Digital Pathology-Based Assessment of the CD4/CD8 Ratio for Differentiating Early Mycosis Fungoides from Benign Inflammatory Dermatoses

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Introduction

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. Early diagnosis is clinically significant, as it influences prognosis and overall survival. However, it remains challenging due to the histological overlap between early MF and benign inflammatory dermatoses. One proposed criterion to distinguish between early MF and BIDs is the CD4:CD8 ratio on tissue immunohistochemistry, but it is subject to interobserver variability . In this study, we used a digital pathology workflow to quantify the CD4:CD8 ratio in early MF versus BID and to assess its diagnostic performance

Methods

We analyzed 51 paired whole-slide images stained for CD4 and CD8 from early MF (n=39) and benign inflammatory lesions (n=12). A semi-automated workflow was implemented in QuPath, consisting of manual annotation of regions of interest followed by automated cell segmentation with the Cellpose-SAM segmentation model. The CD4:CD8 ratio was computed per case from the resulting positivity rates.

Results

The MF cases showed a significantly elevated CD4:CD8 ratio compared with benign inflammatory dermatoses (mean 5.59 ± 4.27 vs. 3.08 ± 1.72; median 4.31 vs. 2.78; **p = 0.023**). ROC analysis showed fair discriminative performance, with an AUC of 0.72. The Youden-optimal cutoff was **CD4:CD8 ≥ 3.82**, yielding **64% sensitivity** and **75% specificity**. At this cutoff, **PPV** was **89%**, whereas NPV was **39%**.

Performance traded off predictably along the threshold range: a more permissive cutoff (≥ 2.5) reached 79 % sensitivity but only 50 % specificity, whereas a more stringent cutoff (≥ 5) achieved 92 % specificity at the cost of 46 % sensitivity.

