Selected Abstracts Presented at the 13th International Congress of Iranian Organ Transplantation Society (IRSOT)

Bedside Diagnosis of Lymphorrhea in Kidney Transplantation

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Background: Lymphorrhea and lymphocele are the common surgical complications of kidney transplantation that sometimes cause significant effects on the allograft kidney function. Lymphorrhea is diagnosed by comparing the creatinine and urea levels in discharged fluid from the wound, serum and urine samples, because urine is the single fluid that may be mistaken for lymphorrhea.

Objective: To assess a method with for bedside diagnosis of lymphorrhea.

Methods: 25 kidney transplant recipients operated in Kidney Transplant Ward, Imam Hospital, between 2001 and 2013 who had post-operative drainage of fluid through the inserted drain catheter were studied. The patients consisted of 15 males and 10 females aged between 14 and 62 years. To determine the nature of the discharged fluid, creatinine and urea of three samples of discharged fluid and serum and urine were measured and compared with each together. All of the patients were given 100 mg phenazopyridine (pyridium). Therefore if the color of the discharged fluid was changed, we considered it urine leakage.

Results: In 5 of 25 cases (those with urine leakage) the amount of creatinine and urea in the discharged fluid were near to those in the urine samples, while they were very different with those in serum. Furthermore, the color of urine and discharged fluid changed to deep yellow (for consumption of phenazopyridine), which reflects urine leakage. In the remaining 20 cases with lymphorrhea, while the amount of creatinine and urea of the discharged fluid and serum were almost similar they were significantly different from those in urine samples. Moreover, the color of discharged fluid did not change to deep yellow as it did in urine.

Conclusion: Administration of phenazopyridine is an alternative bedside diagnostic tool for lymphorrhea in kidney transplant recipients.

Effects of High-dose Anti-thymocyte Globulin on Blood Profile, CMV Infection, and Graft Rejection Rate in Kidney Transplant Recipients

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Background: There are controversial reports on the role of anti-thymocyte globulin (ATG-F) induction therapy in early and late functionality and performance of kidney transplant.

Objective: To evaluate the functionality and graft rejection rate in kidney transplant recipients who received

ATG-F *vs* those who did not.

Methods: 265 kidney transplant recipients who received ATG-F (9 mg/kg, single dose) during 2010–2012 were studied enrolled in this study. A group of patients who did not receive ATG-F and had complete follow-up for 3 months were served as the control group. Complete blood count and CMV screening had been performed for these patients monthly for 3 months. The two studied groups were compared for the occurrence of CMV infection, thrombocytopenia, leukopenia and frequency of early and delayed graft rejection.

Results: There were no significant differences between the two groups in terms of age and sex ratio. The mean±SD hemoglobin level was 9.8±2 g/dL in the case and 9.5±1.9 g/dL in the control group ($p>0.05$). The mean±SD WBC count was $10±4.5×10^3/\mu L$ in ATG-F group and $9.9±4.7×10^3/\mu L$ in the control group ($p>0.05$). The mean±SD platelet count was $220.1±67.7×10^3/\mu L$ and $214.1±97.4×10^3/\mu L$ in the case and control groups, respectively ($p>0.05$). In ATG-F group, 12.5% developed early graft failure and 16.7% developed delayed graft failure. In contrast, 14.2% and 7.6% of patients in the control group developed early and delayed graft failure, respectively ($p<0.001$). Frequency of CMV infection in ATG-F group was significantly ($p<0.001$) lower than that in the control group. However, only patients who received ATG-F also received ganciclovir prophylaxis.

Conclusion: Considering the lower rate of early and late rejection in patients who received ATG-F, it is recommended to use high-dose ATG-F as induction therapy in our patients. This form of induction therapy is a part of standard care in many transplantation centers in order to reduce the risk of early and late graft failure.

Duct to Duct Anastomosis *vs* Roux-en-Y Hepaticojujenostomy for Biliary Reconstruction in Patients with Primary Sclerosing Cholangitis

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Background: Traditionally, Roux-en-Y hepaticojujenostomy was the method of choice for biliary reconstruction in primary sclerosing cholangitis (PSC) in patients undergoing orthotopic liver transplantation.

Objective: To compare the results of duct to duct anastomosis *vs* Roux-en-Y hepaticojujenostomy for biliary reconstruction in patients with PSC who underwent liver transplant in Shiraz Organ Transplant Center.

