Keynote Speech

Tribute to Professor Mehmet Haberal

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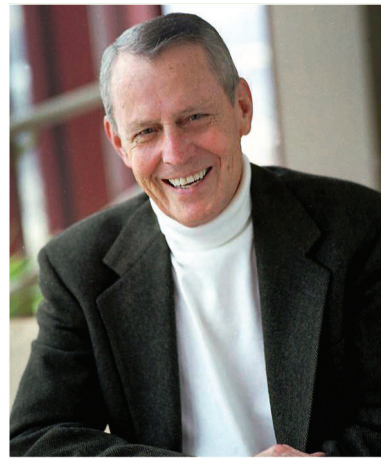

I am honored indescribably by having my name attached to this important meeting. It goes without saying that the primary purpose of the conference is to celebrate the Silver Anniversary of the first liver transplantation in Turkey. It was, in fact, the first such operation in the Middle East and portions of adjacent Eastern Europe, Asia, and Africa.

Because of the importance of this milestone, it is appropriate to ask who made it possible, and how. The person was a truly exceptional young man who joined my transplant program at the University of Colorado almost 40 years ago with the specific intention of bringing back to his beloved country a new technology that did not exist there.

Dr. Haberal had a list of steps that had to be taken before reaching his ultimate objective of liver replacement. The first was effective treatment of end stage kidney disease with dialysis and kidney transplantation. Within little more than a year after returning home, Mehmet had founded the beginning of a network of dialysis centers and begun the kidney trail that eventually led to his historical liver operation on December 8, 1988.

The presence in Turkey of the young superstar did not go unnoticed. Mehmet's presence at medical meetings brought distinction and international respect for his country. For the record, he is the only Turkish citizen ever to be elected as an Honorary Foreign Member of the prestigious American Surgical Association, and the even more elite Institute of Medicine of the United States National Academy of Science.

Professor Haberal's instincts always were those of an educator. Between 1982 and the summer of 2007, I made 5 visits to Turkey. During that quarter century, I saw the birth and growth of one of the country's finest universities in which medicine was only one of the disciplines. It was an accomplishment that I look back at, even now, as nearly miraculous.

Along the way, Mehmet founded the Turkish Transplantation Society, the Middle East Society for Organ Transplantation (MESOT), and the new journal, Experimental and Clinical Transplantation - the official organ of MESOT. It was during this rich and productive period of his life that Mehmet started his liver transplant program on December 8, 1988.

It is interesting to reflect on the status of liver transplantation at that time. There only had been about 2000 liver transplants done in the world. Objectives that had been accomplished included better control of blood coagulation, better means of liver preservation, a more thorough understanding of infections, and guidelines for the use of veno-venous bypasses.

The most important advances up to 1988 had been with immunosuppression. While it was true that liver transplantation with survival for at least one year was first accomplished in July 1967, the one year survival was too poor to allow liver replacement to be viewed as a service. Thus, liver transplantation had reached the status of "feasible but impractical".

Although the one year survival never rose above the 50% level, the continued existence of liver recipients who had reached this milestone and remained alive was a constant reminder of the operation's potential value. Four of these pioneer patients, all treated in Colorado while Mehmet Haberal was working there, have now born their hepatic allografts for 40 to 44 years. These are the longest-surviving liver recipients in the world.

As of 1980, 4 new liver transplant centers had been added to our original one in Denver. All of the new ones were in Europe: the center founded in Cambridge, England by Roy Calne, followed in succession by the Paris program of Henri Bismuth, the Hannover, Germany center of Rudolf Pichlmayr, and the Dutch center of Rudi Krom. Most of the policies of liver transplantation that exist today were developed by the transatlantic alliance of the 5 centers.

The seemingly grim future of liver transplantation dramatically changed with the arrival of cyclosporine. When we combined cyclosporine with prednisone, our one year survival rose to 80%. Liver transplantation had now become a "clinical service" rather than an experimental procedure. In a 17-page article that I published in The New England Journal of Medicine in October 1989, the text began with the following statement:

"The conceptual appeal of liver transplantation is so great that the procedure may come to mind as a last resort for virtually every patient with lethal hepatic disease." It was already evident that there would be a large disparity between the availability of, and demand for, livers. Discussions and disputes now centered around the most efficient and fair way to allocate the organs.

Meanwhile, we had set in motion preclinical studies of tacrolimus in Pittsburgh that led to its substitution for cyclosporine and fast-track FDA approval. With tacrolimus, there were further improvements in survival with liver and ultimately all kinds of organ transplantation. In addition, procedures that included the intestine, or consisted of intestine-alone, were elevated by tacrolimus to the status of "clinical service". The world's longest surviving multivisceral recipient, now a school teacher, is 24 years post-transplantation.

There is little point in going into more detail about the problems and progress of organ transplantation overall or those of the liver specifically. These issues make up much of the fine program that will begin as soon as I am finished. Suffice it to say, an early start was given to Turkey and to the Middle East generally by Mehmet Haberal's historical case.

LI

Honoring Courage and Dedication: The Legend of Prof. Thomas E. Starzl

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Of all the branches of medicine, transplantation, since its first inception as a simple idea, has aroused some of the most controversy. The issues are tied deeply with ethical and moral concerns often grounded in religious and cultural beliefs and, dare I say, prejudices.

The first physicians and surgeons to begin experimenting with transplantation faced the derision of many, often accused of having "God complexes" and meddling with nature in a manner more suited for science-fiction novels and movies. It is true, many patients could not be saved and many methods were tried and discarded before success was achieved. Thomas Starzl faced this and more in his quest to follow a "hunch." Dedicating much of his research to the liver, he believed that there was a way to perform the elusive transplant – elusive, as it had never been performed with any organ in any living species to date.

In their attempt to discover the intricacies of the field, Starzl and his team performed the first series of successful kidney transplants in the world. However, the success of the kidney could not be replicated in the liver. Losing a patient is always a source of pain for a surgeon, and eventually the program was stopped. But an inquisitive mind cannot be reined and back to the drawing board they went. Starzl believed in what he was doing, in the possibilities offered by successful liver transplantation, and his successful attempts with dogs gave him the confidence to turn down prestigious positions and dedicate himself to the liver.

His previous failures were, in his own words, "a scar to be removed" and what a fine excision it was! Starzl and his team performed that first successful liver transplant in 1967. A seemingly impassable mountain revealed a pathway – though rocky, it was a route to take and to lay paving stones for those who followed. I was one who followed. I remember my time in Colorado from January 1974-June 1975 studying with Starzl, learning his techniques and the treatments available, and feeling the exhilaration of success and the grave disappointment of a failure. I too chose this path and fought my own battles on my return to Turkey. With Thomas Starzl as my guide and my inspiration, I too fought against my opponents and circumstances to finally succeed, and to give life to those who had lost all hope of one.

The countless lives saved are testament to the miracles borne out of the desire to succeed. Starzl's achievements did not only benefit those suffering from liver failure, but many other patients requiring transplants of other organs. He taught others, like me, who in turn passed on the constant accumulation of knowledge to their own students. Several generations of surgeons will continue to benefit from Starzl's inquisitive mind and determination. It is not a secret that the world owes him some of the best doctors the profession has to offer.

Today, the controversies continue, regarding patient choice, treatment options, organ donation, transplant tourism… the list can go on for as long as you choose. It seems to be woven into the very fabric of transplantation on every level, whether scientific, social or economic. The physicians that are active in the field or newly entering it will continue to face many adversities, yet they are lucky – few other fields are so thoroughly defended; in fact many of our colleagues here today are dedicated to ensuring the ethical execution of every aspect of transplantation. And of course, we must never forget that the example that has been set by their predecessors, legends and pioneers with a vision and a steel will. They are the Starzl's of our profession, fighting against the current to extend the horizon for us, for their patients, for mankind everywhere.

The risks a surgeon must take are great, for the results may often be fatal. It takes courage and determination indeed to weather such storms, to stand tall in the face of hostility and adversity and to persevere. Such a man is Thomas Starzl, and we must celebrate such mean and women who change the world with their dedication. It is a privilege for me to have this opportunity to honor Prof. Starzl and it shall always remain a great source of pride for me to call him a teacher, a mentor, and a true friend.

L2
Liver Transplantation: Past, Present and Future

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Although experimental attempts at most solid organ transplants can be traced to the early 1900s, experimental liver transplantation was not performed until 1952 when Vittorio Staudacher performed an orthotopic liver transplant in a dog model. In 1963, Thomas Starzl performed the 1st human orthotopic liver transplant. Although this patient died, Dr. Starzl was successful in transplanting a young child in 1967 who lived over one year. Although several other surgeons including professors Calne, Bismuth and Pichlmayr in the late 1960s through the late 1970s had modest success in liver transplantation, it was not till the discovery and use of calcineurin inhibitor immunosuppression in the late 1970s-early 1980s that liver transplantation was considered a justifiable and truly therapeutic treatment for patients with end stage liver disease.

As an example, in 1984 there were 5 liver transplant centers in the US, while today, there are over 130. With the development and standardization of surgical techniques, organized organ procurement strategies and teams, improved organ preservation, as well as immunosuppression protocols, liver transplantation has become universally accepted as the definitive therapy for patients suffering from liver failure of all causes.

Today in most experienced centers, liver transplantation results in approximately 85%, 75% and 60% 1, 5, and 20 year patient survival. In general pediatric patients fare better than adults and even the sickest patients, with MELD scores of 40 or greater can achieve a better than 70% long term survival. Despite these amazing results of long term survival in patients with end stage liver disease or primary hepatocellular carcinoma, complications with immunosuppression and recurrent disease continue to remain problematic.

In the future these are the major goods which need to be addressed:

1. To improve the organ donor shortage by providing means to decrease ischemia reperfusion injury and thus increase the donor pool.
2. Continued refinement of living donor liver grafting to improve recipient outcomes and to assure maximal donor safety.
3. To find novel ways to reduce recurrence of hepatitis C, which is the number one indication for liver transplantation in the US.
4. To develop new ways to characterize tumor biology in patients with HCC to better determine their risk of recurrence after liver transplantation besides sole reliance on tumor size and number.

L3
Starzl's Heritage or 50 Years of Liver Transplantation

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The first liver transplantation (LT) has been performed by T.E. STARZL in March 1963. All different difficulties encountered to develop this "impossible operation" were made very clear by the fact that only 540 liver transplantations were performed worldwide during the period 1963-1983. The results of this rather small experience were finally the subject of the 1983 -NIH consensus conference (CC) on liver transplantation. This CC stated that LT could once become a valid therapeutic alternative for patients presenting with end-stage liver disease. After the introduction of the new immunosuppressive drug, Cyclosporine, in the eighties LT became more and more practiced all over the world. Most surgical groups performing this operation were trained by Professor STARZL himself first in Denver and later on in Pittsburgh. The CC identified five relative and ten absolute contraindications to LT as well as the profile of the "ideal" recipient to be 'submitted' to such an important surgical and medical undertaking.

This lecture will highlight all the progresses that have been made during 50 years. In fact, all relative and all, but one, absolute contraindications to LT have nowadays being eliminated. LT can be done successfully in nearly all patients presenting acute and chronic liver failure.

The very good early results obtained nowadays after LT, have shifted the attention of the transplant teams not only to the long term survival but even more to the quality of life.

Further improvement of results will most likely be linked more and more to a reduction of immunosuppressive therapies which are still the main culprits of many (lethal) cardiovascular, infectious and malignant tumor complications.

The lecture will give an overview of the huge progresses that have been made during half-century in the field of liver transplantation and hepatotology.

L4

The Legacy of Dr. Thomas Starzl in New Zealand

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Background: One of Dr Starzl's early transplant fellows in Denver, CO was Dr Ruud Krom from the Netherlands. Dr Krom returned to his homeland and established a liver transplant program in Groningen. The results were excellent, even without the availability of calcineurin inhibitors, and Dr Krom was recruited to the Mayo Clinic in Rochester, MN in 1985 where he established a second successful program. I was a transplant surgical fellow at Mayo from 1986 and was on staff at Mayo until 1997 when I returned to set up a liver transplant unit in Auckland, New Zealand (NZ). The population of NZ is only 4.2 million and there is only one liver transplant unit located at Auckland City Hospital.

Materials and Methods: The NZ Liver Transplant Unit database was reviewed and the data collected on the first 514 patients was collated for this report. The period of time over which these transplants were performed was from February 1998 to December 2012. Descriptive statistics were used to describe patient demographics and outcomes.

Results: 922 adult and paediatric patients were assessed for transplantation of which 680 (74%) were listed. Of these 514 (76%) were transplanted, 22 (3%) were waiting and 144 (21%) were delisted (105 [73%] for deterioration). Most patients received deceased donor livers but 12.5% received living donor liver segments. Adults were transplanted most frequently for viral hepatitis (HBV and HCV) with or without hepatocellular carcinoma and most children were transplanted for biliary atresia. Transplant procedures have taken an average of 6 hours and average length of hospital stay has been 14 days for adults and 25 days for children. Overall patient survival following liver transplantation at 1, 5 and 10 years is 96%, 89% and 81%. Re-transplantation has been required in 3.4% of patients. Average waiting time for a transplant has increased from 44 days in 1998 to 213 days in 2012. This is a result of the growing waiting list and a shortage of deceased donor organs. NZ has, on average, only 10 deceased donors per million of population per year which presents a significant challenge given the demand for organs. NZ has a socialized medical system and therefore all the costs associated with the transplant including patient assessment, transport, accommodation, transplant surgery, post-transplant cares (including immunosuppressive drugs) are covered by public health funding.

Summary: The important Hippocratic principle of training younger doctors has been applied in the liver transplant arena. The world-wide influence of Dr Tom Starzl's pioneering efforts continues to be seen, even at the 'ends of the earth'. Excellent results can be achieved even in small volume liver transplant programs provided careful attention is given to both surgical and medical details as advocated by Dr Starzl.

L5

Progress of Pediatric Liver Transplantation in Japan

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Introduction: The Japanese liver transplantation society (JLTS), a cooperative research consortium, was established in 1980, in order to characterize and follow trends in patients and graft survival in all liver transplants in Japan. This study analyzes comprehensive factors that may influence outcome of pediatric patients who underwent LDLT in largest cohort in the world.

Methods: Between November 1989 and December 2010, 2224 patients received LDLT in Japan. The survival of each of the donor and recipient variants were evaluated.

Results: There were 998 male (44.9%) and 1,226 female donors (55.1%) with a median age of 35.2 years (range: 17~70 years) and body weight of 59 kg (range: 36~103kg). There was no donor mortality related to the surgery. There were 946 male (42.5%) and 1,278 female (57.5%) recipients with a median age of the recipient of 4.0 years (range;13 days~17.9 years) and body weight of 16.6kg (range:2.6~90kg). Cholestatic liver disease was the leading indication for LDLT (n=1,649; 76.2%), following metabolic disorders (n=194; 8.7%), acute liver failure (n=192; 8.6%), and neoplastic liver disease (n=66; 3.0%). The 1/ 5/ 10/ 20 year patient survival were 88.3/ 85.4/ 82.8/ 79.6%. Blood type incompatibility, recipient age, etiology of liver disease and transplant era were significant predictors for overall survival.

Conclusons: We conclude that pediatric LDLT is a safe and an effective treatment modality without compromising live donors. The significant factors affecting survival could be overcome by technical and immunological refinements in recent years.

Lecture

L6

High Volume of Living Donor Liver Transplant Without Deceased Donor Backup: Outcomes, Insight and Lessons To Be Learned

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Introduction: Living donor liver transplantation (LDLT) is a well established and acceptable therapeutic modality for end stage liver diseases especially in countries like Egypt where transplantation from a deceased donor is not a viable alternative. We present the outcomes of 1905 LDLT cases from the Egyptian registry performed in eleven years and discuss the lessons learned from our collectible experience.

Methods: Between August 2001 to December 2012, 1905 LDLT cases were performed in ten centers, adults represented 93.5% (1781 patients, mean age 53.65 years) while 124 (6.5%) were pediatrics cases (mean age 7.7 years). The main indication for LDLT in adults was HCV cirrhosis (92%, with or without hepatocellular carcinoma [HCC]) with a mean MELD score of 18. HCC cases were 450 (27%) and 86% of them were within Milan criteria. Down staging was performed in 42 cases (12%) either by liver resection, radiofrequency ablation and/or trans-arterial chemo-embolization (TACE). The main indication in the pediatric was biliary atresia (52%). A single pediatric case with central hepatoblastoma received LDLT and chemotherapy.

Results: Operative mortality occurred in 22 recipients (1%). Donor mortality occurred in four donors (0.21%); the first died3 months post donation due to biliary leak followed by severe infection, septicemia and multi organ failure, the 2nd died 12 days after donation due to portal vein thrombosis, in the3rd donor mortality occurred due to right sub-clavian artery injury during central line insertion with massive hemo-thorax and the 4th died one month after donation due to hepatic insufficiency and hepatic failure Major morbidity: Hepatic insufficiency and LDLT was done after 4 weeks post donation. In the adult recipients mortality was 31.4% versus 22.7% for the pediatrics. Biliary complications occurred in 24.7% and clinical HCV recurrence was 11% requiring anti-viral treatment. In adult recipients with HCC, first year recurrence was 10%, 3 years recurrence was 15%. Five year survival was 58% and the mortality rate due to tumor recurrence was 13.6%. The hepatoblastoma case has been doing well for the last 8 years with no recurrence.

