Differentiating Interstitial Lung Abnormalities and Interstitial Lung Disease In Lung Cancer Screening

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Introduction

Interstitial lung abnormalities (ILAs) are common incidental findings in lung cancer screening (LCS) and the presence of ILA is an independent predictor of mortality. LCS is rolling out in England so that by 2030, it is estimated that nearly one million subjects will be invited for an annual CT scan.

AIM : To address the challenges in differentiating clinically relevant ILAs, as highlighted in a recent ERS/ESTS/ESTRO/ESR/ESTI/EFOMP statement, by analysing ILAs identified in the SUMMIT Study, the largest LCS study in Europe.

Method

Of 11,635 LCS individuals, 417 screen detected ILAs were evaluated using:

- A new simple visual classification system focused on traction bronchiolectasis (categorising non-fibrotic [NFILA] and fibrotic ILA [FILA] and advanced ILA [AILA])(Figure 1).
- A quantitative computer tool CALIPER.
- An age, sex and smoking history matched control group was analysed alongside the ILA cohort to examine associations between baseline ILA and forced vital capacity (FVC), hospitalisations (Students T-Tests) and mortality (univariable and multivariable Cox proportional hazards models).

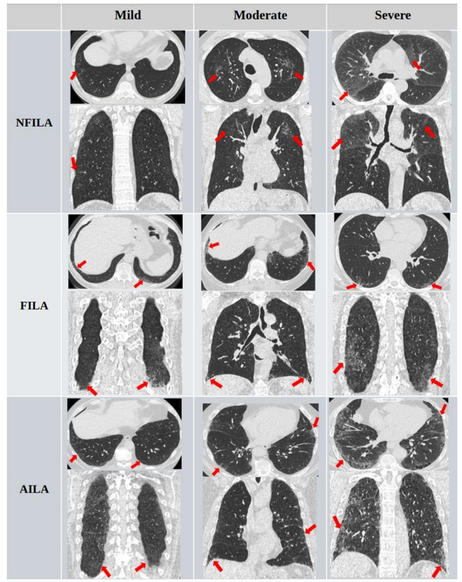
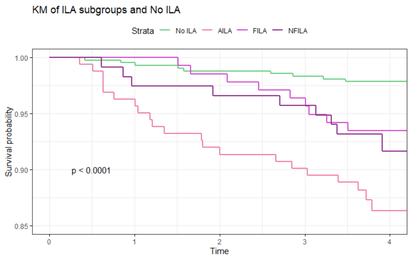


Figure 1: Axial and coronal CT examples of non-fibrotic interstitial lung abnormality (NFILA), fibrotic interstitial lung abnormality (FILA), and advanced interstitial lung disease (AILA). NFILA= presence of non-dependent ground glass opacities and/or reticulation with no associated traction bronchiolectasis evident in any lobes. FILA required traction bronchiolectasis (coexisting with reticulation with/ without non-dependent ground glass opacities) in a maximum of 2 lobes. AILA required traction bronchiolectasis (coexisting with reticulation with/ without non-dependent ground glass opacities) to be evident in more than 2 lobes.

Results

- Our visual ILA classification system showed superior interobserver agreement versus existing ILA criteria (K=0.76 v K= 0.64). Observer variation for ILA subtypes (no ILA, NFILA, FILA and AILA) was excellent (K=0·84).
- Participants with AILA had a 6- fold higher mortality rate, while fibrotic and non-fibrotic ILA subtypes had a 3-fold increased mortality compared to controls (Figure 2)
- CALIPER-quantified ground glass opacities and vessels were increased in ILAs (Figure 3) and independently associated with mortality (p=0·02 and p=0·03 respectively); in contrast to baseline FVC (p=0·49 and p=0.57 respectively) (Figure 4)



Number at risk table by time

Time

status	t0	t1	t2	t3	t4
No ILA	417	415	412	410	408
NFILA	117	114	113	112	108
FILA	138	138	136	133	129
AILA	162	156	149	146	141

Figure 2: Kaplan-Meier Survival Curves for participants with and without interstitial lung abnormalities/disease (ILA) on CT (top); and for participants with and without subtypes of ILA on CT (bottom).

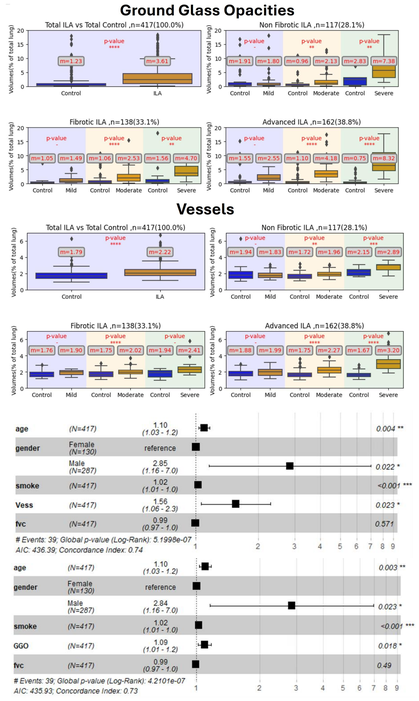


Figure 3: Box-Plots showing CALIPER-derived quantitative outputs of ground glass opacities (top) and vessels (bottom) on CT imaging in subjects ILAs. ILA=interstitial lung abnormality, ILD=interstitial lung disease. *p<0·05; **p<0·01, ***p<0·001, ****p<0·0001.

Figure 4 : Multivariable Cox regression analyses for CALIPER variables derived from CT analysis. Results are shown for SUMMIT participants identified with interstitial lung abnormalities. GGO=ground glass opacities, Vess=vessels; fvc=forced vital capacity

Conclusion

We demonstrate a new reproducible classification to characterise prognostically important ILAs and ILDs in LCS, to help facilitate early referral to ILD services. We highlight advantages of quantitative analysis and limitations of FVC in delineating ILA mortality associations