scanners, reconstruction kernels, segmentation methods, and acquisition protocols remains challenging(18,24,25). Current recom-

mendations emphasize standardized CT protocols, consistent breath-holding or controlled ventilation where feasible, and the use of reproducible feature definitions aligned with the Image Biomarker Standardisation Initiative (IBSI)(7,18).

MRI has the major advantage of avoiding ionizing radiation, which is critical for pediatric CF patients requiring repeated imaging(5,7,14,29). UTE MRI can approximate lung density and may support morphological assessment, although consistent image quality for robust radiomics remains an ongoing challenge(14). Functional MRI techniques, including hyperpolarized gas MRI, could eventually synergize with radiomics to measure ventilation heterogeneity(30).

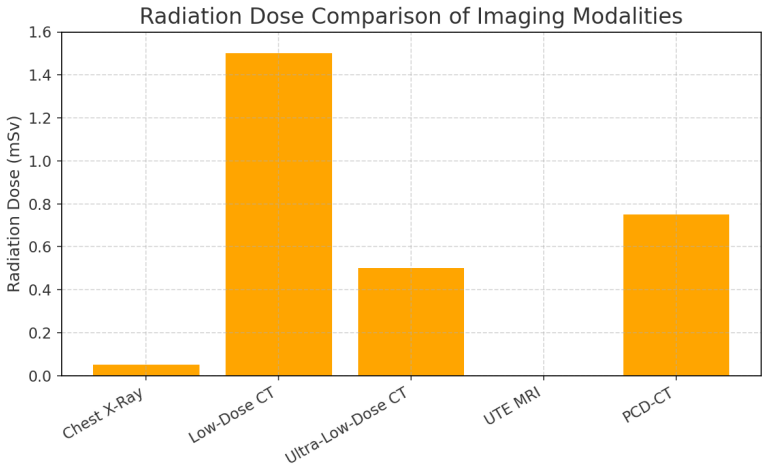
Photon-counting CT (PCD-CT) is also emerging, with potential advantages in spatial resolution, spectral information, and dose efficiency compared with conventional detector technology (31). The synergy between advanced hardware and radiomics workflows may provide more detailed characterization of CF lung microstructure.

The following table (Table 2) summarizes the main imaging modalities used in cystic fibrosis lung assessment, highlighting their relative advantages and limitations in terms of radiation exposure, spatial resolution, structural and functional information, and suitability for radiomics analysis. This comparison is intended to contextualize the role of conventional and emerging imaging techniques within CF care, particularly in relation to their potential integration into quantitative radiomics workflows. The accompanying radiation dose chart (Chart 1) further illustrates the balance between diagnostic performance and cumulative radiation burden, which is especially relevant in pediatric CF patients requiring repeated imaging over time.

Table 2. Comparison of Imaging Modalities in Cystic Fibrosis

Modality	*Radiation Dose (mSv)*	*Resolution*	*Structural Findings*	*Functional Findings*	*Radiomics Suitability*
Chest X-Ray	*0.01–0.1*	*Low*	*Gross pathology, lung opacities*	*None*	*Low*
Low-Dose CT	*1–2*	*High*	*Bronchiectasis, mucus impaction*	*Indirect (air trapping)*	*High*
Ultra-Low-Dose CT	*<1*	*Moderate–High*	*Bronchiectasis, air trapping*	*Indirect (air trapping)*	*High*
UTE MRI	*0*	*Moderate*	*Lung signal intensity, density approximation*	*Emerging (ventilation/perfusion mapping)*	*Moderate*
PCD-CT	*0.5–1*	*Very High*	*Airways, small vessels, better contrast detail*	*Potential (not yet routine)*	*High*

