PT2.17.03 : Association of accelerated biological ageing with early-onset lung cancer and its prognosis: insights from a multicenter case–control study and the UK Biobank

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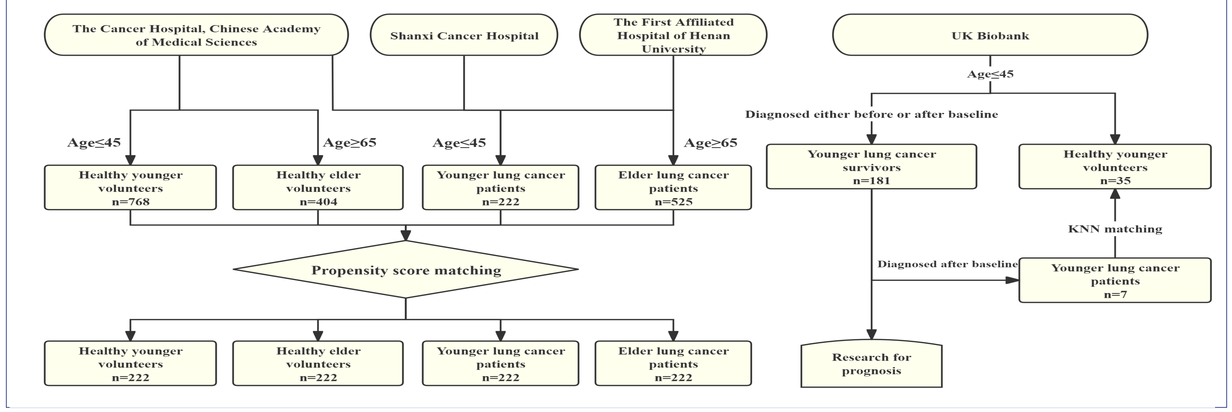
INTRODUCTION

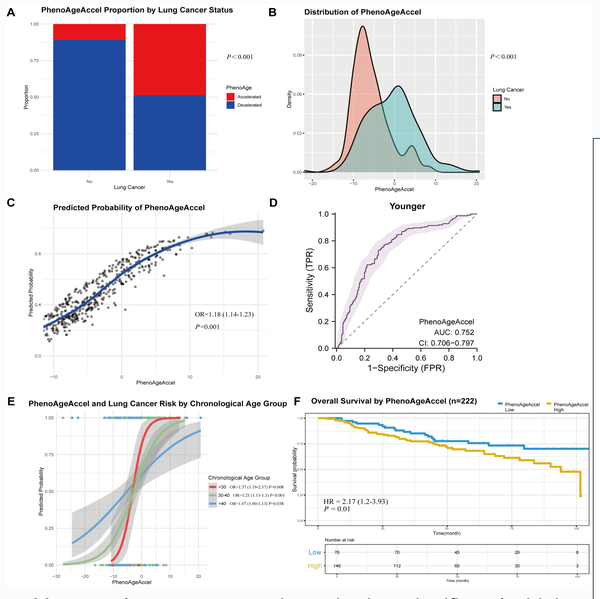
- Early-onset lung cancer (commonly defined as <40–50 years) is increasingly recognised and represents an important public-health concern.
- Earlier detection is crucial, yet widely accessible, cost-effective screening methods for younger populations are lacking.
- Studies investigating accelerated biological ageing (PhenoAgeAccel for representation) and cancer risk have produced heterogeneous findings. Several reports describe clear links between accelerated PhenoAge and cancer susceptibility, including lung cancer, whereas others do not find a significant association.
- Evidence on whether accelerated biological ageing influences cancer prognosis is sparse.