Lessons learned from our collectible experience.

1. Assessment of CT arteriography, portography and MRCP for all donors for anatomical variations. Exclusion of donors if the graft includes more than 3 ducts. This because of the problems of high incidence of biliary complications and its impact on the results. Increased incidence graft congestion and failure due to increase number of hepatic veins (V5and V8).
2. Liver biopsy for all donors, and the remaining liver volume not less than 35% because, abundance of donor operation (12cases) due to liver quality. Also because of the prevalence of liver diseases, donor mortality and major morbidity that leads to Hepatic insufficiency and LDLT for a donor 4 weeks post donation.
3. Age limit of the recipients Males 65years females 60 years.
4. Recipients having HCC must be within Milan criteria.

Conclusion: LDLT is a potentially safe procedure especially when cadaveric liver transplantation is unavailable in countries like Egypt. The long term survival and disease free survival rate in patients with HCC transplanted by LDLT is comparable to those using diseased donors. Although LDLT had reasonable outcomes; yet, it carries considerable risks to healthy donors, lacks cadaveric back up and is not feasible for all patients.

L7

Organ Transplantation Services Organization in Jordan: International, Regional Support and Cooperation

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Jordan is one of the countries in the region who started organs transplantation activity in the early seventeen's of past century where is first kidney transplant done 1972.

Legislation (Utilization of organs and tissues of the human body Law) was issued in Jordan in 1977, and in 2000 Instructions of organs and tissues Transplantation of the human body was issued.

First liver transplant program started in the Royal Medical Services with the support of Turkey June 2004, where is the liver transplant program in the Private sector started later in the same year in cooperation with France and Germany.

After several visits of Prof. Mehmet Haberal to Jordan Organ transplant program started in Ministry of Health institutions in 2007 where first kidney transplant done with the support of Baskent University –Ankara- Turkey.

Executive program for cooperation in the field of organ donation and transplantation between the Ministry of Health in Saudi Arabia and in Jordan was signed in Jan 2010, and in Apr. 2010 the Jordanian Center of Organ Transplant Directorate at (Ministry of Health) for the organization of the transplant services in the country was established which started functioning on Oct. 2011.

Sep. 2010 Twining ship was signed between Al-Bashir Hospital (Ministry of Health) Amman-Jordan and Niguarda Hospital – Milan-Italy in the field of Organ transplantation where more than 35 persons (physicians, nurses, technicians,…etc) were trained.

Sep. 2012 a Memorandum of Understanding between Jordanian Center of Organ Transplant Directorate Amman-Jordan and Center of Organ Transplantation in Moscow Russia was discussed.

With the aim of strengthening of the transplant program in MESOT countries Jordan has got two fellowships from MESOT countries in 2012.

Although many things still needed to be done especially in the field of organ donation and procurement, the above mentioned besides other factors played and playing a major role in the improvement of transplant services in the country and it can serves as an example for fruitful international and regional cooperation in the field of organ transplant services.

L8
The Impact of Living Unrelated Transplant on Establishing Deceased Donor Liver Program in Syria

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Liver transplantation is the gold standard of care in patients with end-stage liver disease. The estimated need for liver transplant in Syria is 1000 cases every year. Yet there is no liver transplantation in Syria. Traveling to Iran or Europe for a liver transplant is a luxury few Syrian can afford, not to mention the bureaucratic hurdle of obtaining governmental financial support if any.

There is currently an on-going debate on which type of donor for liver transplant shall we start with in Syria; living donor liver transplant (LDLT) versus deceased donor liver transplant (DDLT). The program should initially depend on deceased donors because a) LDLT requires good experience which is presently lacking in Syria and b) living donor partial hepatectomy carries a considerable risk of morbidity and mortality as reported by many large centers in the west

In 2003, a new national Syrian legislation was enacted and authorized the use of organs from both volunteer strangers and deceased donors. As a result, the kidney transplant rate jumped from 7 kidney transplants per million populations (pmp) in 2002 to 17 pmp in 2007. This increase was from unrelated donors. Regrettably, practices have developed that have gone beyond the limits of ethical and legal acceptability. Under-the-table payments by the recipient family to the vendor's broker are customary and well known. This model is considered to be in violation of the Istanbul Declaration. Paid kidney donation has increased from none in 2002 to about 70% of total transplants in year 2010 as poverty makes this option attractive

Starting an unrelated kidney donor program in Syria has decreased the urge or need to start a deceased donor program as most patients manage to buy kidneys rather than wait for a deceased donor and also economically is more attractive for the state. In such a scenario, many transplant physicians would favor unrelated donation which is less expensive and readily available with better outcome over deceased program. Furthermore, the health authorities remain silent on "organ selling practices" which saves them money spent on dialysis. Consequently, the reputation of transplantation has been tarnished making it difficult to gain the trust of the public to donate after death. The interest in deceased donation has been negatively affected by that systematic approach to use the poor people as the source of organ. As a result, ten years after the enactment of the 2003' law that permits retrieval of organs from deceased, there is no deceased donor program in Syria.

This lack of interest has affected starting the liver program which relies on deceased donation especially that the need for kidneys is more than livers.

In addition there is a concern that an unrelated living donor liver program might lead to death of many donors who will be coerced in donation by poverty. Therefore, the transplantation society and the transplant community have to define how much risk we are willing to accept in LDLT for both donor and recipient.

Conclusion: Paid kidney donation in actual effect becomes a hindrance to establishing deceased liver donation, as it decreases the urge to start a deceased program and tarnishes the reputation of transplantation.

Lecture

L9
Immunology of Liver Transplantation

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The past four decades have observed the evolution of liver transplantation research procedures, and as they had witnessed a high mortality and morbidity they now serve as a successful therapeutic measure for end-stage liver disease.At the present time, one year and five years survival for elective cases are often in excess of 85%-88% and 70%-75% and with an excellent quality of life. Compared with other solid-organ transplants, liver allografts have long been considered to be immunologically privileged, as manifest by an absence of hyperacute rejection despite a positive T cell cross-match, a low incidence of graft loss due to chronic rejection. Despite this special status, the liver can display destructive immunologic processes, since acute liver allograft rejection occurs in approximately 50% to 75% of liver transplant recipients.Immunosuppressive drugs produce significant toxic effects that increase patient morbidity and mortality. Moreover the current immunosuppressive regimens do not prevent the development of chronic rejection, which is a major cause of graft loss.

Allograft Rejection and Immunology

Related to liver transplantation, grafts mostly originate from different members of the human species. The genetically encoded immunologically mediated barrier to transplantation was recognised and defined over the course of the last century. The immunological study of transplantation has played an extremely important role in the development of clinical transplantation. The rejection mechanism is very complex and has been shown to be caused by transplantation antigens,including minor histocompatibility antigens, major histocompatibility antigens and other alloantigens .

a. Allografts and cell-mediated rejection

Antibody-mediated, hyperacute vasculitic rejection can take place in individuals with preformed antibodies against the donor's MHC class I antigens after liver transplantation. Under most other circumstances, acute allograft rejection is launched by the large number of recipient T cells that recognise donor alloantigens.Tcell-dependent pathway to rejection,graft alloantigens are processed by specialised antigen presenting cells (APCs). Acute cellular rejection is the best-characterised graft-specific form of immune rejection.

b. Allografts and humoral-mediated rejection

The production of anti-donor MHC antibodies is related with acute and chronic graft damage, usually in the form of graft vasculopathy.Donor specific antibodies can damage the graft by activating complement and mononuclear cells with Fc receptors that recognise the heavy chain of antibodies. Anti-donor antibodies can also directly inhibit signalling cascades within endothelial cells. Humoral mediated rejection of allografts is often perceive following kidney, heart and lung transplantation, but liver allografts appear to recover in relation to the development of humoral-mediated rejection.

c. Allografts and memory T cell mediated rejection

With regard to organ transplantation, upon re-exposure to donor antigens donor-reactive memory T cells are more sensitive to antigens, function more rapidly, produce effector cytokines, survive longer than naïve T cells and directly or indirectly produce cytolytic effects on the transplanted tissue.

d. Co-stimulatory pathways

T cells must receive two distinct but coordinated signals in order to achieve optimal activation. The first signal is provided by the TCR engagement with recognition of peptide/ MHC I or II on APCs, and the second signal is achieved by the interaction of costimulatory molecules on the T cells and their ligands on APCs. There are two co-stimulatory pathways that are important in the generation of a complete T cell response are CD28/B7 and CD40/CD154 in the co-stimulatory field.

The graft rejection has been divided into three groups;hyperacute ,acute and chronic rejection.Allograft rejection principal involves host-versus-graft reaction in liver transplantation,which is the rejection of the transplant by the recipient's body.

Prevention of allograft rejection

Allograft rejection is prevented by graft selection before transplantation, such as ABO blood
group and HLA matching. The majority of liver transplant centres regard blood group compatibility as the primarily immunological selection criterion. A liver from a donor with a compatible ABO and Rh blood group is easy and feasible, with well-documented reports of this being performed inurgent situations. In recent years, many transplantation centres have also carried out the operation with ABO-incompatible grafts, and the outcomes of ABO-incompatible liver transplantations have been similar to that of blood-type-matched transplantations in some centres. Retrospective data has not shown any clear survival advantages associated with good HLA matching. Interestingly, some studies suggest that there is a clear disadvantage with certain aspects of HLA-matching.Generaly,The immunological system of liver transplantation is very complex.

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L10
Operational Tolerance By a Regulatory T Cell-Based Cell Therapy in Living Liver Transplantation: A Preliminary Report

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Background: Liver transplantation (LT) has become an accepted modality for the treatment of patients with end-stage liver failure. However, a life-long intake of immunosuppressants (IS) to prevent rejection always accompanies immunological and non-immunological risks. Freedom of the recipients from these problems, e.g. Operational Tolerance (OT), has been an ultimate goal in LT.

Objects: To determine whether a regulatory T cell (Treg)-based cell therapy afford OT in living donor LT (LDLT).

Materials and Methods: Consecutive 10 adult patients underwent LDLT. Indications were HCV, HCC, alcohol, PBC, PSC and NASH. Peripheral blood mononuclear cells (PBMNs) were collected from both donor and recipient by leukapheresis and Tregs were expanded ex vivo by a 2-week culture of recipient PBMNs with irradiated donor PBMNs under the presence of anti-CD80/anti-CD86 mAbs. They were infused into the recipient on postoperative day (POD) 13. Cyclophosphmide (CP) was given on POD5, and steroids and MMF were stopped within one month, while the patients were left on culcineurin inhibitor (CI) monotherapy. At 6 months after LDLT, when graft function and histology were normal, CI was gradually tapered by spaced doses until it was discontinued 12 months later.

Results: Results were shown below. Of the 10 recipients, 5 are free from IS for 1 month to 10 months, 3 are under smooth weaning processes, and the other 2 resume low dose CI monotherapy. All of them have normal liver function without histological evidence of rejection. Of the expanded cells by the culture, Tregs were found as a major cell type with suppressive function. Although they were supposed to have specificity against donor antigen, serial tests of mixed lymphocyte reaction (MLR) using recipient PBMNs revealed no consistency, indicating OT by Treg suppression is not systemic event, rather it is local.

Conclusion: A preliminary results of our experience suggest that OT in LT is approaching a clinical reality by a Treg-based cell therapy. The protocol is safe and promising not only in LDLT but also for diseased donor LT.

Case	CP[1](mg/kg)	Infused cells Total ($x10^8$)	Infused cells $CD4^+CD25^+$ $Foxp3^+$ ($x10^7$)	Days after LDLT[2]	IS at present[2](trough level: ng/ml)	LFTs[2]:AST/ALT/γGTP(IU/L)	Time off IS[2]	Remarks
#1	50	6.1	3.1	920	**off**	29/18/14	**10mos**	CMV Hepatitis (POD 35)
#2	50	25.4	46.6	843	**off**	29/29/13	**10mos**	Graft MHV thrombus (POD 608)
#3	30	7.9	9.4	815	**off**	25/27/77	**9 mos**	FK neurotoxicity (POD 14) CsA conversion
#4	40	24.5	44.1	710	**off**	10/8/9	**6mos**	-
#5	40	6.3	4.3	626	**FK 4 mg/d (6.9)**	21/10/19	-	Mild ACR during IS weaning (POD 394)
#6	40	11.8	27.2	584	**CsA 75 mg, x3/wk (40) + PSL 2.5 mg/d**	34/29/20	-	Brachial plexus neuritis (POD 206) →CsA conversion + PSL
#7	40	25.9	31.8	563	**off**	27/22/28	**1 mos**	-
#8	40	7.0	30.4	486	**CsA 75 mg, x2/wk (53.8)**	19/18/15	-	-
#9	40	5.9	3.3	423	**FK 4 mg/d (3.9)**	19/12/38	-	Mild ACR during IS weaning (POD 365)
#10	40	12.0	28.9	328	**FK 2 mg, x3/wk (<1.5)**	25/19/16	-	-

[1]CP: Cyclophosphamide
[2]Data collected on July 7, 2013

Lecture

L11
Aspects of Liver Transplant Tolerance

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The liver is recognized to be the most "tolerogenic organ". Liver transplants are always accepted in mouse models and in some rat strains across complete MHC mismatches and in some outbred pigs. Transplantation of the liver in some rat strains can prevent rejection of skin, heart and kidney allografts and can in fact turn off an ongoing rejection episode. In humans antibody rejection is rare and it is recognized that chronic rejection is uncommon and some patients can accept allografts long term without immunosuppression. It is clear that tolerance in humans can be observed if bone marrow chimerism becomes established but this is rare. In the absence of chimerism it is best to think of liver tolerance as two separate but possibly linked processes namely the induction phase followed by a maintenance phase .It is know from experiments in our group and those of others that the induction of liver tolerance versus rejection occurs in the first week of transplantation. (1)During this phase liver transplantation is not due to Tregs as tolerance at this stage can not be transferred by recipient splenocytes. In fact liver transplantation tolerance during this phase is an active deletion process whereby there is an actual allograft "rejection" episode that does not lead to full blown rejection but tolerance. This process requires two mechanisms 1) Donor leucocytes leaving the allograft and activating recipient CD8 T cells in systemic lymphoid tissues but triggering their deletion; 2) Recipient CD8 cells entering the allograft, either as naïve T cells or as activated cells from systemic lymphoid tissue. These cells are partially activated but do not form CTLs .They are eliminated within the allograft by suicidal emperipolesis (hepatocyte induced degradation) or Bim dependent cell death. These processes combine and lead to effect early deletion of the CD 8 allograft response and hence tolerance and acceptance of the liver allograft.

Following acceptance of the allograft tolerance to other allografts (skin, heart kidney) also occurs and by 100 days in the rat this tolerance is then transferable by recipient splenocytes (Tregs).Thus the maintenance phase mechanisms seem quite different to the early induction phase although CD 8 T cell deletion may still occur. This maintenance phase has now been studied in humans where about 5% of adults can been seen as tolerant from the ITT perspective post transplant. If patients are highly selected by successful weaning before the withdrawal of immunosuppression then about 20-23 % of adults and perhaps up to 40% of children can be defined as tolerant (i.e. no allograft rejection when immunosuppression is withdrawn: so called Prope Tolerance)

These patients have been studied for gene signatures in PBLs and within the allograft itself that may identify tolerance before IS withdrawal. Groups in the USA and Europe have defined gene signatures enriched for Tregs, Gamma/ Delta T cells and NK cells in the tolerance signature (2,3).One group has identified a 3 gene signature in PBLs from children that may define tolerance (3).These signatures define patients many years (> 5 Years) who may be tolerant. Challenges occur in identifying similar patterns in additional cohorts and in studying the timing of the onset of these signatures i.e. how early do they develop and what is their link to the early induction phase in experimental animals but not yet studied in humans. There are exciting times ahead in meeting these challenges.

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L12
Can We Achieve Tolerance for All Transplant Recipients?

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Short-term results following organ transplantation have been significantly improved by the use of increasingly efficacious immunosuppressive agents. However, their chronic use results in significant morbidity, especially from an increased incidence of cardiovascular disease, infection, malignancies, de novo diabetes and other metabolic derangements. Additionally, the potent immunomodulatory effects of current therapeutic protocols do not prevent the development of chronic rejection, despite their administration being pushed to toxic levels. Therefore, induction of tolerance, defined as the absence of destructive immune responses to a transplanted tissue without ongoing immunosuppressive therapy, remains the ultimate goal of organ transplantation.

Since the seminal work reported by Billingham, Brent and Medawar on neonatal tolerance in 1956, numerous tolerance induction strategies have been identified in

rodents. However, only a very limited number of these have been successfully translated to large animals and even fewer to primates. Among the few protocols that have been applied in humans, induction of donor chimerism, either transient or permanent, currently appears to be the most promising strategy to achieve renal allograft tolerance. Initial results of clinical trials for tolerance induction in three centers have so far been reported.

Using TLI and DBMT, the Stanford group has reported successful induction of stable chimerism and renal allograft tolerance in HLA identical kidney transplant recipients. Extension of this approach to recipients of HLA-mismatched renal allografts has not yet been reported. More recently, the Northwestern group has reported the use of a Fludarabine-based conditioning regimen, donor hematopoietic stem cells, and a unique "Facilitator Cell" for induction of tolerance in HLA-mismatched kidney transplant recipients. Although the follow-up is still brief, persistent donor chimerism without GVHD has been reported, allowing weaning from all maintenance immunosuppression in approximately half of their patients.

