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INHIBITION OF ALLO-IMMUNE RESPONSE IN HUMAN AFTER EXPOSURE OF T LYMPHOCYTES TO ALLOGENEIC APOPTOTIC CELLS

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Introduction: The apoptotic bodies emanate particularly from mononuclear cells in early stages of apoptosis have immunomodulatory properties and may modulate notably the alloimmune response. This immunomodulatory effect has been demonstrated in various murine models of transplantation but few studies have examined the effect of apoptotic cells (AC) on the human allogeneic response and the mechanisms involved are not yet fully demonstrated. Here we present the characteristics of human AC and analyze their immunomodulatory properties *in vitro*.

Methods: The AC are obtained by UV-A treatment after 8-MOP sensitization of human PBMC (from healthy donors). AC were then incubated with PBMC from a second allogeneic donor (mixed lymphocyte reaction, MLR). Proliferative capacity, activation marker and of cytokine synthesis of responders PBMC were analyzed.

Results: Stimulation of allogeneic lymphocytes by AC causes a low proliferation (1.76%, divided cells) compared to a conventional MLR (27%) at D5. In addition, T-cell activation markers like CD25 and CD69 are weakly expressed on the surface of CD4⁺ and CD8⁺ cells stimulated by AC. The synthesis of pro-inflammatory cytokines IL-6, TNF α and IFN γ obtained by standard MLR is absent upon stimulation with AC. A second stimulation of PBMC by the same initial antigen does not induce any proliferative response.

In a situation of indirect presentation, the culture of AC with allogeneic APCs shows a weak activation of the latter (decreased expression of HLA-DR and CD86, decreased secretion of IL-6 and TNF α). Stimulation by these APC leads to a very low proliferation of autologous lymphocytes compared to stimulation of APC by PBMC untreated.

Conclusion: Apoptotic cells induce a weak allogeneic response of lymphocytes *in vitro* whether in direct or indirect presentation showing for the first time the immunomodulatory capacities of AC in human allogeneic condition.

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IMPACT OF LATE MYCOPHENOLIC ACID EXPOSURE ON GRAFT SURVIVAL IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The clinical benefit of therapeutic drug monitoring of mycophenolate mofetil (MMF) in kidney transplantation remains unclear and it is not currently recommended by transplantation guidelines. It has been demonstrated that early mycophenolic acid (MPA) exposure was well correlated with acute rejection within the first year posttransplant but data are lacking on the added value of MPA monitoring to predict long-term outcome.

Methods: The charts of 354 consecutive kidney transplant recipients who underwent MPA monitoring at day 15 and month 3 posttransplant were retrospectively studied. MPA exposure was assessed by area under the curve (AUC) calculation using a Bayesian estimator and clinical outcome (acute rejection, patient and graft survival) at three years was compared between patients who were adjusted to reached the MPA therapeutic target of 30–60 mg.h/l and those who were not.

Results: Only 32% of patients had a MPA-AUC measurement at day 15 while 70% had one at month 3, underlying the difficulty to obtain an early measurement of MPA exposure in a daily routine practice. No association was shown between AUC value at day 15 or month 3 and short-term clinical outcome at one year. However, patients with MPA-AUC value below the therapeutic target of 30 mg.h/l and no dose adjustment at month 3 had a seven-fold increased risk of graft loss at three years. There was no correlation between MPA exposure at month 3 and the occurrence of bacterial or viral infections, but a MPA-AUC >60 mg.h/l without dose adjustment at month 3 was significantly associated with a higher incidence of fungal infections.

Conclusion: This is the first study to analyse the association between late MPA exposure and long-term graft survival. Determination of MPA concentration and adjustment of MMF dosing at month 3 could be a feasible and efficient strategy to improve long-term outcome in kidney transplant recipients, but these results should be confirmed in a prospective study.

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CLINICAL PHARMACIST (CP) AND MEDICATION RECONCILIATION (MR) IN KIDNEY TRANSPLANTATION

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Drug related problems (DRP), and cardiovascular risk factors (CVRF) can lead to severe consequences in kidney recipients. We assessed the impact of the MR at the admission of the patient on the incidence of DRP.

A first study, without the intervention of a CP, evaluated the number of DRP, their severity and their avoidability. A second study, with a MR (medication history, detection of intentional and unintentional discrepancies), was realised. We compared both populations: demographics, stage of CKD, time since transplantation, CVRF (hypertension, dyslipidemia, and smoking history), number of drugs prescribed and kidney disease. In both studies we collected avoidable DRP.

Of 44 patients were included versus 35 (65 vs. 41 cases of DRP) out of 159 and 164 kidney transplant patients, respectively. Patients concerned, were mainly men, 56 years old, stage 3 of CKD, transplanted for <3 months or more than 1 year, with CVRF and receiving an average of nine drugs prescribed per day. In both studies, 20% of DRP were avoidable (lack of drug monitoring, drug-drug interaction, drugs not indicated in CKD patients), and half needed a hospitalisation. No death was observed. During the second study, 56 patients had a MR: 30% presented discrepancies among whom 40% were unintentional discrepancies (omission, error of prescription). And 14% of the patients were non adherent (Girerd score>2). DRP were numerically, but not significantly, more frequent in the first study (27.7%) compared to the second (22%) (p = 0.18); and the incidence of avoidable DRP was similar in both studies (4.5%).

A numerical reduction of DRP was observed with MR, but it was not significant. Consequently we have improved pharmaceutical interventions, during the hospitalisation (narrow drug monitoring, dose adaptation according to the kidney function), and added a MR at discharge (targeted information to the patient, medication intake plan). We hope to be more efficient in the reduction of avoidable DRP.

P16

THE TRANSFORM TRIAL DESIGN: A LARGE RANDOMIZED, MULTICENTER, OPEN-LABEL STUDY OF EVEROLIMUS WITH REDUCED CALCINEURIN INHIBITORS IN DE NOVO RENAL TRANSPLANTATION

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Background: Immunosuppressive regimens allowing both freedom from rejection and reduction calcineurin inhibitors (CNI) exposure and their associated nephrotoxicity remain an unmet need in kidney transplantation (KTx). Here, we present a phase IV study, TRANSFORM, designed to evaluate the efficacy and safety of everolimus (EVR) plus reduced CNI exposure in comparison to mycophenolic acid (MPA) plus standard CNI exposure in *de novo* KTx recipients (KTxR).

Methods: TRANSFORM, a 24-month (mo), multicenter, open-label study will be conducted across 200 centers worldwide. Approximately >2000 KTxR will be randomized (1:1) to receive either EVR (C0, 3–8 ng/ml) with reduced CNI exposure or MPA with standard CNI exposure, all with basiliximab or antithymocyte globulin induction and steroids (Figure 1). The primary endpoint will be the composite of (i) treated biopsy-proven acute rejection (tBPAR) rate or (ii) proportion of KTxR with estimated glomerular filtration rate <50 ml/min/1.73 m² (eGFR;MDRD4) at mo 12 post-Tx. The key secondary endpoint is composite efficacy failure rate (tBPAR, graft loss, or death) at mo 12 post-Tx. These endpoints will be also analyzed at mo 24. Patients completing

24 months of treatment will be eligible to participate in an observational extension study for a further 36 months with outcomes analyzed up to 5 years including eGFR, patient and graft survival, and incident cardiovascular disease, malignancy, and infection.

