Nephrology Dialysis Transplantation 28 (Supplement 1): i175–i184, 2013
doi:10.1093/ndt/gft113

CLINICAL NEPHROLOGY - IGA NEPHROPATHY, LUPUS NEPHRITIS, VASCULITIS

SP307 EFFICACY AND SAFETY OF TELMISARTAN, CLOPIDOGRELIN, AND LEFLUNOMIDE IN PATIENTS WITH IgA NEPHROPATHY – A MULTICENTRE, PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND AND -DUMMY CONTROLLED CLINICAL TRIAL

Jie Wu[1], Shuwei Duan[1], Wenge Li[1], Yaping Wang[1], Wenhu Liu[1], Jianrong Zhang[1], Lide Lun[1], Xuemei Li[1], Chunhua Zhou[1], Ying Zheng[1], Shuwen Liu[1], Yuansheng Xie[1], Guangyan Cai[1] and Xiangmei Chen[1]
[1]*Department of Nephrology, State Key Laboratory of Kidney Disease Beijing China*

Introduction and Aims: To evaluate the efficacy and safety of telmisartan combined with clopidogrelin and/or leflunomide for patients with IgA nephropathy and whether the combination therapy surpass telmisartan in decreasing proteinuria and protecting renal function.
Methods: We enrolled 400 patients aged 18-55 years from 13 centers in Beijing who had proteinuria 0.5~3.5g per day, baseline serum creatinine (SCr) <265.2μmol/L (3mg/dl). All patients were eluted by taking telmisartan 80mg per day for 4 weeks and then randomly assigned to receive at least 24 weeks of treatment with telmisartan 80mg per day + clopidogrelin placebo + leflunomide placebo (group A), telmisartan 80mg per day + clopidogrelin 50mg per day + leflunomide placebo (group B), telmisartan 80mg per day + clopidogrelin placebo + leflunomide 20mg per day (group C), telmisartan 80mg per day + clopidogrelin 50mg per day + leflunomide 20mg per day (group D). Comparison of 24-hr urinary protein excretion, the serum creatinine, eGFR, albumin, cholesterol and uric acid, before and after the therapy were assessed.
Results: No statistically significant differences were observed for any baseline clinical data including age, gender, BMI, blood pressure, proteinuria, serum creatinine, eGFR, serum uric acid in the four groups (P>0.05). After treatment for 24 weeks, a significant decline of proteinuria was observed in the four groups (P <0.05), while those in group C (1.20±0.76 vs 0.77±0.42 g/24h) and group D (1.16±0.63 vs 0.74±0.49 g/24h) were decreased more significantly than in group A (1.15±0.87 vs 0.92±0.58 g/24h) and group B (1.11±0.83 vs 0.89±0.42 g/24h) (P<0.05). Mixed effects were showed that telmisartan, leflunomide, and telmisartan combined with leflunomide were effective in lowering proteinuria (P<0.01) by model analysis. The extent of serum creatinine decline in group C and group D displayed more significantly than that in group A and group B (P<0.05). The levels of eGFR in group C and group D were increased more than those in group A and group B. The decline of serum uric acid in group C and group D displayed more significantly than group A and group B (P<0.05). There were no significant differences in the results of albumin and cholesterol among the four groups ($P > 0.05$). No obvious adverse reactions were found in the four groups.
Conclusions: In the selected patients with IgA nephropathy, telmisartan combined with leflunomide was safe and effective in decreasing proteinura and protecting short-term renal function. Larger randomized studies would be needed to confirm these results in the long run.

SP308 A PROSPECTIVE RANDOMIZED STUDY ON THE EFFICACY OF CORTICOSTEROID COMBINED WITH CYCLOPHOSPHAMIDE OR FK_{506} IN PRIMARY IgA NEPHROPATHY WITH MILD OR MODERATE RENAL INJURY

Pingyan Shen[1], Ya Li[1], Zhaohui Wang[1], Weiming Wang[1], Hong Ren[1], Wen Zhang[1] and Nan Chen[1]
[1]*Department of Nephrology Ruijin Hospital, Shanghai Jiao Tong University School of Medicine Shanghai China*

Introduction and Aims: The aim of this study was to evaluate the efficacy and drug safety of cyclophosphamide or FK_{506} with corticosteroid in primary IgA nephropathy (IgAN) with mild or moderate renal injury.
Methods: From 2010 to 2011,36 primary IgAN patients with 30ml/min≤GFR<90ml/min and urinary protein excretion >1.0g/24h (with or without hypertension) were enrolled to this study prospectively. There were three groups(Corticosteroid, Corticosteroid combined with cyclophosphamide (CTX) or FK_{506}), each group included 12 patients for 24-weeks treatment. In each group, corticosteroid initial dosage was 0.5-0.8mg/kg/d,decreasing the dosage gradually after 8 weeks. Corticosteroid combined with CTX group: CTX 0.5-0.75g/m^2/month; Corticosteroid combined with FK_{506} group: FK_{506} 0.1mg/kg/d (effective serum drug concentration 6~10ng/ml). Maintenance period were 24 weeks: corticosteroid 10-15mg/d; CTX 0.5-0.75g/m^2/8weeks; FK_{506}0.05mg/d. Evaluation of the effect: (1) Remarkable effect:24-hour urinary protein excretion< 0.3g/24h, serum creatinine decreased >10% than baseline; (2) Effect: 24-hour urinary protein excretion decreased over 50% than pre-treatment and serum creatinine was stable; (3) Non-effect:24-hour urinary protein excretion did not meet the above criteria, or serum creatinine increased >8% per year.
Results: 36 patients were enrolled, M 26/F 10, average age 37.53±11.35yrs(20~70). There is no difference among the three groups in their laboratory features at the base line. After 3 months, 6 months and 12 months, 24-hour urinary protein excretion was decreasing 0.90±0.75g, 0.76±0.73g and 0.35±0.35g in corticosteroid group; 1.40±1.24g, 0.87±0.83g, 1.43±2.59g in corticosteroid combined with CTX group and 1.10±1.33g, 0.78±0.69g, 0.69±0.82g in corticosteroid combined with FK_{506} grouprespectively (P<0.05). After 6 months, the serum creatinine decreased both in corticosteroid group (Scr 111.72±31.23umol/L) and corticosteroid combined with CTX group (Scr 111.33 ±22.76 umol/L) (P<0.05); while no change in corticosteroid combined with FK_{506} group. Remarkable effect: corticosteroid group 9 patients(75%), corticosteroid combined with CTX group and corticosteroid combined with FK_{506} group were both 7 patients(58%); Effect: corticosteroid group and corticosteroid combined with FK_{506} group both 3pts(25%),corticosteroid combined with CTX group 5 pts(42%); corticosteroid combined with FK_{506} group had 2pts(17%)non-effect. Adverse events included 1 hyperglycemia and 1 liver dysfunction in corticosteroid group, including 2 hyperglycemia, 1 IGT and 1 liver dysfunction in corticosteroid combined with FK506 group.
Conclusions: It suggested that CTX and FK506 were beneficial for controlling proteinuria without significant serum creatinine increasing.

SP309 RELATIONSHIP BETWEEN THE BODY MASS INDEX AND THE PROGRESSION OF IgA NEPHROPATHY EVEN IN LEAN INDIVIDUALS

Mamiko Shimamoto[1], Isao Ohsawa[1], Hiyori Suzuki[1], Seiji Nagamachi[1], Yoshio Shimizu[1], Satoshi Horikoshi[1] and Yasuhiko Tomino[1]
[1]*Division of Nephrology, Department of Medicine Juntendo University Faculty of Medicine Tokyo Japan*

Introduction and Aims: In chronic kidney disease, obesity is an important risk factor for disease progression. Likewise, in IgA nephropathy (IgAN), several studies reported that excessive body weight (body mass index (BMI): 25 kg/m^2 or greater) had an impact on the prognosis. The impact of BMI, however, remains unclear in smaller individuals like Japanese. The objective of the present study is to determine the impact of BMI and metabolic factors on the prognosis of IgAN patients in Japanese.
Methods: All IgAN patients were diagnosed in the Juntendo University Hospital between 1999 and 2009. Patients with diabetes mellitus or autoimmune disease, purpura nephritis were excluded. There were 95 male (49.2%) and 98 female (50.8%) patients, and median age was 32.8±11.0 years old (range 12-65). Patients were divided into three groups equally according to BMI: Group L (lean group) (n=65, BMI: 15.57-20.18kg/m^2), Group M (middle group) (n=64, BMI: 20.20-23.04 kg/m^2) and Group O (overweight group) (n=64, BMI: 23.11-31.89 kg/m^2). Clinical and pathological data at the time of renal biopsy were analyzed. Levels of serum creatinine (sCr), urinary protein (UP), urinary red blood cell (uRBC) of 1, 2, 3, 4 and 5 years after the renal biopsy were also compared.
Results: In multivariate logistic regression analysis, the excessive BMI (OR 1.19, 95%CI 1.02-1.40) and hypoalbuminemia (OR 0.16, 95%CI 0.05-0.46) at the time of renal biopsy were significant predictors of remission of proteinuria. At the time of renal biopsy, there were no significant difference in UP, the degree of hematuria, serum urea nitrogen, total protein, albumin, IgG, IgM, and IgA. The ratio of female to male was significantly higher in group L, it was much lower in Group O. Systolic blood pressure (BP) and diastolic BP in Group O were significantly higher than those in Group L and Group M. Estimated GFR (eGFR) in Group L was higher than that in Group O. Triglyceride (TG), LDL cholesterol, Uric acid (UA), Hemoglobin (Hb), C-reactive protein, C3 and C4 in Group O were significantly higher than those in Group L and Group M. UA, TG, C4, Hct, Hb, C3, HDL-c, sCr, systolic BP and diastolic BP were significantly correlated with BMI. In five years, although the progression of eGFR and the degree of RBC were similar among the three groups, the remission of urinary protein was significantly delayed in Group O.
Conclusions: This is the first study that shows BMI and metabolic factors have impacts on the prognosis of IgAN even in Japanese whose body is smaller than Caucasian. It appears that the overweight is a risk factor for disease progression. Therefore, BMI should be paid more attention, and we should aggressively recommend patients with IgAN to reduce weight and treat their metabolic factors.

SP310

ALTERED MONOCYTE GENE EXPRESSION AND EXPANSION OF CD14$^+$CD16$^+$ CELL SUBSET IN IgA NEPHROPATHY PATIENTS

Sharon N. Cox[1], Grazia Serino[1], Fabio Sallustio[1,2,3], Francesco Pesce[1,4] and Francesco P. Schena[1,2]

[1]Emergency and Organ Transplantation University of Bari Bari Italy, [2]C.A.R.S.O. Consortium Valenzano, Bari Italy, [3]DiSTeBA Università del Salento Lecce Italy, [4]Genomics of Common Disease, School of Public Health Imperial College London United Kingdom

Introduction and Aims: Immunoglobulin A nephropathy (IgAN) is the most common form of primary glomerulonephritis worldwide. The basic defect lies within the IgA immune system and in peripheral blood leukocytes rather than local kidney abnormalities. Our previous work evidenced a more profound altered gene expression pattern in monocytes compared to B and T cells isolated from IgAN patients and thus our aim here was to study the monocyte subset more closely at a genome wide level. Human monocytes can be classified into two main subsets with distinctive characteristics: classical (CD14$^+$CD16$^-$) and non classical (CD14$^+$CD16$^+$) monocytes, the latter cells characterized by a more marked apoptotic propensity.
Methods: A total of 33 IgAN patients and 33 healthy subjects (HBD) were included in this study. Illumina microarray technology was used to evaluate global differences in gene expression between monocytes isolated from IgAN patients and HBD. Bioinformatic analysis was performed with GenomeStudio and Genespring software. The connectivity between genes was evaluated using Ingenuity Pathway Analysis. Aberrantly expressed genes and pathways were then validated inan independent set of patients with RT-PCR western blot and flow cytometric analysis.
Results: Bioinformatic analysis revealed 710 differently regulated probes with FDR-corrected p value<0.05 in IgAN patients. These probes were primarily involved in *Apoptosis Signaling, mitochondrial dysfunction, tnfr2/1 and death receptor signaling* canonical pathways. Four representative genes belonging to these pathways (TNF, CD83, *TNFRSF1A, NDUFS3)* were chosen for validation purposes and the normalized gene expressions obtained were in line with the gene expression array. All mitochondrial respiratory chain subunits were found modulated. In particular, the protein levels of NDUFS3 were statistically up-regulated in IgAN patients confirming an aberrant mithocondrial homeostasis. The enhanced apoptotic phenotype seen with the gene expression in monocytes was confirmed at the protein level, in fact CD14+ cells exhibited a significantly higher percentage of annexin-V and 7-AAD double positive staining. Next we demonstrated this phenotype was due to a different distribution of monocyte subsets in IgAN patients compared to HBD. Surprisingly we found that CD14$^+$ CD16$^+$subset was significantly expanded in all IgAN patients tested even though the total monocyte count was unchanged.
Conclusions: Taken together, our findings demonstrate an aberrant modulation of the mitochondrial respiratory system in monocytes isolated from IgAN patients and a specific up-regulation of NDUFS3. Furthermore, the aberrant expansion of the CD14$^+$CD16$^+$subset in IgAN patients could explain the enhanced apoptotic function seen in these cells thus, revealing a potential pathogenetic role of these cells in IgAN.

