

A diamond open access online journal | established in 1871 |
published by the SMW supporting association | www.smw.ch

Supplementum 275

ad Swiss Med Wkly 2023;153

November 30, 2023

Abstracts of the 55th Annual meeting of the Swiss Society of Nephrology

Lausanne (Switzerland), December 7–8, 2023



55TH ANNUAL MEETING OF THE SWISS SOCIETY OF NEPHROLOGY (SGN-SSN)

LAUSANNE, DECEMBER 7–8, 2023

TABLE OF CONTENTS

| | | |
|------------------------------|---|------|
| OC 01 – OC 24 | Long oral presentations | 2 S |
| OC 25 – OC 48 | Short oral presentations & Poster presentations (P 01 – P 24) | 22 S |
| OC 49 – OC 63 | Elevator pitch presentations & Poster presentations (P 25 – P 39) | 40 S |
| OC 64 – OC 68 | Young Swiss Nephrology presentations | 52 S |
| Index of first authors | | 55 S |

LONG ORAL PRESENTATIONS

OC 01

Effect of hydrochlorothiazide on bone mineral density in patients with kidney stones: a post-hoc analysis of the NOSTONE trial

Dr. Matteo Bargagli¹, Dr. Dionysios Drakopoulos², Dr. Elias Primetis², Dr. Maria Grazia Cereghetti¹, Dr. Nasser Dhayat³, Prof. Olivier Bonny⁴, Prof. Beat Roth⁵, Dr. Alexander Ritter⁶, Dr. Nilufar Mohebbi⁶, Dr. Nicolas Faller⁷, Dr. Lisa Pellegrini⁸, Dr. Giulia Bedino⁸, Dr. Reto Venzin⁹, Dr. Philipp Grosse⁹, Dr. Carina Huesler¹⁰, Dr. Irene Koneth¹⁰, Dr. Christian Bucher¹⁰, Dr. Rosaria Del Giorno¹¹, Dr. Luca Gabutti¹¹, Dr. Michael Mayr¹², Dr. Urs Odermatt¹³, Dr. Florian Buchkremer¹⁴, Dr. Thomas Hernandez¹⁵, Dr. Catherine Stoermann-Chopard¹⁵, Prof. Daniel Teta¹⁶, Dr. Luca Tamo¹, Prof. Bruno Vogt¹, Prof. Andreas Christe², Prof. Daniel G. Fuster¹

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Radiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 3. B. Braun Medical Care AG, Nephrology & Dialysis Care Center, Hochfelden, Zürich, Switzerland, 4. Service of Nephrology, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland, 5. Department of Urology, Lausanne University Hospital, CHUV, University of Lausanne, Switzerland, 6. Division of Nephrology, University Hospital Zürich, Zürich, Switzerland, 7. Service of Nephrology, Department of Medicine, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland, 8. Department of Nephrology, Regional Hospital Lugano, Lugano, Switzerland, 9. Department of Nephrology, Cantonal Hospital Graubünden, Chur, Switzerland, 10. Department of Nephrology and Transplantation Medicine, Cantonal Hospital St. Gallen, St. Gallen, Switzerland, 11. Department of Internal Medicine, Regional Hospital of Bellinzona, Bellinzona, Switzerland, 12. Medical Outpatient Department, University Hospital Basel, University of Basel, Basel, Switzerland, 13. Department of Nephrology, Luzerner Kantonsspital LUKS, Lucerne, Switzerland, 14. Medizinische Universitätsklinik, Abteilung für Nephrologie, Kantonsspital Aarau, Aarau, die Schweiz, 15. Service of Nephrology, Geneva University Hospitals, Geneva, Switzerland, 16. Nephrology Service, Centre Hospitalier du Valais Romand, Sion, Switzerland

Background: Low bone mass is highly prevalent in patients with kidney stones. Although thiazides lower urine calcium, no pla-

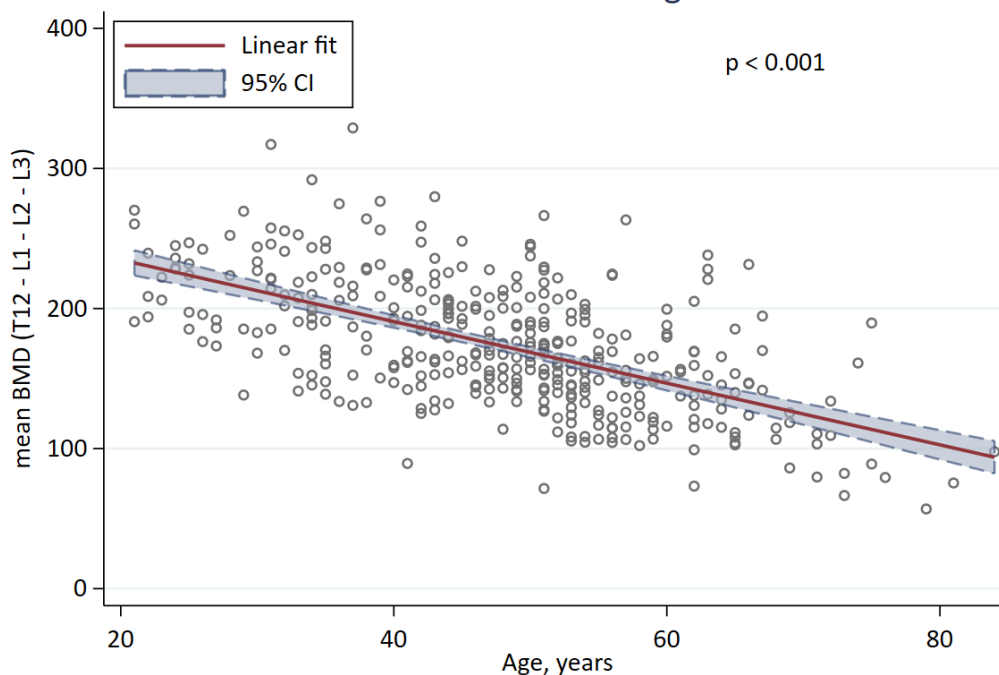
cebo-controlled randomized trial has been conducted to examine the impact of thiazides on bone mineral density (BMD) in patients with kidney stones.

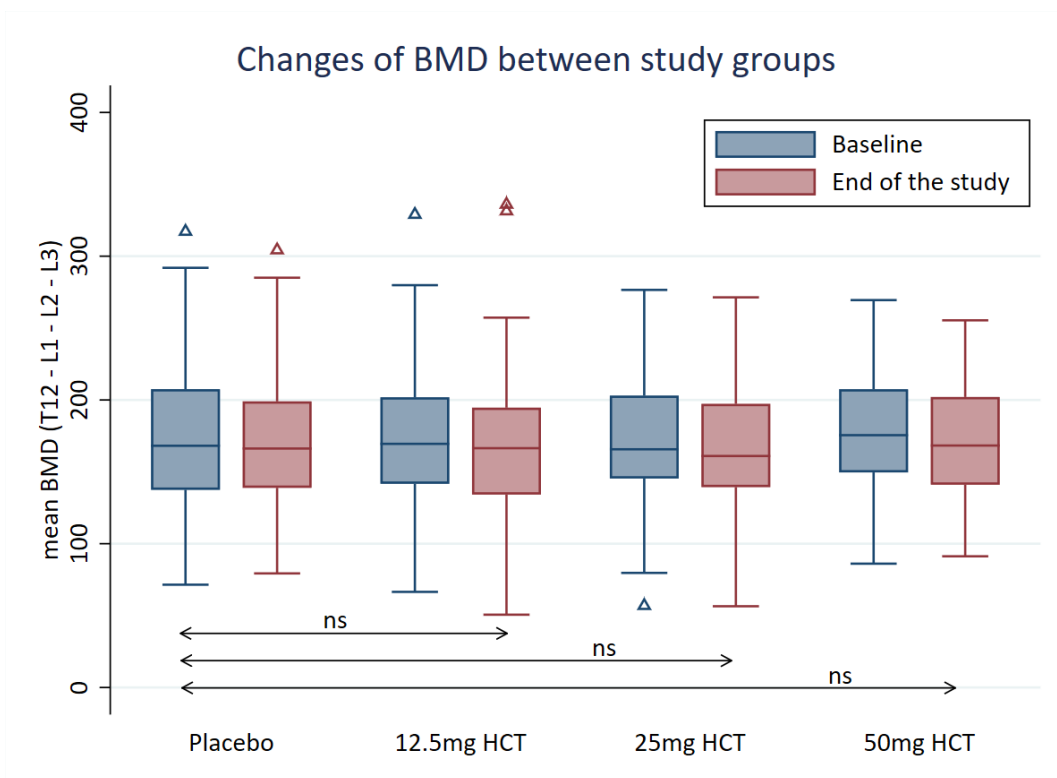
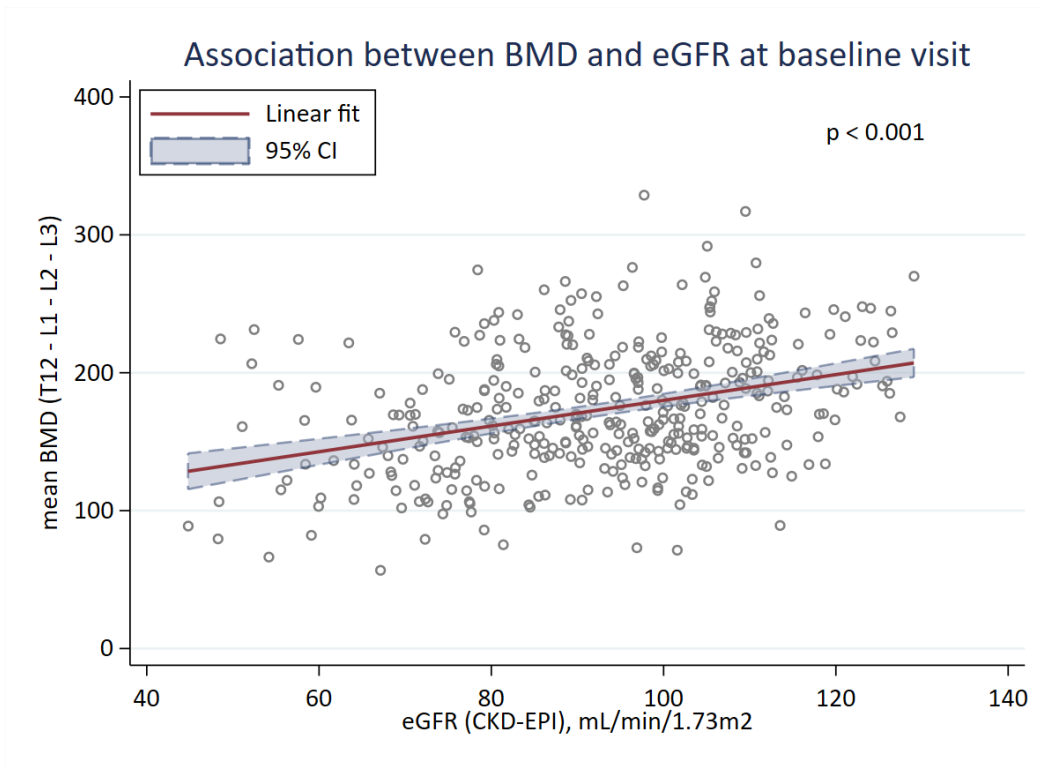
Methods: We conducted a post-hoc analysis of the NOSTONE trial to assess a range of hydrochlorothiazide (HCT) doses or placebo on BMD in patients with recurrent calcium stones. Computed tomography (CT) attenuation was measured at T12-L3 vertebrae in Hounsfield units (HU) at baseline and the end of the study, using a previously validated approach, with lower values corresponding to lower BMD. BMD measurements were performed by two independent readers blinded to the study intervention.

Results: BMD measurements were available in 388 of 416 (93%) randomized patients. Median follow-up time was 2.92 years. At baseline, mean BMD was directly associated with eGFR and inversely with age (figure 1 and 2). Mean BMD decreased by 6.4 ± 15.7 HU in the placebo group, by 5.1 ± 15.1 in the 12.5 mg HCT group (β coefficient vs placebo, 0.368, 95% CI -1.735; 2.472, $p = 0.732$), by 4.1 ± 16.3 in the 25 mg HCT group (β 0.926, 95% CI -1.335; 3.187, $p = 0.422$), and by 4.8 ± 15.9 in the 50 mg HCT group (β 0.699, 95% CI -1.450; 2.848, $p = 0.524$). The results were confirmed in sensitivity analyses for urinary calcium and in per-protocol analyses. Exploratory analyses revealed a negative association between HCT administration and both total alkaline phosphatase (β -0.039 UI/L, 95% CI -0.061; -0.017, $p = 0.001$) and 1,25(OH)₂-Vitamin D₃ (β -0.053 pmol/L, 95% CI -0.086; -0.020, $p = 0.002$), but not with parathyroid hormone.

Conclusion: In patients with recurrent calcium-containing kidney stones, loss of bone mineral density was similar in patients receiving hydrochlorothiazide at a dose of 12.5 mg, 25 mg, or 50 mg or placebo once daily.

YSN submission

Association between BMD and age at baseline visit



OC 02

Lymphocele formation after living donor kidney transplantation negatively affects mid-term allograft function

Dr. Christian Kuhn¹, Dr. Bernd Jänigen², Ms. Laura Matuschik², Prof. Daniel Sidler³, Prof. Stefan Zschiedrich⁴

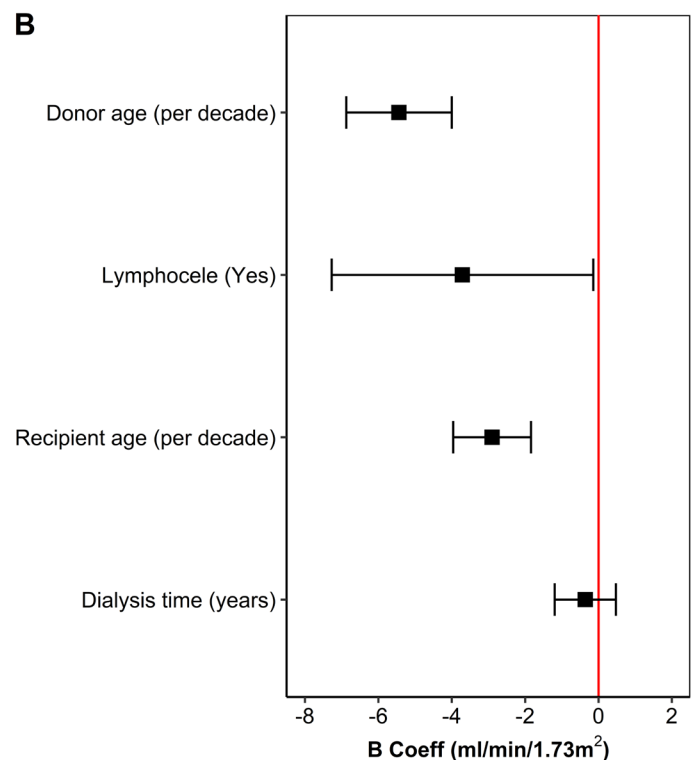
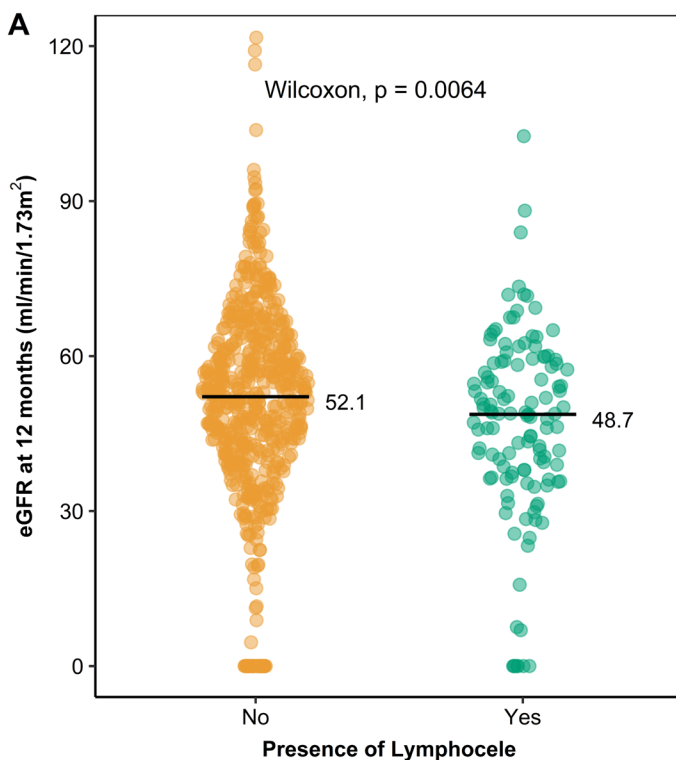
1. Division of Nephrology and Transplantation Medicine, Kantonsspital St. Gallen, St. Gallen, Switzerland, 2. Department of General and Digestive Surgery, Medical Centre, University of Freiburg, Freiburg, Germany, 3. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland, 4. Department of Internal Medicine, Bürgerspital Solothurn, Solothurn, Switzerland

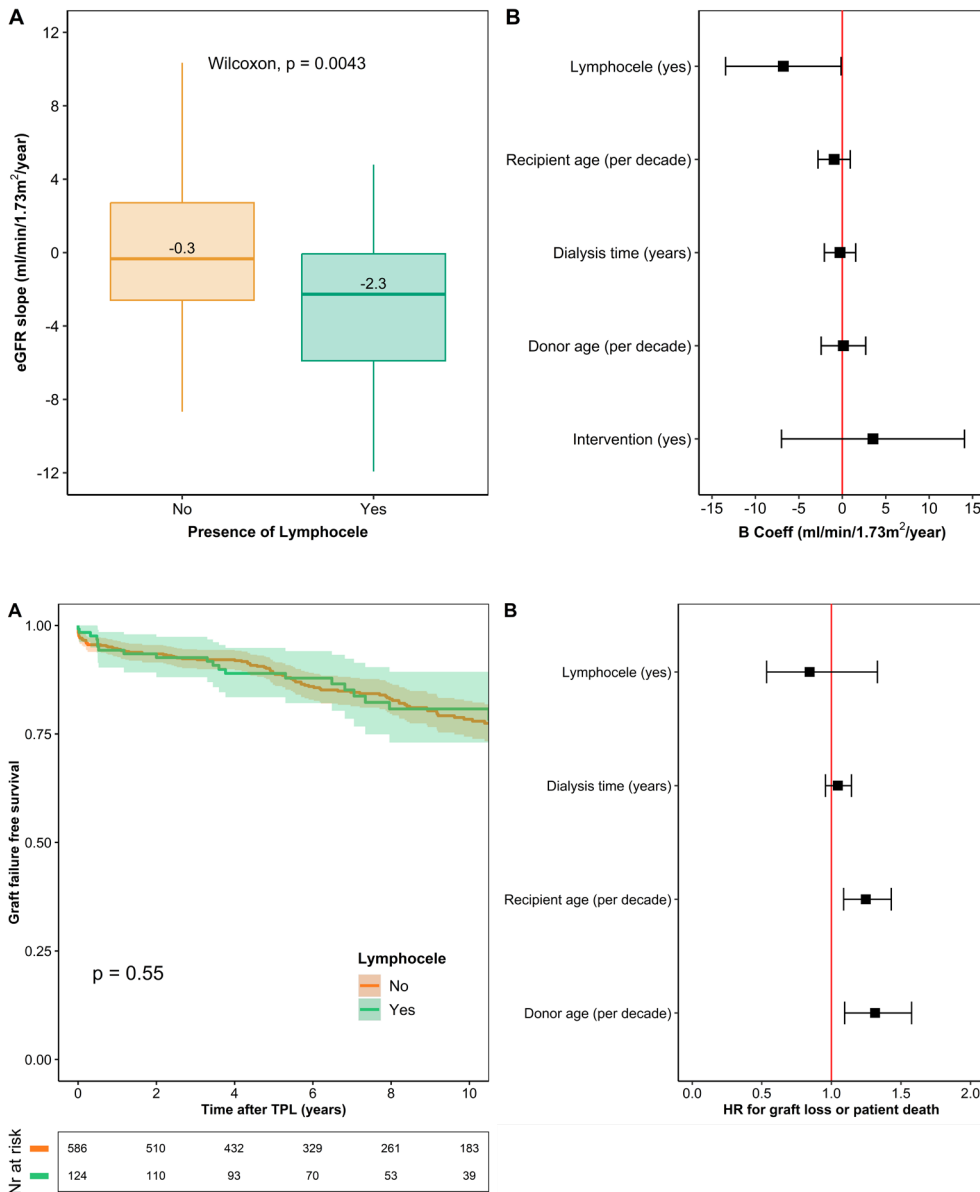
Background: Despite advances in kidney transplant surgery and immunosuppression, lymphoceles remain a common complication in the early postoperative period and may lead to the need for reintervention. While long-term outcomes such as graft and patient survival are well studied, the effect of lymphoceles on mid-term graft function is unknown. This bicentric study investigates the impact of lymphocele formation on eGFR at 12 months, mid-term allograft function assessed by eGFR slope as well as patient and allograft survival after living donor kidney transplantation.

Method: Data from living donor kidney transplantations at the university hospitals of Bern (Switzerland) and Freiburg (Germany) between January 2004 and November 2021 were analysed, comprising a total of 711 living donor transplant recipients. Primary outcome was the impact of lymphocele formation on 12 month eGFR, and secondary outcomes comprised eGFR slope after 12 months as well as allograft survival and patient death.

Results: Lymphocele formation was detected in 124/711 (17.4%) of patients, with a median volume of 129 ml (IQR: 53–289) and an intervention rate of 71.8% (single puncture, drainage, or fenestration). Median eGFR at 12 months was significantly better in patients without lymphocele with 52.1 ml/min/1.73 m² (IQR: 41.7–62.5) compared to patients with lymphocele formation with 48.7 ml/min/1.73 m² (IQR: 36.6–58.6). Furthermore, the latter group had a steeper median eGFR slope (–2.3 ml/min/1.73 m²/year, IQR: –5.0 – –0.1) than the former group (–0.3 ml/min/1.73 m²/year, IQR: –2.6 – +2.7). The composite outcome for allograft survival and patient death was similar.

Conclusion: In summary, our data indicate that lymphocele formation after living donor kidney transplantation has a negative impact on mid-term allograft function in terms of eGFR at 12 months and eGFR-slope. Whether this also applies to deceased kidney transplantation requires further evaluation.





OC 03

Thrombotic microangiopathy associated with metastatic prostate cancer

Mrs. Céline Tümay¹, Dr. Isabel Stiefel², Dr. Anne Sachs³, Dr. MinJeong KIM¹

1. Division of Nephrology, University Clinic of Medicine, Kantonsspital Aarau, Switzerland, 2. Division of Oncology, University Clinic of Medicine, Kantonsspital Aarau, Switzerland, 3. Division of Internal Medicine, Hirslanden Klinik Aarau, Switzerland

Cancer-associated thrombotic microangiopathy (TMA) is a rare disease with a poor prognosis. Although the classical treatment is urgent chemotherapy, the additional role of plasma exchange (PE) or eculizumab is not clearly established.

Case: We report a case of a 74-year-old patient, who presented with subacute lower abdominal pain in a local hospital. He had no relevant medical history. On clinical examination, an elevated blood pressure of 225/100 mmHg and diffuse hematoma of the upper extremities were remarkable. Laboratory examination revealed hemolytic anemia (decrease of hemoglobin from 19.3 g/l to 12.3 g/l within 3 days, elevated LDH 1786 IU/l and bilirubin 65.6 µmol/l, haptoglobin <0.01 g/l, and schistocytes in

peripheral blood smear), thrombocytopenia (18 x 10⁹/l), and acute kidney injury stage 3 (creatinine 619 µmol/l), compatible with TMA. The patient was transferred to our hospital for an urgent plasma exchange therapy (PEX). At the time of the transfer, we obtained the result of ADAMTS 13 activity measurement, which was normal at 69%. We decided not to perform a PEX, but to start eculizumab. Acute hemodialysis was started. In addition, an abdominal CT scan for the evaluation of subacute lower abdominal pain suggested a prostate cancer with bone metastases. The PSA was highly elevated to 4059 ng/ml. After immediate initiation of eculizumab and degarelix (GnRH antagonist), the hemolysis resolved, and thrombocytes normalized in the following days. We were able to stop hemodialysis after 2 weeks with complete recovery of kidney function during the following 4 weeks. The prostate biopsy revealed an adenocarcinoma. Eculizumab was not continued after 1st administration.

Conclusion: Our case demonstrates a favorable course of cancer-associated TMA after immediate initiation of anti-cancer treatment. The therapeutic role of eculizumab remains unclear. This case also emphasizes that a rapid detection of secondary cause of TMA is crucial for a favorable prognosis.

YSN submission

OC 04

Tacrolimus monitoring in hair samples of kidney transplant recipients

Mr. Alexander Born¹, Dr. Federica Bocchi¹, Dr. Christian Kuhn², Ms. Ursula Amstutz³, Dr. Baumgartner Markus⁴, Prof. Daniel Sidler⁵

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Division of Nephrology and Transplantation Medicine, Kantonsspital St. Gallen, St. Gallen, Switzerland, 3. Department of Clinical Chemistry, Inselspital, Bern University Hospital, University of Bern, Switzerland, 4. Center for Forensic Hair analytics, University of Zurich, Kurvenstrasse 17, 8006 Zurich, Switzerland, 5. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland

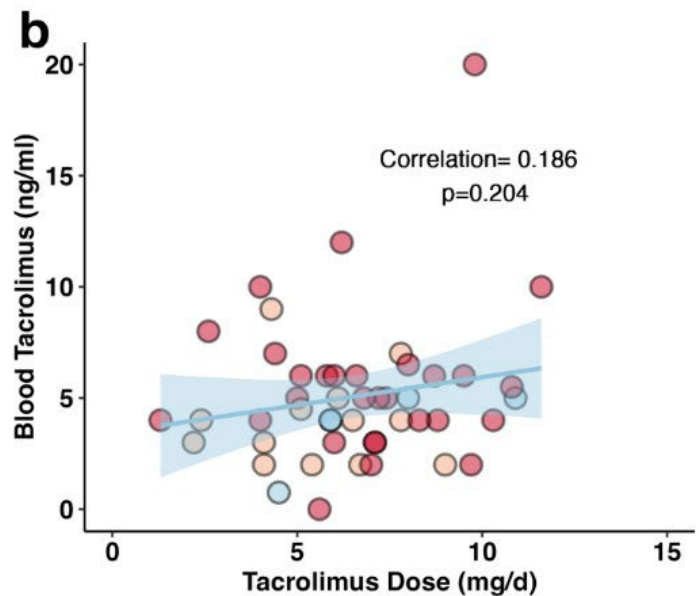
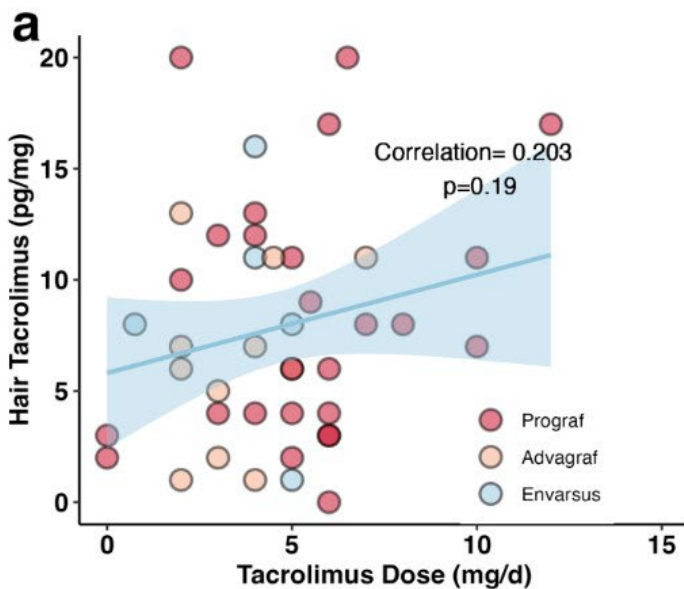
Background: Calcineurin inhibitors (CNI) including tacrolimus remain a cornerstone of immunosuppressive therapy after kidney transplant (KT). However, the therapeutic window is narrow, and nephrotoxic side effects occur with overdose, while the risk of alloimmunization and graft rejection will increase with underdose. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) allows the quantification of tacrolimus in biological samples from patients. This study investigates the feasibility of quantifying tacrolimus in scalp hair from KT recipients, and correlates hair tacrolimus concentrations with tacrolimus dosage and blood trough levels. The aim was to provide proof-of-principle for hair tacrolimus drug monitoring in KT recipients.

Method: Single center prospective study of KT recipients in Bern, Switzerland, from September 09th 2021 to 04th December 2021. Patients under tacrolimus with no active skin- or hair disease and with scalp hair longer than 4 cm were eligible to participate. Scalp hair was collected from the posterior vertex of patients, cut into segments, and analyzed for tacrolimus by LC-MS/MS. In parallel, tacrolimus trough levels were measured in whole blood and correlated with hair tacrolimus concentrations.

Results: 39 consenting KT recipients were included. Tacrolimus was detected in 98% hair samples of patients exposed to the drug. Tacrolimus hair concentration (hC₀) and daily dose showed a correlation coefficient of $r^2 = 0.203$, which was higher compared to correlation between tacrolimus blood concentration (bC₀) and daily dose ($r^2 = 0.186$). Dark hair affected hair tacrolimus measurements, while different tacrolimus formulations (immediate release vs. extended release), hair washes, and permanent coloring did not. Longitudinal measurements in a subgroup of patients indicate that long-term measurement of hair tacrolimus levels is feasible.

Conclusion: Measuring tacrolimus in hair is a potentially reliable method to monitor drug exposure in KT patients. This method provides a simple and low-risk alternative to regular blood sampling, sparing patients from frequent hospital visits by self-collection of hair samples.

YSN submission / student submission



OC 05

Prevalence of chronic kidney disease associated pruritus among hemodialysis patients in the French-speaking part of Switzerland

Dr. Nancy Helou¹, Mrs. Dina Nobre², Prof. Olivier Bonny³, Dr. Hemett Ould Maouloud³, Prof. Daniel Teta⁴, Dr. Floriane Beaud⁵, Dr. Georges Halabi⁵, Dr. David Jaques⁶, Prof. Sophie De Seigneux⁶, Dr. David Fumeaux⁷, Dr. Anne Cherpillod⁷, Dr. Zina Fumeaux⁸, Dr. Gérard Vogel⁹, Dr. Alain Rossier⁹, Dr. Patricia Mehier⁹, Dr. Olivier Phan¹⁰, Dr. Grzegorz Nowak¹¹, Dr. Anne-Hélène Reboux¹², Dr. Robin Chazot¹³, Dr. Antoine Humbert¹⁴, Dr. Menno Pruijm²

1. School of Health Sciences (HESAV), HES-SO University of Applied Sciences and Arts Western Switzerland, Lausanne, Switzerland 2. 2. Lausanne University Hospital (CHUV), Service of Nephrology and Hypertension, Lausanne, Switzerland 3. 3. Hôpital de Fribourg (HFR), Service of Nephrology, Fribourg and University of Fribourg, Fribourg, Switzerland 4. 4. Hôpital du Valais – Centre Hospitalier du Valais Romand (CHVR), Hôpitaux de Martigny, Sierre et Sion, Service of Nephrology, Switzerland 5. 5. Etablissements Hospitaliers

du Nord Vaudois (eHnv), Dialysis Center, Yverdon-les-Bains, Switzerland 6. 6. Geneva University Hospitals (HUG), Service of Nephrology, Geneva, Switzerland 7. 7. Clinique Cecil, Dialysis Center, Lausanne, Switzerland 8. 8. Nyon Hospital / GHOL, Dialysis Center, Nyon, Switzerland 9. 9. Hôpital Riviera-Chablais, Dialysis Center, Renaz, Switzerland 10. 10. Broye Inter cantonal Hospital, Hemodialysis Center, Payerne, Switzerland 11. 11. Hôpital du Valais – Centre Hospitalier du Valais Romand (CHVR), Hôpital de Sierre, Dialysis Center, Sierre, Switzerland, 12. 12. Hôpital du Valais – Centre Hospitalier du Valais Romand (CHVR), Hôpital de Martigny, Dialysis Center, Martigny, Switzerland 13. 13. Dialyse Riviera, Vevey, Switzerland 14. 14. Réseau Hospitalier Neuchâtelois, Service of Nephrology, Neuchâtel, Switzerland

Background: Chronic Kidney Disease Associated Pruritus (CKD-aP) is a frequent symptom in patients with end-stage renal disease. The reported prevalence differs between countries and is estimated between 20–40%; data on the prevalence of CKD-aP in Switzerland are lacking. Objectives: This ongoing study aims to determine the prevalence and severity of CKD-aP among patients on hemodialysis in the French-speaking part of Switzerland and to investigate its association with demographic and clinical factors.

Methods: Patients aged ≥ 18 years, on hemodialysis for ≥ 6 months, and free of cognitive impairment are recruited. Clinical, laboratory and dialysis prescription characteristics are collected by an independent research nurse, who also performs CKD-aP assessment using the Visual Analog Scale (VAS, numeric score 0–10) and the Verbal Rating Scale (VRS, 0 = no itch – 4 = extremely severe itch). Multiple linear regression analysis will be carried-out to investigate associations of CKD-aP with demographic and clinical factors when data collection is completed.

Results: Preliminary data from 354 participants (mean age 68.1 years, SD 13.9; 65% men) shows a CKD-aP prevalence of 26.9%. Most participants with CKD-aP (69%) report generalized itching and 35% waking-up at night because of the itching.

Mean VAS in participants with CKD-aP was 4.78 (SD 2.02) during the last 24 hours and 6.61 (SD 2.25) for the worst intensity itching during the last 24 hours. According to the VRS, most participants with CKD-aP suffered from moderate (57%) to severe itching (25%), and 73% experienced at least one severe to extremely severe episode of itching during the last 24 hours.

Conclusion: Despite high dialysis standards and easy access to medications, CKD-aP affects around 27% of patients on hemodialysis in the French-speaking part of Switzerland, and its intensity is moderate to severe. Results may help to increase clinicians' awareness of CKD-aP, improve its regular screening, severity reporting and treatment.

YSN submission

OC 06

Selective V2R blockade with Tolvaptan increases urinary exosome Pendrin expression in patients with Autosomal Dominant Polycystic Kidney Disease

Dr. Matteo Bargagli¹, Dr. Giuseppe Albano¹, Prof. Bruno Vogt¹, Prof. Pietro Manuel Ferraro², Prof. Daniel G. Fuster¹

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. U.O.C. Terapia Conservativa della Malattia Renale Cronica, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy

Background: Tolvaptan, a selective V2 vasopressin receptor (V2R) antagonist, has shown to improve kidney function and acid retention biomarkers in ADPKD-treated patients. However, the underlying mechanisms of this association remain unclear. Here we investigated the effect of Tolvaptan on renal acid-base handling in ADPKD by analyzing the abundance in urinary exosomes of Pendrin and the B1 subunit of V-ATPase, which regulate HCO_3^- and H^+ transport in the collecting ducts.