Conclusion: TRANSFORM will be the largest clinical trial in KTx and is designed to demonstrate the short- and long-term benefits of *de novo* CNIminimization with an EVR-based regimen.

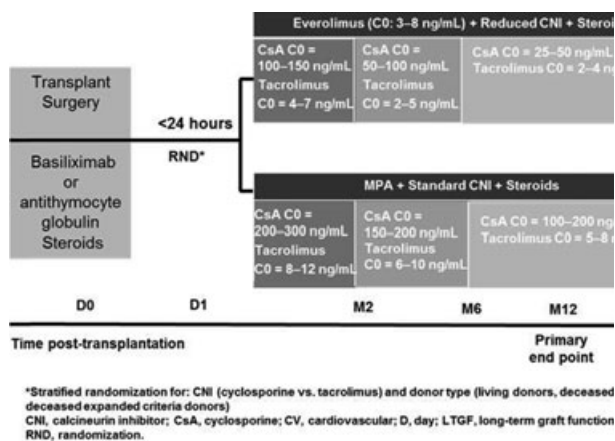


Figure 1: Study design

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IMPACT OF ANOREXIA NERVOSA ON THE RESULTS AT FIVE YEARS IN KIDNEY TRANSPLANTATION

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Introduction: Anorexia nervosa (AN) is an eating disorder, which can be associated to end stage renal disease. The impact of AN at the time of kidney transplantation (KT) on graft outcome has not been described.

Materials and Methods: In this multicentre retrospective study, clinical and biological data from three groups were obtained from KT to 5-year follow-up: patients (pts) with AN at time of KT, pts with low BMI at time of KT (LoBMI), pts with normal BMI at time of KT (NoBMI). The three groups were matched for age, KT centre and period of KT, with a ratio of 3 pts with LoBMI or NoBMI for each pt with AN. Differences between groups were assessed by appropriate statistical tests. Survival analysis techniques were used to identify risk factors for loss of graft function.

Results: One hundred thirty seven pts (all women) were recruited from four centres in this study including 19 AN, 59 LoBMI, 59 NoBMI. AN was significantly associated with lower graft survival (HR 5.5 CI95 [3.4-8.9], $p = 0.005$), while graft survival was not different between LoBMI and NoBMI. In the AN group, BMI increased until 3 months after transplantation and then stabilized during the 1-year follow-up ($17.0 \pm 1.3 \text{ kg/m}^2$ to $17.8 \pm 0.9 \text{ kg/m}^2$, $n = 9$) whereas it increased gradually in both LoBMI and NoBMI (respectively $17.1 \pm 1.0 \text{ kg/m}^2$ to $21.5 \pm 1.5 \text{ kg/m}^2$ and $19.3 \pm 1.9 \text{ kg/m}^2$ to $22.7 \pm 2.7 \text{ kg/m}^2$). There was more cardiovascular disease in the AN group than in LoBMI and NoBMI (respectively, 37%, 6% and 7% during the 5-years follow-up $p = 0.001$). There were no differences in delayed graft function, biopsy proven acute rejection, CMV infection, bacterial infection, cancer, bone disease, diabetes and in psychiatric disorders other than AN among groups.

Conclusion: Pts with AN had a lower graft survival than pts with LoBMI and NoBMI. Pts with AN gained less weight after KT, and had more cardiovascular events post KT. Anorexia nervosa may be considered as a pejorative factor for renal transplantation.

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LATE CD4+ LYMPHOPENIA IN KIDNEY TRANSPLANT RECIPIENTS

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We investigated the pathogenesis and clinical significance of persistent CD4+ lymphopenia detected 10 years or later after renal transplantation.

We undertook a retrospective single-center study of 27 HIV-negative lymphopenic kidney transplant recipients ($\text{CD4} < 300/\text{mm}^3$), compared with 54 non-lymphopenic patients matched for the date of kidney transplantation.

The prevalence of CD4+ lymphopenia at 10 years after transplantation was 5.3%. CD4+ T-cell lymphopenia was associated with a decrease of recent thymic emigrants, and with a B-cell lymphopenia ($p < 0.05$). Duration of pre-transplant dialysis was the sole risk factor significantly associated with T-cell lymphopenia (6.1 vs. 3.0 years, $p = 0.003$). Strikingly, CD4 lymphopenia was associated with an increased risk of opportunistic infections (34.6 vs. 11.48%, $p = 0.01$), skin carcinomas (34.62 vs. 15.09%, $p = 0.04$) and with a hastened decline in graft function ($p = 0.003$). Of note, the recent thymic emigrants/CD4+ lymphocytes ratio was inversely correlated with the dialysis duration before transplantation ($p = 0.037$).

Our study identified the duration of pre-transplant dialysis as the main risk factor for a poor reconstitution of the CD4+ T-cell compartment at late time point after kidney transplantation. This finding is in line with recent studies suggesting that ESRD impairs thymic function. In addition, our study is the first to show that T-cell lymphopenia correlates with an increased risk of opportunistic infections, skin cancer and decline in graft function 10 years or later after transplantation. This study should prompt clinicians to evaluate thymic function in patients who have undergone a long-term dialysis treatment. This may help to tailor the immunosuppressive regimen to the risk of prolonged lymphopenia.

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EARLY ISCHEMIC PRECONDITIONING PROTECTS RAT KIDNEY AGAINST ISCHEMIA REPERFUSION INJURY VIA THE AKT/ENOS/ HIF-1 ALPHA PATHWAY

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Introduction: Although recent studies indicate that renal ischemic preconditioning (IPC) protects the kidney from ischemia-reperfusion (I/R) injury, the precise protective mechanism remains unclear. In the current study, we investigated to what extent the inhibition of nitric oxide (NO) production would abolish these protective effects.

Methodology: Kidneys of Wistar rats (180-250 g) were subjected to 60 min of warm ischemia followed by 120 min of reperfusion (I/R group), or to two cycles of 5 min ischemia and 5 min reperfusion before ischemia (IPC group), or to intravenously injection of NG-nitro-L-arginine methylester (L-NAME, 5 mg/kg) 5 min before IPC (L-NAME+IPC group). The results of these experimental groups were compared to those of a sham-operated group. Sodium reabsorption rate, creatinine clearance, plasma lactate dehydrogenase (LDH) activity, tissue concentrations of malondialdehyde (MDA), hypoxia-inducible factor-1 α (HIF-1 α) and nitrite and nitrate levels were determined. In addition, Western blot analyses were performed to quantify the amounts of protein kinase B (Akt) and endothelial nitric oxide synthase (eNOS).

Results: IPC decreased cytolysis, lipid peroxidation and improved renal function. Parallely, IPC enhanced Akt phosphorylation, eNOS, nitrite/nitrate and HIF-1 α levels as compared to I/R group. However, beneficial effects of IPC were abolished in animals pretreated with L-NAME.

Conclusion: These findings suggest that kidney protection with early IPC is mediated by phosphorylation of Akt, eNOS activation and NO production contributing to HIF-1 α stabilization. The beneficial impact of IPC is abolished when NO production is inhibited before IPC application.

