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Fibrotic and vascular abnormalities quantified by an AI-based model are associated with outcomes in patients with idiopathic pulmonary fibrosis

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Abstract

Background Idiopathic pulmonary fibrosis (IPF) is a progressive fibrosing interstitial lung disease associated with high morbidity and mortality despite specific anti-fibrotic therapies. Management of IPF is complex and relies on pulmonary function tests (PFT) to evaluate severity and monitor progression. CT provides non-invasive morphologic assessment and emerging software techniques enable quantitative analysis.

Methods We included 319 individuals with IPF from the OSIC dataset. A cross-sectional analysis was made for all patients, with a longitudinal evaluation for 143 of them. We used LungQ software (Thirona, The Netherlands) to quantify lung and pulmonary vessel volumes, as well as the extent of interstitial lung disease and to assess correlation with PFT and mortality.

Results Quantitative extent of fibrotic abnormalities was correlated with baseline FVC and DLCO (r -0.47, $p < 0.0001$ and r -0.55, $p < 0.0001$ respectively) and longitudinal modifications over time (r -0.48, $p < 0.0001$ and r-0.43 $p < 0.0001$, respectively). Median baseline extent of ILD, expressed as a percentage of lung volume, was 16.5% (10.8–25.5) and increased to 17.3% (11.6–29) on follow-up ($p < 0.001$). The median ILD progression was of 9.8% (-9.5-40.0). Vascular enlargement quantification as well as ILD quantification were predictive marker of death ($p < 0.0001$). However, vascular abnormalities' independent predictive value could not be assessed in multivariate models due to multicollinearity with other variables.

Conclusions LungQ allows to quantify interstitial and vascular lung features and their changes over time in a large cohort of patients with IPF. Imaging markers were negatively correlated with PFT at baseline and follow-ups were predictive of mortality confirming their potential as disease quantifiers. Further clinical validation is needed to specify the potential clinical use.

Keywords Interstitial lung disease, Idiopathic pulmonary fibrosis, Radiology, Imaging, Ai-based model

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Introduction

Idiopathic pulmonary fibrosis (IPF) has widely been recognized to be a severe progressive ILD associated with a high morbi-mortality despite the possibility of treating this severe condition with anti-fibrotic therapies [1, 2]. Physiological measurements (pulmonary function test (PFT)) and CT imaging are typically used to monitor individuals with IPF, but there is a need for improved measures of disease severity. PFTs are an indirect measure of disease activity, and visual assessment of imaging is limited by inter-observer and intra-observer variability [3].

Artificial intelligence (AI) has increasingly been applied in radiology over the last decade [4–6]. As modern medicine is evolving towards precision medicine, offering personalized patient care and treatment, the opportunity for robust imaging biomarkers discovery has gradually increased including in the field of fibrotic lung diseases. Imaging of ILDs is a specialist field and many centers lack the requisite radiology expertise to evaluate these patients. AI offers an opportunity to develop decision support systems which democratize consistent and reproducible diagnosis. Exploring new reliable tools for quantifying disease severity on HRCT is also a growing area of interest for predicting IPF and monitoring treatment response in routine clinical practice as well as stratifying patients in treatment trials.

Clinicians may use the Gender-Age-Physiology (GAP) score to stage the severity IPF [7–9]. Deep learning and radiomic models can be used as complementary tools for diagnosis and differentiate IPF and non-IPF ILDs [9, 10]. Such models could be used to discriminate different types of ILDs and assess their potential of progression towards fibrosis. In order to assess changes through time, longitudinal studies are needed [11–13].

One of the major complications of IPF is the occurrence of pulmonary hypertension (PH). PH in IPF is thought to be due to the chronic pulmonary insufficiency. This specific condition has been recognized to be associated with increased morbidity and mortality. It can be challenging to identify PH in patients suffering from IPF based solely on imaging analysis. Indeed whereas we can identify indirect imaging-based markers (dilatation of right ventricle or enlarged pulmonary artery) a structured quantitative analysis is still challenging. Moreover, the Increase trial has recently opened the field of specific therapies of PH associated with ILD underlying the need of early identification of IPF-associated PH [14].

Therefore, the identification of specific quantitative biomarkers combining ILD analysis and vascular enlargement would help clinicians to evaluate patients suffering from ILD in order to propose an integrated holistic evaluation. We sought to evaluate CT-based imaging biomarkers in a cohort of IPF patients by quantifying both vascular and interstitial abnormalities aiming to predict patient outcome. The model was applied to a multicentric cohort from the OSIC consortium.