Methods: In this study, 24 ADPKD patients were enrolled from the Bern ADPKD registry. Patients were allocated with a 1:1 ratio in the Tolvaptan and no-Tolvaptan groups. All patients performed baseline and 2-year follow-up visits. NAE and NGIA, markers of acid and alkali intake, were calculated from 24h

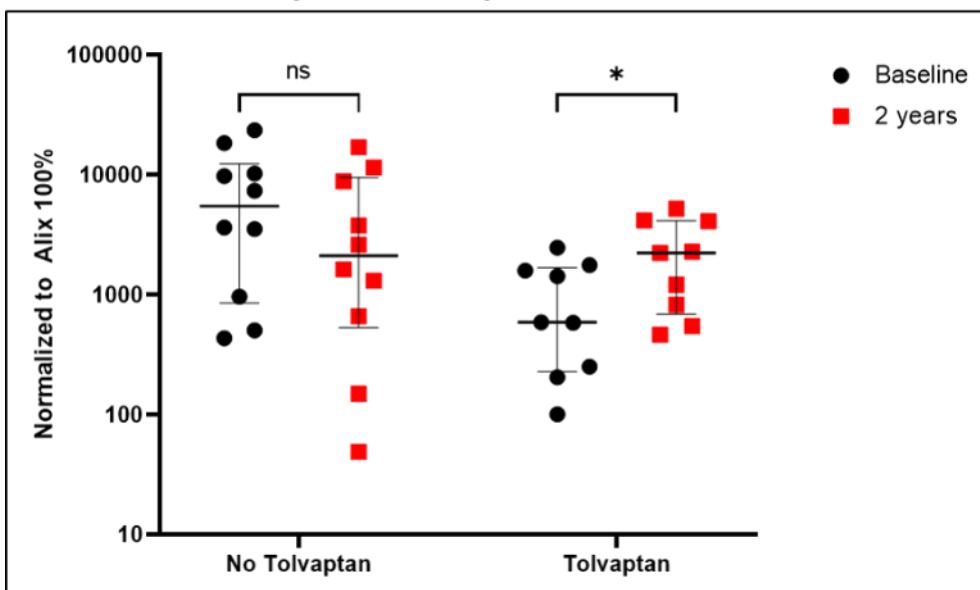
urines. Second morning spot urines with freshly added protease inhibitors were used to isolate urinary exosome proteins with an already established differential centrifugation method. Primary polyclonal anti-rabbit antibodies for Pendrin and the B1 subunit of V-ATPase were used for immunoblotting. Changes in urinary exosome abundance were normalized by Alix (exosome housekeeping protein).

Results: 19 patients (9 with and 10 without Tolvaptan) were included in the final analysis. 5 patients were excluded because Alix was not detectable. Compared to baseline, urinary exosome Pendrin increased by 134.4% only in Tolvaptan-treated patients ($p < 0.01$) after two years. Pendrin abundance strongly and directly correlated with NGIA ($\rho = 0.75$, $p < 0.01$) at baseline, and inversely with NAE ($\rho = -0.51$, $p = 0.03$) during follow-up. Urinary HCO_3^- excretion was associated with Pendrin expression over time ($\rho = 0.73$, $p < 0.01$).

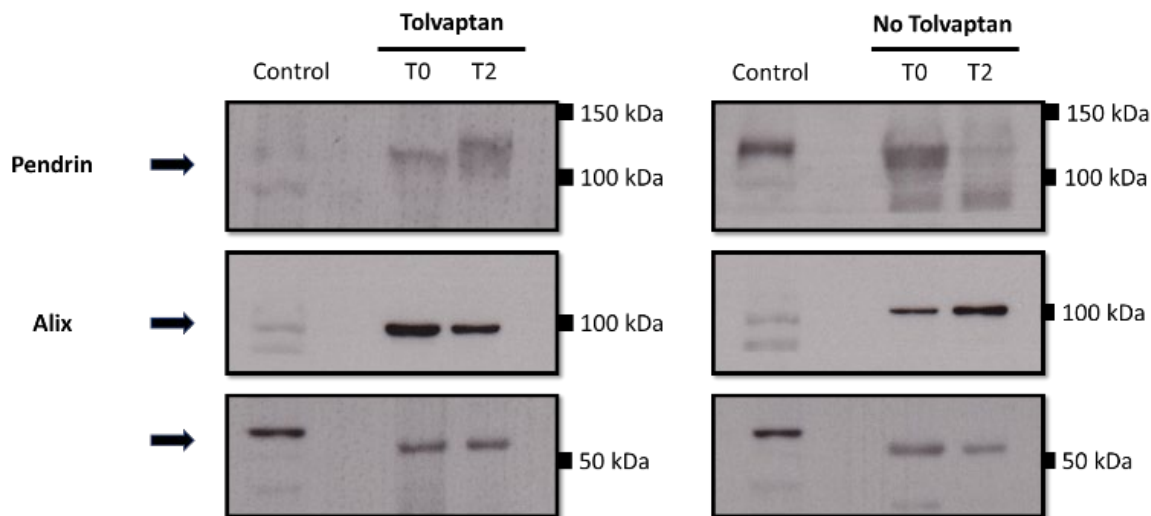
Conclusions: Urinary exosome Pendrin expression is sensitive to subtle changes in the acid-base status of ADPKD patients. Tolvaptan increases the expression of Pendrin in urinary exosomes, supporting the hypothesis that selective V2R blockade exerts an effect on systemic acid-base status of ADPKD patients.

YSN Submission

Urinary exosome pendrin abundance



Representative immunoblots in a patient with and without Tolvaptan



OC 07

Functional characterization of claudin-3 in renal cortical collecting duct

Dr. Ali SASSI¹, Ms. Alexandra Chassot¹, Prof. Eric FERAILLE¹

1. Department of Cellular Physiology and Metabolism, Faculty of Medicine, Geneva, Switzerland

Background: In the kidney, ion and fluid transport across epithelia can occur via the transcellular or paracellular pathways. Tight junctions play a key role in mediating paracellular ion reabsorption in the kidney. The renal collecting duct (CD) is the place of fine tuning of Na⁺ reabsorption and it is mainly regulated by aldosterone. Aldosterone classically regulates Na⁺ transport through the transcellular pathway. We hypothesized that aldosterone modulates also the paracellular pathway. Paracellular ion permeability is mainly dependent on tight junction proteins expressed along the CD.

Methods: We used cultured mouse CD principal cells and mouse models to study the effects of aldosterone on claudin-3. WT and claudin-3 knockout male mice were fed for 7 days with either low (0.01%), normal (0.18%) or high sodium (1.25%) diet. One group of mice fed a low sodium diet received 0.35 mg/100g body wt/day of spironolactone for 7 days.

Results: We showed that aldosterone increased protein levels of claudin-3 in cultured CD principal cells. Overexpression of claudin-3 was associated with a reduction in paracellular permeability to sodium and chloride, whereas silencing of claudin-3 was associated with the opposite effect. We also showed that a low-salt diet, which stimulated aldosterone secretion, was associated with increased claudin-3 abundance in the mouse kidney. Reciprocally, mice treated with spironolactone, a mineralocorticoid receptor antagonist, displayed decreased claudin-3 expression. Importantly, claudin-3 knockout mice displayed increased γ -ENaC and claudin-4 protein abundance under low-salt diet compared to WT mice.

Conclusions: Our results show that aldosterone modulates the expression of claudin-3 and that claudin-3 acts as paracellular NaCl barrier. We also show a specific adaptation of claudin-3 deficient mice to low-salt diet. Claudin-3 may then play an important role in preventing the backflow of reabsorbed NaCl

OC 08

Monogenic disease variants in the Swiss Kidney Stone Cohort and stone-free controls (NCCR project)

Dr. Johannes Münch¹, Dr. Joana Figueiró da Silva², Dr. Elena Cabello², Dr. Isabel Rubio Aliaga¹, Dr. Ivan Ivanovski², Mr. Michael Papik², Dr. Beatrice Oneda², Prof. Daniel Fuster³, Dr. Harald Seeger⁴, Dr. Thomas Hernandez⁵, Dr. Florian Buchkremer⁶, Prof. Gregoire Wuerzner⁷, Dr. Nasser Dhayat⁸, Dr. Alexander Ritter⁴, Dr. Catherine Stoermann-Chopard⁵, Dr. Stephan Segerer⁶, Prof. Anita Rauch², Prof. Olivier Bonny⁹, Prof. Carsten Wagner¹, Prof. Ruxandra Bachmann-Gagescu²

1. Institute of Physiology, University of Zürich, Zürich, Switzerland, 2. Institute of Medical Genetics, University of Zurich, Zurich, Switzerland, 3. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland, 4. Division of Nephrology, University Hospital Zürich, Zürich, Switzerland, 5. Service of Nephrology, Geneva University Hospitals, Geneva, Switzerland, 6. Medizinische Universitätsklinik, Abteilung für Nephrologie, Kantonsspital Aarau, 7. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 8. B. Braun Medical Care AG, Nephrology & Dialysis Care Center, Hochfelden, Zürich, Switzerland, 9. Service of Nephrology, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland

Background: With a lifetime prevalence of 10%, kidney stones (KS) are among the most common diseases. KS disease (KSD) has a complex pathogenesis influenced by a variety of factors, including dietary intake, fluid consumption, metabolic abnormalities, and a genetic predisposition. A thorough understanding of both the genetic and biochemical factors is crucial for a better diagnosis, therapy and prevention.

Methods: The Swiss Kidney Stone Cohort (SKSC) is a multicenter longitudinal observational study consisting of two distinct groups: Kidney stone formers (KSF) and matching non-KSF (NKSF). Blood and urine samples were collected at baseline (KSF, NKSF) and periodically over a 3-year period (KSF). Exome sequencing was performed in all participants, and variants in established KSD genes were assessed according to the ACMG/AMP criteria with subsequent genotype/phenotype analysis for KSF and NKSF.

Results: 731 KSF and 201 NKSF were included. A diagnosis of monogenic KSD was established in 10.1% of KSF. (Likely) pathogenic variants were predominantly located in genes encoding proteins involved in phosphate/calcium metabolism (*SLC34A1*, *SLC34A3*, *ALPL*, *CYP24A1*) or cystinuria (*SLC3A1*, *SLC7A9*). Of note, 4.5% of NKSFs also carried (likely) pathogenic variants in KSD genes and displayed matching biochemical parameters

(e.g., NKSF with *SLC34A1* variants had comparable reduction of Tmp/GFR). Additionally, our follow-up revealed that KSFs with monogenic KSD showed a significantly steeper decrease in eGFR over a 36-month period (Δ eGFR -4.9 vs. -2.0 mL/min/1.73 m², $p = 0.027$).

Conclusion: The SKSC is the hitherto largest genetically analyzed KS cohort, accompanied by a control group of confirmed NKSF. The comparison with NKSFs, who also carried (likely) pathogenic variants in KS genes, suggests that KS occurrence may depend on additional factors that may be either genetic (additional rare or common variants) or environmental. The results from genetic analysis in KS genes can help identify patients at risk for a faster decline in kidney function.

YSN submission

OC 09

Computer based nutritional training in dialysis patients

Dr. Andreas Schliech¹, Dr. Rolf Pachlatko¹

1. Stadtspital Zürich, Zürich, Schweiz

Introduction: Kidney failure forces dialysis patients to follow a strict diet to avoid electrolyte and volume imbalances. Current guidelines recommend reduced consumption of sodium, phosphate and potassium. It is assumed, that better compliance with these guidelines results in improved control of these critical components in the blood.

Method: We developed a computer-based training application in the form of an electronic quiz. Our dialysis population was subjected to this application during dialysis sessions during one month. The working hypothesis was that use of this instrument results in a significant improvement in serum potassium, and phosphate as well as volume status after one month of training.

Results: Forty-eight dialysis patients with a mean age of 66 years solved an average of 1'100 questions within the study period. There was no significant difference compared in blood values and volume status compared to the months before the quiz training. However, improvement of potassium levels was significantly associated with the numbers of questions solved.

Conclusion: A computer-based training application has no beneficial impact on patient's compliance [amp011] regarding better control of serum potassium and phosphate values or intradialytic weight gain. However, the effect may depend on the intensity of training.

OC 10

Residual kidney function at one-year in diabetic and non-diabetic incident patients treated with incremental hemodialysis

Prof. Patrick Saudan¹, Dr. David Jaques¹, Prof. Belén Ponte¹, Dr. Anne Dufey¹, Dr. Fadi Haidar¹, Prof. Sophie De Seigneux¹

1. Service of Nephrology and Hypertension, Department of Medicine, Geneva University Hospitals, Switzerland

Background: Residual kidney function (RKF) is better preserved with incremental haemodialysis (I-HD) as compared to conventional thrice-weekly HD (TW-HD). Presence of diabetes is associated with a faster decline of RKF in TW-HD. We aimed to analyze the RKF decline at one-year in diabetic versus non-diabetic patients initiating dialysis with I-HD.

Methods: We conducted an analysis of a prospectively assembled cohort in a single university centre including all adults initiating I-HD from January 2013 to July 2022. Outcomes were maintenance of incremental dialysis at one year and RKF decline at one year (or transition to TW-HD) according to the presence of diabetes.

Results: Of 289 patients who started hemodialysis, 106 initiated dialysis with I-HD of whom 38 were diabetics. At dialysis initiation, age, eGFR, comorbidity score, daily diuresis and urea clearance (KrU) were similar between non-diabetic and diabetic patients. Transition to TW-HD occurred after a mean duration of 16 +/- 14 months and 11 +/- 9 months in non-diabetic and diabetic patients respectively ($p = 0.03$). At one year, the percentages of non-diabetic patients and diabetic patients still on I-HD were 49% and 40% respectively ($p = 0.046$). At one-year, non-diabetic and diabetic patients had a daily diuresis decline of 31 and 38% ($p = 0.26$) and a KrU decline of 34 and 45% ($p = 0.07$) respectively.

Conclusions: RKF decline is more rapid in incident diabetic patients versus non-diabetic patients treated with I-HD and its duration before transition to TW-HD is shorter in patients with diabetes. Nephrologists should be aware that transition to TW-HD could be faster in diabetic patients.

OC 11

The urine-to-plasma urea concentration ratio: a new marker of kidney function decline in three independent studies

Dr. Lise BANKIR¹, Dr. Ragnar PALSSON², Dr. Dusan PETROVIC³, Prof. Murielle BOCHUD⁴, Prof. Belén Ponte⁵

1. Centre de Recherche des Cordeliers, INSERM, Sorbonne Université, CNRS, ERL 8228, Paris, France 2. Division of Nephrology, Dpt of Medicine, Mass. General Hospital, Boston, Massachusetts, US 3. University Center for General Medicine and Public Health (UNISANTE), Lausanne, Switzerland 4. University Center for General Medicine and Public Health (UNISANTE), Lausanne, Switzerland 5. Department of Nephrology and Hypertension, Geneva University Hospitals, Geneva, Switzerland

Urea is the most abundant solute in the urine, and this large load is markedly concentrated in urine compared to plasma. Urea handling by the kidney participates in overall urine concentration, but it also serves mainly its own concentration. The best way to evaluate the kidney's ability to concentrate urea is to calculate the urine-to-plasma urea concentration ratio (U/P-urea-ratio).

In 2012, Bankir and Bichet described a "urea-specific" urine concentrating defect in patients with ADPKD. This prompted epidemiologic studies evaluating the U/P-urea-ratio as a possible predictor of kidney function decline. Here, we review 3 existing studies (Table 1): in ADPKD patients (Study1), in patients with CKD (excluding ADPKD by design) (Study2), and in a general adult population (Study3).

These studies reveal very similar results, both in cross-sectional and in longitudinal analyses over several years of follow-up (Table 2). In all studies, U/P-urea-ratio was positively associated with eGFR at baseline. Furthermore, a higher U/P-urea-ratio was associated with slower eGFR decline over time, independently of usual biomarkers. In ADPKD patients, cysts compromise the intrarenal urea recycling that promotes high urea concentration in inner medulla. But even without cysts, a decline in the ability to concentrate urea predicts a faster loss of kidney function (Studies 2+3). Moreover, Study 3 shows that the U/P-urea-ratio (based on a 24h urine collection under normal conditions) is more sensitive than the U/P ratio of urine osmolarity or of other individual solutes (Na, K, and uric acid).

The U/P-urea-ratio is an early marker of kidney function decline, independent of glomerular biomarkers. It reflects transport functions that occur along the renal tubule and collecting duct. Urea is easy to measure with well-standardized techniques, and at low cost. Altogether, these three studies should stimulate further investigation of the U/P-urea-ratio as an early prognostic biomarker for chronic kidney disease.

Table 1. Baseline characteristics

| | Study | Reference | N (% males) | Age, y | BMI, kg/m ² | eGFR ml/minx1.73 m ² | U/P urea |
|---|--|-----------------------------|----------------|---------|---------------------------|---------------------------------------|-----------------|
| 1 | ADPKD patients (DIPAK cohort) | Heida et al, CJASN 2021 | 583 (42%) | 47 ± 11 | 26.0 ± 4.6 | 64 ± 24 | 20 [17-36] |
| 2 | CKD patients, (CRIC cohort) | Liu et al, AJKD 2023 | 3723 (55%) | 58 ± 11 | 32.1 ± 7.8 | 44.3 ± 15.0 | 14.8 [9.5-22.2] |
| 3 | General population cohort (SKIPOGH) | Petrovic et al, NDT 2023 | 1043 (48%) | 48 ± 17 | 25.1 ± 4.5 | 96.4 ± 17.9 | 51.3 ± 23.7 |

Table 2. Associations of the U/P-urea-ratio with eGFR decline during follow-up

| | Follow-up duration | Selected Outcomes and Results |
|---|--|---|
| 1 | 4.0 [2.6-5.0] y | <ul style="list-style-type: none"> • Association of ln(U/P-Urea) with eGFR decline, per 1 unit higher: $\beta = 0.57$, $p=0.02$ after adjusting for age, sex, eGFR, PKD mutation, and Mayo Clinic htTKV class. • Odds ratio for rapidly progressive disease (defined as decline by ≥ 3.0 mL/minx1.73m²), per 10 unit decrease in U/P-Urea: 1.35 (95% CI 1.19-1.52; $P<0.001$), after adjusting for sex, PKD mutation, and Mayo Clinic htTKV class. • Combining Mayo Clinic htTKV class, PKD mutation, and the U/P-urea-ratio into a disease severity score predicted rapidly progressive disease better than these predictors individually. |
| 2 | 7.0 [3.0-11.0] y | <ul style="list-style-type: none"> • Association of ln(U/P-Urea) with eGFR slope, per 1-SD lower: $\beta = -0.38$ (CI, -0.46 to -0.30) in fully adjusted model • Lower U/P-urea at baseline associated with more rapid eGFR decline and with development of kidney failure, independent of other major risk factors for CKD progression. |
| 3 | Two study visits, separated by 36.3 ± 4.7 m | <ul style="list-style-type: none"> • Association of U/P-Urea with eGFR difference in fully adjusted model: $\beta = 0.08$ (95% CI, 0.04-0.13), $p < 0.001$ • When stratified by eGFR, the above association was significant only among those with eGFR < 90 ml/minx1.73m², but not among those with eGFR > 90 ml/minx1.73m² • Participants with a lower U/P-Urea at baseline displayed a greater decline in eGFR than those with a higher U/P-Urea at baseline |

Notes: eGFR, estimated glomerular filtration rate; PKD, polycystic kidney disease; htTKV, height-adjusted total kidney volume; U/P-Urea, U/P-urea-ratio; SD, standard deviation.

OC 12

Apixaban drug level monitoring in hemodialysis

Dr. Simeon Schietzel¹, Dr. Andreas Limacher², Dr. Matthias Moor¹, Dr. Cecilia Czerlau³, Prof. Bruno Vogt⁴, Dr. Fabienne Aregger¹, Prof. Dominik UEHLINGER⁵

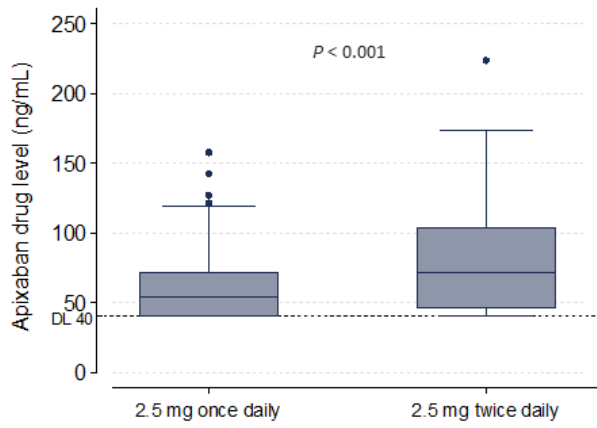
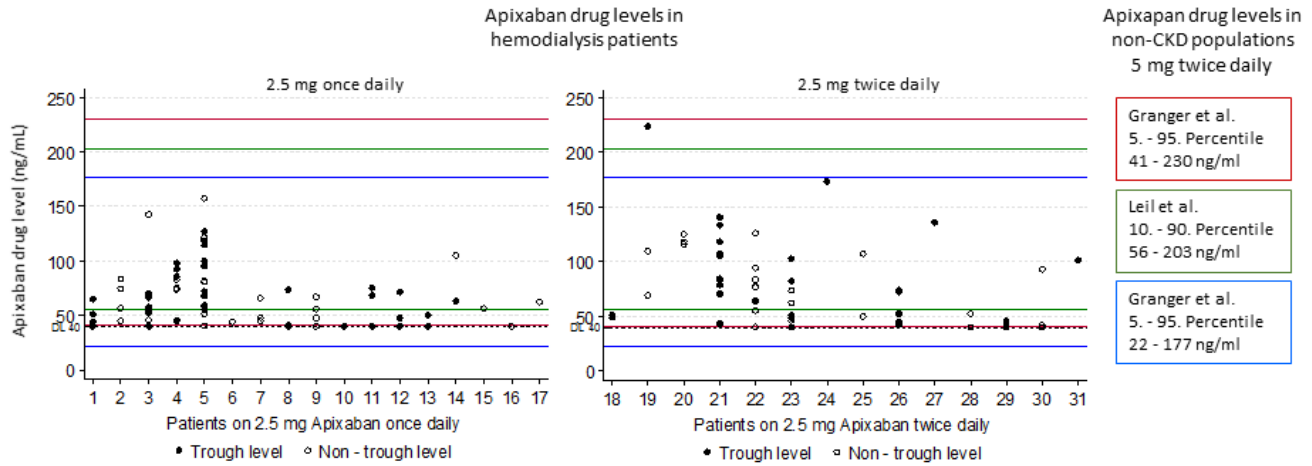
1. Division of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., 2. CTU Bern, University of Bern, Bern, Switzerland., 3. Division of Nephrology, Central Hospital Biel, Biel, Switzerland., 4. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland., 5. Universitätsklinik für Nephrologie und Hypertonie, Inselspital Bern

Background: Apixaban is increasingly being used in hemodialysis patients. However, uncertainty remains regarding appropriate dosing and risk of accumulation.

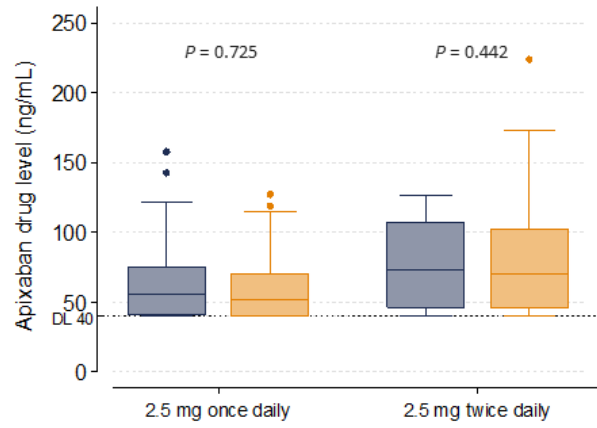
Methods: We analyzed apixaban drug levels from a tertiary care dialysis unit collected between August 2017 and January 2023. We compared 2.5 mg once versus twice daily dosing. We applied mixed-effects models analyses including dialysis modality, adjusted standard Kt/V, ultrafiltration and dialyzer characteristics.

Results: We analyzed 143 apixaban drug levels from 24 patients. Mean (SD) age was 64.2 (15.3) years (45.2% female), median (IQR) follow up 12.5 (5.5 – 21) months. For the 2.5 mg once and twice daily groups, median (IQR) drug levels were 54.4 (<40 – 72.1) and 71.3 (48.8 – 104.1) ng/mL ($P<0.001$). Drug levels were below the detection limit in 30% and 14%. Only dosing group (twice versus once daily) was independently associated with higher drug levels ($P= 0.002$). Follow-up did not suggest accumulation. 95th percentile did not exceed those of non-CKD populations taking 5 mg twice daily. Drug levels before a bleeding (8 episodes) were significantly higher than those without a subsequent bleeding: 115 (SD 51.6) versus 65.9 (SD 31.6) ng/mL ($P<0.001$). Patients with versus without a bleeding took concomitant antiplatelet therapy in 86% versus 6% ($P<0.001$). In 21% of patients, drug level monitoring resulted in change of dosing.

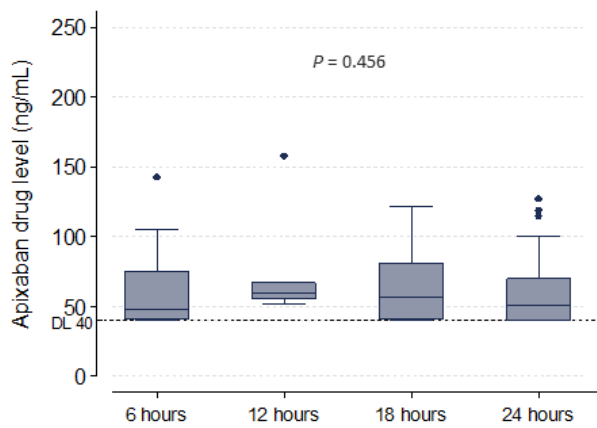
Conclusions: Apixaban drug monitoring might be a contributory tool to increase safety in patients on hemodialysis. Further prospective outcome studies are warranted to investigate possible target levels.



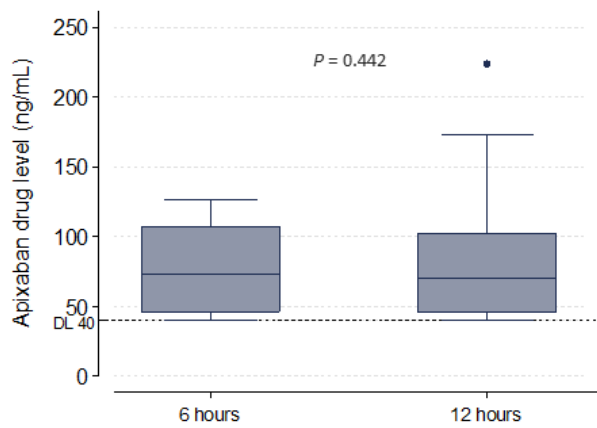
1a. Drug levels (all) per dosing group.



1b. Non - trough (blue) vs. through levels (yellow).



1c. Drug levels per time point after intake (2.5 mg once daily).



1d. Drug levels per time point after intake (2.5 mg twice daily).

Table 3. Mixed-effects model with 3 level of multivariate adjustments.

| Log Apixaban drug level | Model 1 | | Model 3 | | Model 3 | |
|---|-----------------------------|--------|----------------------------|-------|---|----------------------|
| | Coefficient (95% CI) | P | Coefficient (95% CI) | P | Coefficient (95% CI) | P |
| Dosing 0 = 1 x 2.5 mg, 1 = 2 x 2.5 mg | 0.16 (.09 to -.24) | <0.001 | .142 (0.055 to 0.228) | 0.001 | .13 (0.05 to 0.22) | 0.002 |
| Age (y) | -0.002 (-0.005 to 0.001) | 0.30 | -.002 (-0.005 to 0.001) | 0.27 | -.002 (-0.005 to 0.001) | 0.15 |
| Sex 0 = female, 1 = male | .001 (-0.091 to 0.093) | 0.98 | -.003 (-0.095 to 0.089) | 0.95 | .028 (-0.06 to 0.11) | 0.51 |
| BMI (Kg/m²) | .000 (-0.005 to 0.006) | 0.93 | -.000 (-0.006 to 0.006) | 0.97 | .003 (-0.002 to 0.009) | 0.25 |
| Time after intake 6, 12, 18, 24 (h) | | | -.002 (-0.007 to 0.003) | 0.35 | -.002 (-0.007 to 0.003) | 0.35 |
| UF-adj. standard Kt/V | | | | | .104 (-0.02 to 0.23) | 0.1 |
| Dialysis modality 0 = HD, 1 = HDF | | | | | .061 (-0.02 to 0.14) | 0.15 |
| Dialyzer surface area (1 - 2.5 m ²) | | | | | -0.03 (-0.14 to 0.08) | 0.63 |
| Dialyzer Brand / Material 1 = Baxter Nephral/Actyl* 2 = Fresenius CorDiax/PES** 3 = Braun Xevonta/PSU*** 4 = Fresenius CorAL/PSU-PVP**** | | | | | Reference -0.02 (-0.16 to 0.12) -0.1 (-0.23 to 0.04) - 0.09 (-0.23 to 0.04) | 0.77 0.16 0.18 |
| Ultrafiltration per week L | | | | | -0.002 (-0.011 to 0.008) | 0.72 |
| Wald Chi2 | 21.8 | | 22.7 | | 35.7 | |
| No participants | 24 | | 24 | | 24 | |
| No observations | 143 | | 143 | | 143 | |

* Acrylonitrile and Sodium methallyl sulfonate blend. ** Polyethersulfone. *** Polysulfone.

**** Polysulfone + increased polyvinylpyrrolidone

OC 13

The Swiss Kidney Biopsy Registry - rationale and design

Prof. Andreas KISTLER¹

1. Kantonsspital Frauenfeld, Frauenfeld, Switzerland

Background: Apart from hypertensive and diabetic kidney disease, most etiologies of CKD are relatively rare. Many of these renal diseases are diagnosed by kidney biopsy. Their treatment options are still limited, but promising therapeutic approaches are emerging. Owing to the decentralized Swiss health care system, epidemiologic data on specific kidney diseases are largely unavailable and patient recruitment for observational, translational and interventional studies is challenging.

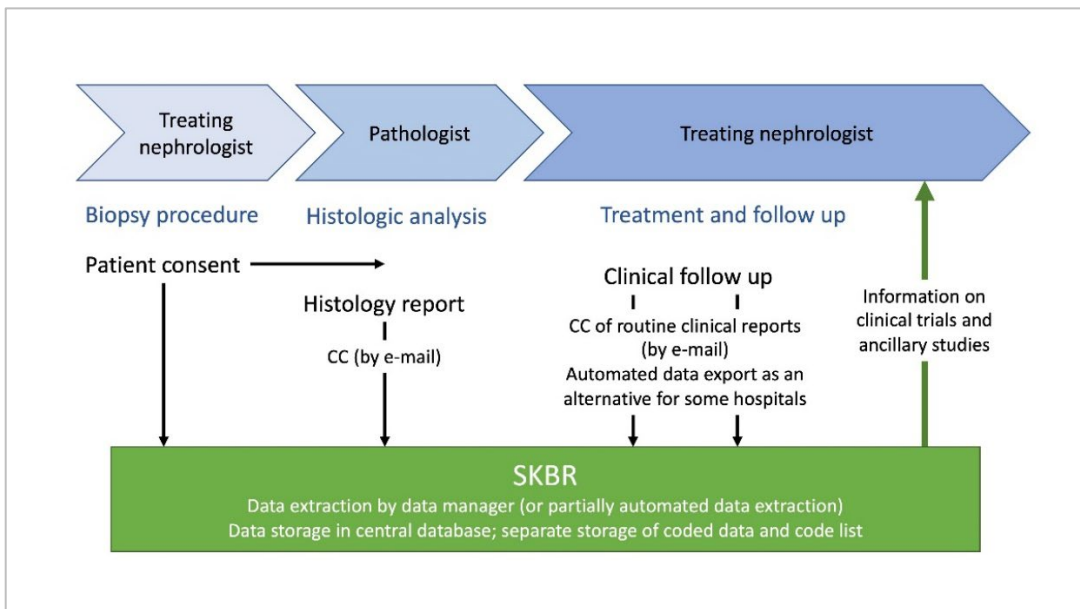
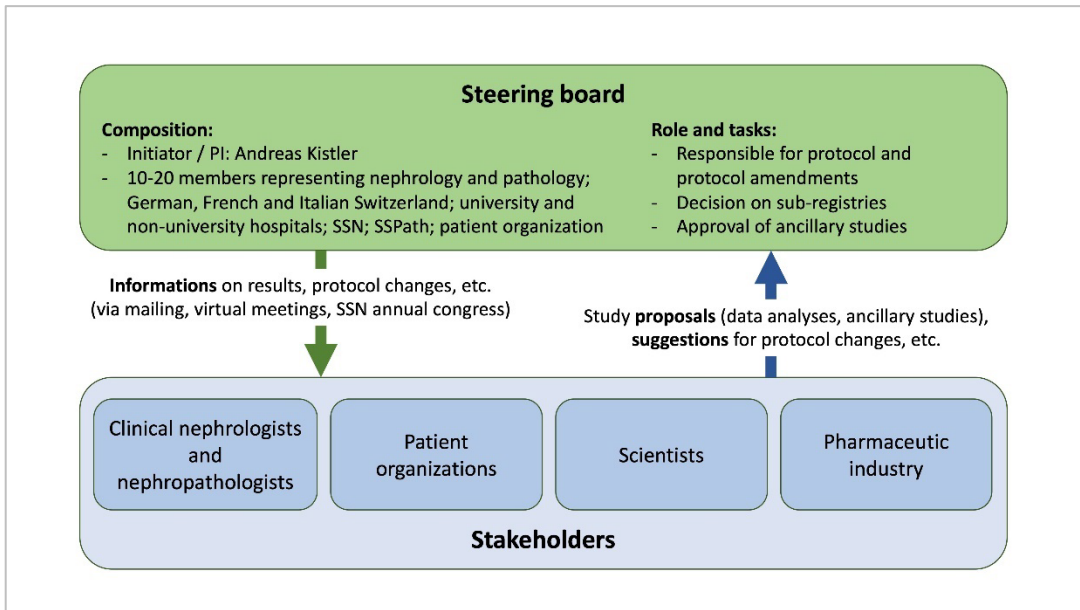
Methods: A Swiss Kidney Biopsy Registry (SKBR) steering board has been constituted with nephrologists and nephropathologists from university- and non-university-hospitals of all parts of Switzerland (Figure 1). Patient inclusion is planned to be started in early 2024. Before kidney biopsy, consent for the SKBR will be sought from patients together with their consent for the biopsy procedure. The data collection process will be

organized in a way that imposes minimal work load to clinicians (Figure 2), using primarily data extraction from routine clinical reports to be sent in CC by secure e-mail to the SKBR, or by automated electronic health record data transfer for select hospitals. Baseline data will be collected about all adult patients undergoing kidney biopsy in Switzerland and a subset of patients with specific diseases will be followed longitudinally in sub-registries. Data transfer to registries with an overlapping scope will be aimed for (Figure 3). Kick off funding for the project has been raised from pharmaceutical companies. Long term funding will be sought from industry, foundations and public sources.

