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Medical Center

The prognostic value of the tumor-stroma ratio validates in subgroups of breast cancer, especially in grade III tumours

TSR in breast cancer

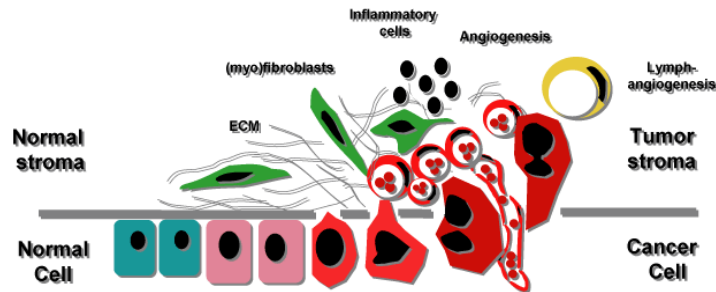
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AUTHORS DECLARE NO CONFLICT OF INTEREST

Tumor-stroma interaction

- The stroma surrounding cancer cells plays an important role in the development and **behavior of the tumor**.
- Studies including cell isolation, gene expression and cultures demonstrated that stroma can promote cancer and **influences outcome**.



Tumor-stroma ratio (TSR)

- The TSR is based on the amount of stroma within the primary tumor
stroma-high = worse patient outcome.
- Scoring of TSR is performed at **routine pathology** analysis in short time (<2 min), without additional costs and is highly reproducible ($K > 0.80$).

Review literature

Breast Cancer Research and Treatment (2019) 173:55–64
<https://doi.org/10.1007/s10549-018-4987-4>

REVIEW



The prognostic value of tumour–stroma ratio in primary breast cancer with special attention to triple-negative tumours: a review

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Abstract

Purpose There is a strong need to improve the prognostication of breast cancer patients in order to prevent over- and undertreatment, especially when considering adjuvant chemotherapy. Tumour stroma characteristics might be valuable in predicting disease progression.

Methods Studies regarding the prognostic value of tumour–stroma ratio (TSR) in breast cancer are evaluated.

Results A high stromal content is related to a relatively poor prognosis. The most pronounced prognostic effect of this parameter seems to be observed in the triple-negative breast cancer (TNBC) subtype.

Conclusions TSR assessment might represent a simple, fast and reproducible prognostic factor at no extra costs, and could possibly be incorporated into routine pathological diagnostics. Despite these advantages, a robust clinical validation of this parameter has yet to be established in prospective studies.

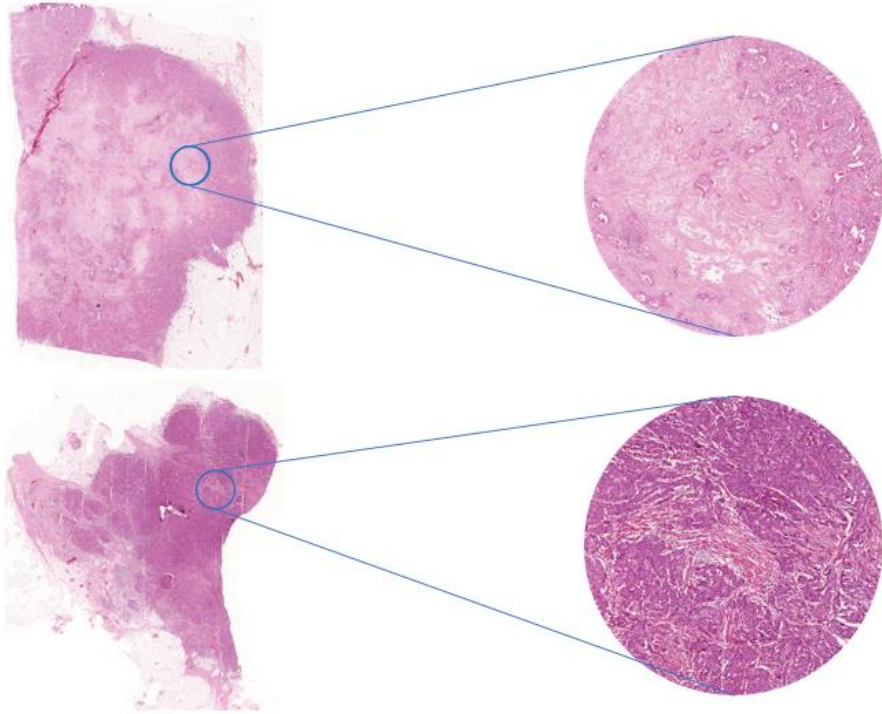
Keywords Breast cancer · Triple-negative breast cancer · Tumour–stroma ratio · Prognosis · Review

Good prognostic parameter for BC overall and TNBC, but applicability in other subgroups may differ.

