on the expression of EMT markers. Thirteen patients (22%) had borderline changes or acute rejection lesions (from grade I to grade II) detected by the protocol biopsy. EMT scores were significantly higher in this subgroup of patients when compared to patients with a normal kidney graft (expression of vimentin: 2.28 ± 0.9 vs 1.24 ± 0.7, p=0.001; translocation of beta catenin: 2.08 ± 0.6 vs 1.33 ± 0.9, p=0.006).

Conclusions: Together, these data suggest that EMT is an early (three months) and frequent (41%) phenomenon in kidney transplants, that could be triggered by ischemic and/or immunologic tubular injury. Its impact on the long-term function of the graft should now be further studied, but our findings suggest that EMT might be involved in the pathophysiology of CAN.

SO004 INSULIN PROTECTS FROM ACCELERATED SENESCENCE SECONDARY TO ISCHAEMIA/REPERFUSION INJURY IN STZ DIABETIC RATS

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Introduction and Aims: Diabetic organs are under elevated oxidant stress. We have hypothesised that such stress may accelerate ageing in these organs and predispose to further pathology. We have investigated telomere biology and associated cell damage responses in rat kidneys following ischemia reperfusion injury, to determine if cell ageing processes are affected by diabetes.

Methods: Wistar rats were rendered diabetic by streptozotocin treatment, and two weeks later, complete ischemia was induced in the left kidney of both diabetic and non-diabetic rats. These left kidneys, and the corresponding non-right kidney controls, were removed at 6 hours, 24 hours, 1 week and 2 weeks later, complete ischemia was induced in the left kidney of diabetic and non-diabetic groups) Telomere lengths were determined by PFGE. Senescence associated gene expression was determined by real time PCR (Taqman).

Results: We report that diabetic kidneys exhibit accelerated senescence and are preferentially susceptible to ischemia/reperfusion injury. We demonstrate that diabetic rats exhibit shorter telomeres than non-diabetic controls (p <0.009) and that this situation is preferentially exacerbated in diabetic animals by ischemia reperfusion injury (p<0.008) Diabetic kidneys exhibited elevated p21 (p<0.04) and XRCC5 (p<0.03) expression, indicative of increased oxidative damage. This is matched by changes in the expression of the anti-apoptotic gene Bcl-2 (p<0.006) Elevated p21 expression is similar in CKD stages 2 to 4/5. The proportion of patients with U-proteinuria >300 mg/24h significantly increased with advancing renal disease, both in males and females. Although proteinuria was prevalent and progressive, 11% of males and 33% of females with eGFR >< 60 ml/min/1.73m2 had U-proteinuria ><300 mg/24h. Conversely, proteinuria was detected in a significant proportion of patients with estimated GFR >90 ml/min, more so in males than in females.
(TAE) showed great effect to enlarged polycystic kidneys (Am J Kidney Dis, 39, 2002), we treated enlarged PLD patients, whose condition was poor unable to undergo hepatic transplantation, by this TAE technique for the first time in the world (Am J Kidney Dis, 43, 2004). However, treatment outcomes and liver volume changes were obscure. The aim of this study is to reveal the effects of hepatic TAE in patients with huge PLD and discuss about mechanism of cystic growth in liver.

Methods: Among 115 huge PLD patients between June 2001 and November 2005, 12 patients died before treatment and 103 patients undergo hepatic TAE. We analyzed them and followed their outcomes. Patients with massive ascites, hepatic failure (total bilirubin \(>2.0 \text{ mg/dL}\)), or diffusely distributed intrahepatic cysts were excluded. After the diagnosis of PLD, we tried to embolize using microcoils only cystic segments with neither portal vein flow nor intact intrahepatic parenchyma by using computed tomography, portography, and multi-angle angiography. Laboratory data were measured for a few weeks and 3, 6, and 12 months after the procedure. Total hepatic volume, total volume of intrahepatic cysts and intrahepatic parenchyma were measured 0, 12 months after the therapy by using computed tomography and NIH image.

