MO404 AUTOPHAGY AND FIBROTIC RESPONSE IS GENETICALLY DETERMINED IN MOUSE MESANGIAL CELLS

Anna Manzeger, Krizstina Mikone, Miklos Mozies and Gaxor Kokeny
Samuelweis University, Institute of Translational Medicine, Budapest, Hungary

BACKGROUND AND AIMS: CS786(1) (B6) mouse strain is resistant to several experimental models of renal fibrosis. Mesangial cells play an important role in the pathogenesis of glomerulosclerosis. Also, autophagy dysregulation was recently related to fibrosis. However, it is unclear whether autophagy dysregulation could be genetically determined in mice. Thus, we investigated autophagy and fibrotic response in primary mesangial cells isolated from fibrosis resistant (B6) and fibrosis prone (CBA) inbred mouse strains.

METHOD: Primary mesangial cells were isolated from 6-week old B6 and CBA male mice via magnetic bead separation technique. Glomerular outgrowths were maintained in RPMI medium for 21 days when cells were subcultured and characterized for mesangial markers. Mesangial cells with passage numbers P5 to P8 were seeded onto 24-well plates. Gene expressions were analyzed after 48-h of PBS (CT1) or TGF-β (10 ng/mL) treatment (n = 6/group). Data (mean ± SD) were analyzed using Kruskal–Wallis test.

RESULTS: Tgfb1 and Coll1α1 expressions increased by 2.5-fold and 8-fold in TGF-β treated CBA cells as compared to B6 (P < 0.01, respectively). The expression of Egfr (early growth response factor 1) that participates in both fibrosis and autophagy increased by 2-fold in TGF-β treated CBA cells but remained unchanged in B6 cells (P < 0.05). Similarly, the expression of core autophagy molecule Lc3b did not change in TGF-β treated B6 cells, but increased by 60% in CBA cells (P < 0.05) accompanied by 1.5-fold increase of Sqstm1/p62. On the other hand, the expression of Mtmr14 that negatively regulates autophagy decreased by 30% in TGF-β treated CBA cells but remained unchanged in B6.

CONCLUSION: We conclude that genetic background of mice highly influences the TGF-β induced fibrotic and autophagy response of mesangial cells. Our results corroborate previous reports on autophagy dysregulation associated to fibrosis.

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REFERENCES
1. Zhang A, Fang H, Chen J. et al. Role of VEGF-A and LRG1 in abnormal angiogenesis associated with diabetic nephropathy. Front Physiol 2020; 11: 1064
2. Lee HS, Song CY. Differential role of mesangial cells and podocytes in TGF-beta-induced mesangial matrix synthesis in chronic glomerular disease. Histol Histopathol. 2009; 24: 901–908

MO406 LEUCINE-RICH ALPHA-2-GLYCOPROTEIN AS A POTENTIAL MARKER OF MESANGIAL CELL PROLIFERATION IN IMMUNOGLOBULIN A NEPHROPATHY

Anna Popova1,2,3, Kārlis Rācenis2,1, Viktoria Kuznerova2,4, Anna Jana Saulute1,2, Mikus Saulute1,2, Renārs Broks1, Kristīne Opiejekans1,2, Baiba Silsere1,2, Aivars Petersens1,2,4, Avrijs Laurinavicius9, Harijs Cernevskis4, Aivars Lēnīte1,10, and Juta Krolči1
1 Riga Stradins University, Department of Biology and Microbiology, Riga, Latvia, 2 Pauls Stradiņš Clinical University Hospital, Nephrology department, Riga, Latvia, 3 Pauls Stradiņš University, Department of Internal Diseases, Riga, Latvia, 4 Riga Stradins University, Department of Internal Diseases, Riga, Latvia, 5 Riga Stradins University, Department of Human Physiology and Biochemistry, Riga, Latvia, 6 Boston Children’s Hospital, Boston, USA, 7 Harvard Medical School, Boston, USA, 8 Pauls Stradiņš Clinical University Hospital, Riga, Latvia, 9 State Pathology Center, Branch of Santaros Clinics, Vīnuvi University Hospital, Vīnīu, Lithuania and 10 Riga East Clinical University Hospital, Riga, Latvia

BACKGROUND AND AIMS: Leucine-rich alpha-2-glycoprotein (LRG1) is a novel proangiogenic factor involved in the abnormal angiogenesis and renal fibrosis in experimental models of renal fibrosis. Mesangial cells play an important role in the development of kidney damage, classic biomarkers, such as plasma creatinine, are not useful to detect this kidney injury [1]. In this sense, innovative diagnostic methods have been developed, such as early biomarkers capable of detecting subclinical kidney damage in the initial stages of the disease [2, 3]. In fact, studies carried out in our laboratory have shown that smoking patients suffer subclinical kidney damage evidenced by the excretion of these urinary biomarkers [4]. The aim of this work was to study the evolution of kidney damage associated with tobacco consumption using these biomarkers after monitoring smoking patients for 2 years.