SP311

RELIABILITY OF STATISTICAL MODELS TO PREDICT AN IGA NEPHROPATHY

Emilie Kalbacher[1], Michel Ducher[1], Denis Fouque[1], Brigitte MacGregor[1], Francois Combarnous[2] and Jean Pierre Fauvel[1]

[1]Nephrology hopital E Herriot Lyon France, [2]Nephrology Clinique du Tonkin Lyon France

Introduction and Aims: Models are increasingly used in clinical practice to improve the accuracy of diagnosis. The aim of our work was to compare Bayesian network to logistic regression to forecast an IgA nephropathy (IgAN) from simple clinical and biological criteria.
Methods: Retrospectively, we pooled the results of all biopsies (n=155) performed by nephrologists in a specialist clinical facility between 2002 and 2009. Two groups were constituted at random. The first sub-group was used to determine the parameters of the models adjusted to data by logistic regression or Bayesian network, and the second was used to compare the performances of the models using Receiver Operating Characteristics (ROC) curves.
Results: An IgAN was found in 45 patients. Areas under the ROC curves provided by both methods were highly significant but not different from each other. Based on the highest Youden indices, sensitivity reached (100% vs 67%) and specificity (73%vs 95%) using the bayesian network or the logistic regression respectively.
Conclusions: A Bayesian network is at least as efficient as a logistic regression to estimate the probability of a patient suffering IgAN, using simple clinical and biological data obtained at consultation.

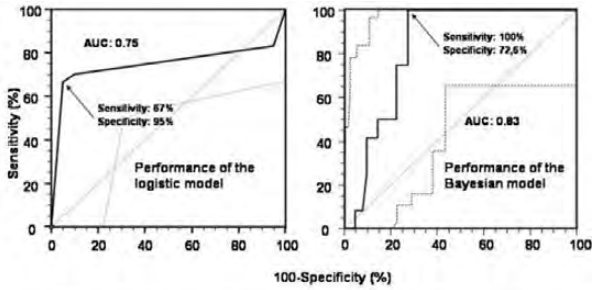


Figure 1. Receiver-operating-characteristic curves used to assess the predictive values of the 2 models to diagnose an IgAN in the validation sample of 74 patients. AUC means area under the curve.

SP312

CORTICOSTEROID THERAPY IS THE MOST IMPORTANT FACTOR INFLUENCING TA PROTEINURIA AND RENAL SURVIVAL IN IgA NEPHROPATHY (IgAN)

C. Sarcina[1], F. Ferrario[1], V. Terraneo[1], A. Pani[2], G. Fogazzi[3], G. B. Visciano[1], I. De Simone[1], F. Rastelli[1] and C. Pozzi[1]

[1]Nephrology and Dialysis Unit Bassini Hospital Cinisello Balsamo Italy, [2]Brotzu Hospital Cagliari Italy, [3]Maggiore Hospital Milan Italy

Introduction and Aims: Time Average Proteinuria (TAP) is an important prognostic factor in patients (pts) with IgAN: when proteinuria remains <1 g/d, progression towards ESRD is rare. The aim of this study is to search for association between proteinuria <1 g/d (favourable prognostic factor) and some clinical variables, especially the treatment.
Methods: From 1989 to 2005, we enrolled 325 pts affected by IgAN, presenting any plasma creatinine values and proteinuria above 1 g/d. Mean follow-up was 65.3±31 months and pts were evaluated six months after the enrollment and then every year. The considered variables were: age, sex, histological score, blood pressure (BP), immunological therapy, RAS blockers and statins. Pts were divided in 3 groups according to mean proteinuria values at follow-up: group 1, pts with proteinuria steadily >1 g/d; group 2, pts with proteinuria in turn > or <1 g/d; group 3, pts with proteinuria steadily <1 g/d. Considered endpoints were ESRD, 100% and 50% increase of plasma creatinine.
Results: Pts were distributed as follows: 51 (15.7%) in group 1, 156 (48.0%) in group 2, 118 (36.3%) in group 3. At last observation, the percentage of pts who reached the endpoints of ESRD, 100% and 50% increase of plasma creatinine in group 1 was 46.15%, 48.7% and 64.1%, respectively, in group 2 10.6%, 17.5% and 30.0%, respectively, and in group 3 3.1%, 5.5% and 11.1%, respectively. In group 3 a stable reduction of proteinuria occurred in 66.9% by 6 months and in further 18.7% by 12 months. Therefore, proteinuria reduction occurred especially when pts received immunological treatment (first six months). Considering the immunological therapy, 43 pts had no treatment, 171 received steroids (ST) and 111 steroids+azathioprine (ST +A); in group 1, 41.0% of patients had no treatment, whereas 17.9% received ST and 41.1% ST+A; in group 2, 9.4% had no treatment, 58.1% received ST and 32.5% ST+A; in group 3, 9.52% had no treatment, 56.35% received ST and 34.15% ST+A. At logistic univariate analysis pts treated with ST or ST+A, compared to not treated pts, had more possibilities of reducing proteinuria <1 g/d (RRR 7.0 and 3.2 respectively; p <0.01). Age, sex, histological score, BP at baseline and use of statins were not associated with proteinuria steadily below 1 g/d; the use of RAS blockers resulted significant only in group 2 (p 0.03).
Conclusions: Our data show that the only factor associated with proteinuria steadily below 1 g/d was the immunological treatment. Particularly, ST resulted effective in reducing TAP, whereas the add of A didn't produce further advantages. Histological grade and hypertension at baseline didn't seem to be associated with a low TAP. Use of RAS blockers had a significant role in pts with more variability of proteinuria values.

SP313

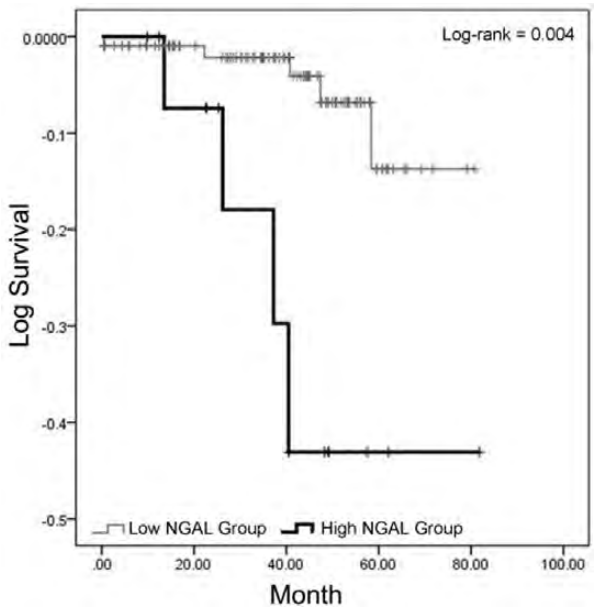
HIGH SERUM AND URINE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) LEVEL IS AN INDEPENDENT PREDICTOR OF RENAL PROGRESSION IN PATIENTS WITH IgA NEPHROPATHY

Ihm Soo Kwak[1], Eun Young Seong[1], Harin Rhee[1], Dong Won Lee[2], Soo Bong Lee[2], Byung Yoon Yang[1], Min Ji Shin[1] and Il Young Kim[2]

[1]Nephrology Pusan National University Hospital Busan Republic of Korea, [2]Yangsan- Pusan National University Hospital Yangsan Republic of Korea

Introduction and Aims: Tubulo-interstitial injury plays an important role in the progression of Immunoglobulin A(IgA) nephropathy and the neutrophil

gelatinase-associated lipocalin (NGAL) is one of the most sensitive tubule markers. The aim of our study is to investigate if the serum or urine NGAL might predict the prognosis in patients with IgA nephropathy.
Methods: From January 2005 to December 2010, patients with biopsy proven IgA nephropathy whose serum and urine samples at the time of kidney biopsy were conserved in a frozen state, were enrolled in this study. We retrospectively reviewed their clinical data and followed them up till October 2012. Serum and urine NGAL levels were measured using ELISA kit. Renal progression was defined as eGFR decline more than 50% or progression to end-stage renal disease (ESRD).
Results: A total of 121 patients were enrolled in this study. During the median follow up period of 41.49 months, renal progression was found in 9 patients(7.4%). In our study, serum or urine NGAL alone could not predict renal progression, however, when the serum and urine NGAL levels were combined, the high NGAL group independently predicted the renal progression (HR=4.58,95% CI=1.13−18.59, p=0.033) along with the tubular damage graded by the Oxford classification T2 (HR=6.61, 95% CI=1.51−28.91, p=0.004). The Kaplan-Meier curve for renal survival showed a significantly higher renal progression in the high NGAL group(Log rank, p=0.004).
Conclusions: In patients with IgA nephropathy, high serum and urine NGAL levels at the time of kidney biopsy, predicted renal progression.



SP313

SP314 UP-REGULATION OF URINARY MARKERS PREDICTS OUTCOME OF IgA NEPHROPATHY BUT THEIR PREDICTIVE VALUE IS INFLUENCED BY TREATMENT WITH IMMUNOSUPPRESSION

Maria J. Stangou[1], Christos Bantis[1], Stratis Kasimatis[1], Maria Skoularopoulou[1], George Toulkeridis[1], Afroditi Pantzaki[2], Aikaterini Papagianni[1] and George Efstratiadis[1]
[1]Department of Nephrology Hippokration Hospital Thessaloniki Greece, [2]Department of Pathology Hippokration Hospital Thessaloniki Greece

Introduction and Aims: Steroids and immunosuppressants can delay progression of renal function in IgAN, but their possible effect in local cytokines has not been studied.
Methods: Histology in 53 IgAN patients [M/F 35/18 age 40.5yrs (17-65)] was evaluated by Oxford classification system. IL-1β, -2, -4, -5, -6, -10, -12 and -17, INF-γ and MCP-1 were measured subsequently by multiplex cytokine assay in first morning urine samples taken at the day of renal biopsy. After a 6 month course with RAASinhibitors+fish oils, 35/53 patients, group A, responded and continued on the same treatment, while in 18/53 who did not respond, group B, steroids+azathiopine were added.
Results: The presence of endocapillary proliferation had significant correlation with the urinary excretion of pro-inflammatory and pro-fibrotic cytokines (IL-1β, MCP-1, IL-17, INF-γ, IL-6 and IL-10). Serum creatinine at time of diagnosis had significant correlation with proteinuria (p=0.02), urinary levels of IL-1β (p=0.03), IL-2 (p=0.01) and MCP-1 (p=0.03). GFR was reduced from 65±29 to 57±34ml/min, p=0.005 in group A and stayed stable in group B patents (GFR from 63±24 to 61±30ml/min, p=NS). Most of the measured cytokines in the urine predicted deterioration of renal function in group A, but the urinary excretion of IL-1β, and IL-6 seemed to predict renal function outcome in both groups of patients.
Conclusions: Several cytokines are excreted in the urine of patients with IgAN, and their levels predict outcome of the disease. Steroids+aza may exert their beneficial effect through production or activation of most cytokines.