Results: Before the treatment, total hepatic volume were ranged from 4063 to 14112(mean 8367 \(\pm 1411\) cm\(^3\)), of which only 7.2 to 37.5(mean 14.9 \(\pm 7.0\)) % were intrahepatic parenchyma volume. After 1 year, the total hepatic volume and the total volume of intrahepatic cysts were decreased to 86.4 \(\pm 13.4\), 81.1 \(\pm 14.0\)% of pretreatment value, respectively (P < 0.001, P < 0.0001). On the other hand, the total volume of intrahepatic parenchyma were increased to 119.3 \(\pm 31.3\)% of pretreatment value (p=0.004). Fever and mildly elevated liver function tests (AST 101 \(\pm 123 \text{ IU/L}\) and ALT 42 \(\pm 57 \text{ IU/L}\) in day 1) after TAE resolved within 2 weeks. Liver functions were preserved over a year. We could not cure 14 patients but there was no treatment-related death.

Conclusions: Most of all the patients received this treatment have had good clinical course and better quality of life without serious complications. Hepatic TAE may be a safe and new treatment for the patients with poor conditions by symptomatic PLD. Better still, it may increase intrahepatic parenchyma volume. Our study also suggests a hypothesis about mechanism of cystic growth in liver. With growth of intrahepatic cysts and regression of the portal vein, total volume of intrahepatic parenchyma might decrease and the hepatic artery continue to develop by angiogenesis, which is probably induced by portal venous ischaemia. This results in cystic growth, since the cysts is fed by the hepatic artery.

TOLERANCE OF HIGH DOSE ENALAPRIL AND LOSARTAN FOR PROTEINURIA AND BLOOD PRESSURE REDUCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction and Aims: Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) are widely used in proteinuric or hypertensive chronic kidney disease (CKD) patients. The optimum doses for these drugs are debated and studies on the effect of greater dose are few. The aim of this study was to observe whether increasing the dose of Enalapril and Losartan alone or in combination to a higher dose to reduce proteinuria (UTP) or blood pressure (BP) is safe and effective.

Methods: Total 150 patients were selected. Patients of diabetic nephropathy (DN) and primary glomerulonephritis (GN) with proteinuria >0.5 g/day were recruited after a wash period of 3-4 weeks. They were randomly allocated ACEI (group E: Enalapril from 5 mg to 40mg/day, ATRB (group L: Losartan from 25mg to 100 mg/day) or their combination (group E+L: Losartan from 25mg to 50 mg/day). Primary end point was BP reduction to 120/80 mmHg. Patients were evaluated at base line (phase1) and after attainment maximum allocated/tolerated dose (phase3). Patients were excluded when serum creatinine (Scr) elevated >30% in four weeks period, persistently raised serum potassium (K+ >5.5 mmol/l) or for manifestations of distressing side effect of the drug.

Results: Number of patients from DN group was 90 (30 in each drug group of E, L and E+L). 84% patients were hypertensive (>140/90mmHg) at recruitment, 47% patients had renal failure (Scr >1.5 mg/dl) and 7% patients required diuretic (HTZ/Frusemide) to control edema. At phase 1 and phase 2 (11±5 weeks) systolic BP was (150±21 & 141±24, mmHg, P<0.01; diastolic BP (87±10 & 81±12, mmHg, P<0.003); UTP (2.7±2 & 1.6±0.7, g/dl,P<0.02);SCr (1.6±0.5 & 1±0.3, mg/dl, P=NS) and K+ (4.7±0.4 & 4.5±0.7, P=NS) respectively. Due to rising Scr (>30% in 1st month) 2 patients discontinued the trial, 3% patients couldn’t attain full dose for low BP, 3% developed CVA, 4% dry cough and 14% developed hyperkalemia (K+ >5.5 mmol/l).