Methods: We reviewed records of 69 patients with PSC who underwent liver transplant. We performed duct to duct reconstruction in those patients who had a grossly normal bile duct during hepatectomy (n=29). Roux-en-Y hepaticojujenostomy was used in the remaining 40 cases. Data collected included biliary complications (leakage, stricture, stone, and cancer in the remnant bile duct), documented episodes of rejection, and morbidity.

Results: The studied patients had a mean follow-up of 27 (range: 9–46) months. In duct to duct group, 2 patients presented with anastomotic stricture and 1 developed cholangiocarcinoma in distal bile duct and underwent pancreaticoduodenectomy. In Roux-en-Y group, 5 patients developed anastomotic stricture in the follow-up. The difference was not significant. The rate of documented episodes of rejection was similar in the two groups ($p=0.66$).

Conclusion: Duct to duct reconstruction is safe and can be the method of choice for biliary reconstruction in patients with PSC. Furthermore, considering the innovations in ERCP, management of strictures in duct to duct group can be easier and more feasible in comparison to revision of Roux-en-Y hepaticojujenostomy.

Renal Function and Regulatory T-Cell Assessment in Kidney Transplanted Patients Receiving Cyclosporine A *versus* Sirolimus after 2 Years

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Background: One way to overcome the calcineurin inhibitor (CNI)-induced nephrotoxicities and rejection events in routine immunosuppressant protocols is their replacement with mammalian target of rapamycin (mTOR) inhibitors that are not nephrotoxic and cause better tolerogenic properties.

Objective: To evaluate the conversion effects of cyclosporine A (CsA) with sirolimus (SRL) on GFR and T-regulatory (Treg) cell numbers 2 years after kidney transplantation.

Methods: 88 primary kidney recipients, all receiving clinically adjusted doses of MMF plus steroids, were randomized through adaptive method to remain on CsA (n=59) or to switch to SRL (n=29) after early phase of 3–6 months post-transplantation. GFR and 2 subsets of Tregs, $CD4^+/CD25^+/FoxP3^+$ and $CD8^+/CD28^-$ cells were counted by 3-color flow cytometry before conversion and at year 2 after transplantation.

Results: 2 years after transplantation, GFR decreased in CsA group (p=0.002). In CsA and SRL groups, 2 years after transplantation the frequency of $CD4^+/CD25^+/FoxP3^+$ (p<0.001, p=0.018, respectively) and $CD8^+/CD28^-$ (p=0.028, p<0.001, respectively) Tregs were significantly increased. At year 2 after transplantation, there was no correlation between the frequency of Treg subpopulations and various variables including GFR, Cr, ALT, AST, LDL cholesterol, biopsy proven acute rejection episodes, UTI, respiratory infection, and CMV and BK infection in each drug group. In both drug groups, the changes of $CD8^+/CD28^-$ Tregs remained significant after controlling the likely confounding effects of GFR changes, acute rejection episodes, UTI, respiratory infection, and CMV and BK infection (p=0.006).

Conclusion: Our study suggests that stable kidney recipients on maintenance SRL therapy have a high circulatory percentage of $CD4^+/CD25^+/FOXP3^+$ and $CD8^+/CD28^-$ Tregs as well as a better graft function compared with recipients on CsA. In the long run, if it be tolerated by the patient, the CNI may be replaced by an mTOR inhibitor which has been demonstrated to prevent both acute and chronic rejection and to play a pivotal role in tolerance induction.

Biliary Complications Management after Liver Transplantation

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Background: Although patient and graft survival rates have been increased, biliary complications after liver transplantation are associated with significant morbidity and mortality. There is a multidisciplinary approach to solve this problem.

Objective: We reviewed our experience in management of biliary complications after deceased donor liver transplantation in 105 patients over a 13-year period.

Methods: We reviewed records of 105 patients who underwent deceased donor liver transplantation at Nemazee Hospital, Shiraz, southern Iran, who presented with clinical or biochemical signs of biliary complications between January 2000 and September 2013. All patients presented with abnormal results on liver function tests and a variety of clinical symptoms such as fever, icter, and cholangitis. In addition, if the find-

ings of a liver biopsy were not conclusive for rejection or for recurrent HCV infection, sonography or MRCP was performed to rule out any biliary complications. If we suspected to any biliary problems, ERCP or PTC was performed for the patients. If the complication was not resolved by the above-mentioned procedures, exploration of common bile duct and Roux-en-Y choledochojejunostomy was done for the patients.