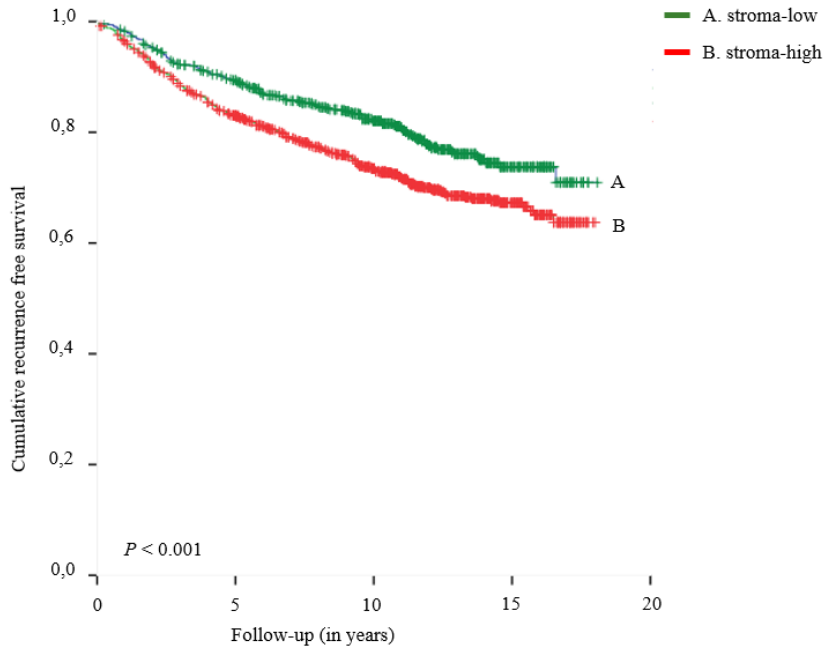
Validation in large study with clinical subgroups

- The prognostic value of TSR in clinically relevant subgroups is evaluated.
Age, grade, size, histological type, PR status, ER status, HER2 status, TN status, lymph node status.
- Whole tissue slides of 1809 primary BC patients from the Nottingham Breast Cancer Series (patients <70 years, M0).
- Validation in cohort of 737 Dutch patients from the Antoni van Leeuwenhoek.
- TSR was visually assessed on digital H&E stained slides.

Tumor-stroma ratio (TSR)



Nottingham Breast Cancer series: TSR



Univariate

RFS: HR 1.19, 95% CI 1.19-1.78, $P < 0.001$

BCSS: HR 1.60, 95% CI 1.25-2.04, $P < 0.001$

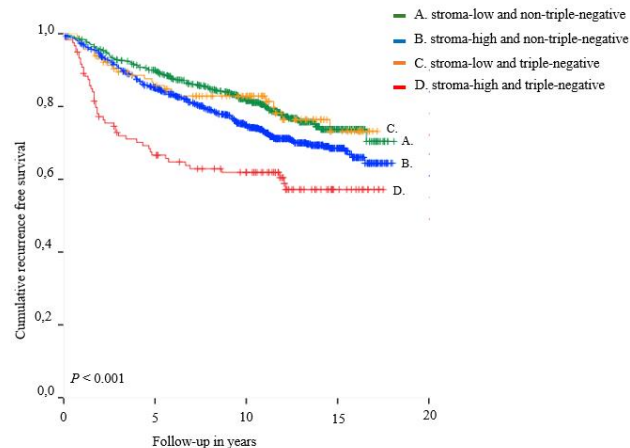
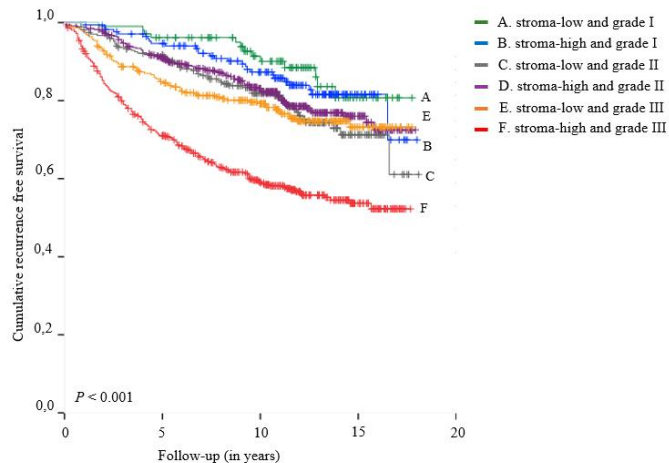
Multivariate