METHOD: A longitudinal study was carried out that included 150 smokers and 150 non-smokers, without previous kidney damage and risk factors for kidney disease, from a Salamanca Health Centre (Spain). Urine samples were collected at the time of inclusion and after 2 years, and the biomarkers of subclinical kidney damage N-acetyl-β-D-glucosaminidase (NAG), neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1) and total proteins, were quantified using ELISA and colorimetric techniques. The data obtained were analyzed with the statistical software SPSS®.

RESULTS: The results showed a higher excretion of NAG, NGAL, KIM-1 and total proteins in smoker patients with respect to non-smoker ones, measured at baseline, which was maintained after 2 years.

CONCLUSION: Our research suggests that subclinical kidney damage associated with tobacco consumption would remain stable in the 2 years studied and could become chronic and it could constitute the basis for the development of chronic kidney failure.

REFERENCES
1. Orth SR, Ritz E. The renal risks of smoking: an update. Curr Opin Nephrol Hypertens 2002; 11: 483–488
2. Bonventre JV, Vaidya VS, Schmouder R. et al. Next-generation biomarkers for detecting kidney toxicity. Nat Biotechnol 2010; 28: 436–440
3. Malyszko J, Malyszko J. Biomarkers of Acute Kidney Injury in Different Clinical Settings: A Time to Change the Paradigm? KBR. 2010; 33: 368–382
4. Tascón J, Casanova AG, Jiménez-Lozano S. et al. Kidney damage associated with tobacco consumption. Role of oxidative stress. Toxicol Lett. 2021; 350S: S146

MO407 CLINICAL FEATURES & OUTCOME OF 352 COVID-19 POSITIVE MAINTENANCE HAEMODIALYSIS PATIENTS IN SECOND COVID WAVE IN TERTIARY CARE CENTRE IN SOUTH INDIA

Pratul Chege1 and Manjusha Yadla2
1 Gandhi Medical College, Nephrology Department, Secunderabad, India and 2 Gandhi Medical College, Nephrology Department, Secunderabad, India

BACKGROUND: Coronavirus disease (COVID-19) infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is an ongoing pandemic with high mortality and morbidity rates. The second COVID-19 wave was...
GDF-15 is a predictor of mortality in chronic kidney disease patients with type 2 diabetes.

**Table 1.**

| Variable                  | No.   |
|---------------------------|-------|
| Mean age (years)          | 50.7  |
| Male : Female             | 269:83|
| DM                        | 157   |
| HTN                       | 320   |
| CAD                       | 28    |
| Access : AVF/IFV/Femoral/Permcathe | 303/35/10/4 |
| Haemoglobin (gm/dl)       | 8.1   |
| Platelet count (lakhs/mm3)| 1.18  |

observed between April–July 2021. Patients with underlying CKD > 65 years, immunocompromised, post-transplants are at high risk for COVID-19 infection.

**Aims and objectives:** Clinical features and outcome of 352 COVID-19 positive maintenance hemodialysis (MHD) patients in a tertiary care centre in South India.

**Method:** Patients admitted with respiratory symptoms with nasal RTPCR positive and on MHD referred to us from April to July 2021, were included. The study design was an observational study. The analysis included clinical profile, epidemiological data, vascular access, lab parameters and outcomes. Data analysed using SPSS version 17 (P-value < 0.05 significant).

**Study design:** This is an Observational Retrospective study.

**Results:** Clinical profile constituted fever (82.6%), SOB (61.2%), cough (29.8%). Baseline characteristics were: Oxygen was required in 244 patients (69.31%), CPAP in 71 patients (20.17%) and mechanical ventilation in 21 patients (5.96%). Mortality seen in 132 patients (37.5%). Factors affecting mortality were age (P = 0.001), thrombocytopenia (P = 0.004), q SOFA score > 1 (P = 0.001), CPAP (P = 0.002) and mechanical ventilation (P = 0.0001).

**Conclusion:** The mortality rate was 37.5%. The factors associated with mortality were age, thrombocytopenia, q SOFA score > 1, hypoxemia, patients on oxygen support, CPAP, mechanical ventilation.

**MO408 Hepatic steatosis in patients with type 2 diabetes and chronic kidney disease**

Therese Adrian1, Mads Hornum1, Filip K. Knop2, Thomas Peter Almad1, Peter Rossing1, Lisa Lica1, Niels Sondergaard Henriksen1, Vincent Boer1, Anouk Marsman1, Esben Petersen3, Hartwig Siebner4 and Bo Feldt-Rasmussen5

1Copenhagen University Hospital —Rigshospitalet, Nephrology, Copenhagen, Denmark, 2Copenhagen University Hospital —Gentofte Hospital, Center for Clinical Metabolic Research, Denmark, 3Copenhagen University Hospital —Rigshospitalet, Endocrinology, Denmark, 4Copenhagen University Hospital, Steno Diabetes Centre Copenhagen, Denmark and 5Copenhagen University Hospital—Amager and Hvidovre Hospital, Danish Research Centre for Magnetic Resonance, Denmark.