Methods

Data repository

We selected all patients from the *Open Source Imaging Consortium (OSIC) Cloud Data Repository* with a clinical diagnosis of IPF. At the time of the study there were 581 patients in the repository with a total of 761 scans available for download. From this data 319 patients with a total of 462 scans were processable by LungQ due to input requirements on the input images. CT scans were considered not adequate for detailed quantitative assessment in case any of the following occurred: (1) slice thickness was too large (>1.5 mm), (2) inconsistency of the spacing between slices (>5%), (3) image orientation was not axial, (4) the patient was not positioned in a head first prone or feet first prone position, (5) image contained to few slices (< 150), or (6) DICOM file was incomplete. Survival data were available for all the subjects. We then used baseline CT-scan of those 319 patients in whom 143 follow-up CTs were available for a longitudinal analysis. In this study, Thirona's AI-based lung quantification platform (LungQ, Thirona, The Netherlands) was used to analyze all acquired CT scans [15]. The software uses state-of-the-art deep learning based algorithms to segment anatomical structures and disease manifestations (e.g. the lung, lobes, airways and pulmonary vessel) to quantify the total lung volume (TLV), the extent of interstitial lung abnormalities, and to phenotype pulmonary vascular volume distribution (AVX). As a pre-processing step of the CT data, the software leverages image normalization techniques to provide robust and repeatable quantitative information in CT scans acquired with varying scanner parameters, typically found in a clinical setting. The quantitative information is presented as the volume percentage of ILA and volume percentage of the affected area for the whole lung.

ILD scores were expressed as both the total volume of interstitial abnormalities (ILD_{ml}) and the total volume percentage of within the total lung volume ($ILD_{\%}$). We additionally calculated the extent of emphysema within the lungs expressed as normalized LAA-950HU [16]. The novel AI-based pulmonary artery-vein phenotyping (LungQ AVX) analysis was performed to provide a deep characterization of the pulmonary vasculature on thoracic CTs with or without contrast. The analysis starts by automatically segmenting the arterial and venous trees on CT using a deep learning-based algorithm and separates the vascular trees into individual branches. For each arterial or venous branch, the diameter, length, and vascular volume is computed, allowing for a detailed characterization of the pulmonary vascular volume distribution and

shifts. This study primarily focuses on total vessels, arteries, and veins with a diameter >2 mm (i.e. $AVX_{LV,}$ $AVX_{LAV,}$ and $AVX_{LVV,}$ respectively). The values are expressed as the volume of large vessels >2 mm as a percentage of the volume of all detected vessels. A visual representation of the detected and quantified regions is shown in Fig. 1.

Statistical analysis

Results are expressed as median (interquartile range: IQR). The evolution of PFT and lung abnormality over time was analyzed with the Wilcoxon-matched pairs signed rank test. The Spearman Rank test was used to test the correlation between PFT and lung abnormalities at baseline and between variation over time (follow up minus baseline) of the PFT and Lung abnormalities. A p value < 0.05 was considered to be statistically significative. Statistical analysis was performed using *TIBCO Statistica*, v. 13.5.0, TIBCO Software Inc, Palo Alto, CA, USA and graphs using GraphPad Prism software version 9.0.0 for Windows, GraphPad Software, San Diego, California, USA.

The survival probability based on ILD extent was calculated with Kaplan-Meyer survival analysis and comparison between survival curve were performed with Log-rank test for trends (graphs performed with the Python lifelines survival package version 0.27.3).

Cox regression univariate and multivariate models were used to analyze the overall survival concerning ILD extension, FVC %pred.val. and demographic parameters (Age, gender and smoking status). The variance inflation factor (VIF) was used to exclude covariable parameter.

Results

Patients demographics and functional characteristics

A total of 319 patients were evaluated with a mean age of 68.5 years and a male predominance (83.4%). The median (IQR) FVC at baseline was of 80% predicted (68–91) whereas DLCO was 11 $mmol.min^{-1}.Kpa^{-1}$ [9–15](Table 1).