Chart 1. Radiation dose comparison of imaging modalities



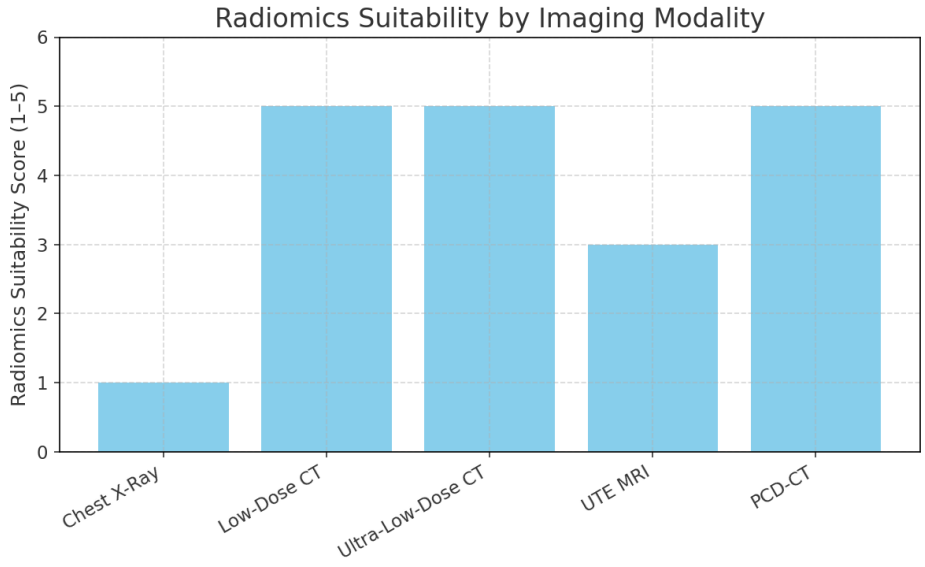
3.2 Radiomics Suitability

To evaluate the appropriateness of various imaging modalities for radiomics-based analysis in cystic fibrosis (CF), we developed a semi-quantitative scoring system ranging from 1 (lowest suitability) to 5 (highest suitability), as shown in Table 3 and Chart 2. This score was determined based on five core criteria adapted from prior radiomics evaluation frameworks and recent literature(15,18–20,22):

Table 3. Radiomics scoring system

Criterion	*Scoring Consideration*
1. Spatial Resolution	*Determines ability to extract fine-grained textural and morphological features.*
2. Image Consistency / Noise	*Influences feature reproducibility across timepoints or patients.*
3. Feature Richness	*Ability to extract large numbers of shape, intensity, and texture features.*
4. Clinical Usage in CF	*Extent to which the modality is currently used or validated in CF radiomics studies.*
5. Radiation Safety	*Especially critical in pediatric CF; safe modalities receive higher practical suitability.*

Chart 2. Radiomics suitability score by modality



4. Discussion

Traditionally, CF severity has been gauged by lung function tests or qualitative imaging scores(1,5). While these methods retain clinical utility, they may overlook early or regional lung pathology, particularly in children(6,13,23). Radiomics addresses part of this limitation by extracting large numbers of image-based features that quantify texture, shape, intensity, and spatial patterns(15,16).

Recent studies indicate that radiomic or quantitative CT parameters can detect treatment response to CFTR modulator therapy (21,22), predict exacerbation risk(20), and

track subtle longitudinal structural changes (26). Combined with ultra-low-dose imaging protocols (12,13), radiomics could support longitudinal CF lung monitoring with lower radiation burden, which is especially important in pediatric patients requiring frequent follow-up.

In CF, irreversible lung changes usually begin in childhood. Identifying these changes early may allow targeted preventive interventions and improved long-term outcomes (5,23). PRAGMA-CF has demonstrated that systematic quantitative CT assessment in young children is feasible and correlates with markers of airway inflammation(23).

Research using ultra-low-dose CT in children shows encouraging accuracy for detecting bronchiectasis and air trapping (13), and longitudinal automated CT analysis has shown that quantitative CT may capture subtle disease progression in school-age children with mild CF(26). In parallel, UTE MRI suggests that quantitative MRI signals can approximate CT-like lung densities (14). Additional standardization and multicenter evaluation are necessary before pediatric MRI radiomics can be widely adopted clinically.