At Massachusetts General Hospital, based on decades-long basic studies in animal models, we have applied combined kidney and donor bone marrow transplantation (CKBMT) for induction of allograft tolerance in both HLA matched and mismatched kidney transplant recipients. Ten patients with renal failure secondary to multiple myeloma have been treated with CKBMT from HLA-matched siblings, following a nonmyeloablative preparative regimen consisting of cyclophosphamide, local thymic irradiation, ATG and a brief course of post transplant cyclosporine. All recipients developed mixed chimerism and renal allograft tolerance. Two patients have died, of recurrent myeloma, 4 and 8 years after CKBMT. The remaining 8 are alive with normal allograft function with F/U periods of up to 14 years.

Following similar conditioning, CKBMT has been performed in 10 recipients of HLA-mismatched kidney allografts. Stable renal function without immunosuppression has been achieved for periods of 2.6 – 9 years in seven of these recipients. The protocol is currently being modified in non-human primates in order to extend it to recipients of deceased donor allografts.

In conclusion, observations from three clinical trials, utilizing the mixed chimerism approach to tolerance induction, emphasize that the consistent induction of tolerance in human allograft recipients may finally be achievable.

L13
Are We Over Immunosuppressing Liver Transplant Recipients? Do We Need a Biological Marker To Monitor Over All Immunosuppression?

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Lecture

With development of newer immunosuppressing agents and using them in various combinations (poly pharmacy therapy) the rate of acute rejection currently is very low after liver transplantation. We have reported a rate of acute rejection of< 5% with use of intravenous Mycophenolate Mofetil, steroid and tacrolimus without any need of antibody preparation. Currently, the only monitoring performed is the measurement of the concentration of calcineurin inhibitor or Rapamycin when used. Monitoring of MPA levels have not found to be useful for LTx recipients. Monitoring the concentration of one medication does not reflect the overall cumulative effect on individual patient after LTx. Further more it is well known that every patient needs different amounts of immunosuppression (IS), yet we practically provide the same amount of immunosuppression to all patients. Fortunately, the rate of infection is not alarming either. However, metabolic morbidity in terms of hypertension, diabetes mellitus and impaired lipid profile and weight gains posses an additional challenge after successful LTx. Currently there is no biological monitoring with proven benefit. ImmuKnow (Cylex) assay, which measures the ATP generated by CD4 proliferation in vitro, although FDA approved, has not been useful in LTx patients.

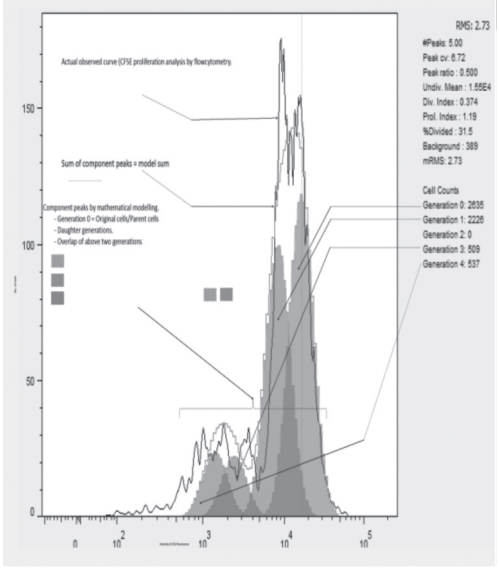
Aim of the study is to develop biomarker that can quantify the overall IS in LTx recipient.

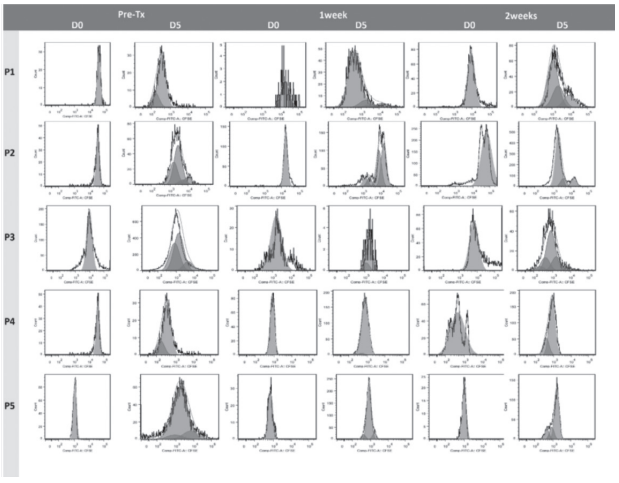
We developed ex-vivo stimulation of peripheral blood lymphocyte with CD3 and CD28 mono clonal antibodies and observed the generations of division over 7 days (figure on the left). We simultaneously compared the soluble CD30 (sCD30) and ImmuKnow values. The study was conducted just before LTx and on post-op day 2, 4, 6, 14, 21, 28, 42, 60 and 90 days. We also measured the peripheral leucocyte counts and ratio of CD4 and CD 8 counts.

Results: Preliminary results in 5 patients with 2 months of follow-up shows a diminution of division of recipient lymphocytes using CFSE stain and flowcytometry. In the figure on the right (pre LTx, one and two weeks post LTx) we see that lymphocyte proliferation slows down with duration after transplant, and more lymphocytes remain in earlier generations of division. Correlation with sCD30 and ImmuKnow are awaited.

Conclusion: Preliminary observations suggest that the test may have utility in evaluating overall immunosuppression if the generation of proliferation can be quantified. More than one modality of monitoring may be necessary to have clinical utility.

Future: In the future we are planning to measure immunologically relevant Cytokines and tissue array to identify the cytokine phenotypic and genomic differences between individuals of allo reactivity. This could improve our understanding of allogeneic response of the host to the graft with overall biological measurement of immunosuppression requirement after successful LTx.





LI4
History of Organ Transplantation

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Organ transplantation is one of the most remarkable therapeutic advances in medicine. What started as a clinical experiment is nowadays a routine life-saving and cost-effective practice that brought about remarkable evolution in several medical fields – surgery, organ preservation, immunology, immunosuppression, infectious diseases, critical care medicine. Many are the major milestones of this multidisciplinary clinical science, and the challenges that organ transplantation still faces. Among these, such issues as the shortage of organ supply, graft longevity, the development of immunologic tolerance between host and graft, but also the threath of organ traffic, the promise of xenotransplantation, and of other innovative techniques that might make traditional transplantation surgery as we know it obsolete.

Organ transplantation has always been present in the mithology of many different cultures, but it was only in the second half of the 19th century that surgeons realised that diseased tissues could be removed and replaced without risking the patient's death.

In July, 1883, Theodor Kocher transplanted thyroid tissue into a patient who had undergone radical thyroidectomy. This operation can be considered the first organ transplant of modern times.

Researchers used experimental animals under the controlled conditions of the laboratori and later began to use xenotransplants and allotransplants for treating patients.

In 1905, Alexis Carrel performed the first heart transplantation in a dog. Carrel's technique of blood vessel suture made it possible to link up transplanted organs to their vascular connections in the host organisms.

Carrel noticed that the successful transplantation between individuals was blocked by a problem that could not be solved by surgical means, and that he called biological incompatibility.

A number of researchers undertook to study the effect of the immune system on the outcome of transplanted tissues. Among these, Sir Peter Medawar, now considered the father of transplant immunology, investigated why transplanted skin grafts so often failed. The descriptions of rejection, immunological memory, and tolerance earned him the Nobel Prize in medicine in 1960.

Meanwhile, in 1954, the team led by Joseph Murray in Boston, ushered in the modern era of organ transplantation

with the first successful organ transplant between humans, a kidney transplant between two identical twins.

In December 1967, Christiaan Barnard performed the world's first human heart transplant, after having become acquainted with the technique perfectioned in the US by Norman Shumway, who had done much of the pioneering research in the field.

In the same year, Thomas E. Starzl, in Denver, performed the first successful human liver transplant, which earned him the definition of "the father of modern transplantation."

Physicians soon realized that tools were needed to prevent rejection. A dramatic change in immunosuppression came when Sir Roy Calne, drawing on laboratory work of Jean Borel, introduced cyclosporine A to clinical practice. This discovery was followed by a series of advancements including monoclonal antibodies, tacrolimus, mycophenolate mofetil, sirolimus, and polyclonal antilymphocyte preparations.

Technical avances have prompted the need for legal, ethical, and social changes. One of these was how to establish when someone was dead. The traditional concept of death as cardiopulmonary collapse became inadequate. In 1964, the concept of coma depasse was introduced, and in 1981, the Guidelines for the Determination of Death were published in the US, which declared that death was defined by the cessation of brain function.

The largest problem affecting transplantation today is the shortage of organs. Efforts are directed toward maximizing living donation. Many believe that xenotransplantation could become a reality and that the best source of potential organs would come from pigs, once hyperacute rejection is avoided. Two strategies that are also currently promising are mixed hematopoietic chimerism and costimulatory blockade.

L15
Clinical Experience in Organ Transplant; The Shiraz Transplantation Center

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The first kidney transplantation in Iran was performed in 1968 in Shiraz from living related donor, but after a short term activity and transplantation of few cases it was stopped in 1981. Kidney transplantation was started again in Tehran. Shiraz Transplanted Center (STC) was established in 1988. From the beginning we were interested in to institute a deceased donor program. In 1989 the religious permission to utilize deceased donor organs was obtained and in 2001 the brain dead law was approved by parliament. The first kidney and liver transplantation were performed in 1992 and 1993 respectively in Shiraz.

Since 2001 organ transplantation in Shiraz progressed very rapidly and till now, we have done more than 2000 liver, >3000 kidney, 150 pancreas and 25 small bowl and Multi visceral in our center.

L16
Liver Transplantation in Saudi Arabia

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The achievements of the organ transplantation program in the Kingdom of Saudi Arabia (KSA) during the year 2012 reflect the progressive success in the number of organ donation and transplantation, but with escalating numbers of end-stage organ failure patients awaiting transplantation. The estimated need for liver transplantation in Saudi Arabia is 20 per million populations per year. The KSA has an active deceased transplant program under the supervision of the Saudi Center for Organ Transplantation (SCOT). At the end of the year 2012, a total of 9451 possible deceased cases have been reported to SCOT of which 631 were reported during year 2012 from 97 intensive care units around the Kingdom. By the end of year 2012, a total of 570 living donor and 671 deceased donor liver transplantation have been performed inside the KSA of which 147 were transplanted in 4 active liver transplant centers during that year. In addition, by the end of year 2012, a total of 4852 living donor and 2349 deceased donor renal transplantation have been performed inside the KSA of which 553 were transplanted in 16 active renal transplant centers during that year. By the end of year 2012, a total of 206 deceased donor heart transplantation have been performed inside the KSA, and 540 were used as source for heart valves; 19 whole hearts were transplanted in one active heart transplant center during that year. In addition, by 2012, 70 lung transplant operations and 19 harvested pancreas were successfully transplanted. We still have much work in order to achieve the self-sufficiency of organ donation and transplantation; however, we believe that we have made major strides towards this goal in the KSA.

Lecture

L17
Twenty Eight Years of Liver Transplantation in Australia and New Zealand

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Australia and New Zealand (ANZ) are considered to be the same region for the purpose of organ allocation and data collection in the context of Liver Transplantation although funding and oversight of individual programmes remains the duty of separate state and national governments.

Between Jan 1985 and Jan 2013, 4302 orthotopic liver transplants (OLT) were performed in ANZ on 3980 patients. There were 3266 adult patients (82%) and 714 (18%) children.

In contrast to regions elsewhere in the world, the predominant source of organ donation comes from brain dead deceased donation rather than from living donors. A small but growing number of DCD donors have contributed over the last few years. An agreed priority allocation system operates between centres for urgent patients based on Kings College criteria. Allocation within individual jurisdictions largely follows MELD score. Liver splitting occurs in most centres and partial grafts are shared between programmes. Split grafts provide approximately 24% of all paediatric transplants, 45% are from other reduced size grafts including only 63 from living donors. In adult patients 245 have received reduced size grafts, 203 from splits, 29 others from reduced sized cadaveric donors and 13 from living donors.

Similar listing criteria are followed in each centre. As a result the annual waiting list mortality using "an intent to treat" basis has not exceeded 15% for adults in the last decade and it is currently <4% for children. The number of patients listed for transplantation increased slightly in 2012 and 182 patients remained on the waiting list at January 1 2013. Patient delistings due to death, becoming too ill or tumour [HCC] progression accounted for 10% of all delistings while 268 [50%] were transplanted. Thirty five patients were listed as urgent in 2012 [16 Category 1 and 19 Category 2]. Thirteen [81%] of Category 1 and 17 [89%] of Category 2 patients had a positive outcome.

Potential organ donors are voluntarily registered on a national data base in Australia and this data is accessible at any hour by local donor co-ordinators. A national authority has been set up to oversee policy and performance in relation to organ and tissue donation.

Overall 1 year patient survival of all patients is 89% at 1 year, 81% at 5 years and 72% at 10 years. Children have a significantly better survival rate than adults with an actuarial survival of 71% at 25 years post-transplant. Nine hundred and forty eight patients (25%) developed 3809 skin cancers with 555 patients having multiple skin cancer types and 29 had melanoma. The cumulative risk of developing cancer of any description post transplant is approaching 40% by 20 years.

Data provided is from the Australian and New Zealand Liver Transplant Registry's 24th annual edition which compiles and analyses the key cumulative data on every liver transplant performed in both countries since the establishment of the first liver transplant unit in the region in 1985. On-line real time data entry is via secure connection. Data is de-identified centrally and outcome comparisons are available for individual programmes versus all centres as a whole. Comparison of one centre against another is not available. Data is audited and checked for accuracy and duplication.

L18
Current Status of Liver Transplantation in Turkey

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Liver transplantation (LT) is the definitive treatment option for end-stage liver diseases. The first successful LT was performed in the US by Thomas Starzl in 1967. The first successful solid organ transplantation in our country was a living related kidney transplantation performed in 1975 by Haberal. In 1979 the Turkish parlament was enacted the law about organ transplantation with great efforts of Dr Haberal. After clinical and experimental studies the first liver transplantation in Turkey was also performed by Dr Haberal in 1988. This was also the first successful deceased-donor liver transplantation for Middle East region and North Africa. The first succesful partial living donor liver transplantation in children were performed by the same team in March 15, 1990. In April 24, 1990 Dr Haberal also performed the first successful partial living-donor liver transplantation in adult in the world. Two years later in May 16, 1992 he performed the first succesful liver and kidney transplantation from the same living donor in the world. After these pioneering efforts liver transplantation activities widened all over Turkey and liver transplantation centers reached to 30. According to data of Ministary of Health; nowadays, in our country 2065 patients are waiting for liver transplantation. Between January 2002 and June 2013, 6091 liver transplantations

were performed in Turkey. 4020 (66%) of these were living-donor LT and 2071(34%) were deceased-donor LT. Between January 2011 and June 2013, 2514 patients underwent liver transplantation, and 437(17,3%) of them passed away due to various reasons. For the year 2012, the liver transplantation numbers for Turkey had been exceeded the limit of 1000/year. According to these increasing numbers Turkey will be one of the most populer country in a couple of years with its high volume and high survival rates of over 90% for the first year.

L19
Preoperative Evaluation for Liver Transplantation

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Liver transplant is the gold standard therapy for end-stage liver disease and many patients are on the waiting list for a transplant. In the preop assessment, patients should be evaluated for the presence of liver failure and the complications of end stage liver disease, which include the following:

Pulmonary System
Assessment of the patient's pulmonary system should include review of a recent chest radiograph, lung function tests and ABG. Pulmonary complications associated with liver disease include:

a) Restrictive Lung Disease
b) Intrapulmonary shunts
c) Pulmonary Hypertension

Cardiovascular System
The cardiovascular system is difficult to evaluate in patients with severe liver disease. The typical high cardiac output state with low systemic vascular resistance seen in most patients with cirrhosis can masquerade as an athletic heart, disguising severe cardiomyopathy. Severe coronary artery disease is found in less than 3% of this patient population. It is thought that cirrhosis may offer some protection from coronary atherosclerosis.

CNS
Hepatic encephalopathy is a life-threatening complication of endstage liver disease. Causes include accumulation of toxins such as ammonia, GABA agonists and other neuroactivesubstances. Cerebral metabolism and the blood-brain barrier may also be abnormal in these patients.

Gastrointestinal System
Portal pressure increases because of increased hepatic vascular resistance and increased portal venous inflow. The anatomic site of the increased intrahepatic vascular resistance varies according to the etiology of the cirrhosis. Portal hypertension is sustained by the development of increased portal venous inflow from a generalized hyperdynamic circulation in both acute and chronic liver failure. Problems related to portal hypertension:

a) Oesophageal varices
b) Hypersplenism
c) Ascites
d) Spontaneous Bacterial Peritonitis (SBP)

Haematological System
a) Thrombocytopenia due to portal hypertension-induced splenic sequestration and alcohol or sepsis induced bone marrow suppression is common. DIC (consumption) also may lead to low platelet counts.
b) Anaemia normally occurs because of chronic disease, malnutrition, or bleeding.