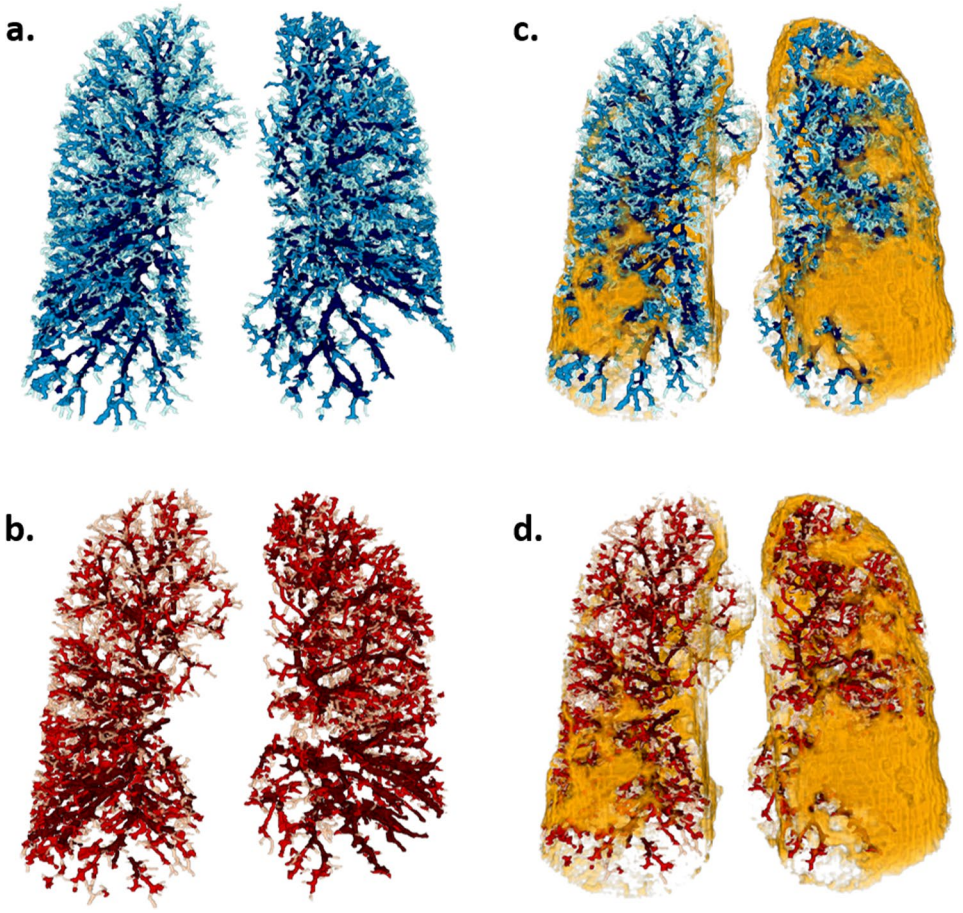

Fig. 1 Results of Thirona's AI-based lung quantification platform (LungQ, Thirona, The Netherlands). A visual representation of the pulmonary artery (**a**) and vein (**b**) phenotyping using LungQ AVX, where darker colors represent larger vessels. (**c**) and (**b**) show the AVX analysis with additional overlay of interstitial lung abnormalities (ILD) in orange

Table 1 Parenchymal abnormalities and patient functional characteristics

	N **= 319**
TLV, ml	3865 (3149–4623)
Emphysema score,%	0.4 (0.07–1.5)
$ILD_{\%}$ score,%	17 (11–25)
ILD_{ml} score, ml	640 (450–860)
AVX_{LV} (Large vessels > 2 mm),%	69 (65–74)
AVX_{LVV} (Large veins > 2 mm), %	28 (26–31)
AVX_{LAV} (Large arteries > 2 mm), %	41 (38–45)
FVC, % pred.	80 (68–91)
FVC, L.	2.7 (2.3–3.3)
FEV-1, L.	2.2 (1.9–2.6)
DLCO, $mmol.min^{-1}.Kpa^{-1}$	11 (9–15)

Data are expressed as median (IQR). *TLV* Total Lung volume, *ILD* Interstitial Lung Abnormalities, *FVC* Forced vital capacity, *FEV-1* Forced expired volume in 1 second, *PFT* pulmonary functional tests

ILD analysis and correlation with functional characteristics

The median (IQR) lung volume was 3865 ml (3149–4623) with a median extent of emphysema of 0.4% (0.07–1.5) whereas the median volume of ILD_{ml} at lung level was 640 ml (450–860). The median (IQR) $ILD_{\%}$ extent was 17% (11–25) (Table 1). ILD scores were moderately negatively correlated with both FVC (% predicted) and DLCO ($mmol.min^{-1}.Kpa^{-1}$) (n = 171)(r=−0.47, p < 0.0001 and r=−0.55, p < 0.0001 respectively)(Fig. 2).

ILD longitudinal study

Results of longitudinal analysis for participants with serial CTs is shown in Table 2. In this cohort we had a median (IQR) follow up of 54 (46–61) weeks with a median (IQR) FVC decline of −2.3% (−8.6–3.2) predicted and an increase in ILD extent of 9.8% (−9.5–40). Baseline characteristics of this subgroup of patients showed that the median FVC was of 80% predicted (68–91). The median lung volume was 3964 ml (3259–4664) with an extent of emphysema of 0.5% (0.1–1.5) whereas ILD_{ml} median extent was of 630 ml (480–840). Median baseline $ILD_{\%}$ score was of 16.5% (10.8–25.5) at baseline for a median follow-up quantification of 17.3% (11.6–29), with a significant increase (p < 0.001) of 9.8% (−9.5–40.0) (Table 2).

Table 2 Imaging and functional characteristics of the longitudinal cohort

	BASELINE	FOLLOW-UP	% change
Lung volume, ml	3964 (3259–4664)	3818 (2915–4551)***	−3.7 (−9.7–2.8)
Emphysema score,%	0.5 (0.1–1.5)	0.5 (0.1–1.4)	−3.2 (−51.8–131.3)
$ILD_{\%}$ score,%	16.5 (10.8–25.5)	17.3 (11.6–29)***	9.8 (−9.5–40.0)
ILD_{ml} score, ml	630 (480–840)	660 (480–1000)**	8.3 (−11.6–27.1)
AVX_{LV} (Large vessels > 2 mm),%	68.7 (64.7–73.8)	69.3 (66.4–75.2)**	1.1 (−2.3–6.9)
AVX_{LVV} (Large veins > 2 mm), %	27.8 (25.6–30.6)	28.5 (26-31.1)	1.5 (−6.6–11.3)
AVX_{LAV} (Large arteries > 2 mm), %	41.4 (38.4–44.7)	41.7 (39-44.9)*	2.4 (−3.8–7.6)
FVC, % pred.	80 (68–91)	76 (63–92)**	−2.3 (−8.6–3.2)
FVC, L.	2.8 (2.3–3.4)	2.7 (2.1–3.2)****	−3.2 (−10.5–2.3)
FEV-1, L.	2.3 (1.9–2.7)	2.2 (1.8–2.6)****	−2.9 (−10.2–1.5)
DLCO ($mmol.min^{-1}.Kpa^{-1}$)°	11.6(8.9–15.1)	11.4 (8.0-14.1)***	−6.4 (−17.8–1.3)