SP315 EFFECT OF LEUKEMIA INHIBITORY FACTOR (LIF) ON IgA1-PRODUCING CELLS FROM TONSILS OF PATIENTS WITH IgA NEPHROPATHY (IgAN)

Koshi Yamada[1,2], Hitoshi Suzuki[1,2], Yusuke Suzuki[2], Milan Raska[1,3], Zhi-Qiang Huang[1], Colin Reily[1], Zina Moldoveanu[1], Krzysztof Kiryluk[4], Bruce A. Julian[1], Yasuhiko Tomino[2], Ali G. Gharavi[4] and Jan Novak[1]
[1]University of Alabama at Birmingham Birmingham AL United States, [2]Juntendo University Tokyo Japan, [3]Palacky University Olomouc Czech Republic, [4]Columbia University New York NY United States

Introduction and Aims: IgA1-producing cells from tonsils of patients with IgAN secrete galactose-deficient IgA1 (Gd-IgA1), a key factor in the IgAN pathogenesis. Upper-respiratory-tract infections frequently associate with episodes of macroscopic hematuria in IgAN patients, but little is known about the role of tonsils and production and glycosylation of IgA1 by tonsillar cells. Moreover, genetic studies revealed an association of a locus encompassing the gene encoding LIF with serum IgA levels in patients with IgAN. LIF, a member of IL-6 family of cytokines, is involved in mucosal immunity. Here, we assessed the effect of LIF on IgA1 production and glycosylation using IgA1-secreting cells derived from tonsils of IgAN patients and controls.
Methods: We assessed the effect of LIF, as compared to IL-6 as a control, on production and *O*-glycosylation of IgA1 in EBV-immortalized IgA1-secreting cells derived from tonsils of IgAN patients (IgAN-T) and controls (patients with sleep apnea syndrome; HC-T). IgA1-secreting cells derived from the circulation of IgAN patients (IgAN-P) and healthy controls (HC-P) served as controls. Gd-IgA1 was determined by lectin ELISA with *Helix aspersa* agglutinin (HAA).
Results: LIF decreased production of IgA1 in IgAN-T and HC-T (-22.4%±14.4% and -3.7%±1.2%), as well as in IgAN-P and HC-P (-9.1%±6.1% and -6.7%±4.1%). Conversely, IL-6 increased production of IgA1 in IgAN-P and HC-P by 55.8% and 16.9%, respectively, wheras the increases in IgA1 production in IgAN-T and HC-T were less robust (14.5% and 3.5%). Cells from IgAN patients (IgAN-T and IgAN-P) secreted more Gd-IgA1 compared to the cells from controls (HC-T and HC-P) (28.0% and 24.2%, 13.5% and 15.5%; expressed as HAA reactivity; 100% is binding to standard Gd-IgA1). LIF increased Gd-IgA1 production by IgAN-T but not by HC-T (relative change, 24.2%±3.7% *vs.* -0.1%±0.1%). LIF increased production of Gd-IgA1 in IgAN-P but not in HC-P (relative change, 15.3%±3.6% *vs.* -1.5%±2.8%; p<0.01). IL-6 increased production of Gd-IgA1 in IgAN-T but not in HC-T (relative change, 32.5%±3.7% *vs.* -0.1%±0.1%) and increased Gd-IgA1 production in IgAN-P but not in HC-P (relative change, 24.0%±15.9% *vs.* -4.0%±4.2%; p<0.01). Thus, LIF or IL-6 stimulation of IgA1-secreting cells from IgAN patients increased production of Gd-IgA1.
Conclusions: IgA1-secreting cells from IgAN patients responded abnormally to a cytokine encoded in a locus identified by genetic association studies. Understanding the abnormalities will aid development of new diagnostic approaches and future IgAN-specific therapy.

SP316 TONSILLECTOMY IN A PAN-EUROPEAN COHORT OF 1147 PATIENTS WITH IgA NEPHROPATHY

Roberta Camilla[1], Rosanna Coppo[1], Shubha Bellur[1], Daniel Cattran[1], Terence Cook[1], John Feehally[1], Stephan Troyanov[1], Ian Roberts[1], Luca Vergano[1] and Laura Morando[1]
[1]On behalf of VALIGA Study Group Italy

Introduction and Aims: The beneficial effect of tonsillectomy in patients with IgA nephropathy (IgAN) is controversial. Tonsillectomy has been proposed with the aim of removing a source of pathogens and reducing Gut Associated Lymphoid Tissue (GALT) and decreasing polymeric IgA synthesis. In Asia, particularly Japan, benefits of tonsillectomy have been claimed from uncontrolled studies and from recent RCTs, mostly in association with steroids. In Europe small single center uncontrolled studies failed to show any benefit of tonsillectomy in IgAN. There is a lack of a European multicenter study on tonsillectomy in IgAN.
Methods: The 1147 patients with IgAN enrolled in the European validation study of the Oxford Classification of IgAN (VALIGA), from 55 Centers of 13 European Countries, has offered a unique opportunity to investigate the effect of tonsillectomy in IgAN paztients very well characterized both histologically and clinically. Retrospective data were obtained over a mean follow-up >5 years.
Results: Data on tonsillectomy were available in 1049 patients: tonsillectomy was performed in 62 patients (5.9%), 10 children and 52 adults; 95% were Caucasian and 77% males. Mean values in the 62 tonsillectomized patients versus 987 non-tonsillectomized are reported in table1.

SP316

	NO tonsillectomy	YES tonsillectomy	p value
Age at renal biopsy (years)	35.8 ± 16.5	37.4 ± 16.2	ns
Follow-up (years)	5.71 ± 4.48	5.62 ± 4.12	ns
eGFR at renal biopsy (ml/min/1.73m^2)	76.7 ± 34.6	73.4 ± 31.76	ns
Proteinuria at renal biopsy (g/day/1.73m^2)	1.20 (0.52-2.56)	1.35 (0.59-2.83)	ns
Mean proteinuria over follow-up (g/day/1.73m^2)	0.78 (0.40-1.62)	0.73 (0.37-1.68)	ns
Loss of eGFR during follow-up (ml/min/1.73m^2/year)	-2.08 ± 8.08	-1.01 ± 7.75	ns
ESRD	112/987 (11.3%)	9/62 (14.5%)	ns
50% loss of initial eGFR	137/987 (13.9%)	9.62 (14.5%)	ns
Combined end-point (ESRD or 50% loss of initial eGFR)	156/987 (15.8%)	10/62 (16.1%)	ns

e-GFR was calculated using the MDRD formula in adults and Schwartz formula in children. The slope of e-GFR was calculated form serial measurements over the follow-up. The end-points were end stage renal disease (ESRD) and 50% loss of e-GFR. A propensity score estimating the probability of receiving tonsillectomy after renal biopsy permitted the pairing of 41 patients with tonsillectomy and 41 without tonsillectomy with similar risk of progression (gender, age, race, mean blood pressure, proteinuria, e-GFR at renal biopsy, previous treatments and Oxford MEST scores). No significant difference was found in the combined end point (3 events in tonsillectomized vs 8 in non tonsillectomized patients, p NS).
Conclusions: The VALIGA retrospective study of a large cohort of European subjects with IgAN did not demonstrate a significant correlation between tonsillectomy and survival from the end point of ESRD or 50% loss of e-GFR.

SP317 RISK OF PROGRESSION OF IgA NEPHROPATHY (IgAN) IN CHILDREN BASED ON OXFORD CLASSIFICATION (OC) AND IgA/C3 SERUM RATIO

Malgorzata Mizerska-Wasiak[1], Jadwiga Maldyk[2], Agnieszka Rybi-Szuminska[3], Agnieszka Firszt-Adamczyk[4], Beata Bienias[5], Katarzyna Gadomska-Prokop[6], Ryszard Grenda[6], Malgorzata Zajaczkowska[5], Roman Stankiewicz[4], Anna Wasilewska[3] and Maria Roszkowska-Blaim[1]

[1]Dept. of Pediatrics and Nephrology Medical University of Warsaw Warsaw Poland, [2]Dept of Children Pathology Medical University of Warsaw Warsaw Poland, [3]Dept of Pediatrics and Nephrology Medical University of Bialystok Bialystok Poland, [4]Dept of Pediatrics and Nephrology Children's Hospital Torun Poland, [5]Dept of Pediatric Nephrology Medical University of Lublin Lublin Poland, [6]Dept of Nephrology and Kidney Transpalnatation The Children's Memorial Health Institute Warsaw Poland

Introduction and Aims: The aim of the study was to assess the risk of progression of IgAN in children at the onset of the disease, based on OC and IgA/C3 serum ratio.
Methods: A total 58 children, in mean age 9.56 ± 4.99 yrs, with IgAN from 5 nephrology centers in Poland were enrolled. Renal biopsy was performed in 0.9, median 0.5 (0.08-4.75) yrs after the first symptoms of IgAN. The histological features were scored ac. to OC: (M-mesangial hypercellularity, E-endocapillary hypercellularity, S-segmental sclerosis, T-tubular atrophy/interstitial fibrosis; absent =0, present=1). Proteinuria (mg/kg/day), IgA/C3 serum ratio were analyzed depending on MEST and histological number of risk factors.

SP317

MEST	Proteinuria (mg/kg/day)	P	IgA/C3 serum ratio	P
M0	19.59 ± 21.34	NS	1.82 ± 1.03	<0.05
n= 13	Median 14.1 (0-76.0)		Median 1.71 (0.69-4.4)	
M1	41.23 ± 84.10		2.70 ± 1.31	
n=45	Median 16.0 (0-500.0)		Median 2.57 (0.58-6.14)	
E0	31.38 ± 77.53	<0.05	2.47± 1.30	NS
n= 48	Median 14.55 (0-500.0)		Median 2.45 (0.58-6.14)	
E1	58.39 ± 58.42		2.63 ± 1.34	
n=10	Median 26.50 (6.40-177.0)		Median 2.02 (0.67-4.97)	
S0	25.05 ± 77.53	<0.05	2.17 ± 1.07	<0.05
n=36	Median 12.90 (0-202.0)		Median 2.15 (0.67-5.14)	
S1	53.45 ± 104.69		2.96 ± 1.47	
n=22	Median 24.0 (0.10-500.0)		Median 2.74 (0.58-6.14)	
T0	36.71 ± 79.06	NS	2.33 ± 1.19	<0.05
n=51	Median 15.0 (0-500.0)		Median 2.21 (0.58-5.19)	
T1	32.69 ± 34.50		3.58 ± 1.55	
n=7	Median 16.0 (0.10-91.0)		Median 3.58 (3.30-1.93)	

Results: Results of proteinuria and IgA/C3 ratio in MEST groups are presented tabl. 1. Most commonly histological lesions were: M1-77.6% pts, S1-37.9% Proteinuria was higher (p<0.05) in pts with E1, S1 vs. E0, S0. IgA/C3 serum ratio was significantly higher (p<0.05) in children with M1, S1 and T1 vs. M0,S0,T0, in E1 vs E0 NS. Significantly higher values of IgA/C3 (p<0.05) were revealed in pts with 4 risk factors of poor histological prognosis in OC (M+E+S+T=4) vs. pts without risk factors (M+E+S+T=0).
Conclusions:
1. The serum IgA/C3 ratio may be a marker severe histological lesions in children with IgAN.
2. The renal biopsy Oxford Classification performed in children at the onset of the disease is useful in evaluation of IgAN severity.

