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POSTER ABSTRACTS

722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Soluble Urokinase-Type Plasminogen Activator Receptor (suPAR) and Growth Differentiation Factor-15 (GDF-15) Leves Are Significantly Associated with Edothelial Injury Indices in Adult Allogenic Hematopoietic Cell Transplantation Recipients

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Introduction: Endothelial dysfunction is a common denominator of graft-versus-host disease (GVHD) and transplant-associated thrombotic microangiopathy (TA-TMA). Among endothelial injury indices, the Endothelial Activation and Stress Index (EASIX) has been studied in allogeneic hematopoietic cell transplantation recipients (allo-HCT) recipients, while others including suPAR and GDF-15 have been determined only in other patient populations with hematologic diseases, such as in patients with Multiple Myeloma, AL- amyloidosis and Sickle Cell Disease. We hypothesized that suPAR and GDF-15 would reflect endothelial injury in allo-HCT recipients.
Methods: We enrolled consecutive adult TA-TMA (classified according to current standardized criteria), acute and/or chronic graft-versus-host-disease (GVHD), control allogeneic hematopoietic cell transplantation (alloHCT) recipients and apparently healthy individuals of similar age and gender in a 1:1:1:1 ratio. Plasma was collected and stored immediately at -80 °C at the first day of confirmed TA-TMA or GVHD diagnosis and at a similar post-transplant period in control recipients. EASIX [lactate dehydrogenase (U/L) × creatinine (mg/dL)/thrombocytes (10^9 cells per L)] was calculated at day 0, 30, 100 and at last follow-up. Soluble C5b-9/membrane attack complex, suPAR and GDF-15 levels were measured using immunoenzymatic techniques.
Results: We studied 20 TA-TMA, 20 GVHD, 20 control alloHCT patients, and 20 healthy controls. We found significantly higher suPAR and GDF-15 levels in TA-TMA and GVHD patients compared to alloHCT and healthy controls ($p<0.001$, Bonferroni's correction). Then, we further analyzed characteristics of the alloHCT population.
TA-TMA developed at a median of 125 post-transplant day (range 9-2931); whereas the first day of confirmed GVHD diagnosis was at a median of 78 post-transplant day (range 16-145). Both GDF-15 and suPAR concentrations were associated with EASIX at day 100 ($r=0.351$, $p=0.012$ and $r=0.338$, $p=0.015$, respectively) and last follow-up ($r=0.473$, $p<0.001$ and $r=0.410$, $p=0.020$, respectively). Among the laboratory values used to calculate EASIX (LDH, creatinine, platelets), suPAR was associated with creatinine and platelets at day 100 and last follow-up; while GDF-15 only with platelets at both time points, suggesting that the association with EASIX is not driven by laboratory values *per se*. Interestingly, only suPAR and not GDF-15 levels was associated with soluble C5b-9 levels ($p=0.013$), a marker reflecting high risk in TA-TMA.
Conclusion: Our study shows for the first time that suPAR and GDF-15 reflect endothelial injury in allo-HCT recipients. In accordance with other patient populations, suPAR emerges as a marker of renal dysfunction, characterizing high-risk in endothelial

injury syndromes and in particular, TA-TMA. However, prior to their clinical usefulness, these biomarkers must undergo through rigorous validation in multiple cohorts.

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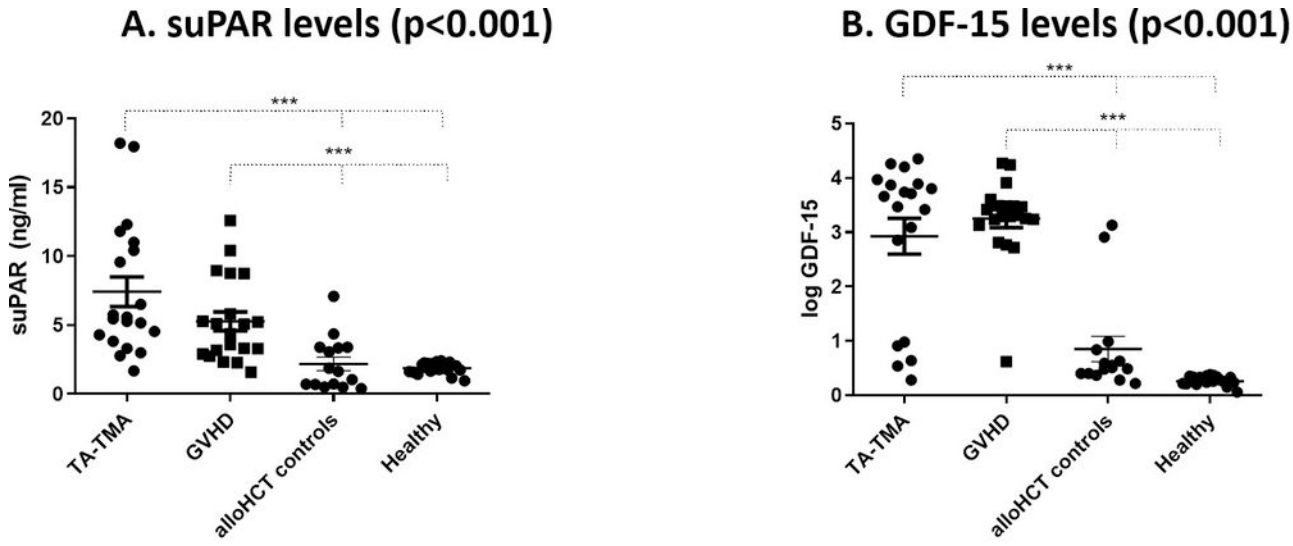

Figure 1

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