**Background and aims:** Non-alcoholic fatty liver disease (NAFLD) is suggested as being a risk factor for chronic kidney disease (CKD). The incidence of NAFLD is rising globally parallel to the increasing incidences of obesity and type 2 diabetes. As diabetes remains the leading cause of CKD the co-existence of NAFLD, CKD and type 2 diabetes needs to be explored. Here, we evaluated the prevalence of hepatic steatosis in patients with type 2 diabetes and CKD and patients with type 2 diabetes without CKD.

**Method:** This cross-sectional study included 50 patients with type 2 diabetes and CKD stages 3–5 and 50 patients with type 2 diabetes without CKD. Liver fat content was estimated by proton magnetic resonance spectroscopy (1H-MRS) and magnetic resonance imaging proton density fat fraction (MRI-PDFF) by the multi-echo Dixon-technique in a 3 Tesla full-body MRI scanner. Hepatic steatosis was defined as ≥ 5.56% liver fat. Further, continuous glucose monitoring (CGM) was performed for 4 days.

**Results:** Mean age 72.0 ± 4.9 years and body mass index (BMI) 28.6 ± 3.5 kg/m² in patients with CKD, and mean age 65.9 ± 7.8 years and BMI 27.0 ± 4.0 kg/m² in patients without CKD with a predominance of men in both groups. Hepatic steatosis was identified in 22 (44%) patients with CKD and 19 (38%) patients without CKD (P = 0.68). Median (IQR) values of percentage liver fat were 4.7% (3.0–8.5) and 4.1% (2.9–7.7) in patients with and without CKD, respectively, corresponding to 5.3% higher levels of hepatic fat percentage in patients with CKD [95% confidence interval (CI) − 23; 45, P = 0.75]. Mean sensor glucose from CGM was 9.0 ± 1.6 mmol/L and 8.7 ± 1.8 mmol/L in patients with and without CKD, respectively (P = 0.47). There was no statistically significant difference between the two groups regarding the percentage of time spent in different CGM ranges: time-below-range, < 3.9 mmol/L (P = 0.83), time-in-target-range, 3.9–10.0 mmol/L (P = 0.20) and time-above-range, > 10.0 mmol/L (P = 0.20). Pooled data from both groups showed no significant association between the mean sensor glucose from CGM and hepatic fat percentages (P = 0.38).

**Conclusion:** These findings do not support any association between hepatic steatosis and CKD stages 3–5 in patients with type 2 diabetes.

**MO409 GDF-15 is a predictor of mortality in chronic kidney disease patients with COVID-19 infection**

Paola Ciceri, Valeria Bono, Lorenza Magagnoli, Matteo Sala, Luisa Artici, Roberta Rovito, Mohamad Adla, Valthav Yelenki, Antonella D’armino Montforte, Andrea Galassi, Camilla Tincati, Giulia Marchetti and Mario Gennaro Cozzolino

University of Milan, Health Sciences, Italy

**Background and aims:** A cytokine storm drives the pathogenesis of severe coronavirus disease (COVID-19) and several biomarkers with different mechanisms of action have been linked to mortality. Chronic kidney disease (CKD) emerged as a very common risk factor for severe COVID-19. Indeed, CKD patients are at increased risk of premature death from many causes, including, but not limited to, cardiovascular disease (CVD) and infections. In this study, we aimed to investigate the associations between the growth differentiation factor 15 (GDF-15), an established cardiovascular and inflammatory biomarker and outcomes in CKD patients hospitalized for COVID-19.

**Method:** A retrospective study on COVID-19 hospitalized subjects in the acute phase of the disease. A broad range of cytokines (CD25, IL-18, TNF-α, TNF RI, TNF RII, GDF-15, IL-7, IL-6, CHITINASE3_LIKE1, RAGE and Pentraxin-3) were assessed in plasma (Lumix, ELISA) collected upon hospitalization. A total of 77 subjects were divided into two groups according to their estimated glomerular filtration rate (eGFR, by CKD-EPI formula), ≥45 mL/min (n = 44), or <45 mL/min (n = 33).

**Results:** In patients with type 2 diabetes and CKD and patients with type 2 diabetes without CKD.

**Conclusion:** In conclusion, hepatic steatosis, determined by MRI, is a predictor of mortality in CKD patients with COVID-19 and could be used as a prognostic marker in this setting.