Results: Our study group comprised 105 patients; 64 (61%) men and 41 (39%) women with a mean±SD age of 33.6±14.8 (range: 3–66) years. The interval between orthotopic liver transplantation and the clinical onset of biliary complications ranged from 1 to 122 (mean±SD of 18.8±28.2) months. The most common indications for liver transplantation were cryptogenic cirrhosis (n=29), HBV-induced liver cirrhosis (n=15), primary sclerosing cholangitis (n=13), autoimmune hepatitis (n=13), and Wilson's disease (n=11). The biliary tract was reconstructed with choledochocholedochostomy (duct to duct anastomosis) in 87 (87%) and Roux-en-Y choledochojejunostomy in 13 (13%) liver transplantations. ERCP and PTC were performed in 73 (69.5%), and 25 (23.8%) suspected patients with biliary complications, respectively. Secondary operation and biliary exploration was performed in 39 (37.1%) patients. 21 (28%) of patients who underwent ERCP, and 12 (48%0 of those who underwent PTC needed biliary exploration.

Conclusion: ERCP and PTC are effective management for biliary complications after liver transplantation.

Split Liver Transplantation: Our Experience in Shiraz Organ Transplant Center

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Background: Orthotopic liver transplantation (OLT) is the only treatment modality for patients with end-stage liver disease. Because of the limited organ pool, other ways like splitting of the donated liver should be kept in mind. Split liver transplantation (SLT) has been perceived as an important strategy to increase the supply of liver grafts by creating 2 transplants from 1 allograft. The bipartition of a whole liver also carries utmost importance by increasing the available grafts for the pediatric patients, where size-matched whole liver allografts are scarce, leading to increased incidence of waiting list mortality in this group of patients. In the common approach of the split liver procedure, liver is divided into a left lateral segment graft (LLS) to be transplanted to a child and a right extended liver lobe graft for an adult recipient but liver may be split to left and right lobes. The liver can be split on the back table (*ex situ*) or in the donor hospital before the donor cross-clamp using *in situ* splitting technique The most important advantage of *in situ* splitting is to decrease the total ischemia time.

Objective: To report our experience with SLT between September 2002 and May 2013 at our center.

Methods: We analyzed the results of 115 patients who underwent SLT at our center between September 2002 and May 2013 including 55 (47%) adults and 60 (53%) children.

Results: 1-year survival of the recipients was 92%; 5-year survival was 72%. The pediatric patient survival and graft survival after 1 and 5 years were 91% and 72%, and 85% and 75%, respectively. Adult patient survival and graft survival after 1 and 5 years were 92% and 71%, and 88% and 77%, respectively. The most common causes of liver cirrhosis were cryptogenic, biliary atresia, and autoimmune hepatitis.

Conclusion: The use of split liver for adult and pediatric patients allows us to expand the cadaveric donor pool and has the potential to significantly reduce the waiting list mortality.

Predictors of Tumor Free Survival after Liver

Transplantation for Hepatocellular Carcinoma

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Objective: To identify the potential predictors of both overall survival and tumor-free survival of a cohort of 88 patients with HCC, who were treated with orthotopic liver transplantation at Shiraz Organ Transplant Center.

Methods: We preformed this retrospective study after reviewing the transplant database of all patients who underwent orthotopic liver transplantation secondary to HCC and liver cirrhosis at Nemazee Hospital, Shiraz, southern Iran, a referral organ transplant center in Iran. We performed approximately 1000 liver transplantations at Nemazee Hospital Between January 2008 and December 2013. HCC were diagnosed in 70 patients before liver transplantation and 18 at histological examination of the explanted livers (*ie*, incidental HCC). Cox regression analysis was used to identify independent factors that affected post-transplantation survival.

Results: The 5-year overall survival rate was 83%; the tumor-free survival rate was 79.5%. The overall survival of patients with incidental and non-incidental HCC were 94.4%, 80% at 5 years, respectively. Tumor-free survival of patients with incidental and non-incidental HCC were 94.4%, and 75.7% at 5 years, respectively. Independent factors for tumor recurrence in Cox regression analysis were Milan criteria, α-fetoprotein levels before operation ≤400 ng/mL, grade of tumor, age, and vascular invasion. Vascular invasion, and tumor grade were statistically significant in this analysis ($p=0.05$; OR: 5, 95% CI: 0.985–25.496; and $p<0.001$, OR: 14.4, 95% CI: 3.65–56.95, respectively).