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EVALUATION OF PERIODONTAL STATUS IN RENAL TRANSPLANT PATIENT: CASE-CONTROL STUDY

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Introduction: Renal transplantation has experienced a considerable progress. The emergence of new drugs even the side effects have allowed better management of immunosuppression. Many studies have shown there relation with gingival enlargement. The aim of this study is to evaluate periodontal status and assess the impact of RT and adjuvant therapy in renal transplants

Materials and Methods: A comparative cross-sectional epidemiological survey conducted in the Department of Nephrology CHU Ibn Rochd (December 2012–April 2013) of 35 transplanted for at least 6 months with at least 10 teeth and 106 controls from Consultation and Dental Treatment Center in Casa-blanca consulting for any pathology other than periodontal diseases. The plaque index (PI) and hyperplasia index (HI) were evaluated. The immunosuppression, the oral hygiene and the muco-gingival status were studied.

Results: The age of patients is between 25 and 50 years for 60% of cases. In both groups, patients and controls, no significant gender difference. 22.9% of patients are under mycophenolatémofétil (MMF), associated with corticosteroids in 2.90% of cases. 60% are under cyclosporin A, associated with MMF in 54.30%. 17.10% are under tacrolimus and MMF. In both groups brushing was done between 1, 2 to 3 times a day against 14.2% of control group who did not brushed their teeth. 62.9% of transplant patients have good control plate (IP is between 0.1 and 0.9) against only 21.7% in control group. The average PI is 0.730 ± 0.569 for transplant and 1.188 ± 0.518 for controls with a significant difference ($p = 0.000019$). The index of hyperplasia is significantly higher in renal transplant patients (mean: 0.236 ± 0.290) than in controls (mean: 0.055) ($p = 0.000257$).

Conclusion: Oral hygiene is not sparing renal transplant periodontal problems, particularly gingival hyperplasia. The close collaboration between nephrologist and periodontist is necessary for proper management of transplant patients.

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THE NOCARDIOSIS IN A RENAL TRANSPLANT ABOUT EIGHT CASES

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Introduction: The nocardiosis is a rare and serious opportunistic infection, attached to bacteria of the genus *Nocardia*. *Nocardia* asteroids whose strain is most frequently reported in immunocompromised patients. The frequency of this infection appears augmented as systemic infections frequently associated with cerebral localization burdened with significant mortality. Rare series, comprising only a few cases are described. Bacteriological knowledge, diagnostic and therapeutic methods are evolving. We wanted our reported cases.

Materials and Methods: Retrospective review of records of patients with *Nocardia* infection, the strain has been identified by the bacteriology laboratory of the University Hospital of Marseille between January 2004 and December 2011. The identification of cases was made from the Bacteriology Laboratory computerized register.

Results: During the reporting period, have supported in our service, eight cases of proven nocardiosis, seven cases occurring in renal transplant patients, and one case in a heart transplant hemodialysis. We can assess the impact of nocardiosis in our patients to 146 cases/100 000 patients/year. The average age was 52 years with a male predominance (6H/1F). Average infection occurred 14.9 months after transplantation. The clinical picture was characterized by constant fever with a peak temperature averaged 38.9°C, impaired general condition in all patients. All our patients had a systemic form with multiple tissue locations, and in 71% of cases at least three bodies were achieved. In our cohort, the most common location is secondary joint/muscle, found in about 60% of cases. A predominant lung disease and multi-organ localization constant and varied, liver, thyroid or graft. The brain damage was classic, and neurological symptoms (headache, delirium) were present in 50% of our patients, associated with cerebral radiological localization once two. At diagnosis, a biological inflammatory syndrome was frequently found, with an average CRP 151.25 mg/l and leukocytosis 12.39 giga/l, associated with acute alteration of renal graft function, with a decline in glomerular filtration close 20 ml/min. Contributing bacteriological samples were cultivation of aspirates of abscess lesions, and rarely growing bronchoalveolar lavage. Blood cultures were often sterile. The strains were most frequently isolated *Nocardia* abscessus in three cases and *Nocardia* otitidiscaviarum /farcinica in two cases, *Nocardia* neocaledoniensis in one case. According to the protocol of immunosuppression at our center, the majority of patients were treated with tacrolimus and corticosteroids had a short long. It may be noted that four patients were immunized before transplantation, and two patients received a second transplant. All patients were treated with imipenem and triméthoprine/sulphaméthoxazole association for a period of total antibiotic averaged 12.5 months. Antibiotic therapy has been associated with a reduction in immunosuppression. Three taken into surgical charges were made with a total thyroidectomy and two evacuations brain abscess diagnostic purposes. No deaths were noted.

Conclusion: Diagnostics methods and *Nocardia* with much advanced over the past 10 years. The key to diagnosis is usually based on an invasive procedure such as stereotactic puncture of an abscess, or more rarely the culture of a specimen such as during enucleation. *Nocardiosis* post kidney transplant is a rare condition, occurring mainly during the first year of transplantation, with a prognosis in a specialized environment remains favorable, the price of prolonged antibiotic therapy and a take -invasive and rapid diagnostic support.

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SEROPREVALENCE/SEROCONVERSION OF THE VHE IN POST RENAL TRANSPLANTATION AFTER PLASMATIC EXCHANGE

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The infection by virus hepatitis E is an emergent disease with a risk of evolution towards chronic hepatitis in post transplantation. Some Cases of transmission per blood transfusion were described. The seroprvalence in post transplantation varies between 6% and 15.6%

Objective: To determine the seroprevalence, the seroconversion of the infection by the VHE and a possible contamination in post renal transplantation after plasmatic exchange (EP)

Methods: It is about a retrospective study with pairing at the age of two groups with and without plasmatic exchanges. The criteria of inclusion were: a renal graft between January 2009 and February 2013, the availability of three serums in virology in pre renal transplantation, 3 months after the renal transplantation and before the plasmatic exchanges. Serology was done by the Wantai test and PCR VHE by the Ceeram test

Results: Of 25 patients with an average age at 48 years (25–65 years) were included in this study having plasmatic exchanges before renal transplantation. The use of plasma was noted at 100% of the patients having had recourse to the EP because of the hemorrhagic risk (recent transplantation and/or biopsy of the graft). Of 30 patients were included in the group controls with an average age at 47.7 years (27–65 years).

Seroprevalence VHE before the renal transplantation is 20%, after transplantation 36.4%.

The seroprevalence before the renal transplantation in the group without EP is 23.3%, and in the group with EP 16%. The seroprevalence post renal transplant is 30% in the group without EP and 44% in the groupe with EP

The seroconversion is to 8.7% (2/23) in the group without EP versus 33.3% (7/21) in the group with EP ($p = 0.043$)

None the patients having a seroconversion presented detectable plasmatic viral replication.

Conclusion: The rate of seroconversion in this study is more important in the group with plasmatic exchange but it could exist a passive transfer of Ig anti VHE of the donors. A longitudinal follow-up of the patients presenting a seroconversion after renal transplant could be useful to differentiate the passive transfer from a seroconversion.

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FATAL HUMAN HERPESVIRUS-6 INFECTION 5 MONTHS AFTER RENAL TRANSPLANTATION

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Introduction: HHV-6 is an underestimated cause of opportunist infection after renal transplantation although its reactivation is frequent.

Methods: A 66-year-old man was admitted 5 months after the transplantation to investigate chronic diarrhea and weight loss.

Results: He suffered from asthenia, weight loss, liquid chronic diarrhea, daily fever with bicytopenia, mild inflammatory syndrome and graft dysfunction was added. An ulcerative ileitis has been diagnosed by colonoscopy with HHV-6 PCR in biopsy material without associated viremia, followed by oral ulcerations despite GANCICLOVIR introduction. It was complicated with a inhalation pneumonia with severe sepsis, which was followed by a hemophagocytic syndrome, *multiple organ dysfunction syndrome and death*.