Value are represented in median (IQR) for each value (n=143). Data are analysed with the Wilcoxon-matched pairs signed rank test for the non-parametric variable or with the paired T test for the parametric variables *P<0.05,**P<0.01, ***P<0.001, ****P<0.0001. °*DLCO* Number of pairs = 102. The variation is (Follow-up – Baseline)/Baseline) in %

In order to evaluate the potential value of LungQ ILD, we constructed a Kaplan-Meier curve after having separated patients in 3 tertiles based on the ILD-extent (Annex 1). The 3 tertiles were associated with a median (IQR) lesional extent of 9.0% (6.6–11.1); 16.9% (14.8–19.8) and 31.9% (25.5–45.1) respectively.

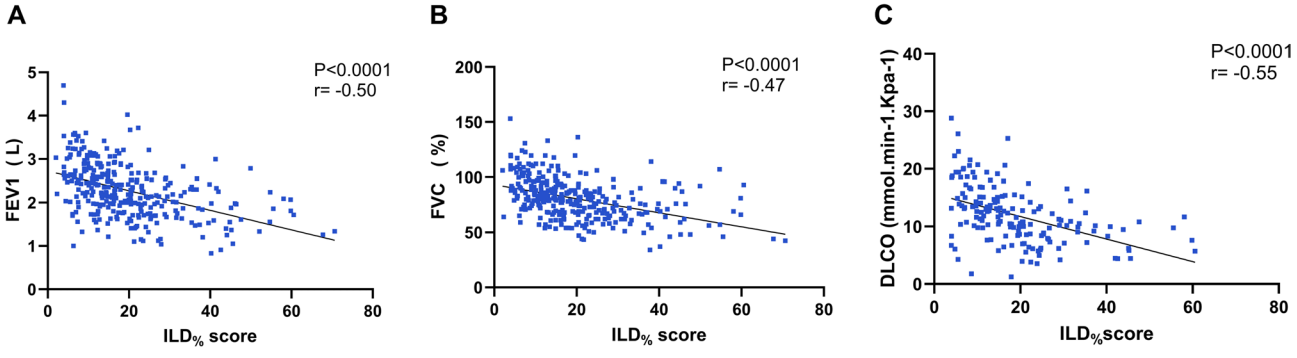

Fig. 2 Correlation between PFT and $ILD_{\%}$. Panel of correlation curve representing the correlation between FEV-1 and % of ILD in the lungs **A**); FVC and % of ILD in the lungs (**B**); DLCO and % of ILD in the lungs (**C**). ILD: Interstitial Lung Abnormalities; FVC: Forced vital capacity; FEV-1: Forced expired volum in 1 second; PFT: pulmonary function tests

Longitudinal analysis : Correlation between ILD progression and PFTs

Correlations between CT-based quantification of ILD and functional markers were also evaluated. The change in total lung volume (ml) was specifically correlated with FVC, FEV-1 and DLCO change (in % of the absolute value)($r = 0.45$, $p < 0.0001$; $r = 0.40$, $p < 0.0001$ and $r = 0.27$; $p = 0.0059$ respectively. FVC, FEV-1 and DLCO change over time were negatively correlated with ILD change in extent ($r = -0.48$, $p < 0.0001$; $r = -0.42$, $p < 0.0001$ and $r = -0.43$, $p < 0.0001$)(Fig. 3).

Survival analysis based on ILD quantification

We constructed Kaplan-Meier curves for each group of patients based on their $ILD_{\%}$ extent in Tertiles (Fig. 4). The three cohorts compared with the log-rank test for trend (lower, medium or upper tertiles) exhibit a median survival of 428, 270 and 131 weeks respectively ($p < 0.0001$).

Vascular analysis

The median (IQR) AXV_{LV} was of 69% (65–74) (Table 1).

Correlation between PFTs and pulmonary vascular volume distribution

We correlated pulmonary vascular volume distribution scores (AVX) with PFTs and found that there was a negative correlation with FEV-1, FVC and DLCO for each parameter arterial and total vascular enlargement (Fig. 5). Of high interest, vascular abnormalities were negatively correlated with DLCO ($r = -0.40$; $p < 0.0001$) in a similar extent to the correlation of FVC ($r = -0.32$; $p < 0.0001$).