Hepatic Synthetic Function
Plasma concentrations of albumin, plasma cholinesterase and coagulation proteins are decreased in patients with liver disease (decreased synthesis volume).

a) Haemostatic abnormalities in patients with liver disease: In patients with liver disease, impaired haemostasis reflects decreased production of clotting factors because of hepatic synthetic dysfunction and, in some cirrhotics, depletion of vitamin K stores (clotting factors II, VII, IX and X) due to malnutrition or decreased intestinal absorption. Increased fibrinolytic activity with laboratory features of mild disseminated intravascular coagulation is also frequent in patients with cirrhosis.

b) Albumin: Hypoalbuminaemia contributes to low serum oncotic pressure, which predisposes to intravascular hypovolaemia, interstitial oedema, ascites and pleural effusions. Drug protein binding is also affected.
c) Pseudocholinesterase: Plasma cholinesterase concentrations are lower due to decreased production.
d) Metabolic dysfunction: Diminished hepatic glycogen stores as well as impaired gluconeogenesis in patients with liver disease may result in severe hypoglycaemia. The blood urea nitrogen level may therefore be low in patients with endstage liver disease, whereas the ammonia concentration may be markedly elevated. Ammonia itself is neurotoxic and its accumulation in the blood is associated with hepatic encephalopathy.

Renal Function
Renal function may be impaired in patients with liver failure. This can be due to the same disease process that damaged the liver, or the result of prerenal azotemia, acute tubular necrosis, or hepatorenal syndrome. In end-stage liver disease, the renin-angiotensin system is activated with little

or no sodium excretion. In addition, antidiuretic hormone activity is increased, causing water retention that exceeds sodium retention, resulting in hyponatremia. Hepatorenal syndrome is characterized by normal urinary sediment, low urinary sodium, azotemia, and oliguria. This picture is similar to prerenal azotemia; it is therefore important to exclude hypovolemia. Patients with hepatorenal syndrome usually recover renal function following OLTX. If a renal biopsy demonstrates irreversible renal disease, then a combined liver and kidney transplant should be considered.

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L20
Management of Perioperative Period

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Introduction
Nowadays, sickest patients are guided for LT and performed in patients who urgently need them due the policy of organ allocation according to MELD score system.

There are few data that influence how transplant anesthesia care is delivered. If anesthesia care had little effect on outcomes, it would not be important. However, there are some evidence that anesthesia care makes a significant difference on outcomes.

Preoperative Period
Any liver disease affects almost all organ system, especially neurologic, pulmonary, cardiovascular, renal and coagulation systems.

Intraoperative Period
Monitoring
Hemodynamic monitoring for recipient becomes even more important. However, the type of monitoring differs among transplant centers and is mainly determined by personal experiences or institutional practice.

Hemodynamic monitoring for LT usually includes at a minimum one arterial line and one central venous line. In addition, transesophageal echocardiography (TEE), or continuous cardiac output (CCO) has been described for advanced hemodynamic monitoring.

Dissection Phase
Blood loss during this phase of operation may be significant. Previous abdominal surgery or previous spontaneous bacterial peritonitis may make this phase of surgery more difficult and may cause significant bleeding. Therefore, intravascular volume management becomes more important in that phase. In these patients, blood salvage techniques can be useful and associated with a significant reduction in allogenic transfusion requirements.

Administration of blood products can be guided according to clinical findings or monitors of coagulation. Administration of fluid should be balanced between maintaining low CVP and adequate filling pressure. Although there is relatively evidence that lower CVP during liver surgery can reduce blood loss, the use of lower CVP in LT is still debated.

Liver diseases cause alterations in glucose metabolism. As a result of high dose steroid therapy hyperglycemia is common during the operation. On the contrary, hypoglycemia is the most important problem in patients undergoing LT due to fulminant hepatic failure. For that reason, strict plasma glucose monitoring becomes important issue throughout the operation.

Hypocalcemia and hypomagnesemia are frequently seen during LT. They all need to be corrected gradually because of altered clotting indices.

Anhepatic Phase
This phase is a unique period in LT surgery. In this period, the diseased liver is removed. Because of reduction in venous return and cardiac output by up to 50%, it is needed to support the circulation with a potent vasoconstrictor. Volume replacement therapy also is necessary. However, overtreatment of this condition with aggressive volume replacement can lead to hypervolemia at the time of graft reperfusion.

The important result of removal diseased liver is lactic acidosis due to exclusion of the native liver from the circulation. Thus, there is a rise in plasma lactate and decrease in plasma pH. This lactic acidosis is exacerbated when the graft liver is reperfused, and maximal acidosis and base deficit is therefore seen in the first several minutes after graft reperfusion. Thus, to treat the acidosis during the anhepatic phase to reduce the risk of severe acidosis with reperfusion may be useful in critical patients.

Neohepatic Phase
Vital role of anesthesiologists is to prevent high central venous pressure, which may cause graft congestion. Close communication about venous congestion of the graft and its color between the anesthesiologist and the surgeon has important role to optimize the graft survival.

At the begining of neohepatic phase, an acute clot lysis syndrome frequently develops. Thromboelastography demonstrates this pattern as typically graphic, which is poor clot initiation and rapid dissolution of clot, is called secondary fibrinolysis. Strategies for reducing fibrinolysis include use of antifibrinolytic agents such as tranexamic acid, and ε- aminocaproic acid.

At the end of the operation, the anesthesia team also prepares for the early extubation (i.e., in the operating room). Although it is reported that extubation rates varied from 5% to 80%, early extubation after liver transplant is often possible because of improvements in both surgical and anesthetic techniques. Its proponents argue that early extubation reduces the risk of pneumonia and improves both splanchnic and liver blood flow. Early extubation has been shown to decrease ICU length of stay and diminish resource use.

Postreperfusion Syndrome (PRS)
Despite improvements in the operative procedures of LT, PRS remains serious concerns for anesthesiologists. Even severe PRS may pose a direct threat to life during operation. Moreover, intraoperative PRS was associated with significantly higher intraoperative and postoperative mortalities and more frequent postoperative renal dysfunction. Incidence of PRS is 8-55%. The exact mechanism of PRS remains unknown, but the potential risk factors may include cold and acidotic components released from graft, severe graft ischemia- reperfusion injury, disorder of electrolyte and acid-base balance, and cirrhotic cardiomyopathy.

There are various suggestions to prevent or modify the severity of this syndrome including vasopressors, bicarbonate, ischemic preconditioning, calcium, methylene blue, N-acetylcysteine, and even flushing the graft with autologous blood.

Postoperative Period
All intraoperative modalities of monitoring and medication are continued in ICU. Early weaning from mechanical ventilation after LT is possible in selected patients with an uneventful intraoperative course. That does not only lower the risk of ventilator associated pneumonia but also improves the splanchnic and liver blood flow and reduces hepatic venous congestion. However fast tracking following LT is not a routine practice.

For postoperative care in liver transplant recipient, close collaboration between intensivist (anesthesiologist) and surgeon is needed. The main goals are hemodynamic stabilization, prevention of graft rejection and renal injury, and infection.

L21
Intensive Care Management of Liver Transplant Recipients

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Lecture

Advances in perioperative care of liver transplant recipients and improvements in treatment of graft rejection and postoperative infectious complications have made liver transplantation the best therapeutic option in patients with end-stage liver transplantation. However, despite these achievements, early postoperative management of liver transplant recipients remains to be one of the most challenging scenarios in the intensive care unit. The burden of the end-stage liver disease and its systemic manifestations such as hepatopulmonary syndrome, hepatorenal syndrome, and cirrhotic cardiomyopathy, the effects of the major surgery itself, and the graft related problems such as hepatic artery thrombosis and acute rejection are the main reasons of this challenge. Furthermore, the facts that recently sicker patients with more comorbidities have undergone liver transplantation and grafts from marginal donors have been extensively used significantly increases the intensive care management of liver transplant recipients.

As sicker patients with multiple comorbidities receive liver transplants from more marginal donors, an appropriate intensive care management becomes even more crucial for decreasing postoperative morbidity and mortality in this group of patients. Meticulous prevention, timely recognition, and immediate treatment of postoperative complications should be the goals of intensivists who are involved in the early postoperative care of liver transplant recipients. A multidisciplinary approach, close monitoring of organ system functions, understanding the pathophysiologic changes in these patients, intensive and collaborative efforts, and a skillful and knowledgeable leadership are the key components for a better overall outcome in liver transplant recipients.

L22
Infectious Complications After Liver Transplantation

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Transplantation has been established as accepted therapy for end-stage liver diseases for nearly 30 years. Although survival rates have insistently improved during the past decade, infections still represent a major cause of morbidity and mortality after liver transplantation.

Up to 80% of liver recipients have at least one infection during the first year after the transplantation Moreover, throughout the initial three years following the transplantation opportunistic infections are considered to be a leading cause of mortality.

Identification of risk factors for possible post-transplant infections is necessary to establish the optimal use of strategies to prevent infections in the post-transplant setting such as;

- latent or unrecognized infection of donor or recipient before transplantation
- pre-transplant colonisation of liver transplant recipients with multi drug resistant (MDR) microorganisms such as MRSA, VRE, ESBL positive enterobacteriaceae and non-albican candida
- surgical complications of the transplant operation such as prolonged operative time (>12 hours) reoperation, patients who had undergone Roux-en-Y biliary anastomosis.

Timetable Of Infections
With relatively standardized immunosuppressive regimens in clinical practice, different infectious processes tend to occur at specific times during the post-transplant course.

First Month
Most of the infections occurring in this period are nosocomial infections which are also seen after other complicated abdominal surgical operations.

1 to 6 Months (opportunistic period)
Infections caused by CMV, EBV and Aspergillus present clinically during the "opportunistic" period characterized by intense immunosuppression.

After 6 Months
Infections occurring in this period can categorized under three headings

1. Community-acquired infections
2. Chronic and/or progressive viral infections with HBV, HCV, CMV, EBV, and papillomavirus
3. Opportunistic infections due to intense immunosuppression because of allograft rejection and dysfunction

L23
The Clinical Course and Management of HCV Infection After Liver Transplantation

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Hepatitis C virus (HCV) infection is one of the major causes of all chronic liver disease and HCV-associated cirrhosis is one of the most common indication for orthotopic liver transplantation (OLT) among adults. Recurrence of HCV following orthotopic liver transplantation (OLT) occurs in almost every patient (1). HCV infection remains a serious problem after liver transplantation and recurrent hepatic infection is the leading cause of graft failure.

Pathogenesis: Variables that influence the progression of recurrent HCV following orthotopic liver transplantation (OLT) are incompletely understood, but donor characteristics (donor type, age), viral characteristics (genotype, viral load), the inflammatory grade of the explanted liver, and the patient's immune status and immunosuppressive regimen may be important (2). The degree of inflammation present in the patient's explanted liver at the time of transplantation correlate well with fibrosis progression in recurrent HCV (3). The level and type of immunosuppression following transplantation likely influence the severity of disease recurrence.

Clinical Course: The course of HCV infection accelerates after OLT and progression to cirrhosis occur in 10-20 % during the first five years time.

Diagnosis: HCV RNA levels and liver biopsy is important in establishing diagnosis. Features that are supportive of recurrent HCV are lobular activity, interface hepatitis, piecemeal necrosis, and lymphocyte predominance or lymphoid follicles

Management: Several strategies for HCV treatment in the setting of transplantation have been attempted: treatment prior to transplantation to prevent infection of the graft, immediate or peri-operative prophylaxis, early preemptive HCV therapy, and treatment of established recurrent disease. Eradication of HCV infection prior to transplantation would be the ideal approach, as patients who undergo transplantation in the absence of viremia are much less likely to have recurrent infection. However, treatment of patients with decompensated cirrhosis is difficult. Genotype 1 patients

have approximately 15 percent sustained virologic response (SVR) rate with the cost of exacerbations of encephalopathy, infections and other serious adverse events (4). There is no consensus on the role of prophylactic or preemptive therapy following transplantation prior to HCV-related liver injury from recurrent infection (2). The combination of peginterferon and ribavirin treatment after OLT has been associated with the best treatment responses overal. SVR rates are approximately 25% however discontinuation to therapy is also about 25% (5). The future of direct acting antiviral agents (protease and polymerase inhibitors) is promising, and the promise of interferon-free regimens may become a reality in the next several years (6). Indications and contraindications for retransplantation remain unclear and practices vary widely among institutions.Unfortunately, the prognosis for such patients is generally poor.

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L24
Isn't It Time to Use Immunonutrition for Liver Transplants?

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A series of experiments using cardiac transplants in rats showed that a variety of amino acids and lipids when added to the diet in relatively high concentrations increased the survival of allografts when given with a short course of several immunosuppressive drugs in subtherapeutic doses. A prospectively randomized clinical trial was then done in patients with renal transplants which showed that the administration of nine grams of arginine and 30 ml of canola oil reduced the incidence of rejection significantly (p=0.01) during the posttransplant period between 30 days and 3 years. It also reduced the incidence of biopsy-proven calcineurin inhibitor toxicity (35.3% vs. 9.2%, p=0.002), sepsis (18.9% vs. 6.5%, p=0.05), new onset diabetes (14.5% vs. 2.3%, p=0.04) and cardiac events (17.1% vs. 4.6%, p=0.05). In a subsequent study in kidney transplant patients, some patients were treated with arginine and fish oil rather than arginine and canola oil. Fifty-four patients had blood samples performed preoperatively and postoperatively and 49 of these patients also had plasma amino acid profiles. When the concentration of omega-3 fatty acids in red blood cells was <6%, rejection rate was 18.5% compared to no rejections when the percentage of omega-3 fatty acids was >6% (p=0.01). An inverse relationship was seen with the omega-6 fatty acids and similar findings were seen with omega-3:omega 6 ratio and concentrations of docosahexaenoic acid and eicosapentaenoic acid independently. The concentration of omega-3 fatty acids in the red blood cell membranes have no significant relationship to the development of new onset diabetes mellitus, nor did the concentration of arginine. However, ornithine, the metabolic product of arginine, was significantly associated with prevention of new onset diabetes after transplant.

It is now evident that a combination of arginine and omega-3 fatty acids provides a more powerful effect than either alone, possibly through the development of myeloid-derived suppressor cells (MDSC). A proposed definitive prospective, placebo-controlled clinical trial of the use of arginine and fish oil is planned for the United States in the near future, but no studies have been done in liver transplant patients. It is highly probable that this simple, inexpensive and nontoxic therapeutic modality will have the same beneficial effects in hepatic transplantation that it has in kidney transplants.

L25
Pharmacogenetics Relevance in Clinical Immunosuppression Monitoring

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It is becoming increasingly clear that pharmacokinetic-based approach in immunosuppressive drug therapy monitoring has its limitations. Its clinical relevance seems to be questionable, especially in the era of applied therapeutic individualization. A number of genetic and environmental factors in both donor and recipients influence pharmacokinetics, intra-cellular concentrations and pharmacodynamic of immunosuppressive drugs

(ISD). Their mode of action is the result of an interaction between the distinct recipient-donor polygenic profiles with several recipient environmental factors. Pharmacogenetics (PG) identifies genes and establishes their influence and possibly predicts their effects on drug disposition, transport and biological effects. The main application of PG in the field of organ transplantation is to establish genetic profiling for each patient that will assist clinician in individualizing immunosuppressive therapy with optimal efficacy and minimal side effects. Significant number of recently published papers assessed mainly the impact of different gene polymorphisms (GP) on drugs bioavailability in whole blood or plasma in stead on intracellular concentrations or target enzyme activity known to be more biologically and clinically relevant. Whole blood or plasma levels correlate weakly with target cell concentration and clinical outcome. While the transplant recipient is a hybrid complex environment resulting from the interaction between the combination of both recipient-donor distinct genetic makeup and recipient environment, most of these studies evaluated mainly the effect of one recipient individual candidate gene, which could be negated or enhanced by the interaction with other candidate genes or other environmental factors. Moreover, the majority are retrospective or prospective and involved small cohorts of patients. Few assessed the influence of GP on patient and graft outcome in term of efficacy and toxicity and most of them investigated the relationship with short term outcome defined by biopsy proven acute rejection (BPAR), while long term outcome defined by graft and patient survival is determined by recipient and donor factors. Most trials assessed the effect of one single GP on one ISD in the context of an immunosuppressive therapy involving multiple drugs. The overall immunosuppressive effect of a particular immunosuppressive regimen is a cumulative one and is the result of the interaction of all drugs-specific candidate genes among each other and within the recipient–donor hybrid environment. Although several genetic mutations of different candidate genes have been identified to influence drugs metabolizing and target enzymes and transporters, only one PG strategy of CYP3A5 genotyping for Tacrolimus has made it through to testing in a clinical trial in a randomized fashion with rather deceiving results where no significant impact was observed in the short term on the incidence of BPAR, renal function and graft and patient survival. Whether a monogenic PG-guided dosing strategy for Tacrolimus or any other IS drugs can improve clinical outcome remains to be proven and will probably be unlikely. A polygenic approach using a haplotypic rather then a single polymorphism profiling the donor-recipient pair for the different ISD within a specific immunosuppressive startegy in combination with intracellular drug monitoring post-transplantation will hopefully improve clinical outcome by optimizing efficacy and minimizing toxicity.

