Semiquantitative Evaluation Of TILs In Breast Cancer Shows Differences Among Histotypes And Tumor Grade

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Background & objectives

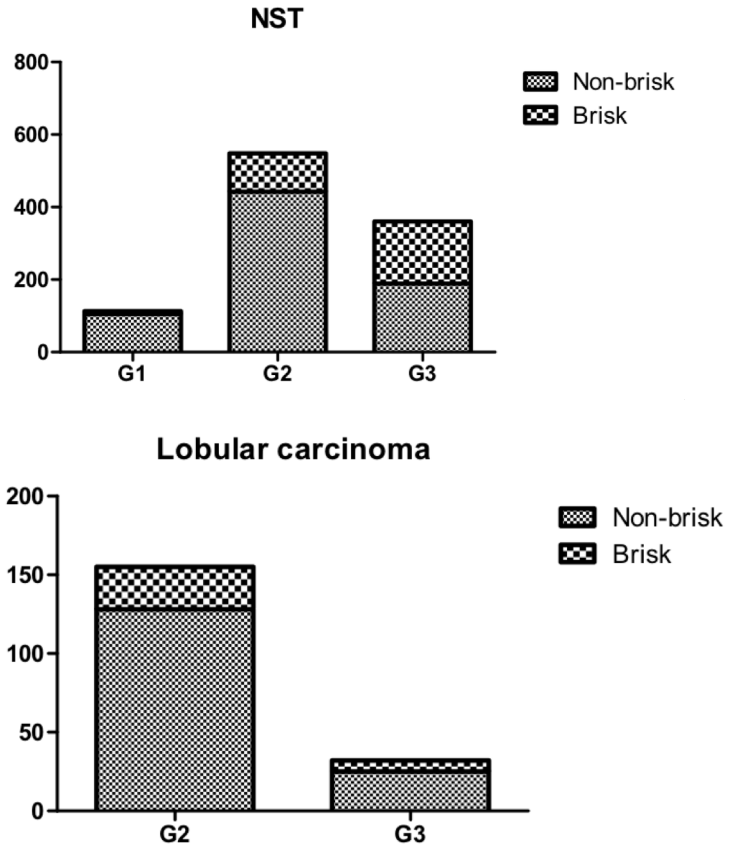
Current research in tumor microenvironment (TME) of breast cancer focuses mainly on molecular subtype and receptor status. In this work, we compare TME characteristics between no special type and lobular breast cancer to ascertain if a correlation with histotype exists.

Methods

At our Institution, 1724 patients underwent surgery for breast cancer (January 2012-December 2018). Patients who received neoadjuvant therapy were excluded. A final cohort of 1395 invasive breast cancer was considered; 1047 were diagnosed as no special type, 190 as lobular, and 158 as other histotypes. Stromal tumor-infiltrating lymphocytes (TILs) were assessed according to the recommendations by Salgado et al (1) and semi-quantitatively grouped into a "brisk" (≥5% of immune cells in stromal tissue within the invading border of the tumor) and "non-brisk" category, similar to previously published works (2-4). Contingency analysis was performed on GraphPad Prism with the Pearson Chi-Squared test.

Results

Among the 1021 no-special type cases in which TILs were assessed, "brisk" TILs were found to be significantly associated with histologic grade of the tumor **(P<0.0001)**: 7% in the G1 group (8/113), 19% of the G2 group (106/548), and 48% of the G3 group (171/360). In contrast, grade did not seem to impact the adaptive immune response in lobular carcinoma **(P = 0.5519)**, and "brisk" infiltrate showed an analogous distribution: 17% in the G2 group (27/155) and 22% in the G3 group (7/32). This is not unexpected, as the no-special type histotype includes most of the triple-negative and HER2-enriched invasive breast cancer, which are found to be associated with increased TILs.



Conclusion

Our data suggest that in no-special type breast cancer TILs appear to parallel histologic grade and could reflect the increased genomic instability of high-grade cancers. In contrast, lobular carcinoma may represent a subtype of breast cancer in which adaptive immune response is underregulated, possibly underlying a low genomic instability and consequent low burden of neoantigens. As more therapies emerge for which TILs could represent a predictive factor, a more comprehensive understanding of its significance in breast cancer is needed.

References

(1) Salgado R et al. The evaluation of tumor-infiltrating lymphocytes (TILs) in breast cancer: recommendations by an International TILs Working Group 2014. *Ann Oncol*. 2015
(2) Loi S et al. Tumor infiltrating lymphocytes are prognostic in triple negative breast cancer and predictive for trastuzumab benefit in early breast cancer: results from the FinHER trial. *Ann Oncol.* 2014
(3) Salgado R et al. Tumor-Infiltrating Lymphocytes and Associations With Pathological Complete Response and Event-Free Survival in HER2-Positive Early-Stage Breast Cancer Treated With Lapatinib and Trastuzumab: A Secondary Analysis of the NeoALTTO Trial. *JAMA Oncol.* 2015
(4) Denkert C et al. Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: a pooled analysis of 3771 patients treated with neoadjuvant therapy. *Lancet Oncol*. 2018