SP318 CRESCENTS IN IGA NEPHROPATHY:A CLINICAL-PATHOLOGICAL STUDY

Xiaoyan Zhang[1], Jingyuan Xie[1], Weiming Wang[1], Xiaoxia Pan[1], Shanmai Guo[1], Pingyan Shen[1], Wen Zhang[1] and Nan Chen[1]

[1]Department of Nephrology, Rui Jin Hospital, Shanghai Jiao Tong University, School of Medicine Shanghai China

Introduction and Aims: Previous studies found crescent may be associated with clinical outcomes in patients with IgA nephropathy (IgAN). However, due to the small sample size and the controversial results of these studies, the clinical significant of crescents in IgAN remain fully elucidated. The aim of this study is to evaluate clinical-Pathological characteristics of IgAN patients with crescents formation and compare renal outcomes between patients with or without crescent in an extended Chinese IgAN cohort.
Methods: We recruited 539 biopsy-proven IgAN patients in this study. IgAN patients secondary to systemic diseases were excluded. All participants in this study were divided to two group (Cre+ group and Cre- group) based on whether crescents were found in the renal tissue. Clinical data was recorded at baseline and during follow-up. Histological parameters were scoring semi-quantitatively by one experienced pathologists. Cresent was defined as cellular cresent or fibrocellular cresent that involved >10% of the circumference of Bowman's capsule.
Results: There are 226 patients in Cre+ group and 313 patients in Cre- group. The mean follow-up time is 3 years. Mean age was 37.1±12.2 in Cre+ group and 35.0 ± 12.1 years in Cre- group. Of all patients in Cre+ group, 91(40.3%), 94(41.6%), 30(13.3%), 11 (4.8%) had the percentage of crescent was <10%, 10-25%, 25-50%, >50% respectively. At renal biopsy, patients in Cre+ group had lower Hemoglobin (12.4±2.1 vs 13.1±2.1g/dl, p=0.001), higher proteinuria [1.76(0.04-11.26) vs 1.26(0.03-13.91)g, P=0.001] than in Cre- group. On histology, Cre+ group had a higher percentage of mesangial hypercellularity (44.1% vs 37.1%, P=0.015) and endocapillary hypercellularity (60.6% vs 17.0%, P<0.001,) higher intensity of C3 deposition (83.0% vs 73.4%, P=0.016). In total, ESRD occurred in 56 individuals. Patients in Cre+ and Cre- group had a similar renal survival time. By multivariate Cox proportional hazards model, four bvariables were independently related to ESRDwhich including serum albumin [HR = 0.53(0.32–0.88), p = 0.02], systolic blood pressure[HR = 1.02(1.00–1.04), p =0.04], eGFR [HR = 0.96(0.94–0.97), p =0.00], hemoglobin [HR = 0.83(0.72–0.94), p =0.01]. In Cre+ group, There are three baseline variables associated with ESRD :sex[HR = 0.17(0.04–0.85), p =0.03], systolic blood pressure[HR = 1.05, 95% CI 1.02–1.09, p <0.001], eGFR [HR = 0.94(0.91–0.97), p<0.001].
Conclusions: Our study suggested cresent is associated with clinical and pathological characteristics in patients with IgAN. While cresent is not associated with ESRD, IgAN paitents with crescent have different risk factors for ESRD compare with that without crescent.

SP319 EVALUATION OF CELIAC DISEASE IN CHILDREN WITH HENOCH SCHOENLEIN PURPURA

Alper Soylu[1], Yeşim Öztürk[1], Yavuz Doğan[2], Derya Özmen[1], Özlem Yilmaz[2] and Salih Kavukçu[1]

[1]Pediatrics Dokuz Eylül University Medical Faculty İzmir Turkey, [2]Microbiology Dokuz Eylül University Medical Faculty İzmir Turkey

Introduction and Aims: Prevalence of celiac disease (CD) in children is around 1 per cent in Europe and United states. The rate of seropositivity has been reported to be 2.42% in healthy Turkish children. The frequency of other autoimmune diseases is increased in CD. IgA associated skin and systemic disorders (IgA nephropathy) are found among these diseases. Henoch Schoenlein purpura (HSP) is an IgA associated autoimmune disease. However, apart from two case reports, there is no study evaluating the association of HSP with CD. We aimed to evaluate the presence of latent CD in children with HSP.
Methods: Children with HSP over 3 years of age were enrolled in the study. They were evaluated for demographic, anthropometric, clinical and laboratory data including urinalysis, complete blood count, serum albumin, creatinine, IgA levels. In addition, anti-tissue transglutaminase IgA (ELISA), anti-endomysium IgA (IFAT), antigliadin (GAF3X, deaminated) IgA (IFAT) and anti-gliadin (GAF3X, deaminated) IgG (ELISA) antibody levels were determined. Seropositive patients were evaluated by endoscopic small bowel biopsy. The rate of CD seropositivity in HSP patients was compared to the rate in healthy Turksih children by the test for the statistical significance of two percentages.
Results: Celiac serology was evaluated in 42 children (25 male, mean age 11.2±3.6 years) with HSP. There was no patient with growth failure or having symptoms

associated with CD like abdominal pain, abdominal distention or diarrhea. In addition, none of the patients had IgA deficiency, anemia or hypoalbuminemia. Celiac serology was positive in 5 (12%) children. Endoscopic evaluation was performed in 3 patients and one of them was diagnosed as CD. Prevalence of CD in children with HSP was significantly higher compared to healthy Turkish children (p<0.001).
Conclusions: Celiac seropositivity was 12% in children with HSP and this rate is significantly higher than the rate in healthy children. Although the number of children with HSP is small in this preliminary study, this result suggests that celiac screening may be considered in children with HSP.

SP320 PLASMA NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS A NEW INDEPENDENT PREDICTOR OF PROGNOSIS IN PATIENTS WITH IGA NEPHROPATHY

Ji-Young Choi[1,2], Ga-young Park[1,2], Hee Yeon Jung[1,2], Kyung Hoon Kim[1,2], Owen Kwon[1,2], Jang-Hee Cho[1,2], Chan-Duck Kim[1,2], Yong-Lim Kim[1,2] and Sun-Hee Park[1,2]

[1]Division of Nephrology, Department of Internal Medicine Kyungpook National University School of Medicine Daegu Republic of Korea, [2]Clinical Research Center for End Stage Renal Disease in Korea Daegu Republic of Korea

Introduction and Aims: The clinical course of IgA nephropathy (IgAN) is variable. Neutrophil gelatinase-associated lipocalin (NGAL) is well known as a novel specific biomarker of acute kidney injury (AKI). We aimed to evaluate the value of plasma NGAL as an independent predictor associated with disease prognosis in IgAN.
Methods: A total of 93 patients with biopsy-proven IgAN in a single center were evaluated. Plasma NGAL was measured by commercial ELISA kit (R&D Systems, Minneapolis, MN). Adverse renal outcome was defined as CKD stage 3 or above at last follow-up. Pearson's correlation coefficient and Cox regression were used for analysis.
Results: There were 50 men and 43 women with a mean age of 35 years (18˜77 years). Plasma NGAL ranged between 21.67 and 446.40 ng/ml (median 125.13 ng/ml) and it was correlated with age (r=0.326, p=0.001), creatinine (r=0.403, p<0.001), eGFR (r=-0.432, p<0.001), uric acid (r=0.309, p=0.003) and protein/creatinine ratio (PCR) (r=0.308, p=0.003). Plasma NGAL was also significantly associated with tubular injury in pathology (p=0.026). During mean follow-up of 37.6 months, the patients with CKD stage 3 or above were 13 (14%). In a multivariate Cox regression model, hypertension (HR=7.289, CI 1.448-36.682, p=0.016), proteinuria >1g/day (HR=4.724, CI 1.227-18.182, p=0.024) and plasma NGAL (HR=1.010, CI 1.002-1.018, p=0.018) were independent predictors associated with the outcome of CKD stage 3 or above.
Conclusions: Plasma NGAL was well correlated with other clinical parameters previously known as predictors of disease prognosis of IgAN and it was independent predictor of adverse renal outcome. We suggest plasma NGAL as a new independent predictor of prognosis in IgAN, while further studies are needed to confirm the usefulness of plasma NGAL as a predictor.

SP321 THE ABSOLUTE RENAL RISK OF DIALYSIS/DEATH IS VALIDATED IN ADULTS WITH IGA NEPHROPATHY SECONDARY TO HENOCH-SCHÖNLEIN PURPURA: A MONOCENTRIC COHORT STUDY

Francois C. Berthoux[1], Hesham Mohey[1], Blandine Laurent[1] and Christophe Mariat[1]

[1]Nephrology, Dialysis, and Renal Transplantation University Hospital of Saint-Etienne Saint-Etienne France

Introduction and Aims: We established earlier the absolute renal risk (ARR) of dialysis/death (D/D) in primary IgA nephropathy (IgAN) which permitted accurate prospective prediction of final prognosis. This ARR was based on the eventual presence at initial diagnosis of three major, independent, and equipotent risk factors such as hypertension, quantitative proteinuria ≥ 1 g per day, and severe pathological lesions appreciated by our local classification, global optical score, GOS ≥ 8 (range 0 -20) or by the Oxford classification, MEST≥ 2 (range 0-5). We studied the validity of this ARR concept in secondary IgAN to predict future outcome and focused on Henoch-Schönlein purpura (HSP) nephritis.
Methods: This is an observational cohort study over 3 decades. This cohort of adults with IgAN concerned 1064 patients with 101 secondary IgAN and was focused on 74 patients with HSP (59 men), a mean age of 38.6 at initial diagnosis and a mean follow-up of 11.8 years. Three major risk factors: hypertension, proteinuria ≥1g/d, and severe pathological lesions appreciated by our GOS ≥8 (integrating all elementary histological lesions), were studied at biopsy-proven diagnosis and their presence defined the ARR scoring: 0 for none present, 3 for all present, 1 or 2 for the presence of any 1 or 2 risk factors. The primary end-point was composite with occurrence of dialysis or death before dialysis. We used classical statistics and both time-dependent Cox regression and Kaplan-Meier survival curve methods.
Results: The cumulative rate of D/D event at 10 and 20 years post- disease onset was respectively 0 and 14% for ARR=0 (23 patients);10 and 23% for ARR=1 (N=19); 27 and 33% for ARR=2 (N=24); and 81 and 100% (before 20 y) in the 8 patients with ARR=3 (P=0.0007). Prediction at time of diagnosis (time zero) of 10y cumulative rate of D/D event was 0% for ARR=0, 10% for ARR=1, 33% for ARR=2, and 100% by 8.5y for ARR=3 (P=0.0003) in this adequately treated cohort (ACE inhibitors; ARBs; steroids; and in few immunosuppressive agents).
Conclusions: This cohort study clearly validated the Absolute Renal Risk of Dialysis/Death concept also in secondary IgAN with utility to individual management and for the design of future clinical trials.

SP322 RE-EVALUATION OF CHINESE ANCA-ASSOCIATED RENAL VASCULITIS PATIENTS WITH HISTOPATHOLOGICAL CLASSIFICATION

Yong-Xi Chen[1], Wen Zhang[1], Jing Xu[1] and Nan Chen[1]

[1]Department of Nephrology Ruijin Hospital Shanghai China

Introduction and Aims: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) includes microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), Churg–Strauss syndrome and their localized forms. Renal involvement is present in more than half of the patients at disease onset and affects the prognosis. Recently, a histopathological classification of AAV was proposed and validated in Caucasians. Little is known of its application in Asian population.
Methods: Patients with biopsy proven AAV diagnosed in Ruijin hospital from 1997 to 2011 were retrospectively analyzed. According to definition proposed, patients were classified into "focal", "mix", "crescentic" and "sclerosis" group. Patients with anti-glomerular basement membrane disease or secondary causes of vasculitis were excluded.
Results: There were 116 patients enrolled in current study, with 90 MPA (90/116, 77.5%), 8 GPA (8/116, 6.9%), 15 renal limited vasculitis (RLV) (15/116, 12.9%) and 3 CSS (3/116, 2.7%) . The mean age at presentation 56±15 yrs with the male to female ratio of 1:1.03 (57/59). Mean serum creatinine at diagnosis was 388±310 μmol/L and proteinuria was 1761±1684mg/d. The mean BVAS was 21±6 at diagnosis. According to classification, there were 20 (20/116, 17.2%) patients with "crescentic" group, 33 (33/116, 28.4%) "focal" group, 55 (55/116, 47.4%) "mix" group and 26 (26/116, 22.4%) "sclerosis" group. There were no significantly difference regarding extra-renal involvement including fever, pulmonary involvement, digestive involvement, neurological involvement among the patients with different histopathological classifications (p>0.05). During follow-up, 34 patients progressed to end stage renal disease (ESRD) and depended on dialysis. 41 patients died during follow-up. The probability of developing ESRD increased with the ascending category of focal, crescentic, mix and sclerosis (p<0.01). And the total survival decreased with the descending category of focal, crescentic, mix and sclerosis (p<0.05).
Conclusions: We validated the new histopathological classification in Chinese population. The result showed that patients with sclerotic category had the worst outcome. The patients with focal, mixed and crescentic ANCA-associated glomerulonephritis were all at decreased risk for developing ESRD compared with the patients with in the sclerotic category.