Discussion: Most HHV-6 infections are asymptomatic or associated to mild clinical course. The non-specific case delayed the antiviral treatment initiation. Two cases of HHV-6 infections after renal transplantations were fatal with colitis followed by a hemophagocytic syndrome were found in the literature but some examples of fatal infections can be found in other solid or stem cell transplantation. HHV-6 reactivations occur early, but late infections up to 24 months have been also described. Only 1% of transplant recipients will develop clinical illness associated with HHV-6 infection. Nevertheless our patient developed the disease 5 months post-transplantation without any identified risk factor. Thus it seems important to mention HHV-6 infection, even far from the transplant.

Conclusion: Any chronic diarrhea must lead to a colonoscopy after the exclusion of the main causes not to forget an opportunist infection as the DIDACT study showed since the presentation may be insidious and late just like this case and delay the antiviral treatment initiation.

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DO IMMIGRANT HAVE DIFFERENT KIDNEY TRANSPLANTATION OUTCOMES OR HARDER ACCESS TO WAITING LIST, IN FRANCE?

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Introduction: Transplantation results and access is influenced by patient ethnic group in USA. Ethnicity is difficult to study, because it is subjective, flexible and dynamic. Health anthropologist thinks that the migratory pathway is more pertinent: it shapes patients behaviours towards their disease, their treatments and caregivers. Does migratory pathway influence kidney transplantation outcomes or access?

Methods: We interviewed patients who underwent renal transplantation from 1999 to 2019 at the Medical University Center of Bordeaux about their nationality and their place of birth. We collected data about transplantation results, time on dialysis and waiting time in Cristal and RAN (software used in the region for recipients follow up).

Among the 299 patients who answered, 189 were French born in France and 48 were foreign immigrant. 46 of these foreign immigrant were match to 92 native French on age, sex, immunisation and suppressive therapy. Survival (patient and graft), rejection rate, GRF were similar in both groups after 83 months of follow up. The time on dialysis was longer in immigrant group 50.6 ± 43 vs. 43.5 ± 67 , $p = 0.02$, when no difference was found on time in waiting list. In multivariate analyse, graft rank (OR = 8.7), B blood type (OR = 5.2), O blood type (OR = 3) and immigrant migratory pathway (OR = 3.8) were linked to a long time on dialysis (>24 months).

Before the beginning of the study we asked 50 nephrologist's opinion about immigrant's graft survival: 30 answered, 14 used to think that immigrant's graft survival is poorer than the rest of recipients.

Conclusion: Migratory pathway does not change kidney transplantation results but immigrant stay a longer time in dialysis before transplantation. Nephrologist have to be careful about this.

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BAFF POLYMORPHISMS AND SERUM LEVELS OF BAFF IN TUNISIAN KIDNEY TRANSPLANTATION

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Introduction: Current advances provide that elevated serum BAFF (B-cell activating factor) levels correlate with an unfavorable outcome in kidney allograft. To analyze this hypothesis in Tunisian renal transplant patients and to determine whether increased levels BAFF are due to genetic variations in the promoter region of the BAFF gene, a cross-sectional analysis of serum BAFF levels (s-BAFF), single nucleotide polymorphisms (SNPs) and clinical variables was performed.

Materials and Methods: Ninety three kidney recipients are included in this cohort. 6 of them (6.45%) have developed acute allograft rejection (AR) and 9 (9.67%) have anti-HLA antibodies before transplantation. Two SNPs: -2701 (A/T) and -2841 (T/C) in BAFF 5' regulatory region were investigated by direct sequencing and (s-BAFF) levels were measured by ELISA (R&D systems).

Results: AA (-2701) and CC (-2841) homozygous genotypes were increased in AR cases compared to other recipients (83.3% vs. 66.6%, $p = 0.063$ and 50% vs. 11.5%, $p = 0.036$, respectively). Moreover, haplotype analysis revealed that A(-2701) C(-2841) was associated to AR episode (AR (+): 75% vs. AR (-): 32%, $p = 0.011$). However, s-BAFF was not correlated with acute kidney rejection (AR(+): 1234.8 ± 447.55 vs. AR (-): 1132.15 ± 949.46 pg/ml) or anti-HLA antibodies production before and after transplantation. Moreover, single allele, genotype and haplotype association analyses showed no significant association with s-BAFF levels variations or better kidney survival.

Conclusion: Despite the small number of AR cases inducing certain limitations to this study, our results show that BAFF variants do contribute to the susceptibility to AR in Tunisian allograft recipients. Further expression studies are needed to investigate the potential pharmacologic role of these variants in immunosuppression therapy.

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IVIG NEPHROTOXICITY IN KIDNEY TRANSPLANTATION

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Nephrotoxicity of intravenous immunoglobulin (IVIG), which are frequently used in renal transplantation, is conventionally attributed to carbohydrate excipients through a mechanism of osmotic nephrosis.

We aimed to analyze the renal tolerance of IVIG containing no carbohydrates in patients with a recent kidney transplant.

We retrospectively studied 84 kidney transplant recipients considered at high immunological risk receiving 183 infusions of IVIG within 3 months after transplantation. A graft biopsy was performed before implantation and 3 months after transplantation. These patients were matched to 50 transplant recipients who did not receive IVIG. The dose of IVIG was 2 g/kg per infusion and the mean infusion rate was 0.5 ml/kg/h and was associated with intravenous hydration.

The mean patient age was 50.9 ± 14.4 years (47M/37F). Serum creatinine before infusion was 139 ± 71 $\mu\text{mol/l}$. We didn't observed any case of acute renal failure and the median change in creatinemia was -6% [-42%, 39%]. Renal histology at three months showed more severe tubular toxicity in patients who received IVIG, with more frequent vacuolization of tubular cytoplasm (36% vs. 14%, $p = 0.01$). The IVIG infusion, however, was not accompanied by a worsening of renal function at one year after transplantation.

Our study is the first to evaluate the safety of IVIG without carbohydrate excipients in renal transplant recipients. Our results show an excellent clinical safety of these products since no case of acute renal failure was reported, but a tubular histological damage without significant impact on renal function at one year was observed.

P36

KIDNEY TRANSPLANTATION UNDER LOCAL ANESTHESIA: IS IT POSSIBLE ?

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Introduction: The choice of appropriate anesthetic technique for patients undergoing kidney transplantation is crucial and should have minimal side effects on the patients as well as the transplanted organ. In fact, this will, particularly, impact allergic patients to general anesthetics. We have reported two cases related to two patients undergoing a kidney transplant and having multiple allergies to intravenous anesthetics.

Case 1: Patient of 28 years old, with chronic renal failure in lupus glomerulonephritis and hemodialysed for 4 years. This patient is allergic to most intravenous anesthetics and has undergone a single shot spinal anesthesia (15 mg of bupivacaine 0.5%); the surgery lasted 110 min with a good postoperative assessment.

Case 2: Patient of 38 years old, with chronic renal failure of unknown origin and hemodialysed for 3 years. The patient is allergic to penicillin as well as intravenous anesthetic agents and has undergone a spinal anesthesia using 15 mg of bupivacaine 0.5%, 25 micrograms of Clonidine and the implementation of an epidural catheter. The surgery lasted 190 min with injection in the 120th minute 15 ml Lidocaine 2% for 15 min without hemodynamic compromise with a normal postoperative assessment.

Conclusion: The regional anesthesia is a good alternative that may replace the general anesthesia during kidney transplantation for allergic patients.

