Conclusions: In the previous reports, tight junction proteins were downregulated and as Occludin and ZO-1 expressions.

Although it is reported that gut microbiota and colon barrier function were deteriorated in CKD state, the detailed mechanism or pathological relevance has not been elucidated. Oral activated charcoal adsorbent (AST-120) has been reported to delay the progression of CKD by adsorbing uremic toxin from the intestine. However, the effects of AST on the gut environments in CKD and its impact on CKD progression have not been fully elucidated.

Methods: Six-week-old spontaneously hypertensive rats (SHR) were rendered CKD by 5/6th nephrectomy (Nx). The SHRs were divided into four groups; group 1, sham-operated SHR (SHR, n=10); group 2, SHR given AST-120 (SHR+AST, n=10); group 3, 5/6th nephrectomized SHR (Nx, n=10); group 4, 5/6th nephrectomized SHR given AST-120 (Nx+AST, n=10). AST-120 was orally given at a dose of 4g/kg/day by mixing with regular chow. After 12 weeks, rats were sacrificed and biochemical parameters, histological analysis of the kidney and colon, and molecular changes were compared among the groups. The distribution of the intestinal flora was examined by T-RFLP (Terminal Restriction Fragment Length Polymorphism) and real time PCR.

Human colon cell line, Caco-2 cell were treated with uremic toxin precursor, indole. The results showed the decrease of the protein excretion were increased in Nx, which were attenuated in Nx+AST. The analysis of the gut flora showed the decrease of the Lactobacillus in Nx. This decrease was also reversed in Nx+AST. Regression analysis revealed that the number of Lactobacillus in colon was significantly associated with serum creatinine levels. In Caco-2 cells, treatment with indole, precursor of IS produced in the colon downregulated mucin-2 expression as well as Occludin and ZO-1 expressions.

Conclusions: In addition to the traditional endpoints, the gut environment in CKD is also affected by the gut microbiota. The changes in gut flora may contribute to the progression of CKD through various mechanisms, including altered nutrient metabolism and the release of inflammatory mediators. Therefore, interventions that modulate the gut microbiota may offer therapeutic benefits in the treatment of CKD.

Fiber intake can also influence kidney function and inflammation. A low energy-adjusted dietary fiber intake was linked to reduced kidney function and inflammation in this community-based cohort. Moreover, in individuals with reduced kidney function, low fiber intake was independently associated with mortality.

Methods: A low energy-adjusted dietary fiber intake was linked to reduced kidney function and inflammation in this community-based cohort. Moreover, in individuals with reduced kidney function, low fiber intake was independently associated with mortality.

Introduction and Aims: The gut microbial metabolism contributes substantially to the human metabolome and is a well-known source of so-called uremic retention solutes. Mounting evidence indicates that the gut microbial metabolism can be disease-specific. Whether chronic kidney disease is associated with a distinct gut microbial metabolism has not been studied to date.

Methods: A low energy-adjusted dietary fiber intake was linked to reduced kidney function and inflammation in this community-based cohort. Moreover, in individuals with reduced kidney function, low fiber intake was independently associated with mortality.

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Results: Fecal samples of 20 hemodialysis patients, 20 unrelated healthy controls and 20 household contacts on the same diet were included for analysis. A total of 286 different metabolites were identified. Partial least square discriminant analysis demonstrated a clear distinction between fecal metabolite profiles of hemodialysis patients and healthy controls (see figure). A total of 92 volatile organic compounds were significantly different between the 2 groups with, among others, an increased generation of indole and p-cresol in hemodialysis patients. According to chemical classes, there was an upregulation of alcohols, aldehydes, benzenes, BCFA, furans, indoles and SCFA, while alka/enes and ketones were downregulated in hemodialysis patients. In contrast, the discrimination between hemodialysis patients and their household contacts on the same diet was less pronounced (see figure) with an increased generation of aldehydes and furans in hemodialysis patients.

Conclusions: The renal phenotype is associated with a distinct gut microbial metabolism. Secondary, there is an increased generation of indole and p-cresol as precursors of the uremic retention solutes indoxyl sulfate and p-cresyl sulfate, respectively. While there is a clear role of dietary and other chronic kidney disease related factors on the gut microbial metabolism, possibly aggravated in the presence of renal dysfunction, the influence of renal function loss per se is less pronounced. The potential beneficial effect of therapeutics targeting the gut microbiota in patients with renal disease has to be awaited.