4.1 Software and Automation

Multiple tools are currently used for quantitative lung analysis in CF, such as YACTA, Chest Imaging Platform-related segmentation methods, Myrian XP-Lung, and PyRadiomics(20,22,24,25). While commercial or proprietary solutions may offer convenience, open-source platforms can encourage reproducibility by disclosing algorithms. This transparency is particularly important in CF, where sample sizes are often small and multicenter collaborations are essential for robust findings(18,19).

Advances in machine learning have also driven automated segmentation and scoring. For example, PRAGMA-AI automates a previously manual pediatric CT scoring approach, accelerating analysis and showing promising correlation with visual PRAGMA-CF for bronchiectasis, disease extent, and mucus plugging (27). Ongoing developments should converge on standardized pipelines that can be shared across CF centers, ultimately facilitating broad clinical implementation.

In line with narrative review methodology, a formal risk-of-bias tool was not applied. However, a narrative assessment of methodological quality was performed for each included study based on study design, sample size, use of standardized imaging protocols, segmentation independence, and presence of internal or external validation. Bayfield et al.(13) and Weinheimer et al.(26) provided the most directly pediatric CT-focused quantitative evidence among the included studies. Chassagnon et al. (20) and Campredon et al. (21) used larger retrospective datasets and internal validation strategies but lacked robust pediatric external validation. Dettmer et al. (22) and Zeimpekis et al. (14) had smaller or exploratory designs. Overall, the evidence base is limited by small and heterogeneous cohorts, variable acquisition protocols, and absence of multicenter external validation, which restricts generalizability. Radiomics-based predictive models also face overfitting risks when high-dimensional feature sets are applied to small CF cohorts. Best practices include predefined feature extraction, partitioned training/validation/testing, cross-validation, cautious feature selection, and independent external validation(18,19,25).

4.2 Clinical integration and future directions

Pediatric CF radiomics holds considerable promise for personalized care across the lifespan. By identifying risk phenotypes, detecting early or subclinical progression, and quantitatively monitoring treatment response, radiomics may complement established clinical and functional assessment approaches. However, it is not yet ready

for routine clinical use: the current evidence is limited by small samples, heterogeneous protocols, and absence of multicenter external validation in pediatric cohorts. Standardization of acquisition, segmentation, and feature extraction is a prerequisite for clinical implementation(18,19,32).

In pediatric practice, the adoption of ultra-low-dose CT or MRI can facilitate repeated imaging while reducing unjustified radiation exposure (11,13,14,29). As imaging hardware evolves, including photon-counting CT (31) and hyperpolarized MRI(30), the synergy with advanced analytical frameworks such as radiomics should be accelerated. To realize these benefits, multicenter collaboration is needed to harmonize imaging protocols, validate radiomic features, and develop user-friendly software integrated with CF registries.

In addition to chronic structural progression, future pediatric CF imaging research should also account for the potential impact of acute respiratory infections and viral co-infections on disease trajectory. Major respiratory viruses such as SARS-CoV-2, influenza, and respiratory syncytial virus may influence hospitalization risk, respiratory deterioration, and intensive care need in vulnerable pediatric populations. A recent systematic review reported that viral co-infections, although not highly frequent, are associated with longer hospital and intensive care unit stay, higher oxygen requirement, and more severe outcomes(33). Longitudinal radiomics and quantitative imaging could help clarify how acute infectious events interact with pre-existing CF lung disease and whether specific imaging biomarkers predict incomplete recovery after exacerbations.

5. Conclusions

Radiomics and other advanced quantitative imaging analysis methods offer a transformative step in CF lung disease evaluation, particularly in the pediatric setting. Current evidence indicates that radiomics-derived or quantitative imaging features from CT and MRI can correlate with clinical outcomes, evaluate treatment response, and track subtle disease changes that spirometry or qualitative scores may miss. Ultra-low-dose CT and new MRI sequences further mitigate radiation risks for children. Future research should prioritize harmonized imaging protocols, open data sharing, and dedicated multicenter pediatric validation studies. Radiomics is a promising but still investigational tool. Its integration into routine clinical practice requires standardized acquisition, segmentation, and feature extraction, as well as prospective validation in pediatric CF cohorts before clinical recommendation can be made.

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