SP323 SERUM SOLUBLE LECTIN-LIKE LOW-DENSITY LIPOPROTEIN-1 RECEPTOR IN ANCA-ASSOCIATED RENAL VASCULITIS

Dóra Bajcsi[1], Ágnes Haris[3], György Ábrahám[1], Péter Légrády[1], Kálmán Polner[3], Benedek Rónaszéki[1], Zsolt Balla[1], Zoltán Rakonczay[1], Béla Iványi[2] and Sándor Sonkodi[1]

[1]Nephrology and Hypertension Center, First Dept. of Med. Szeged Scientific University Szeged Hungary, [2]Institute of Pathology Szeged Scientific University Szeged Hungary, [3]Nephrology Department St. Margit Hospital Budapest Hungary

Introduction and Aims: Circulating levels of soluble Lox-1 (sLox-1) are increased in inflammatory and atherosclerotic conditions. In our previous study we found an overexpression of Lox-1 gene in renal bioptic tissue and in circulating leukocytes of ANCA-associated vasculitic patients (presented earlier at this forum, not yet published). It seemed worthwhile to investigate the sLox-1 level in ANCA-associated renal disease.
Methods: 22 patients with ANCA-associated vasculitis (age 63.5 ± 12.5 years; 8 males) and 7 control subjects without renal disease (age 44.6 ± 17.2; 4 males) were investigated. All patients had renal biopsy at clinical onset of their renal involvement. ANCA serology was performed by using indirect immunofluorescence technique and ELISA was performed for antibodies to PR3 and MPO. The serum soluble (sLox-1) receptor concentration was measured in serum by using the Human Lox-1 ELISA Kit (CELL BIOLABS, INC.). The ANCA-associated disease activity was evaluated with the Birmingham Vasculitis Activity Score (BVAS).
Results: Twelve patients had pANCA and 10 had cANCA positivity. Twelve patients showed signs of the disease activity (6 with cANCA and 6 with pANCA positivity), 10 patients were in complete remission. Circulating sLox-1 receptor concentrations of ANCA vasculitic patients (142.8 ± 19.6 pg/mL) were not significantly differ from the controls (139.0 ± 33.8 pg/mL). However, when we separately analysed the serum receptor concentration of the diseased patients in the active phase compared to the values of patients in remission, we received significantly lower receptor concentration in the active phase patients (85.2 ± 18.2 pg/mL vs. 200.5 ± 24.8 pg/mL; p < 0.001). There was no significant difference in the sLOX-1 levels between the pANCA positive

and the cANCA positive patients. We found a significant inverse correlation between the sLox-1 and BVAS values ($n = 22$; $r^2 = -0.43$; $p < 0.001$).
Conclusions: Our present finding of a decreased concentration of circulating soluble Lox-1 in ANCA vasculitic patients, with regard to previous observations of the overexpression of Lox-1 gene in the organ tissue, raises the possibility that Lox-1 may be highly expressed locally in response to proinflammatory stimuli, and via a feed-back effect decreases the circulating soluble receptor level. It could be suggested that serum soluble Lox-1 concentration might be a useful marker for the disease activity in ANCA-associated renal vasculitis. Further investigations are needed to clarify the pathomechanism of the decreasing receptor concentration in active ANCA vasculitis.

SP324 INCIDENCE AND OUTCOMES OF RENAL ANCA-ASSOCIATED VASCULITIS IN SOUTHWEST IRELAND 2007-2012

Philip H. Bredin[1], Mark Canney[2], Claire Kennedy[2], Liam D. Plant[2] and Michael R. Clarkson[2]
[1]School of Medicine University College Cork Cork Ireland, [2]Department of Renal Medicine Cork University Hospital Cork Ireland

Introduction and Aims: ANCA-associated vasculitis (AAV) is a rare, life-threatening disease with a one-year mortality of approximately 80% in untreated patients. Renal involvement is a common manifestation, and may lead to end-stage kidney disease (ESKD). Treatment requires systemic immunosuppression and carries inherent risks, including sepsis. Our unit is the sole tertiary referral centre for renal AAV in Southwest Ireland. We identified all patients diagnosed with Renal AAV from 2007 - 2012. Our objectives were to calculate the incidence of Renal AAV in Ireland and to describe the clinical features and outcomes of Renal AAV in this patient population.
Methods: We identified a cohort of patients with a first diagnosis of AAV with clinical evidence of renal involvement, over a six year period using our integrated laboratory and patient database. A retrospective review of patient charts, correspondence and laboratory results was performed.
Results: 59 patients met the inclusion criteria. Of these, 34 (58%) were male. The median age at diagnosis was 62 years (IQR 55-72). 42% had clinical, radiological or histological evidence of pulmonary involvement; 36% had upper airway involvement. 64% were MPO positive and 36% were PR-3 positive. The incidence of AAV with renal involvement in Southwestern Ireland over the six year period was 15.4 cases per million person years (95% CI 11.9-18.9). Median creatinine at presentation was 285µmol/L (IQR 152-420). Median creatinine at one year was 137µmol/L (IQR 112-174). 22 (37%) patients were admitted with sepsis in the follow-up period. 32% (12 out of 38) of patients treated with oral cyclophosphamide (CYC) were admitted with sepsis during the follow-up period as compared to 15% (2 out of 13) of patients treated with IV CYC. 17 (29%) patients received Plasma Exchange (PEX). The median creatinine of PEX-treated patients at presentation compared to non-PEX treated patients was 428µmol/L (IQR 147-892) vs 276µmol/L (165-344), with 71% of patients receiving PEX having significant pulmonary involvement. At one year the PEX treated patients had a median creatinine of 170µmol/L (IQR 112-219)vs 134µmol/L (IQR 112-168) in the non-PEX treated group reflecting the more severe initial presentation in the former group. The patient survival rate at one year was 92% (n=48) comparing favourably to international published outcomes. 10 patients (17%) developed ESKD during the follow-up period. Two of these patients were subsequently transplanted without complication. Only one patient not dialysis-dependent at 6 months developed ESKD thereafter.
Conclusions: These data suggest that the incidence and one year mortality rates of renal AAV in Ireland fall within international norms. Furthermore, they support the observation from randomized clinical trials that pulse IV cyclophosphamide is associated with fewer infectious adverse events as compared to daily oral therapy.

SP325 RITUXIMAB MONOTHERAPY (WITHOUT CYCLOPHOSPHAMIDE) IN ANCA ASSOCIATED VASCULITIS IN PATIENTS WITH SERUM CREATININE ABOVE AND BELOW 500 µmol/l

Noshaba Naz[1], Mrityunjay Hiremath[1], Anindya Banerjee[1] and Yaser Shah[1]
[1]Renal Wirral University Teaching Hospital Wirral Merseyside United Kingdom

Introduction and Aims: There is limited data on using rituximab (without cyclophosphamide combination) as the primary immunosuppressive agent in ANCA associated vasculitis with serum creatinine > 354 µmol/l. RAVE excluded such patients; in RITUXIVAS patients received at least 2 doses of intravenous cyclophosphamide along with rituximab. We used rituximab as the main immunosuppressive agent (without cyclophosphamide combination) as induction therapy in 32 ANCA associated vasculitis patients including 15 patients with serum creatinine > 354µmol/l. We grouped our patients into a presenting creatinine of higher or less than 500µmol/l. Our aim was to investigate the renal outcome in these two groups in the first year of presentation and to identify rates of infection, relapse, malignancy and mortality between these groups.
Methods: We retrospectively assessed new ANCA associated vasculitis with acute renal failure. Patients were grouped into two based on their presenting serum creatinine. Group A with serum creatinine < 500µmol/l and Group B with serum creatinine >500µmol/l. Serum creatinine at 3, 6 and 12 months of presentation was compared with baseline serum creatinine. Incidence of infection, mortality, malignancy and relapse rate was also compared in these 2 groups at their first 12 months of treatment.
Results: All patients received IV methyl prednisolone followed by oral prednisolone with rituximab 375 mg m^2 weekly for 4 weeks. 11 (7 with serum creatinine >500 µmol/l) also received plasma exchange. Table 1 show a significant improvement in serum creatinine in both groups at 3, 6 and 12 months of presentation. Serum creatinine plateaued at 3 months in Group A but took more than 3 months in Group B suggesting severe ischemia and acute tubular necrosis in group.We also found no statistically significance difference in infection, relapse, mortality and malignancy rate in the 2 groups at their first year of rituximab therapy.
Conclusions: We concluded that rituximab was a very effective and well tolerated induction agent without cyclophosphamide combination in ANCA associated vasculitis irrespective of the level of renal failure.

SP326 CARDIOVASCULAR OUTCOMES AND PROGNOSTIC PREDICTORS IN ANCA-ASSOCIATED VASCULITIS

Claudia Yuste[1], Alina Casian[2], Cristina Jironda[3] and David Jayne[2]
[1]Nephrology Gregorio Marañon Hospital Madrid Spain, [2]Vasculitis and Lupus Clinic Addenbrookés Hospital Cambridge Cambridgeshire United Kingdom, [3]Nephrology Carlos Haya Hospital Malaga Andalucia Spain

Introduction and Aims: ANCA associated vasculitis (AAV) (granulomatosis with polyangiitis (GPA), and microscopic polyangiitis (MPA)) is associated with an increased frequency of cardiovascular events (CVE). **Objectives:** To characterize cardiovascular outcomes and predictors, including the role of vasculitis therapies, for CVE/death in AAV.
Methods: A single center retrospective review of 307 AAV patients (173 GPA, 134 MPA, 47% male, 12% diabetic; mean age 53 [±17] years with follow-up 6.1 (±5.3) years. The primary end-point was CVE (defined as acute coronary syndrome, new onset angina, symptomatic peripheral vascular disease, stroke or transient ischaemic attack), or death.
Results: Fifty-one CVE occurred in 42 patients (13.6%) with 28 (9%) deaths. 15.7% CVE occurred at the onset of AAV, 57.4% CVE/death occurred within first year of AAV diagnosis, and 27.8% between 1 - 5 years. Independent predictors for the end-point (CVE/death) were: maintenance prednisolone dose (hazard ratio (HR) 169.6 (95% CI 1.18-24200), cumulative cyclophosphamide dose (HR 15.98 [0.005-0.83]), haemoglobin level at the end of follow-up (HR 0.6 [0.262-0.987]), serum PR3-ANCA levels at onset (HR 0.97 [0.995 – 0.99] and history of prior CVE (HR 5.3 [1.015-27.69]). A cumulative RTX dose <6g was associated with higher maintenance prednisolone dose ($p=0.016$).
Conclusions: CVE/death risk in AAV patients is especially high within the first 1 and 5 years of diagnosis. Prior CVE, low serum PR3-ANCA levels at onset and lower haemoglobin at the end of follow-up are associated with increased cardiovascular risk. Intensive immunosuppressive treatment of AAV at onset and avoidance of high long-term prednisolone dosage may have a protective effect against atherosclerosis. Rituximab therapy was associated with a steroid-sparing effect.

