Influence of Different Age Cutoff Points on the Prediction of Prognosis of Cancer Patients Receiving ICIs and Potential Mechanistic Exploration

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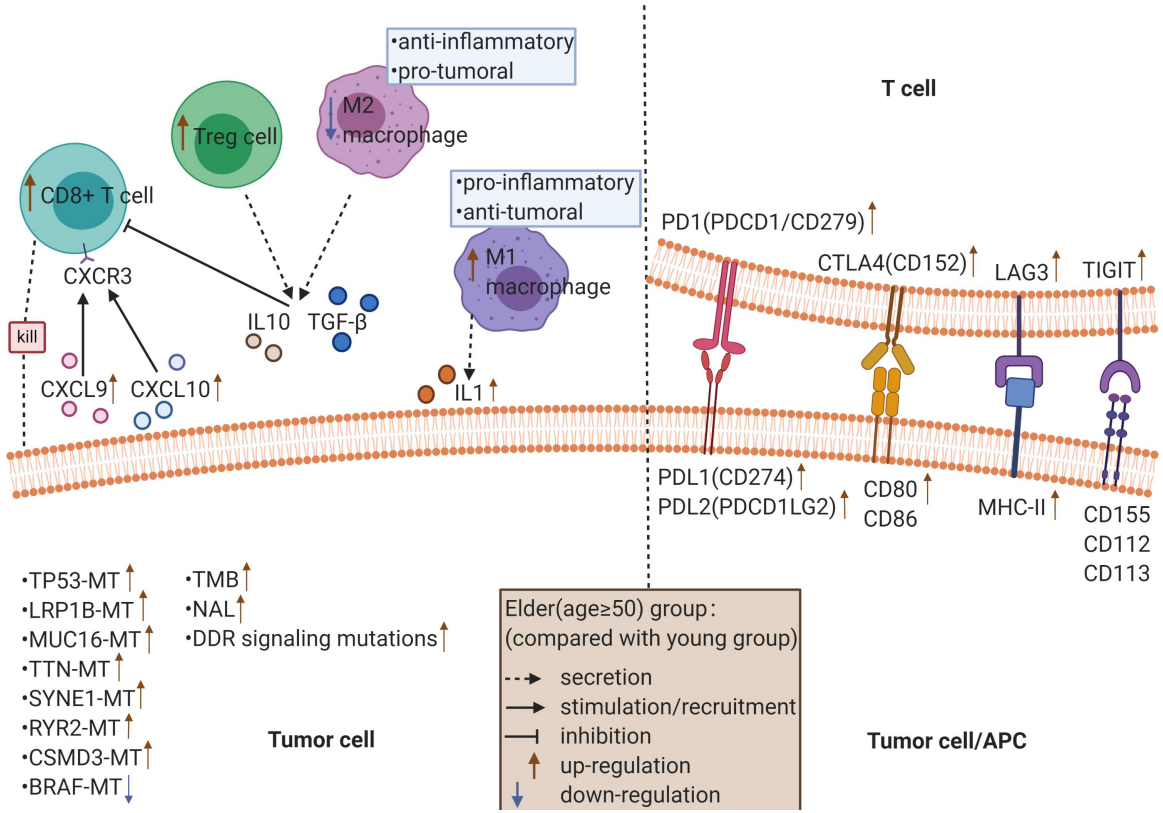

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Backgroud: Age is a potential predictive marker for the prognosis of cancer patients treated with immune checkpoint inhibitors (ICIs), but the appropriate age cutoff point is still controversial.

Methods: We applied cutoff points of 50, 55, 60, 65, 70, and 75 years old to divide 1660 patients from the Memorial Sloan-Kettering Cancer Center(MSKCC) immunotherapy cohort into older and younger groups and performed survival analysis of the six subgroups. And we explore the mechanism underlying the appropriate age cutoff point from the aspects of gene mutation and expression, immune cell infiltration and so on.

Results: The results showed that older patients had better survival than younger patients in accordance with the cutoff point of 50 years old [median overall survival (OS) (95% CI): 13.0 (10.5-15.5) months vs. 20.0 (16.7-23.3) months; p=0.002; unadjusted hazard ratio (HR) (95% CI): 0.77 (0.65-0.91)], whereas no significant difference was observed with other cutoff points. Further analysis of The Cancer Genome Atlas (TCGA) database and the MSKCC immunotherapy cohort data showed that the tumor mutation burden (TMB), neoantigen load (NAL), DNA damage response and repair (DDR) pathway mutation status, mutation frequencies of most genes (except IDH1, BRAF and ATRX), the expression of most immune-related genes and the degree of infiltration of most immune cells (such as CD8+ T cells and M1 macrophages) were higher in the elderly group (aged ≥50 years).

Conclusion: Cancer patients aged ≥50 years can benefit more from ICIs than younger patients. This may be related to specific gene mutations, gene expression levels and the degree of immune cell infiltration related to age. In the future, prognostic data are still needed to directly verify the underlying mechanisms behind the age cutoff point of 50 years.