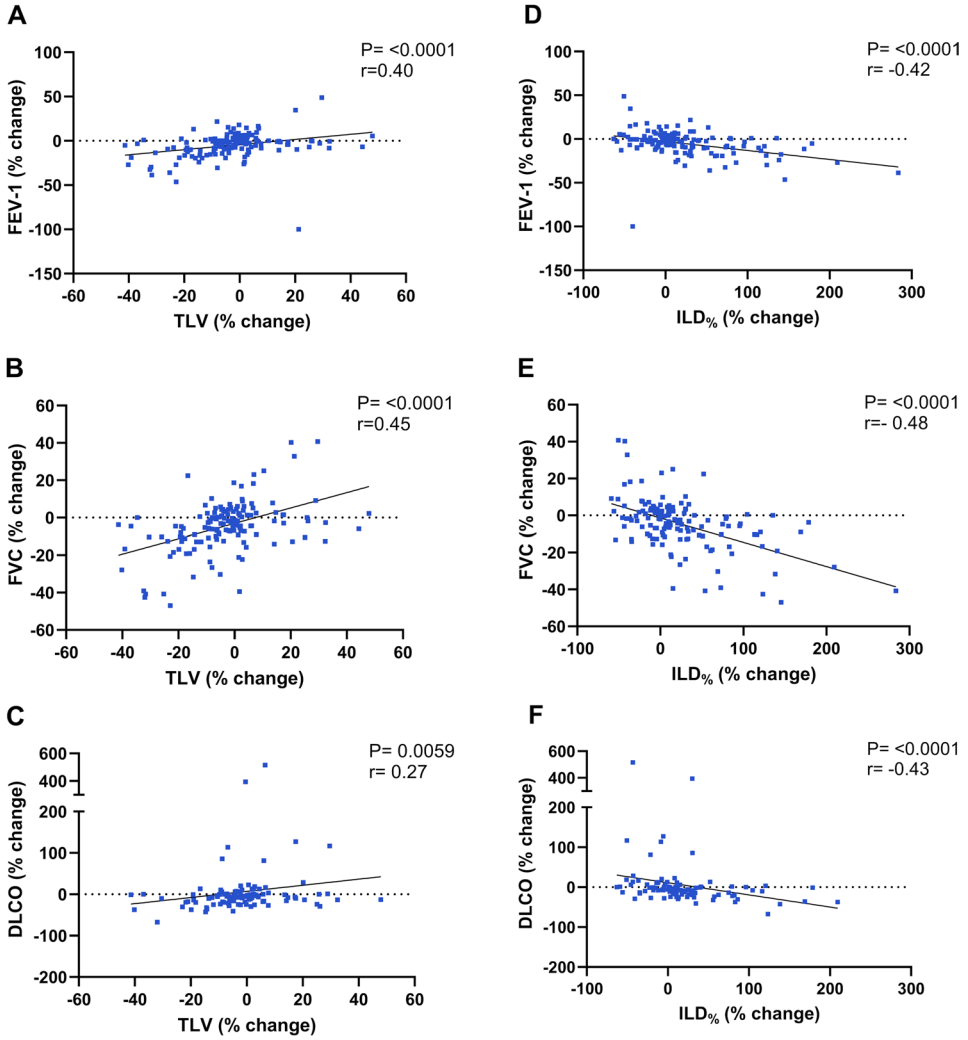

Fig. 3 Correlation between longitudinal change in PFTs and ILD quantification. Pannel of correlation curve representing the correlation between FEV-1 and change of TLV (**A**); FEV-1 and % of ILD change in the lungs (**D**); FVC and change of TLV (**B**): FVC and % of ILD change in the lungs (**E**); DLCO and change of TLV (**C**); DLCO and % of ILD variation in the lungs (**F**). TLV: Total Lung Volume; ILD: Interstitial Lung Abnormalities; FVC: Forced vital capacity; FEV-1: Forced expired volum in 1 s; PFT: pulmonary functional tests