SP327 RITAZAREM: AN INTERNATIONAL, OPEN LABEL, RANDOMISED CONTROLLED TRIAL COMPARING RITUXIMAB WITH AZATHIOPRINE AS MAINTENANCE THERAPY IN RELAPSING ANCA ASSOCIATED VASCULITIS

Rona Smith[1], Michelle Lewin[1], Rachel Jones[1], Peter Merkel[2] and David Jayne[1]
[1]Medicine Addenbrookes Hospital Cambridge United Kingdom, [2]Rheumatology University of Pennsylvania Philadelphia PA United States

Introduction and Aims: Prior to the availability of effective therapy, ANCA associated vasculitis (AAV: granulomatosis with polyangiitis (GPA, Wegener's), microscopic polyangiitis (MPA)) had a mortality of 93% within two years, primarily due to renal

SP325

TABLE 1: Group A (Serum creatinine <500µmol/l), number=19

Baseline creat µmol/l (iqr)	Creat at 3 months (iqr)	Significance compared to baseline	Creat at 6 months (iqr)	Significance compared to baseline	Creat at 12 months (iqr)	Significance compared to baseline
209(190)g	154(66)	0.09	15(189)	0.79	146(145)g	0.94
Group B (serum creatinine >500 µmol/l), number 13						
649(454)	352(66)	0.002	294(180)	0.003	349(186)	0.006

and respiratory failure. The introduction of glucocorticoids and cyclophosphamide has transformed survival, with five year survival rates nearing 80%. AAV has become a chronic relapsing disorder, with progressive organ damage and disability affecting over 95% of patients. Cumulative exposure to glucocorticoid and immunosuppressive drugs contributes to toxicity and organ damage. 50% of patients relapse within five years and 10-20% have a refractory disease course. Novel therapeutic strategies are required for these patients.
Methods: RITAZAREM (EudraCT 2012-001102-14; ClinicalTrials.gov NCT01697267) is a 1:1, parallel, open randomized trial evaluating the efficacy of rituximab or azathioprine maintenance therapy in relapsing AAV. 190 patients with relapsing AAV will be enrolled across Europe, North America, and Australasia to receive rituximab (4 x 375mg/m^2), and glucocorticoid, induction therapy. Those with stable disease at month 4 will be randomised to receive repeat rituximab (1g at 4, 8, 12, 16, 20 months) or azathioprine (2mg/kg/day, stopping at month 27) maintenance therapy. All patients will receive glucocorticoids (standardized taper) concomitant with their allotted maintenance regimen. The primary objective is to demonstrate whether or not fixed interval, repeat rituximab is superior to azathioprine in the prevention of disease flare in AAV patients with relapsing disease. Secondary objectives are to demonstrate sustained disease remission beyond the 24 month treatment period, long term safety of rituximab administration, and the optimal remission maintenance therapy in AAV following induction of remission with rituximab. The primary endpoint is the time to disease relapse from randomisation. Patients will be followed, after the 24 month treatment period, for 12 months (minimum) and 24 months (maximum) . There will be a common close-out of the trial when the last patient reaches 12 months follow-up, 36 months after entry.
Results: RITAZAREM is a joint venture of two international collaborative networks, the European Vasculitis Study Group (EUVAS) and the Vasculitis Clinical Research Consortium (VCRC). Rituximab is supplied free of charge by Roche and Genentech. RITAZAREM will inform the future standard of care for patients with AAV, and provide data describing the long term safety of rituximab therapy in AAV patients.
Conclusions:
Bibliography Smith, R. *et al*, 2012. Rituximab for remission maintenance in relapsing ANCA-associated vasculitis. *Arthritis Rheum*. Nov; 64 (11) pp3760-9.

SP328 ANTI-PHOSPHOLIPID NEPHROPATHY ONLY BELONGS TO MYAKIS I E IIA CLASSES, ALWAYS IN ASSOCIATION WITH LUPUS ANTICOAGULANT, BUT NEVER ANTI-b_2GP1 ANTIBODIES

Cristina Izzo[1], Marco Quaglia[1], Elisabetta Radin[1], Andrea Airoldi[1], Roberta Fenoglio[1], Elisa Lazzarich[1] and Piero Stratta[1]
[1]Clinical and Experimental Medicine, Nephrology and Transplantation Amedeo Avogadro University - Maggiore Hospital Novara Italy

Introduction and Aims: Updated Sapporo criteria have provided a tool which should allow clinicians to better classify patients (pts) with anti-phospholipid antibodies (aPL) and anti-phospholipid syndrome (APS).
Methods: In pts with biopsy-proven lupus nephritis (LN) and positivity for Lupus Anticoagulant (LA), anticardiolipin antibodies (aCL) and anti-β2-glycoprotein antibodies (anti-β2GPI) we analysed: APS, APS-associated nephropathy (APSN) and main clinical outcomes, employing as classifying criteria Myakis-Class I (any combination), IIa (LA only), IIb (aCL only) and IIc (anti-β 2GPI only).
Results: Out of 101 patients, 70 were aPL negative and 31 aPL positive: 18 Class I, 10 Class IIa, 1 Class IIb, 2 Class IIc. Overall LA was present in 27/31 (87%), triple association in 4/18 (22.2%) and anti-β2GPI in 8/31(25.8%). APS was present in 15/31 aPL-positive pts: 7 Class I, 7 Class IIa and 1 Class IIb. APSN was present in 9 pts, 5 of Class I and 4 of Class IIa; all pts with APSN were LA positive and anti-β2GPI negative. In 3 pts (2 pts of Class I and 1 of Class IIa) APSN was an isolated histological picture, whereas in 6 other pts (3 pts of Class I and 3 of Class IIa) typical lesions of LN coexisted (5 diffuse proliferative LN and 1 Membranous nephropathy). Multivariate analysis showed that aPL significantly worsen thrombosis-free survival but do not reduce renal survival, which is instead much worse in proliferative classes of LN (HR 5,37). These classes were significantly less represented in aPL positive pts than in negative ones (35% vs 60%, p = 0.01). Five pts who started dialysis had APSN (χ2=7.52, p 0.006).
Conclusions: These findings confirm that LA is a strong risk factor for APSN and suggests that anti-β 2GPI antibodies positivity may have a protective role. aPL positivity alone does not worsen renal survival, probably because of a lower frequency of proliferative classes in this subset of pts, whereas coexistence of APSN is a risk factor for ESRD.

SP329 THE DELETERIOUS IMPACT OF ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY ON THE OUTCOME OF LUPUS NEPHRITIS: A CASE-CONTROL STUDY

Vivian L. Onusic[1], Maria J. Araujo[1], Ligia C. Battaini[1], Lecticia B. Jorge[1], Cristiane B. Dias[1], Myrthes Toledo-Barros[2], Rui Toledo-Barros[1] and Viktoria Woronik[1]
[1]Nephrology University of São Paulo São Paulo Brazil, [2]Clinical Immunology University of São Paulo São Paulo Brazil

Introduction and Aims: Few studies have analyzed the impact of anti-neutrophil cytoplasmic antibody (ANCA) on the outcome of lupus nephritis (LN). The aim of this study was to evaluate the influence of ANCA seropositivity in the renal outcome of LN.
Methods: A retrospective analysis was carried out on all SLE patients (345) submitted to a kidney biopsy between 1999-12. Patients that fulfilled ACR lupus criteria and tested for ANCA were enrolled. Positive ANCA patients (POS) were randomly matched to ANCA seronegative patients (NEG) according to the type of LN and baseline clearance(MDRD simplified formula). Clinical and laboratory data were collected at baseline, after one year and at the end of follow up. Treatment was decided by the clinical staff based on conventional literature protocols.
Results: We included 128 patients (32 POS/96 NEG). Perinuclear ANCA was detected in 87,5% (n=28) of POS patients. At baseline, POS and NEG groups were similar regarding age, complement level, ANA, anti-DNA antibody, eGFR (46±36vs44±29ml/min/1.73), proteinuria (3.4±2.6 vs 4.6±4.4 g/day), WHO LN classes, histological activity index, chronicity index, vascular lesions and follow up time. Interestingly, after one year of follow up, Pos group was significantly associated with a lower serum C3 (86,7±22vs106,5±32mg/dl p=0,01) and positive Anti-dsDNA (66%vs31% p<0,01). At the end of follow up, the POS group showed a tendency to have a lower eGFR (56 ±37vs71±36ml/min/1.73 p=0.09) as well as more patients with eGFR<60ml/min(56,3% vs33,3% p=0,03). Finally, logistic regression analysis showed that ANCA is an independent predictor of eGFR<60ml/min during follow up, even after adjustments for inicial eGFR and chronicity index .
Logistic Regression Analysis

SP329

	OR	95%IC	p
ANCA	3.62	1.3-9.96	0.013
Initial eGFR	0.98	0.97-1.0	0.064
CI	1.4	1.1-1.7	0.002

Conclusions: In our study, positive ANCA was significantly associated with a worse renal outcome of LN when compared to matched negative ANCA patients.

SP330 LUPUS NEPHRITIS AND PREGNANCY: MATERNAL AND FETAL OUTCOMES, RENAL RISK FACTORS, THERAPEUTIC PERSPECTIVES

Calogero L. Cirami[1], Pamela Gallo[1], Elena Romoli[1], Federico Mecacci[2], Serena Simeone[2], Enrico E. Minetti[1] and Giorgio Mello[2]
[1]Nephrology Unit, Careggi Hospital Florence Italy, [2]Obstetric Unit, Careggi Hospital Florence Italy

Introduction and Aims: Systemic Lupus Erythematosus (SLE) predominantly affects women, especially during fertile ages. Lupus Nephritis (LN) was considered one of the risk factors for maternal and fetal complications during pregnancy.The aim of our study is to compare pregnancies of women with SLE/LN and pregnancies in women with SLE, without LN, to evaluate the role of LN on the maternal and fetal outcome. We have also sought to identify renal risk factors for preeclampsia, preterm delivery before 34th week of gestation and IUGR below the tenth percentile.
Methods: A retrospective study was conduct on 99 pregnancies in 88 women with SLE, since 2003 to 2011.The data were analyzed by a multivariate logistic regression.
Results: The results showed that there aren't significant differences in terms of pregnancy-outcome between nephropatics women and not,except for the incidence of renal flare, greater in nephropatics women. There were no differences between the two groups for fetal outcome.

SP330

Characteristics	Previous Nephritis (n=27)	No previous Nephritis (n=59)
Thromboembolic events, n°(%)	0	0
Flare n° (%)	9(33.3%)	12(20.3%)
Renal flare, n°(%)	5(18.5%)	2(3.3%)
Preeclampsia/HELLP, n° (%)	4(14.8%)	4(6.78%)
Cesarean birth, n° (%)	15(55.5%)	29(49%)
Preterm delivery (< 34 weeks), n°(%)	4(14.8%)	4(6.78%)
Live birth, n°	27	59
Perinatal death, n°	1(25 weeks)	1(25 weeks)
Gestational age at delivery (mean±SD)	37+3.50	37.7+2.82
Preterm delivery (< 34 weeks), n°(%)	4(14.8%)	4(6.78%)
Mean birth weight, g, (mean±SD)	2560+758	2878+743
Weight centile (mean±SD)	35+27	43+29
IUGR < 10° centile, n°(%)	5(18.5%)	6(10.1%)
Apgar < 7 at 1° min	1(2indeterminated)	2(3indeterminated)

Risk factors for maternal and fetal complications are: decreased renal function at conception and pre-existing chronic hypertension. Thrombophilia and nephropathy were not risk factors for maternal and fetal adverse events.

SP330

Outcome	OR	Std.Err.	Z	P>Z	IC95%
Thrombophilia	0.34	0.18	-1.99	0.05	0.12 0.98
Nephropathy	0.38	0.23	-1.66	0.11	0.12 1.23
Hypertension	2.75	1.33	2.1	0.04	1.07 7.09
Proteinuria	2.45	1.5	1.46	0.14	0.74 8.16
SCr>1.2mg/dl	1.25	0,45	0.63	0.53	0.62 2.53
Quiescence	0.87	0.39	-0.32	0.75	0.36 2.11
eGFR<90ml/min/1.73m^2	18.73	13.96	3.93	0	4.35 80.70

Conclusions: Our study shows that pregnancy in patients with LN can be completed successfully, thanks to a multi-disciplinary approach in specialized centers, with the preconception assessment of the relative risk and trought adequate prophylaxis of adverse events.