L26
Logical Approach to Transplant Patient Monitoring

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Acute and chronic graft rejections as well as tolerance are true representation of the specificity, complexity, sophistication and redundancy of an elegantly and meticulously designed immune system. Thus in order to predict, diagnose and treat (control) graft rejection it is necessary to determine and understand the steps leading to recognition, stimulation, activation, and amplification of the immune system. It is generally accepted that the first steps leading to the initiation of the immune system cascade, leading to graft rejection, is recognition. Recognition is followed by the ligation of a series of adhesion molecules starting with an antigen to its specific T-cell receptor (TCR)/cluster of differentiation (CD) complex, expressed on the surface of the T cell. In order for the activation to proceed additional costimulatory signals, such as ligation of the CD28/B7, CD4/HLA class II and CD/HLA class I antigens are required. During the activation process, the lymphocyte, begins to acquire new CD molecules such as CD25 (IL-2R), CD69, CD71 and HLA-DR. This is accompanied by an increase of cytokines production by the primed T cell. The cytokines are essential for the differentiation, proliferation and amplification of the T-cell The most important of these cytokines is interleukin (IL)- 2, which is essential for activated T-cell proliferation. The complexity and the polymorphic nature of the immune system have necessitated to design agents that inhibit the immune system at different levels. Cyclosporine (CYA) and Tacrolimus (FK) seems to act on the IL-2 by inhibiting its production thus leading to a decrease in the proliferation of the activated lymphocyte. Some earlier reports have indicated that CYA also blocks the receptor for the HLA-DR antigen on T cells. The newly introduced immunosuppressive agent Cellcept (MMF) reduce the proliferation of T cell by inhibiting purine synthesis and by its action on the type II isomer of inosine monophosphate dehydrogenase16,17. Anti-lymphocyte antibodies (ATG) deplete circulating lymphocytes while selective monoclonal antibodies are directed against IL-2 receptor thus reducing the rate of proliferation of activated T cells. Recently antibodies to the CD40/CD40 ligand have been shown to induce long term graft survival with the inhibition of the Th1 cytokines interferon gamma (INF), IL-2 and IL-12 and upregulating the Th2 cytokines IL-4 and IL-1020,21. Lastly graft rejection can be reduced by blockade of the B7/CD28 costimulation pathway with the fusion protein CTLA-4Ig22.

L27
The Role of Genomics in Predicting Chronic Allograft Dysfunction

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Chronic graft dysfunction is a major cause of graft loss after renal transplantation and is characterised by interstitial fibrosis, tubular atrophy, vascular changes and glomerulosclerosis. Multiple immune and non-immune mechanisms have been implicated in its pathogenesis. However, the molecular pathways and signaling networks involved are poorly defined. Whilst there are many potential causes of injury, there are limited biological pathways that result in fibrosis. It is likely that is also true after liver transplantation. At present the pathogenesis of renal allograft fibrosis is controversial. In all likelihood the key initiating events change over time and differ between different patient cohorts. Fibrosis is the result of ongoing activation of myofibroblasts, which can be derived from multiple sources. Some studies have identified EMT as an important source. Others have identified myofibroblasts to be of recipient origin. In the context of renal transplantation, early inflammatory events are important in the recruitment of myofibroblasts. Acute cellular rejection and subclinical rejection have been identified as important causes of IF/TA in the first two years of transplantation. In mechanistic studies of fibrosis, chemokines such as CCL2 and CCL3 are important for the recruitment of myofibroblasts and Th2 T cell responses induce dysregulated alternatively activated (M2) macrophages that secrete TGFβ. This link between inflammation and fibrosis may be an important initiator of fibrosis after transplantation. Gene array studies have been undertaken in several renal transplant cohort studies and show a consistent pattern of gene expression pathways linking immune and fibrotic gene expression profiles. In longitudinal studies gene expression profiles predictive of fibrosis can predate histological evidence and has the potential to be predictive of future damage. Data linking macrophage infiltration and T-cell mediated immune activation with the development of fibrosis will be presented, whilst evidence of EMT in longitudinal cohort studies was largely lacking. In the GoCar study gene expression profiles early after transplantation that are predictive of future fibrosis have been developed as a biomarker assay that is a better predictor than histology or clinical data and has the potential to better define the pathogenesis of the condition.

L28
Minimal Immunosuppression in Liver Transplantation

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The early outcome after liver transplantation (LT) has nowadays become excellent as indeed shown by the one- and five years survival rates of about 90 and 70 to 80 %.

Despite these results still (too) many successfully transplanted patients die of cardiovascular, infectious and tumor diseases whilst having a well-functioning graft. Most such unfortunate outcomes are mainly related to the immunosuppression (IS).

The liver transplant unit of the Catholic University of Brussels has a long-standing interest in the development of minimization of IS in the field of LT.

During this lecture, the several steps necessary to minimize the IS will be discussed. At the end a final note on the actual developments in the search towards operational tolerance in this field will be highlighted.

L29
Organ Donation and Transplantation in Iran: With Brief History of Developments

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Studies have shown a correlation between organ transplant (Tx) activity and human development index (HDI). Iran is a country with high HDI and its organ donation & Tx activity specially from deceased-donors is steadily increasing. The first renal Tx was carried out in Iran in 1967, which was also the first organ Tx in current MESOT counties. From 1967 to 1985, only approximately 100 renal Txs were performed. Twelve of these 100 kidneys came from Euro-transplant that were transplanted prior to 1979. Between 1979 and 1985, more than 400 patients travelled abroad and received a renal Tx using governmental funds. In 1985, the high expenses of renal Tx abroad prompted health authorities to increase renal Tx activity inside the country. Two renal Tx teams were organized, and between 1985 and 1987, only 274 renal Txs from living related

donors were performed. In 1988, because of a long renal Tx waiting list at the Ministry of Health for Tx in abroad, a regulated living unrelated donor renal Tx program was adopted. As a result, the number of Tx teams and the number of Txs that were performed increased rapidly such that by 1999, the renal Tx waiting list was eliminated. In 1989 a religious decree from supreme religious leader was obtained recognizing the concept of brain death and allowing deceased donor organ Tx. This was followed by performing a number of deceased donor kidney Txs. In 1982 the first liver Tx was performed by Dr. Malek Hosseini in Shiraz. In 2000, the legislation of Organ Trans¬plantation and Brain Death Act legalized organ donation from deceased donors. This was also followed by establishing Organ Procurement Centers and Brain Death Identifica¬tion units all over the country. At first, Organ Tx Center in Shiraz University started performing increasing number of deceased donor kidney, liver and pancreas Txs and remained a successful deceased donor organ Tx model in the country. Then other Tx centers increased their deceased donor organ Tx activities.

By the end of 2012, a total of 34,166 kidney Txs (4,436 from deceased donors),2021 liver Txs (1788 from deceased donors),147 pancreas Txs, 482 heart Txs, 63 lung Txs, several intestine Txs have been performed . Since2000, the annual number of deceased donor kidney, liver, heart, lung and pancreas Txs has increased steadily in the country. In 2000, only 2.2% of all renal Txs were from deceased donors. This increased to 10%, 20% and 38% by the years 2003, 2008 and 2012 respectively. In 2011, Iran by performing 2771 solid organ Txs(37pmp) ranked 33rd between 50 most active countries globally and 2nd after Turkey between MESOT countries. But in donation and Tx from deceased donors Iran was ahead of all MESOT countries including Turkey, Kuwait and Saudi Arabia. In 1012, a total of 3002(39.2pmp) solid organ Txs were performed . Again Iran was the 2nd after Turkey in all solid organ Tx activity but ahead of all MESOT countries in deceased donor organ Tx.

L30
National Efforts to Develop Transplant Coordination System in Turkey

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Taking into consideration that the first succescssful solid organ transplantion was performed in 1975 and the organ transplant act was passed in 1979, it is unfortunate that the national coordination system as the constituent component of organ supply efforts was founded with a 20-years delay. The importance of bureaucratic and political commitment should not be underestimated with regard to health policy in general and organ transplantation in particular.

Although Turkey has had important achievements in transplant applications in recent years, it still has a long way to go to improve its current organ supply system. Systematic working of transplant coordination system, incorporation of transplant coordinators into the system and practices of the importance of intensive care unit professionals have lead us to a different understandig of organ supply. However, our efforts to improve organ supply have not resulted in a significant success yet. Organ shortage brings about serious differences in clinical applications of transplant centres. Nothwitstanding the fact that the supply does not meet the demand in organ transplantation, the central coordination authority has put great effort into sustaining the system for the last 10 years. It should be noted that the countries with considerable success in donation and transplantation reached their goal in a time period of 20 to 25 years. Bearing this time period in mind, we should continue working to develop the transplant coordination system in Turkey.

Referring to this point, we can analyse our efforts during the last 10 years and thus see clearly what we have got so far:

Strengths;

- Air, land, sea ambulance systems
- Adequate technological equipments and ease of access to intensive care units
- Intensive care experience
- Fair and transparent allocation/sharing of organs
- Sufficient number of certified organ transplant coordinators
- Ease of access to transplant centres
- Experience in organ transplants, especially in living donor transplants
- Organ transplant treatments to be guaranteed by pay back system
- The adequacy of the legal regulations in major issues

Weaknesses;
- Shortage of deceased donors
- Inefficiency in donor detection system
- High refusal rates in organ donation
- Inadequate use of extended donor criteria
- The lack of a methodological professional training
- 75% of transplant centres work with very low activity
- The lack of quality and audit system
- The lack of organ transplant logistics system
- Challenges in organ supply chain to meet social demands
- Overwork in national transplant coordination system and insufficiency in qualified task force

Threats;
- Dramatic decrease in donation rates
- Aggressive increase in the number of patients with chronical organ failure
- Uncontrolled expansion of waiting lists
- Increasing number of candidates on the waiting lists, who are not suitable for transplantation
- Imbalances in mortality, morbidity and survival rates
- Excessive inclination to living donor transplantation and the risk of organ trafficking
- Inability to sustain experience in transplant centres with low activity
- Demotivation of organ transplant coordinators due to uncertainty in work conditions as a result of the new organisational structure of the Ministry of Health

Opportunities;
- Political and bureaucratic commitment and possibility to change legal regulation
- Young and dynamic work force
- Donor transplant centres and transplant team meeting the expanding pool of donors
- Our ability to express ourselves in the field of transplant practices in neighbouring countries
- Constituting an attraction centre for foreign patients in organ transplant services due to high quality and economic reasons
- Interest of non-governmental organisations in the development of organ donation
- Potential significant contribution of educated young people to the social awareness about organ donation

As a result, our efforts would play a key role in improving the innovative ability of central health authority, decreasing the workload by integrating non-governmental organisations into the system, adopting and applying sustainable and reformist donation and transplantation policies in compliance with international norms without ignoring the health care system and social structure of Turkey, and developing organ transplant services.

L31
The Important Role of the Health Professionals in a Deceased Organ Procurement System

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No organs equal No transplantations
Although, over used, this famous equation is often not seriously taken into consideration. As long as human organs are the only valid source of organs, organ shortage will remain a problem. A Lebanese system (adapted from the Spanish model) has been implemented. We need to inform the public and particularly the health professionals about it through continuous medical education.

Health professionals are an integral part of society. They share the same culture and are often influenced by the same taboos. Their main advantage is that: They form a more compact group, smaller and easier to reach. They have an important role as privileged counselors in all health matters. We have thus, concentrated our efforts on the motivation, formation and education of the health professionals and we are hoping that their motivation will incite society to participate more actively in this very vital project.

L32
Meeting the Demand for Livers From Deceased Donors, the Way Forward

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Although liver transplantation has become widespread and routine in developed world, it is still uncommon in most Middle East (ME) countries. There are many reasons for this but lack or shortage of deceased donors (DD) is a crucial factor in establishing or sustaining a program of liver transplantation.

Deceased Donation in the ME
Only few countries in the ME have viable DD programs, even so, the rate of deceased donors is far below those in western countries. The best in Europe is 35 donors per million population whereas the best in the ME does not exceed 6.

This discrepancy is because there is a lack of donation culture in most ME countries resulting from an eastern culture of respecting the deceased body and misunderstanding the provisions of Islam which dominates the lives of the people in the ME.

Meeting the demand

In Spain, which has the highest DD rate in the world, organ donation has become a national program, receiving support and pride by the population. A similar model should be followed in the ME to increase DD in the long term. This requires a concerted effort by the state, organ procurement organizations, other professional organizations, media and religious authorities in promoting donation. The governments should be made accountable to achieve self sufficiency in organ donation as advocated by the WHO. Iran is one of the countries which has applied this model in recent years and has succeeded in increasing DD year after year.

Providing incentives to donor families

Some Gulf countries managed to achieve good rates of DD by providing financial incentives to donor families. This practice remains controversial especially after the declaration of Istanbul, against commercialism in transplantation, which allows removal of disincentives, by covering the costs incurred by the donors, but rejects providing financial incentives.

This model can be modified to provide humanitarian support to donor families, if needed, within an ethically acceptable framework, not including fixed cash payments. This could be done in the form of educational grants provided to deceased's children to continue their education or providing long term interest free loan to allow the family start a small business to sustain them. This support can be provided and managed by charities.

L33
Is Meld Score Sufficient to Manage Graft Allocation in Turkey?

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Liver transplantation (LT) has been the prominent treatment option in patients with end-stage liver failure, however procurement of adequate number of liver grafts remains a major problem. "The model of end-stage liver disease (MELD)" was described in 2006 in order to provide a fair allocation of the grafts. Despite MELD enabled an important decrease in death rates on waiting list, 1-year survival has also been decreased from 90% to 80% owing to prioritization of patients with poorer MELD scores. This situation led to discuss MELD score in different points of view.

In Turkey, patients who are candidate to cadaveric liver transplantation (CLT) for the treatment of hepatocellular carcinoma (HCC) gain a substantial amount of additional MELD score according to tumor size. This may push end-stage patients who do not have HCC but need earlier CLT urgently regarding other MELD criteria (high total bilirubin, creatinin and INR levels, uncontrolled ascites or hepatic encephalopathy [HE]) down in the waiting list and result in lower survival rates. Therefore additional MELD scores for HCC patients should be revised. Patients with metabolic disease or unresectable parasitary disease (alvelolar hydatid cyst) are effected by the same issue. A large amount of these patients cannot reach required MELD score and progress into more complicated disease which hinder previously possible improved survival.

Acute on chronic liver failure is a novel concept in prognosis of liver disease which is not accepted as an indication for urgent CLT in Turkish Liver Allocation System. Patients with acute on chronic liver failure are not considered as acute liver failure, whereas outcome after graft procurement is promising in this group.

In our country, Central Transplantation Coordination System procures grafts to the end-stage liver disease patients with a MELD score more than 14, whereas liver transplantation centers are allowed to manage living donor transplantation (LDT) with an insitutional internal-auditing. Social security institution finances CDT as well as LDT. The advantage of this financing is controversial and revisions should be considered for LDT.

In conclusion, a health care service should fight for good health, but not only for good results.

L34
Acute Liver Failure in Children

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Acute liver failure (ALF) is an uncommon condition in which the rapid deterioration of liver function results in coagulopathy and alteration in the mental status of a

previously healthy person. There are important differences between ALF in children and ALF in adults. The main difference is encephalopathy which may be absent, late, or unrecognized in children.

Pediatric acute liver failure (PALF) is a complex, rapidly progressive clinical syndrome that is the final common pathway for many disparate conditions, some known and others yet to be identified. The pediatric acut liver failure group recommended PALF definition as (1) evidence of liver dysfunction within 8 weeks of onset of symptoms (neonates may have only deranged liver functions without overt symptoms) (2) uncorrectable (6-8 hours after administration of one dose of parenteral vitamin K) coagulopathy with International Normalized Ratio (INR) >1.5 in patients with hepatic encephalopathy, or INR> 2.0 in patients without encephalopathy and (3) no evidence of chronic liver disease either at presentation or in the past. Staging of encephalopathy in infants and children is difficult as compared to adults. The group recommends the following grades: Grades I and II are indistinguishable with clinical features of inconsolable crying, inattention to task: with normal or exaggerated deep tendon reflexes: Grade III encephalopathy manifests as somnolence, stupor, combativeness and hyperreflexia. In grade IV, child is comatose [arousable with painful stimuli (IVa) or no response (IVb)] with absent reflexes and decerebration or decortication.

Incidence: The estimated frequency of acute liver failure (ALF) in all age groups in the United States is about 17 cases per 100,000 population per year, but the frequency in children is unknown. PALF accounts for 10 to 15 percent of pediatric liver transplants performed in the United States annually.

Etiology: The causes and natural history of ALF in neonates and infants differ from those in older children. In neonates, the commonest etiology reported in Western literature is neonatal hemochromatosis, Herpes simplex virus and less common causes are hemophagocytic lymphohistiocytosis and metabolic disorders (galactosemia, tyrosinemia, mitochondrial cytopathy). In infants, metabolic causes are common (type I tyrosinemia, mitochondrial cytopathy, galactosemia, and hereditary fructose intolerance). Drug-related hepatotoxicity, viral infections, autoimmune hepatitis, Wilson'sDisease are the main causes of ALF in older children. Nearly 15-20% of cases remain of indeterminate etiology.