TO020

COMPARING SCORES ASSESSING NUTRITIONAL STATUS IN CHRONIC HEMODIALYSIS PATIENTS: A CONTRAST SUBANALYSIS

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Introduction and Aims: To address the need for standardizing the syndrome of wasting, malnutrition and inflammation the term Protein Energy Wasting (PEW) has been introduced to describe the state of decreased body stores of protein and energy fuels. As PEW may occur in up to 50% of hemodialysis (HD) patients and is positively associated with all-cause mortality, it is important to detect PEW in patients accurately and easily. In the present study, we investigated which nutritional scoring list or individual parameter related to nutritional status best predicts all-cause mortality in HD patients.

Methods: Data were used from the CONVective TRansport Study (CONTRAST, NCT 00205556), a cohort of end stage renal disease (ESRD) patients treated with HD or hemodialfiltration (HDF). The Subjective Global Assessment (SGA), the Malnutrition Inflammation Score (MIS), the Geriatric Nutritional Risk Index (GNRI) and the composite Protein Energy Nutrition Score (cPENS) were assessed or calculated at study enrolment. Calibration was tested using the Hosmer and Lemeshow Goodness-of-Fit test. Ultimately, four groups were created of every score and parameter to compare 1) hazard ratios (HR, worst group versus best group), 2) increase in HR per group and 3) HR of worst group versus the other three groups combined.

Results: In 489 out of 714 patients, all scores and parameters were available for analysis. In this cohort, ROCs showed significant predictive value regarding mortality for SGA, MIS, GNRI, cPENS, albumin and creatinin with areas under the curve (AUCs) between 59.5-66.5% (p<0.0005). Comparison of the 95% confidence intervals (CI) of these AUCs demonstrated no added value of one test over the other. The Hosmer-and-Lemeshow Goodness-of-Fit test showed an inadequate fit for cPENS, GNRI and creatinin (p-values 0.002, 0.040 and 0.007, respectively). Of the remaining parameters (SGA, MIS and albumin), high had a significant better predictive value regarding mortality over the other in either test.

Conclusions: Out of the 4 scores and 4 individual parameters, SGA, MIS and albumin predicted mortality best in ESRD patients. As none has an added value over the other, it appears that PEW is most easily estimated by regular albumin measurements.

TO021

INFLUENCE OF A HIGH PROTEIN DIET ON THE HUMAN METABOLOME

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Introduction and Aims: In the nephrology community there is a long held belief that protein restriction may attenuate progression of pre-existing renal disease. Lately, there is a renewed interest in metabolites originating from protein fermentation as potential driving force behind adverse outcomes in patients with renal dysfunction. p-Cresyl sulfate and indoxyl sulfate, both protein fermentation metabolites, have repeatedly been associated with progression of chronic kidney disease in observational and mechanistic studies, supporting the so-called protein metabolite hypothesis. The influence of protein intake on p-cresyl sulfate, indoxyl sulfate and other relevant metabolites has not been fully elucidated.

Methods: After a 2 week run-in period with normal protein intake, 29 healthy volunteers were randomized to either a high protein diet or a low protein diet for 2 weeks. Blood and urine were sampled after the run-in period and again after dietary intervention. All samples were analyzed with a dedicated liquid chromatography mass spectrometry method for measurement of a panel of metabolites, including indoxyl sulfate, indoxyl glucuronide, indole-3-acetic acid, kynurenine, kynurenic acid, quinolinic acid, tryptophan, phenylacetic acid, p-cresyl sulfate, p-cresyl glucuronide, phenyl sulphate, phenyl glucuronide, hippuric acid and 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid (CMPF). Urinary collections were used to calculate 24h urinary excretion of the various metabolites as a surrogate of their generation rates. Differences in plasma levels and urinary excretion rates were compared with the wilcoxon rank sum test.

Results: After randomization, 14 subjects received a high protein diet and 15 subjects were allocated to a low protein diet. There were no significant between-group differences in age, gender and body mass index. In addition there were no significant differences in baseline plasma levels and urinary excretion rates of the abovementioned metabolites. In the high protein diet, we observed a significant increase in plasma levels of indoxyl sulfate (median 19% increase in high protein diet group vs. 18% decrease in low protein diet group, P 0.004). When considering urinary excretion rates, we also noted significant increases of indoxyl sulfate (+33% vs. -11%, P 0.002), indoxyl glucuronide (+78% vs. -19%, P 0.01), kynurenine (+35% vs. -5%, P 0.006), quinolinic acid (+12% vs. -6%, P 0.05) and p-cresyl sulfate (+73% vs. -23%, P 0.04).

Conclusions: High protein intake is associated with increased plasma levels and generation rates of different metabolites, including indoxyl sulfate, indoxyl glucuronide, kynurenine, kynurenic acid, quinolinic acid and p-cresyl sulfate. As part of these metabolites are known uremic retention solutes possibly contributing to progression of chronic kidney disease, these findings give additional insights in the presumed beneficial effects of protein restriction in renal disease, thereby further supporting the protein metabolite hypothesis.