Patients from GN group were 60 in number (20 in each drug group of E, L and E+L). 23% patients were hypertensive (>140/90mmHg) at recruitment, 10% had renal failure (Scr >1.5 mg/dl) and 23% required diuretic (HTZ/Frusemide) to control edema. At phase 1 and phase 2 (12±6 weeks) systolic BP was (115±19 & 108±14, mmHg, P<0.02); diastolic BP (76±12 & 69±14, mmHg, P<0.003); UTP (4.2±1.5 & 2.7±2.6, g/dl,P<0.007);SCr (1.1±0.3 &1.2±0.5, mg/dl, P=NS) respectively. 2.6% patients developed cough, 5.3% discontinued drug due wide search using 400 microsatellite markers on the biggest pedigree, and using the Affymetrix GeneChip 10K 2.0 on all the families. We calculated pair-wise and multipoint ELOD scores using the FASTLINK 4.1 and Simwalk 2 programs, respectively. The model used for the parametric analysis was autosomal dominant with disease gene frequency = 0.001, penetrance = 0.85, phenocopy rate = 0.001. Traditional thresholds for declaring and excluding linkage were used.

Results: After the first genome scan, 5 loci with heterogeneity LOD score >1 were found. All the suggestive signals were pursued with high resolution microsatellite genotyping in order to extract complete genetic information. The analysis demonstrated a significant linkage on chromosome 1p31-35, with a maximum heterogeneity LOD score of 3.85 and 43% of families linked. The biggest pedigree showed a maximum LOD score of 3.5, achieving genome wide significance on its own. The results were robust to alternative analyses, including changes of penetrance from 0.65 to 0.95 and phenocopy rate from 0.0001 to 0.01.

Conclusions: In the present study we characterized a previously unrecognized autosomal dominant form of congenital abnormalities of the kidneys and urinary tract and we demonstrated the first locus linked to this disease. These studies constitute the first step towards the identification of the underlying gene. The discovery of the responsible gene will improve our understanding in kidney pathophysiology and development.
Vascular access and bioengineering

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Introduction and Aims: Maintenance of long term function of vascular access is a challenge in hemodialysis patient management. Early detection of the dysfunction of hemodialysis vascular access (stenosis is a major cause) and prompt intervention seem to be the crucial step. The purpose of this study was to assess multislice computed tomographic angiography (MSCTA) for detecting stenosis of hemodialysis vascular accesses and guiding the revising operation or percutaneous transluminal angioplasty (PTA).

Methods: Contrast-enhanced 16 slice spiral CT was used to examine 22 hemodialysis subjects with various dysfunctions of vascular access. Parameters for the MSCT angiographic acquisition were 1.0mm section thickness, 0.8mm section interval, pitch of 3 (high-quality mode), 120-135kVp, 200-300 mAs. The scanning volume extended from the AV fistula level to right atrium. 90 ml of iohexol was administered intravenously with a power injector at a rate of 3 ml/sec through the other upper limb peripheral vein. The transverse source images were reformatted as maximum intensity projection (MIP), volume rendering (VR) and curved planar reconstruction (CPR) images. The whole procedure was usually accomplished in 20-30 minutes in outpatient setting and no hospitalization was needed for this examination.

Results: High-spatial-resolution images of vascular accesses were obtained with MSCTA in all patients. MIP, VR and CPR images displayed whole spectrum the AV fistula with the feeding artery, anastomoses and outflow tract up to the superior caval vein. On MSCTA, the stenotic segments of vascular access were mostly string-like. The access distal to the stenosis dilated and distorted locally and the borders between the dilated access and the stenoses were usually obvious. Numerous venous collateral branches were seen in 4 patients. According to the results of MSCTA, AV fistula revising surgery was done in 11 patients and PTA under the guide of digital subtraction angiography (DSA) was done in 5 patients. The results of MSCTA coincide with the finding of surgery or DSA in these 16 subjects.

Conclusions: In our opinion, MSCTA is a good non-invasive diagnostic technique to detect various hemodialysis vascular access abnormalities. It is more economical than DSA at present medical setting, and could replace DSA in the imaging of hemodialysis vascular access and provide important information for further AVF revising surgery or PTA.

Edema and extracellular water

SO009 ◆ MULTISLICE COMPUTED TOMOGRAPHIC ANGIOGRAPHY IN EVALUATING HAEMODIALYSIS VASCULAR ACCESS

Edema and extracellular water

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