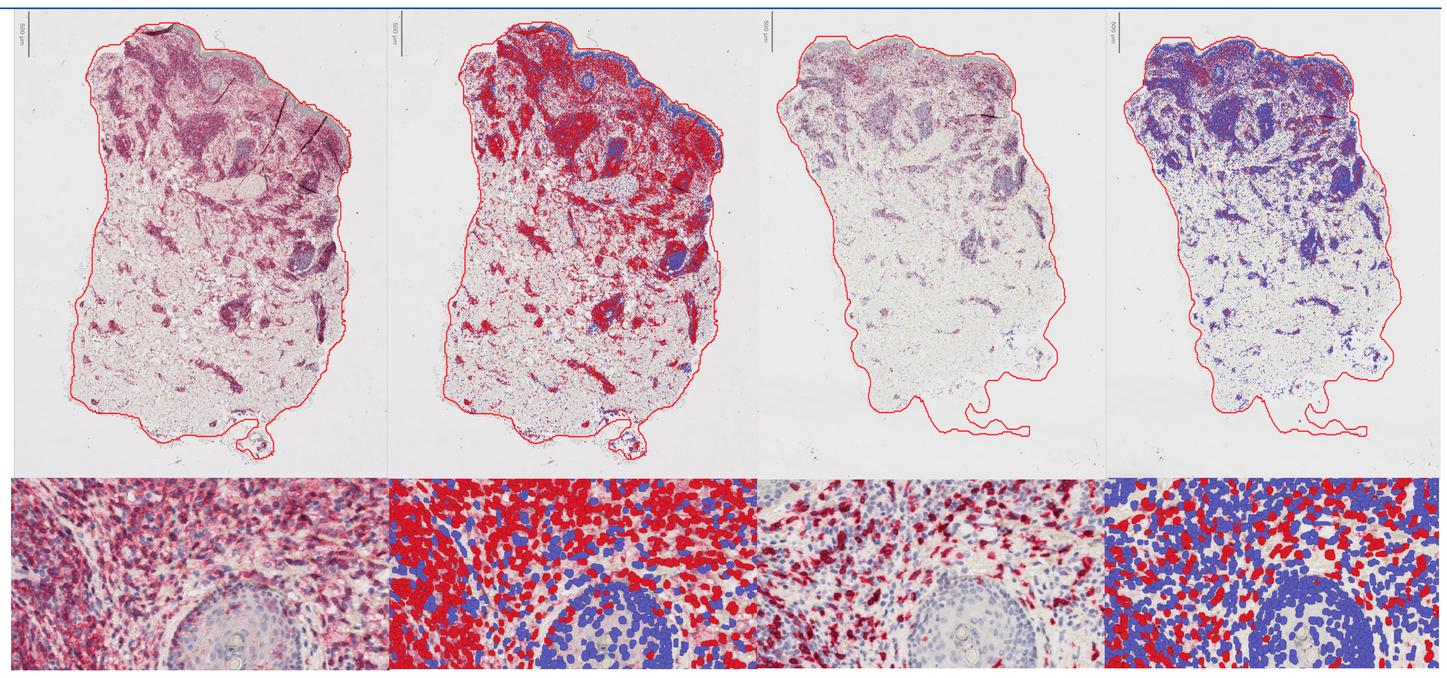

Figure 1. Paired CD4 (columns 1–2) and CD8 (columns 3–4) IHC stains of the same lesion. **Top:** whole-section overview with the manually annotated region of interest outlined in red. **Bottom:** corresponding exemplary high-magnification detail. For each marker, the original IHC (columns 1, 3) is shown alongside the cell-classifier output (columns 2, 4; red = positive, blue = negative), from which the CD4/CD8 ratio within the ROI was computed.

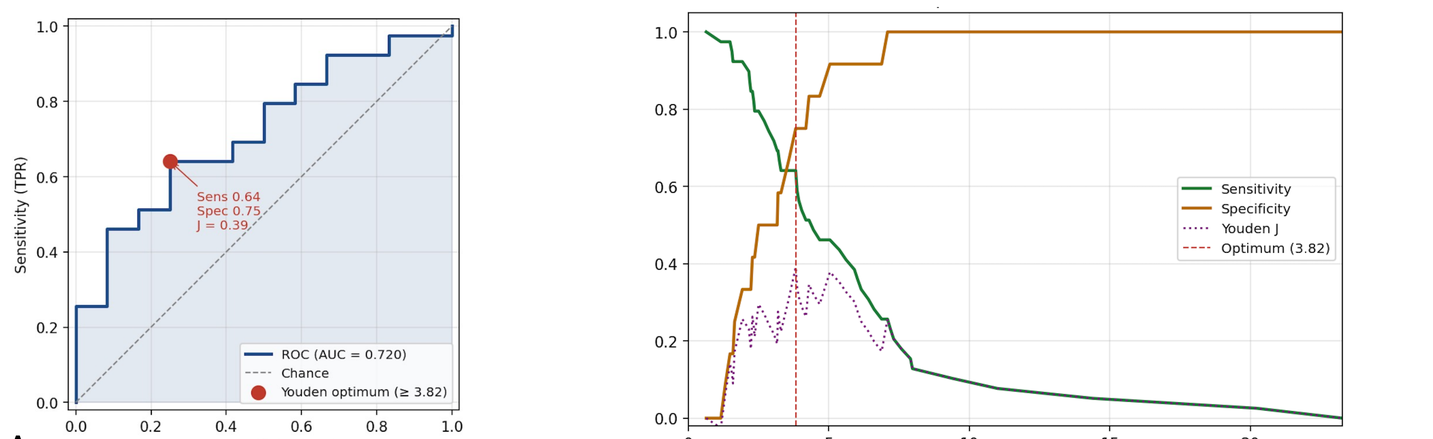

Figure 2. Diagnostic performance of the CD4:CD8 ratio (A) Receiver operating characteristic (ROC) curve. TRP = True Positive Rate. FPR = False Positive Rate. (B) Sensitivity, specificity and Youden's J across CD4:CD8 ratio cutoffs

Discussion & Conclusion

These findings suggest that a reliably calculated CD4:CD8 ratio using a digital workflow can contribute to the diagnostic workup of suspected MF, addressing the interobserver variability of manual scoring. The limitations of this study include the single-center design and the imbalanced cohort (39 MF vs 12 BID). Analysis of a larger cohort would allow derivation of more robust threshold values and a more precise assessment of diagnostic performance. Extending the workflow to additional immunophenotypic markers, such as the CD3:CD8 ratio, may further enhance diagnostic accuracy.

References

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