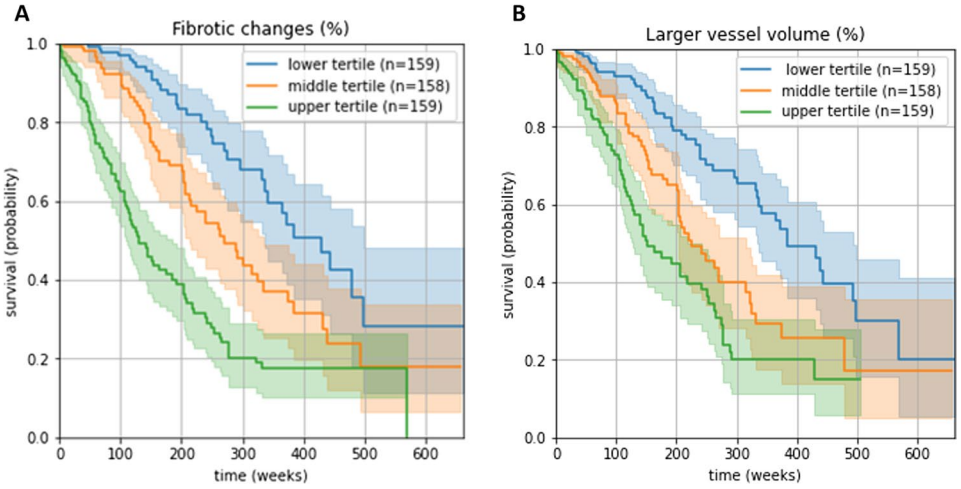

Fig. 4 Survival curve based on the ILD extension. Kaplan-Meier curve for the 3 IPF group based on their ILD extent (**A**) and Vascular abnormalities (**B**). **A** The three tertiles are associated with a median (IQR) extension of 9.0% (6.6–11.1); 16.9% (14.8–19.8); 31.9% (25.5–45.1) for the lower, medium and upper tertiles respectively. The survival rate was of 428, 270 and 131 weeks respectively. **B** The three tertiles are associated with a median (IQR) of vascular abnormalities of 64.3% (62.6–65.8); 69.5% (68.2–70.1); 76.7% (74.6–80.5) for the lower, medium and upper tertiles respectively. The survival rate was of 385, 225 and 152 weeks respectively

Longitudinal analysis

Correlation between Vascular abdnormalities progression and PFTs.

The correlation between imaging-based quantification of vascular enlargement in the lungs and functional markers were also evaluated. FVC, FEV-1 and DLCO variation over the time were negatively correlated with change in vascular metrics ($r = -0.34$; $p < 0.0001$, $r = -0.32$; $p < 0.0001$ and $r = -0.32$; $p = 0.0012$) (Annex 2).

Survival analysis based on vascular abnormalities quantification

We constructed Kaplan-Meier curves for each group of patients based on their vascular enlargement % of total vascular volume (Fig. 4; Annex 3). The three cohorts (lower, medium or upper tertiles) exhibit a median survival of 385, 225 and 152 weeks respectively ($p < 0.0001$) (Fig. 5).

Univariate and multivariate survival Cox models analysis

Univariate analysis shows that FVC, ILD%, AVX and age are predictive of survival, but smoking and gender are not predictors when used alone. For the multivariate analysis, a strong collinearity was observed between FVC, AVX and Age; and between AVX and ILD%. Two models were selected after the exclusion of those covariates. The multivariate analysis (adjusted on demographic characteristics) confirmed that ILD% was an independent risk factor of mortality. Age, gender and smoking status were also as expected independent risk factor of mortality. Harrel's C-statistic concordance test showed that in the univariate models, the C-statistic was higher for the ILD% indicating a better ability to predict survival than compared to other parameters (Annex 4).

Cox model for multivariate analysis did not allow to identify a significant impact of age, gender and smoking status confirming that CT-based markers remained significant even after demographic adjustment.

Correlation between ILD quantification and vessels enlargement

Thinking beyond the pathophysiological process leading to vascular abnormalities in IPF, we aimed to correlate those to markers with a spearman test (Annex 5). We identified a significant correlation between vascular and interstital markers ($r = 0.61$, $p < 0.0001$)(Annex 6).

Discussion

In our study we evaluated the potential of the AI-based lung quantification platform LungQ for quantification of both parenchymal and vascular modifications in a cohort of IPF patients from the OSIC initiative. We showed that automatically quantified interstitial lung abnormalities were correlated with physiological values and associated with mortality. In addition, pulmonary vessel enlargement was correlated with overall mortality and alveolo-capillary dysfunction. Taken together, those imaging-based markers have the possibility to integrate IPF severity and IPF-associated pulmonary hypertension.

In IPF, disease quantification is one of the major challenges to tackle. Assessing disease severity and change in fibrotic lung images over the time through visual scoring approach is still difficult even for expert senior radiologists underlying the need of automatized quantification tools [17, 18].