Results: Results from first analyses on epidemiological data are to be expected by the end of 2024. The current status of the SKBR project will be presented at the meeting.

Conclusions: The SKBR will close a knowledge gap on the epidemiology of histologically defined kidney diseases in Switzerland and provide a platform for observational, translational and interventional research and to optimize patient care.

YSN submission



OC 14

The Molecular Microscope Diagnostic System (MMDx®) does not identify ABMR in the presence of DSA but absence of histological antibody-mediated changes

Dr. Dusan Harmacek¹, Mr. Kai Castrezana Lopez¹, Dr. Nicolas Schmid¹, Dr. Lukas Weidmann¹, Dr. Raphael Korach², Dr. Nicola Borte¹, Dr. Birgit Maria Helmchen³, Dr. Ariana Gaspert³, Dr. Elena Rho¹, Prof. Thomas F. Mueller¹, Dr. Thomas Schachtner¹

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. Division of Nephrology, University Hospital Zurich, Switzerland, 3. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland

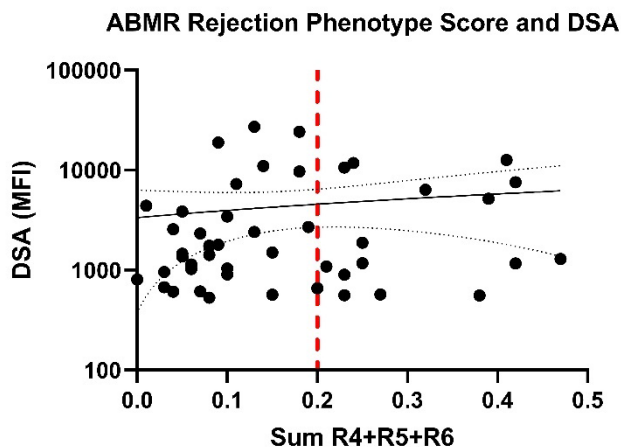
Background: The development of de novo donor-specific antibodies (DSA) or an increase in MFI values of preformed DSA are common indications for kidney allograft biopsies. If changes in transcript patterns analyzed by the Molecular Microscope Diagnostic System (MMDx®) may precede histological antibody-mediated changes and identify subclinical antibody-mediated rejection (ABMR) remains uncertain.

Methods: In this single-center cohort of 326 kidney transplant biopsies assessed by histology and MMDx® at the University Hospital Zurich, we analyzed 128 cases with no glomerulitis (g0) and no ABMR (not meeting Banff 2019 ABMR criteria 1 and 2) concerning the presence (n = 47) and absence (n = 81) of DSA (DSA+ and DSA-, respectively).

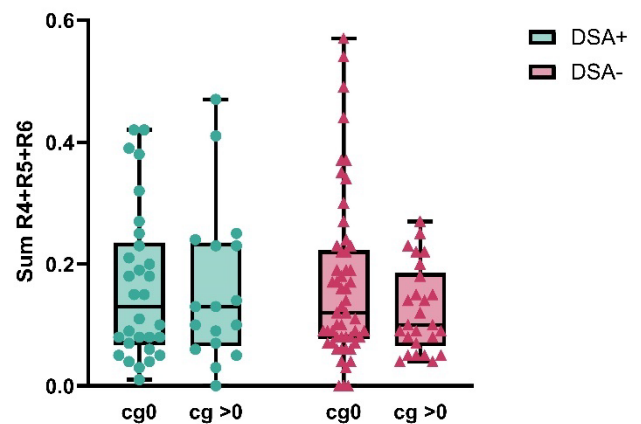
Results: Kidney allograft biopsies in the presence of DSA were performed later post-transplantation (median 47 months, IQR 15–89) compared to DSA- biopsies (median 13 months, IQR 3–98; p = 0.03). Molecular ABMR was observed in 0/47 cases (0%) in the DSA+ and 3/81 cases (4%) in the DSA- group (all 3 cases of mixed molecular ABMR/TCMR; 2 with histological TCMR). The median all ABMR rejection score (sum of scores R4+5+6) did not differ between the DSA+ (0.13, IQR 0.07–0.23) and DSA- (0.11, IQR 0.075–0.21; p = 0.77) group. We did not detect any association between all ABMR score and MFI of DSA. We found a weak correlation between all ABMR score and serum creatinine (r = 0.2870 (95% CI 0.1143 to 0.4429), p = 0.001). Patients with a higher all ABMR score had a higher serum creatinine (p < 0.001) and were more often retransplanted (p = 0.04). The proportion of biopsies with cg>0 was the same irrespective of DSA status.

Conclusion: MMDx does not differentiate subclinical ABMR in the presence of DSA and/or transplant glomerulopathy but in the absence of histological antibody-mediated changes. If minor molecular changes are meaningful, at least in a subgroup of cases, needs to be assessed in the context of follow-up biopsies.

YSN submission



ABMR Rejection Phenotype Score and cg Score



OC 15

First successful treatment of a patient with a primary immune complex-MPGN with iptacopan – a selective inhibitor of factor B

Dr. Simone Arnold¹, Dr. Manuela Nickler², Prof. Michael Dickmann¹, Dr. Thomas Menter³, Prof. Helmut Hopfer³, Dr. Patricia Hirt-Minkowski¹

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 2. Division of Nephrology/Haemodialysis Cantonal Hospital Olten, Olten, Switzerland 3. Institute for Pathology, University Hospital Basel, Basel, Switzerland

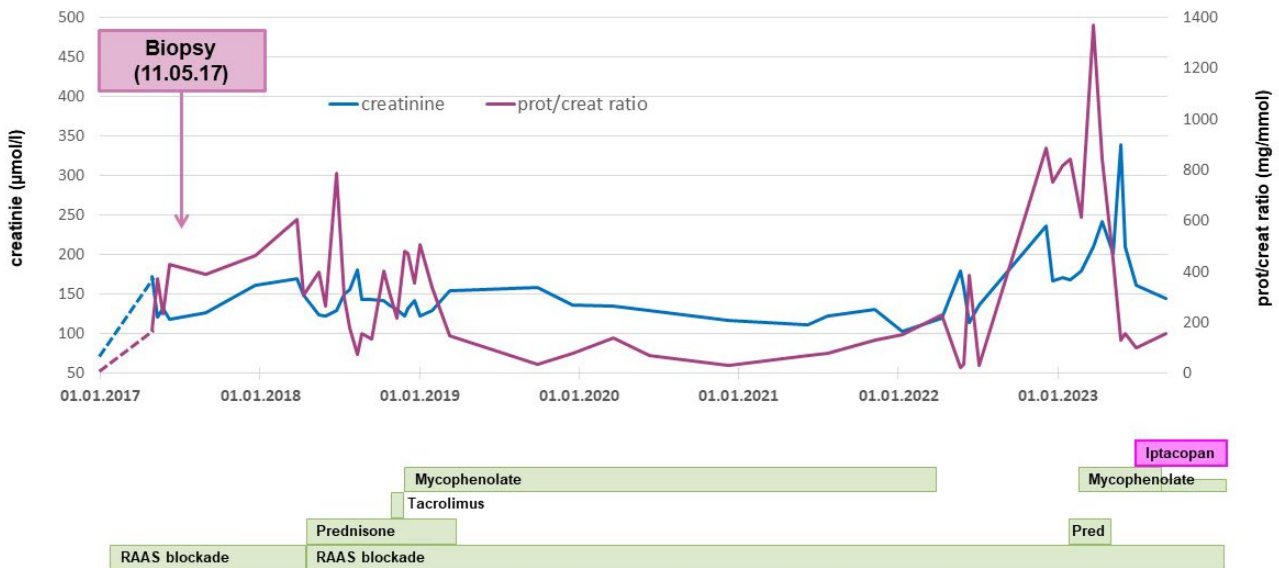
Background: Nowadays, there is insufficient evidence for the recommendation of management patients with a primary membranoproliferative glomerulonephritis (MPGN), taking into account the new classification system. We report the first successful treatment of a 47-year-old man suffering from a biopsy-confirmed primary immune complex-MPGN with iptacopan.

Case description: A male patient with newly diagnosed primary immune complex-MPGN was first treated with a conservative therapy with blockade of the renin-angiotensin-system (RAS). However, despite RAS blockade urine protein-creatinine ratio (UPCR) raised to a maximum of 607 mg/mmol within the following months which no longer justified a sole conservative therapy. Briefly, a therapy with glucocorticosteroids was started, followed by an immunosuppressive therapy with mycophenolate (Figure 1). As during the follow-up, the established immunosuppressive therapies failed to control the disease, there was an urgent need for an experimental rescue therapy. Thus, a request was made to the company to timely obtain iptacopan for this patient. Three months after starting the treatment with iptacopan UPCR decreased impressively to a level of around 100-150 mg/mmol (Figure 1).

Learning point: Although a better understanding of the pathogenesis of idiopathic MPGN has led to the reclassification of the glomerular disease, we must keep in mind that nowadays no evidence from randomized clinical trials or case series exists for the treatment of primary immune-complex MPGN based on the new classification. However, there is consensus that for the management of patients with primary immune-complex MPGN newer data do not longer support the global application of broad-spectrum immunosuppression, but rather a more individualized approach.

Conclusions: Our case report provides evidence that iptacopan may be a promising treatment option for primary immune complex-MPGN with respect to efficacy and safety. However, to address this issue, further studies are warranted.

YSN submission / student submission



OC 16

The Molecular Microscope Diagnostics System (MMDx) may have the potential to differentiate molecular T Cell-mediated rejection among kidney transplant recipients with chronic-active T cell-mediated rejection

Dr. Nicola Borte¹, Dr. Dusan Harmacek¹, Dr. Lukas Weidmann¹, Mr. Kai Castrezana Lopez¹, Dr. Nicolas Schmid¹, Dr. Raphael Korach², Dr. Birgit Maria Helmchen³, Dr. Ariana Gaspert³, Dr. Elena Rho¹, Prof. Thomas F. Mueller¹, Dr. Thomas Schachtner⁴

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. Division of Nephrology, University Hospital Zurich, Switzerland, 3. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland 4. department of Nephrology, University Hospital Zurich, Switzerland

Background: Treatment of chronic-active T Cell-mediated rejection (caTCMR) lacks consensus, causing many different therapeutic approaches. If changes in transcript patterns analyzed by the Molecular Microscope Diagnostic System (MMDx) may differentiate among these cases with caTCMR and offer additional diagnostic value needs to be evaluated.

Methods: In this single-center cohort of 341 indication kidney transplant biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 18 cases with caTCMR after the exclusion of overlapping pathologies such as BK nephropathy, pyelonephritis, and acute interstitial nephritis. 9 cases with combined acute TCMR and caTCMR were compared to 9 cases with caTCMR only.

Results: 3 of 9 cases (33%) with combined acute TCMR and caTCMR, and 1 of 9 cases (11%) with caTCMR only showed pure molecular TCMR. In addition, 4 of 9 cases (44%) with combined acute TCMR and caTCMR, and 3 of 9 cases (33%) with caTCMR only showed mixed molecular ABMR/TCMR with histologic ABMR in 4 of 7 cases (57%). Among 4 of 9 cases (44%) with caTCMR only but no molecular rejection, 2 cases showed an all ABMR rejection phenotype score (sum of R4, R5, and R6) ≥ 0.20 , and 1 case showed a TCMR phenotype score (R2) ≥ 0.10 .

Conclusion: The MMDx may have the potential to differentiate histologic caTCMR into molecular TCMR, molecular ABMR/TCMR, or no molecular rejection. Whether the observed minor molecular findings are attributable to undetected overlapping findings other than rejection, cortex/medulla sampling variations, or a suspected continuum of caTCMR needs to be studied.

YSN submission / student submission

OC 17

Acute post-renal kidney graft dysfunction due to cytomegalovirus-positive nephrogenic adenoma after deceased donor kidney transplantation

Dr. Nicola Hosek¹, Dr. Matteo Montani², Dr. Laila-Yasmin Mani³

1. Department of medicine, Division of Nephrology and Dialysis, Kantonsspital Graubünden, Chur, Switzerland, 2. Institute of Tissue Medicine and Pathology, University of Bern, Bern, Switzerland, 3. Service of Nephrology, Bern University Hospital, Switzerland

Background: Tissue-invasive cytomegalovirus (CMV) disease represents a well-recognized complication after kidney transplantation. However, direct involvement of the urogenital tract and CMV-ureteritis occur less frequently. Nephrogenic adenomas are benign lesions of the urinary tract preferentially reported in kidney transplant recipients. We herein report the case of a kidney transplant recipient with acute post-renal allograft dysfunction due to CMV-positive ureteral nephrogenic adenoma.

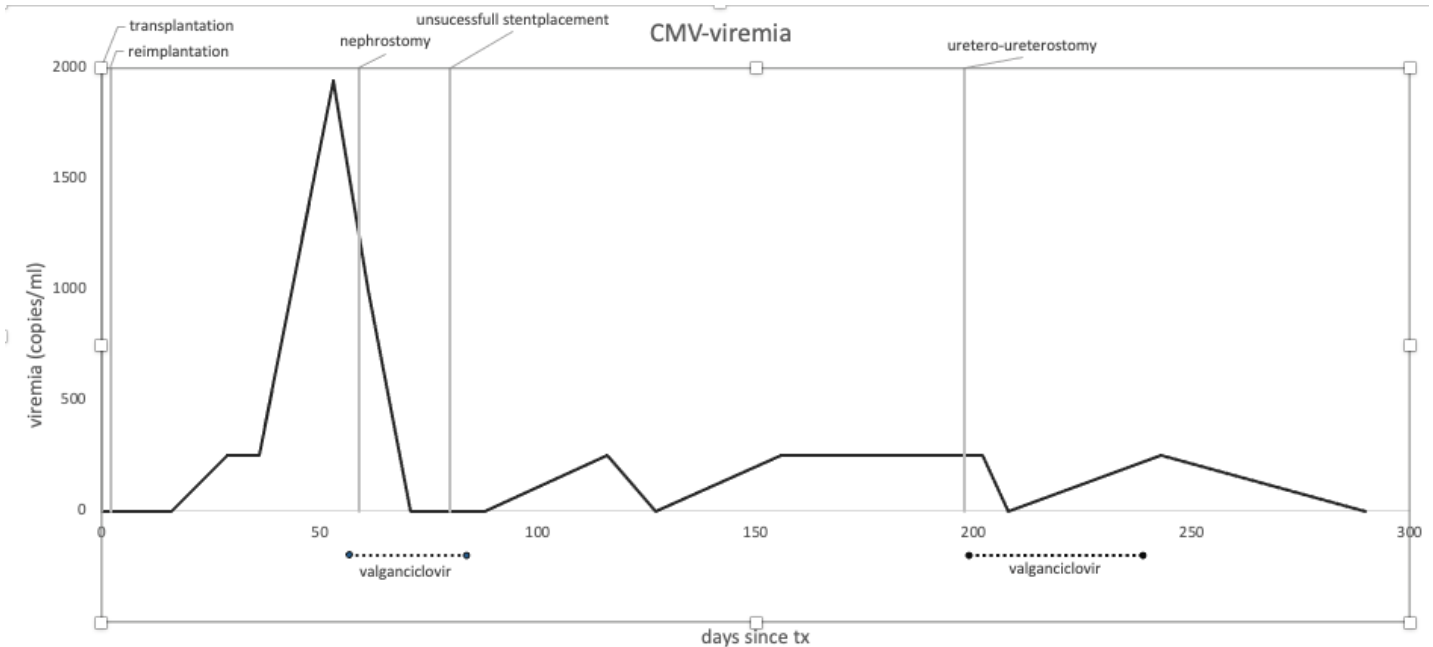
Case description: A 33 year-old male African patient with end-stage kidney disease due to hypertensive nephropathy received a kidney transplant from a deceased donor. Postoperative dissection of the common iliac artery required explantation, arterial reconstruction and allograft re-implantation. The immunosuppressive regimen included basiliximab, ciclosporin, mycophenolate mofetil and steroids. According to preemptive approach and serologic constellation (donor and recipient CMV-positive), regular CMV viremia monitoring was performed. Two months after transplantation, an acute rise in serum creatinine and new-onset hematuria were noted. Duplex ultrasound of the graft showed new-onset hydronephrosis grade III. In addition, CMV viremia of 1940 copies/ml was detected. Percutaneous nephrostomy was placed and antiviral therapy with valganciclovir was started for four weeks until clearance of CMV viremia. Antegrade pyelography visualized a stenotic lesion in proximity to the bladder motivating uretero-ureterostomy with the native ureter after unsuccessful ureteral stent placement. Histological analysis showed nephrogenic adenoma of the resected ureter with positive CMV immunohistochemical staining without evidence of concomitant graft involvement. Another

trial of valganciclovir was introduced for six weeks following surgery with uneventful further clinical course.

Learning point: CMV-ureteritis as well as nephrogenic adenomas are causes for post-renal kidney graft dysfunction. Diagnosis of tissue-invasive CMV disease generally requires histological evidence of CMV infection at the affected site.

Conclusions: To the best of our knowledge, this is the second published case of ureteral nephrogenic adenoma with evidence of CMV infection in a kidney transplant recipient. A causal link might be expected.

YSN submission



OC 18

Machine Learning Models for the Prediction of Kidney Stone Composition and Recurrence

Dr. Matteo Bargagli¹, Dr. Stephan Peischl², Prof. Bruno Vogt¹, Dr. Rémy Bruggmann², Prof. Daniel G. Fuster¹

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Interfaculty Bioinformatics Unit, University of Bern, Bern, Switzerland

Background: Kidney stones are prevalent and cause high patient morbidity and healthcare cost. Kidney stone treatment depends on stone type and recurrence risk. We hypothesized that machine learning (ML) methods provide higher accuracy compared to current approaches for stone type and recurrence risk prediction.

Methods: Data from three comprehensively phenotyped Swiss cohorts comprising 1505 kidney stone formers with demographic, anthropometric and clinical information, stone composition analysis, and 24-h urine measurements were included. Several supervised ML models, including logistic regression, parallel-tree boosting (XGBoost), random forests, and neural networks, were trained independently to predict the stone type and the 5-year recurrence risk.

Results: XGBoost performed with generally high specificity (>90%), except for calcium oxalate stones which demonstrated lower sensitivity. The algorithm achieved an accuracy of 85% when distinguishing between uric acid-containing and calcium phosphate-containing stones. Key features informing the model included age at first stone event, body mass index, 24h urine calcium and pH. The 5-year recurrence risk predicted by the neural network ranged between 48% and 83%, closely aligning with observed recurrence risk (R2 = 0.913).

Conclusion: The developed ML models demonstrated remarkable accuracy in predicting the risk of stone recurrence. These findings have the potential to address an unmet clinical need by assisting healthcare specialists in clinical decision-making, and ultimately enhancing patient outcomes and quality of life for those affected by recurrent kidney stone disease.

YSN submission

OC 19

Impact of natural killer cell functional genetics on microvascular inflammation in the presence of donor-specific antibodies

Dr. Matthias Diebold¹, Dr. Hannes Vietzen², Ms. Laura Kühner², Ms. Sarah Berger², Dr. Andreas Heinzl³, Dr. Carsten Herz³, Dr. Katharina Mayer³, Dr. Farsad Eskandary³, Dr. Konstantin Doberer³, Dr. Alexander Kainz³, Ms. Susanne Haindl³, Dr. Nicolas Kozakowski³, Prof. Elisabeth Puchhammer-Stöckl², Prof. Philip F. Halloran⁴, Prof. Georg A. Böhmig³

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, 2. Center for Virology, Medical University of Vienna, Vienna, Austria, 3. Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria, 4. Alberta Transplant Applied Genomics Centre, ATAGC, University of Alberta, Edmonton, AB Canada

Background: Antibody-mediated rejection (ABMR) is a leading cause of graft failure. While the exact mechanisms behind antibody-triggered injury are still unclear, there is emerging evidence for a contribution of natural killer (NK) cells to microvascular inflammation (MVI). To investigate whether genetically determined NK cell functionality affects ABMR activity, we conducted a cohort study to analyze associations of distinct NK cell receptor polymorphisms and the degree of killer immunoglobulin-like Receptor (KIR)-dependent missing self with the development of donor-specific antibody (DSA)-triggered MVI.

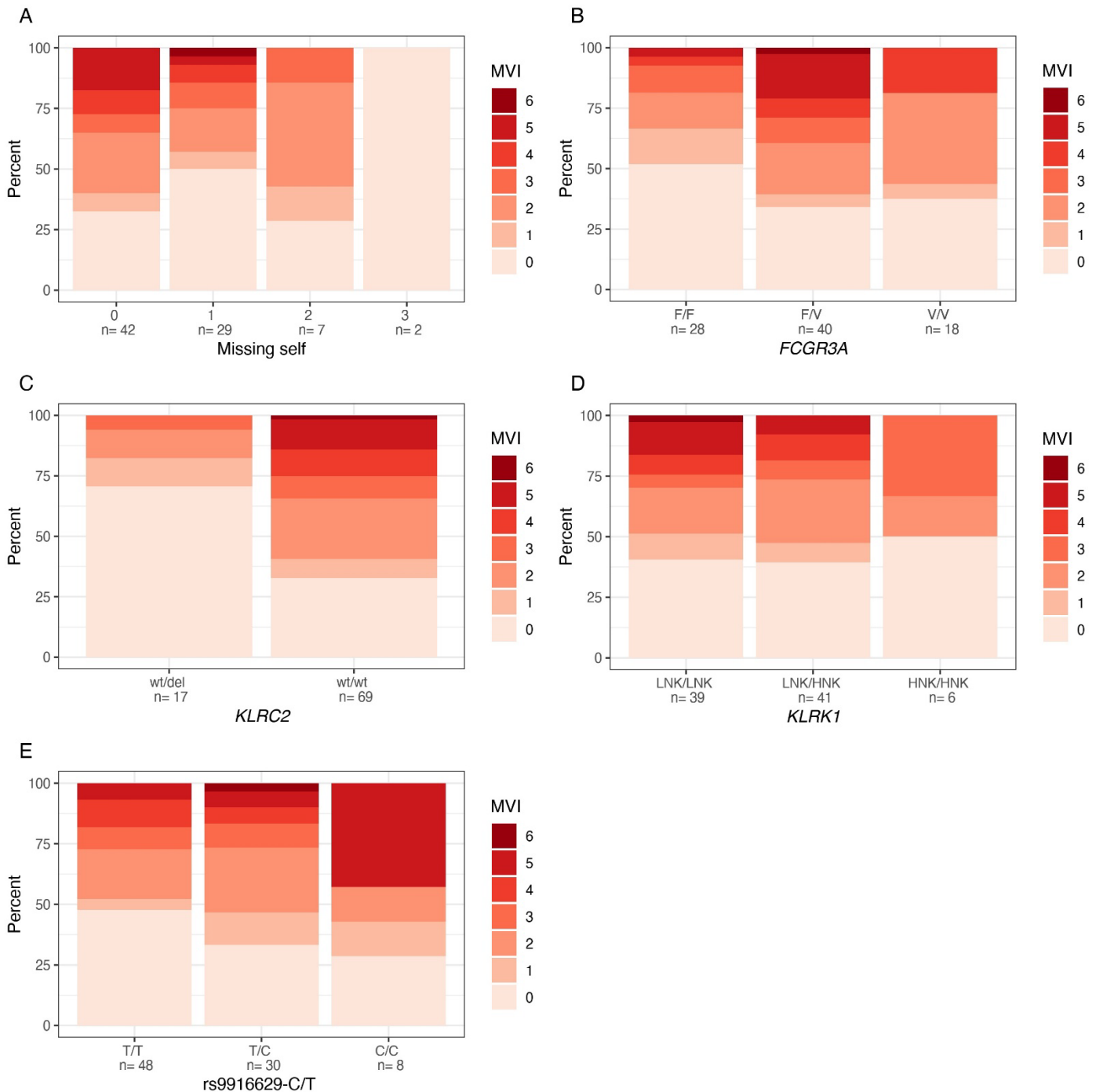
Methods: We enrolled 86 DSA-positive kidney transplant recipients in this study, all of whom underwent systematic biopsies during the screening phase of the BORTEJECT trial (NCT01873157). Patients were genotyped for polymorphisms known to determine NK cell activity and phenotypic composition (FCG3A[158-F/V], KLRK1[HNK/LNK], KLRC2[wt/del], rs9916629[C/T]). We also performed KIR typing for the calculation of missing self, defined as the absence of corresponding donor HLA in the presence of educated inhibitory KIR gene.

Results: Forty-four of the 86 patients had ABMR associated with higher levels of MVI and NK cell transcripts. Among tested genetic polymorphisms, only KLRC2^{wt/wt} was associated with a higher MVI score: 2 (median; interquartile range: 0– 3.2) versus 0 (0–1.0); Spearman’s rho = 0.349, p = 0.001 (Figure 1). No such

association, however, was observed for missing self. NK cell genetics did not impact death-censored graft survival or eGFR slope. In multivariable logistic ordinal regression model, only KLRC2^{wt/wt} was associated with MVI (OR 7.84, 95%CI 2.37–30.47, p = 0.001). A risk score combining variants important in univariable analysis (p <0.1) (KLRC2^{wt/wt} and FCG3A[158-F/V]) did not differ from a sum score of all polymorphisms plus missing self.

Conclusion: In this thorough analysis of NK cell genetics only a polymorphism of KLRC2 turned out to be a significant determinant of ABMR activity. No additive effect of other functional NK cell gene polymorphisms and missing self were found.

YSN submission



OC 20

RapGEF1 (C3G) is necessary for intact podocyte foot processes in mice

Dr. Carolin Eul¹, Mrs. Laura Stöveken¹, Prof. Hermann Pavenstädt¹, Prof. Britta George¹

1. Medical Clinic D, Department of Nephrology, University Hospital Münster, Münster, Germany

Background: Podocytes are key players in maintaining proper kidney filter function. In glomerular diseases podocyte foot processes are often altered, resulting in proteinuria and podocyte loss. The intercellular junctions of podocytes – called slit-diaphragms (SD) – make up one part of the three-layered kidney filter. A central protein of the slit-diaphragm is nephrin, that signals to the actin cytoskeleton and to integrin β 1 at focal adhesions *via* the small GTPase Rap1 and its guanine nucleotide exchange factor C3G. Thus, we hypothesize that C3G – alike nephrin – is also essential for an intact slit-diaphragm. Therefore, the aim of this study is to understand the role of C3G in glomerular podocytes *in vivo*.

Methods: C57BL/6 C3G flox mice were crossed to C57BL/6 Six2-Cre transgenic mice to generate a C3G knockout (C3G-KO) in the metanephric mesenchyme. Mice were examined for proteinuria, histological and ultra structural abnormalities. Bulk RNA-sequencing of C3G-KO and littermate control glomeruli was performed.

Results: Nephron-specific C3G-KO mice exhibited proteinuria 4 to 6 weeks after birth, concomitant with foot process effacement and podocyte loss progressing to focal segmental glomerulosclerosis. Immunofluorescence analyses unveiled mislocalization of slit-diaphragm as well as focal adhesion proteins. Bulk RNA-sequencing of C3G-KO glomeruli revealed significantly enriched gene regulation in pathways involved in cell adhesion, neurogenesis, organization of extracellular matrix (ECM), and cell signaling processes.

Conclusions: Our results show, that C3G is necessary for an intact glomerular filtration barrier. Moreover, C3G might play a role in anchoring podocytes to the ECM as C3G deficiency in the nephron results in podocyte loss. Bulk RNA-sequencing supports this hypothesis as C3G regulates the expression of genes, that operate in cell adhesion, cell signaling processes and organization of the ECM.

YSN submission

OC 21

Frequency and Impact on Renal Transplant Outcomes of Urinary Tract Infections Due to Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* and *Klebsiella* species

Dr. Jakob E. Brune¹, Prof. Michael Dickenmann¹, Prof. Daniel Siedler², Dr. Laura N. Walti³, Prof. Dela Golshayan⁴, Prof. Oriol Manuel⁵, Dr. Fadi Haidar⁶, Dr. Dionysios Neofytos⁷, Dr. Aurelia Schnyder⁸, Dr. Katia Boggian⁹, Prof. Thomas F. Mueller¹⁰, Dr. Thomas Schachtner¹⁰, Prof. Nina Khanna¹¹, Prof. Stefan Schaub¹, Dr. Caroline Wehmeier¹²

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland, 3. Department of Infectious Diseases, Inselspital, Bern University Hospital, Bern, Switzerland 4. Transplantation Center, Lausanne University Hospital, Lausanne, Switzerland 5. Infectious Diseases Service, Lausanne University Hospital, Lausanne, Switzerland 6. Nephrology and Hypertension Service, Division of Medicine, University Hospital Geneva, Geneva, Switzerland 7. Transplant Infectious Disease Service, Division of Infectious Diseases, University Hospital Geneva, Geneva, Switzerland 8. Clinic for Nephrology, Kantonsspital St. Gallen, St. Gallen, Switzerland 9. Division of Infectious Diseases and Hospital Epidemiology, Kantonsspital St. Gallen, St. Gallen, Switzerland 10. Clinic for Nephrology, University Hospital Zürich, Zürich, Switzerland 11. Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, Basel, Switzerland 12. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Switzerland

Background: *Enterobacteriales* are often responsible for urinary tract infection (UTI) in kidney transplant recipients. Among these, *Escherichia coli* or *Klebsiella species* producing extended-spectrum beta lactamase (ESBL) are emerging. However, there are only scarce data on frequency and impact of ESBL-UTI on transplant outcomes.

Methods: We analyzed frequency and impact of first-year UTI events with ESBL *Escherichia coli* and/or *Klebsiella species* in 1482 kidney transplantations performed between January 2012 and December 2017, which were captured in the Swiss Transplant Cohort Study. In this study, we focused only on kidney transplants having at least one UTI with *Escherichia coli* and/or *Klebsiella species*.

Results: Overall, 389/1482 (26%) patients had at least one UTI with *Escherichia coli* and/or *Klebsiella species*. In total, 139/825 (17%) first-year UTI events in 69/389 (18%) transplant recipients were caused by ESBL-producing strains. Both UTI phenotypes (colonization, UTI and urosepsis) and proportion among all UTI events over time were not different compared with UTI caused by non-ESBL-producing strains. However, hospitalizations in UTI with ESBL-producing strains were more often observed (39% versus 26%, $p = 0.04$). Transplant recipients with at least one first-year UTI event with an ESBL-producing strain had more frequently recurrent UTI (33% versus 18%, $p = 0.02$) but there was no significant difference in one-year kidney function as well as longer-term graft and patient survival between patients with and without ESBL-producing strains.

Conclusions: First-year UTI events with ESBL-producing *Escherichia coli* and/or *Klebsiella species* are associated with a higher risk for hospitalization, but do neither impact allograft function nor allograft and patient survival.

YSN submission

OC 22

Natural history of patients with familial focal segmental glomerulosclerosis associated with TRPC6 mutations

Dr. Heidi Sarrasin¹, Prof. Daniel Sidler², Dr. Deborah Bartholdi³, Prof. Christiane Zweier³, Prof. Bruno Vogt¹, Dr. Federica Bocchi¹

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland, 3. Inselspital Bern, Department for Human Genetics, Bern, Switzerland

Background: TRPC6 gene mutations have been identified in families with adult-onset of autosomal dominant inherited FSGS. This gene, located on chromosome 11, encodes for the canonical transient receptor potential cation superfamily C member 6 (TRPC6) ion channel. The latter, located on the slit diaphragms within the podocytes, seems to determine appropriate structure and function of podocytes. As evidence suggests a role of the TRPC6 channel in acquired forms of glomerular diseases, this channel is considered as promising drug target. The impact on structural nephropathies, its clinical-pathological relationship, genotype-phenotype correlation and outcome has never been thoughtfully studied. The study aim is to describe the renal disease phenotype and evolution in patients with proven TRPC6 mutations.

Methods: single centre cohort study (Bern, Switzerland) of patients and their first-degree relatives with TRPC6 mutations. Screening of patients from 102 reports at the university hospital in Bern with the key words "TRPC6". Patients' clinical and genetic data were obtained by interviews and medical records. We analysed the renal and subclinical renal disease phenotype, its evolution as well as the genotype-phenotype correlation of TRPC6 pathogenic variants.

Results: 9 consenting participants from 4 different families were included in the study and underwent interviews. All patients had signs for structural nephropathy and the most frequent presentation was sub-nephrotic proteinuria with slowly progressive eGFR deterioration. 8/9 patients had a proteinuria A3, 8/9 patients had an eGFR <90 ml/min/1.73 m² among those 6/9 patients needed a renal replacement therapy (RRT). Median age at first RRT was 35 years. 4 patients had multi-organ (>3) involvement (rheumatology, hematology, cardiology, neurology, urology) with unclear genotype-phenotype involvement.

Conclusion: this study characterizes and correlate the phenotype and genotype of patients with TRPC6 mutations and first-degree relatives, permitting a better understanding of this rare condition and improving patient's counselling and care.

YSN submission

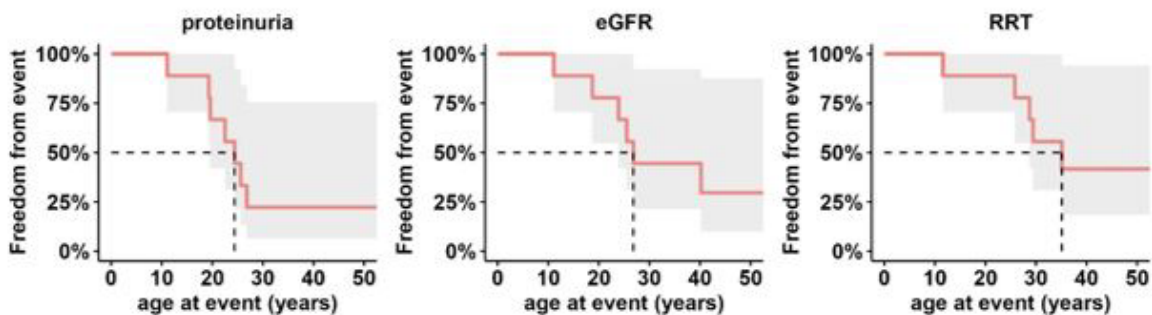


Figure 1

Development of proteinuria, eGFR <90ml/min and need of RRT over time. 50% of patients developed A3 proteinuria around 25 years, 50% of patients developed chronic kidney disease around 28 years and RRT was required in 50% of patients around 35 years.

