NEW ASPECTS REGARDING MARKERS FOR THE CLINICAL COURSE IN THE BLOOD OF PATIENTS WITH SARS-COV-2 INFECTION. A TOOL TO PROTECT OUR ONCOLOGY PATIENTS

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Purpose: SARS-CoV-2 is still a challenge for our oncology patients. During radiochemotherapy some patients are not able to develop protective antibodies after vaccination against SARS-CoV-2. These patients are at more risk to develop Covid-19. A few investigations have detected a correlation between HLA variants and differential COVID-19 outcomes and have demonstrated that HLA genotypes are associated with differential immune responses against SARS-CoV-2, especially in severe ill patients. We wanted to find out which of our oncology patients are of high risk for a severe clinical outcome and if we could detect them with blood samples.

Materials and Methods: Next generation sequencing based-HLA typing was performed in 303 female and 231 male non-hospitalized North Rhine Westphalian patients infected with SARS-CoV2 during the first and second wave. For HLA-Class I we obtained results from 528 patients, and for HLA-Class-II from 531. In those patients, who became ill between March 2020 and January 2021, the 22 most common HLA class I (HLA-A, -B, -C) or HLA class II (HLA –DRB1/3/4, -DQA1, -DQB1) haplotypes were determined. The identified HLA haplotypes as well as the presence of a CCR5 32D mutation and number of O and A blood group alleles were associated to disease severity and duration of the disease.

Results: The influence of the HLA haplotypes on disease severity and duration was more pronounced than the influence of age, sex, or AB0 blood group. These association were sex dependent. The presence of mutated CCR5 resulted in a longer recovery period in males.

Conclusions: Certain HLA haplotypes are associated with a more severe clinical outcome. Therefore HLA testing could be an option to detect patients who are at risk for a more severe clinical outcome