STUDY DESIGN



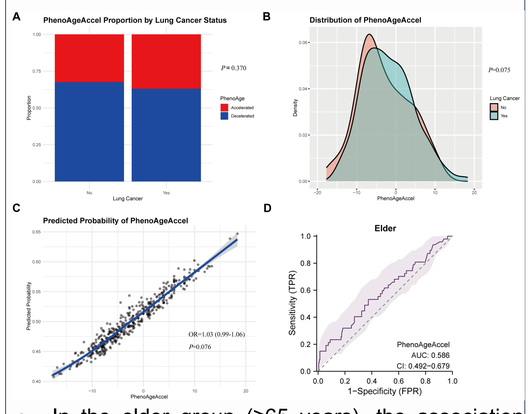
RESULTS

Figure 1 Association between accelerated biological ageing and early-onset lung cancer in the case-control study



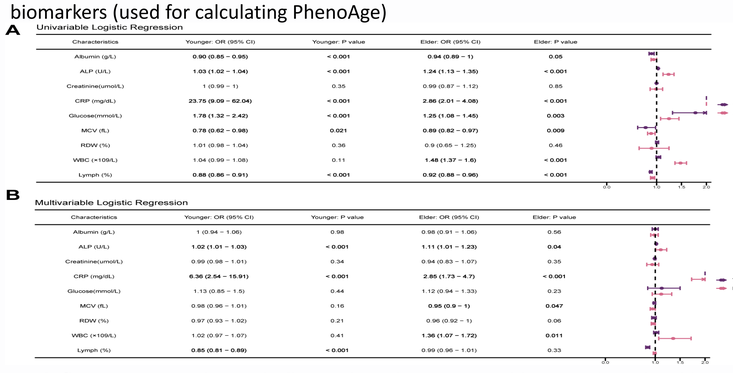
- Younger lung cancer patients had a significantly higher proportion of accelerated biological ageing (PhenoAgeAccel) than healthy volunteers (Figure 1A). The distribution of PhenoAgeAccel was shifted towards higher values in younger patients (Figure 1B).
- PhenoAgeAccel was positively associated with lung cancer risk in younger adults (per SD increase: 18% higher risk; Figure 1C).
- The ROC analysis of PhenoAgeAccel yielded an AUC of 0.752, indicating good discriminatory capacity (Figure 1D).
- Regression slopes were steeper in younger adults, indicating a stronger impact of PhenoAgeAccel on lung cancer risk earlier in adulthood (Figure 1E).
- Patients in the low-PhenoAgeAccel subgroup had significantly better OS than those in the high-PhenoAgeAccel subgroup (HR = 2.17, Figure 1F).

Figure 2 Association of accelerated biological ageing with cancer risk in elderly lung cancer patients for contrast



- In the elder group (≥65 years), the association was weaker and non-significant (Figure 2C, OR = 1.03, P = 0.076).
- Elder lung cancer patients showed no significant differences in PhenoAgeAccel compared to age-matched controls (Figure 2A) and exhibited no significant distributional differences (Figure 2B).
- Predictive performance was poor in this group (AUC=0.586; Figure 2D).

Figure 3 Univariable and multivariable logistic regression analyses of nine PhenoAge biomarkers (used for calculating PhenoAge)