Conclusion: Vascular invasion and tumor grade were two independent predictors for tumor-free survival after liver transplantation for HCC.

Expanding the Indications of Pancreas Transplantation Alone

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Background: Total pancreatectomy (TP) is associated with post-operative endocrine and exocrine insufficiency, steatohepatitis and potentially liver failure. Insulin therapy, in particular, requires good patient compliance, reduces patients' quality of life, and may lead to long-term diabetes-associated complications.

Objective: We reviewed the literature with regard to the potential option of pancreas transplantation alone (PTA) following TP in patients with chronic pancreatitis or benign tumors.

Methods: A Medline search (1958–2013) using the terms [Pancreas Transplantation], [Pancreas Transplantation Alone], [Total Pancreatectomy] and [Morbidity] and [Mortality], [Insulin Therapy] and [Quality of Life] was performed. Current textbooks and congress proceedings were also reviewed.

Results: The number of patients undergoing TP for benign or borderline tumors of the pancreas as well as chronic pancreatitis (rarely) is continuously increasing. Despite improvement of exogenous insulin therapy, >50% of these patients experience severe glucose control problems, which cause up to 50% long-term mortality. PTA can cure not only endocrine but also exocrine insufficiency and reduce the associated risk for

cardiac, ophthalmic and renal diseases. The 3-year graft and patient survival rates after PTA are up to 73%, and 100%, respectively.

Conclusion: PTA following TP in patients with pancreatitis or benign tumors improves the recipient's quality of life and reduces long-term mortality. This is attributed to elimination of exogenous insulin replacement, frequent daily blood glucose measurements and many of the dietary restrictions imposed after TP. Considering the amount of available organs and potential candidates, PTA can be a treatment option for patients following TP with chronic pancreatitis or benign tumors.

Renal Transplantation in HTLV-1 Recipients: a Single-Center Study

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Background: Renal transplant recipients are susceptible to viral infections because of their immunocompromised background. HTLV-1 is a retrovirus that leads to adult T-cell leukemia/lymphoma or myelopathies. Great Khorasan in northeastern Iran is an endemic region for HTLV-1, with a prevalence of 1.97%.

Objective: Considering the high prevalence of HTLV-1 infection in our region and few reports of such cases, we report our experience in these patients.

Methods: This historical cohort study was conducted in Imam Reza Hospital between May 2002 and September 2012. 14 patients with HTLV-1 infection who underwent renal transplantation (group A) were compared with 14 sex- and age-matched uninfected patients (group B). The immunosuppressive drugs were also similar in the studied groups. Patient characteristics and medical history were recorded and the outcome of renal transplantation has been followed carefully.

Results: During the mean follow-up of 4.3 (range: 1–12) years, there was only one rejection in group A and one in group B. In other patients the mean creatinine level did not have any significant difference 1, 3 and 5 years after operation. The rate of post-operative infections was similar in the two groups. One patient in group A developed urinary incontinence and gait disturbance 10 years after transplantation, which was approved to be due to HTLV-1 infection.

Conclusion: Although HTLV-1 myelopathy may likely be developed after renal transplantation, HTLV-1-positive patients can undergo renal transplantation with confidence of acceptable prognosis and minimal complications.

Outcome after Renal Transplantation in Pediatric Patients: Results of 20 Years of Experience in a Single Center

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Background: The incidence of renal failure in children under 19 years of age is almost 11 per million (US data system). In the recent years, the number of children who survive renal disease and who become candidates for renal transplantation, has been increased.

Objective: In this study we reviewed 20 years of our experience in Pediatric Renal Transplantation to determine the rate of patient morbidity and graft survival.

Methods: Of 1600 renal transplantation performed in our center between 1989 and 2010, 190 were done on children (aged 6–18 years). Causes of renal failure were neurogrnic bladder in 22, reflux nephropathy in 31, posterior urethral valve in 6, prunebelly syndrome in 2, and chronic glomerulonephritis in 65 patients. The remaining failures were of unknown etiology. 16% of kidneys were harvested from related living donors, 66% were from unrelated living donors, and 22% from cadaveric donors. Immunosuppressive therapy was given with three drugs (prednisolone, azathioprine or mycophenolate mofetil, and cyclosporine). All but 11 recipients of HLA-identical sibling, received cyclosporine. Kaplan-Meier survival analysis and long-rank test were used to assess the effect of kidney source and date of renal transplant.

