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Abstract #MP55-11

Modified Immunoscore improves prediction of survival outcomes in patients undergoing radical cystectomy for bladder cancer

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Objectives

- Tumor-Infiltrating Lymphocytes (TIL) has been shown to predict disease outcome in several types of cancers.
- Immunoscore (IS), known as a prognostic factor in colon and lung cancer, offers a method to quantify TIL. Immune activation is involved in genomic subtypes of BC however, data on IS in BC is scarce.
- The aim of this study was to evaluate the prognostic value of a modified IS in a cohort of bladder cancer (BC) patients undergoing radical cystectomy (RC).

Methods

- Two tissue microarrays (TMAs) containing 159 BC patients (Two tissue cores/patient) who all underwent radical cystectomy were immunohistochemically stained for CD4/CD8/FoxP3 and CD45RO.
- Automated analysis was performed by digital pathology to detect stained TIL. Output was cumulated, averaged and reported as density (positive count per mm2). The four candidate predictors were explored for normality, extreme values and multicollinearity.

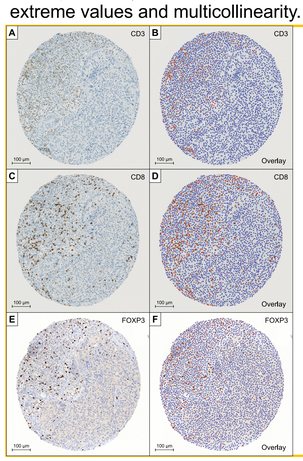


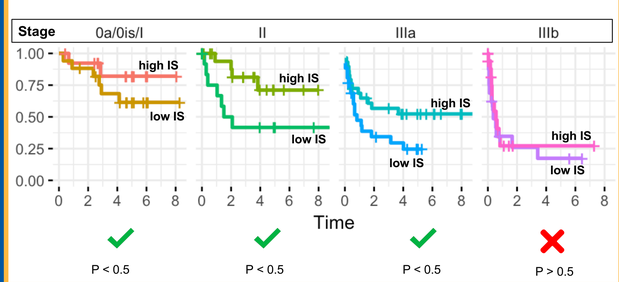
Figure 1: Trouble-free evaluation

Representative samples of the scanned TMA-sections stained with antibodies for CD3 (A), CD8 (C), and FOXP3 (E) and the corresponding overlays generated by QuPath (B, D, and F). Red dots highlight the lymphocytes that where rated positive, while the blue dots are showing the remaining detected cells that where counted as negative.

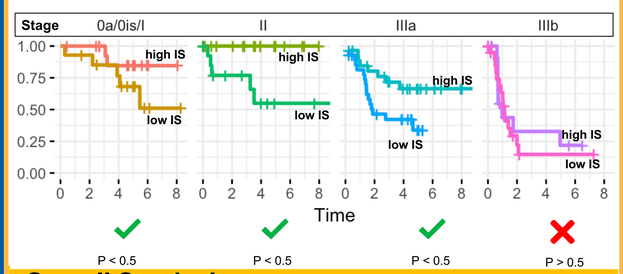
- Cox proportional hazards regression was used to predict progression free survival (PFS), cancer specific survival (CSS) and overall survival (OS).
- Patients were stratified as “high IS / favorable risk” and “low IS / unfavorable risk” (cut-off: median of linear predictor). Kaplan-Meier analysis were used to test IS within each American Joint Committee on Cancer (AJCC) stage group for BC.

Patient characteristics	N / (% or Range)
Number of patients (n)	159
- Male	122 (77)
- Female	37 (23)
Age (y, range)	68 (44-87)
AJCC Stage (n)	
- 0a/0is/I	31 (19.6)
- II	34 (21.5)
- IIIa	57 (36.1)
- IIIb	36 (22.8)
Median Follow-up (m)	35.8

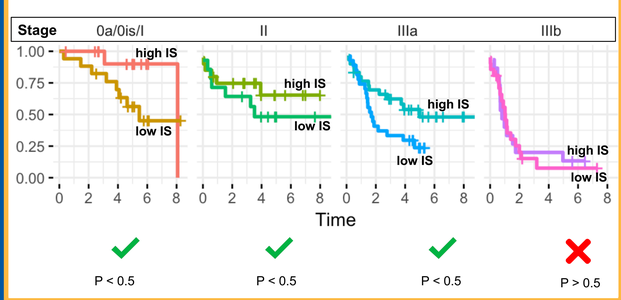
Progression Free Survival



Cancer Specific Survival



Overall Survival



Results

- The median age in our cohort was 68 years (range: 44-87) and 77% patients were male.
- AJCC stage distribution was 31 (19.6%) for 0a/0is/I, 34 (21.5%) for II, 57 (36,1%) for IIIa and 36 (22.8%) for IIIb.
- Median follow-up time after surgery was 35.8 months.
- The four candidate predictors were log-transformed and reduced to three (CD8/FoxP3 and CD45RO) due to very strong correlation between CD4 and CD8.
- By using the modified IS we were able to sub-stratify patients within AJCC stages 0is/0a/I, II and IIIa.
- PFS, CSS and OS were significantly longer for patients with high IS as compared to low IS ($p < 0.05$).
- IS was not prognostic for stage IIIb patients ($p > 0.05$).

Conclusions

- Our study provides evidence that IS is of prognostic value in BC patients undergoing RC.
- The modified IS was able to stratify patients within AJCC stages. IS might serve as a prognostic marker to guide treatment or follow-up strategies post RC if confirmed in further studies.
- Since this study was performed on TMAs, the determination of IS on selected areas of whole tumor slides might even reveal more precise and reproducible results

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