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Background

- Systemic sclerosis (SSc) is a complex connective tissue disease often complicated by interstitial lung disease (ILD), which contributes significantly to morbidity and mortality. **Krebs von den Lungen-6 (KL-6) has been identified as a potential biomarker for ILD severity. Nailfold videocapillaroscopy (NVC) is a non-invasive tool to detect microvascular changes in SSc, but its role in predicting ILD progression and outcomes requires further investigation.** This study aimed to assess whether baseline NVC findings in SSc patients could **predict pulmonary function decline and changes in serum biomarkers, inflammatory markers, disease activity indices (EUSTAR 2017, SCTC-DI), and other clinical parameters over a two-year follow-up.**

Methods

- This prospective longitudinal study included SSc patients diagnosed according to the 2013 ACR/EULAR criteria, stratified by the presence of ILD. **Baseline assessments included NVC, chest high-resolution computed tomography (HRCT), pulmonary function tests (PFTs), and serum biomarker measurements (KL-6, IL-18, IL-18BP) using quantitative ELISA.** The annualized rate of change in forced vital capacity (FVC) was calculated as a surrogate for ILD progression. Associations between baseline NVC patterns and longitudinal changes in %DLCO, %FVC, biomarkers, inflammatory markers, and disease indices were analyzed using correlation and multivariate regression modeling.

Results

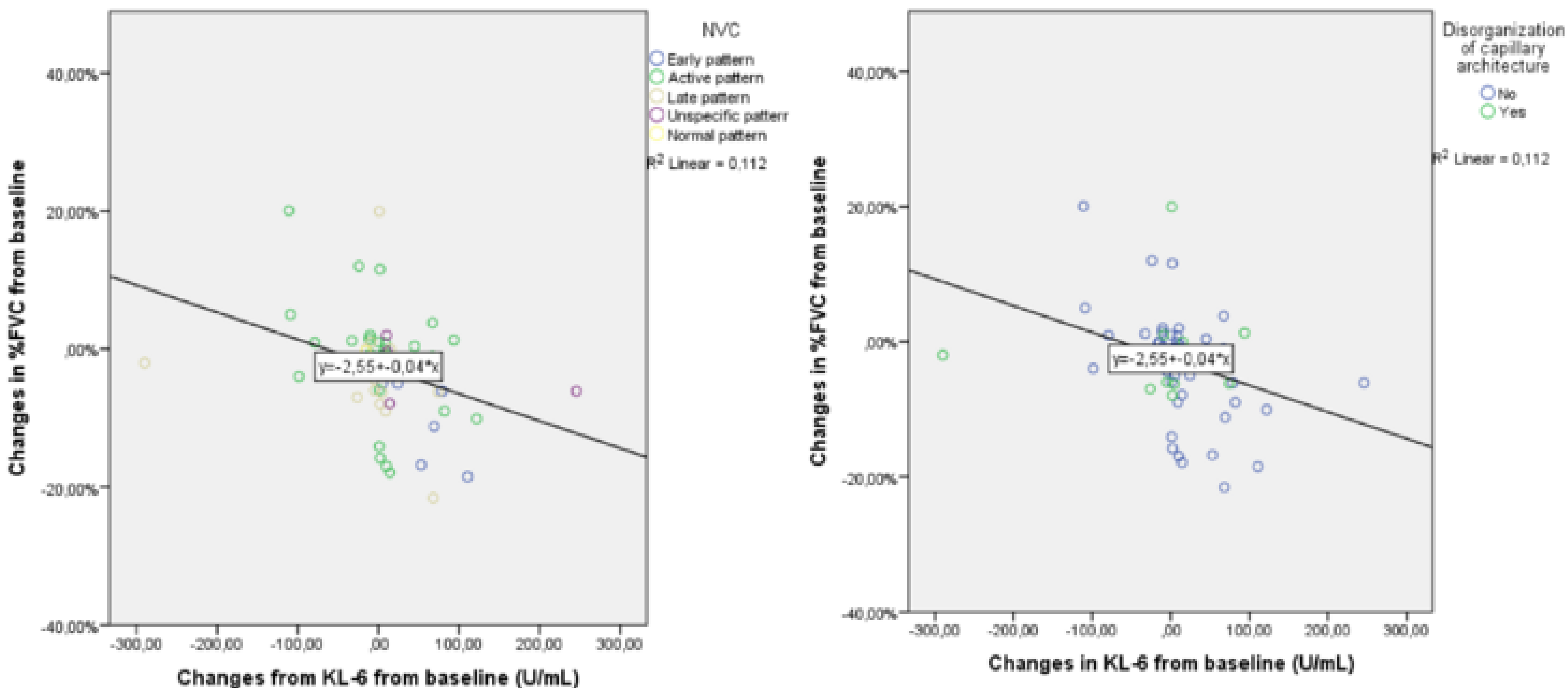
- 74 patients** (27% male, mean age 57.5 ± 15 years) were included, with a **mean disease duration of 7.67 ± 8 years.** At baseline, 38% had ILD, which increased to 51% after two years, while the proportion with $\geq 20\%$ lung involvement on HRCT rose from 32% to 43%.
- Disorganization of capillary architecture** at baseline predicted faster declines in %FVC ($\beta = -0.75$, $p = 0.03$) and %DLCO ($\beta = -0.24$, $p = 0.03$), as well as worsening modified Rodnan skin score (mRSS) ($\beta = 0.23$, $p = 0.03$) at two-year follow-up.
- A late NVC pattern** was associated with worsened mRSS ($\beta = 0.47$, $p = 0.004$), larger increases in KL-6 ($\beta = 0.18$, $p = 0.04$), and a more rapid decline in %DLCO ($\beta = -0.38$, $p = 0.04$). **A higher baseline SCTC-DI score** predicted progression of semiquantitative fibrosis on HRCT ($\beta = -0.32$, $p = 0.003$) and elevated CRP levels ($\beta = 0.38$, $p = 0.003$) at two years.

Conclusions

- Capillary disorganization and late NVC patterns at baseline** predict faster declines in pulmonary function, increased serum KL-6 levels, and worsening skin fibrosis over two years in SSc patients. Additionally, **higher baseline SCTC-DI scores** at baseline are associated with fibrosis progression on HRCT and elevated CRP levels.

| NVC scleroderma spectrum abnormalities, % | SSc-ILD (N=28) | SSc (N=46) | P value |
|-------------------------------------------|----------------|------------|---------|
| Early pattern | 1 (4%) | 8 (17%) | 0.11 |
| Active pattern | 11 (39%) | 24 (52%) | 0.28 |
| Late pattern | 15 (43%) | 10 (22%) | 0.006 |
| Loss of capillary density | 16 (57%) | 10 (22%) | 0.002 |
| Avascular areas | 11 (39%) | 11 (24%) | 0.16 |
| Enlarged and giant capillaries | 17 (61%) | 33 (72%) | 0.33 |
| Tortuous capillaries | 13 (46%) | 35 (76%) | 0.01 |
| Haemorrhages | 23 (82%) | 20 (44%) | 0.002 |
| Disorganization of capillary architecture | 7 (25%) | 11 (24%) | 0.02 |

Table 1: Nailfold Videocapillaroscopy Abnormalities in SSc Patients With and Without Interstitial Lung Disease



Graph 1: Relationship between changes in KL-6 Levels and %FVC decline across NVC patterns in SSc Patients.

Graph 2: Association Between Changes in KL-6 Levels and %FVC Decline in SSc Patients, Stratified by Capillary Disorganization.