Results: Immediate diuresis occurred in all grafts. Surgical complications included 2 urinary fistulae, two ureteral strictures, and 3 clinical lymphocele, which were all managed surgically. The most common causes of graft failure were chronic rejection and recurrence of primary renal disease. The graft survival rate after 1, 2, 5, 10 and 15 years were 97%, 88%, 79%, 65%, and 53%, respectively.

Conclusion: Renal transplantation in children results in improved physical growth and mental development. The rates of graft survival, chronic rejection, recurrence of primary renal disease, and medical noncompliance continue to be problematic.

Urinary Tract Infection in Renal Transplant Patients in Sina University Hospital

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Background: Renal transplantation is the treatment of choice in patients with end-stage renal disease. Urinary tract infection (UTI) is one of the most common complications after renal transplantation and has serious consequences.

Objective: To assess UTIs in renal transplant patients and evaluation of risk factors associated with post-transplantation UTI.

Methods: In this prospective study, 173 patients (48 hospitalized patients and 125 outpatients) were enrolled in this study. These renal transplant recipients were evaluated for bacterial UTI in Urology Research Center at Sina Hospital. After collecting urine samples from symptomatic and asymptomatic patients, urinalysis and colony count were performed. Identification of bacteria was performed by routine microbiological tests conducted at the Department of Pathobiology, School of Public Health, Tehran, Iran, in 2011.

Results: UTI was observed in 47 patients. The most prevalent microorganism was *Escherichia coli* in 18 (38.2%) patients. Nearly 71% of UTI cases were diagnosed during the first 3 months post-transplantation. Female gender, older age, and length of hospitalization were risk factors for UTI. Female patients were more susceptible than males (OR=2.0, p=0.047) to contract UTI. There were no significant difference between diabetes mellitus and UTI. Most of the isolated bacteria were susceptible to imipenem and resistant to tetracycline and trimethoprim+sulfamethoxazole.

Conclusion: Bacterial UTI remains the most common infectious complication in the early post-transplantation period. Antibiogram rather than empirical treatment is needed to find the best effective antibiotics. Moreover, risk factors such as female gender, older age, and length of hospitalization are predisposing factors for UTI in renal transplantation.

A Single Center Experience of 1000 Liver Transplants Using the Modified Piggyback Technique by Belghiti

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Background: Over the past 4 decades, the surgical techniques of liver transplantation (LTx) have been evolving. Among these, the modified piggyback (MPB) technique by Belghiti offers specific advantages.

Objective: To present our single-center experience with the MPB technique in 1000 cases.

Methods: Recipients' perioperative data were prospectively collected and evaluated. Post-operative and specific complications, stay in the intensive and intermediate care unit, and the mortality rate with cause of death were analyzed.

Results: Most (46%) recipients were classified as Child C. For the patients who underwent LTx for the first time, alcoholic (22%) and viral (21%) cirrhosis and hepatocellular carcinoma (15%) were the most common indications. The overall median warm ischemia time, anastomosis duration, and operative time were 47, 108, and 325 minutes, respectively. The median intra-operative blood loss was 2000 mL. A veno-venous bypass was never needed to maintain hemodynamic stability. Only in a few cases, temporary inferior vena cava clamping was necessary. Most prominent surgical complications were hemorrhage, hematoma, and wound dehiscence. Renal failure occurred in 8.1% of patients. The overall median stay in the intensive and intermediate care unit was 16 days. The mortality rates within 30 and 90 days were 6% and 14%, respectively. Only one technique-related death occurred.

Conclusion: The MPB technique by Belghiti is a feasible and simple LTx technique. The caval flow is preserved during the anhepatic phase, and this minimizes the need for venovenous bypass or portocaval shunt. This technique requires only 1 caval anastomosis, which is easy to perform with a short anhepatic phase. To minimize the risk of outflow obstruction, attention should be paid by doing a wide cavocavostomy cranially to the donor inferior vena cava in a door-lock manner. This technique can be applied in almost all patients undergoing LTx for the first time and liver retransplantation as well.