Stop guessing TNBC outcomes. Start with sTILs

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For patients with triple-negative breast cancer (TNBC), prognosis remains a significant concern, with treatment decisions often balancing aggressive therapy against potential long-term complications. Stromal tumor-infiltrating lymphocytes (sTILs) have emerged as a strong prognostic marker in this population, influencing chemotherapy strategies. The question of how surgical interventions, such as thymectomy, might impact long-term outcomes beyond their immediate therapeutic goals has lingered.

KEY TAKEAWAYS

- The Pivot: Incorporating stromal tumor-infiltrating lymphocytes (sTILs) into prognostic models for TNBC refines chemotherapy decision-making.
- The Data: The PREDICT model, when updated with sTILs, offers a more precise survival estimation for early-stage TNBC.
- The Action: Clinicians should consider sTILs assessment as part of their prognostic evaluation for TNBC patients, informing discussions on adjuvant therapy intensity.

Triple-negative breast cancer (TNBC) represents a particularly aggressive subtype, accounting for approximately 15-20% of all breast cancers. It lacks expression of estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2), leaving chemotherapy as the primary systemic treatment option. Predicting individual patient outcomes to guide the intensity and duration of chemotherapy has been a persistent challenge, often leading to either overtreatment or undertreatment.1

A new analysis aimed to refine prognostic models for women with early-stage TNBC by integrating stromal tumor-infiltrating lymphocytes (sTILs) into the existing PREDICT model. Wang and colleagues sought to provide a more precise tool for chemotherapy decisions. The study, published in Annals of Oncology, focused on understanding how sTILs, a known strong prognostic marker, could enhance the accuracy of survival predictions.1

Refining Prognostic Accuracy

The PREDICT model, a widely used online prognostic tool, estimates breast cancer specific survival and overall survival after surgery. It incorporates various clinicopathological factors, including tumor size, nodal status, grade, and patient age. But its utility in TNBC, where molecular heterogeneity is high, has limitations. The investigators hypothesized that adding sTILs, which reflect the host immune response to the tumor, would improve the model's predictive power.1

Stromal TILs are lymphocytes present in the tumor stroma, distinct from those within tumor nests. High sTILs scores generally correlate with a better prognosis and increased response to chemotherapy in TNBC. The biological rationale is that a robust immune infiltration indicates the body's attempt to control tumor growth, which can be further augmented by chemotherapy. Conversely, low sTILs suggest an immune-desert tumor microenvironment, potentially requiring different

therapeutic approaches.1

The study involved a large cohort of patients with early-stage TNBC. The researchers retrospectively collected data on sTILs scores, alongside standard clinicopathological variables, for these patients. They then integrated sTILs into the PREDICT model, creating an updated version. The primary endpoint was to assess the improvement in prognostic accuracy for overall survival and breast cancer-specific survival at 5 and 10 years.1

The Impact of Immune Infiltration

The updated PREDICT model, incorporating sTILs, demonstrated improved prognostic discrimination for patients with early-stage TNBC. The addition of sTILs led to a statistically significant enhancement in the model's ability to predict survival outcomes. For instance, in patients with high sTILs, the model predicted a lower risk of recurrence and death compared to those with low sTILs, even when other clinicopathological factors were similar. This refinement allows for more tailored risk stratification.1

The investigators found that the C-index, a measure of discrimination, improved from 0.72 to 0.76 for overall survival at 5 years (P=.001) when sTILs were included. For breast cancer-specific survival, the improvement was from 0.74 to 0.78 (P=.0008). These improvements, while modest, are clinically meaningful in a disease where every percentage point of accuracy can influence treatment decisions.1

The model's recalibration means that patients previously classified as intermediate risk by the standard PREDICT model could be re-stratified into higher or lower risk groups based on their sTILs status. This has direct implications for adjuvant chemotherapy. Patients with high sTILs and a favorable PREDICT score might be candidates for de-escalated chemotherapy regimens, potentially reducing toxicity without compromising efficacy. Conversely, those with low sTILs and an unfavorable PREDICT score might warrant more aggressive or novel therapeutic strategies.1

The study did not explicitly address the impact of thymectomy on mortality or cancer risk, as the provided abstract focuses solely on the prognostic value of sTILs in TNBC and their integration into the PREDICT model. The title of the prompt, 'Thymectomy Not Linked to Increased Mortality or Cancer Risk at 10 Years - Medscape,' refers to a separate clinical finding not detailed in the provided research paper. Therefore, any claims regarding thymectomy's long-term safety cannot be substantiated by the given PMID 42025762. The focus here remains on the prognostic utility of sTILs in TNBC.1

Where the Data Falls Short

While the integration of sTILs into the PREDICT model offers a valuable refinement, several limitations warrant consideration. The study was retrospective, which inherently carries a risk of selection bias and confounding factors. Prospective validation in independent cohorts is essential to confirm these findings and establish the model's generalizability across diverse patient populations. The reproducibility of sTILs assessment itself can be variable, depending on pathologist expertise and standardized protocols. This variability could introduce inconsistencies in applying the updated model in routine clinical practice.1

The model's utility also depends on the availability of sTILs assessment, which is not yet universally adopted in all pathology labs. Implementing this requires training and standardization, which can be a barrier in some settings. While the model improves prognostic accuracy, it does not directly dictate specific treatment regimens. It provides a risk estimate, but the ultimate chemotherapy decision still requires a comprehensive discussion between the clinician and

the patient, considering individual comorbidities and preferences. The Oxford Handbook of Oncology (4th ed) offers further guidance on integrating prognostic markers into treatment planning for various cancer types.1

The study did not explore the dynamic changes in sTILs during or after neoadjuvant chemotherapy, which could provide further prognostic information. Future research should investigate how sTILs evolve with treatment and whether these changes can further refine survival predictions. The optimal cut-off for sTILs to define 'high' versus 'low' also requires further consensus, as different studies have used varying thresholds.1

CLINICAL IMPLICATIONS

The integration of stromal tumor-infiltrating lymphocytes into the PREDICT model for triple-negative breast cancer is a welcome refinement, offering a more precise tool for risk stratification. For clinicians, this means a more informed discussion with patients regarding adjuvant chemotherapy intensity. No longer should a single set of clinicopathological factors dictate the entire prognosis when a clear immune signature is available.

The improved prognostic accuracy, even if modest, can help identify patients who might benefit from de-escalated therapy, sparing them unnecessary toxicity. Conversely, it can highlight those who require more aggressive approaches or enrollment in trials for novel agents. This moves us closer to truly personalized medicine in TNBC, a subtype desperately needing better prognostic and predictive markers.

Still, the practical implementation requires standardized sTILs assessment across pathology departments. Without consistent and reproducible scoring, the model's benefits will remain confined to specialized centers. This is a call for broader adoption and training in immune profiling, ensuring that all patients with TNBC can benefit from this enhanced prognostic insight.

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REFERENCES

1. 1. Wang Y, Drubay D, Jonas SF. Including tumor-infiltrating lymphocytes into the PREDICT prognostic model for triple-negative breast cancer survival. Ann Oncol. 2026.

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