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P01.08 SARCOPENIA AS BIOMARKER FOR IMMUNOTHERAPY OUTCOMES AND IMMUNE-RELATED ADVERSE EVENTS – A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background Sarcopenia is an established risk factor for oncologic treatments like surgical interventions and conventional chemotherapy. However, the impact of sarcopenia on treatment and immune-related adverse events (irAEs) of cancer patients treated with immune checkpoint inhibitors (ICIs) continues to be debated. Therefore, we performed a systematic review and meta-analysis of all published articles evaluating the effects of sarcopenia on survival outcomes and irAEs of patients undergoing ICI treatment.

Materials and Methods In analogy to the Cochrane guidelines for systematic reviews, we performed a systematic literature search including all published articles in PubMed until February 2021 for the key terms ‘sarcopenia’ or ‘sarcopenic obesity’ in combination with several terms for ICI treatments, irrespective of cancer entity and ICI used. Further selection criteria for meta-analysis included defined cut-offs for sarcopenia. Reported outcomes included progression-free survival (PFS), overall survival (OS) and the frequency of irAEs. For the random effects meta-analysis, we used Hazard Ratios (HR) for OS and PFS and Odds Ratios (OR) for occurrence of irAEs with corresponding 95% confidence intervals (95%CI), respectively.

Results A total of 15 studies with 1,428 patients were selected to be eligible for meta-analysis. To evaluate muscle mass, all studies used CT-derived body composition parameters at the third lumbar vertebrae level and defined sarcopenia by using skeletal muscle index (SMI), psoas muscle index (PMI) or skeletal muscle density (SMD). Sarcopenic patients showed an inferior survival compared to non-sarcopenic patients with a combined HR for PFS with 1.53 (95%CI 1.23-1.91, $p = 0.0001$) and for OS with 1.6 (95% CI 1.23-2.09, $p = 0.0005$). Frequency of irAEs did not differ between sarcopenic and non-sarcopenic patients regardless of irAE grade (irAEs of grade ≥ 3 : OR 1.14, 95%CI 0.65-2.01, $p = 0.64$, irAEs of any grade: OR 0.96, 95%CI 0.65-1.42, $p = 0.85$).

Conclusions This is the first meta-analysis that assessed sarcopenia in a mixed cohort of cancer patients. It revealed that sarcopenia is an adverse risk factor for survival of patients undergoing ICI treatment without affecting the risk of developing irAEs. Future studies may address sarcopenia as a patient-derived risk factor emphasizing the importance of nutrition and physical activity interventions.

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P02 Tumor microenvironment and microbiome in Immunotherapy

P02.01 T- AND B-CELL ABUNDANCE ARE REMARKABLY REDUCED IN THE IMMUNE MICROENVIRONMENT OF POST-TRANSPLANT MALIGNANCIES

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Background Immunosuppressive medication is mandatory in the majority of solid organ transplant recipients to reduce the risk of allograft rejection. An increased risk to develop cancer is a negative side effect of long-term immunosuppression and impaired cancer immunosurveillance is assumed as underlying mechanism. However, the impact of immunosuppression on the tumor immune microenvironment (TME) is poorly understood. In this study we aimed to elucidate differences between immune infiltrates of post-transplant malignancies and cancer of non-immunosuppressed patients.

Materials and Methods 117 resected tumor samples of 80 organ transplant (kidney, heart, lung and liver) recipients were included. Immunohistochemistry and digital image analysis of whole section slides was used to quantify T- (CD3, CD8) and B-cell (CD20) abundance in the TME of 14 different cancer types. These data were used to calculate the Immune-score and to quantify tertiary lymphoid structures in the TME. Expression of Human-Leucocyte-Antigen-I (HLA-I) and programmed cell death ligand 1 (PD-L1) were analyzed in tissue microarrays. Clinical parameters were included in statistical analyses.

Results The increased risk of cancer in organ transplant recipients was reflected by a remarkably reduced immune infiltrate in the central region (CT) and the surrounding tissue (invasive margin, IM) of cancer areas. T cell abundance was decreased in IM and CT of skin (814 vs. 1440 CD3⁺ cells/mm², $p < 0.01$) and non-skin tumors (479 vs. 781 CD3⁺ cells/mm², $p < 0.01$), when compared to non-immunosuppressed controls. These differences were more pronounced in the IM than in the CT and larger when comparing abundance of CD8⁺ T cells. The Immune-score integrating results from CT and IM was also decreased in transplant recipients. Similar to the results observed for T cells, B cell abundance and density of tertiary lymphoid structures were lower in cancer samples of transplant recipients. Decreased expression of HLA-I was more common in transplant recipients whereas the fraction of samples with PD-L1 expression was higher in controls.

Conclusions Our study demonstrates that post-transplant malignancies show a low immune infiltrate and supports the hypothesis of reduced anti-tumor immune response as an important mechanism underlying increased risk of cancer in organ transplant recipients. Optimized immunosuppressive protocols may be able to reduce cancer incidence and cancer therapies need to consider the distinct immune microenvironment of post-transplant malignancies.