P42

CENTRAL PRESSURE ASSESSMENT IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Enhanced augmentation of the central aortic systolic pressure by the increased effect of arterial wave reflection, as defined by the augmentation index (Alx) has been shown to be a powerful predictor of cardiovascular mortality and cardiovascular disease in general population, in patients with chronic hemodialysis and in renal transplant recipients (RTR) making from arterial stiffness a therapeutic target.

Some studies suggest an association between Alx and non traditional risk factors which may lead to the development of new therapeutic strategies to reduce the cardiovascular risk in RTRs.

The aim of this study is to evaluate the Alx in a large cohort of RTRs and to assess exhaustively his main determinants.

Patients and Methods: All RTRs attending the annually outpatient clinics were eligible for the study. Every measurements of Alx were performed with a validated, automatic, oscillometric device (ARTERIOGRAPH™). We also performed standard biology, cystatin C and homocystein measurements. Vascular calcifications was evaluated by assessing the kauppilla score.

Results: Of 215 patients were included. The mean age was 55.9 years (± 13), 67.4% were male and the mean duration of transplant was 8.3 yrs (± 6.3). The mean Alx was $+25.7\%$ and varied from -3% to 59.1% . The duration of transplant was associated with a decrease of Alx ($p = 0.02$) with a more important effect for transplant whose duration was less than 8 years ($p = 0.005$). The most significantly associations with Alx were the duration of hemodialysis ($p = 0.01$), the recipient's age ($p < 0.001$), cystatin C, eGFR and and vascular calcifications assessed with the Kaupilla score.

Conclusion: These results suggest the role of supplementary factors in aortic stiffness. The impact of new determinants independently associated with AIx must be prospectively assessed to better anticipate the cardiovascular risk in RTRs.

P43

POORLY DIFFERENTIATED ADENOCARCINOMA OF THE RENAL GRAFT

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Introduction: Follow-up of renal transplant patients is important in tumor pathology. In most cases, cancers take their origin from recipient's tissues, but there are rare cases where the cancer is transmitted from the donor. We describe a case of poorly differentiated adenocarcinoma of an undiagnosed malignancy in the donor discovered 4 months after transplantation.

Method: The patient is a 44 years old with past medical history: End-Stage Renal Disease from unknown origin, who was on hemodialysis for 3 years before the transplant. His pre-transplant evaluation didn't shows any signs of malignancy and he received a cadaveric kidney transplant in November 2012 with an immunosuppression (IS) regimen. His nadir creatinine was 1.5 mg/dl. The patient presented within 2 months of progressive renal failure with serum creatinine 2.4 mg/dl and an increase in the volume of graft with ultrasound. A chest radiograph showed multiple pulmonary nodule with canon ball pattern and the patient underwent diagnostic kidney biopsy revealing a poorly differentiated adenocarcinoma of unknown origin. PET SCAN showed increase metabolism in the lung and within the renal graft. No gross evidence of tumor was present during surgical exploration of the transplanted kidney and the donor had no necropsy. Concurrent recipients from the same donor (contralateral kidney) were later diagnosed with graft carcinoma of unknown origin.

Outcome: The patient underwent a transplantectomy of the graft and the IS was stopped. He received chemotherapy. Follow up imaging 10 months after the diagnosis showed significant regression of the lesions. The recipient of the contralateral kidney who developed generalized cancer was treated with graft removal and immunosuppression withdrawal only with sustained clinical remission.

Conclusion: Cancers transmitted by the donor are extremely rare, but may know a favorable outcome after transplantectomy of the graft, the withdrawal of immunosuppression and chemotherapy.

P44

RECURRENCE OF SCLEROSIS RENAL CRISIS IN A KIDNEY TRANSPLANT RECIPIENT

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Introduction: Scleroderma renal crisis (Src) is a rare but severe complication of systemic sclerosis. Physiopathology is currently not well known but overexpression of endothelin (ET)-1 could be involved. Recurrent Src in the graft can drive to graft loss.

Method: Here we describe the case of a 34-year-old female patient with systemic sclerosis and Src under dialysis during 3 years. She developed a new Src 105 days after the procedure.

Results: She underwent a deceased donor renal transplant. Induction was pulses of methylprednisolone and Thymoglobulin[®] followed by tacrolimus, mycophenolate mofetil and prednisone with fast decrease under 15 mg/day. Angiotensin-converting enzyme inhibitor (ACEi) was introduced on day 7. The best creatininemia was 90 µmol/l (1 mg/dl). ACEi was discarded because of hypotension on day 20. Since day 50 progressive increase of creatininemia has occurred. On day 109 creatininemia was 169 µmol/l (1.9 mg/dl) with light haptoglobinemia decrease. On the graft biopsy, there were fibrous thrombus in a glomerulus and onion skin lesion in an artery. ACEi was reintroduced. She underwent plasmapheresis, tacrolimus was switched by belatacept. The greatest creatininemia was 326 µmol/l (3.7 mg/dl). Bosantan was then started at 62.5 mg bid (ScS REINBO protocol) 12 days after biopsy. Creatininemia started to decrease 15 days after its introduction. Currently creatininemia is 147 µmol/l (1.7 mg/dl).

Conclusion: In Src, guidelines recommend to keep ACEi after procedure and steroids have not to exceed 15 mg/day. In this case, plasmapheresis seemed to be inefficient. Switch from tacrolimus to belatacept and adjunction of bosantan allowed improvement in renal function.

P50

FACE TRANSPLANTATION WITH COMBINED HEMATOPOIETIC STEM CELL INFUSION AND VASCULARIZED BONE MARROW TRANSPLANTATION IS NOT ASSOCIATED WITH MIXED CHIMERISM IN HUMANS

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Background: In rat models of limb allograft transplantation, vascularized bone marrow (VBM) transplantation is associated with mixed chimerism (MC) and donor-specific tolerance. The objective of the study was to analyze the development of MC in face transplant recipients treated by the combination of VBM and hematopoietic stem cell infusion.

Methods: Three face allotransplantations were performed in severely disfigured patients (pts), one male and two females, aged of 27, 38 and 52 year-old respectively.

Facial allograft included nose, lips, cheeks and chin in pt 2, bilateral mandible (VBM), cheeks, lips and chin in pt 1, and bilateral maxilla and mandible (VBM), cheeks, lips, chin and tongue in pt 3. Donor BM was infused after transplantation on day 4 and 11 in pt 2; day 4 in pt 1 and day 7 in pt 3.

Immunosuppression included Thymoglobulin, tacrolimus, prednisolone and mycophenolate mofetil. Chimerism was assessed by RQ-PCR on whole blood and on CD3+ cells at days 8, 14, 26, 39, 53, 69, 88, 124, 174, 330, and 545 after transplantation, and on total and purified CD34+ BM cells at days 14, 26, 53, 90, 174, 370, and 545. The lower limit of the assay was 0.1%.

Results: Microchimerism was detected once at M2 (0.1% donor cells among the CD34+ enriched population of BM cells) in pt 2. Transient microchimerism was evidenced in pt 1 in the BM at d7 (0.4% donor CD34+ cells), d14 (0.6% donor CD34+ cells), and d56 (0.4% donor CD34+ cells) and was detected once in peripheral blood (0.6% donor CD3+ lymphocytes at d28). Chimerism remained undetectable in pt 3. No graft versus host disease has developed in the 3 pts. Two episodes of acute rejection occurred in pt 2, 6 in pt 1, and 1 pt 3.