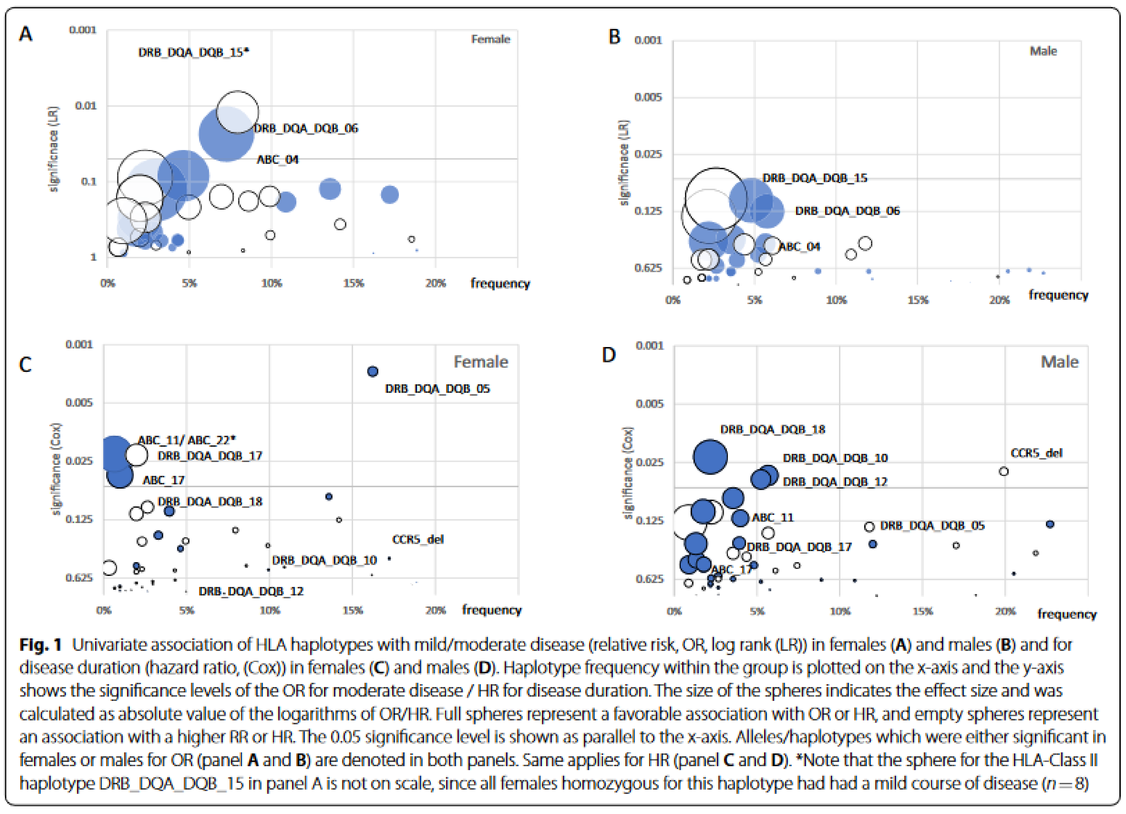

Fig. 1 Univariate association of HLA haplotypes with mild/moderate disease (relative risk, OR, log rank (LR)) in females (**A**) and males (**B**) and for disease duration (hazard ratio, (Cox)) in females (**C**) and males (**D**). Haplotype frequency within the group is plotted on the x-axis and the y-axis shows the significance levels of the OR for moderate disease / HR for disease duration. The size of the spheres indicates the effect size and was calculated as absolute value of the logarithms of OR/HR. Full spheres represent a favorable association with OR or HR, and empty spheres represent an association with a higher RR or HR. The 0.05 significance level is shown as parallel to the x-axis. Alleles/haplotypes which were either significant in females or males for OR (panel **A** and **B**) are denoted in both panels. Same applies for HR (panel **C** and **D**). *Note that the sphere for the HLA-Class II haplotype DRB_DQA_DQB_15 in panel A is not on scale, since all females homozygous for this haplotype had had a mild course of disease ($n = 8$)

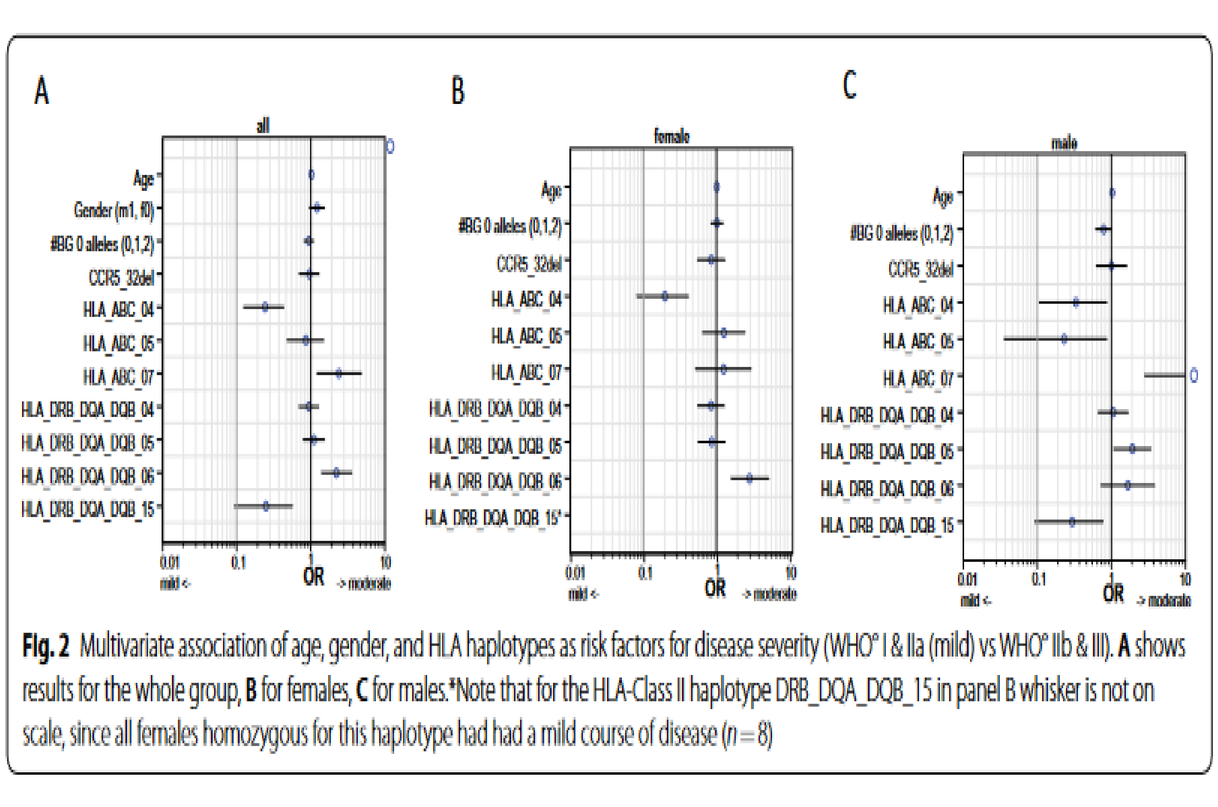

Fig. 2 Multivariate association of age, gender, and HLA haplotypes as risk factors for disease severity (WHO° I & IIa (mild) vs WHO° IIb & III). **A** shows results for the whole group, **B** for females, **C** for males.*Note that for the HLA-Class II haplotype DRB_DQA_DQB_15 in panel B whisker is not on scale, since all females homozygous for this haplotype had had a mild course of disease ($n = 8$)