Assessment and treatment: The most important step in the assessment of patients with acute liver failure is to identify the cause, as certain causes demand immediate and specific treatment. Planning for early transfer is important as the risks involved with patient transport may increase or even preclude transfer at later stages. The development of cerebral edema is the major cause of morbidity and mortality in patients with ALF. Another consequence of ALF is multisystem organ failure, which is often observed in the context of a hyperdynamic circulatory state that mimics sepsis; therefore, circulatory insufficiency and poor organ perfusion possibly either initiate or promote complications of ALF. So management should be in an intensive care setting in select situations. Patient should be monitorized hemodinamically. Electrolyte disturbances and hypoglycemia should be prevented with appropriate intravenous solution. Supportive management which included n-acetyl cystein and proton pump inhibitors is recommended in all cases of ALF irrespective of etiology. Despite coagulopathy is poor prognostic sign, routine correction of coagulopathy and thrombocytopenia is not recommended. Infection still remains one of the major causes of death in patients with ALF. The most commonly isolated organisms are gram-positive cocci (Staphylococci, Streptococci) and enteric gram-negative bacilli. Fungal infections, particularly Candida albicans, may be present in one third of patients with ALF. Empirical antibiotics are recommended for patients listed for liver transplantation (LT), since infection often results in delisting and immunosuppression post- LT is imminent. Though ammonia is an accepted triggering factor in cerebral edema, L-ornithine L-aspartate, lactulose and other non-absorbable antibiotics have not been found to be beneficial. However, if lactulose is administered (preferred in grades I-II HE) care should be taken to avoid over distension of the abdomen. Brain edema should be treated mannitol, hypertonic saline or head cooling.

Malnutrition affects pre- and post-transplant survival, and nutritional assessment should be a priority in children with liver disease. There is no role of protein restriction in children with HE. Energy intakes should be increased appropriately to counter the energy catabolism and also factor-in the requirement for maintenance, growth and physical activity.

Prognosis: Several prognostic scoring systems have been devised to predict mortality and to identify those requiring early LT. These include King's College Hospital (KCH) criteria , pediatric end-stage liver disease (PELD) score, APACHE II, and Clichy criteria. However none of them is accepted ideal tool for determine to outcome.The outcome of acute liver failure is related to the etiology, the degree of encephalopathy, and related complications. Patients with ALF caused by acetaminophen have a better prognosis than those with an indeterminate form of the disorder. Patients with stage 3 or 4 encephalopathy have a poor prognosis. The risk of mortality increases with the development of any of the complications, which include cerebral edema, renal failure, adult respiratory distress syndrome (ARDS), and infection.

In more than 50% of children with ALF there is poor survival unless LT is offered at the appropriate time. Before LT, the mortality rate was generally greater than 80%.

L35
Management of the Post Liver Transplantation Period in Children

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Post liver transplantation management of children can be reviewed as in early and late post transplantation periods. During the first weeks of post transplantation period, complications of surgery such as bleeding, bile leakage and thrombotic events may necessitate immediate intervention. Immunosuppression started following liver transplantation usually prevents graft rejection. In intensive care unit, opportunistic infections partly due to immunosuppression, are important factors for morbidity and mortality. Immunosupressive treatment may cause some further adverse effects such as hypertension, nephrotoxicity, and neurotoxicity. In long-term intensive care, the most important concerns are severe infections, ventilator dependency, and insufficient nutritional support. Nutritional support for children in the ICU is of paramount importance.

Nephrotoxicity, neurotoxicity, de novo malignancy, and late infections are among the important risks during long-term immunosuppression. Noncompliance in teens is a particular problem that might lead to graft loss and patient death. Because of the long life expectancy in children, optimal growth and development with a high quality of life should be the main goal in the long term.

L36
Few Experiences in Rare Indications in Pediatric Liver Transplantation

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In some genetic defects mainly liver cells are affected and leads to liver injury and liver failure. In some genetic defects and inherited metabolic disorders defective gene expression in liver cells leads not to liver disease but to other organ damage due to production abnormal proteins or lack of enzymatic function to clear toxic metabolites. Alpha-one antitrypsin deficiency, Wilson disease, cystic fibrosis, neonatal hemochromatosis, tyrosinemia, galactosemia, organic acidemia, urea cycle defects, fatty acid oxidation defects, glycogen storage diseases, primary hyperoxaluria type 1, liver restricted mitochondrial respiratory chain disorders, Crigler Najjar syndrome, progressive familiyal intrahepatic cholestasis type 1,2,3, protein C deficiency, hemophilia A and B, familial hypercholesterolemia, Alagille syndrome, polycystic liver-kidney disease are such disorders that can be treated with liver transplantation or combined liver-kidney transplantation. Timing, selection, and management of these patients with this rare disorders shows significant improvements. Liver transplantation effectively treats both the underlying defect for those disorders mainly the liver is affected. Inherited diseases that can be treated with liver/liver-kidney transplantation is frequent in Turkey due to high rate of consanguinity. In Baskent University Liver Transplantation Unit, out of 166 pediatric patients with liver transplantation, 54 (32%) had metabolic diseases. 31 (57%) Wilson disease, 7 tyrosinemia, 5 Crigler Najjar disease, 3 glycogen storage disease, 3 primary hyperoxaluria type 1, 2 familial hypercholesterolemia, 1 deoxyguanosine kinase deficiency, 1 3-methyl crotonyl CoA carboxylase deficiency, 1 ornithine transcarbamylase deficiency patients successfully liver transplanted. In addition to 54 metabolic cases, 10 patients with PFIC also underwent liver transplantation in our unit.

L37
Intestinal Transplantation: An Unexpected Journey

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The introduction of tacrolimus and the development of the abdominal multiorgan procurement techniques allowed for the development of intestinal transplantation in the early 1990's; indeed, with the early success of this procedure it would be possible to tailor various types of intestine containing grafts which can include other intra-abdominal organs such as the liver, pancreas, and stomach. This has been critical to the application of this type of organ transplant, given the wide scope of diseases for which replacement of the intestine may be necessary. Also, the understanding that the liver protects the intestine against rejection had been suggested by previous combinations of liver plus other organs such as the kidney. The first survivors of intestine transplantation would also go on to demonstrate the interaction (host-versus-graft and graft-versus-host) between recipient and donor immunocytes (brought with the allograft), which

under the cover of immunosuppression allows varying degrees of graft acceptance and eventual minimization of drug therapy. However, included in the success of intestine transplantation survival outcomes has been the concomitant development of strategies to better manage intestinal failure (IF; describes a patient who has lost the ability to maintain nutritional support with his or her intestine and is permanently dependent on total parenteral nutrition [TPN]). This has been accomplished largely through the establishment of Intestinal Rehabilitation services, which incorporates a multidisciplinary team approach to medical and surgical care (including transplantation and corrective surgeries).

Intestinal transplantation is the standard of care for patients with intestinal failure who have significant complications of total parenteral nutrition. It is hoped that with the minimization of immunosuppression strategies currently used, the long-term survival will plateau, as occurs with other organ transplants; also, rehabilitation and quality-of-life studies have shown that >80% of survivors reach total independence from TPN and have meaningful life activities.

As a result of the success of intestinal transplantation, multidisciplinary intestinal centers have focused on intestinal rehabilitation and improving the devastating effects of TPN on the liver.

L38
Techniques and Results of Pediatric Liver Transplantation

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L39
Status of Liver Transplantation in the Arab World

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Pan Arab Liver Transplant Society (PALTS); [1]Qatar, [2]Egypt, [3]Saudi Arabia, [4]Jordan, [5]Lebanon, [6]Algeria, [7]Tunisia, [8]Iraq, [9]Libya, [10]UAE, [11]Kuwait.

Background: The Arab world comprises the 22 countries of the League of Arab States founded in 1945. The Arab world has a combined population of around 422 million people and is united by Arabic language, culture, religion and geographic contiguity. The high prevalence of viral hepatitis in certain Arab countries has led to an increasing number of patients suffering from end-stage liver disease and who are in need for liver transplantation (LT). The first deceased donor liver transplant (DDLT) in the Arab World was performed in 1990 at Riyadh Military Hospital in Saudi Arabia; and the first Living Donor Liver transplant (LDLT) was performed in 1991 at the National Liver Institute in Egypt. Since then, both DDLT and LDLT have been routinely performed in many Arab countries. Herein, we summarize the liver transplant activity in the Arab World.

Material and Methods: After extensive search, liver transplant activities were found in 11 Arab countries and divided between 27 liver transplant centers. In June 2012, an email questionnaire was sent to all 27 centers requesting simple information including; date of the first LT, total number of LT, number of DDLT, number of LDLT, in addition to the most common indication for LT in those centers.

Results: Out of 27 liver transplant centers, 26 centers (96.3%) responded to the questionnaire and agreed to provide their data. Up to June 2012, a total of 3207 liver transplants were performed in the Arab World divided between 11 countries and 26 transplant centers. Out of the 3207 liver transplants, 2550 (79.5%) were LDLT and 657 (20.5%) were DDLT. The highest LT activity was found in Egypt (56%) mostly performing LDLT, followed by Saudi Arabia (35%) performing both DDLT and LDLT, and finally Jordan (5%) mostly performing LDLT. The most common indication for LT was end-stage liver cirrhosis due to Hepatitis C virus (HCV) or Hepatitis B virus (HBV), with or without

Hepatocellular Carcinoma (HCC). Liver transplantation activity in the Arab World is summarized in the table below.

Country	First LT	LDLT	DDLT	Total	(%)
Saudi Arabia	1990	532	604	1136	35%
Egypt	1991	1795	2	1797	56%
Tunisia	1998	7	29	36	1%
Lebanon	1998	4	15	19	1%
Algeria	2003	34	-	34	1%
Jordan	2004	146	2	148	5%
Libya	2005	21	-	21	1%
UAE	2007	2	-	2	0.1%
Kuwait	2010	-	2	2	0.1%
Iraq	2011	9	-	9	0.3%
Qatar	2011	-	3	3	0.1%
	Total	2550 (80%)	657 (20%)	3207	

Conclusions: Both DDLT and LDLT have been routinely and successfully performed in the Arab World. As elsewhere, severe organ shortage remains the biggest hurdle facing the increasing need for LT in most of the Arab countries. Although deceased organ donation has been legalized in many Arab countries, its implementation remains limited to few countries mostly due to cultural and logistical barriers. The increasing demand and limited supply of organs in the Arab World has generated many concerns especially related to organ trafficking and transplant tourism. These shared challenges can only be faced through continued collaboration between various liver transplant programs in the Arab World. The Pan Arab Liver Transplant Society (PALTS) is developing a comprehensive registry and an online forum aiming to discuss all shared problems related to liver transplantation in the Arab World including medical, ethical, social and legal aspects.

Lecture

L40

Twenty Five Years of Liver Transplant at the University of Colorado, School of Medicine

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Dr. Thomas Starzl joined the faculty at the University of Colorado as the Chief of Surgery at the Denver Veterans Administration Medical Center (VAMC) in 1961. He performed the first kidney transplant in March of 1962. Dr. Starzl pioneered liver transplant with the first attempt on March 1st of 1963. With Dr. Starzl's departure to Pittsburgh, the Liver Transplant Program was closed at the University of Colorado until November 1988. The new era started on July 1st, 1988 with the arrival of Dr. Igal Kam, an Israeli transplant surgeon who spent two years with Dr. Starzl in Pittsburgh. Dr. Kam completed his two years of fellowship with Dr. Starzl and became a faculty member in Pittsburgh in 1985.

Upon Dr. Kam's arrival to the University of Colorado, he immediately recognized the need to build a multidisciplinary team combined of surgeons, hepatologists and nephrologists. Together with the hospital commitment a team was created with nursing and a designated hospital space for the new transplant unit.

With better outcomes in liver transplant more programs appeared in the United States and other parts of the world.

At the University of Colorado the initial team efforts gave them experience in 10 cases with no death paved the road to the success of the team.

After completion of the first series of 110 cases with veno-venous by-pass, we had trouble with case number 111. We were unable to introduce the veno-venous by-pass. The case was completed without the bypass and as a result we gradually terminated the use of the by-pass between 1992-1995. Since 1995, veno-venous by pass has not been used at the University of Colorado during liver transplant surgery.

Around the same time the use of T-tube in liver transplant was stopped. This small change significantly reduced the hospital stay for patients after liver transplant.

The next step of practice change was obtained with early extubation. As a result of the elimination of veno-venous bypass we changed the intraoperative management of liver transplant patients. The use of more vasopressors and less fluids was used. Over 70% of our recipients including some of the very sick patients are extubated. Most of these patients do not need SICU post liver transplant.

With the increased numbers of patients on the waiting list for liver transplant in the U.S., the Scientific Registry of Transplant Recipients (SRTR) reports indicate that in some centers including ours that the one year wait list mortality reaches the level of more than 10%. As a result we began our live donor liver transplant (LDLT) program. Positive outcomes from Japan stimulated our efforts. We decided to use of the right lobe of the liver instead of the left one.

The University of Colorado Transplant Program in 1997, was the first one in the western hemisphere to report the initial success of the Right lobe liver donor transplant. The controversy surrounding LDLT continues in the US and other countries especially regarding the donor safety. In Colorado we had a donor death after 140 LDLT. The impact of a death on the family of the donor and on the transplant team is devastating.

The last technical modification was in 2000; with the reintroduction of choledochoduodenostomy instead of a roux-en-y anastomosis. This technical change was first used in hostile abdomens when roux-en-y limb was difficult to create.

In the mid 1990's we started protocols of steroid withdrawal after liver transplant which has led to complete cessation of steroid use after liver transplant except for some of the autoimmune hepatitis cases. We also achieved better results with Denovo use of Rapamycin after liver transplant

Over the last 25 years our program has done over 1800 liver transplants in adult and pediatric patients with over 90% one year patient survival and one over 70% for ten years.

To conclude; the team effort and need for improvement was the driving force behind the coordinated success of the liver transplant program at the University of Colorado School of Medicine.

L41

Experience With 500 Cases of Living Donor Liver Transplantation in Egypt

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The absence of a cadaveric liver transplantation program in Egypt has led us to start the first living donor liver transplantation (LDLT) program in Egypt in August 2001. Since then we have performed more than 500 cases of LDLT in three transplant programs. This is mainly an adult program with only three paediatric cases and only three left lobe donations. the remaining 497 cases were right lobe donations of which two were for retransplants.

Donor safety has been of primary concern in our programs. Donors were 18 to 45 years of age with a mean of 30 and ABO-compatible. Liver biopsy was done routinely in all donors and 30% revealed abnormal findings in spite of normal tests stressing the importance of routine liver biopsy in donors.

There were no donor mortalities and donor complications were classified using the Clavien grading system with all complications within grades I and II. The residual liver volume was always kept at or above 35.

The mean age for recipients was 44 years, MELD 21. and BMI 26 with HCV constituting 95% of the cases.

Associated Hepatocellular carcinoma (HCC) has been the indication in 19% of cases with 98% of those within the Milan criteria.

Biliary complications have been an initial challenge being a cause of mortality in 0.5% and morbidity in > 10% of cases in the initial 130 cases analysed. Modification of the surgical technkque and selection criteria has eliminated the mortality from biliary complications in LDLT.

L42

Evolution of Liver Transplantation in Lebanon

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Background: Liver transplantation was performed for the first time in Lebanon in 1998; this was followed by several transplants over the years.

Material/Methods: From 1998 to present, 21 liver transplants were performed in our institution. Of these, 14 were adults and 7 children. Indications for adult transplants were: 2 alcoholic liver cirrhosis, 2 autoimmune liver cirrhosis, 5 cryptogenic, hepatitis B, hepatitis C with HCC, 1 subacute liver failure, 1 Budd Chiari syndrome, 1 biliary cirrhosis secondary to iatrogenic common bile duct injury, and 1 multiple hydatid disease of the liver. Pediatric transplant indications were: 4 cryptogenic liver cirrhosis, 1 extra hepatic biliary atresia, 1 familial

hypercholesterolemia, and 1 congenital hepatic fibrosis. Of the 21 transplants, 4 were living related liver transplants.

Results: Patient survival was 76% at 1, 5 and 10 years. There were 5 deaths at a median of 9 days (range 1-56) post-transplantation. The causes of death were: 2 primary non-functions, 1 intraoperative cardiac arrest, 1 portal and hepatic artery thrombosis, and 1 severe cellular rejection. There were 2 biliary complications and 2 major vascular complications. All survivors are well, with normal liver function tests at a median follow-up time of 70 months (range 2-131) after transplantation.

Conclusions: Although our numbers are small, the 10-year survival rate is acceptable compared to other series. Cadaveric organ donations and transplantations should be encouraged so that more transplants can be performed. Living related liver transplant is an important alternative source of organs, but should not replace cadaveric donation.

L43
Clusters, Derivatives and Uterine Transplants

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Mass homotransplantation of abdominal organs was introduced by Dr Starzl in 1960 as a model for the study of the physiology of the denervated graft. It was the beginning of the "cluster" concept according to which the abdominal organs are like the clumps of a cluster. They can be used as composite or solitary grafts.

Clinical attempts started in the mid 80s, the first series of such Transplants was started in the early 90s. Now we are able to analyze their use and long term results.

Almost 20 years after after transplantation, more than 1/3 of the pediatric and about 25% of the adult patients are alive.

Short term survival improved overtime, all surviving patients are independent of intravenous treatments except patients who lost or are losing their grafts.

Their BMI on oral nutrition is normal or nearly normal.

Still, patients and grafts, alive and well at 5 years, have a high rate of attrition on further follow up.

In an elegant study Dr. Kareem AbuElmagd showed that there were 2 major risk factors: the absence of the liver from the graft, which was expected and then something we all suspected but were never able to prove: the lack of social support. Indeed the lack of social support had just as much an impact as the liver!