Abbreviations: eGFR, estimated Glomerular Filtration Rate; RRT, Renal Replacement Therapy.

OC 23

Interleukin 6 blockade reduces age-related sensitivity to renal ischemia-reperfusion injury

Mr. Arnaud Lyon¹, Mr. Thomas Agius², Mr. Kevin Kiesworo², Dr. Matthieu Halfon¹, Dr. Louis Stavart¹, Dr. Michael MacArthur³, Dr. Sébastien Déglise², Prof. Alejandro Ocampo⁴, Dr. Sarah Mitchell⁵, Dr. Florent Allagnat², Prof. Dela Golshayan⁶, Dr. Alban Longchamp⁷

1. Transplantation Center, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 2. Department of Vascular Surgery, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland., 3. Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ, USA, 4. Department of Biomedical Sciences, University of Lausanne, Switzerland, 5. Ludwig Princeton Branch, Princeton University, Princeton, NJ, USA, 6. Transplantation center, Lausanne university hospital, Lausanne, Switzerland 7. Transplant Center, Dept. of Surgery, Massachusetts General Hospital, Boston, MA, USA

Background: Recipient mean age at time of kidney transplantation (KTx) has globally increased in the last decades and was found to be associated with increased susceptibility to renal ischemia-reperfusion injury (IRI), with subsequent poor graft and patient outcome. Specific treatments need to be found to limit early graft injury in this older population.

Methods: Patients data were analyzed from the Swiss Transplant Cohort Study (STCS) and CHUV transplantation center. Experimentally, IRI was modelled in 10- and 70-weeks old C57BL/6 mice using unilateral nephrectomy and 12min contralateral ischemia and reperfusion. Visium spatial mRNA sequencing was carried out on paraffin-embedded mouse renal tissue.

Results: STCS data analysis revealed an association between recipient age and long-term death-censored graft survival. CHUV data analysis (n = 23 patients) revealed that serum concentrations of interleukin (IL)-6, at day 2 post KTx, correlated with donor and recipient age. Serum IL-6 levels were also associated with donor type (living *versus* deceased) and organ total ischemia time. Experimentally, following IRI, old mice had lower renal function and increased tubulointerstitial damages compared to their younger counterparts, together with increased IL-6 renal expression and serum concentration at day 2 post IRI. Spatial RNA sequencing identified age-dependent transcriptomic changes in proximal tubular cells in response to IRI. Finally, *in vivo* IL-6 blockade reduced IRI in aged mice.

Conclusions: Clinical data showed an association between donor and recipient age and early blood concentrations of IL-6 following KTx. In old mice, IL-6 contributed to renal damage in IRI as observed by specific transcriptomic changes in proximal tubular cells towards increased injury and cellular death. Blocking IL-6 significantly reduced IRI in mice. As IL-6-mediated signaling pathway can be targeted by clinically approved drugs, rapid translation into clinical trials could improve KTx outcomes. Similarly, therapeutics against IRI could enable an extended and safer use of marginal organs.

YSN submission / student submission

OC 24

The effect of dark and white chocolate on renal perfusion as assessed with Doppler ultrasound in healthy volunteers

Mrs. Louise Garciulo¹, Ms. Mariëlle Hendriks-Balk², Dr. Kenji Theiler², Ms. Wendy Brito³, Dr. Menno Pruijm²

1. Department of Medicine, Service of Nephrology and Hypertension, University Hospital of Lausanne and University of Lausanne, Lausanne, Switzerland, 2. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 3. Service of Nephrology and Hypertension, Lausanne University Hospital, Lausanne, Switzerland

Background: Chocolate consumption in Switzerland is among the highest in the world, but its effects on health remain incompletely understood. Dark chocolate (DC) is rich in calories but also in cocoa, a substance with anti-oxidative and antihypertensive properties. Acute intake of DC induces vasodilatation of

coronary arteries, but the effect on renal hemodynamics is unknown. The aim of this randomized, placebo-controlled study was to investigate whether DC induces changes in renal perfusion as assessed with Doppler ultrasound, both at rest and during sympathetic stimulation.

Methods: Seventeen healthy volunteers were randomized to eat 1g/kg of DC (70% cocoa) or 1g/kg of white chocolate (WC). The renal resistive index (RRI), a proxy of intra-renal vascular resistance, was measured just before and two hours after chocolate consumption. Blood pressure (BP) and heart rate were measured with a Finapres® device. At each time point, a 3-minute handgrip test was performed as sympathetic stimulus; during the handgrip, supplementary RRI values were measured. Two weeks later, the same exams were repeated with the other type of chocolate (see Figure 1).

Results: DC intake decreased RRI from 0.62 ± 0.04 to 0.60 ± 0.04 ($p = 0.039$), whereas RRI did not change after the intake of WC (before: 0.62 ± 0.05 , after: 0.62 ± 0.04 , $p = 0.47$), see Figure 2. No changes were observed in blood pressure. Handgrip exercise also lowered the RRI, both before and after chocolate intake, especially in young participants <35 years, while increasing BP. In women, the effect on RRI was attenuated by the ingestion of DC (see Table).

Conclusions: The ingestion of DC lead to an acute reduction in RRI, suggesting intra-renal vasodilatation, whereas WC had no effect. Handgrip exercise led, surprisingly, also to reductions in RRI, especially in young participants. Whether this is a sign of sympathetically induced intra-renal vasodilatation or vascular reactivity needs further study.

YSN submission / student submission

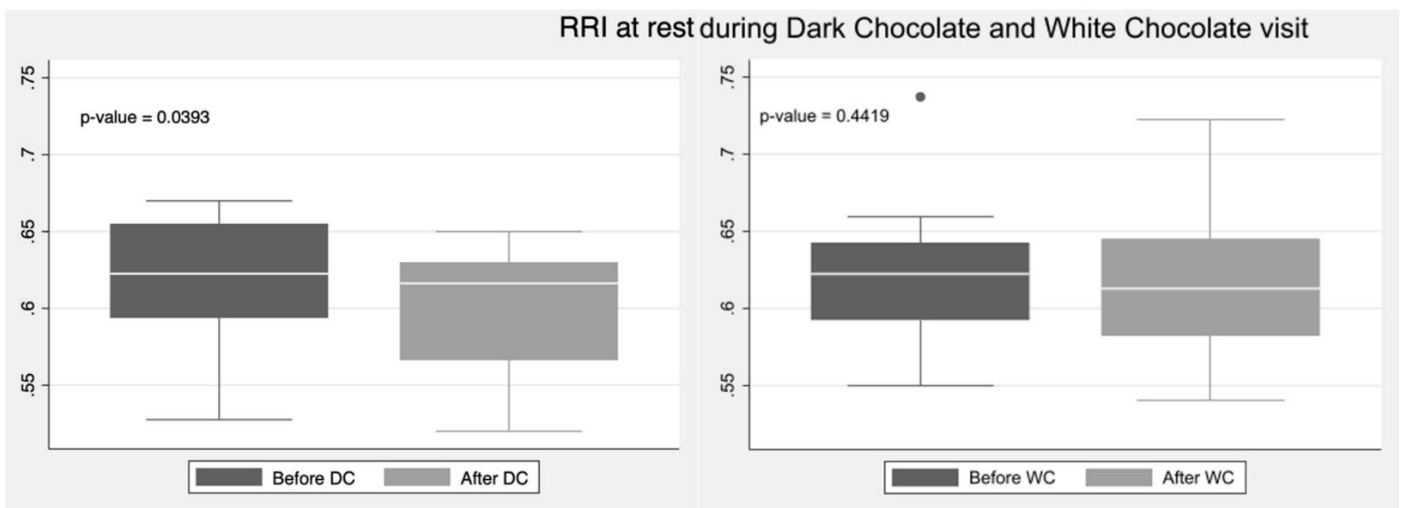
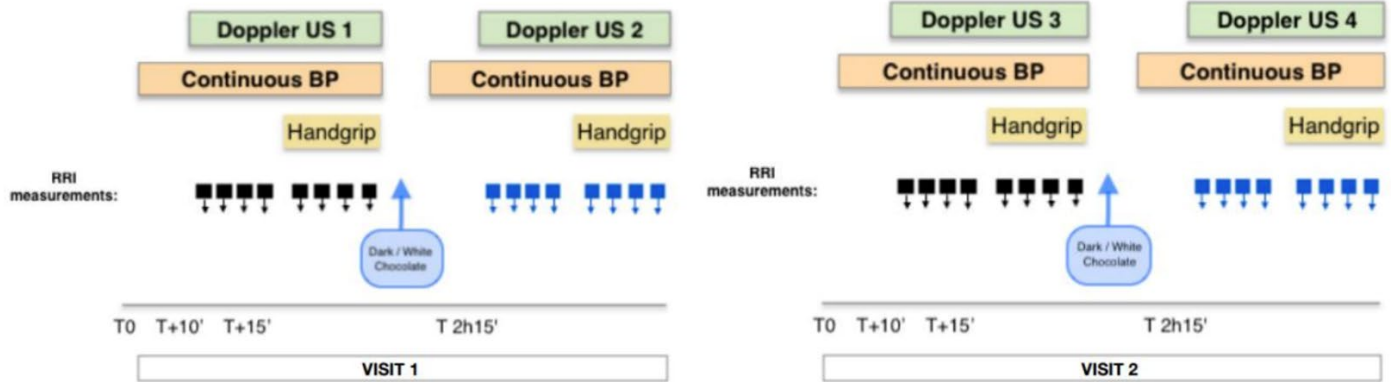


Table: Changes in RRI induced by the handgrip test, before and after respectively DC and WC intake.

| | N | Before DC | p-value | After DC | p-value |
|--------------------------|----|---------------|---------------|---------------|---------------|
| All | 16 | -0.044 ± 0.04 | 0.0006 | -0.031 ± 0.05 | 0.0275 |
| Women | 7 | -0.043 ± 0.03 | 0.0112 | -0.015 ± 0.04 | 0.3010 |
| Men | 9 | -0.045 ± 0.05 | 0.0259 | -0.043 ± 0.06 | 0.0591 |
| < 35 years old | 8 | -0.070 ± 0.03 | 0.0001 | -0.055 ± 0.05 | 0.0128 |
| > 35 years old | 8 | -0.018 ± 0.04 | 0.2162 | -0.007 ± 0.04 | 0.6858 |
| | | Before WC | | After WC | |
| All | 17 | -0.049 ± 0.05 | 0.0003 | -0.046 ± 0.04 | 0.0002 |
| Women | 8 | -0.037 ± 0.02 | 0.0002 | -0.039 ± 0.03 | 0.0066 |
| Men | 9 | -0.060 ± 0.06 | 0.0166 | -0.052 ± 0.05 | 0.0106 |
| < 35 years old | 8 | -0.080 ± 0.03 | 0.0002 | -0.066 ± 0.04 | 0.0032 |
| > 35 years old | 9 | -0.022 ± 0.04 | 0.1045 | -0.028 ± 0.03 | 0.0132 |

SHORT ORAL PRESENTATIONS & POSTER PRESENTATIONS

OC 25 / P 01

Plasma untargeted metabolomics characterizes residual kidney function in chronic hemodialysis patients

Dr. David Jaques¹, Dr. Julien Boccard², Dr. Gioele Visconti², Prof. Patrick Saudan¹, Prof. Sophie De Seigneux¹, Prof. Serge Rudaz², Prof. Belén Ponte³

1. Service of Nephrology, Department of Medicine, Geneva University Hospitals, Geneva, Switzerland, 2. School of Pharmaceutical Sciences, University of Geneva, Geneva, Switzerland, 3. Department of Nephrology and Hypertension, Geneva University Hospitals, Geneva, Switzerland

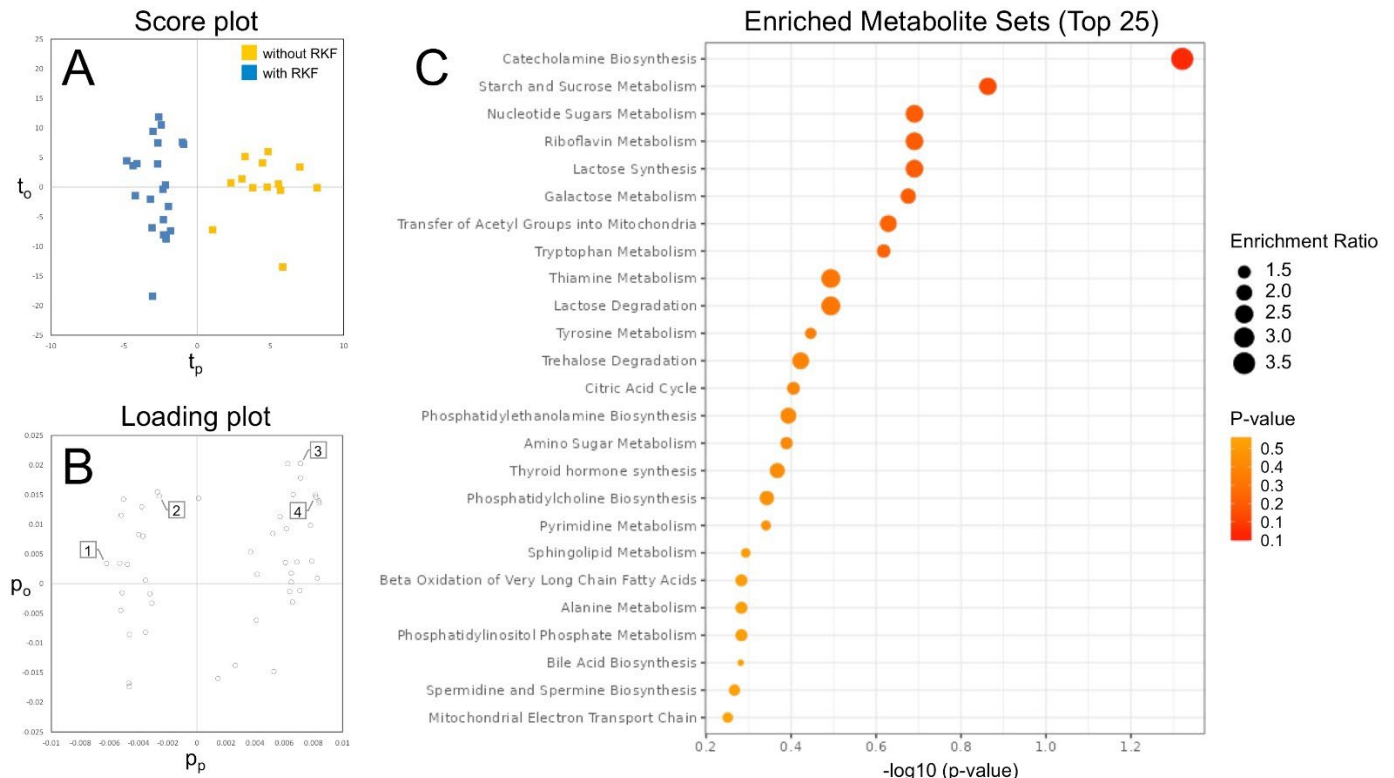
Background: Observational data suggest that patients undergoing haemodialysis (HD) with preserved residual kidney function (RKF) have improved outcomes as compared to anuric patient. The reason for this beneficial effect of RKF is not formerly understood. This raises the question of the contribution of RKF to metabolic homeostasis in chronic HD patients.

Methods: We performed an observational study using an existing cohort recruited at a single tertiary centre (Geneva University Hospitals, Geneva, Switzerland) and including 35 prevalent patients on chronic HD for at least 3 months on a standard regimen of 4 hours 3x/week. An untargeted liquid chromatography-mass spectrometry workflow was used to identify 278 plasma metabolites. Uninformative variable elimination and orthogonal projections to latent structures-discriminant analysis (OPLS-DA) were computed.

Results: We included 13 anuric patients and 22 with preserved RKF. Mean age was 66.3 +/- 15.7 with 25 (71.4%) men, 24 (68.5%) suffering from hypertension and 15 (42.8%) from diabetes. A model based on a subset of 47 metabolites showed clear separation between patients with and without RKF. Scores and loadings of this model are represented in figure 1a and 1b, respectively. Among the 47 metabolites, 28 were found in lower concentration in patients with preserved RKF as compared to anuric patients. On the opposite, 19 out of the 47 identified metabolites were found in higher concentration in patients with preserved RKF as compared to anuric patients. Finally, enriched metabolite sets are represented in figure 1c.

Conclusions: We found clinically relevant alterations in metabolic profiles of chronic HD patients depending on the presence of RKF. Those results suggest that metabolomics could be used as an additional tool to better characterize RKF. Whether health benefits related to RKF preservation could be partly explained by improved metabolic homeostasis in HD patients still needs to be determined in larger dedicated studies.

YSN submission



OC 26 / P 02

Minimal Change Glomerular Disease associated with solid neoplasms: a systematic review

Dr. Domenico Cozzo¹, Dr. Francesca Orlando², Prof. Adam Ogna³, Dr. Valentina Forni Ogna⁴

1. Servizio cantonale di nefrologia, Ente Ospedaliero Cantonale (EOC), Locarno-Lugano, Switzerland 2. Servizio di medicina interna, EOC Ospedale "La Carità", Locarno, Switzerland 3. Servizio di medicina interna, EOC Ospedale "La Carità", Locarno AND Università della Svizzera Italiana (USI), Lugano, Switzerland 4. Servizio cantonale di nefrologia, Ente Ospedaliero Cantonale (EOC), Locarno-Lugano AND Università della Svizzera Italiana (USI), Lugano, Switzerland

Background: Among paraneoplastic glomerulopathies, membranous glomerulonephritis (GN) is commonly associated with solid malignancies, whilst minimal change disease (MCD) has predominantly been reported in association with hematological disease. In this systematic review of literature we describe the characteristics and outcome after treatment of MCD associated with solid malignancy.

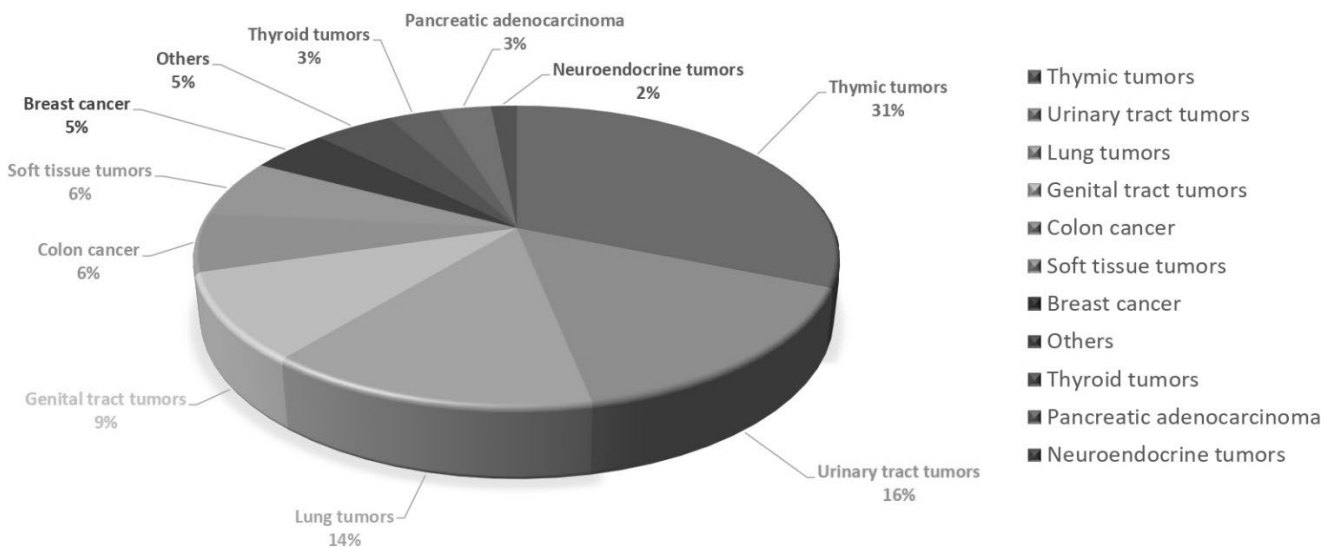
Methods: We performed a systematic review of the MEDLINE and COCHRANE databases, including case reports of adult patients with biopsy-proven MCD and solid malignancy, without language or time restriction. The references of the identified articles were further searched for additional original cases.

Results: A total of 57 papers were included, presenting 62 original clinical cases. The mean age was 57.2 ± 15.6 years, exactly 50% were women. The initial presentation was nephrotic syndrome in all patients, with acute kidney injury in 68%. In 45% of the cases, MCD preceded the neoplasm diagnosis by 163 ± 240 weeks, and in 55% the tumor diagnosis had already been established since 56 ± 102 weeks. Thymic tumors were the most frequent malignancy (31%), followed by urinary tract (16%), lung (14%) and genital tract tumors (9%). In 87.5% of cases, an immunosuppressive therapy was started (steroids and/or other immunosuppressants), leading to a complete remission of the nephrotic syndrome in 45% of cases. In 24% of patients, remission was obtained after tumor treatment (surgery and/or chemotherapy and/or radiotherapy).

Conclusions: An association between MCD and solid neoplasms is consistently described in the literature. Interestingly, steroids could induce nephrotic syndrome remission in almost half of the cases, and most of the remaining cases responded to neoplasm treatment. A solid neoplasm screening should probably be suggested in MCD of unclear origin, although a definitive statement would require more data on the prevalence of solid neoplasm-associated MCD.

YSN submission

RELATIVE FREQUENCY OF SOLID MALIGNANCIES ASSOCIATED WITH MINIMAL CHANGE DISEASE



OC 27 / P 03

Natural Killer Cell Receptor NKG2C Encoding KLR2C Gene and Kidney Transplant Outcome

Dr. Matthias Diebold¹, Dr. Hannes Vietzen², Dr. Andreas Heinzl³, Ms. Susanne Haindl³, Dr. Carsten Herz³, Dr. Katharina Mayer³, Dr. Konstantin Doberer³, Dr. Alexander Kainz³, Ms. Laura Kühner², Ms. Sarah Berger², Prof. Elisabeth Puchhammer-Stöckl², Dr. Nicolas Kozakowski³, Prof. Jürg Steiger⁴, Prof. Stefan Schaub¹, Prof. Georg A. Böhmig³

1. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 2. Center for Virology, Medical University of Vienna, Vienna, Austria, 3. Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria, 4. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, University of Basel, Basel, Switzerland

Background: Antibody-mediated rejection (ABMR) is a leading cause of long-term graft failure. Increasing evidence suggests that natural killer (NK) cells play a pivotal role in the pathogenesis of ABMR. A potential activating pathway might involve polymorphism in the KLR2C gene, which encodes the NK cell receptor NKG2C.

Methods: All consecutive kidney transplant recipient in Basel between 2015 and 2021 were included in this cohort. Clinical data as well as routine laboratory analysis were prospectively collected during regular clinical visits. All patients were genotyped for the KLR2C wt/del variants.

Results: Among 506 transplant recipients, 35 (6.9%) were diagnosed with ABMR. Microvascular inflammation (MVI) was detected in 69 patients (13.6%) with a median score of 2 (IQR 1-3). KLR2C^{wt/wt} was identified in 343 (67.8%), KLR2C^{wt/del} in 130 (25.7%) and KLR2C^{del/del} in 33 (6.5%) patients. In the overall cohort associations between the KLR2C genotypes and higher MVI scores, ABMR or TCMR were not significant (Figure 1). However, for the cohort of 33 KLR2C^{del/del} recipients, markedly less MVI and no case of ABMR was recorded. While this did not translate into differing graft survival, the mean yearly eGFR slope was significantly lower among KLR2C^{wt/wt} versus KLR2C^{wt/del} patients, with an inter-group difference of 1.31 (95%CI: 0.16 to 2.24) ml/min/1.73 m² per year (p = 0.026). Interestingly, in a stratified analysis of 112 patients (22.1%) with a delayed graft function (DGF), we found a correlation between KLR2C risk variants and MVI, but without reaching the conventional boundaries for statistical significance (Spearman's rho 0.17, p-value 0.079) (Figure 2).

Conclusion: In our present cohort we were unable to demonstrate a significant effect of NKG2C genetics on the development of MVI, ABMR or TCMR. However, an association was found for eGFR trajectories. Interestingly, DGF and the resulting ischemia-reperfusion injury might serve as a possible trigger for NK cell activation.

YSN submission

Figure 1 Full Cohort

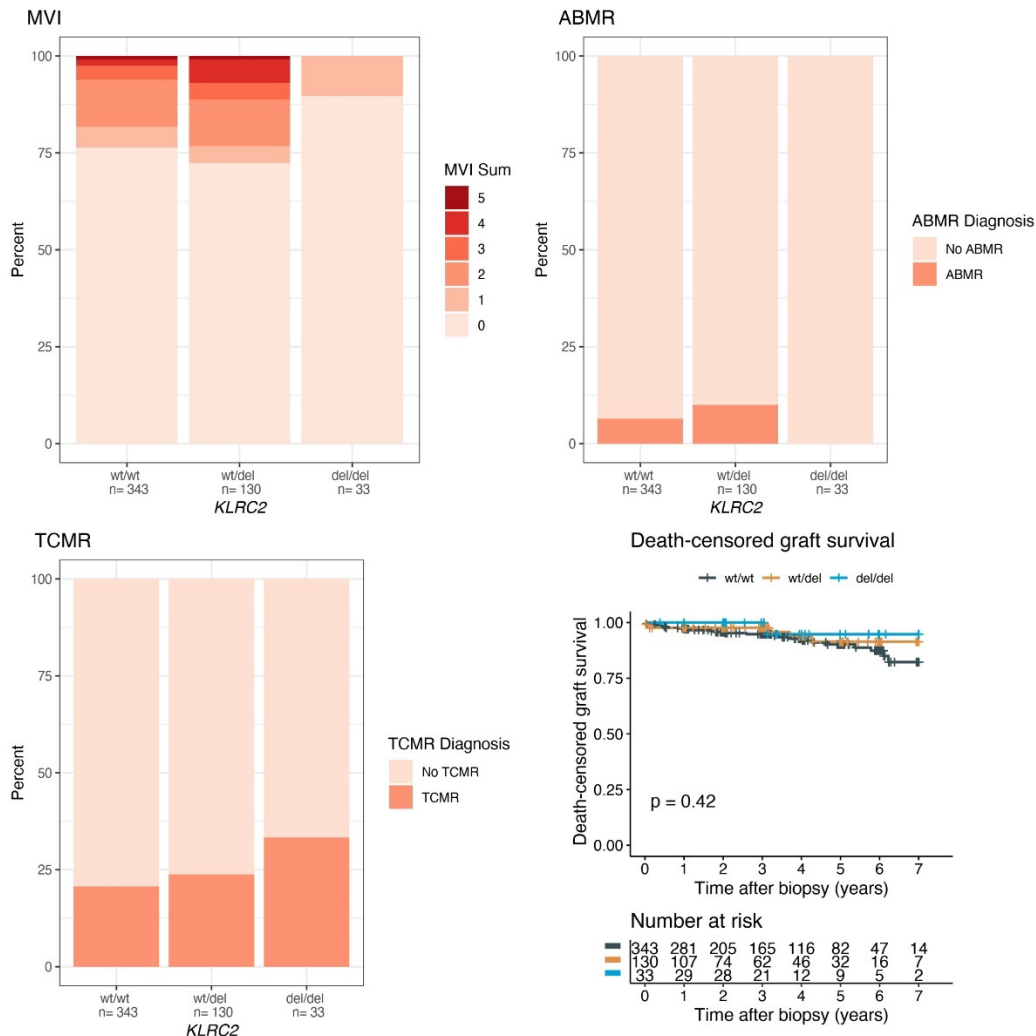
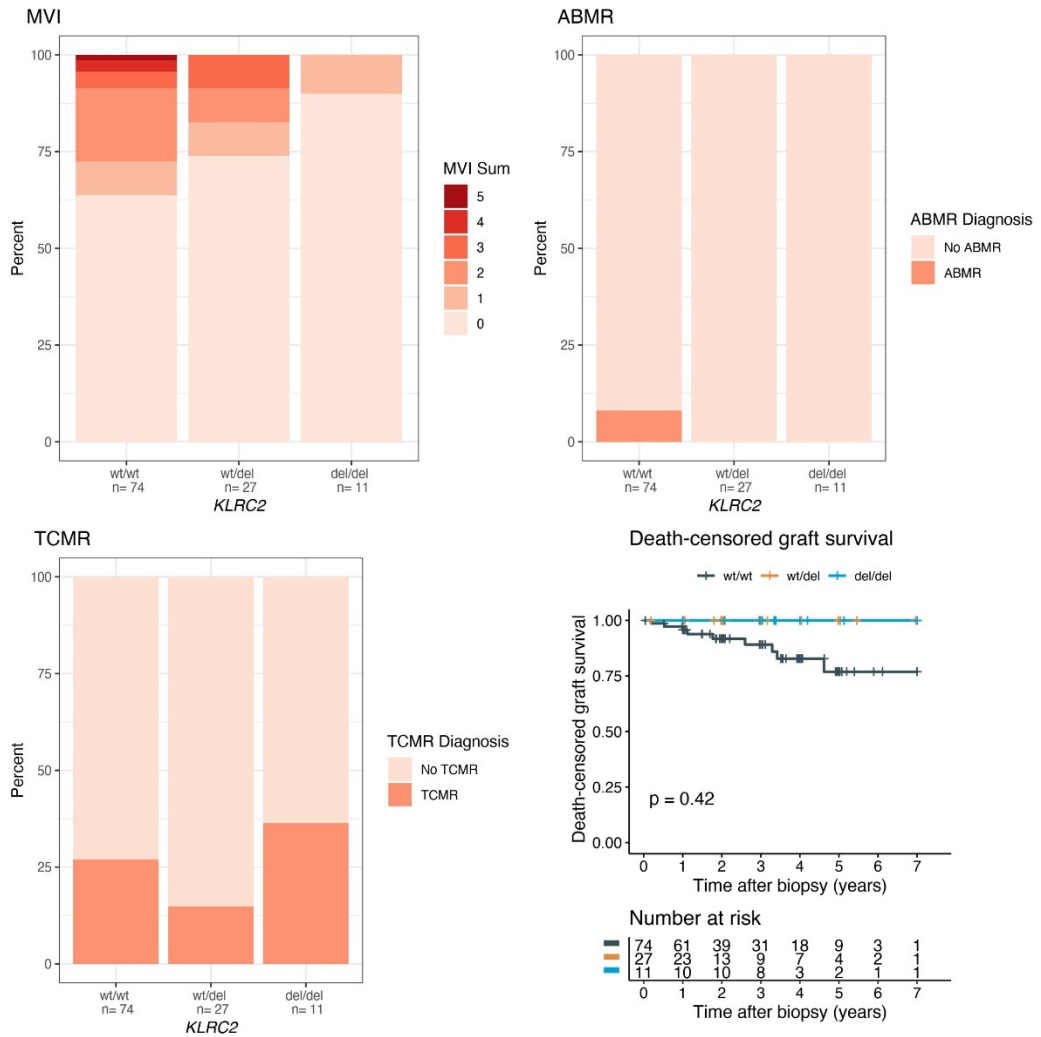


Figure 2
Delayed graft
function



OC 28 / P 04

Age-adapted Chronic Kidney Disease Definition and long-term impact on renal function and Mortality in a population based-study

Dr. Delal Dalga¹, Dr. Anne Dufey¹, Dr. Peter vollenweider², Prof. Sophie De Seigneux³, Dr. Lena Berchtold¹, Prof. Belén Ponte⁴

1. HUG, Geneva, Switzerland 2. Department of Urology, Lausanne University Hospital, CHUV, University of Lausanne, Switzerland, 3. UNIGE, Geneva, Switzerland 4. Department of Nephrology and Hypertension, Geneva University Hospitals, Geneva, Switzerland

Introduction: Chronic Kidney Disease (CKD) diagnosis is on a glomerular filtration rate (eGFR) below 60 ml/min/1.73 m² or a urine albumin-to-creatinine ratio >30 mg/g. Adopting age-specific GFR thresholds could influence CKD prevalence. Debate also exists on indexing GFR to body surface area (BSA). We aimed to compare age-specific, BSA-adapted, and standard CKD-EPI 2021 GFR thresholds to assess CKD prevalence. We compared then renal function decline (RFD) and global mortality risk between those 3 classifications.

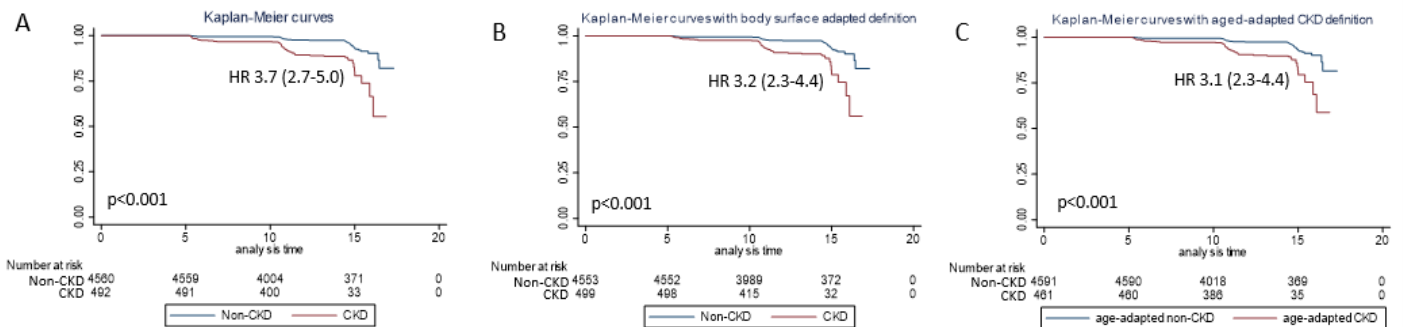
Method: We used a prospective longitudinal population-based study from Lausanne (CoLaus), with a 15-year follow-up. We defined 3 CKD groups all including albuminuria but different

eGFR: (1) CKD-EPI <60 ml/min/1.73 m²; (2) eGFR BSA-indexed <60 ml/min/1.73 m²; (3) age-stratified eGFR of <75 ml/min/1.73 m² under 40 years old, <60 ml/min/1.73 m² for 40-65, and <45 ml/min/1.73 m² over 65. We performed adjusted Cox regression analyses using those 3 CKD classifications compared to non-CKD participants, focusing on rapid RFD (>30%) and mortality.

Results: We analysed 5052 participants (Table 1). For renal survival (Figure 1), the Kaplan-Meier curves for decline-free survival, stratified by CKD and non-CKD patients, were based on (A) the CKD epi 2021 equation, (B) the CKD epi 2021 equation adapted for body surface, and (C) the CKD epi 2021 equation adapted for age. These curves show worse survival in the CKD groups independently of the group with similar hazard ratios (HR). We observed the same for the mortality, with similar HR in the 3 groups: CKD-EPI HR 3.2 (95% CI: 2.3-4.5, p <0.001), BSA-indexed HR 2.9 (95% CI: 2.0-4.1, p <0.001), and age-stratified HR 2.3 (95% CI: 1.6-3.3, p <0.001).