Conclusion: VBM transplantation combined with HSC infusion did not induce MC in face transplant recipients treated by Thymoglobulin and tacrolimus. This study suggests that a non-myeloablative regimen is necessary to induce MC and tolerance in the context of donor VBM and HSC infusion.

P53

NEPHRECTOMY FROM LIVING DONOR: WHICH TECHNIQUE TO CHOOSE?

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Nephrectomy for transplantation in the living donor has become a common procedure, standardized and safe that can be practiced open pit or by laparoscopy.

The aim of this work is to evaluate the morbidity of open nephrectomy in living donor and graft function and the occurrence of complications in the recipient; identify later, through literature feasibility, morbidity and functional outcomes of laparoscopic nephrectomy.

We prospectively compiled data transplants performed between 2010 and 2012 by open surgery and 43 pre settings, per- and postoperative have been studied.

P58

ORGAN AND TISSUES DONATION AND HARVESTING FROM BRAIN STEM DEATH. SURVEY REALIZED BY MEDICAL STUDENTS

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Introduction: The organ and tissues harvesting of a brain stem death patient is a recent activity in Morocco. This notion is still unknown in our cultural context. In order to raise awareness, we conducted a survey to assess the knowledge of medical students in death brain and organs and tissues harvesting.

Materials and Methods: Anonymous questionnaire with 15 questions, distributed over 500 students in the second cycle. We assessed their knowledge about brain stem death and organ donation.

Results: 336 copies were completed. The average age was 20.15 years (18-30 years old). 63.4% were female.

285 students had a preconceived notion of the brain stem death.

147 students ignored the existence of a register of consent in court and 121 students didn't know that the Moroccan law allows the organ harvesting from brain stem death patients.

Only 35 students knew the hospital coordination, among them five students knew its different tasks.

265 students were not opposed to the harvesting of their own organs after death.

43.46% of students opposed to the organ and tissues harvesting after death of familie's member.

Among the refusal reasons we find:

- Sociocultural with 43.66%
- Personal reasons with 28.16%
- Religious reasons with 26.76%
- One case of ignorance of the Moroccan law

Discussion: Following these results, we find that our students ignore the major information about the brain stem death and also organ and tissue's donation. However, we find that is very important to start (at first targeting the medical student) some awareness companion for addressing different aspects of organ and tissue donation.

P59

FACTORS ASSOCIATED WITH URINARY TRACT INFECTIONS (UTI) IN ENTEROBACTERIACEAE PRODUCING BETA -LACTAMASES WITH EXTENDED SPECTRUM (ESBLE): CASE-CONTROL STUDY IN RENAL TRANSPLANT PATIENTS BETWEEN 2008 AND 2012 AT THE UNIVERSITY HOSPITAL OF NANTES

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Introduction: Renal transplant recipients are more likely to present UTI. Scarce clinical symptoms, frequent recurrences and lack of guidelines leads the practitioner to treat most of the bacteriuria, therefore increasing the antibiotic pressure, whereas the prevalence of ESBLE increases. Our study purpose is to evaluate the factors associated with ESBLE UTI compared to non ESBLE (NESBLE) UTI.

Patients and Methods: We conducted a retrospective and monocentric matched case control study on patients transplanted between 2008 and 2012 at the University Hospital of Nantes. The main goal was to identify the factors associated with ESBLE UTI compared to NESBLE UTI among factors related to the host, hospitalization and drug exposures. Cases were transplanted less than three years ago and presented at least 1 ESBLE UTI during this period. Each case was matched to two controls transplanted the same year and which had similar number of ITU (1, 2–3, more than 4) from the transplantation to the ESBLE UTI case.

Results: Of 21 patients were selected and matched with 42 controls. Differences were shown on antibiotic exposure (ESBLE: 80.9%, NESBLE: 54.7%, $p = 0.05$), urological complications (61.9% against 21.4%, $p = 0.002$), pyelonephritis occurrences between transplantation and the ESBLE or NESBLE ITU (52.4% against 28.6%, $p = 0.05$) and delay graft function (42.7% against 16.7%, $p = 0.03$).

Discussion and Conclusion: There seems to be a population of renal transplant recipients more likely to present UTI in ESBLE for which special monitoring would be interesting. Besides, guidelines for antibiotic prescriptions should be set, especially for asymptomatic bacteriuria, in order to prevent the emergence of resistances causing morbidities.

P62

ASSESSMENT OF CYTOMEGALOVIRUS SPECIFIC MEMORY T CELLS IN RENAL TRANSPLANT AND CORRELATION WITH VIRAL INFECTION

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Introduction: Assessment of Cytomegalovirus (CMV) specific memory T cells could potentially allow to evaluate the patient viral risk and to provide a tool guiding the use of preemptive or prophylactic anti-viral treatment.

Methods: In a pilot prospective study, we compared by multiparametric flow cytometry, CMV specific T cells subpopulations of five healthy controls and 11 recent allograft recipients (before transplantation, at 6 weeks and 3 months

after transplantation and at time of CMV infection) in studying the polyfunctionality (i.e. concomitant cytokine secretion by one cell) and the differentiation subsets distribution of CMV-specific T cells: naive, central (TCM) and effector (TEM) memory, terminally differentiated (TD) and memory stem T cells (TSCM).

Results: Five patients presented CMV infection (three reactivations and two primary infections). CMV-specific T cells differentiation is more advanced in transplant recipients than healthy controls (expansion of TEM CD4⁺ and TD CD8⁺ T cells) with an expansion of TSCM CD8⁺ T cells in transplant recipients free of CMV reactivation ($* = p < 0.05$).

T cell polyfunctionality is more greater in transplant recipients (<1% in controls against 20–40% in transplant recipients, $p > 0.05$).

Conclusion: Our study suggest that operational CMV specific memory immunity with a large reconstitution capacity could allow the CMV control in renal transplantation and could be a tool guiding the use of preemptive or prophylactic anti-viral treatment.

P66

ACQUISITION OF EXTENDED SPECTRUM BETA-LACTAMASE PRODUCING ENTEROBACTERIA DURING THE FIRST MONTHS OF RENAL TRANSPLANTATION: EPIDEMIOLOGY AND CLINICAL IMPACT

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Introduction: Epidemiology of extended-spectrum beta-lactamase producing enterobacteria (ESBL-PE) is not well documented in renal transplantation (RT). The purpose of this study is to determine the prevalence of ESBL rectal or clinical colonization at admission for RT and its clinical impact during the first following three months.

Patients and Methods: Monocentric and retrospective analysis of microbiological data of patients admitted for RT between May 2007 and December 2010 were performed. Our center proposes systematic screening of rectal or urinary multiresistant bacteria by rectal swabs on admission and every week, as well as urine examination twice a week. Medical files of every ESBL-positive patient were analyzed looking for sepsis related to the ESBL-bacteria.

Results: Out of the 467 screened patients on admission, 11(2.4%) were positive, every time E. coli. In 2009, 15% of patients acquired rectal colonization, 28.2% in 2010. Clinical prevalence was respectively 16.5% and 16.1%. Eighteen patients (3.6%) developed sepsis related to ESBL-PE, mostly from urinary tract (83.3%), and was preceded by rectal colonization in 6 patients (33.3%).

