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A MACHINE LEARNING APPROACH TO PATIENT BENEFIT BY ANALYZING IMMUNE-RELATED PROGNOSTIC MARKERS IN COLON CANCER PATIENTS RANDOMIZED TO SURGERY OR SURGERY AND ADJUVANT CHEMOTHERAPY, IN SEARCH OF PREDICTIVE SIGNATURES.

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Background: The immune contexture of malignant colon tumors has been shown to correlate with patient outcomes(1). Important markers that help characterize this immune environment include HLA genotype, MHC class I and HLA-G expression, CD8+ lymphocyte infiltration, and the microsatellite instability (MSI) status of the tumor (2, 3). Predictive algorithms are increasingly being employed in cancer treatment to manage the complexity of novel prognostic and predictive markers (4-6).

Aim: This study aimed to utilize a machine learning approach to analyze clinical trial data of colon cancer patients who were randomized to either surgery alone or surgery followed by adjuvant chemotherapy. By incorporating clinical variables, immunological biomarkers like Her3-expression, and MSI status, we sought to identify risk factors for treatment failure and to distinguish sub-cohorts of patients who could significantly benefit from adjuvant chemotherapy.

Materials and Methods: Clinical data, including age, gender, tumor stage, and location, along with FFPE samples of primary tumors, were collected from 520 colon cancer patients who were followed for overall survival over 120 months. Immunological biomarkers such as HLA-A*02 genotype, MHC class I, and HLA-G expression, as well as CD8+ lymphocyte infiltration, were assessed using immunohistochemistry. Her3 expression and MSI status were also evaluated through immunohistochemical analysis.

Results: Using clinical categorical variables (7), we developed a risk-based algorithm called CLICAL©, which organized the clinical variables into predictive signatures. Validation of these signatures was performed using a machine learning algorithm (SRF-CLICAL©), resulting in the identification of distinct patient groups with significant variations in their response to adjuvant chemotherapy (Figure 1).

Conclusion: This machine learning-based approach demonstrated the ability to generate predictive signatures with a 95% confidence level, providing a valuable tool for clinical decision-making. By accurately identifying patient subgroups who are likely to benefit from adjuvant therapy, this method could enhance personalized treatment strategies in colon cancer.

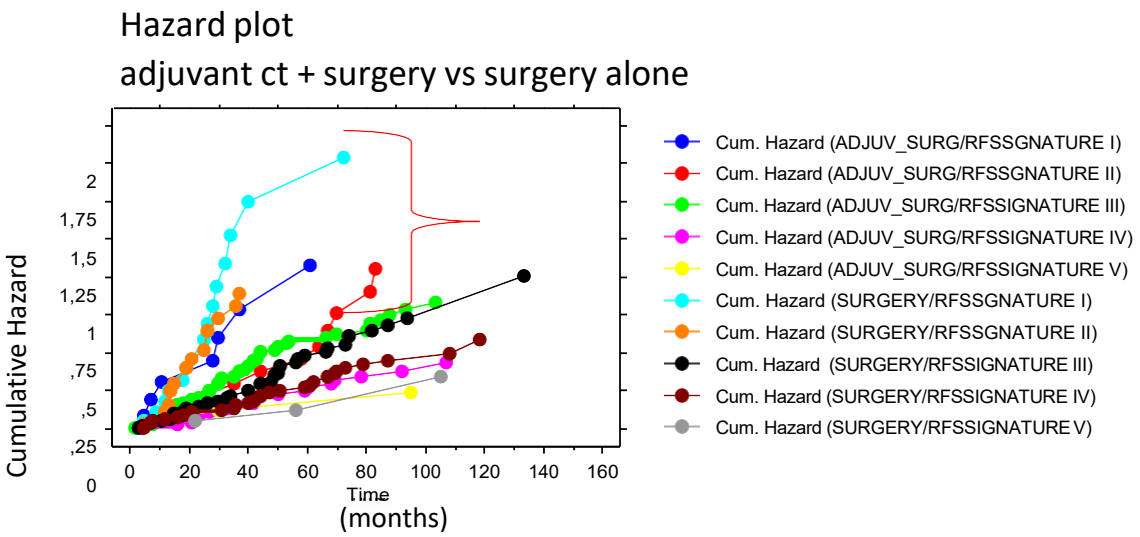

Figure 1. Cumulative hazard plot of the risk of death over time for colorectal cancer patients receiving surgery and adjuvant chemotherapy or surgery alone. Signatures of risk groups suggested by SRF-CLICAL©. Red curly bracket indicates for signatures with least benefit of treatment choice.

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