SP331 MYCOPHENOLATE AS MAINTENANCE THERAPY FOR LUPUS NEPHRITIS WITH IMPAIRED RENAL FUNCTION

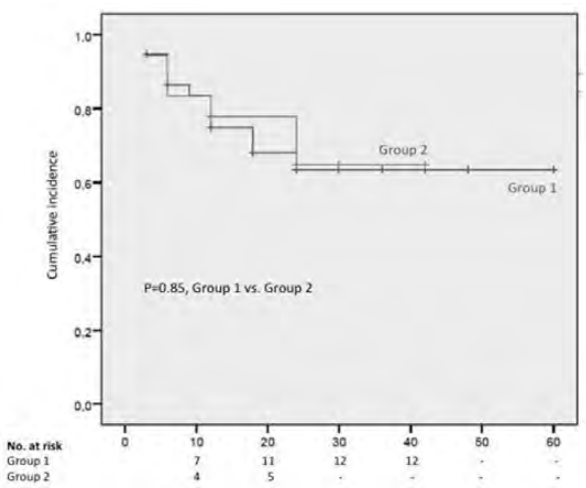
Francisco Rivera[1], Alfons Segarra[2] and Manuel Praga on behalf for the Glomerular Spanish Glomerular Study Group (GLOSEN)[3]

[1]Nephrology Hospital General de Ciudad Real Ciudad Real Spain, [2]Nephrology Hospital Vall d'Hebron Barcelona Spain, [3]Nephrology Hospital Universitario 12 de Octubre Madrid Spain

Introduction and Aims: Mycophenolate (MF) is effective as maintenance treatment after induction therapy in patients with lupus nephritis (LN). However, little is known about its role in patients with impaired renal function. The purpose of this study was to evaluate the efficacy and safety of MF as maintenance therapy for LN and its association with renal function.
Methods: Data were obtained for 56 patients from 13 Spanish renal units who were receiving MF as maintenance therapy for LN. All of them had received intravenous cyclophosphamide as induction therapy. Patients were classified into 2 groups according to renal function at the onset of MF treatment: Group 1 (estimated glomerular filtration rate [eGFR] ≥60 mL/min/1.73m^2) and Group 2 (eGFR <60 mL/min/1.73m^2). Primary endpoints of the study were the rates of renal relapses and responses (partial or complete) and their relationship with baseline renal function. Secondary outcomes were the appearance of side effects during treatment.
Results: At initiation of MF treatment, there were no differences between groups except age, hemoglobin levels, anti-DNA antibody titer, proteinuria and renal function. In Group 1 (n=38) eGFR was 98±34 mL/min/1.73m^{2}and in Group 2 (n=18) was 43±14 mL/min/1.73m^2. Exposure to prednisone and MF was similar. The number and percentage of cases that relapsed are indicated in Table 1.

SP331

	6th month (n=51)	12thmonth (n=49)
Relapses, n (%)	11 (21.6)	11 (22.4)
Responses, n (%)	35 (68.6)	35 (71.4)



SP331

No significant differences were observed in the rate of relapses at 6 months (Group 1: 20% and Group 2: 23%, p=0.81) and at 12 months (Group 1: 25% and Group 2: 17%, p=0.72). Response rates were also similar in both groups (76% and 52% at 6 months and 71% and 70% at 12 months). The cumulative rate of responses over time was similar in both groups.Side effects were unremarkable, without differences between groups.
Conclusions: MF is effective and safe as maintenance therapy for LN both in patients with normal renal function and in those with renal impairment.

SP332 WHY HAVE OUTCOMES OF LUPUS NEPHRITIS BEEN IMPROVING OVER THE LAST 40 YEARS? A MONOCENTRIC EXPERIENCE

Marco Quaglia[1], Elisabetta Radin[1], Cristina Izzo[1], Andrea Airoldi[1], Elisa Lazzarich[1], Roberta Fenoglio[1] and Piero Stratta[1]

[1]Translational Medicine Amedeo Avogadro University, "Maggiore della Carità" Hospital, Nephrology and Transplantation Novara Italy

Introduction and Aims: Outcomes of patients with lupus nephritis (LN) have been improving due to a variety of reasons and relative contributions are difficult to assess.
Methods: We included all patients with biopsy-proven LN followed-up at our center and analysed evolution of epidemiological, clinical, histological features and therapeutic immunosuppressive protocols over the last 4 decades.
Results: We enrolled 130 patients stratified by diagnosis over the following periods: ≤1980, n = 43; >1980≤1990, n = 34; >1990≤ 2000, n = 33; >2000, n =20. Age at diagnosis decreased from 30 to 26 years old and the interval between diagnosis of Lupus and that of LN has extended from 1 to 3 years. The mortality rate fell from 41.8 % to 0%, paralleling decrease in complications. The proliferative classes remained the most represented (59.2 %); the need for dialysis has been dramatically reduced (from 23% to 0%). The most significant therapeutic changes in induction therapy between the first and fourth decade were the increasing use of pulse steroid (ST) (from 0% to 65 %) and the association of cyclophosphamide (CYCLO) (from 25% to 65 %) . Cumulative load of oral drugs was sharply reduced: ST decreased from 533 to 269 mg/Kg and CYCLO from 505 to 180 mg/Kg over the first 5 years. Multivariate analysis showed that survival improvement is mainly associated with the youngest age at diagnosis and on more recent historical periods. The renal prognosis was worse in male, age>30 years, renal failure, proliferative classes with indexes of chronicity, while it appeared to improve with induction therapy other than only oral STER and with high activity index.
Conclusions: The most important factors which determined improved outcomes of LN over the last 4 decades were a progressively earlier diagnosis (from 30-31 to 26-29 years old) and qualitative/quantitative modifications in therapeutic strategies. Adoption of sequential schedules of aggressive induction and fast tapering of immunosuppression have been crucial to achieve better control of the acute phase and reduced toxicity long-term.

Covariates	HR	95% CI	p
Period of diagnosis:			
≤1980	1		
1980≤1995	0.397	0.093-1.696	0.2126
>1995	0.058	0.004-0.859	0.0384
Age at diagnosis:			
<20 years	1		
>20<30 years	2.037	0.598-6.936	0.255
>30 years	4.086	1.336-12.499	0.013
SLEDAI	1.081	1.006-1.160	0.013
Sex (m)	1.123	0.409-3.082	0.050
Proliferative classes	13.550	1.743-105.325	0.012
Chronicity index continuous variable	2.986	1.151-7.743	0.024
Activity index			
≤4	1		
>4	0.24	0.084-0.681	0.007
Serum creatinine a biopsy	2.233	1.009-4.942	0.047
Proteinuria mg/24h	0.870	0.362-2.089	0.754
Renal flare up	4.238	0.887-20.447	0.072
Induction therapy different from oral steroid alone	0.072	0.006-0.913	0.042

SP332

SP333 CD68 POSITIVE CELLS IN RENAL BIOPSY PREDICT LONG TERM PROGNOSIS IN PROLIFERATIVE LUPUS NEPHRITIS

Cristiane Bitencourt Dias[1], Jin Lee[2], Letícia Jorge[1], Denise Malheiro[2], Rui Toledo Barros[1] and Viktoria Woronik[1]

[1]Nefrologia Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo São Paulo Brazil, [2]Patologia Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo São Paulo Brazil

Introduction and Aims: Studies in proliferative lupus nephritis (LN) showed that in more severe clinical forms the renal histology showed increase macrophages detected by immunohistochemistry. However no long-term assessment of this data is known. *The aim of this study was to describe any relations of renal outcomes with tecidual macrophages ($CD68^+$) expressed in renal biopsy specimens obtained on the diagnosis.*
Methods: Forty six newly diagnosed patients with proliferative LN were prospectively followed-up during 3.5 (3.2 - 4.0) years. Conventional laboratory tests were collected on diagnosis and on last follow-up. Renal biopsy was done on diagnosis and immunohistochemical study was performed with monoclonal antibody anti-CD68 (DAKO) and macrophages MCP-1 (R&D), and results expressed as cells/microscopic fields. Patients were stratified in two groups according to renal outcome: GFR ≤ 60 mL/min/1.73m^2 at the end of follow-up (n=24) and GFR > 60mL/min/1.73m^2 (n=22). Considering treatment, all patients received prednisone and 6 pulses of cyclophosphamide (CYA) on induction. Maintenance treatment was conventional and applied in both groups.
Results:
Considering all patients (n=46) tubule and interstitial $CD68^+$ cells showed negative correlation with final MDRD (r= - 0.3, p=0.01 and r= -0.45, p=0.001). Macrophages MCP-1 interstitial had positive correlation with chronicity index (r=0.4, p=0.0031).
Conclusions: Tubule and interstitial $CD68^+$ cells expression on renal biopsies may predict long term GFR in proliferative lupus nephritis.

SP334 USAGE OF CYCLOSPORINE IN LUPUS NEPHRITIS CLASS III, IV AND V – ONE CENTRE EXPERIENCE

Elena V. Zakharova[1] and Ekaterina S. Stolyarevich[2]

[1]Nephrology City Clinical Hospital n.a. S.P. Botkin Moscow Russian Federation, [2]Pathology City Nephrology Center Moscow Russian Federation

Introduction and Aims: Current KDIGO Guidelines for Glomerulonephritis and EULAR/ERA-EDTA Recommendations for Management of Lupus Nephritis suggest cyclosporine (CYC) as alternative option for initial treatment of lupus nephritis (LN) class V with persistent nephrotic proteinuria, resistant disease not responding to more than one of the recommended initial regimens, and for subsequent treatment of pure class V, or class III/IV intolerant of mycophenolate mofetil and azathioprine (AZA). CYC is also acceptable during pregnancy. We aimed to evaluate retrospectively efficacy of CYC in our cohort of LN patients.
Methods: Using electronic clinical and pathology database we searched 106 LN patients, treated in our nephrology unit since 2002, when we introduced CYC for LN, to 2012. Patients with class I, II and VI, and those who never received CYC were excluded from analysis. Study group included 14 patients, 12 female and 2 male, median age 27.5 [17;39] years. 2 patients had class III, 6 – class IV and 6 – class V LN. Disease duration prior to switching to CYC was 60 [5;168] months, previous treatment included prednisolone in all, cyclophosphamide (CP) "pulses" in 12, mycophenolate mofetil/micophenolic acid (MMF/MPA) in 5, and AZA in 4 cases. Indications for CYC were non-responsiveness or intolerance of CP and MMF/MPA in 6, renal flare after CP and/or MMF/MPA initial and re-induction regimens in 4, and subsequent treatment in 4 patients intolerant of MMF/MPA and AZA. Initial dose of CYC was 200 mg/day [150;250], with dose adjustment to plasma concentration. Duration of therapy constituted 14.5 [1;84] month, duration of follow-up – 18 [1;84] months.
Results: 6 patients (42.8%) achieved and/or sustained complete remission, 6 (42.8%) – partial remission, and only in 2 (14.3%) cases CYC was non-effective. Changes in proteinuria and kidney function and distribution of efficacy in different LN classes are shown in tables 1 and 2

SP334 **Table 1.** Influence of CYC on proteinuria and kidney function

	Before CYC	At last evaluation	P value
Medinan proteinuria g/day	2.6 [0.15;15.0]	0.3 [0.0;9.5]	<0.05
Median creatinine µmol/l	102 [68;300]	100 [74;441]	NS

SP334 **Table 2.** Results of CYC treatment in different LN classes

	Complete response achived/sustained	Partial response achived/sustained	No response
Class III	0/1	1/0	0
Class IV	1/0	2/1	2
Class V	2/2	2/0	0
Total	3/3	5/1	2

In one case of LN class V after 5 years of treatment with sustained partial remission 2-nd kidney biopsy did not show any signs of CYC-toxicity. 3 patients had 4 normal pregnancies and delivered healthy babies, in 1 case after delivery developed renal flare, successfully treated with MMF. There were no other flares in patients treated with CYC.
Conclusions: In our cohort of 106 LN patients 13% were treated with CYC. In 85.6% of cases complete or partial remissions were achieved/sustained with lowering of median proteinuria from 2.6 to 0.3 g/day and nicely preserved kidney function. The best results were seen in LN class V (100% of remissions, mostly complete), the worst - in class IV (only 66.6% of remissions, mostly partial).