Conclusion: Our results suggest that prevalence of ESBL-EP rectal colonization in candidates to RT is similar to the general population. They confirm the high risk of nosocomial acquisition underlying the need for sparing broad-spectrum antibiotic regimens and strict hand hygiene. The small associated infection rate does not seem to justify the use of carbapeneme in front of post-RT sepsis without severity, even if there is a known rectal ESBL-colonization. A study of risk factors for ESBL-infections is necessary.

P69

LATE CYTOMEGALOVIRUS (CMV) INFECTION IN RENAL TRANSPLANT RECIPIENTS: CLINICAL PRESENTATION AND RISK FACTORS: A CASE-CONTROL STUDY

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Introduction: Few data deal with late cytomegalovirus (CMV) infection occurring beyond one year after transplantation. Some case reports described an atypical clinical presentation (less fever and leucopenia). The aim of our study was i) to compare clinical presentation and graft outcomes in early (ECMV) versus late CMV (LCMV) disease and ii) to identify risk factors of developing LCMV disease.

Methods: We conducted a retrospective case-control (1:2) study at Montpellier's kidney transplantation center. Between 2000 and 2010, 15 patients who developed late CMV infection were identified. They were matched with 30 controls transplanted at the same time (± 2 months) who developed ECMV infection. CMV disease was defined as positive viremia and clinico-biological symptoms (fever, leucopenia) with or without tissue invasion.

Results: Patients who developed LCMV disease had significantly higher gastrointestinal symptoms and higher CMV disease (70 vs. 33%) as compared

	Healthy controls	Transplant recipients with CMV reactivation	Transplant recipients free of CMV reactivation
TEM CD4 ⁺	35.9% [28.7–56.5]*	72% [60.4–82.7]	69.3% [59.8–70.2]
TD CD8 ⁺	27.3% [13.6–41.5]*	66.1% [57.1–87.6]	58.4% [51.7–72.4]
TSCM CD8 ⁺	Not significant	3.2% [0.9–4]*	6.3% [6.2–7.3]

with controls ($p = 0.02$). There was no difference between the two groups concerning fever, leucopenia and liver cytolysis. Two independent risk factors of developing LCMV were identified: age beyond 60 years (adjusted HR: 18.3, 95% CI [1.4–248.3], $p = 0.03$) and transplantation range beyond 1 (adjusted HR: 76.1, [2.6–2270.7], $p = 0.01$). Graft rejection and outcomes were similar between the two groups. The duration of antiviral therapy was significantly shorter amid patients who developed LCMV (17.76 v/s 11.87 days, $p = 0.0006$).

Conclusion: In this work, we compared for the first time LCMV and ECMV infection occurring among kidney transplanted patients. We showed that LCMV infection presented frequently as a CMV disease, with significantly higher gastro-intestinal symptoms. LCMV disease should be suspected in transplant patients when exploring GI symptoms and particularly diarrhea.

P75

EFFECT OF CYP3A5 POLYMORPHISM ON TACROLIMUS DOSE AND BLOOD LEVELS IN RENAL TRANSPLANTATION IN CLINICAL PRACTICE

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Tacrolimus is an immunosuppressive drug used for prevention of allograft rejection in kidney recipients. It exhibits a narrow therapeutic index and large PK variability. Tacrolimus is mainly metabolized by cytochrome P450 3A5. It shows cytochrome P450 (SNP) in intron 3, which consisted of a change of base, G for A, producing a stop codon. The result is a nonfunctional protein (allele*3). Allele *1 is the wild type. The aim of this study was to evaluate this effect in clinical practice post renal transplantation.

Methods: Kidney transplant recipients undergoing treatment with tacrolimus were genotyped by Taqman[®] for CYP3A5 *1*3 polymorphism. DNA was extracted from peripheral blood and polymerase chain reaction (PCR) was used to amplify intron 3 of the CYP3A5. Tacrolimus blood concentrations were measured with immunoanalyse assay (Xpand[®]) and concentration/dosage (C/D) and concentration/body weight (C/P) ratio were evaluated.

Results: Of 67 transplant patients were included, 43 men and 24 women. The average age was 49.5 years (22–69). The dosage received of TAC was 8.5 mg/j (1–32). We observed that 50.7% of the patients were homozygous for CYP3A5 1 and 49.3% were CYP3A5 3 carriers. African patients were 2.8% and 62.5% respectively in the two groups. The tacrolimus blood concentrations among 2 groups did not significantly differ ($p = 0.64$). The ratio (C/D) and (C/p) were significantly lower in CYP 3A5 *3 carriers ($p = 0.000001$ and $p = 0.008$ respectively). Tacrolimus doses were significantly higher in CYP3A5 *3 carriers ($p = 0.001$).

Conclusion: This study showed that patients carrying a CYP3A5 *3 allele require a higher tacrolimus dose compared with homozygous carriers of CYP3A5 *1 variant allele. Genotyping for the CYP3A5 *3 variant allele could contribute to a better and more individualized immunosuppressive therapy in renal transplant patients.

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LOOKING FOR CYCLOSPORINE AUC TARGETS IN RENAL TRANSPLANTATION

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Introduction: The individual dose adjustment of cyclosporine (CsA) is historically performed by measuring trough levels (C_0). The area under the curve (AUC) is known to be a better exposure index, but is not routinely used mainly because no targets have been consensually accepted. On the basis of a large database of CSA pharmacokinetic (PK) profiles collected in renal transplant patients, our objectives were: (1) to explore the relationships between AUC and C_0 , and (2) to define AUC targets which may be proposed in renal transplantation.

Material and Methods: The requests for a dose adjustment of CsA in adult renal transplant patients posted on the ISBA website ⁽¹⁾ between 2007 and 2013 were retrospectively studied. Regression analyses between observed C_0 values and estimated AUC were performed taking into account the post-transplantation period. Using the different regression equations, AUC targets were defined that corresponded to the C_0 targets proposed in the Symphony study ⁽²⁾ (150–300 µg/L over the first 3 months post-transplantation, then 100–200 µg/L).

Results: Of 6121 CSA PK profiles obtained from 1468 patients of 27 different transplantation centers were collected. The regression analyses yielded the following equations: $AUC = 0.0163C_0 + 2.3378$ ($r^2 = 0.64$) and $AUC = 0.0191C_0 + 1.1582$ ($r^2 = 0.62$), for the <3 months and >3 months post-transplantation periods, respectively. The derived AUC targets were: 4.8–7.2 mg.h/l for the <3 months period and 3.1–5.0 mg.h/l for the >3 months period.

Discussion – Conclusion: Using a very large database of CSA PK profiles, we have defined CSA AUC targets taking into account those used for C_0 . These values may be used in concentration-controlled studies testing the efficacy of a therapeutic drug monitoring based on AUC estimation.

(1) ISBA web site; <http://pharmaco.chu-limoges.fr/>; (2) Ekberg H et al. N Eng J Med 2007.

P84

SYSTEMATIC SCREENING OF INTRACRANIAL CEREBRAL ANEURYSM IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE BEFORE RENAL TRANSPLANTATION: RETROSPECTIVE ANALYSIS ABOUT 116 PATIENTS

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Introduction: Intracranial aneurysms (ICA) represent one of the main complications of autosomal dominant polycystic kidney disease (ADPKD) and recommendations do not specify if screening is mandatory before transplantation. Since 1999, we do a systematic screening for ICA with a cerebral imaging before renal transplantation at our institution.

Methods: We reviewed all transplanted patients with ADPKD between January 1999 and June 2013. The aim of this study was to estimate the exact prevalence of ICA and how to manage them.