RFS: HR 1.35, 95% CI 1.10-1.66, $P = 0.004$

BCSS: HR 1.51, 95% CI 1.18-1.95, $P = 0.001$

Observer variation TSR scoring: $K > 0.87$

Nottingham Breast Cancer series: TSR combined with grade and triple negative status



Multivariate Cox regression analyses showed the highest effect of the TSR for RFS in:

Grade III: HR 1.89, 95% CI 1.43-2.51, $P < 0.001$

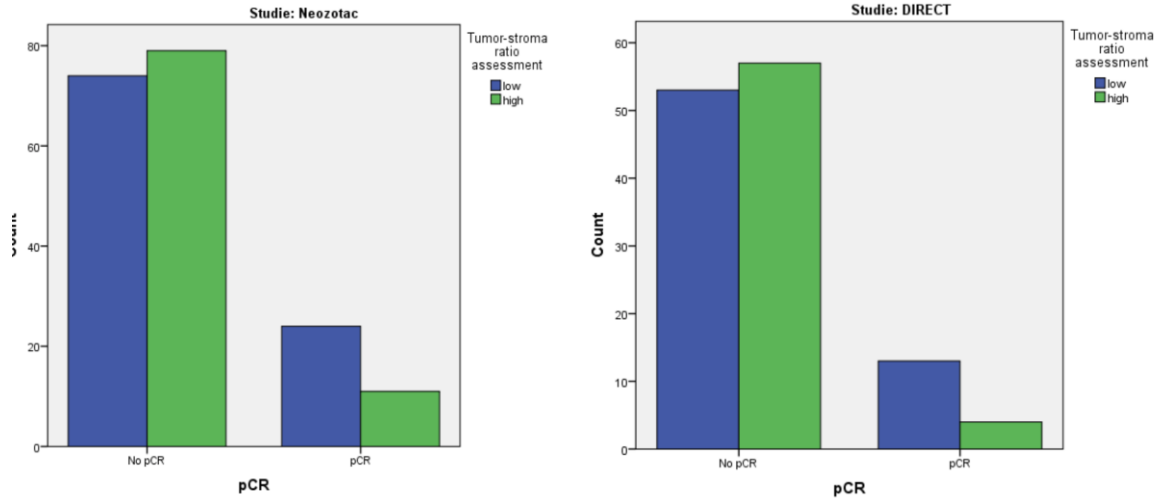
Triple negative: HR 1.86, 95% CI 1.10-3.14, $P = 0.020$

Data are confirmed in the AvL series

Conclusions

- TSR can be scored on routine H&E sections **and** on digital images.
- Strong survival difference for stroma-low and stroma-high patients.
- **The prognostic value of the TSR is most pronounced in grade III tumors and triple negative tumors.**
- The prognostic value of the TSR is not influenced by age, tumor size, histology, ER status, PR status, HER2 status and lymph node status.

Response to therapy



In the prospective DIRECT and NEOZOTAC trials the association between TSR before treatment and efficacy of neoadjuvant chemotherapy in HER2 negative breast cancer patients was evaluated.

Stroma-low was associated with a better pathological complete response (pCR Miller and Payne) (OR 2.570, 95%CI 1.343-4.919, P=0.004).

Benefit for the patient

- Validation of the TSR in a prospective study
- Further improve clinical decision making for chemotherapy
- Implementation in the PREDICT tool



Know more?

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