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Spread through air spaces (STAS) and its molecular landscape predict relapse after curative resection of localised lung adenocarcinoma (LUAD)

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Background

STAS is an intrapulmonary pattern of dissemination in early-stage (LUAD), but its prognostic value and molecular correlates are seldom used in postoperative management.

Methods

We retrospectively reviewed resections with curative intent for LUAD at La Paz University Hospital (January 2015 – December 2024). STAS extent—defined as the greatest distance from the tumor edge to the outermost detached cell cluster—was dichotomised at 1.2 mm using bootstrap-corrected, maximally selected log-rank statistics. Molecular testing was performed using PCR, FISH, IHC or NGS (Oncomine Precision Assay) according to institutional protocols. Recurrence-free survival (RFS) was defined as the time from surgery to recurrence or death.

Results

307 patients were included. STAS was identified in 175 patients (57.0 %). Median follow-up was 41 months (95 % CI 33.8–47.7). Median RFS was not reached; 3-year RFS was 77.6 % (95 % CI 72.4–82.8). In multivariable analysis, the presence of STAS independently shortened RFS (adjusted HR (aHR) 2.29, 95 % CI 1.13–4.66[LG1]) after adjustment for other risk factors (Table). Extension beyond 1.2 mm further increased risk (aHR 2.48, 95 % CI 1.38–4.46[LG2]). Three- and five-year RFS rates were 70.5 % and 61.8 %, respectively, for STAS-positive tumors vs 86.1 % at both time points for STAS-negative tumors. STAS-positive tumors harboured fewer *MET* Exon 14 skipping alterations (OR 0.08, p = 0.004) and *EGFR* mutations (OR 0.52, p = 0.032), whereas *KRAS*, *ALK* and *ROS1* alterations were not associated.Table: 1798P

Variable	HR (95 % CI)	*p*	HR (95 % CI)	*p*
STAS (yes vs no)	2.29 (1.13 – 4.66)	0.022	—	—
STAS (> 1.2 mm vs ≤ 1.2 mm/none)	—	—	2.48 (1.38 – 4.46)	0.002
Clinical stage	1.78 (1.30 – 2.37)	<0.001	1.75 (1.28 – 2.39)	<0.001
Grade	1.81 (1.07 – 3.08)	0.028	1.85 (1.09 – 3.13)	0.022
Perineural invasion	1.61 (0.94 – 2.75)	0.083	1.88 (1.10 – 3.21)	0.020
Lymphovascular invasion	1.67 (0.92 – 3.02)	0.091	1.28 (0.85 – 1.94)	0.23

Conclusions

STAS, particularly when it extends more than 1.2 mm from the tumor edge, independently predicts relapse after resection of localized LUAD and, when combined with selected genomic and histopathologic variables, further refines postoperative risk stratification.

Legal entity responsible for the study

A. Rueda Lara.

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Disclosure

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