A Univariable Logistic Regression

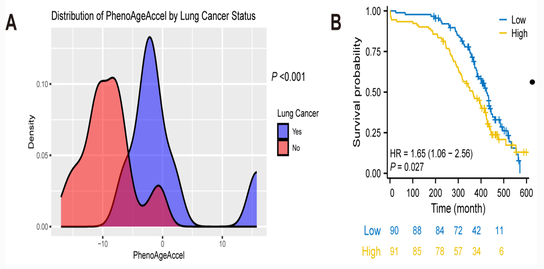
Characteristics	Younger: OR (95% CI)	Younger: P value	Elder: OR (95% CI)	Elder: P value
Albumin (g/L)	**0.90 (0.85 ~ 0.95)**	**< 0.001**	**0.94 (0.89 ~ 1)**	**0.05**
ALP (U/L)	**1.03 (1.02 ~ 1.04)**	**< 0.001**	**1.24 (1.13 ~ 1.36)**	**< 0.001**
Creatinine(umol/L)	1 (0.99 ~ 1)	0.35	0.99 (0.87 ~ 1.12)	0.85
CRP (mg/dL)	**23.75 (9.09 ~ 62.04)**	**< 0.001**	**2.86 (2.01 ~ 4.08)**	**< 0.001**
Glucose(mmol/L)	**1.78 (1.32 ~ 2.42)**	**< 0.001**	**1.25 (1.08 ~ 1.45)**	**0.003**
MCV (fL)	**0.78 (0.62 ~ 0.98)**	**0.021**	**0.89 (0.82 ~ 0.97)**	**0.009**
RDW (%)	1.01 (0.98 ~ 1.04)	0.36	0.9 (0.65 ~ 1.25)	0.46
WBC (×109/L)	1.04 (0.99 ~ 1.08)	0.11	**1.46 (1.37 ~ 1.6)**	**< 0.001**
Lymph (%)	**0.88 (0.86 ~ 0.91)**	**< 0.001**	**0.92 (0.88 ~ 0.96)**	**< 0.001**

B Multivariable Logistic Regression

Characteristics	Younger: OR (95% CI)	Younger: P value	Elder: OR (95% CI)	Elder: P value
Albumin (g/L)	1 (0.94 ~ 1.06)	0.98	0.98 (0.91 ~ 1.06)	0.56
ALP (U/L)	**1.02 (1.01 ~ 1.03)**	**< 0.001**	**1.11 (1.01 ~ 1.23)**	**0.04**
Creatinine(umol/L)	0.99 (0.98 ~ 1.01)	0.34	0.94 (0.83 ~ 1.07)	0.35
CRP (mg/dL)	**6.36 (2.54 ~ 15.91)**	**< 0.001**	**2.85 (1.73 ~ 4.7)**	**< 0.001**
Glucose(mmol/L)	1.13 (0.85 ~ 1.5)	0.44	1.12 (0.94 ~ 1.33)	0.23
MCV (fL)	0.98 (0.96 ~ 1.01)	0.16	**0.95 (0.9 ~ 1)**	**0.047**
RDW (%)	0.97 (0.93 ~ 1.02)	0.21	0.96 (0.92 ~ 1)	0.06
WBC (×109/L)	1.02 (0.97 ~ 1.07)	0.41	**1.36 (1.07 ~ 1.72)**	**0.011**
Lymph (%)	**0.85 (0.81 ~ 0.89)**	**< 0.001**	0.99 (0.96 ~ 1.01)	0.33

- Inflammatory and metabolic markers incorporated into ageing algorithms (e.g., CRP, albumin, glucose) contribute to lung cancer development.
- However, these biomarkers should not be interpreted as isolated predictors, but rather within the broader context of age-related physiological dysregulation, such as PhenoAgeAccel.

Figure 4 Association between accelerated biological ageing and early-onset lung cancer in the UK Biobank for validation



- A rightward shift in PhenoAgeAccel among patients relative to healthy individuals (Figure 4A).
- In a multivariable Cox analysis of long-term survivors, higher PhenoAgeAccel was associated with poorer OS (HR = 1.65, Figure 4B).

INTERPRETATION & RESOURCES

- PhenoAge acceleration (PhenoAgeAccel) was defined as the residual from a linear regression of PhenoAge on chronological age, reflecting whether an individual appears biologically elder (positive values) or younger (negative values) than their chronological age.
- PhenoAge was calculated according to previously described methods, with further details provided in the following QR code.
- The ePDF can also be acquired in the following QR code.

CONCLUSIONS

Accelerated biological ageing is a key factor in the risk and prognosis of early-onset lung cancer. Consistent findings across cohorts support PhenoAgeAccel as a promising biomarker for early detection, risk stratification, and potentially, therapeutic targeting. These results underscore its clinical relevance for guiding personalised screening and management strategies in younger patients with lung cancer.