Long term survivors had lots of problems: hearing loss, developmental delay, depression, substance abuse, impaired cognitive functions.

Nevertheless, most patients completed education, 84% maintained marital status, 75% were appropriately employed.

Other Composite abdominal transplants have been byproducts of the clusters and have two main advantages:

A technical: there are only 2, large vascular anastomoses, the abdominal Aorta and Inferior Vena Cava and an immunologic: protective effect of the liver.

Disadvantage is that one has to consider the 3 dimentional fit of the composite grafts before implantation to avoid technical imperfections.

En block Liver Kidney transplants is such a variant, we had done 9 such transplants in Miami with my associate, Dr. Akin Tekin.

All patients were children, 8 of 9 suffered from congenital hepatic fibrosis and autosomal recessive polycystic kidney disease, one from hyperoxaluria.

All are alive with functioning grafts except one who died of rejection due to non compliance

A variant of this procedure is the combined Liver, pancreas and K Tx for Wolcott Rallison Syndrome. This is a rare genetic disorder caused by mutations in the gene which controls protein unfolding. It is the most common cause of neonatal diabetes. Death usually occurs in childhood from fulminant liver and kidney failure. We have performed one such successful case which, for the first time, resulted in control of the syndrome. The child is alive and has been well for almost 2 years following the transplant**

The composite abdominal wall transplants have been byproducts of the cluster transplants.

Initially presented in 2003, the blood supply was through the inferior epigastric arteries, anastomoses through the iliac vessels of the donor which were anastomosed onto the lower abdominal vessels of the recipient.

It is pretty adaptable and can cover practically any abdominal wall defect. The same, or a different, compatible donor can be used, at the same or subsequent surgical session.

In Miami we did a total of 10 such grafts.

Other programs have used a variant with microvascular anastomoses.

And then: the Intestinal/multivisceral autotransplants, designed to treat otherwise unresectable lesions of the

route of the mesentery, as desmoid tumors and severe vascular malformations. Usually, the head of the pancreas is removed en block with the intestine, the pathology is resected in the bloodless field of the back table as well as any vascular reconstructions. Then the graft is reimplanted.

In our series of Ten patients, four children and six adults, who underwent these procedures since January 1999, * 7 patients are alive up to 13 years later, 6 with functioning autografts; one had to be rescued with an allotransplant.

UTx is a procedure devised for the treatment of uterine infertility which is a very common problem. It is due to to congenital absence, as in the Rokitansky syndrome, surgical resection or damage from abortions or infections.

At the moment, there are 2 options for these women: adoption and surrogacy. They are good for many. The reason uterine transplants are needed is because it is impossible for many others.

UTx just like face, extremity and other composite tissue transplants is not a vital transplant.

Unlike any other transplant performed till now, it is an ephemeral transplant: the first transplant not intended to last for the duration of the patient's life but only till the delivery of one or more healthy offspring. After that time, the immunosuppression is stopped and the graft left to reject or removed.

Three lives are at risk: the mother, the donor and the offspring. One has to be sure that they are protected.

Ideally, the procedures involved are tested in animals with anatomy and physiology like the humans and only then applied clinically.

It's for a fact that the anatomy and physiology of reproduction is species specific. The closest one can get are the non human primates.

Non human primates have anatomy and physiology that is closest to human, techniques used are directly applicable to humans. But there are problems with them:

The number of experiments that can be performed with primates is very limited. There are emotional difficulties due to their humanoid features and their use is very restricted. They are also very expensive.

Long term Immunosuppression is notoriously difficult in baboons, which are the most accessible non human primates. They are also subject to TB and Simian CMV.

Male baboons have frequently low sperm counts.

IVF is tenuous. So, one can only go so far with Baboons.

For these reasons data have accumulated by pasting together findings from different species.

*The group of the U Gothenburg, Sweden led by Dr. Mats Brannstrom, has the most extensive experience. They showed in small animals that transplantation of the vascularized uterus can be performed safely. The graft can tolerate cold ischemia, can become pregnant and deliver offspring not different than controls. They also showed that autotransplantation in baboons is safe, information which is directly transferable to a living donor situation.

We performed UTx on mini swine. We used a heterotopic location and exteriorized the graft.

This allowed us to perform numerous hysteroscopies and study rejection and its treatment.

We showed the safety of donor and recipient procedures and that longterm survival can be achieved in these animals.

We had the opportunity to collaborate with the Swedish group which has included Dr. Michael Olausson for the past several years. Together we performed U allografts in baboons in a procedure mimicking deceased donor UTx and showed its safety and longterm survival.

Other groups showed that healthy offspring can be delivered from allografts in sheep and autograft in baboon.

There have been 11 clinical cases:
First case in SA from a living donor 13 years ago, without any experimental preparation, the graft had to be explanted 3 months postoperatively.

Second case in 2011 in Antalya, Turkey, from a deceased donor, again without any experimental preparation. The graft is intact, without evidence of rejection. Attempted IVFs have not been successful as yet.

Then there has been a series of 9 Transplants from living donors at the U Gothenburg by a team led by Profs Brannstrom and Olausson which I was privileged to attend.

This is very exciting times because, at this moment the team is preparing the first patients for IVF, scheduled to start 1 year after the transplant.

A successful outcome will be hope to many women who's desire to bear a child is unfulfilled due to Uterine Infertility.

L44
Big- and Small-for-Size

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L45
Split-Liver Should Be Done More Often

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Over the last 30 years split-liver transplantation has become a victim of its own success. The shortage of organs and the resulting death risk during the waiting time has become the most important factor for survival in many indications.

Apart from direct measures to increase donation the transplant surgeon has several ways to deal with this. First of all we tailor indications to the availability of organs. Further we can try to open resources by transplanting extended criteria donor grafts or livers from DCD donors. Finally we can use technical options like domino transplantation, split-liver transplantation or living donor liver transplantation.

Split-liver transplantation started in the end of the 80s with the aim of providing grafts for children, then the most deprived group of patients. The technique was hampered by bad results for the right graft and poor reproducibility. In 1995 the experience with living donor liver transplantation translated in the introduction of in-situ splitting. This technique was completely designed to safeguard the right graft. During this initial period, single experiences of experienced centers showed similar results for split- and whole grafts, while registry data still clearly identified split-liver transplantation as a risk factor for the adult recipient. This situation is now turned around with registry data, both in Europe and the US, confirming comparable results in the last years while inferior results are only reported by a few centers.

While this way of splitting has practically solved the organ availability for children and preserves the numbers of grafts for adults, our ultimate goal should be to develop split-liver transplantation for two adults. Despite several technical improvements, the size of the grafts and the damage to the vascularisation of the bile ducts remains a problem. Split-liver transplantation for two adults is therefore a procedure in development with large potential if the small-for-size problem can be solved.

In view of our increasing willingness to accept ECD donor organs we should be willing to look at our best organs and make optimal use of them.

L46
Challenging Anatomical Problems and Innovative Solutions in Liver Transplantation: Vascular Problems

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Vascular complications after living donor liver transplantation are one of the most feared problems which frequently result in graft and patient loss. The leading causes of these complications are mostly due to challenging anatomical problems in the living donor. These problems can be divided into four groups.

1. Problems regarding vena cava inferior:
Retrohepatic vena cava may not exist in the recipient. The venous circulation of the lower extremity and kidney is provided by the collateral veins. In these cases the venous drainage of the partial liver graft is generally assured by the vena cava inferior present at the level of diaphragm. On the other hand if the venous circulation of the kidney of the patient is supplied by v. azygous system, an attempt to recreate the vena cava inferior should not be done (1).

2. Problems regarding hepatic venous system:
The necessity of providing venous drainage to the right anterior sector of a right lobe graft is controversial (2,3). The middle hepatic vein was included in the right lobe graft in the original design (4), but many transplant centers avoided this procedure assuming that the risk to the donor would substantially increase (5,6). However congestion and failure in the graft did occur without provision of the hepatic venous drainage to the right anterior sector(4,5). Therefore the crucial point in the venous drainage of the anterior sector in right lobe living donor liver transplantation is direct or indirect anastomosis of the segment V and VIII hepatic veins to the inferior vena cava by variable reconstruction methods (5,7,8).

3. Problems regarding vena porta:
Adult-to-adult right lobe living donor liver transplantation (LDLT) has become popular, because it provides a larger size liver graft that is necessary for adult recipients. However anomalous portal venous branching (APVB) resulting in two venous openings in a right lobe graft is one of the most common anatomic variations encountered during evaluation of a living donor candidate. Several authors reported the incidence of anatomic variations of the portal vein as 6% - 22% (9,10). Reconstruction of these vessels during transplantation can be challenging and even donors with such APVB had often been disqualified as right lobe donors (11). Several reconstruction methods have been attempted for this anomaly and thus donors with such APVB became available for right lobe liver grafts (12,13). However, all these surgical techniques have their pitfalls.

4. Problems regarding hepatic artery:

Hepatic artery reconstruction is one of the crucial steps for living donor liver transplantation. Arterial complications including thrombosis, stenosis and aneurysm formation are life threatening in living donor liver transplantation leading to graft failure and irreversible biliary damage. Arterial reconstruction has remained as a major problem in living donor liver transplantation due to small diameter until introduction of microvascular anastomosis techniques by surgical microscopes or loupes. The incidence of arterial thrombosis has declined dramatically from 25% without a microscope to 0-3.8% with a microscope (14,15,16). Nevertheless, technical failure of the reconstruction usually leads to retransplantation or even death and the procedure is complicated by anatomical variations (e.g. two hepatic erteries to the right lobe), vascular consistency and the hemodynamic situation of the recipients during the operations.

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Lecture

L47
The Biliary Anastomosis: Technical Considerations

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The technical aspects of the biliary anastomosis should be discussed separately for cadaveric and living donor liver transplantation.

In cadaveric transplantation, the most preferred technique is a duct-to-duct anastomosis. The use of a T-tube declined markedly in the last decade although practices still vary widely. A tension-free anastomosis between well-vascularized ends should be constructed with fine, monofilament absorbable sutures. Bile duct redundancy and inadvertent suture closure of the cystic duct should be avoided to prevent kinking and mucocele formation respectively. The major complications are leakage and stricture, which can usually be managed by endoscopic methods. Recurrent anastomotic stricture after multiple ERCP procedures may be an indication for a Roux-Y reconstruction. A biliodigestive anastomosis is performed in patients with primary sclerosing cholangitis (PSC), damaged bile ducts (inadvertent embolization during radiologic treatment of hepatocellular carcinoma, retransplantation) or biliary atresia. The use of a transanastomotic catheter depends on physician preference. The major complications are leakage and stricture, which can usually be managed by percutaneous methods. Graft loss due to a biliary anastomotic complication is rare in the absence of concomitant vascular problems.

In living donor liver transplantation, a Roux-Y reconstruction is preferred for left-sided grafts (mandatory in children with biliary atresia) because a tension-free duct-to-duct anastomosis is not usually possible and traction of an originally acceptable anastomosis may occur during graft regeneration. The use of a transanastomotic catheter depends on physician preference. The major complications are leakage and stricture. For right-sided grafts, a duct –to-duct anastomosis is preferred for technical ease, avoidance of intestinal contamination and the possibility of endoscopic treatment of complications. Keeping the dissection plane very close to the vascular structures in the hepatoduodenal ligament and cutting the biliary tree transparenchymally at the end of the recipient hepatectomy preserves a well-vascularized, multiple-ended 'pedicle' that may make it possible to reconstruct multiple bile ducts of the right lobe. The cystic duct may also serve as a conduit. The use of a transanastomotic catheter depends on physician preference. The major complications are leakage and stricture, which can usually be managed by endoscopic and radiologic methods, depending on center experience. A Roux-Y

reconstruction is used if the biliary tree of the recipient is unsuitable for anastomosis or special situations such as PSC are present. In living donor liver transplantation, biliary anastomotic leakage is a risk factor for early hepatic artery thrombosis with catastrophic consequences and for late stricture formation. Graft loss due to a biliary anastomotic complication is an infrequent but well-recognized problem that is further complicated by the fact that the recipient may have to turn to one more family member for donation.

The reported complication (10-35% for cadaveric and 15-50% for living donor liver transplantation) and treatment success rates vary widely depending on definitions, center experience and length of follow up. Biliary anastomotic complications remain significant causes of morbidity, potential graft loss and even mortality.

L48

Improved Outcomes in Overall and Kidney Graft Survival Among Simultaneous Liver-Kidney Transplant Recipients in Post-MELD Era – Does the Diagnosis of HCV Play a Role?

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Background: Since the United Network for Organ Sharing (UNOS) implemented MELD system to determine liver graft allocation in 2002, the number of simultaneous liver-kidney transplants (SLK) has increased. Previous studies have shown that patient survival in post-MELD era is improved in those with long-term dialysis (>3months.), compared to patient survival in liver transplant alone (LTA). Our study is aimed to compare survival outcomes among SLK after MELD era according to their specific diagnosis, HCV vs non-HCV.

Methods: In this IRB-approved retrospective study, clinical data review was performed in all patients who underwent combined liver-kidney transplants at Johns Hopkins Hospital from January 31, 1995 to October 31, 2012. Combined but non-simultaneous transplants, in which liver and kidney transplants took place more than 24-hour apart, were excluded. All cases with prior LTA, kidney transplant alone (KTA) or SLK were also excluded. Differences in patient demographics and characteristics among two groups were compared using independent-samples t-test. Survival analysis and the distributions were calculated using Kaplan-Meier method and Mantel-Cox log-rank test.

Results: Out of total 43 (48) CLKs, 30 (31) SLK cases (24 (25) post-MELD and 6 pre-MELD), were included. Proportions of age, gender, ethnicity, pre-transplant MELD score; pre-transplant renal replacement therapy (RRT) requirement, hypertension, diabetes mellitus and follow-up period were similar in two groups. Median follow up period was 30 months. Both overall and kidney-graft survival in pre-MELD era were 50%, but they were 91.7% in post-MELD era (p=0.02). However, when compared to the diagnosis, there was no statistical significance between overall and kidney-graft survival among 9 (10) HCV and 15 non-HCV subgroups in post-MELD patients (p=0.670 and p=0.403).

Conclusion: Literature suggests lower risk of liver graft loss in SLK compared to LTA, but not much information is

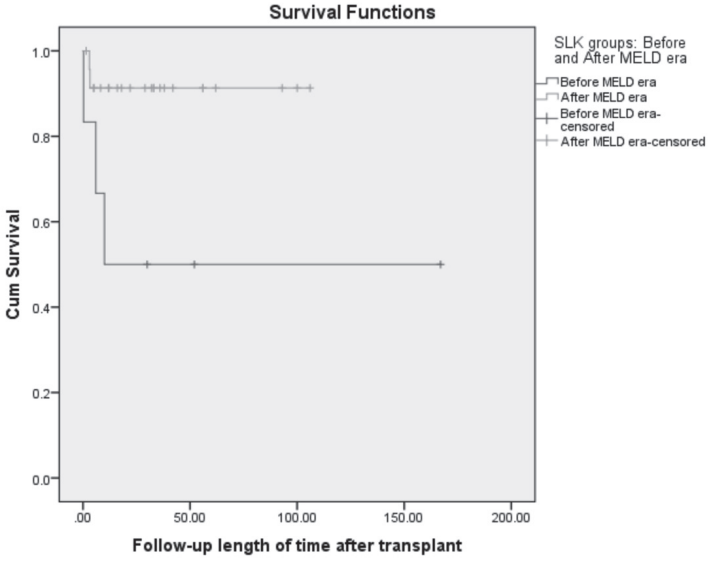
Case Processing Summary

SLK groups: Before and After MELD era	Total N	N of Events	Censored	
			N	Percent
Before MELD era	6	3	3	50.0%
After MELD era	24	2	22	91.7%
Overall	30	5	25	83.3%

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	5.428	1	.020

Test of equality of survival distributions for the different levels of SLK groups: Before and After MELD era.

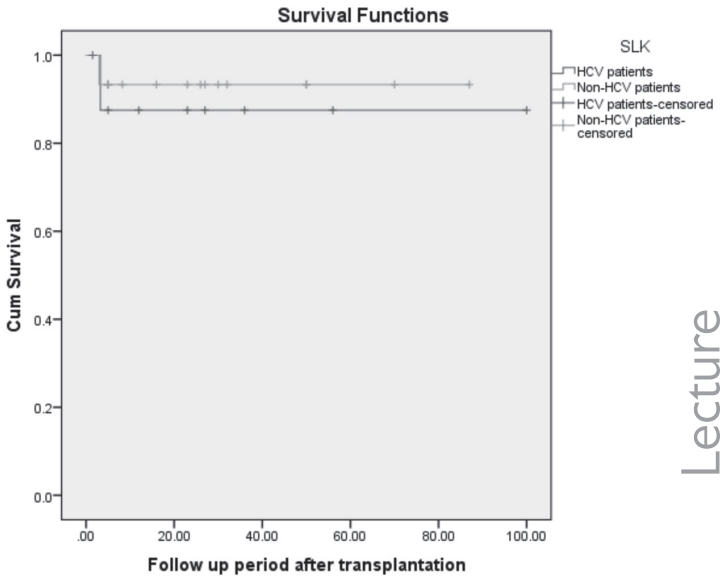


Means and Medians for Survival Time

SLK groups: Before and After MELD era	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Before MELD era	86.208	33.003	21.522	150.895	10.000	.	.	.
After MELD era	97.054	6.044	85.208	108.901	.	.	.	.
Overall	137.966	11.812	114.814	161.118	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

available regarding the specific diagnosis of the underlying liver disease, HCV vs non-HCV. In our study, we have again demonstrated statistically significant difference in overall and kidney graft survival between the post-MELD era and the pre-MELD era. Subgroup analysis of this group showed no statistically significant difference in overall and kidney-graft survival, when compared to their specific diagnosis of HCV. This observation needs to be further studied and verified in larger cohort of patients to fully identify the impact of Hepatitis C infection in this group of patients since it can affect both liver and kidney grafts, post transplantation.



