

RESULTS (CONTINUED)

Figure 2. AI-Based TIL Quantification & Agreement with Pathologist (A) Representative H&E images (left) and AI-processed outputs (right) for low TIL (upper) and high TIL (lower) cases. Tissue classification: carcinoma (purple), stroma (green); detected lymphocytes marked with red bounding boxes. TIL ratio = lymphocytes + monocytes + plasma cells / stromal area $\times 10^3$. (B) Scatter plot showing significant correlation between pathologist TIL score and AI TIL ratio (Spearman $\rho=0.662$, $p<0.001$, $R^2=0.553$). ICC analysis demonstrated good inter-method reliability (ICC=0.749, 95% CI: 0.541–0.864). Quadratic weighted $\kappa=0.724$ (substantial agreement).

Figure 1: Correlation analysis of TIL ratios and clinical variables.

A: Central TIL Ratio vs Stromal TIL Ratio Correlation. Scatter plot showing the relationship between Central TIL Ratio (X-axis) and Stromal TIL Ratio (Y-axis). The correlation coefficient is $\rho = 0.513$ and $p < 0.001$. The regression line is shown as a red dashed line. The formula for the correlation coefficient is $\rho = 1 - \frac{\sqrt{2d}}{\sqrt{d^2 + 1}}$.

B: Correlation Matrix with Significance. Heatmap showing the correlation matrix for Central TIL Ratio, Stromal TIL Ratio, age, pT category, and LVI. The color scale ranges from -0.2 (blue) to 1.0 (red). Significance levels are indicated by asterisks (*, **, ***).

	Central TIL Ratio	Stromal TIL Ratio	age	pT category	LVI
Central TIL Ratio	1.00 ***	0.51 ***	-0.05	-0.24	-0.11
Stromal TIL Ratio	0.51 ***	1.00 ***	-0.03	-0.21	-0.19
age	-0.05	-0.03	1.00 ***	-0.03	-0.25 *
pT category	-0.24 *	-0.21	-0.03	1.00 ***	0.08
LVI	-0.11	-0.19	-0.25 *	0.08	1.00 ***

C: Variance Inflation Factor (VIF) Analysis. Bar chart showing the VIF scores for each variable. The VIF scores are: age (19.04), Central TIL Ratio (4.56), Stromal TIL Ratio (4.60), pT category (16.83), and LVI (1.17). The red dashed line indicates the threshold for VIF = 5.

Figure 3. Correlation & Multicollinearity Analysis of Prognostic Variables (A) Moderate positive correlation between central and stromal TIL ratios ($p=0.513$, $p<0.001$). (B) Correlation matrix showing weak associations between TIL measurements and clinicopathologic variables ($|p|<0.3$ for all). (C) VIF analysis: severe multicollinearity identified for age (VIF=19.04) and pT category (VIF=16.83); central and stromal TIL ratios demonstrate acceptable collinearity (VIF=4.56 and 4.60). Dashed line = conventional VIF threshold of 5.

Figure 4 Kaplan-Meier Survival Analysis: Primary & Validation Cohorts. Kaplan-Meier curves stratified by AI-assessed central TIL ratio at median cutoff (12.5×10^{-3}). **(A)** Primary cohort RFS (n=75 with complete follow-up): significantly improved RFS in TIL-high group (log-rank $p=0.043$; 5-yr RFS: 62.4% vs. 36.8%). **(B)** Primary cohort OS: trend toward improved survival without significance ($p=0.159$). **(C)** Validation cohort RFS (n=44): confirmed protective effect of high central TIL ratio ($p=0.032$; 5-yr RFS: 72.4% vs. 53.8%). **(D)** Validation cohort OS: significantly improved OS in TIL-high group ($p=0.008$; 5-yr OS: 95.5% vs. 84.6%).

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- **AI-assessed Central TIL ratio is an independent predictor of RFS** (HR 0.964, 95% CI 0.931–0.998, $p=0.037$), significantly stratifies recurrence-free survival (log-rank $p=0.043$); 5-year RFS **62.4%** (TIL-high) vs. **36.8%** (TIL-low). **Confirmed in independent external validation cohort** ($p=0.032$; 5-yr RFS: 72.4% (TIL-high) vs. 53.8% (TIL-low)).
- **AI-assessed TIL ratio shows significant correlation with human pathologist TIL score.** (Spearman $\rho=0.662$, $p<0.001$, $R^2=0.553$).
- Ragged tissue edges and thermal artifacts inherent to TURB specimens may favor central TIL density as a more reliable prognostic indicator than invasive-front TIL.