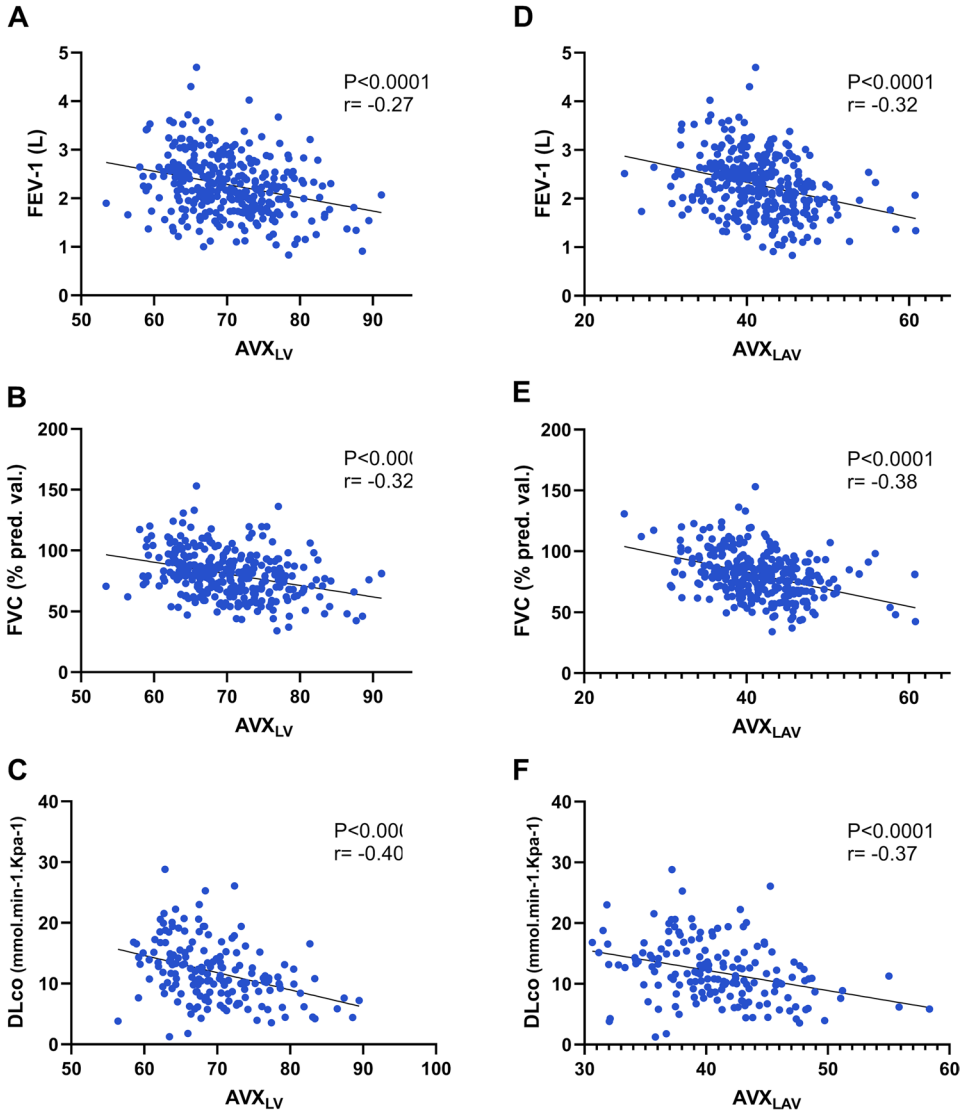

Fig. 5 Correlation between PFTs and vascular metrics. Panel of correlation curve representing the correlation between PFTs and vascular abdnormalities quantification. FEV-1 and % of vascular enlargement in the lungs (**A**) and specific pulmonary arterial enlargement (**D**); FVC % of vascular enlargement in the lungs (**B**) and specific pulmonary arterial enlargement (E); DLCO and % of vascular enlargement in the lungs (**C**) and specific pulmonary arterial enlargement (**F**). FVC: Forced vital capacity; FEV-1: Forced expired volum in 1 s; PFT: pulmonary functional tests

LungQ allowed us to specifically address the question of ILD quantification. We were able to confirm a significant correlation between ILD extent and physiological values (FVC, FEV-1, DLCO) at baseline but also over the time. Moreover, ILD quantification enabled the prediction of overall mortality by separating patients into 3 groups based on ILD extent. The use of automatic software is of great interest for providing reliable and reproducible evaluation in the specific context of IPF [10, 19–21]. Previously, Kim et al. have demonstrated that quantitative CT analysis in IPF was able to quantify the extent of disease severity and assess longitudinal changes, with good correlation to lung function [12]. More specifically, Shi et al. established that baseline HRCT scans could be used to predict fibrosis progression at 6 months to 1-year follow-ups using artificial intelligence [22]. They also hypothesized that the performance of their predictive model could be enhanced by adding further information on patients' demographics and pulmonary function tests, which have been proven to be useful in assessing IPF prognosis. Moreover, several studies showed that quantitative HRCT analysis could predict mortality [11, 23, 24]. For example, Humphries et al. confirmed the potential of predicting transplantation-free survival with a HR of 1.2 using a data-driven texture analysis independently to PFT [25–27].

Through our study we evaluated the potential of an integrated automatic CT based ILD score aiming to

propose an efficent way for helping clinicians to evaluate disease status and predict patients outcome. Todate it is still challenging to propose a unique image-based modelization of fibrotic lung changes over time as disease behaviour is highly variable even in a unique pathological entity like IPF.

The quantification of pulmonary vessels (arteries and veins) and associated structures (perivascular fibrosis), generally known as vessel-related structures (VRSs), which cannot be performed by the human eye, has been demonstrated to be strongly correlated with survival in a series of IPF patients [28]. Jacob et al. previously showed that VRSs was helpful in the prediction of patient outcome in IPF and also in RA-ILD [21, 29]. However, despite those preliminary results the usefulness of vascular analysis on CT imaging in order to identify patients at risk of rapidily progressive IPF is not yet clearly defined. Moreover, the occurrence of pulmonary hypertension due to lung disease can act as a confounding factor increasing vascular diameter.