Conclusion: Modifying the CKD classification based on different criteria did not significantly impact rapid decline kidney function and mortality outcomes.

YSN submission



| Table. Baseline Characteristic | | No.(%).(n=5052) | |
|---|----------|-----------------|-----------------|
| | | Rapid declin | No rapid declin |
| Demographic characteristics | | n=203 (4) | n=4849 (96) |
| Female | | 92 (45) | 2616 (54) |
| Male | | 111 (55) | 2233 (46) |
| BMI | | | |
| | >30 | 55 (27) | 661 (14) |
| | (30-25) | 93 (46) | 1752 (36) |
| | <25 | 55 (27) | 2436 (50) |
| BSA (mean) | | 1.9 | 1.84 |
| Laboratory parameters | | | |
| First eGFR <i>ckd-epi-2021</i> , (median) | | 86.7 | 89.66847 |
| Albuminurie | | | |
| | Presence | 40 (20) | 273 (6) |
| Cardiovascular risk | | | |
| Myocardial infarction | | | |
| | Presence | 25 (12) | 163 (3.4) |
| HTA | | | |
| | Presence | 135 (67) | 1576 (3.3) |
| Diabete | | | |
| | Presence | 44 (22) | 249 (5) |
| Dyslipidemia | | | |
| | Presence | 43 (21) | 492 (10) |
| Smoking | | | |
| | Yes | 54 (27) | 1263 (26) |
| Stroke | | | |
| | Presence | 23 (11) | 208 (4) |
| Angina pectoris | | | |
| | Presence | 15 (7) | 161 (3) |
| Heart failure | | | |
| | Presence | 20 (10) | 92 (2) |

OC 29 / P 05

HLA-specific memory B cell detection in kidney transplantation: First results from a prospective explorative study

Mrs. Joëlle Handschin¹, Dr. Gideon Hönger¹, Mrs. Aynur Gubelmann², Mrs. Beatrice Gujer², Mr. Marc Kleiser², Mrs. Claudia Petit², Mrs. Amanda Puglia², Mrs. Dominique Roubaty², Prof. Stefan Schaub³, Dr. Caroline Wehmeier⁴

1. Transplantation Immunology, Department of Biomedicine, University of Basel, Basel, Switzerland, 2. HLA-Diagnostics and Immunogenetics, Department of Laboratory Medicine, University Hospital Basel, Basel, Switzerland, 3. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, 4. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Switzerland

Background: Exposure to foreign HLA may lead to the formation of plasma cells and dormant memory B cells. While screening for HLA antibodies is part of the pre-transplant immunological work-up in kidney transplantation, the presence of HLA-specific memory B cells is not yet routinely assessed. However, these cells can differentiate into antibody-producing cells upon antigen re-encounter.

Methods: In this single-center prospective explorative study, we included 34 kidney transplant candidates with a history of HLA-sensitizing events. Importantly, patients were only eligible for study inclusion if the immunizing HLA (previous pregnancies and/or former transplantations) was known and high-resolution typing data of all loci could be obtained. Of all patients, we collected peripheral blood mononuclear cells (PBMC) in order to perform a novel memory B cell assay. In the latter, memory B cell-derived HLA antibodies can be detected by Luminex single antigen bead (SAB) assay following in-vitro polyclonal stimulation of PBMC and subsequent collection of culture supernatants. HLA antibody profiles deriving from the memory B cell compartment and serum were comparatively analyzed.

Results: In the whole cohort, there were 324 HLA mismatched alleles resulting from previous immunizing events. Of these, 59 (18%) specificities were assigned as positive in SAB assay in either serum and/or memory B cell culture supernatants. Memory B cell-derived antibodies could be detected against 26/59 (44%) specificities, either alone (10/59; 17%) or with concurrent serum antibodies (16/59; 27%), and mainly for class II. On the patient level, 14/34 (41%) had detectable HLA-specific B cell memory. Depending on the signal intensity, memory B cell-derived antibodies could be attributed to immunizing HLA epitopes.

Conclusions: Assessment of previous HLA sensitization by analyzing memory B cell-derived antibodies differs from serum antibody profiles and reveals “hidden memory” in a subset of patients. Better characterization of the clinical impact of detectable B cell memory is needed.

OC 30 / P 06

Five scenarios across the AMR continuum: the added value of MMDx confirmed by follow-up biopsies

Dr. Raphael Korach¹, Dr. Dusan Harmacek², Mr. Kai Castrezana Lopez², Dr. Nicolas Schmid², Dr. Lukas Weidmann², Dr. Nicola Bortel², Dr. Birgit Maria Helmchen³, Dr. Ariana Gaspert³, Dr. Elena Rho², Prof. Thomas F. Mueller², Dr. Thomas Schachtner⁴

1. Division of Nephrology, University Hospital Zurich, Switzerland, 2. Division of Nephrology, University Hospital Zurich, Switzerland 3. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland 4. department of Nephrology, University Hospital Zurich, Switzerland

Background: The Molecular Microscope Diagnostic System (MMDx) has evolved to be an essential tool in suspected antibody-mediated rejection (AMR). However, cost and availability limit a generalized use, underscoring the necessity to define

specific contexts where MMDx offers substantial diagnostic benefits.

Methods: We present a comprehensive case series comprising 23 kidney allograft biopsies, including 10 follow-up biopsies employing histology and MMDx. Across the spectrum of AMR, we elucidate five distinct scenarios wherein MMDx proved pivotal in achieving accurate diagnoses.

Results: “Isolated glomerulitis”: In two patients with donor specific antibodies (DSA) and mild microvascular inflammation (MVI), MMDx helped to exclude AMR initially and at follow-up. “DSA-negative, C4d-negative moderate MVI”: In one case, MMDx confirmed AMR and showed persistent rejection after treatment at follow-up. In the second case, MMDx repeatedly allowed exclusion of AMR. “MVI in ABOi transplantation”: Two patients after ABOi transplantation were diagnosed with TCMR (confirmed by MMDx). On follow-up biopsy, persistent MVI raised suspicion of AMR. MMDx negated rejection in both cases. “Mixed rejection”: In two cases with malcompliance, AMR could not be diagnosed according to Banff due to concomitant TCMR, but MMDx suggested AMR/TCMR in both cases. After treatment, both patients had mild MVI and MMDx could exclude ongoing AMR. “Early active AMR”: One case showed no rejection on histology one week post-transplant, but minor AMR by MMDx. On follow-up biopsy two weeks later, AMR was confirmed by histology and MMDx. Four other cases with early active AMR showed AMR by histology and MMDx.

Conclusion: MMDx provided significant diagnostic benefit and facilitated therapeutic decisions in histologically and clinically ambiguous cases along the AMR spectrum. Scenarios in which MMDx can be expected to provide added value include DSA-positive, mild MVI, DSA-negative and C4d-negative moderate MVI, mixed rejection and cases with MVI in ABOi transplantation.

YSN submission / student submission

OC 31 / P 07

Intrauterine hypoxia promotes premature placental senescence: role of Klotho

Dr. Stefan Rudloff¹, Prof. Uyen Huynh-Do²

1. Clinic of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Service of Nephrology, Bern University Hospital, Switzerland

Background: The placenta is essential for the exchange of oxygen, nutrients, and waste products between the mother and the fetus. Klotho plays an important role for proper renal function and is also well known for its systemic anti-aging properties. It is expressed in various adult tissues including the kidneys, but is also temporarily expressed in the placenta during development. Adverse conditions during gestation such as chronic hypoxia lead to intrauterine growth restriction of the fetus and through unfavorable “programming” increase the risk for chronic kidney disease (CKD) later in life. We hypothesize that cellular senescence (permanent withdrawal from the cell cycle), that can be prematurely induced by various exogenous or endogenous stress factors, plays an important role during this process. Here, we report on the effect of chronic hypoxic conditions on placental health with a special focus on premature placental senescence and Klotho expression.

Methods: Pregnant dams were exposed to chronic hypoxic conditions (10% O₂) from E11.5 to E18.5. Placentas, fetal trunk blood, and fetal kidneys were collected and analyzed for senescence-associated markers and Klotho expression levels.

Results: Senescence-associated β-galactosidase (SABG), and cyclin dependent kinase inhibitors p16 and p21 showed differential expression patterns in the placentas and kidneys derived

from fetuses exposed to chronic hypoxia compared to normoxic controls. Furthermore, Klotho expression was reduced in hypoxic placentas and hypoxic kidneys, as well as in the serum of hypoxic fetuses.

Conclusions: Enhanced SABG activity, increased expression of p16, but reduced expression of Klotho in hypoxic placentas indicate a premature withdrawal from the cell cycle during late fetal development. These findings corroborate our hypothesis that placental-derived Klotho protein might be a key factor that affects long-term fetal health and that its exogenous replenishment might be a potential rescue mechanism counteracting the negative consequences of fetal programming under adverse developmental conditions.

OC 32 / P 08

The impact of the molecular HLA-epitope mismatch load on allosensitization after kidney transplantation is most pronounced in childhood, adolescence, and early adulthood

Mr. Kai Castrezana Lopez¹, Ms. Cecilia Brunner¹, Dr. Jakob Nils-son², Prof. Thomas F. Mueller¹, Dr. Giuseppina Sparta³, Dr. Thomas Schachtner⁴

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. Department of Immunology, University Hospital Zurich, Switzerland 3. Division of Nephrology, University Children's Hospital Zurich, Switzerland 4. department of Nephrology, University Hospital Zurich, Switzerland

Background: Patients who undergo kidney transplantation during childhood (0–9), adolescence (10–19), or early adulthood (20–25) face distinct long-term survival threats for poor long-term survival due to varying alloimmune responses and a higher likelihood of non-adherence, leading to donor-specific antibody (DSA) development and antibody-mediated rejection (ABMR).

Methods: We studied 153 kidney transplant recipients (KTRs) transplanted at Zurich University Hospital and University Children's Hospital Zurich from 1990 to 2018 in the 0–25 age range and compared them to 862 later adult KTRs. DSA and ABMR development was assessed, and HLA-epitope mismatches were calculated using the Predicted Indirectly Recognizable HLA-Epitopes (PIRCHE-II) algorithm. High-resolution re-typing was performed from kidney allograft biopsies if necessary.

Results: Among the 0–25 group, 49% developed DSA, with 20% progressing to ABMR. Notably, high PIRCHE-II scores for HLA-DRB plus DQB significantly increased DSA (HR 1.019, CI95% 1.010–1.027, $p < 0.001$) and ABMR risk (HR 1.021, CI95% 1.011–1.036, $p < 0.001$). The impact on DSA development was most pronounced in childhood (HR 1.045, CI95% 1.007–1.084, $p = 0.019$) compared to adolescence/early adulthood (HR 1.018, CI95% 1.008–1.027, $p < 0.01$) and later adulthood (HR 1.005, CI95% 1.002–1.008, $p < 0.001$).

Conclusions: An increase of the molecular HLA-epitope mismatch load for HLA-loci DRB plus DQB by 20 epitopes has 2.41 times the risk for developing DSA in childhood, 1.43 times the risk in adolescence and early adulthood, but only 1.10 times the risk in later adulthood. Factors explaining these differences are likely primarily nonadherence and higher alloimmune responsiveness. This result is of particular importance for allocation policies and immunosuppressive strategies alloimmune responsiveness. This result is of particular importance for allocation policies and immunosuppressive strategies.

YSN submission / student submission

OC 33 / P 09

Prospective assessment of the need, discrepancies, and added value of molecular diagnostics of kidney allograft biopsies – An evaluation in clinical practice

Dr. Nicolas Schmid¹, Dr. Seraina Von Moos², Dr. Birgit Maria Helmchen³, Dr. Ariana Gaspert³, Dr. Lukas Weidmann¹, Mr. Kai Castrezana Lopez¹, Dr. Dusan Harmacek¹, Dr. Raphael Korach⁴, Dr. Nicola Bortel¹, Dr. Elena Rho¹, Dr. Thomas Schachtner⁵

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. Division of Nephrology, Kantonsspital Luzern, Switzerland 3. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland 4. Division of Nephrology, University Hospital Zurich, Switzerland, 5. Department of Nephrology, University Hospital Zurich, Switzerland

Background: The Molecular Microscope Diagnostic System (MMDx) may resolve inconclusive histology findings, as preserved biopsy material can be examined after histology findings have been obtained. The extent to which this proposed approach can be implemented in clinical practice remains an open question.

Methods: We prospectively analyzed 102 consecutive indication kidney allograft biopsies by histology and MMDx at the University Hospital Zurich from April to September 2022. Pathologists and clinicians with experience in MMDx assessed the need for MMDx by questionnaire when the histology report was available. Clinicians then assessed the discrepancy rate and assumed added value by questionnaire when the MMDx report was available.

Results: The need for MMDx was most frequently assessed for suspected AMR (12/20) and mixed AMR/TCMR (9/18), but less frequently for proven AMR (1/11), TCMR/borderline (1/6), DSA only (1/20), and no AMR/TCMR (3/28). Discrepancies were observed most frequently in cases with proven/suspected rejection (36/55), but rarely in the absence of histologic rejection (1/47). Clinicians considered an added value of molecular diagnostics mostly in suspected AMR (3/20), mixed AMR/TCMR (7/18), and TCMR/borderline (3/6). Classification into molecular AMR occurred in 9 of 32 cases with suspected AMR. However, classification into molecular TCMR was not observed in any of the 17 cases with suspected TCMR.

Conclusions: The need for MMDx in clinical practice goes beyond the recommendation for suspected AMR. While discrepancies appear to be limited to cases with histologic rejection, an added value of MMDx is particularly suspected along the AMR continuum. Because MMDx aims to overcome the inter-observer variability of histology, the potential added value of MMDx must be determined for each center individually.

YSN submission / student submission

OC 34 / P 10

Peripheral blood mitochondrial DNA fraction as a biomarker of renal involvement in systemic lupus erythematosus

Dr. Matthieu Halfon¹, Dr. Ashfaque Menon², Prof. Manuel Pascual¹, Prof. Kristina Sundquist², Dr. Anna Hedelius², Prof. Camillo Ribi¹

1. Lausanne University Hospital, Lausanne, Switzerland 2. Lund university, Lund, Sweden

Background: Kidney damage is of major concern in systemic lupus erythematosus (SLE). Mitochondrial dysfunction plays a significant role in SLE pathophysiology, particularly in case of renal involvement. Changes in circulating mitochondria specific DNA could serve as proxy for metabolic dysfunction in SLE, especially in subjects with lupus nephritis. To evaluate whole blood (WB) mitochondrial(mt) to nuclear (nuc)DNA fraction subjects with SLE compared to healthy controls (HC), and within the SLE group in those with and without renal involvement.

Methods: All SLE subjects were adults recruited at Lausanne University Hospital within the Swiss SLE cohort study, with clinical data and corresponding WB samples. SLE kidney involvement was defined by eGFR below 60 ml/min and/or proteinuria exceeding 0.7g/d. HC consisted of Swedish volunteers. After DNA extraction, the mt/nucDNA ratio was determined by the number of *ND1* gene copies divided by the *EIF2C1* gene copies. We used a logistic regression model with the mt/nucDNA ratio as dependent variable and SLE characteristics as covariates.

Results: Of the 195 patients with SLE, 168 (88%) were women. Median age was 42 years, IQR: 34–54. Median disease duration was 97 months, IQR: 37–194, and 61 (31%) patients had renal involvement. Median SLE Disease Activity Index was 4 points, IQR: 2–9. Median eGFR was 93 ml/min, IQR: 77–114, with mean proteinuria of 1 ± 3.3 g/day. The mt/nucDNA ratio was lower in SLE patients compared to HC (median 129, IQR: 113–151 vs 119, IQR: 99–144 respectively; $P = 0.001$). In SLE with renal involvement, the mt/nucDNA ratio was even lower than in non-renal SLE (median 105, IQR: 86–133 vs 123, IQR: 105–149; $P < 0.001$). The association with reduced mt/nucDNA ratio in renal SLE persisted when adjusting for age, eGFR, proteinuria, leucocyte count, hemoglobin concentration, thrombocytes count, and SLE Disease Activity Index.

Conclusion: SLE and renal lupus in particular are associated with a reduced mt/nucDNA ratio in WB, suggesting mitochondrial dysfunction. mtDNA demonstrates promise as a biomarker for assessing and managing renal involvement in SLE.

YSN submission

OC 35 / P11

Proteinuria and type of allograft injury identify kidney transplant recipients benefiting most from Belatacept conversion

Dr. Lukas Weidmann¹, Mr. Kai Castrezana Lopez¹, Dr. Nicolas Schmid¹, Prof. Thomas F. Mueller¹, Dr. Thomas Schachtner²

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. department of Nephrology, University Hospital Zurich, Switzerland

Background: Conversion to belatacept is associated with an improvement in kidney allograft function. Yet, not all kidney transplant recipients (KTRs) benefit equally from this change of maintenance immunosuppression. Both type (alloimmune vs. non-alloimmune) and severity of kidney allograft injury (assessed by proteinuria) may influence the functional response to a belatacept conversion.

Methods: We studied 49 KTRs from belatacept conversion to 1-year post-conversion. KTRs were categorized based on injury types (group 1: calcineurin inhibitor (CNI)-toxicity; group 2: antibody-mediated rejection (AMR); group 3: unspecific) in pre-conversion biopsies; and pre-conversion proteinuria (low = <500 mg/day, moderate = 500–1000 mg/day, high = >1000 mg/day). KTRs were analyzed for change of proteinuria (whole cohort) and change of kidney allograft function (injury- and proteinuria-categories).

Results: 43 of 49 (87.7%) individuals stayed stable or improved regarding proteinuria course over the first year of conversion. eGFR-Slopes were significantly positive in the CNI-toxicity group (+9.1 ml/min/year, $p < 0.001$), the low proteinuria group (+4.6 ml/min/year, $p < 0.001$) and the moderate proteinuria group (+3 ml/min/year, $p = 0.031$). Upon multivariate regression for 5% eGFR-increase over the 1-year post-conversion patients with low proteinuria and CNI-toxicity (non-alloimmune injury) benefited independently from age, baseline-eGFR or timepoint of conversion.

Conclusions: KTRs with low proteinuria and non-alloimmune injury benefit independent of kidney function before conversion. While aggravation of proteinuria post-conversion is rare, some KTRs show improvement of proteinuria post-conversion. If belatacept conversion is still beneficial compared to calcineurin inhibitor-based immunosuppression among KTRs with high proteinuria and alloimmune injury needs to be studied.

YSN submission / student submission

OC 36 / P 12

High rate of assisted Peritoneal Dialysis in an aging dialysis population: A single center observation

Dr. Stefan Achermann¹, Mrs. Stephanie Markiewicz¹, Mrs. Kloudija Mozzillo-Lackovic¹, Mrs. Iris Damdinsuren¹, Dr. Katrin Koenig¹, Dr. Felix Burkhalter¹

1. Division of Nephrology, University Clinic of Medicine, Kantonsspital Baselland, Liestal, Switzerland

Background: The annual incidence of end-stage renal disease (ESRD) has stabilized in Switzerland in recent years due to prophylaxis programs for patients with chronic kidney disease. At the same time, an increase in the proportion of elderly patients with ESRD was observed, which represents a challenge in the context of promoting home dialysis and in achieving the required 20% incidence rate for home dialysis in Switzerland.

Methods: We retrospectively analyzed the incidence of home dialysis, the rate of assisted home dialysis and the type of assistance at our center from 01.01.2015 until 30.06.2023.

Results: In total there were 206 patients initiating chronic dialysis treatment at our center during the observation period. 51 patients started on peritoneal dialysis, none on home hemodialysis and 155 patients on in-center hemodialysis, leading to an overall incidence rate of home dialysis of 25% (51/206). The incidence rate of assisted PD was 37% (19/51). The assistance was provided by family members in six patients (partners $n = 4$, parents $n = 1$, other family member $n = 1$), by outpatient nursing team in eight patients and in five patients by nursing home staff. There was a significant difference in the mean age between the independent PD patients and the assisted-PD patients with a median age of 65.0 versus 78.8 years.

Conclusion: Due to the increase in the proportion of elderly patients with ESRD there is a need to implement an assisted PD program to promote home dialysis and to achieve the required rate of home dialysis by the health authority in Switzerland.

YSN submission

OC 37 / P 13

Ventricular hypertrophy and stroke risk in chronic haemodialysis: a single-center study at the western French Guiana hospital

Dr. Arriel MAKEMBI BUNKETE¹, Ms. Florence FERMIGIER¹, Dr. Kazi Anga Muamba², Dr. Modi SIDIBE¹, Dr. Mohamed SIDIBE³, Dr. Malika BELGRINE³, Dr. Timoté DAVODOUN³, Dr. Tanguy GBAGUIDI³, Dr. Irénée DJICONKPODE¹

1. Department of nephrology and dialysis, Western French Guiana Hospital Center, French Guiana 2. Intensive Care Department, Western French Guiana Hospital Center, French Guiana 3. Department of Nephrology and dialysis, Cayenne Hospital Center, French Guiana

Introduction: Left ventricular hypertrophy (LVH) is the major cardiac abnormality in chronic haemodialysis patients. It is, independently of other cardiovascular risk factors, associated with the risk of stroke, which represents the third cause of cardiovascular mortality in dialysis patients. However, the magnitude of the association between LVH and stroke occurrence in

this population is not sufficiently described and particularly in the Guyanese population, hence the aim of this study.

Methods: Retrospective, descriptive and analytical study from June 2018 to June 2023, including all chronic haemodialysis patients at the west French Guyana hospital the primary endpoint was the occurrence of ultrasound left ventricular hypertrophy (LVH) and the secondary endpoint was the notion of stroke. We described the characteristics of patients with LVH in whom a stroke occurred. A logistic regression model was constructed to define the association between LVH and stroke, with a significance threshold equal to $p < 0.05$.

Results: A total of 35% of patients had left ventricular hypertrophy (LVH), of whom 32% had a history of stroke. The sex ratio M/F was 1.2. They were older, with a median age of 66 years. They had a mean NT-pro BNP doubling and 86% had hypertension. They had a higher mean pre-dialytic urea level (19.6 VS 16.7) and were equivalent with patients without LVH in terms of dialysis efficiency (mean KT/V 1.2), haemoglobin level (mean HB 11 g/dl). 11% of the population had a stroke, and all had LVH. The distribution of LVH was equivalent across the different stroke types, and these associations were significant ($p < 0.001$).

Conclusion: Left ventricular hypertrophy is an independent risk factor for stroke in chronic haemodialysis patients of all types.

KEYWORDS: Left ventricular hypertrophy, stroke, chronic haemodialysis

YSN submission

OC 38 / P 14

Loss of TrkC in the nephron aggravates tubular kidney injury in mice

Dr. Carolin Eul¹, Dr. Malte Krakow¹, Prof. Hermann Pavenstädt¹, Prof. Britta George¹

1. Medical Clinic D, Department of Nephrology, University Hospital Münster, Münster, Germany

Background: Acute tubular injury often progresses to chronic kidney disease. Neurotrophic tyrosine kinase receptor C (TrkC) regulates neuronal differentiation and survival signaling. In the kidney, TrkC is expressed in podocytes and in a tubular fraction consisting of cortical collecting duct and thick ascending limb in mice. Loss of TrkC in the nephron (TrkC-KO) results in proteinuria progressing to FSGS while tubuli appear unaffected histologically. However, TrkC is differentially expressed in tubuli of CKD biopsy samples of different etiologies. Thus, we aim to analyse the role of TrkC during tubular injury.

Methods: Three months old C57BL/6 nephron-specific TrkC-KO mice and littermate controls were fed a 0.2% adenine-enriched, or a control-diet for 8 days. Weight and blood urea nitrogen (BUN) were measured. Kidney sections were evaluated with histology, electron microscopy and immunofluorescence. HEK293T cells were treated with adenine to analyse the effects on TrkC signaling.

Results: Adenine-enriched diet causes the precipitation of crystals, acute tubular injury, inflammation, and consecutive fibrosis. TrkC-KO mice fed an adenine-enriched diet lost significantly more weight and displayed a significantly higher BUN, than adenine-fed controls. Histologically, adenine-fed TrkC-KO mice presented with more severe acute tubular injury in histology than adenine-fed control mice. Immunofluorescence analyses showed that distal tubules of adenine-fed TrkC-KO mice expressed more NFκB, and Ki67, compared to adenine-fed

controls. Moreover, leucocytes and macrophages were enriched in the kidney cortex of adenine-fed TrkC-KO mice, compared to adenine-fed controls. *In vitro*, HEK293T cells overexpressing TrkC exhibited increased TrkC phosphorylation and down-stream signaling when treated with adenine.

Conclusion: Adenine-induced acute tubular injury is aggravated upon loss of TrkC in the nephron of mice. Furthermore, tubulo-interstitial inflammation is increased in TrkC-KO mice fed an adenine-enriched diet. Taken together with the *in vitro* data TrkC signaling in tubules may be protective during adenine-induced acute tubular injury.

YSN submission

OC 39 / P 15

mTOR inhibitors in combination with calcineurin inhibitor after lung transplantation: a real-life experience with focus on kidney function

Ms. Katja Schmucki¹, Dr. Thomas Gaisl², Dr. Patrick Hofmann³, Dr. René Hage², Dr. Carolin Steinack⁴, Prof. Thomas Fehr¹, Prof. Silvia Ulrich², Dr. Macé Schuurmans²

1. Department of Internal Medicine, Cantonal Hospital Graubünden, Chur, Switzerland. Faculty of Medicine, University of Zurich, Zurich, Switzerland, 2. Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland. Faculty of Medicine, University of Zurich, Zurich, Switzerland, 3. Department of Internal Medicine, Cantonal Hospital Graubünden, Chur, Switzerland., 4. Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland.

Background: The mammalian target of rapamycin inhibitors (mTOR inhibitors) in combination with calcineurin inhibitors (CNI), antimetabolites and corticosteroids for immunosuppression after lung transplantation (TPL) have gained importance in patients with chronic kidney disease (CKD). The goal of this study was to characterize lung transplant recipients (LTR) treated with mTOR inhibitors, with a special focus on kidney function.

Methods: LTR transplanted at the University Hospital Zurich between December 1992 and April 2023 were analyzed. Demographics, estimated glomerular filtration rate (eGFR) before and after mTOR initiation, TPL circumstances, immunosuppressive regimens, and allograft function were recorded. We used linear regression to calculate the Mitch curves and a linear mixed-effects model to compare the eGFR.

Results: Of the LTR, 70/593 (12%) ever received mTOR inhibitors. Intolerance or adverse events of antimetabolites were the most common indication for mTOR inhibitor introduction, and discontinuation of 34/70 (49%) was often related to planned or urgent surgery. The mean annual eGFR decline changes significantly from -16.19 ml/min/1.73 m²/year (95% CI -22.27 to -10.11) before to -6.16 ml/min/1.73 m²/year (95% CI -13.37 to 1.05) after mTOR initiation ($p = 0.009$) with better outcomes with early mTOR inhibitor initiation.

Conclusions: This retrospective study suggests stabilization of kidney function after mTOR inhibitor initiation in LTR documented by a slower eGFR decline after mTOR inhibitor introduction with better outcomes early after lung TPL. Intolerance or adverse events of antimetabolites are important indications for the introduction of mTOR inhibitors. A relatively high discontinuation rate can be explained by the anticipation of impaired wound healing.

YSN submission

Figure 1. Alluvial plot on mTOR inhibitor indication, tolerance, and outcome. (Created with flourish studio app). Numbers indicate counts.

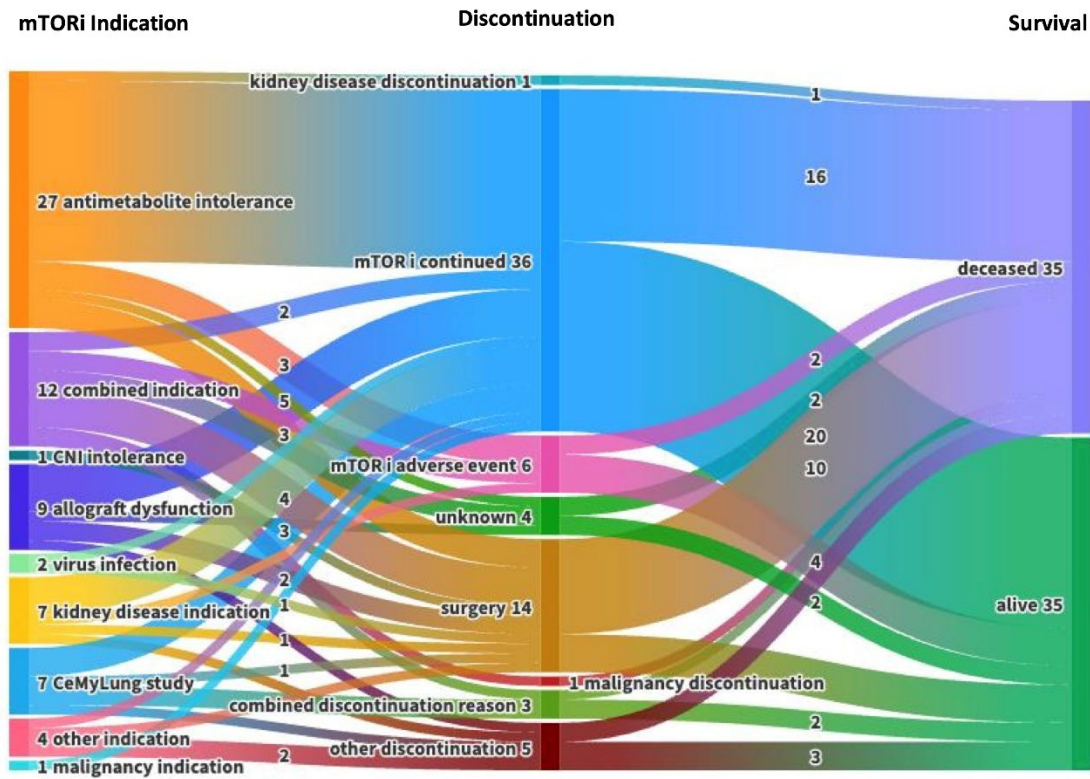
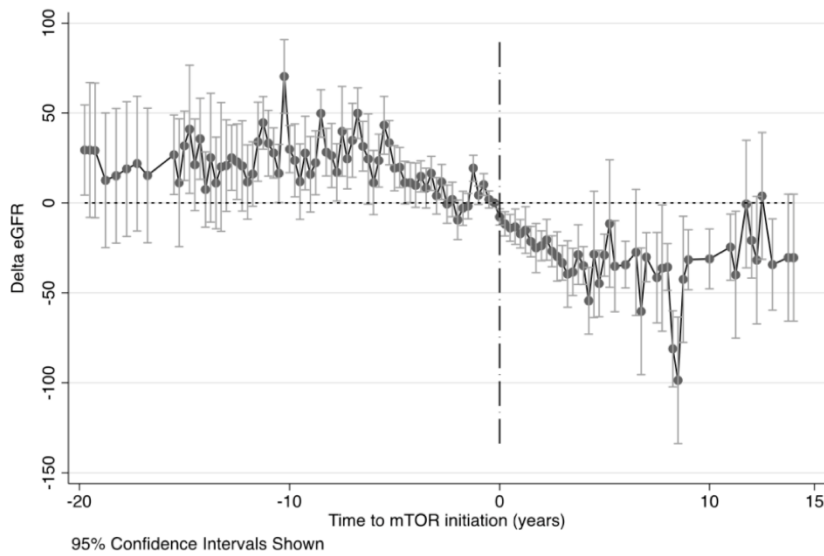
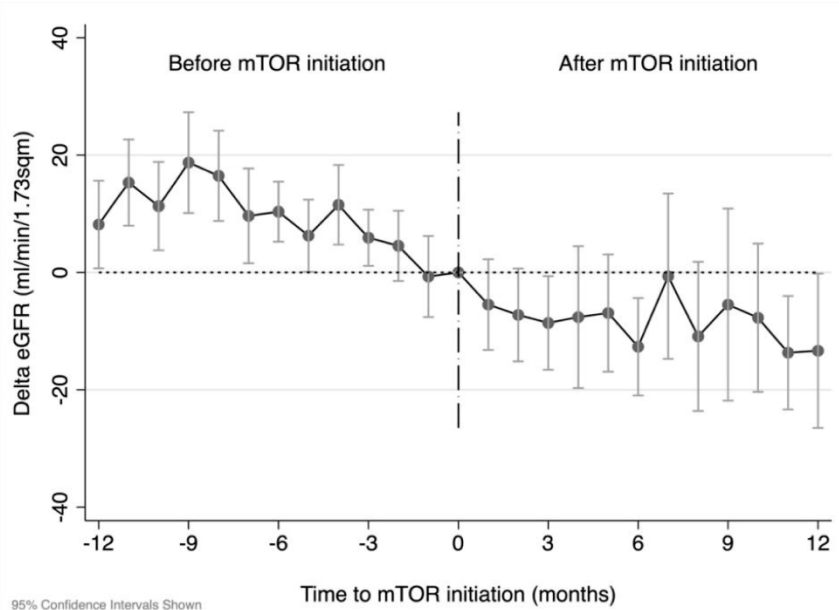


Figure 4. Dynamic difference-in-differences graph (two-way fixed effects event study regressions) on
 A) the whole group (rounded for quarters) and B) truncated to +/- 12 months (rounded for months).



A)



B)

OC 40 / P 16

Decline of living kidney donors: a Swiss monocentric study

Dr. Alexander Ritter¹, Dr. Aurelia Schnyder², Dr. Christian Kuhn³, Mr. Wolfgang Ender¹, Dr. Patrick Folie⁴, Dr. Isabelle Binet¹

1. Clinic for Nephrology and Transplantation Medicine, Cantonal Hospital St. Gallen, Switzerland 2. Clinic for Nephrology, Kantonsspital St. Gallen, St. Gallen, 3. Division of Nephrology and Transplantation Medicine, Kantonsspital St. Gallen, St. Gallen, Switzerland, 4. Clinic for General, Visceral, Endocrine and Transplant Surgery, Cantonal Hospital St. Gallen, Switzerland

Background: There is a survival benefit and more quality of life after kidney transplantation compared to dialysis for many patients with end-stage renal disease (ESRD). In view of the large demand, living kidney donation helps to increase the availability of donor kidneys. Demographical changes and the increasing prevalence of health issues like diabetes or obesity augment the pressure to accept medically complex living kidney donors. However, donor safety is a priority in the ethical conflict between avoidance of harm to the donor, respect for the autonomous donor decision and care for the recipient in need. Health or psychosocial risks for the donor and organ quality or unsuitable anatomical or immunological organ features may lead to donor decline. Given these constraints a thorough knowledge

of the current and past practice is fundamental to enable physicians to better evaluate future donation policies and donor outcomes.