Results: During the period of the study, 884 renal transplantations were performed, 135 for ADPKD. Nineteen patients had been excluded by lack of information, 116 were included. 58.6% were men and the age at the time of the transplantation was 55 ± 9 years. Four patients (3.4%) had a personal history of aneurysm rupture. We detected an aneurysm in 8 patients (6.9%), four men and four women, two patients had two lesions. Aneurysms were in the anterior circulation ($n = 5$) or in the posterior circulation and the average size was 4.1 ± 1.4 mm (2.5–5.6 mm). Only one patient had a family history of aneurysm rupture. All patients had liver cysts and one had abdominal aortic aneurysm. Five had surgical repair and one had endovascular treatment, two had no treatment considering the localization of aneurysm and the surgical risk. After transplantation, the size of the untreated aneurysms was stable and we diagnosed one aneurysm in two other patients. None aneurysm rupture occurs during a mean follow-up of 65 ± 30 months.

Conclusion: The prevalence of ICA in our study is 12%, higher than previously described. Eleven of these 14 patients had no family history. Aneurysm rupture is a rare event and its risk does not seem to increase after renal transplantation. Our practice allowed us to detect an aneurysm in 8 patients before renal transplantation and to propose a surgical or endovascular treatment to 6 of them.

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ANALYSIS OF ROUTINE DOSE ADJUSTMENTS OF SIROLIMUS IN HEPATIC TRANSPLANT PATIENTS

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Background: Sirolimus is an oral immunosuppressant that selectively inhibits T-cell activation and indicated for the prophylaxis of organ rejection in adult patients. Due to variable individual pharmacokinetics and narrow therapeutic ranges, therapeutic drug monitoring (TDM) is critical to the success of post-transplantation patient care. The aim of this study is to evaluate the therapeutic monitoring of sirolimus in hepatic transplantation realized at Pitié-Salpêtrière hospital (Paris, France).

Methods: For 20 months, 59 different patients (outside any clinical trial) with a hepatic transplantation were included in this study; 13 women and 46 men. At the time of dosages, the average age of all patients was 59.0 ± 8.9 years. Two hundred sixty-three dosages of sirolimus were realized at residual concentration on total blood samples by a mass spectrometry method.

Results: This retrospective study showed that (1) according to a consensually recommended 4.0- to 12.0 µg/l (in monotherapy) and 12.0- to 20.0 µg/l (in association with ciclosporin) targets, dose adjustment was needed for approximately 76.4% of dosages, among which 88.6% being underexposed and 11.4% overexposed; (2) only 59 dosages were the object of a dose adjustment against 136 dosages without any dose adaptation; (3) a high interindividual variability of sirolimus residual concentrations was observed considering a daily dose of 2 mg of sirolimus per os (coefficient of variation of 56.4%).

Conclusion: According to the high interindividual variability and of the narrow therapeutic ranges, the therapeutic monitoring of residual concentrations of sirolimus is essential. Nevertheless, these outcomes must be confirmed by a larger study.

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EFFICACY AND SAFETY OF PERITONEAL DIALYSIS IN RENAL TRANSPLANT PATIENTS FROM NON-HEART BEATING DONOR REQUIRING RENAL REPLACEMENT THERAPY IN THE IMMEDIATE POST-GRAFT PERIOD

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Background: Delayed graft function is a frequent complication of renal transplantation, especially in the kidney transplantation from non-heart beating donor. In this case, patients need dialysis for a long time. Most often they are treated with hemodialysis even if they were treated with peritoneal dialysis before transplantation. In this case, use of venous central catheter is necessary and can conduct to some severe complication. Efficacy and safety of peritoneal dialysis in immediate post graft from non-heart beating patients had never been described.

Patients and Methods: We reported five cases of peritoneal dialysis patients which need dialysis because of DFG because they were transplanted with non-heart beating donor between 2007 and 2010.

Results: The median period of treatment by PD was 14 days. All patients with the exception of one were treated with peritoneal dialysis until graft function start. One patient had a pyocianc tunellitis infection secondary to strong neutropenia caused by mycophenolate mofetil. This patient whom underwent hemodialysis is on a central venous catheter. No infectious or mechanical complication is noted for the others patients. The mean creatinemia level for the 4 patients transplanted successfully was 154 $\mu\text{mol/l}$ [110–190 mol/l] at 12 months after renal transplantation.

Conclusion: This study highlights for the first time the efficacy and the safety of the use of PD early after delayed graft function in renal transplantation from NHBD. For the successful result of this replacement therapy, experimented nurses are highly recommended.

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EFFICACY AND SAFETY OF GASTRIC BALLOON IN OBESE PATIENTS CANDIDATES TO RENAL TRANSPLANTATION

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Background: The number of obese patients candidates to a renal transplantation are considerably increased. The complications in immediate post transplantation are more severe and frequent. The weight loss is often difficult with a simple dietary. We have studied the efficacy and tolerance of intragastric balloon in obese patients which are dialyzed and candidates to a renal transplantation.

Patients and Methods: Obese patients (BMI >30 kg/m²) candidates to a renal transplantation are included prospectively between 2010 and 2012. The placing and the removal of the balloon are realized during a gastric endoscopy with general anesthesia. The period of the treatment was 6 months. The end point was the decrease of BMI after 6 months. Impedancemetry, homa-test, nutritional statute, quality of life have been evaluated initially and after the removal of the gastric balloon.

Results: Of 17 (nine females and eight males) with a median age of 53 years [40–72] have been included. The diminution of body mass index (BMI) during

the 6 months was 4 kg/m² (37 vs. 33 kg/m²). The mean weight loss was 7 kg. The tolerance was good without complication. The analysis of the other parameters is in process.

Conclusion: The efficacy of the gastric balloon in dialyzed patients candidates to a renal transplantation is similar at this of obese patient without renal failure. The safety is well. The weight loss is variable. BIG in obese patient candidates to renal transplantation can be use efficacy and safety.

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IVIG IN KIDNEY AND HEART TRANSPLANTATION: A FRENCH NATIONAL SURVEY

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Introduction: Intravenous immunoglobulin (IVIG) are increasingly used for controlling patients' immune response in kidney or heart transplantation to achieve desensitization, or for prophylaxis/treatment of humoral acute rejection (HAR). In France, little is known about the management of renal and heart transplant patients treated by IVIG. A French national survey aimed to identify indications requiring treatment with IVIG in transplant recipients and to evaluate management of these patients in each indication.

Methods: Of 28 kidney and 16 heart transplant centers (76% of French centers) participated to face-to-face interviews between November 2011 and April 2012.

Results: The number of highly sensitized patients increased between 2009 and 2011: 168% in heart centers and 162% in kidney centers.

The set up of a HAR treatment remained stable between 2009 and 2011, the majority of them using the association of IVIG, plasma exchanges and rituximab (PHRC RITUX-ERA).

Desensitization protocol is rarely used in cardiology compares to nephrology.

Prophylaxis increased between 2009 and 2011.

Prophylaxis protocol	Kidney (19 centers)	Heart (7 centers)
Plasmapheresis alone	26%	14%
Plasmapheresis+IVIG	11%	29%
Plasmapheresis+IVIG+rituximab	16%	14%
IVIG alone	68%	57%
IVIG+rituximab	21%	14%

Conclusion: Heterogeneity of therapeutic care in transplantation underlines the need for further studies and for joint recommendations.