SP335 MYCOPHENOLATE MOFETIL TREATMENT FOR RESISTANT LUPUS NEPHRITIS: A SINGLE CENTER EXPERIENCE

Arzu Velioglu[1], Derya Guler[1], Serdar Nalcaci[1], Gurdal Birdal[1], Hakki Arikan[1], Mehmet Koc[1], Haner Direskeneli[2], Serhan Tuglular[1] and Cetin Ozener[1]

[1]Nephrology Marmara University, School of Medicine Istanbul Turkey, [2]Rheumatology Marmara University, School of Medicine Istanbul Turkey

Introduction and Aims: Lupus nephritis (LN) is one of the major complications of systemic lupus erythematousus. Mycophenolat mofetil (MMF) is the prominent treatment for maintenance of remission, prevention of recurrence and progression to chronic renal disease. In our study, we evaluate the long term results of MMF treatment in patients with resistant LN.
Methods: Twenty-seven patients (23 female, four male; mean age 36.5±10.6 years) were included into the study. All patients received induction therapy with cyclophosphamide. SLEDAI scores, creatinine levels, estimated glomeruler filtration rates, 24-hour protein excretions, C3 and C4 levels were collected both at the beginning and the last visit. Patients were compared according to previous maintenance immunosuppressive therapy. The end stage renal disease (ESRD) development and mortality rates were also recorded.
Results: Renal biopsies were showed WHO Class I LN in 14 patients, Class III LN in 10 patients, Class V in one patient and Class II in one patient. In one patient, renal biopsy was not performed because of the coagulation problem. Mean time of MMF treatment was 32.9 months. Mean MMF dose was 1592.6±651 g/day. The first and last SLEADI scores and 24-hour protein excretion were significantly reduced by MMF treatment (6,7±1,05 vs. 1,9±0,51, p<0,001; 0,89±0,2 vs. 0,50±0,12 g/day, p=0,043, respectively). The data are summarized in Table 1. Sixteen patients were under previous maintenance immunosuppressive treatment. There were no differences between

SP333

	GFR > 60ml/min/1.73m^2 (n=22)	GFR ≤ 60ml/min/1.73m^2 (n=24)	p
Age (years)	24.4 ± 7.2	29.5 ± 11.6	ns
Gender (F/M)	21 / 1	21 / 3	ns
Activity Index (renal biopsy)	5.0 ± 1.5	4.1 ± 2.1	ns
Chronicity Index (renal biopsy)	2.0 ± 2.1	4.0 ± 2.1	0.01
Initial GFR – MDRD (ml/min/1,73m^2)	58.1 ± 37.1	35.1 ± 24.9	0.01
Initial Proteinuria (g/day)	4.0 ± 2.7	4.4 ± 2.8	ns
Initial C3 complement (mg/dL)	51.3 ± 28.4	50.4 ± 16.6	ns
Initial C4 complement (mg/dL)	5.5 (4.5-8.0)	8.0 (6.0-11.5)	ns
Last GFR – MDRD (ml/min/1,73m^2)	93.0 (78.0-116.5)	10.5 (6.0-46.	<0.0001
Last Proteinuria (g/day)	0.6 ± 0.7	1.7 ± 1.7	0.008
$CD68^+$ cells tubule /field	2.0 (0.8-30.0)	6.4 (1.9-11.8)	0.0064
$CD68^+$ cells Interstitial /field	4.9 (3.2-9.0)	36.2 (10.1-101.4)	0.0003
$CD68^+$ cells glomerulus/field	5.1 (2.9-11.6)	6.7 (3.0-20.0)	ns
Macrophages MCP1 tubule /field	0.1 (0-0.39)	0.2 (0.0-0.65)	ns
Macrophages MCP1 interstitial /field	5.7 (1.2-12.5)	12.6 (3.6-105.5)	0.03

SP335 **Table 1.** Clinical and Laboratory findings of patients

	Result	p
Initial SLEDAI score	6.7±1.05	0.0001*
Last SLEDAI score	1.92±0.51	
Initial creatinine (mg/dL)	1.48±0.25	0.756
Last creatinine (mg/dL)	1.58±0.3	
Initial eGFR (ml/min)	75.7±8.8	0.806
Last eGFR (ml/min)	74±7.9	
Initial 24-hour protein excretion (g/day)	0.890±0.19	0.043*
Last 24-hour protein excretion (d/day)	0.505±0.12	
Initial C3 (g/L)	1.04±0.13	0.977
Last C3 (g/L)	1.03±0.06	

*p<0.05, Statistically significant

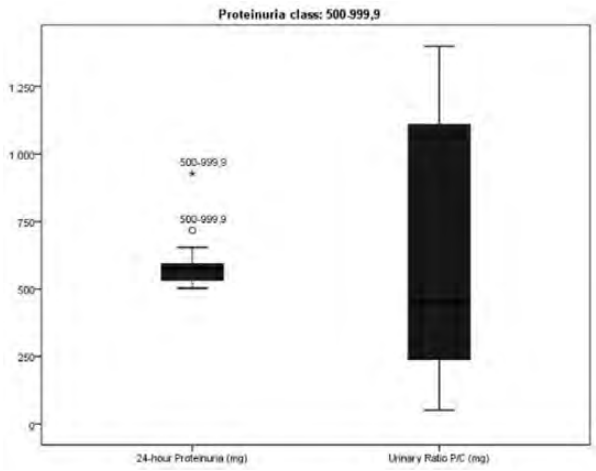
patients regarding to previous treatment. The mean follow-up time was 50.5 months. One patient died due to sepsis. ESRD was developed in three patients.
Conclusions: MMF treatment has provided an improvement in SLEDAI score and proteinuria in resistant LN patients. There was no deterioration in renal function. MMF is an ideal treatment for patients who were not on complete remission after induction therapy with cyclophosphamide.

SP336 RANDOM SPOT URINE PROTEIN/CREATININE RATIO: A RELIABLE METHOD FOR MONITORING LUPUS NEPHRITIS?

Maria Guedes Marques[1], Patrícia Cotovio[1], Francisco Ferrer[1], Cristina Silva[1], Carlos Botelho[1], Karina Lopes[1], Pedro Maia[1], Armando Carreira[1] and Mário Campos[2]

[1]Nephrology Centro Hospitalar Universitário de Coimbra - Hospital Geral Coimbra Portugal, [2]Nephrology Centro Hospitalar Universitário de Coimbra - HUC Coimbra Portugal

Introduction and Aims: Lupus nephritis (LN) is a common and severe manifestation of Sistemic Lupus Erythematosus (SLE) that can lead to End Stage Renal Disease (ESRD) and death. There have been numerous reports on the use of random spot urine protein/creatinine (P/C) ratio to estimate 24-hour proteinuria in non-SLE Cronic Kidney Disease (CKD). However, few papers have been published regarding SLE patients and some of those authors wrote that random spot urine P/C ratio is unreliable to monitoring proteinuria in SLE GN patients. According to Kidney Disease Outcomes Global Improving (KDIGO) clinical practice Guidelines for Glomerulonephritis, random spot urine P/C ratio should be used for monitoring LN. The aim of our study was to evaluate the agreement of urine P/C ratio in untimed specimens with proteinuria measured by 24 h urinary collection in patients with SLE.
Methods: A prospective observational study was performed. A total of 53 paired (106) spot and 24-hour urine collections were evaluated, as part of routine monitoring of their disease activities. Statistical analyze was performed by SPSS 20.0 Statistical Analysis.
Results: Paired-samples T test didn't revealed significant differences between the two assay methods (p 0,216) and a statistically significant correlation was observed between them: Pearson coefficient 0,847 (p < 0,001). After stratifying by degrees of proteinuria, the correlation between 24-hour proteinuria and P/C ratio was maintained in the proteinuria range lower than 500mg/24h (Pearson 0,471, p 0,006) and above 1000mg/24h (Pearson 0,917, p 0,010), but this correlation was not observed between 500 and 1000mg/24h (Pearson -0,106, p 0,718).When stratifying according to background of LN, paired-samples T test didn't revealed significant differences between the groups.
Conclusions: Our study demonstrated a negative , not significant, correlation between urine P/C ratio and 24 h proteinuria for a range of 500 to 1000mg/24h. This finding is of greater importance and concern because this range is quite common among patients with LN in remission, in whom it is essential to monitoring and detect renal flares early. Until further clarification, to the best of our knowledge, we maintain reluctant to completely substitute the 24-hour collection by P/C ratio especially when (according to other activity parameters) a renal flare is suspected; as well as, before any change in therapy.



SP336

SP337 URINARY NEUTROPHIL GELATINASE – ASSOCIATED LIPOCALIN (uNGAL) AND MONOCYTE CHEMOATTRACTANT PROTEIN-1 (uMCP-1) IN LUPUS NEPHRITIS

Sabah Alharazy[1], Norella C.T. Kong[1], Marlyn Mohammad[2], Shamsul A. Shah[3], Halim Gafor[1] and Arbaiyah Báin[1]

[1]Medicine National University of Malaysia Cheras Kuala Lumpur Malaysia, [2]Immunobiology & Microbiology National University of Malaysia Cheras Kuala Lumpur Malaysia, [3]Biostatistics & Community Medicine National University of Malaysia Cheras Kuala Lumpur Malaysia

Introduction and Aims: Several small studies have indicated a role for urine neutrophil gelatinase – associated lipocalin (uNGAL) and urine monocyte chemoattractant protein-1 (uMCP-1) as markers of lupus nephritis (LN) disease activity.We therefore compared the urinary levels of these two biomarkers in SLE patients with biopsy-proven LN.
Methods: This was a prospective, cross-sectional observational study in which consecutive SLE patients with biopsy-proven LN attending the Nephrology/SLE Clinic were recruited. Two x10 ml samples of early morning urine were collected for urinalysis, urine protein creatinine ratio and for both uNGAL (ng/mg of urinary creatinine) and uMCP-1 (pg/mg of urinary creatinine). The last two were measured from frozen stored urine at end visit using an enzyme-linked immunosorbent assay (ELISA). Their renal function test, serum albumin, urinary parameters, lupus serology and renal SLEDAI-2K (global, renal, extra-renal) were also measured.
Results: Of the 100 patients recruited, 47 had active and 53 inactive LN. uNGAL levels (ng/mg creatinine) and uMCP-1 levels (pg/mg creatinine) were significantly higher in patients with active LN compared to those with inactive renal disease ($p = 0.01^{*}$ and $p < 0.001^{**}$ respectively). Both uNGAL and uMCP-1 levels were highly associated with SLEDAI-2K (renal) (uNGAL: $r_{sp} = 0.32$, $p = 0.001^{**}$; uMCP-1: $r_{sp} = 0.39$, $p = 0.001^{**}$). Both biomarker levels also correlated with SLEDAI-2K (global) (uNGAL: $r_{sp} = 0.19$, $p = 0.05^{*}$; uMCP-1: $r_{sp} = 0.28$, $p = 0.006^{*}$). However, there were no associations between uNGAL and uMCP-1 with SLEDAI-2K (extra-renal). Using receiver operating characteristic (ROC) curve, the area under the curve (AUC) for uNGAL was 0.83 (95% CI = 0.74 – 0.92, $p = 0.001^{**}$). With a cut-off value at 91.25 ng/ mg creatinine, uNGAL had a sensitivity of 0.89 and specificity of 0.67 for prediction of LN activity. Whereas, the AUC of uMCP-1 was 0.84 (95% CI = 0.75 – 0.92, $p = 0.001^{**}$). With a cut-off value at 4247 pg/ mg creatinine, uMCP-1 had a sensitivity of 0.89 and specificity of 0.61 for early diagnosis of LN activity.
Conclusions: Both uNGAL and uMCP-1 were highly correlated with LN activity. Since renal flares portend a worse prognosis for the renal outcome, serial measurements of one or both these noninvasive urinary biomarkers may be of great clinical value in predicting early flares of LN thus permitting earlier intervention.