Methods: This retrospective study comprises the assessment results of all potential living kidney donors at the cantonal hospital St. Gallen from January 2007 to December 2020. Pending decisions at the end of the study period were followed up until December 2021.

Results: During the study period a total of 275 living donor-recipient pairs with a mean age of 54.2 (\pm 11.9) years were assessed. 61.1% of donor candidates were female. Living unrelated donation accounted for 50.9% of assessments. 71.6% of donor candidates were declined. The main reasons for decline of potential donors as shown in figure 1 were immunological considerations comprising 20.7% followed by psychosocial aspects in 11.3% and renal causes in 8.4% of donor candidates.

Conclusion: The majority of donor candidates is declined for various reasons. More research is necessary on how these barriers for donation can be overcome and on long-term outcomes of medically complex living kidney donors, including psychosocial risks and risk factors for ESRD.

YSN submission

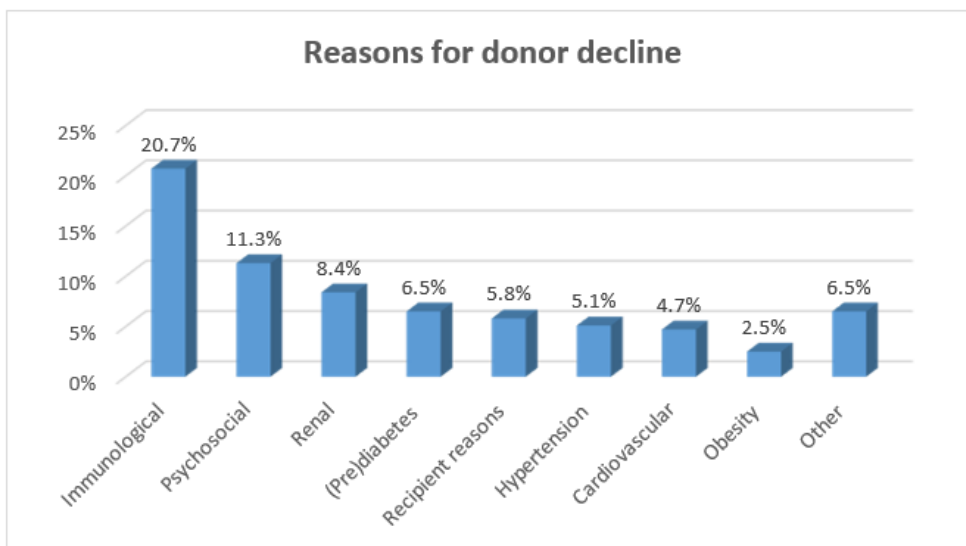


Figure 1: Categories of reasons for donor decline. Declined donor candidates comprising 71.6% (197) of all assessments.

OC 41 / P 17

Overview of Covid-19 vaccinations in dialysis patients in SwitzerlandMrs. Rebecca Guidotti¹, Prof. Patrice M. Ambühl¹¹. Stadtspital Zürich, Zürich, Schweiz

Background: The last few years were dominated by Covid-19. Vaccination has given many people hope for better health and return to normalcy. The aim of this study is to give an overview of the vaccination status among dialysis patients in Switzerland and to identify factors associated with vaccination.

Methods: All medical establishments in Switzerland (N = 96) providing chronic dialysis treatment, provided data from 2020–2022.

Results: In contrast to the general population, vaccination rate in rural areas was higher among dialysis patients. The willingness of patients in French-speaking Switzerland and Ticino to be vaccinated was higher versus in those from German-speaking Switzerland, similar to the general population. Among ethnicities, Asian patients (except Singhalese) were the most likely to have been vaccinated. Covid-19 vaccination did not prevent Covid-19 infection or positive testing. To the contrary, more vaccinated patients were tested positive for the coronavirus. However, non-vaccinated patients had a 2.7-fold higher risk of dying from a viral infection than dialysis patients who were vaccinated.

Conclusion: Although vaccination does not protect from infection and results even in higher risk for getting affected by Covid-19 compared to non-vaccinated patients, vaccination seems to reduce mortality associated with corona virus infection.

Table 1: Vaccination status in dialysis patients compared to the general population, stratified by age groups

| Age (years) | Vaccinated (%) | |
|-------------|--------------------|--------------------|
| | Dialysis patients* | General population |
| 0-9 | 0.0 | 3.7 |
| 10-19 | 71.4 | 50.4 |
| 20-29 | 80.0 | 73.4 |
| 30-39 | 79.7 | 43.6 |
| 40-49 | 80.9 | 77.9 |
| 50-59 | 83.1 | 81.3 |
| 60-69 | 84.5 | 84.8 |
| 70-79 | 89.1 | 90.6 |
| 80+ | 89.1 | 93.1 |
| Overall | 86.3 | 69.8 |

OC 42 / P 18

The Molecular Microscope Diagnostics System does not identify molecular TCMR in cases with isolated tubulitis, borderline changes, or isolated intimal arteritis in the absence of microvascular inflammationDr. Lukas Weidmann¹, Mr. Kai Castrezana Lopez¹, Dr. Birgit Maria Helmchen², Dr. Ariana Gaspert², Dr. Dusan Harmacek¹, Dr. Raphael Korach³, Dr. Nicola Bortel¹, Dr. Nicolas Schmid¹, Prof. Thomas F. Mueller¹, Dr. Seraina Von Moos⁴, Dr. Elena Rho¹, Dr. Thomas Schachtner⁵

¹. Division of Nephrology, University Hospital Zurich, Switzerland ². Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland ³. Division of Nephrology, University Hospital Zurich, Switzerland, ⁴. Division of Nephrology, Kantonsspital Luzern, Switzerland ⁵. department of Nephrology, University Hospital Zurich, Switzerland

Background: Isolated tubulitis, borderline changes, and isolated intimal arteritis suspicious for T-cell mediated rejection (TCMR) represent a particular challenge regarding treatment decisions. Even though the Molecular Microscope Diagnostics System (MMDx) has not been trained on those lesions, it has been suggested that MMDx may reclassify a subgroup of cases to molecular TCMR.

Methods: In this single-center cohort of 326 kidney allograft biopsies assessed by histology and MMDx from 2021 to 2023, we analyzed 214 cases with isolated tubulitis (i0, t1–3, v0; n = 101), borderline changes (according to Banff; n = 9), isolated intimal arteritis (i0, t0–2, v1; n = 37) and no lesions suspicious for TCMR (i0, t0, v0; n = 67) in the presence (n = 68) and absence (n = 146) of moderate microvascular inflammation (moMVI; g+ptc≥2, g≥1).

Results: 32/58 cases (55.1%) with TCMR-suspicion and moMVI showed molecular rejection (5 minor antibody-mediated rejections (AMR), 25 AMR, 2 AMR/TCMR) compared to 4/10 cases (40.0%) without TCMR-suspicion but moMVI (1 AMR/TCMR, 3 AMR; p = 0.375). Only 5/89 cases (5.6%) with TCMR-suspicion but no moMVI showed molecular rejection (2 minor AMR, 3 AMR). No pure molecular TCMR was identified in any subgroup. 9/147 cases (6.1%) with TCMR-suspicion showed a TCMR-specific rejection score (R2) ≥0.10 compared to 4/67 cases (6.0%) without TCMR-suspicion (p = 0.965).

Conclusions: MMDx does not identify molecular TCMR in cases with isolated tubulitis, borderline changes, or isolated intimal arteritis in the absence of moMVI. MMDx in TCMR-suspicion may be more useful to identify concomitant AMR in cases with MVI. TCMR scores do not quantify TCMR activity in cases suspicious for TCMR.

YSN submission / student submission

OC 43 / P 19

Association of ACE Gene Polymorphism with Retinopathy in Type 2 Diabetic Nephropathy Patients of BangladeshDr. MM Iqbal¹, Dr. MZ Hassan², Dr. AN Malik³, Dr. MZA Bhuiyan⁴, Dr. HU Rashid⁵, Dr. MS Hassan⁶

¹. NIKDU, Bangladesh ². BUHS, Bangladesh ³. KCL, UK ⁴. LGE, Lausanne, Switzerland ⁵. KF, Bangladesh ⁶. BIRDEM, Bangladesh

Background: Activation of Renin Angiotensin System (RAS) affects significantly in development and progression of diabetic microvascular complications. In this study the association of diabetic retinopathy (DR) with Angiotensin Converting Enzyme (ACE) gene polymorphism is observed in a group of nephropathy (DN) subjects

Methods: Pre-diagnosed stable non dialysis DN subjects were included. The fundal ophthalmoscopy report was recorded.

The Insertion / deletion (II, ID, DD) polymorphism of Angiotensin Converting Enzyme (ACE) gene was identified by PCR in genetic lab. Relevant clinical (age, sex, systolic and diastolic BP) and laboratory test reports (renal and glycaemic) was recorded. The DR was classified according to ETDRS criteria.

Results: Total 381 DN subjects were included where 65% were male. The DR like changes, based on direct ophthalmoscopy, was present in 27% and absent in 73% DN subjects. The types of DR present was mild pre-proliferative in 19% (gr1), mod to severe pre-proliferative in 66% (gr2) and proliferative in 15% (gr3). In the three groups respectively age was $59 \pm 7, 56 \pm 7$ and 54 ± 7 years; diabetes duration $12 \pm 7, 12 \pm 6$ and 11 ± 7 years; serum creatinine $1.8 \pm 0.7, 1.7 \pm 0.6$ and 1.8 ± 0.5 mg%; 24hours urinary protein $1.85 \pm 1.7, 1.7 \pm 1.8$ and 1.8 ± 1.7 g/day and HbA1c $8.3 \pm 1.7, 8.2 \pm 1.85$ and $7.7 \pm 1.6\%$; ($P = NS$). The distribution of II, ID, DD genotypes of ACE gene among all the study subjects were 38%, 40% and 22% respectively. The distribution of ACE genotypes were similar among DR present versus DR absent groups (II 36 vs 39%, ID 43 vs. 39% and DD 21 vs. 22%, $p = 0.699$) respectively. Also distribution of 3 genotypes II, ID & DD was similar in all DR types like mild (5, 50 & 45%), mod to severe pre-proliferative (24, 41 & 35%); and proliferative (25, 44 & 41%) ($p = 0.453$).

Conclusion: The ACE gene insertion/deletion polymorphisms are similarly distributed among diabetic nephropathy subjects with or without retinopathy. The II and ID genotypes are frequent ones.

OC 44 / P 20

Quantification of ionized and total magnesium in kidney transplant patients

Mr. Federica Bocchi¹, Dr. Simeon Schietzel², Prof. Uyen Huyhn-Do³, Prof. Bruno Vogt¹, Prof. Daniel Sidler⁴

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Division of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 3. Service of Nephrology, Bern University Hospital, Switzerland, 4. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, Bern, Switzerland

Background: in kidney transplant (KT) patients, Magnesium (Mg) deficiency is widespread. It is often encountered early after KT, may persist longer, and is frequently promoted by cal-

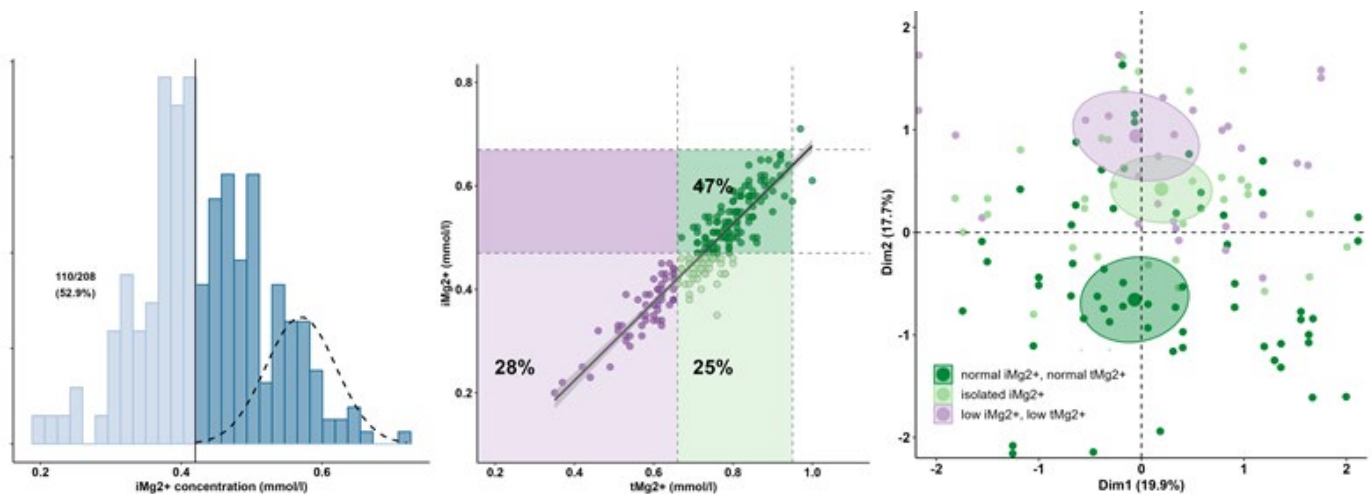
ciurein inhibitors (CNI) and tubular leakage. Studies demonstrated that post-KT hypomagnesemia promotes allograft dysfunction. The concentration of the active form, ionized Mg (iMg), is not measured clinically, and total Mg (tMg) and iMg correlations are conflicting. We assess the cross-sectional prevalence of hypomagnesemia in KT patients. Correlation with demographic and anthropometric parameters were also studied.

Methods: prospective, single-center analysis of KT patients in Bern (March 16th 2023 – 11th August 2023). Blood samples were collected at least twice for the majority of patients. tMg has been quantified from a plasma sample at the Clinical Chemistry Department of the University Hospital Insel Bern. The pHox[®] Ultra blood gas analyzer (Nova Biomedical, USA) provided results for iMg. Following co-variables were considered: age, comorbidities, kidney disease, transplant history, eGFR and treatment (including Mg supplementation and immunosuppression).

Results: 208 measurements in 104 patients were performed (once in 9/104 patients (8.7%), twice in 86/104 (82.7%) and trice in 9/104 (8.7%)). Compared to healthy volunteers, mean iMg was significantly lower in KT patients (KT: 0.46 mmol/l (IQR: 0.40–0.50), volunteers: 0.57 mmol/l (IQR 0.54–0.61), $p < 0.01$). Overall, iMg and tMg showed strong category agreement ($r^2 = 0.93$, $p < 0.01$). In linear regression low iMg correlated with CNI exposure and female gender. 110/208 measurements (52.9%) showed a reduced iMg (cutoff: 0.42 mmol/l). In 58/208 (27.9%) both values were reduced and 52/208 (25%) had isolated reduced iMg. In principal component analysis (PCA), patients with isolated reduced iMg clustered with patients with reduced iMg and tMg.

Conclusion: iMg and tMg were strongly correlated. A substantial proportion of patients show isolated low iMg. Currently, it is unclear, if these patients suffer from magnesium-deficiency and if supplementation is indicated.

YSN submission



OC 45 / P 21

Use of Patient-Centered Dialysis in Switzerland: A Rarity or Common Practice?

Dr. Katarina Benackova¹, Dr. Andreas Ebnetter², Prof. Dominik UEHLINGER¹, Prof. Steffen Eychmüller²

1. Universitätsklinik für Nephrologie und Hypertonie, Inselspital Bern, Switzerland 2. Universitäres Zentrum für Palliative Care, Inselspital Bern, Switzerland

Background: Two of the foundational principles for patient-centered dialysis care are a) tailoring the approach to optimize symptom management and b) aligning the dialysis strategy with individual patient's goals. However, the extent to which this approach is prevalent in Switzerland remains uncertain. To fill this gap, we conducted a survey among Swiss nephrologists.

Methods: We conducted a cross-sectional online survey and followed the Checklist for Reporting of Survey Studies (CROSS) guidelines. The survey employed a questionnaire consisting of 11 questions across 2 sections, with multiple answers possible. The first section focused on the dialysis strategy used and the patient (e.g., Do you sometimes deviate from "standard" dialysis regimens? What are the characteristics of patients who receive nonstandard dialysis?), while the other section centered on the setting and the demographics of the physicians (e.g., What type of nephrology clinic do you work in?)

Results: We analyzed a total of 57 responses (response rate 30%). All types of dialysis centers were represented: tertiary-public (35%), secondary-public (38.6%), other-public (10.5%), and private (21%) centers. Deviation from the standard dialysis strategy was frequent, with over half (61%) of the physicians deviating from standard dialysis in 5%–20% of cases. Deviations exceeding 20% of cases were infrequent, with 25% reporting 21%–50% of cases and only 2% reporting over 50%. Only 16% of physicians adhered strictly to the standard dialysis approach. The top three most common reasons for changing dialysis strategy were 1) limited life expectancy (77%), 2) preserved kidney function (70%), and 3) patient preference for less intensive treatment (49%).

Conclusion: Patient-centered dialysis is not unusual in Switzerland and is reported across all types of dialysis centers. It predominantly involves patients with limited life expectancy (palliative dialysis) or those with preserved kidney function (incremental dialysis).

YSN submission / student submission

OC 46 / P 22

Structural and functional echocardiographic changes after renal transplantation (NCCR project)

Ms. Yuansheng Zhang¹, Mr. Marc Fabian Fischer¹, Ms. Anett Romançuk¹, Dr. Patrizia Amico², Prof. Uyen Huynh-Do³, Prof. Sophie De Seigneux⁴, Dr. Lena Berchtold⁴, Prof. Dela Golshayan⁵, Dr. Aurelia Schnyder⁶, Prof. Thomas F. Mueller⁷, Dr. Elena Rho⁷, Prof. Vartan Kurtcuoglu¹, Dr. Diane de Zélicourt¹

1. Institute of Physiology, University of Zürich, Zürich, Switzerland, 2. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel, Basel, Switzerland 3. Service of Nephrology, Bern University Hospital, Switzerland, 4. Service of Nephrology, Division of Medicine, Geneva University Hospitals, Geneva, Switzerland 5. Transplantation center, Lausanne university hospital, 6. Clinic for Nephrology, Kantonsspital St. Gallen, St. Gallen, Switzerland 7. Division of Nephrology, University Hospital Zurich, Zurich, Switzerland

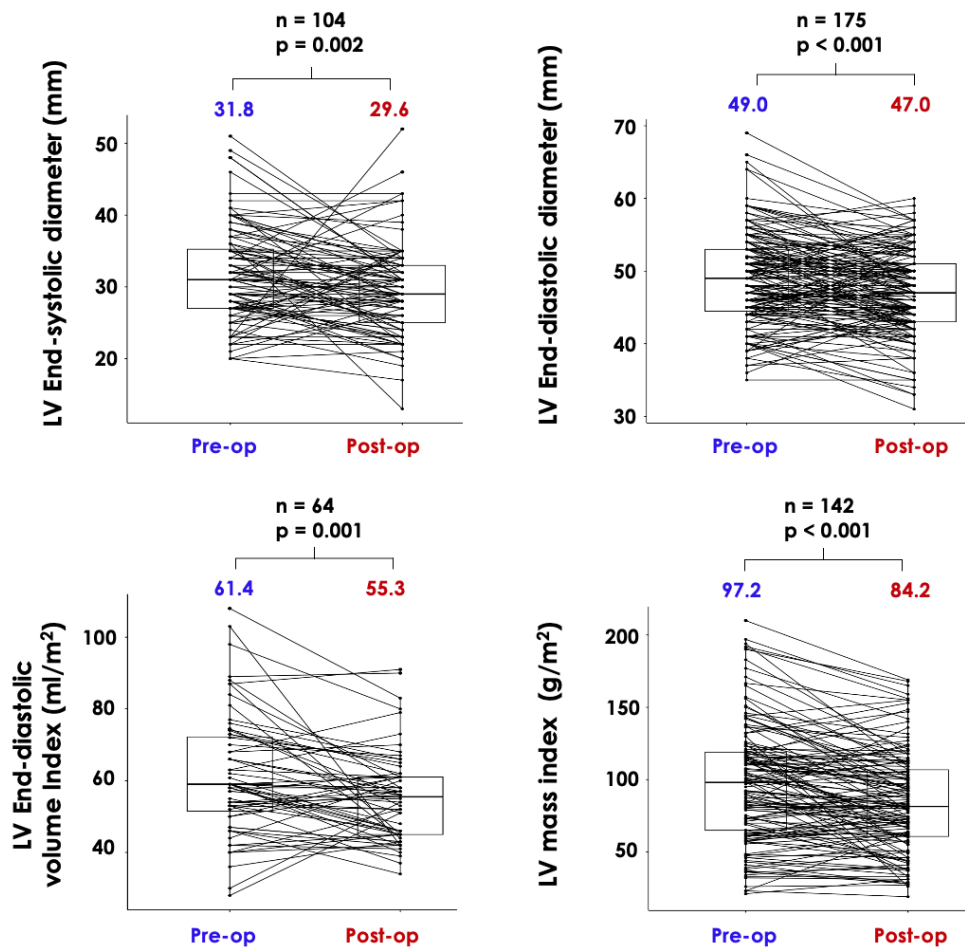
Background: Cardiovascular disease is a leading cause of mortality for renal transplant recipients (RTRs). This study aimed to examine if cardiac changes associated with end-stage renal disease are reversible by renal transplantation (RT) and assessed the prognostic value of pre-operative transthoracic echocardiography (TTE) for predicting major adverse cardiovascular events (MACE).

Methods: We retrospectively analyzed clinical and TTE data of adult RTRs enrolled in the STCS during 2008–2019 and followed until 2021. Included in the current analysis are RTRs from Kantonsspital Sankt Gallen and the University Hospitals of Basel, Geneva and Zurich, with pre-operative TTE at most 2 years before transplantation. Primary outcome was first post-operative MACE. Univariate Cox-regression analysis for MACE was conducted for TTE parameters and traditional risk factors such as: recipient and donor demographics, physicals (BMI, blood pressure), blood chemical analysis (cholesterol, HbA1c), smoking and disease history. Finally, echocardiographic changes were tested in a subset analysis of patients with repeated post-transplant TTEs within 0.5–2 years, using paired t-test.

Results: Of a total of 2149 RTRs, 676 had valid pre-operative echocardiographic data (mean [SD] age, 51.2 [13.7] years; 452 [66.9%] male). Of these, 138 (24.6%) experienced MACE at a median follow-up of 2.4 years (38 fatal and 123 non-fatal events). In addition to traditional risk factors (age, diabetes, hyperlipidemia, and prior MACE), a lower left ventricular (LV) ejection fraction as well as higher left atrial diameter, LV end-systolic diameter and LV mass index were significantly associated with MACE post-transplant upon univariate analysis. Paired pre/post-transplant TTE parameters showed a significant decrease in LV end-systolic and end-diastolic diameters, end-diastolic volume index and LV mass index at a median follow-up of 1.2 years (Figure1).

Conclusion: In our cohort, RT was associated with LV unloading and reverse remodeling. The results further suggest that LV structural and functional parameters may assist post-transplant prognostication.

YSN submission / student submission



OC 47 / P 23

Antibody Response at 6, 24 and 36 Weeks after 2 Doses of Vaccine Against COVID-19 and its Association with Cardio-Renal Risk Factors among Health Care Workers of Bangladesh

Dr. MM Iqbal¹, Dr. SKM Ershad¹, Dr. R Morshed¹, Dr. MZ Hassan², Dr. SR Choudhury³, Dr. M Ishraq³, Mr. MS Alam⁴, Dr. MS Hassan⁴, Dr. SK Banerjee⁵, Dr. MI Arslan⁵

1. NIKDU, Bangladesh 2. BUHS, Bangladesh 3. NHFH&RI, Bangladesh 4. BIRDEM, Bangladesh 5. BSMMU, Bangladesh

Background: COVID-19 posed the healthcare workers at a very high risk during this pandemic. The aim was to assess the antibody responses at 6, 24 and 36 weeks after two doses of vaccine against COVID19 among health care workers.

Methods: Health care workers from 3 tertiary hospital participated. All participants gave blood samples at first visit 6 weeks after second dose of COVID vaccine, then after 6 and 9 months. A quantitative measurement of IgG antibody against (S) protein of SARS-Cov-2 was done by CMIA developed by Abbott. A cut-off value ≥ 50 AIU/L of IgG against spike protein is considered a positive response.

Results: In 350 healthcare workers 47% were doctors, 37% nurses and rest others (supporting staffs, cleaner, guard etc.). Among them some 13% were diabetic, 12% hypertensive, 6% asthma and 3.5% had nephropathy. Vaccine responses measured from neutralizing antibody IgG at 6, 24 and 36 weeks were 99.4%, 99.2% and 98.5% respectively with a mean titer of 14556 ± 1396 , 3024 ± 5293 and 11741 ± 15567 AIU/L (cut-off

value ≥ 50 AIU/L). At 6 weeks, the 50th percentile of IgG level against Spike protein of SARS-Cov-2 among participants with a history of COVID 19 was higher compared to non-COVID participants (11155 vs.6153AIU/L, $p < 0.05$). At an eGFR cut-off of ≥ 90 , 60–90, 30–60 and < 30 ml/min/1.73 m² showed no difference in antibody titer at any of the 6, 12 and 36 months intervals. The correlation studies showed no association of antibody titers with blood pressure, hemoglobin, serum albumin and eGFR. The frequency of COVID-19 re-infection varied between 5%–8% from 12 to 36 weeks post vaccination.

Conclusion: After 2 doses of vaccination for SARS-COV-2, a high antibody response that persisted around 98% up to 36 month post vaccination. There was no apparent association of major renal and cardiac risk factors with vaccine response in this group.

YSN submission

OC 48 / P 24

Rogue docking - theoretical considerations for cardio-renal syndromes

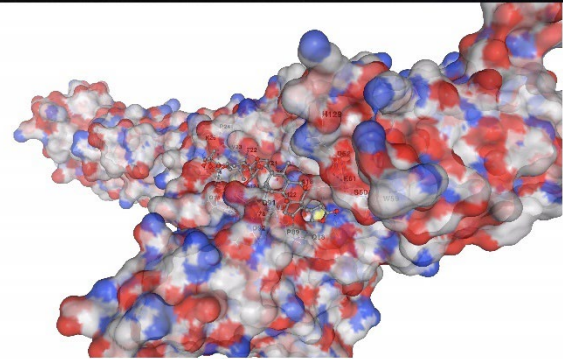
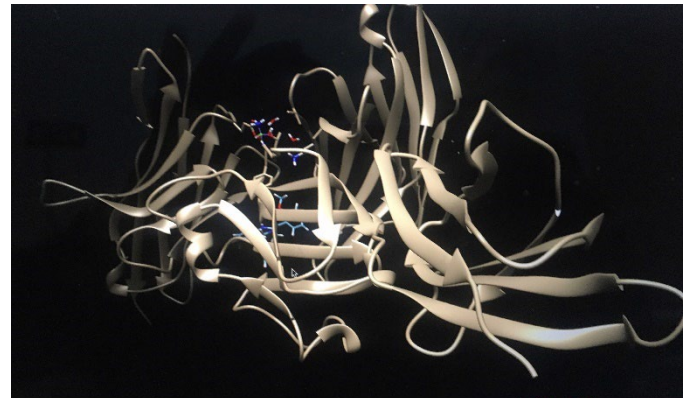
Dr. Mark Christopher Arokiaraj¹
1. 36 Montorsier st, Pondicherry, India

Aims: The incidence of cardio-renal syndromes and its clinical implications are common in clinical practice. This theoretical study was performed to look for potential prevention and treatment solutions for this clinical vignette. The traditional drugs which are not known to be related to cardio-renal-related proteins were tested. Conventionally, the selected proteins and ligands in the study have different targets and receptors. Molecular signalling and the significance of these unconventional docking, which could occur in physiological processes, are largely unknown.

Methods: Using available docking software, docking of proteins - calmodulin and NephtrinMAG1 complex, and various potential ligands was performed. After the docking test, the results were observed, and various parameters were analysed. CD28/PD-D1 was also docked with digoxin. The docking sequences for each interaction was studied through ChimeraX. The selected proteins and the ligands are not known to have interactions in previous literature. Some of the results observed were also studied in another docking software randomly. Dynamic molecular interactions was not performed in the study.

Results: Docking could be seen with molecules like digoxin, levosimendan, arjunin, moringin, nizaminin A with the selected proteins. The docking potential, deltaG, was in the range of -6 to -7.5 Kcal/mol. The full fitness ranged from -525 to -2250 Kcal/mol. H bond formation in the docked molecules could be observed with other forces like Vander wall forces. Surface analysis showed the potential of interactions of these ligands with the selected proteins. Random checking of some of the results also corroborated with other docking software.

Conclusion: There is a theoretical potential for these untraditional molecules to reduce the common clinical problem of cardio-renal syndromes. However, extensive molecular and docking studies are required to identify the potential of these observations.



ELEVATOR PITCH PRESENTATIONS & POSTER PRESENTATIONS

OC 49 / P 25

Pregnancy after kidney transplantation: an observational study on maternal, graft and offspring outcomes in view of current literature

Dr. Louis Stavart 1, Dr. Camille Verly 2, Dr. Jean-Pierre Venetz 1, Prof. David Baud 3, Dr. H el ene Legardeur 3, Prof. Yvan Vial 3, Prof. Dela Golshayan 4

1. Transplantation Center, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 2. Faculty of Biology and Medicine, University of Lausanne (UNIL), Lausanne, Switzerland, 3. Service of Gynecology and Obstetrics, Woman-Mother-Child Department, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 4. Transplantation center, Lausanne university hospital, Lausanne, Switzerland

Background: Pregnancy after kidney transplantation (KTx) is considered to have a high risk of non-negligible maternal, graft, and offspring complications. However, literature regarding long-term outcomes remains scarce.

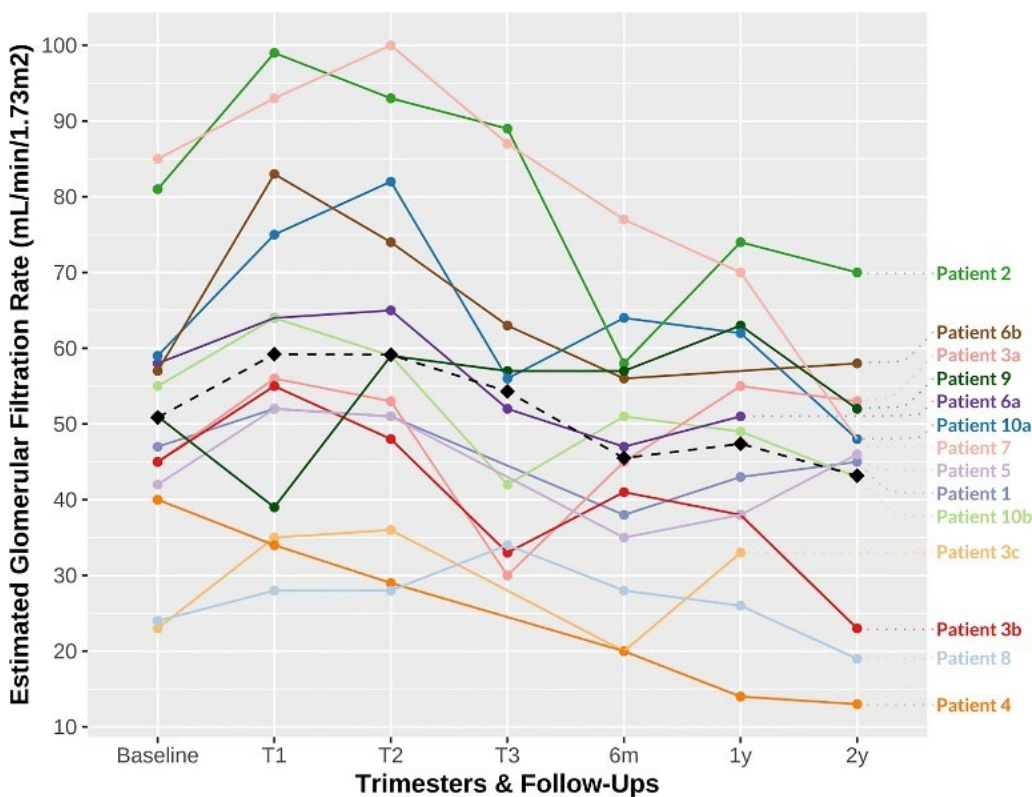
Methods: We retrospectively collected data from all women with at least one live birth pregnancy after KTx who were followed at our tertiary hospital between 2000 and 2021 to study maternal, graft and fetal outcomes.

Results: Ten patients underwent 14 live birth pregnancies after KTx. Preponderant maternal complications were stage 1 acute kidney injury (43%), urinary tract infections (UTI, 43%), progression of proteinuria without diagnostic criteria for preeclampsia (29%), and preeclampsia (14%). Median baseline

serum creatinine at conception was 126.5 $\mu\text{mol/L}$ [median estimated glomerular filtration rate (eGFR) 49 mL/min/1.73 m²], and eGFR tended to be lower than baseline at follow-ups. Overall, there was no increase in preexisting or occurrence of *de novo* donor-specific antibodies. No graft loss was documented within the 2-year follow-up. There were nine premature births (64%). The median birth weight, height, and head circumference were 2,560 g, 45.5 cm, and 32.1 cm, respectively. These measurements tended to improve over time, reaching a higher percentile than at birth, especially in terms of height, but on average remained under the 50th percentile curve.

Discussion: Overall, pregnancies after KTx came with risks for the mother, with a high prevalence of cesarean sections, emergency deliveries, UTI, and preeclampsia, and for the child, with a high proportion of prematurity, lower measurements at birth, and a tendency to stay under the 50th percentile. The short- and long-term impact on the allograft seemed reassuring; however, there was a trend toward lower eGFR after pregnancy. With these data, we emphasize the need for a careful examination of individual risks. More data about the long-term development of children are required to fully apprehend the impact of KTx on offspring.

