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Visual Emphysema on LDCT Predicts Mortality

Low-dose CT screening for lung cancer can reveal more than nodules. Visual emphysema seen at baseline screening is linked with mortality risks that extend decades. In a prospective cohort of 9047 asymptomatic adults aged 40–85 years with a smoking history, a single four-grade visual emphysema score assigned at the first screening was examined against deaths up to 25 years later. After long follow-up through December 2024, emphysema at baseline was associated with higher all-cause mortality and substantially higher chronic obstructive pulmonary disease mortality with signals for cardiovascular disease that diminished in competing-risk analyses. The findings emphasise the prognostic weight of a simple, reproducible visual read made at the outset of screening.

Visual Scoring, Cohort and Follow-up

Participants underwent baseline low-dose chest CT between June 2000 and December 2008 across 12 institutions with annual follow-up under a standardised protocol and causes of death drawn from National Death Index, physicians and family. Emphysema was scored centrally by one of four experienced chest radiologists using a 0–3 visual scale: none, mild, moderate or severe, applied across the whole lung to reduce complexity and interreader variability. This approach, developed by expert consensus before screening implementation, has shown good reproducibility and early prognostic value and has been widely used in routine clinical practice. Coronary artery calcification was also scored ordinally to derive cardiovascular risk categories.

Of 9047 participants, the median age was 65 years, and median smoking history was 43 pack-years. Emphysema was present in 2637 participants (29.1%): mild in 1908, moderate in 512 and severe in 217. Most participants with emphysema at baseline had no prior known diagnosis of emphysema or COPD including individuals with moderate or severe changes. Emphysema was more frequent in current than former smokers, increased with age and cumulative exposure and aligned with higher frequencies of non-zero coronary artery calcification as visual scores rose. By December 31, 2024, 3738 participants (41.3%) had died, cardiovascular disease accounted for 1153 deaths (12.7%) and COPD for 295 deaths (3.3%). Median follow-up estimated with the reverse Kaplan-Meier method was 23.3 years.

Mortality Patterns and Dose–Response Signals

Unadjusted survival curves separated by emphysema presence and severity showed lower overall, COPD and cardiovascular survival among those with emphysema with gradients across mild, moderate and severe categories. Overall survival was 48.1% in those with emphysema versus 62.5% without, COPD survival was 90.9% with emphysema versus 97.7% without, cardiovascular survival was 81.4% with emphysema versus 85.8% without. COPD survival ranged from 94.2% in mild to 70.3% in severe emphysema.

In multivariable Cox models adjusting for sex, age, pack-years and years since quitting, emphysema at baseline independently predicted all-cause mortality (hazard ratio 1.29; 95% CI 1.21–1.38) and COPD mortality (3.29; 95% CI 2.59–4.18). A dose–response pattern was evident: compared with no emphysema, adjusted hazard ratios for all-cause death were 1.15 for mild, 1.54 for moderate and 2.28 for severe; for COPD death they were 2.07, 5.31 and 12.06 respectively. In Fine-Gray competing-risk analyses, the association with COPD mortality persisted but was attenuated (adjusted 3.06; 95% CI 2.40–3.90).

Cardiovascular findings were more nuanced. In Cox models, emphysema was linked to a 14% higher risk of cardiovascular death after adjustment (1.14; 95% CI 1.01–1.29) but there was no dose–response by emphysema severity and the association was not evident once competing risks were accounted for in the Fine-Gray analysis. These patterns suggest that while emphysema presence correlates with cardiovascular mortality in conventional time-to-event models, competing causes particularly COPD deaths may overshadow cardiovascular events over long horizons. The cohort also showed an increasing frequency of non-zero coronary artery calcification with higher emphysema scores underscoring shared risk factors within a screening population of smokers and former smokers.

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Clinical Context and Methodological Considerations

The visual scoring system applied across the entire lung sought to harmonise assessments and reduce interreader variability with prior work indicating superiority over quantitative analysis in some settings and excellent agreement in external experience. The long follow-up, large number of events and cause-specific as well as competing-risk modelling strengthen the mortality insights attributable to a single baseline read. The analysis adjusted sequentially for demographic and smoking variables and examined both presence and extent of emphysema to characterise risk gradients.

Limitations reflect pragmatic screening realities. Visual assessment can be subjective and predates later classification schemes although prior reports indicate broad agreement. Scan parameters evolved over time across multiple centres. Automated quantification or artificial intelligence tools were not used and changes in smoking behaviour, comorbidities or treatments after baseline were not captured leaving scope for residual confounding. Death coding relied on established registries and clinical sources but may include misclassification of COPD or cardiovascular causes.

Implications for Screening Pathways

Within a lung cancer screening pathway, emphysema should not be viewed as incidental. In this cohort, baseline emphysema signalled sustained excess risks of death from all causes and particularly from COPD across a 25-year window. The absence of a consistent dose–response for cardiovascular mortality in competing-risk analyses points to complex interplay between shared risk factors and cause-specific trajectories in smokers and former smokers. Integration of visual emphysema scoring alongside nodule assessment and ordinal coronary calcium scoring may help identify individuals who warrant targeted respiratory management and vigilant cardiovascular prevention within comprehensive screening programmes.

A single standardised visual emphysema score at baseline low-dose CT in a large lung cancer screening cohort predicted long-term mortality with clear dose–response gradients for COPD deaths and consistent excess risk for all-cause deaths. Cardiovascular associations were present in conventional models but were not sustained once competing risks were considered. Incorporating emphysema assessment into screening workflows offers an accessible, reproducible means to refine risk stratification and support early preventive measures for major causes of death in current and former smokers.

Source: **Radiology**

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