In our study, we identified a significant correlation between vascular volume and mortality. AVX quantification is physiopathologically in line with the expected evolution of IPF as it has already been describe that microvascular dilation was potentially due to fibrotic traction [30]. In our study we have mainly studied vessels >2 mm leading us to hypothesize that those observations were more inclined to be the consequence of pulmonary hypertension associated with severe chronic lung disease. This hypothesis is reinforced through its correlation with the severity of ILD. The overall quantification of vascular modifications based on HRCT imaging is not possible for clinicians in daily workflow. For this specific question we also have to disclaim that, even in expert centers, intra- and inter-observer variation will be quite high and not acceptable for clinical use. The identification of pulmonary hypertension is, since we now have potential therapeutic options [14], of major interest in order to include this parameter in patient management. While our study identified a correlation between vascular volume and both ILD severity and mortality, this finding should not be overinterpreted as direct evidence of PH. Vascular enlargement alone is not diagnostic of PH, as definitive diagnosis requires right heart catheterization.

These findings contribute to a growing awareness of the potential of artificial intelligence techniques. Similarly, the LungQ AVX is a unique measure that combines ILD quantification and pulmonary vascular architecture analysis. Previous research have shown that automated pulmonary vasculature assessment is crucial for determining disease severity in IPF patients [20, 28, 31] and associate with worse patient outcome. Recently, Thillai et al. identified the high potential of a deep-learning approach to predict disease progression and mortality in IPF with a high predictive value [32].

A major strength of our study is the usability of the LungQ AVX through its automatization by-avoiding the need for contrast enhanced imaging for vascular evaluation in order to apply disease quantification and help in the prediction of patient outcome as a companion tool for clinicians. We found significant correlation with PFT but also a strong relationship with patient outcome (mainly decreased pulmonary function and mortality). One other interesting point is that we used a multi-center dataset which suggests the potential of this technique for use in the clinic and also in clinical trials.

Our study has several limitations, the most notable being its retrospective design, as opposed to a prospective clinical trial. Additionally, there was a slight male-to-female imbalance that was higher than typically observed in IPF cohorts. Nevertheless its multicentric nature is also a strength as CTs were carried out on multiple scanners in multiple centers without specific gating strategy. The collinearity of the parameters did not permit a multivariate analysis to assess the relative performance of FVC, AVX and ILD% for predicting survival. Of note, including all metrics in a sole model and particularly demographics did not improve the model. Additionally we did not have access to an independent population to further validate the metrics, suggesting a need for further prospective multicentric validation.

Conclusions

In conclusion, we confirm the potential of LungQ AV_X as an AI-based ILD quantification software for IPF patients in a large multicentric cohort. We also identified a potential benefit of vascular quantification in IPF as a marker for the prediction of overall mortality, paving the way of new surrogate markers of pulmonary hypertension in ILD. However, this association remains speculative in the absence of direct clinical or hemodynamic confirmation of pulmonary hypertension and should therefore be interpreted with caution. A dedicated study would be required to explore this relationship more conclusively. The potential of those reliable imaging-based metrics open new perspectives for ongoing or future clinical trials.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03949-7.

Supplementary Material 1

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Clinical trial number
Not applicable.

Authors' contributions
JG, RL and JPC conceived the study. JG, JE, MH and JPC analyzed the results. MH, JE performed statistical analysis. JE and JPC provided the LungQ software. JG, JE, BE, QM, DL, SH and JPC wrote the manuscript. All authors reviewed and validated the manuscript.

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Data availability
Data was obtained from the OSIC-ILD repository (www.osicild.org/).

Declarations

Ethics approval and consent to participate
The OSIC protocol was submitted to the U.S. Central IRB Advarra. The IRB determined that the research project is exempt from IRB oversight. Consent to participate was waived considering the retrospective nature of the study. The study adheres to and is in compliance with the Helsinki Declaration.

Consent for publication
Not applicable.

Competing interests
J.G. has received institutional research grants from Janssen Pharmaceutica, Boehringer Ingelheim, MSD and Roche and has received consulting and honoraria fees from Boehringer Ingelheim, Janssen, BMS, GSK, Roche, AstraZeneca, Aquilon, Volition, Oncoradiomics and Chiesi and has received non-financial support for meeting attendance from AstraZeneca, Chiesi, MSD, Roche, Boehringer Ingelheim and Janssen. J.E. and J-P.C. are employees of Thirona and J-P.C. is shareholder of Thirona. R.L. has received institutional research grants from GSK, AstraZeneca and Chiesi and has received consulting fees from GSK and AstraZeneca and honoraria as lecturer from AstraZeneca and as speaker from GSK and has participated in ANDHI in practice study from AstraZeneca. D.A. Lynch has received consulting fees from Calyx Inc and Beohreinger Ingelheim and honoraria from Clinical Education Alliance and has unlicensed and assigned to institution patents US 10,706,533; US 11,468,564 and US 11,494,902. S.M. Humphries has received grants paid to institution from NHLBI, Boehringer Ingelheim and Calyx and has unlicensed and assigned to institution patents US 10,706,533; US 11,468,564; US 11,494,902; and US 11,922,626.

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