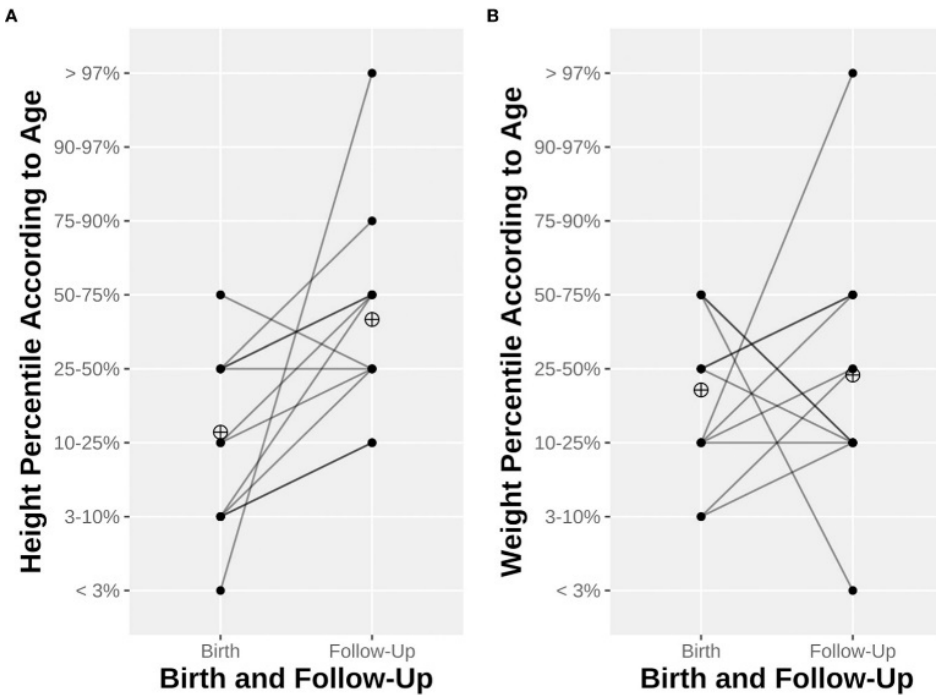
YSN submission / student submission



| Characteristic | Mothers (N = 10, corresponding to 14 pregnancies) |
|---|---|
| At first conception after KTx | |
| Gestation/parity | |
| Previous abortus, <i>n/N</i> (%) | 2/10 (20) |
| Previous miscarriage, <i>n/N</i> (%) | 2/9 (22) |
| Pregnancies before KTx, <i>n/N</i> (%) | 3/10 (30) |
| Time from KTx (months), median (range) [†] | 41 (12–112) |
| CMV seropositive, <i>n/N</i> (%) | 4/10 (40) |
| Weight (kg), median (range) [†] | 61.2 (47.3–68.9) |
| BMI (kg/m ²), median (range) [†] | 23 (17–26) |
| Comorbidities, <i>n/N</i> (%) | |
| Obesity | 0/10 (0) |
| Chronic hypertension | 3/10 (30) |
| Diabetes mellitus | 3/10 (30) |
| Thrombo-embolism history | 3/10 (30) |
| Fecundation technique, <i>n/N</i> (%) | |
| Artificial insemination | 2/14 (14) |
| IVF | 2/14 (14) |
| Nephrological history | |
| RRT, <i>n/N</i> (%) | 9/10 (90) |
| Duration of dialysis (months), median (range) | 10 (2–144) |
| Ever had PD, <i>n/N</i> (%) | 3/10 (30) |
| AVF, <i>n/N</i> (%) | 6/8 (75) |
| Initial nephropathy, <i>n/N</i> (%) | |
| CAKUT | 5/10 (50) |
| Type 1 diabetes | 2/10 (20) |
| Alport syndrome | 1/10 (10) |
| IgA nephropathy | 1/10 (10) |
| Membranoproliferative glomerulonephritis | 1/10 (10) |
| At last KTx before pregnancy | |
| Age (years), median (range) | 35 (23–42) |
| Ethnic group, <i>n/N</i> (%) | |
| Caucasian | 9/10 (90) |
| Asian | 1/10 (10) |
| Second transplantation, <i>n/N</i> (%) | 5/10 (50) |
| Ablation of first graft ablation, <i>n/N</i> (%) | 2/5 (40) |
| Living donor, <i>n/N</i> (%) | 7/10 (70) |
| Preemptive transplantation, <i>n/N</i> (%) | 2/10 (20) |
| Induction therapy <i>n/N</i> (%) | |
| Basiliximab | 6/9 (67) |
| ATG | 3/9 (33) |

AVF, arteriovenous fistula; ATG, antithymocyte globulin; BMI, body mass index; CAKUT, congenital anomalies of the kidney and urinary tract; CMV, cytomegalovirus; IVF, *in vitro* fecundation; KTx, kidney transplantation; PD, peritoneal dialysis; RRT, renal replacement therapy.

[†]Patient 8 was excluded because we only have detailed data following her second pregnancy after KTx.



OC 50 / P 26

Women have a higher renal perfusion index, but their renal circulatory response to a cold pressor test is similar to men

Ms. Mariëlle Hendriks-Balk¹, Dr. Aikaterini Damianaki¹, Dr. Kenji Theiler¹, Dr. Erietta Polychronopoulou¹, Ms. Wendy Brito¹, Dr. Menno Pruijm¹, Prof. Gregoire Wuerzner¹

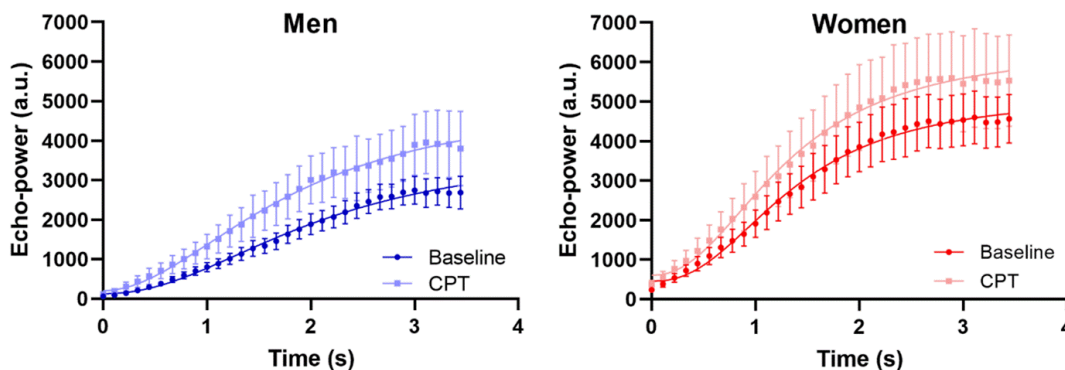
1. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland

Background: Contrast-enhanced ultrasonography (CEUS) enables the quantification of renal microcirculation using a dedicated software to estimate cortical perfusion. We have previously shown that the perfusion index (PI) is lower in hypertensive patients than in healthy participants and that the increase of the PI during a cold pressor test (CPT) is blunted in these patients. Whether a sex-specific response of the PI to a CPT exist is unknown. The objective of this study was to compare the cortical microcirculation between women and men with hypertension, and to assess the response to a CPT.

Methods: This was a prospective observational study. Hypertensive (HT) participants underwent two separate CPT of 2 minutes. Doppler ultrasound was used to measure renal resistive index (RRI) and CEUS was used to measure the PI as a proxy of renal tissue microcirculation. Renal Doppler and CEUS were performed before and during the CPT. A mixed model analysis was used to detect an effect of sex, exposure to the CPT, age and BMI.

Results: Twenty-two HT men and eleven HT women were included. eGFR, age and body mass index were similar for both groups. The PI was higher in women ($p = 0.006$) and the PI increased during CPT in both groups ($p < 0.001$), but there was no significant interaction between the response to CPT and sex (Figure 1). No difference in the RRI was observed between men and women. Age had no effect on the PI, while BMI was associated with a decrease in the PI.

Conclusions: Hypertensive women had a higher PI than hypertensive men, suggesting that microcirculation is better preserved in HT women compared to HT men. The increase in PI during the CPT is similar in both genders suggesting the absence of sex-specific reactivity of the microvasculature during CPT.



OC 51 / P 27

A case of thrombotic microangiopathy as an initial presentation of HIV InfectionDr. Edita Poskaite¹, Prof. Bruno Vogt², Dr. Federica Bocchi²*1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland*

Background: Thrombotic microangiopathy (TMA) is a rare and potentially life-threatening syndrome characterized by a group of medical conditions defined by endothelial injury that triggers abnormal coagulation activation, resulting in microangiopathic hemolytic anemia, thrombocytopenia and microvascular thrombosis, ultimately leading to organ damage. While TMA has been documented in advanced HIV infection, it is an uncommon initial presentation. The exact mechanism of HIV in the pathogenesis of TMA remains unknown. Early recognition and management of HIV-related TMA are essential to improve patient outcomes.

Case description: A 48-year old male Caucasian complaining of fatigue, dyspnea, nausea and emesis, upper abdominal pain, nonbloody diarrhea and weight loss for several weeks. Investigation revealed an acute kidney injury (creatinine 1915 $\mu\text{mol/l}$, urea 48.2 mmol/l) with glomerular microhematuria and nephrotic range proteinuria. A TMA was diagnosed based on a thrombocytopenia (platelet count of 65,000 G/L), a hemolytic anemia (hemoglobin of 62 g/l , LDH of 895 U/l , a haptoglobin <0.10), and a peripheral smear showing multiple schistocytes. A normal ADAMTS13 activity excluded a thrombotic thrombocytopenic purpura. Levels of C3 and C4 were within normal ranges. Stool cultures were negative. HIV was found to be positive; CD4 count was 83 $\text{cells}/\mu\text{L}$. There was no evidence of any opportunistic infections. The kidney biopsy showed signs of acute tubulointerstitial nephritis and chronic thrombotic microangiopathy. He was started on triple antiretroviral therapy (emtricitabin, tenofovir, dolutegravir) and hemodialysis. Despite the treatment, the patient remained dependent on dialysis.

Conclusion: This case highlights the importance of considering TMA as a potential initial presentation of HIV infection, especially in areas with a high prevalence of HIV, to facilitate timely diagnosis and intervention.

YSN submission

OC 52 / P 28

A case of new-onset nephrotic syndrome due to suspected transient receptor potential cation channel subfamily C member 6 mutation in a first pregnancyDr. Dina Ezzat¹, Dr. Heidi Sarrasin², Dr. Anja Kruse³, Dr. Caroline Eggemann¹, Dr. D. Bartholdy¹, Dr. Laila Mani²*1. Department of Gynaecology and Obstetrics, Spitalzentrum Biel, Biel, Switzerland 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 3. Division of Nephrology, Central Hospital Biel, Biel, Switzerland.*

Background: From the start of any pregnancy, regular urinary testing is carried out to detect the presence of proteinuria and other urine abnormalities, which may indicate the presence of kidney disease, including nephrotic syndrome (NS). The causes of NS are numerous including hypertensive disorders of pregnancy as well as underlying pre-existing or de novo kidney disease. Rare genetic forms of NS can be found linked to various mutations in podocyte genes. In this case, NS due to variants in the transient receptor potential cation channel subfamily C member 6 (*TRPC6*) gene was suspected.

Case description: A 21-years old primigravida without medical history presented for her first trimester control. Nephrotic-range proteinuria and microhematuria were detected that had

retrospectively been present during an episode of febrile pyelonephritis several months ago. The patient showed edema and moderate hypalbuminemia with normal blood pressure and kidney function. Serology and protein analyses as well as angiogenesis markers were unremarkable. Duplex ultrasound ruled out renal vein thrombosis. However, family history was positive with hematuria and proteinuria in several family members suggesting autosomal-dominant inheritance pattern. In the grandmother, gene panel analysis had been performed for the suspicion of Alport's syndrome revealing variants of unknown significance in the *TRPC6* (c.253_264dup), *NPHS1* and *CRB2* genes. Hence, NS due to *TRPC6* variant was suspected. The patient was closely monitored during pregnancy and was managed with low molecular weight heparin, ciclosporine, amiloride and loop diuretics. Finally, progressive deterioration of the renal situation with increasing proteinuria, serum creatinine and blood pressure at 36 weeks' gestation led to an induced delivery with a good outcome for both mother and child.

Learning points: This case highlights the potential of pregnancy in uncovering underlying pathologies, which might be exacerbated by it. It also illustrates the therapeutic challenges of an incidental discovery of a nephropathy during pregnancy.

YSN submission

OC 53 / P 29

Overlapping pathologic findings in the kidney allograft biopsy: pitfalls for the Molecular Microscope Diagnostics System (MMDx)Ms. Elena Rho¹, Dr. Nicola Bortel², Dr. Lukas Weidmann², Mr. Kai Castrezana Lopez², Dr. Dusan Harmacek², Dr. Raphael Korach¹, Dr. Nicolas Schmid², Dr. Seraina Von Moos³, Dr. Birgit MariaHelmchen⁴, Dr. Ariana Gaspert⁴, Dr. Thomas Schachtner⁵*1. Division of Nephrology, University Hospital Zurich, Switzerland, 2. Division of Nephrology, University Hospital Zurich, Switzerland 3. Division of Nephrology, Kantonsspital Luzern, Switzerland 4. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland 5. department of Nephrology, University Hospital Zurich, Switzerland*

Background: The Molecular Microscope Diagnostic System (MMDx) has been suggested to add diagnostic value in cases of suspicious antibody-mediated (ABMR) and T cell-mediated rejection (TCMR). Other overlapping pathologies, however, have the potential to mimic molecular rejection.

Methods: In this single-center cohort of 324 indication kidney transplant biopsies assessed by histology and MMDx at the University Hospital Zurich, we analyzed 69 cases with overlapping pathologic findings by histology: 15 cases with pyelonephritis, 21 cases with BK nephropathy (BKN), 5 cases with acute interstitial nephritis (AIN), and 28 cases with recurrent/de novo glomerulonephritis (GN).

Results: **Pyelonephritis:** 8 of 15 cases (54%) with pyelonephritis showed a rejection, which was diagnosed in only 107 cases out of 309 biopsies, (35%), without overlapping pathologies ($p = p = 0.001$). The TCMR phenotype score (R2) was higher in the pyelonephritis group (0.13 vs 0.00, $p = 0.001$). **BKN:** 16 out of 21 cases (76%) showed rejection, compared to 98 cases out of 302 biopsies in the control group, (33%) $p = 0.001$. The phenotype scores for TCMR (R2), mixed rejection (R3) and early ABMR (R4) were higher in the BKN group (respectively 0.07 vs 0.00, $p = 0.001$; 0.02 vs 0.00, $p = 0.001$, 0.065 vs 0.05, $p = 0.001$). **AIN:** 3 of 5 cases (60%) with AIN showed molecular TCMR, of which 2 cases showed mixed ABMR/TCMR in the absence of any antibody-mediated changes by histology. **GN:** 21 of 28 cases (75%) with GN showed no molecular ABMR/TCMR, whereas 2 of 28 cases (7%) showed minor molecular findings, and 5 of 28 cases (18%) showed ABMR.

Conclusions: Minor molecular findings and high global disturbance scores should always suggest the presence of any overlapping pathology. Cases of pyelonephritis, BKN, and AIN mostly mimic molecular rejection and might be misleading in

their interpretation. Although GN often does not show molecular rejection, the elevated ABMR scores suggest a GN-associated phenomenon.

YSN submission / student submission

Figure 1

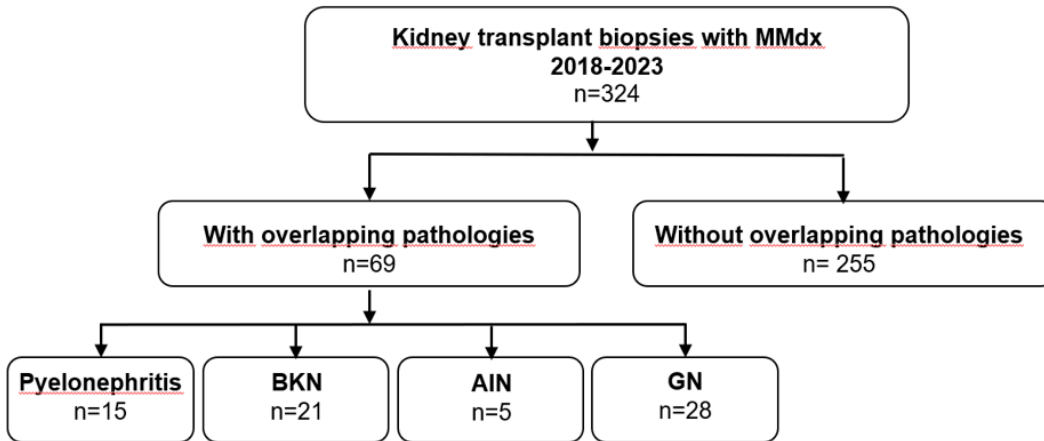


Figure 2

Molecular diagnosis

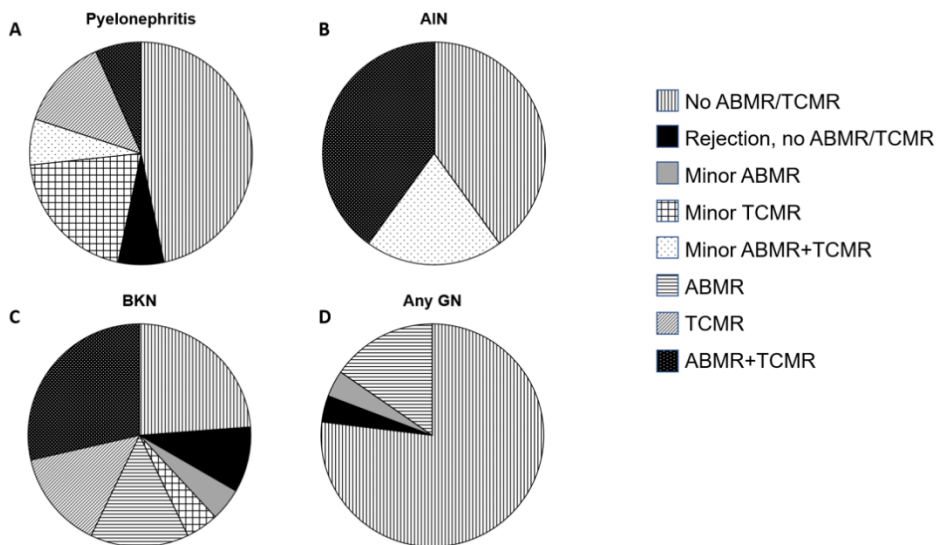
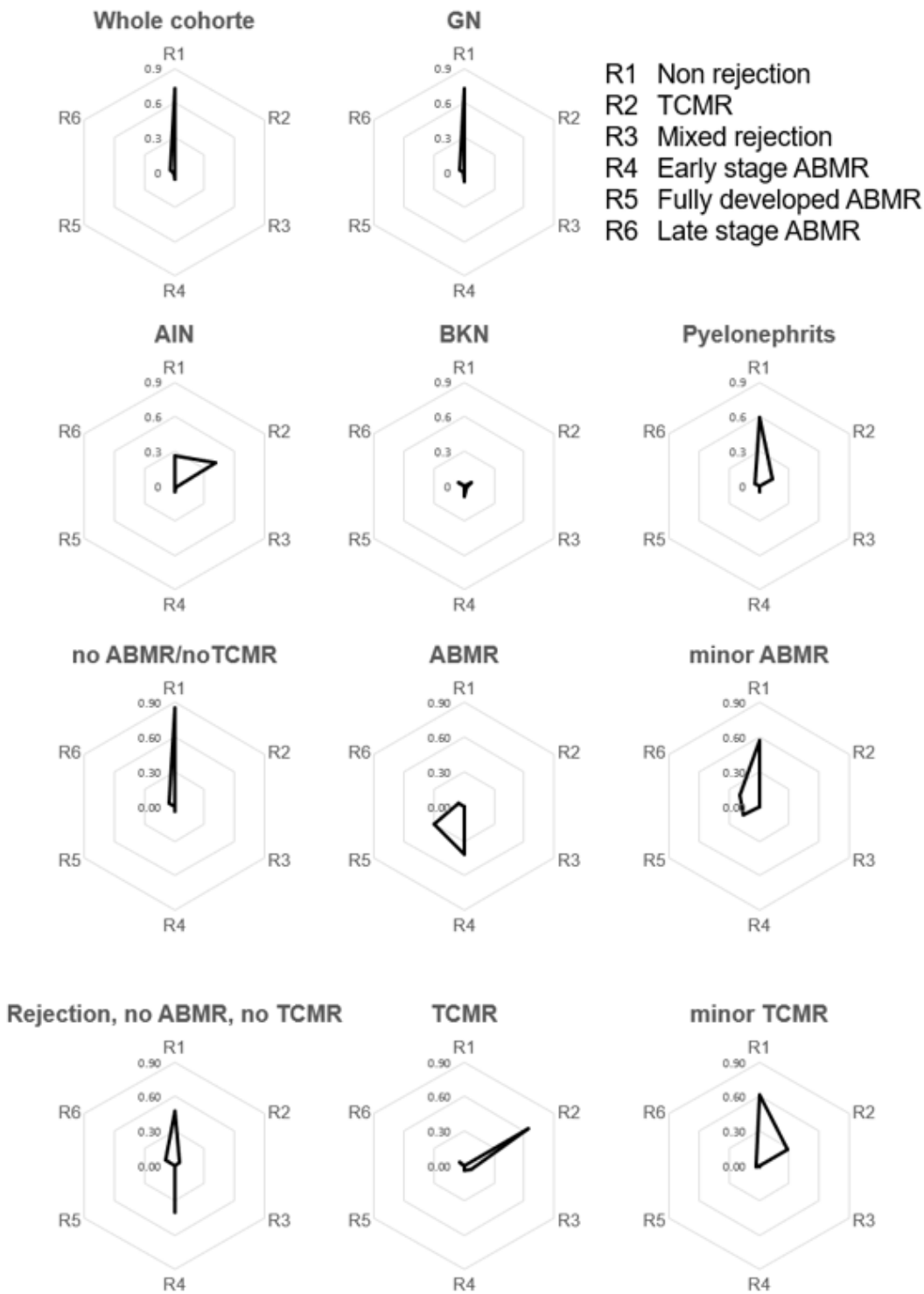


Figure 3



OC 54 / P 30**A case of focal segmental glomerulosclerosis (FSGS) caused by autosomal-dominant Alport syndrome**

Dr. Mélanie Salamin¹, Dr. Cecilia Bracco², Dr. Britta Hartmann², Dr. Stephan Segerer¹, Dr. Ingeborg Fischer³, Dr. Sebastian Rusch², Dr. Florian Buchkremer¹

1. Medizinische Universitätsklinik, Abteilung für Nephrologie, Kantonsspital Aarau, Switzerland 2. Institut für Labormedizin, Abteilung Medizinische Genetik, Kantonsspital Aarau, Switzerland 3. Institut für Pathologie, Kantonsspital Aarau, Switzerland

Background: FSGS is a histopathologic pattern of glomerular injury presenting with proteinuria and chronic kidney disease (CKD). It is categorized as primary, adaptive, genetic, or of undetermined cause. Alport syndrome (AS), caused by mutations of the genes encoding type IV collagen, is one of the most common monogenic forms of CKD. Classically, its renal manifestations are due to alterations of the glomerular basement membrane (GBM). More recently, AS has also been recognized as a common cause of hereditary FSGS.

Case: A 56-year-old male presented with CKD, proteinuria, glomerular hematuria, and hypertension, accompanied by a family history of end-stage kidney disease in his mother and maternal grandmother at ages 62 and 35, respectively. He was found to have an MGUS. A renal biopsy revealed severe vascular damage, widespread glomerular sclerosis, interstitial fibrosis, tubular atrophy, and FSGS with foot process effacement. Notably, the GBM appeared normal, and there were no signs of light chain deposition. Genetic analysis aimed at identifying an autosomal-dominant FSGS variant did not identify a definitive disease-causing variant. However, a variant of unknown clinical significance (VUS) was found: *COL4A3*:c.1723G>A, p.(Gly575Arg). Subsequently, four years later, re-evaluation of the variant, using updated guidelines, which highlighted the importance of glycine patterns in collagen genes, led to the new categorisation of alterations in these motifs as likely pathogenic. Combining this with refined guidelines for molecular diagnosis of CKDs/AS, the patient received a diagnosis of an autosomal-dominant AS.

Conclusion/ teaching points:

AS is the most common cause of hereditary FSGS, with a single *COL4A* variant being sufficient for diagnosis, even in the absence of typical GBM lamellation. Reassessment of previous genetic analysis can be valuable but is not routinely performed.

OC 55 / P 31**A case report of Atezolizumab therapy induced PR3 ANCA vasculitis**

Dr. Laura Gosztonyi¹, Prof. Bruno Vogt², Dr. Federica Bocchi²

1. Inselspital Universitätsklinik Bern, Klinik für Nephrologie und Hypertonie, Bern, Switzerland, 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Background: Immune Checkpoint inhibitors (ICI) are increasingly prescribed as therapy for a broad spectrum of cancers. While these humanized monoclonal antibodies have significantly improved survival rates, they can also cause adverse effects related to the immune system of different magnitude in any organ system, inclusive the kidney (reported frequency of 1–5%). Different types of renal lesion have been described, of which acute kidney injury remains the most common, typically caused by acute interstitial nephritis. Glomerular diseases are less frequent and have been reported sporadically. The most described glomerular disorders are pauci-immune glomerulonephritis, podocytopathy, and C3 glomerulopathy, with reported frequencies of 27%, 20%, and 11% respectively.

Case description: An 83-year-old patient with no renal history was diagnosed with small cell lung cancer and initially treated with 4 cycles of combination chemotherapy with carboplatin, etoposide and atezolizumab, followed by maintenance treatment with atezolizumab. After 8 months therapy, laboratory tests revealed acute kidney injury (creatinine 460 µmol/l, urea 23 mmol/l) with non-nephrotic proteinuria and glomerular hematuria. Immunological analysis revealed positive ANCA-PR3 titers (199.9 UI/ml). Renal biopsy showed acute necrotizing pauci-immune vasculitis, with necrosis and crescents. Atezolizumab therapy-induced vasculitis was postulated which led to permanent discontinuation of ICI. After high-dose intravenous corticosteroid followed by peroral prednisolone with slow tapering, renal function improved and ANCA-PR3 titers decreased.

Conclusion: Cancer patients who develop kidney failure require special attention in order to make an early diagnosis and administer appropriate therapy. Glomerular disease are usually associated with poor outcome. Cessation of ICI and treatment with corticosteroids is recommended. Moreover, the addition of another immunosuppressive treatment should be discussed if there is no improvement. Rechallenge should be reconsidered in any patients once the initial injury has been resolved. Individualized treatment and good collaboration between nephrologists and oncologists is crucial.

YSN submission / student submission

OC 56 / P 32**Diagnosis of C3 glomerulonephritis in a first pregnancy**

Dr. Ayuna Asoyan¹, Dr. Laila-Yasmin Mani², Dr. Jutta Schröder-Braunstein³

1. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 2. Service of Nephrology, Bern University Hospital, Switzerland, 3. Institute of Immunology, University Hospital Heidelberg, Heidelberg, Germany

Background: Most of the pregnancy outcome data reported for membranoproliferative glomerulonephritides does not differentiate between newly defined entities of C3 glomerulopathies. This case describes a woman with C3-glomerulonephritis diagnosed during her first pregnancy.

Case description: A 23-year old primigravida was referred to our nephrology policlinic after proteinuria and hematuria were noticed during an emergency consultation. Nephrotic syndrome was diagnosed, associated with microhematuria and hyperfiltration without arterial hypertension. Previous values obtained 3 years ago showed similar results. The diagnostic work-up including kidney duplex ultrasound, serology tests and protein analyses was unremarkable except for low C3 complement and non-specific antinuclear factor. Advanced complement protein analysis confirmed activation of the alternative complement pathway and revealed the presence of C3 nephritic factor. Gen panel analysis including the parents of the patient was unremarkable. Ophthalmologic examination showed no drusen. Hence, a diagnosis of C3 glomerulonephritis was suspected and the patient managed with low molecular weight heparin, acetylsalicylic acid, calcium and vitamin D. During the pregnancy, the patient remained compensated and normotensive with stable proteinuria and stable preserved kidney function and was delivered after induction at week 39 1/7. C3 nephritic factor was not detectable in the umbilical cord blood of the neonate. Serial urinalysis in the neonate showed no abnormalities. Postpartal kidney biopsy in the patient confirmed the diagnosis of C3 glomerulonephritis.

Learning points: The case illustrates the diagnostic and therapeutic challenges of pregnant women with suspected kidney

disease and adds to the literature of C3 glomerulopathies in pregnant women.

Conclusion: n/a

OC 57 / P 33

Unexpected cause of a generalized seizure

Dr. Katarzyna Szajek¹, Dr. Fabienne Umbricht², Prof. Thomas Fehr³

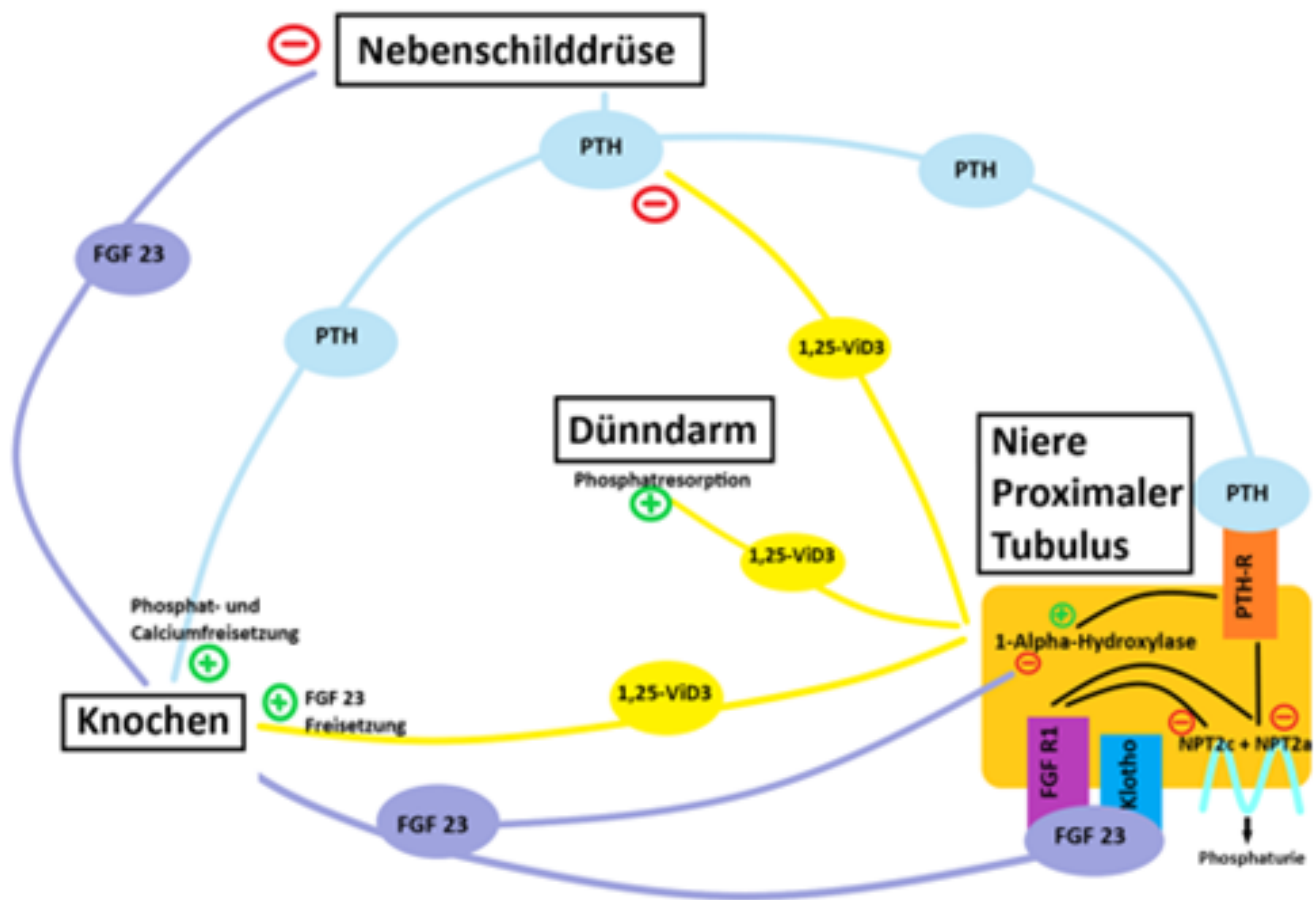
1. Department of Internal Medicine The Cantonal Hospital of Graubünden, Switzerland 2. Department of Internal Medicine, Cantonal Hospital Graubünden, Chur, Switzerland, 3. Department of Internal Medicine, Cantonal Hospital Graubünden, Chur, Switzerland. Faculty of Medicine, University of Zurich, Zurich, Switzerland.

Case Report: A 75-year-old multimorbid patient with dementia, diarrhea, malnutrition and chronic alcohol consumption was referred to the emergency room with suspected cerebrovascular symptoms. She had a history of pulmonary neoplasms (adenocarcinoma, micro-ablation 4 months ago and squamous cell carcinoma, resected 7.5 years ago) and generalized atherosclerosis. Upon admission, a head CT showed carotid stenosis but no acute ischemia or bleeding. The initial diagnosis leaned towards transient cerebral hypoperfusion, possibly related to carotid stenosis in combination with anemia (angiodysplasia in the gastrointestinal tract). Ten days later, the patient experienced a focal onset seizure in her right arm, which progressed into non-convulsive status epilepticus. Emergency treatment with Clonazepam, Levetiracetam and Lacosamide successfully controlled the seizures.

Results (see the table)

Discussion and Conclusion: The patient had severe hypomagnesemia and hypophosphatemia, which predispose to seizures. Hypomagnesemia resulted mainly from extrarenal factors, including reduced intestinal magnesium absorption due to diarrhea, alcohol use, malnutrition and pantoprazole usage. Diuretics exacerbated renal magnesium loss, particularly with hypokalemia. Low vitamin D levels affected calcium and magnesium balance, given their interdependency for vitamin D activation in the kidneys. Hypomagnesemia led to secondary hypoparathyroidism and hypocalcemia, as magnesium is crucial for parathyroid gland function. Magnesium deficiency reduced parathyroid hormone (PTH) secretion and altered PTH responsiveness to blood calcium levels. Following magnesium supplementation, PTH levels increased. Hypophosphatemia had both extrarenal and predominantly renal causes. An elevated fibroblast growth factor 23 reduced phosphate reabsorption in kidney tubules and inhibited the production of active vitamin D. In response to hypophosphatemia, the parathyroid glands released more PTH (following magnesium supplementation), which reduced phosphaturia and activated vitamin D. In our patient, hypophosphatemia and hypomagnesemia returned despite supplementation. There was suspicion of FGF-23 overproduction known to cause oncogenic osteomalacia. The detection of a new lesion in the upper left lung concerns about paraneoplastic involvement.

YSN submission



| Labolatory results | | Normal Range |
|--------------------|---|-------------------------------|
| Potassium | 2.7 | 3.4-4.5 mmol/l |
| Sodium | 153 | 136-146 mmol/l |
| Ionized Calcium | 0.83 | 1.15-1.29 mmol/l (pH 7.4) |
| Magnesium | 0.12 | 0.7-0.95 mmol/l |
| Phosphate | 0.51 | 0.81-1.45 mmol/l |
| Creatinine | 65 | 45-84 μ mol/l |
| eGFR | 80 | >90 ml/min/1.73m ² |
| PTH | 6.3, increased to 15.6 after appropriate magnesium substitution | 1.6 – 6.9 pmol/l |
| FGF-23 | 411.8 | 23.2 – 95.4 pg/ml |
| Vitamin D | 17.8 | > 30 μ g/l |

| |
|--|
| To distinguish whether the electrolyte loss is renal or extrarenal, we measured: |
| - fractional magnesium excretion - 2% (extrarenal) |
| - fractional phosphate excretion - 436% (renal, very high, normal < 5%) |

OC 58 / P 34

A case of idiopathic nodular Glomerulosclerosis

Ms. Claudia Landry¹, Prof. Bruno Vogt², Dr. Federica Bocchi²

1. University Clinic of Nephrology and Hypertension, Inselspital, Bern, Switzerland 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

Background: Idiopathic nodular glomerulosclerosis is a rare disease without clearly distinguishable clinical features. The pathological findings encompass the presence of intercapillary nodular glomerulosclerosis, along with thickening of the glomerular basement membrane, and the presence of arteriolo-nephrosclerosis and hyalinosis, which closely resemble the Kimmelstiel-Wilson lesions typically associated with diabetes. Smoking, obesity, and chronic hypertension are often observed in individuals with this condition. However, their exact contribution to the development of the lesion remains unclear and this poses a diagnostic challenge!

Case description: A 71-year-old Caucasian smoking (60 packs/year) and obese (BMI 48.57 kg/m²) male with a history of chronic obstructive pulmonary disease and untreated hypertension was admitted with progressive worsening dyspnea and lower limbs edema over a week. There was no personal history of diabetes mellitus or renal disease. The physical examination revealed a blood pressure of 165/65 mmHg and a severe anasarca. Laboratory revealed an acute kidney injury (serum creatinine 163 μ mol/L, eGFR 36 ml/min/1.73 m²), a nephrotic syndrome (estimated urinary protein excretion of 13 g/day) with a bland urinary sediment. All immunological markers and viral serologies were negative. Complement and serum protein electrophoresis were normal. Ultrasound showed normal-sized kidneys without obstruction. Renal biopsy showed diffuse nodular expansion of mesangial matrix without significant immune deposits by immunofluorescence and electron microscopy. Taking into account the medical history, laboratory and histological findings, the diagnosis of idiopathic nodular glomerulosclerosis was made. Antihypertensive treatment was introduced allowing blood pressure targets <130/80 mmHg and a reduction in proteinuria in a sub-nephrotic range.

Conclusion: Recognition and early diagnosis of this entity are essential to prevent the progression of kidney disease. Treatment is mainly based on controlling cardiovascular risk factors, in particular treating hypertension, reducing proteinuria and smoking cessation. Glucocorticoid therapy is not recommended. The prognosis is poor and relate to the persistence of nephrotic range proteinuria.

YSN submission

OC 59 / P 35

Tetany and Hypomagnesemia

Michael Möddel,¹ Bujana Batusha-Sopi²

Klinik im Park, Zürich, Switzerland: 1Nephrology, 2Internal Medicine

Background: Hypomagnesemia is a condition that is often overlooked due to its nonspecific symptoms and high prevalence in the context of comorbid diseases. In severe cases, hypomagnesemia can lead to significant cardiovascular and neuromuscular symptoms that require immediate diagnosis and treatment. Managing hypomagnesemia can be particularly challenging in patients with multiple coexisting conditions, as various factors influence magnesium levels. A key factor in differential diagnosis is the measurement of fractional magnesium excretion (FE Mg).

Case Study: A 72-year-old patient with multiple comorbidities presented to the emergency department with acute weakness, tetany, and dizziness. Tachycardia and ventricular extrasystoles were also consistent with electrolyte imbalances. Laboratory tests revealed severe hypomagnesemia (<0.26 mmol/l) and fractional magnesium excretion (FE Mg) below 2%. Clinical symptoms and low FE Mg levels drew attention to potential medication side effects, especially from the use of proton pump inhibitors (PPIs). Intravenous and oral replacement therapy was initiated. The clinical course was uncomplicated following replacement treatment, dietary counseling, and cessation of the PPI, and the patient was discharged symptom-free after normalization of magnesium levels

Learning Point: This case study illustrates the daily challenges of treating patients with multiple comorbidities in the emergency department, particularly when facing tetany induced by hypomagnesemia. For differential diagnostic considerations of hypomagnesemia, the measurement of FE Mg is particularly useful. In this case, it was significantly below 2%. Etiologically, this pointed to side effects from PPIs, inadequate dietary intake following recovery from a COVID-19 illness, and excessive alcohol consumption. An FE Mg greater than 4% could be caused by diuretics, various antibiotics, hypercalcemia, tubulopathies, uncontrolled diabetes mellitus, or a history of acute kidney failure.

The final diagnosis was PPI-induced hypomagnesemia.

YSN submission

OC 60 / P 36

Outcome of patients transplanted for C3 glomerulopathy and idiopathic immune-complex-mediated membranoproliferative glomerulonephritis: a cohort based study

Dr. Matthieu Halfon¹, Dr. Patrick Taffe², Dr. Christian Bucher³, Dr. Thomas Schachtner⁴, Prof. Uyen Huynh-Do⁵, Dr. Caroline Wehmeier⁶, Dr. Laila-Yasmin Mani⁵, Dr. Fadi Haidar⁷, Dr. Jean-Pierre Venetz¹, Prof. Manuel Pascual¹, Prof. Fadi Fakhouri⁸, Prof. Dela Golshayan¹

1. Transplantation center, Lausanne university hospital, Lausanne, Switzerland 2. University Center for Primary Care and Public Health, DESS/Division of Biostatistics, University of Lausanne, Switzerland, 3. service of Nephrology and transplantation, cantonal hospital, Saint-Gall, Switzerland 4. department of Nephrology, University Hospital Zurich, Switzerland 5. Service of Nephrology, Bern University Hospital, Switzerland, 6. Clinic for Transplantation Immunology and Nephrology, University Hospital Basel Switzerland 7. Geneva university hospital, Geneva, Switzerland 8. Service of Nephrology and hypertension, Lausanne university hospital, Lausanne, Switzerland

Background: Approximately 50% of patients diagnosed with C3 glomerulopathy and idiopathic immune-complex mediated membranoproliferative glomerulonephritis (C3G/IC-MPGN) progress to end-stage kidney disease within a decade of diagnosis. Given the relatively young age of these patients, the majority of them become candidates for kidney transplantation. Nevertheless, reported outcomes in patients transplanted for C3G/IC-MPGN remain a subject of considerable variation and controversy, primarily due to reliance on retrospective, single-center reports. This study aims to address this gap by leveraging the ongoing prospective Swiss Transplant Cohort Study to provide comprehensive, multicenter data on patients transplanted for C3G/IC-MPGN.

Methods: We conducted an analysis focused on the risk of graft loss concerning glomerulopathy recurrence and patient survival. Our study exclusively encompassed kidney-alone transplantations and recipients receiving their first kidney allograft. The measurement of risk employed a cumulative risk incidence model.

Results: Our study included 41 recipients transplanted for C3G/IC-MPGN, with a mean age at transplantation of 48 ± 16 years; living donations contributed to 53% of the procured organs. Over a mean follow-up period of 4.7 years, IQR :1.8-6.9, six patients (15%) experienced graft loss within a mean time of 4.7 years, IQR:2.1-7.8, resulting in a cumulative incidence risk of 25.8% at 9 years. Throughout the follow-up period, 7 patients exhibited disease recurrence, with an average time to recurrence of 1.2 years, IQR : 0.4-1.7. Of these, 28% experienced graft loss compared to 11% of patients without recurrence. Notably, disease recurrence emerged as the primary driver of graft loss among these individuals. Additionally, 14% of patients died during the follow-up period.

Conclusion: This study provides vital insights into the post-transplantation outcomes of individuals originally diagnosed with C3G/IC-MPGN. Overall, our data emphasize the substantial risk of recurrence, which significantly impacts overall prognosis. These findings underscore the imperative for continued research aimed at developing targeted therapeutic strategies tailored to this specific patient subgroup post-kidney transplantation.

YSN submission

OC 61 / P 37

Isolated glomerulitis is associated with the absence of molecular AMR in cases with histologically suspected and confirmed AMR

Dr. Nicolas Schmid¹, Dr. Lukas Weidmann¹, Dr. Raphael Korach², Dr. Dusan Harmacek¹, Mr. Kai Castrezana Lopez¹, Dr. Nicola Bortel¹, Dr. Ariana Gaspert³, Dr. Birgit Maria Helmchen³, Dr. Seraina Von Moos⁴, Dr. Elena Rho¹, Dr. Thomas Schachtner⁵

1. Division of Nephrology, University Hospital Zurich, Switzerland 2. Division of Nephrology, University Hospital Zurich, Switzerland, 3. Institute of Pathology and Molecular Pathology, University Hospital Zurich, Switzerland 4. Division of Nephrology, Kantonsspital Luzern, Switzerland 5. department of Nephrology, University Hospital Zurich, Switzerland

Background: According to the 2022 Banff classification, the Molecular Microscope Diagnostic System (MMDx) is indicated in cases when histology is insufficient to diagnose antibody-mediated rejection (AMR) due to an absence of diagnostic criteria groups 2 (antibody interaction with tissue). The impact of mild microvascular inflammation (MVI, g+ptc<2) on the likelihood of molecular AMR appears critical to the implementation of this new biomarker.

Methods: We analyzed 326 kidney allograft biopsies by histology and MMDx at the University Hospital Zurich from July 2021 to March 2023. Histologic findings were classified into: (1) 30 cases with DSA-negative mild MVI, (2) 32 cases with DSA-positive mild MVI (probable AMR), (3) 33 cases with DSA-negative moderate MVI, and (4) 60 cases with confirmed AMR.

Results: MMDx diagnosed AMR in 5/30 cases (17%) with DSA-negative mild MVI, 12/32 cases (38%) with DSA-positive mild MVI, 18/33 cases (55%) with DSA-negative moderate MVI, and 30/60 cases (50%) with confirmed AMR. While only 17/65 cases (26%) with molecular AMR showed isolated glomerulitis, 64/90 cases (71%) without molecular AMR showed isolated glomerulitis (p < 0.001). Among cases with isolated glomerulitis molecular AMR was detected more frequently in cases with proteinuria (p = 0.011), presence of DSA (p = 0.033), and transplant glomerulopathy (cg; p = 0.014).

Conclusions: MMDx confirms AMR in a relevant proportion of cases with mild MVI. However, isolated glomerulitis is associated with absence of molecular AMR in cases with suspected and confirmed AMR. Presence of proteinuria, DSA, and transplant glomerulopathy is associated with molecular AMR among cases with isolated glomerulitis.

YSN submission / student submission

OC 62 / P 38

Is there excess mortality in dialysis patients in Switzerland after the COVID-19 pandemic?

Dr. David Jaques¹, Mrs. Rebecca Guidotti², Prof. Belén Ponte³, Prof. Patrice M. Ambühl²

1. Service de néphrologie et hypertension, Département de médecine, Hôpitaux universitaires de Genève, Switzerland 2. Stadtspital Zürich, Zürich, Schweiz, 3. Department of Nephrology and Hypertension, Geneva University Hospitals, Geneva, Switzerland

Background: Various studies and journals reported excess mortality due to the COVID-19 pandemic. The aim of this study is to determine whether survival in dialysis patients has decreased in the years 2021 and 2022.

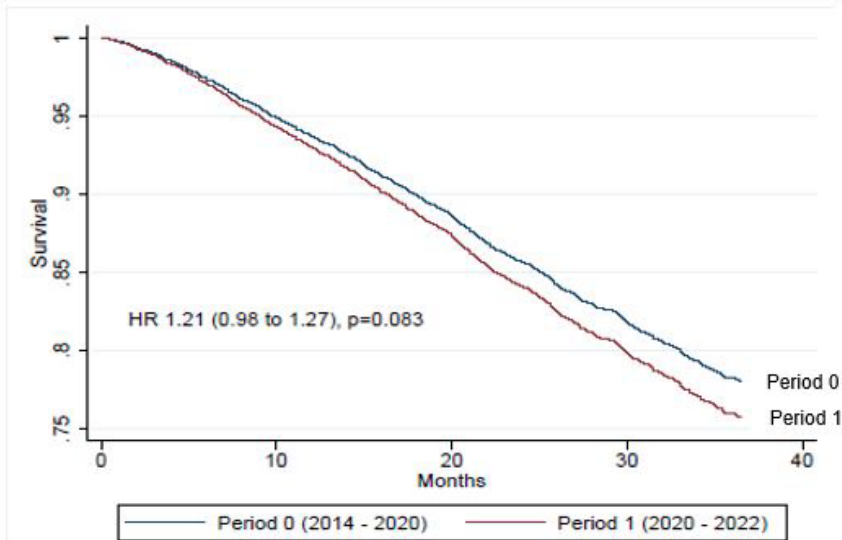
Methods: In this retrospective study, data were retrieved from the Swiss Dialysis Registry (srrqap). Survival rates were analyzed between 2014-2022. We compared survival rates of patients who started dialysis between 2014 and 2019 (period 0)

with those starting between 2020 and 2022 (period 1). All patients were censored after 3 years of follow-up or at January 1, 2020 (whichever comes first).

Results: A total of 7'945 patients were included in this study, with 5'400 in period 0 and 2'545 in period 1. Mean age was 65.5 years and the percentage of male patients was 66.1. Baseline characteristics are given in *table 1*. In Cox regression analysis adjusted for age, sex, ethnicity, BMI, hypertension, diabetes and Charlson comorbidity index, patients starting dialysis during period 1 did not show an increased risk of mortality compared to those starting in period 0, as shown in *figure 1*. Additional Cox regression analysis, adjusted for the same parameters as mentioned in *figure 1*, showed a significant ($p = 0.003$) worse survival probability for those starting in the year 2020, when the Covid-19 pandemic began, compared to all other starting years (grouped).

Conclusion: Our analyses could not show an excess mortality in the years 2021 and 2022, as we would have expected.

Figure 1: Survival probabilities according to study periods (adjusted*)



*Adjusted for age, sex, ethnicity, BMI, hypertension, diabetes and Charlson comorbidity index

Table 1: Baseline characteristics according to study periods

| Characteristics | Period 0 (2014 – 2020) (N=5'400) | Period 1 (2020 – 2022) (N=2'545) | P-value |
|-----------------------------------|--|--|------------------|
| Age (years), mean±SD | 65.2 ± 15.7 | 66.0 ± 15.8 | 0.042 |
| Sex (male), n (%) | 3'578 (66.2) | 1'614 (65.8) | 0.688 |
| Ethnicity (Caucasian), n (%) | 4'976 (92.7) | 2'252 (91.8) | 0.451 |
| BMI (kg/m ²), mean±SD | 25.2 ± 5.6 | 26.1 ± 5.6 | <0.001 |
| Hypertension, n (%) | 4'341 (80.6) | 2'028 (82.6) | 0.034 |
| Diabetes, n (%) | 2'065 (38.2) | 934 (38.0) | 0.870 |

OC 63 / P 39

The challenging diagnosis of hyperaldosteronism in Polycystic ovary syndrome: A case-report

Dr. Claudia Ferrier¹, Dr. Domenico Cozzo², Prof. Bruno Vogt³, Dr. Valentina Forni Ognà⁴

1. University Hospital, Berne, Switzerland, 2 Nefrocentro Ticino, Switzerland, 2. Cantonale di Nefrologia, Ente Ospedaliero Cantonale, Ticino, Switzerland, 3. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 4. Servizio Cantonale di Nefrologia, Ente Ospedaliero Cantonale, Ticino, Switzerland

Background: Polycystic Ovary Syndrome (PCOS) is a complex endocrine-metabolic disorder affecting about 7% of childbearing women. PCOS is characterized by anovulation, hyperandrogenism, insulin resistance and is associated with an increased cardiovascular risk. Clinically, PCOS patients may exhibit symptoms mimicking primary aldosteronism (PA). We discuss a case highlighting the diagnostic pitfalls of PA screening in patients affected by PCOS.

Case Report: A 33yrs old woman attended our renal outpatient clinic because of recurrent episodes of generalized swelling and diuresis contraction. The patient, known for PCOS, was treated with combined oral contraceptives and loop diuretics.

She had no H/O hypertension, but she repeatedly displayed very high aldosterone values.

Results: Clinical examination was unremarkable, in-office and home blood pressure values were normal. Laboratory data showed normal renal function and the absence of acid-base or electrolyte disorders. A CT-scan showed normal adrenal glands. We performed a recumbent saline suppression test (2L NaCl 0.9% infusion in 4 hours) under standardized salt intake (9gr/24h), previous a wash-out period of oral contraceptives and (> 2 weeks) of loop diuretics (> 6 weeks). The results listed below are consistent with a baseline hyperaldosteronism with normal aldosterone adrenal response to volume expansion, excluding PA. Aldosterone and direct renin were determined by chemiluminescent immunoassay technology (DiaSorin®) (see figure 1)

Conclusion: In patients with PCOS the increased adrenal production of aldosterone is probably progesterone-mediated and independent from the renin-aldosterone axis. However, other iatrogenic factors may affect the renin-aldosterone values, such as the use of oral contraceptives and diuretics. Therefore, a NaCl suppression test under standardized conditions is often required, in order to exclude primary versus secondary forms of hyperaldosteronism associated to PCOS.

| Variables | Plasmatic aldosterone <i>pmol/l</i> | Plasmatic direct renin <i>ng/l</i> | Aldosterone-to-renin ratio <i>pmol/ng</i> | Plasmatic K ⁺ <i>mmol/l</i> |
|-----------------------------|--|---------------------------------------|--|--|
| Baseline | 438 (N32-654) | 6.2 (N 1.7-23.9) | 71 (N<55) | 3.6 |
| After NaCl suppression test | 85 (N <140) | | | |

YOUNG SWISS NEPHROLOGY PRESENTATIONS

OC 64

CYP24A1 activity associates with phenotypic traits of idiopathic hypercalciuria

Dr. Nasser Dhayat¹, Dr. Cedric Mattmann², Dr. Harald Seeger³, Dr. Alexander Ritter³, Dr. Thomas Hernandez⁴, Dr. Catherine Stoer-mann-Chopard⁴, Dr. Florian Buchkremer⁵, Dr. Stephan Seeger⁵, Prof. Beat Roth⁶, Prof. Gregoire Wuerzner⁷, Prof. Carsten Wagner⁸, Prof. Olivier Bonny⁹, Dr. Albrecht Popp¹⁰, Prof. Bruno Vogt², Dr. Matteo Bargagli², Prof. Daniel G. Fuster²

1. B. Braun Medical Care AG, Nephrology & Dialysis Care Center, Hochfelden, Zürich, Switzerland, 2. Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland, 3. Division of Nephrology, University Hospital Zürich, Zürich, Switzerland, 4. Service of Nephrology, Geneva University Hospitals, Geneva, Switzerland, 5. Medizinische Universitätsklinik, Abteilung für Nephrologie, Kantonsspital Aarau, 6. Department of Urology, Lausanne University Hospital, CHUV, University of Lausanne, Switzerland, 7. Service of Nephrology and Hypertension, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, 8. Institute of Physiology, University of Zürich, Zürich, Switzerland, 9. Service of Nephrology, Fribourg State Hospital and University of Fribourg, Fribourg, Switzerland, 10. Department of Osteoporosis, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

Background: Hypercalciuria is the most frequent abnormality in kidney stone formers. Underlying mechanisms remain unknown in most cases, hence the designation “idiopathic hypercalciuria”. We hypothesized that the Vitamin D-inactivating enzyme CYP24A1 contributes to the pathogenesis of hypercalciuria in kidney stone formers.

Methods: We conducted association analyses between CYP24A1 activity, estimated by the Vitamin D metabolite diagnostic ratio (25(OH) Vitamin D3/total 24,25 (OH)2 Vitamin D ratio; VMDR), and the phenotype of participants in two observational cohorts of kidney stone formers, the Swiss Kidney Stone Cohort and the Bern Kidney Stone Registry. Linear and logistic regression models adjusted for multiple confounders, including plasma 25(OH) Vitamin D3, were applied. Circulating 25(OH)- and 24,25 (OH)2 Vitamin D were quantified using a validated LC-MS/MS assay.

Results: In all, 974 participants were included in the analysis. We found a positive association of VMDR (and hence negative association of CYP24A1 activity) with total plasma calcium (β 0.009 mmol/L; 95% CI 0.002, 0.016; $p = 0.02$), ionized calcium (β 0.005 mmol/L; 95% CI 0.002, 0.008; $p < 0.01$) and absolute and fractional excretion of urinary calcium (β 0.054 mmol/24h; 95% CI 0.010, 0.097; $p = 0.02$ and β 0.046%; 95% CI 0.018, 0.074; $p < 0.01$, respectively). Further, VMDR was associated with an increased likelihood of forming calcium oxalate dihydrate stones (Odds ratio 1.64; 95% CI 1.22, 2.35; $p < 0.01$) and reduced bone mineral density at the femoral neck (β -0.005 g/cm²; 95% CI -0.010, -0.001; $p = 0.04$). The described associations became stronger when analyzing only idiopathic calcium stone formers.

Conclusion: Our study reveals that CYP24A1 activity is associated with clinical traits previously linked to idiopathic hypercalciuria.

YSN submission

OC 65

Spatiotemporal landscape of kidney tubular responses to glomerular proteinuria

Dr. Anna Faivre¹, Dr. Milica Bugarski², Dr. Anna Rinaldi³, Dr. Thomas Verissimo¹, Dr. David Legouis¹, Dr. Imene B Sakhi², Ms. Sara Correia², Dr. Monika Kaminska², Dr. Delal Dalga¹, Prof. Pietro CIPPA*³, Prof. Sophie De Seigneux¹, Prof. Andrew M Hall²

1. UNIGE, Geneva, Switzerland 2. UZH, Zurich, Switzerland 3. EOC, Switzerland

Background: Large increases in glomerular protein filtration induce major changes in kidney function and body homeostasis, and increase the risk of cardiovascular disease. We investigated how elevated protein exposure modifies the landscape of tubular function along the entire nephron, to better understand the cellular changes that mediate these important clinical phenomena.

Methods: We conducted single nuclei RNA sequencing, functional intravital imaging, and antibody staining to spatially map transport processes along the mouse kidney tubule. We then delineated how these are altered in a transgenic mouse model of inducible glomerular proteinuria (POD-ATTAC) at 7 and 28 days. Results were compared to an ischemia-reperfusion injury (IRI) model of tubular damage.

Results: Glomerular proteinuria activates large-scale and pleiotropic changes in tubular cell gene expression in all major nephron sections, and an injury profile that partially overlaps with IRI, suggesting the existence of both specific and non-specific responses. Extension of protein uptake from the early to late part of the proximal tubule results in a substantial shift in the balance of reabsorptive and secretory pathways. Meanwhile, overflow of luminal proteins to the distal tubule causes transcriptional convergence between specialized regions and generalized dedifferentiation.

Conclusion: Proteinuria is a potent modulator of cell signaling in tubular epithelia and triggers extensive remodeling, in a segment specific manner. These findings could explain some of the well-recognized clinical complications that arise in proteinuric kidney disease, and may also be important for understanding nephron patterning in organ development.

YSN submission

OC 66

Identification of a novel senolytic compound to prevent chronic kidney injury and fibrosis

Dr. Anna Rinaldi¹, Dr. Sara Zumerle^{*2}, Ms. Cristina Torcasio³, Ms. Miriam Saponaro², Ms. Liliana Contu², Mr. Miles Sarill², Dr. Manuel Colucci⁴, Dr. Simone Mosole⁴, Dr. Emiliano Pasquini⁴, Dr. Andrea Giori⁵, Ms. Montopoli Monica², Dr. Jacopo Sgrigani⁶, Ms. Patrizia Locatelli⁶, Dr. Andrea Cavalli⁶, Ms. Martina Troiani⁴, Prof. Lucio Berile^{*7}, Prof. Johan Auwerx^{*8}, Prof. Andrea Alimonti^{*4}, Prof. Pietro CIPPA^{*1}

1. EOC, Switzerland 2. Veneto Institute of Molecular Medicine, Padova, Italy, 3. Division of Nephrology, Ente Ospedaliero Cantonale, Lugano, Switzerland, 4. Institute of Oncology Research (IOR), Bellinzona, Switzerland, 5. R&D Department, IBSA Farmaceutici Italia, Lodi, Italy, 6. Institute for Research in Biomedicine, Università della Svizzera Italiana, Bellinzona, Switzerland, 7. Laboratory for Cardiovascular Theranostics, Cardiocentro Ticino Institute, Ente Ospedaliero Cantonale Lugano, Switzerland, 8. Laboratory of Integrative Systems Physiology, Institute of Bioengineering, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

Introduction: Cellular senescence is involved in different biological processes, including kidney development, acute kidney injury, chronic kidney disease and aging. This study is part of an interdisciplinary project aiming at the characterization of the role of cellular senescence across organs and clinical conditions and at the identification of pharmacological targets to modulate cellular senescence in age-related diseases. Here, we present data on cellular senescence in experimental models of kidney disease and on the discovery of a new kidney-relevant senolytic compound.

Methods: Senescent cells were characterized by a panel of markers measured by single-cell RNA sequencing, RT-PCR and immune-histochemistry in models of kidney disease, including ischemia-reperfusion injury, proteinuria, and aging, and verified in patient-biopsies. Senolytic compounds were identified by *in vitro* cross-validation of two libraries and the most promising compounds were validated *in vivo*. Ultra-high-performance liquid chromatography, computational and surface plasmon resonance analyses were used to investigate the mechanisms.

Results: We confirmed the accumulation of senescent cells in association with aging and chronic kidney disease in different compartments of the kidney, including proximal tubule, podocytes and endothelial cells. Single-cell RNAseq highlighted the peculiar features of senescent cells in each compartment and identified potential pharmacological targets. Depletion of senescent cells by the established senolytic ABT263 resulted in the reduction of senescent cells, fibrosis and inflammation in the kidney. Among the new compounds identified by the pharmacological screening, the luteolin-rich natural compound Haenkenium increased lifespan and displayed favourable effects on kidney aging in mice. Specific analysis on the mechanism of action identified the flavonoid luteolin as the active constituent of Haenkenium, which prevents senescence by disrupting the binding of p16 to CDK6.

Conclusions: Cellular senescence is a target to prevent kidney aging and chronic kidney disease progression. The anti-senescence effects of the natural compound Haenkenium highlight a promising novel treatment in nephrology.

YSN submission

OC 67

Spatial RNA sequencing and mass cytometry identify estrogen-dependent control of neutrophils activation as a protective mechanism in renal ischemia-reperfusion injury

Mr. Arnaud Lyon¹, Mr. Thomas Agius², Mr. Kevin Kiesworo², Dr. Michael MacArthur³, Dr. Sènan D'Almeida⁴, Prof. Sophie De Seigneux⁵, Dr. Thomas Verissimo⁶, Dr. Sarah Mitchell⁷, Dr. Sébastien Déglise², Dr. Florent Allagnat², Dr. Alban Longchamp⁸, Prof. Dela Golshayan¹

1. Transplantation Center, Lausanne University Hospital (CHUV), Lausanne, Switzerland, 2. Department of Vascular Surgery, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland., 3. Lewis-Sigler Institute for Integrative Genomics, Princeton University, Princeton, NJ, USA, 4. Flow Cytometry Core Facility, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland., 5. UNIGE, Geneva, Switzerland 6. Department of Cellular Physiology and Metabolism, Faculty of Medicine, Geneva, Switzerland 7. Ludwig Princeton Branch, Princeton University, Princeton, NJ, USA, 8. Transplant Center, Dept. of Surgery, Massachusetts General Hospital, Boston, MA, USA

Background: Previous experimental and clinical studies have highlighted sex-specific susceptibility to ischemia-reperfusion injury (IRI) in multiple organs, with evidence underlying the potential protective effect of female sexual hormones. Nevertheless, their precise effect in the regulation of immune responses and tissue inflammation following IRI still needs to be investigated.

Methods: Renal IRI was modelled in mice using unilateral nephrectomy, followed by 23min ischemia and reperfusion. Renal function was evaluated by transcutaneous assessment of FITC-Sinistrin clearance. Visium spatial mRNA sequencing was carried out on paraffin-embedded tissue. Mass and multiparameter flow cytometry was applied on peripheral blood mononuclear cells.

Results: Following renal IRI, females had a significantly better glomerular filtration rate and reduced tubulointerstitial lesions compared to age-matched males. Besides the C57BL/6-based initial experimental model, these results were reproducible in various genetically distinct mouse strains. This protection was alleviated after ovariectomy. Spatial mRNA sequencing revealed a differential transcriptomic profile in male and female proximal tubular cells with an upregulation of genes associated with failed damage repair in males. Mass cytometry identified neutrophils as the primarily recruited immune cells in males peripheral blood and in injured renal tissue. *In vivo* depletion of neutrophils with a specific anti-Ly6G monoclonal antibody reduced IRI in males.

Conclusions: Our data showed that female mice were protected from renal IRI independently of genetic background and in an estrogen-dependent manner. Spatial transcriptomics and mass cytometry allowed us to broadly characterize sex-specific tissular gene expression and systemic immune responses following renal IRI. Males proximal tubular cells were shown to have impaired damage repair associated with increased neutrophils recruitment. Sex-specific depletion of neutrophils reduced renal IRI. Overall, our data suggest that neutrophils are necessary in the pathophysiology of IRI and could be targeted, *per se* or via their effector function, to reduce early damage and ameliorate organ preservation for solid organ transplantation.

YSN submission / Student submission

OC 68

PCK1 plays a pivotal role in controlling the metabolic and mitochondrial activities of renal tubular cells

Dr. Delal Dalga¹, Dr. Thomas Verissimo², Dr. Anna Faivre³, Dr. Gregoire Arnoux⁴, Ms. Deborah Paolucci⁴, Mr. Quentin Gex⁴, Prof. Andrew M Hall⁵, Prof. Sophie De Seigneux⁶

1. Department of cellular Physiology and Metabolism, Faculty of Medicine, Geneva, Switzerland 2. Department of Cellular Physiology and Metabolism, Faculty of Medicine, Geneva, Switzerland 3. HUG, Geneva, Switzerland 4. Department of Cellular Physiology and Metabolism, Faculty of Medicine, Geneva, Switzerland., 5. UZH, Zurich, Switzerland 6. UNIGE, Geneva, Switzerland

Introduction: Renal gluconeogenesis is impaired in CKD. Phosphoenolpyruvate carboxykinase 1 (PCK1), a pivotal enzyme in gluconeogenesis, facilitates the conversion of oxaloacetate to phosphoenolpyruvate. In this study, we hypothesize that impaired expression or activity of Phosphoenolpyruvate carboxykinase 1 (PCK1) in kidney proximal cells contributes to the metabolic alterations observed in CKD with a broader impact than glucose generation.

Methods: We developed kidney tubular-specific knockout (KO) and knockin (KI) models for PCK1, using the tubular cell-specific PAX8 promoter. We evaluated the influence of PCK1 expression changes on renal function and kidney metabolism in normal

physiological settings. Subsequently, we examined PCK1's role under two distinct pathological conditions: metabolic acidosis and proteinuric kidney disease.

Results: In basal conditions, PCK1 deletion induced a loss of renal function, modest albuminuria, and hyperchloremic metabolic acidosis. Glucosuria and lactaturia were also observed. This was observed together with major mitochondrial dysfunction and decreased ATP production by Seahorse analysis and morphological alterations by electron microscopy, along with alterations of kidney transporters. During metabolic acidosis, PCK1 KO mice exhibited enhanced tubular damage and acute kidney injury. Finally, mitigating PCK1 downregulation using KI mice in the context of proteinuric renal disease improved kidney function, tubular injury, and fibrosis progression, whereas overexpression of PCK1 at baseline did not modify renal physiology or glycemia.

Conclusion: PCK1 is essential for maintaining renal tubular acid-base balance, mitochondrial energy production, and glucose/lactate stability. PCK1 restoration may be a key target in preventing mitochondrial dysfunction and renal disease progression during proteinuric CKD.

YSN submission.

INDEX OF FIRST AUTHORS

The numbers refer to the numbers of the abstracts.

Achermann S OC 36 / P 12
Arnold S OC 15
Arokiaraj MC OC 48 / P 24
Asoyan A OC 56 / P 32

Bankir L OC 11
Bargagli M OC 01, OC 06, OC 18, OC 64
Batusha-Sopi B OC 59 / P 35
Benackova K OC 45 / P 21
Bocchi F OC 44 / P 20
Born A OC 04
Bortel N OC 16
Brune JE OC 21

Castrezana Lopez K OC 32 / P 08
Cozzo D OC 26 / P 02, OC 63 / P 39

Dalga D OC 28 / P 04, OC 68
Diebold M OC 19, OC 27 / P 03

Eul C OC 20, OC 38 / P 14

Faivre A OC 65

Gargiulo L OC 24
Gosztonyi L OC 55 / P 31
Guidotti R OC 41 / P 17

Halfon M OC 34 / P 10, OC 60 / P 36
Harmacek D OC 14
Helou N OC 05
Hendriks-Balk M OC 50 / P 26
Hosek N OC 17

Iqbal MM OC 43 / P 19, OC 47 / P 23

Jaques D OC 25 / P 01, OC 62 / P 38

Kistler A OC 13
Korach R OC 30 / P 06
Kuhn C OC 02

Landry C OC 58 / P 34
Lyon A OC 23, OC 67

Makembi Bunkete A OC 37 / P 13
Münch J OC 08

Poskaite E OC 51 / P 27
Pruijm M OC 24

Rho E OC 53 / P 29
Rinaldi A OC 66
Ritter A OC 40 / P 16
Rudloff S OC 31 / P 07

Salamin M OC 54 / P 30
Sarrasin H OC 22, OC 52 / P 28
Sassi A OC 07
Saudan P OC 10
Schietzel S OC 12
Schleich A OC 09
Schmid N OC 33 / P 09, OC 61 / P 37
Schmucki K OC 39 / P 15
Stavart L OC 49 / P 25
Szajek K OC 57 / P 33

Tümay C OC 03

Umbricht F OC 57 / P 33

Wehmeier C OC 29 / P 05
Weidmann L OC 35 / P 11, OC 42 / P 18

Zhang Y OC 46 / P 22

SWISS MEDICAL WEEKLY

Editors in chief:

Prof. Adriano Aguzzi
Prof. Gérard Waeber
Academic editors: see www.smw.ch

Managing editors:

Natalie Marty, MD
Susanne Redle, MD
Jan Roth, MD

ISSN online supplement: 2504-1622

© SMW supporting association, 2023.

Published under the CC license**Attribution 4.0 International (CC BY 4.0)**

You are free to share (copy and redistribute the material in any medium or format) and adapt (re-mix, transform, and build upon the material) for any purpose under the following terms:
Attribution – You must give appropriate credit, provide a link to the license, and indicate if changes were made. You may do so in any reasonable manner, but not in any way that suggests the licensor endorses you or your use.

No additional restrictions – You may not apply legal terms or technological measures that legally restrict others from doing anything the license permits.

Guidelines for authors and online submission:

www.smw.ch

Cover image:

© Annanahabed / Dreamstime.com