Case Processing Summary

SLK	Total N	N of Events	Censored	
			N	Percent
HCV patients	9	1	8	88.9%
Non-HCV patients	15	1	14	93.3%
Overall	24	2	22	91.7%

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	.182	1	.670

Test of equality of survival distributions for the different levels of SLK .

Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
SLK	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
HCV patients	87.906	11.313	65.733	110.079	.	.	.	.
Non-HCV patients	81.400	5.410	70.796	92.004	.	.	.	.
Overall	91.576	5.692	80.420	102.732	.	.	.	.

a. Estimation is limited to the largest survival time if it is censored.

Lecture

L49
Cancer After Liver Transplantation

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Cancer mortality after all forms of transplantation provides both physicians and recipients with a significant concern, ranking behind cardiovascular disease and infection as cause of death with a functioning graft. Cancer after liver transplantation is both different and similar to cancer after other forms of transplantation, the similarities driven by the immunosuppression and the differences driven by the diseases that lead to hepatic failure and the inherent behaviour of cancers in the liver.

Cancer should be divided into four groups:

1. Recurrent cancer such cholangiocarcinoma, hepatocellular carcinoma and extra-hepatic cancers which pre-existed in the recipient and may have been an indication for liver transplantation. These are the subject of intense debate and protocols and will not be further discussed here.

2. Donor transmitted cancers which were present in the organ at transplantation and which are screened out quite effectively by history, examination and investigation such that the incidence in the UK is around 0.05% and in the USA up to 1.0% of transplants from deceased donors.

3. Donor derived cancers where the cancer develops in the transplanted liver after transplantation, as may occur in a cirrhotic liver after hepatitis reinfection, or occasionally when a lymphoma is derived from donor rather than recipient lymphocytes. 4. Finally and most commonly, **de-novo cancer** accounts for the majority of cancer deaths in all forms of transplantation .

Donor transmitted cancers are rare after liver transplantation in US, UK and Aus data. The cancers that have been reported include: Neuroendocrine tumour, Adenocarcinoma of the Colon and melanoma. The relative rarity of transmission in liver cancer is notable, likely screened through a high index of suspicion at retrieval.

De-novo cancers are significantly increased from the general population and in liver transplant recipients the additional known risk factors include: Age (RR 1.33), Smoking (1.72), Alcoholic Liver disease (2.14) and Primary Sclerosing Cholangitis (2.62). The increased incidence is highest in the first two years where Lymphoma and Kaposi sarcoma are the highest frequency, but the incidence remains two or

more times higher than the general population. In the UK the risk of de-novo cancer after liver transplantation is 90 per 1000 patient years by 10 years compared to an expected rate of 36 in the general population.

Strategies for avoidance, detection and treatment are all relevant to the long term care of liver transplant recipients.

L50
What Are the Boundaries of HCC Treatment? Transplantation for HCC

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250,000–1,000,000 deaths occur every year due to hepatocellular cancer (HCC) worldwide and HCC is the fifth most common cause among cancer deaths. When diagnosed only 10-30% of HCCs are resectable and even resected 70% of them cannot be cured. Liver Transplantation (LT) offers better survival rates and cure chance for HCC when compared to resection or any other local treatment modalities. Rationale for liver transplantation is the multicentricty of the tumors and the high risk of recurrence after local treatment. LT also cures the underlying chronic liver disease.

Advantages of LT are to provide complete tumor resection, to cure of underlying liver disease and to eradicate liver tissue that may contain occult HCC or dysplastic nodules. Whereas the disadvantages are the surgical risks, organ shortage, long waiting list, higher cost, and lifelong commitment to immunosuppresives.

Live donor LT for HCC has more advantages over LT from deceased donors such as; waiting time is negligible and the surgery is planned, avoids the risk of tumor progression and avoids transplant ineligibility. On the other hand there is considerable risk to the donor which is the main concern in live donor LT.

A debate has been going on for a long time to decide who is going to benefit from transplantation most and efforts have been made to develop inclusion and exclusion criteria for transplantation. Although the initial series without patient selection criteria had dismal results, Milan criteria has increased the survival rates up to 75% for transplantation for HCC and have been applied worldwide. Today selection criteria have been expanded and excellent survival rates are achieved for tumors without major vascular invasion and a total tumor diameter less than 8-10 cm.

L51
Hepatectomy for Hepatocellular Cancer

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Resection is the treatment of choice in HCC patients with near normal liver function. Child classification is still the most practical way of selecting candidates for partial hepatectomy. Patients with Child A cirrhosis and minimal portal hypertension (e.g. platelet count >100,000/mm3 and hepatic venous pressure gradient <10 mmHg) are ideal candidates for resection. Extend of underlying liver disease and metabolic reserve of liver parenchyma determine both resectability and postop patient survival.

Tumor size is not a limiting factor in the determination of resectability. Patients who have circumscribed single tumors are potentially resectable regardless of tumor size. However, patients with muItiple tumors are not good candidates for resection. Presence of multiple tumors strongly implies intrahepatic metastasis and high risk for recurrence. Tumor recurrence in remnant liver frequently originates from a metastatic foci of resected HCC. De-novo tumor may also occur in the potentially tumor producing remnant liver.

Survival rates after resection are in the range 80-92% at 1 year, 61-86% at 3 years, and 41-74% at 5 years. Liver function, including Child, degree of fibrosis, total bilirubin level, presence of clinical portal hypertension and platelet count may predict short-term survival. On the other hand, long-term results are closely related with tumor recurrence, which occurs in approximately 20%, 50% and 75% of patients at 1 year, 3 years and 5 years, respectively. Predictors of recurrence are tumor grade, microscopic and macroscopic vascular invasion, tumor size, number of tumors, presence of satellites, AFP levels, and positive surgical margins.

L52
Local Ablation for HCC

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Early diagnosis of hepatocellular carcinoma (HCC) is important in terms of treatment modalities and success. Surgical options must be considered first, and if the surgical option is precluded, image guided tumor ablation is recommeded in properly selected patients.

The Barcelona Clinic Liver Cancer (BCLC) classification system commonly used for clinical management of patients with HCC. This classification system is also important base for image guided tumor ablation (figure1).

According to BCLC system, percutaneous tumor ablation is recommeded for early stage HCC with no extrahepatic spread and without vascular invasion.

HCC nodules less than 2 cm, not subcapsular or perivascular are the ideal nodules for image guided RF ablation. In patients with early HCC, the rate of complete response is about 97% with a 68% of 5 year survival rate.

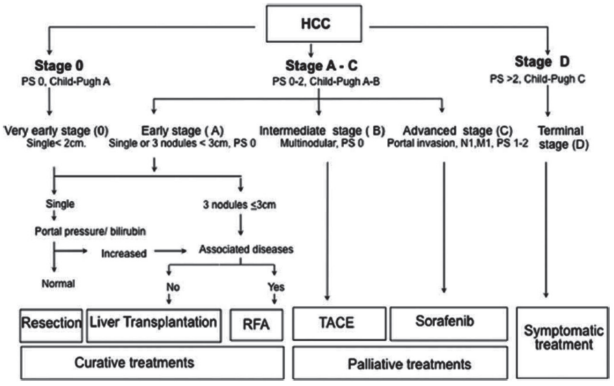
Early stage HCC: Includes patients with preserved liver function (Child pugh A or B), with solitary HCC or up to three nodules less than 3 cm in size.

An important factor affecting the success of RF ablation is to ablate all viable tumor cells and to create tumor free margin. The best results are achieved if the tumor size is less than 3 cm. if the tumor size is between 3-5 cm, the success rate of RF ablation is decreased. Therefore, combination treatment methods are recently emerged to get beter results if the HCC nodule is larger than 3 cm and smaller than 5 cm.

The RF ablation offers beter survival than ethanol injection if the nodule larger than 2 cm.

Microwave (MW) ablation is another alternative to RF ablation. MW ablation cause higher intratumoral temperatures, larger tumor ablation volumes, faster ablation times. However, no statistically significant differences were observed comparing with RF ablation.

A new nonchemical and nonthermal image guided ablation technique is irreversible electroporation (IRE). IRE cause irreversible distruption of cell membrane integrity by changing the transmembrane potential. One advantage of this technique complete ablation of the margin of the vessels. It can be applied to the nodules that is centrally located.



L53
Liver Transplantation For Non-Hepatocellular Liver Cancers

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Lecture

The liver is both a site for primary malignancies as well as for secondary metastasis. While hcc in cirrhosis represents more than 75% of malignancies and is associated with a long-term survival of 70% if specific selection criteria are applied, in selected cases of non-hcc malignancies or even liver metastases, ltx may be indicated.

Hilar Cholangiocarcinoma
Surgical resection and ltx are the only potentially curative treatment options for patients with hilar cholangiocarcinoma. After surgical resection, 5-year survival rates of 20% to 60% have been reported. If surgical resection is limited by proximal tumor extension, ltx has been proposed. Initial results of ltx for hilar cholangiocarcinoma have been disappointing and 5-year survival rates were rarely above 30%. Ltx using neoadjuvant radiochemotherapy, in combination with staging laparotomy to definitely exclude extrahepatic tumor involvement. The long-term patient survival of this cohort was excellent (5-year survival, 76%) and thus may be considered for selected patients. Nevertheless, the role of earlier diagnostic detection, biochemical and genetic markers, and neoadjuvant and/or adjuvant treatment approaches need to be further defined.

Intrahepatic Cholangiocarcinoma
Intrahepatic cholangiocarcinomas might be considered for ltx provided the tumor is either unresectable due to bilobar growth or the recipient has concomitant liver cirrhosis, which occurs in about 5% of patients. Overall, the 5-year survival in a spain cohort and in the unos database is around 40%, whereas it is slightly lower in the european liver transplant registry data for intrahepatic cholangiocarcinoma after ltx.

Hepatoblastoma
Unresectable hepatoblastoma, being the most common hepatic malignancy in early childhood, can be an indication for ltx. In cases of unresectable disease, a total experience of more than 300 cases (mainly us and european patient) demonstrate excellent 5-year survival rates of 70% to 80% after ltx. The results of "rescue transplantation" after previous incomplete tumor resection or after tumor recurrence are less encouraging, leading to 5-year survival rates of only 30% in one series.

Epitheloid Hemangioendothelioma
Epithelioid hemangioendothelioma is a rare malignancy

and predominantly observed in young female patients. A major problem is the precise diagnosis and the prediction of its future course. The main differential diagnosis is hepatic angiosarcoma, which has a very poor prognosis (median survival of 6 months). Whereas ltx is contraindicated in angiosarcoma, epithelioid hemangioendothelioma has a good prognosis after transplantation. Ltx is often the only option, since resection is rarely possible due to the bilobar, multifocal nature of this tumor. A number of transplant centers and registries have analyzed their experience with epithelioid hemangioendothelioma and reported 5-year survival rates of 55% to 75%. Surprisingly, even the presence of extrahepatic metastases did not correlate with long-term survival, and therefore this specific tumor is not necessarily a contraindication for transplantation.

Liver Metastases of Neuroendocrine Tumors

Neuroendocrine tumors often present with unresectable liver metastases. Numerous treatment options have been applied including palliative surgery, chemotherapy, and interventional techniques, but all of these are associated with poor survival rates. Therefore, ltx has been evaluated, resulting in an overall ~50% 5-year survival. The reported results vary between 33% and 80% in various series, presumably due to different patient selection. Several factors associated with a more favorable survival have been defined. These include primary tumor located in the small bowel/lung, no previous extensive operations, no lymph node metastases and no extrahepatic disease, age below 50, normal e-cadherin expression, and ki-67 index < 5%. Ltx can be considered in selected patients, whereas it should be withheld in patients with dismal prognostic factors.

Colorectal Liver Metastases

Colorectal liver metastases were once considered an absolute contraindication for ltx. However, in the 1980s and early 1990s, more than 50 patients with colorectal liver metastases have reported to undergone ltx. The eltr reported 1- and 5-year survival rates of 62% and 18%, respectively. Today, oncological treatment as well as diagnostic imaging techniques have significantly improved, and therefore some to believe that this might also lead to a more specific selection of patients and that adjuvant treatment might help to improve the results after transplantation. Recently, the oslo group reported on 21 patients with various stages of colorectal metastasis who underwent ltx. Their 2- and 5-year survival rates were 89% and 60%, respectively. They reported that patients with large tumors (>5.5 Cm), those in whom primary colorectal resection was less than 2 years before ltx, and with cea >50 ug/l, were at greater risk for recurrence and death. Nevertheless many questions remain about the strategy in these cases, including the need for neo-adjuvant chemotherapy after ltx.

L54
Ethics in Transplantation

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Since the early days of transplantation, ethical issues have arisen and been addressed. In the beginning there were ethical issues with regard to experimentation and new treatments being used on patients. As patient and graft survival improved, it then became unethical not to transplant.

Nations and regions vary in their current state of medical development. In less developed countries, the ethical concept of justice requires that priority must be given to general medical and health programmes. Expensive transplants can help only a few individuals.

Countries also vary in their legal, political, religious and social readiness to undertake human transplantation. Some societies have well-established criteria for 'brain death', others do not recognise a neurological diagnosis of death, therefore despite having the medical knowledge, cadaveric transplantation is not possible.

There is no universally accepted agreement on:
- the use of living donors
- animal donors (xenotransplantation)
- payment for organs
- indications for recipient listing
- donor suitability
- allocation of organs.

The ethical systems of even the most developed of countries are continually challenged by Transplantation. Economic considerations must be weighed against 'the public good'. Even when consensus has been reached, there are always new or special cases which arouse controversy. Countries may learn from the experiences of others.

Use of Living Related Donors
- First live related kidney transplant between identical twins in the 1950s
- Permission was then extended to non-identical twins, subsequently to biologically related then to non-genetically related family members.
- The advantage of living donor graft survival must be weighed again the physical and psychological risks to the donor.

In most countries the ethical basis for live donation has been firmly established in law and confirmed by biological outcome. Waiting times are rising and immediacy is

particularly advantageous for children. Despite improved results with cadaver donor transplants, the scarcity of human organs and the difficulty in providing cadaver organs urgently mean that the role of live donation as an ethical alternative can only increase.

Live Related Transplantation

In live transplantation, the risks and benefits are not equal since the donor bears most of the risk but the recipient receives most of the benefit. C Elliott believed that a distinction should be made between "allowing" a person to risk harm to himself and "encouraging" it: 'Substantial payment to organ donors arguably crosses the line between allowing and encouraging'.

Conclusions

- Should we be determined to maintain life at any cost?
- This attitude can cause distress and suffering to patients, so when do we stop?
- Who do we transplant and with which organs?
- Do we consider the ageing process and our ultimate mortality enough?

L55
Liver Transplant for Patients With Alcoholic Liver Disease: An Ethical Analysis

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Liver transplantation has progressed rapidly from an experimental procedure to standard therapy for patients with end-stage liver disease. However, the demand for liver transplantation far exceeds the supply. As a result, in all countries, there are many deaths per year on the liver transplant waiting list.

The relative organ shortage provides the basis for considering the ethical issues associated with liver transplantation. For example, allocation of organ to patient with alcoholic liver disease, which is one of the most common indications for liver transplantation, is still surrounded by unresolved controversies and ethical dilemma. One critical issue is whether patient's life style should be taken into account in deciding who gets the organ.

In 1993, supported by several studies, the National Institutes of Health Consensus Conference on Liver Transplantation stated that alcoholic liver disease is an appropriate indication for liver transplantation. This led to an increase in the number of transplants performed for these patients.

By presenting an ethical argument about liver transplantation to patients with alcoholic liver disease, reasons provided by proponent and opponents will be discussed. In doing so, controversy about a second liver transplantation to a patient with alcoholic liver disease will be discussed.

L56
A Needed Alliance of the Liver Transplant Community

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WHO, Advisory for Human Transplantation
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The evolution of liver transplantation to today is gratifying. With all of the accolades deservedly recognizing Dr. Starzl, the honor bestowed upon Dr. Starzl by Dr. Haberal is a genuine expression of the appreciation of liver transplant professionals around the world.

However, the past 50 years brings an important challenge to the next period of liver transplantation history. That challenge is the donor source of the liver allograft.

The disparity of living to deceased organ transplantation is striking worldwide. There are countries that are practicing liver transplantation without a deceased donor program. The burden placed upon the living donor is significant when one considers the mortality rate of the donor estimated to be 1 in 300 right lobe donors. This observation should be compelling for liver transplant surgeons to embrace deceased organ donation and propel its development. The potential of deceased organ transplantation has not been realized around the world. Ministries of Health must be engaged to support deceased organ donation by the alliance of the liver transplant community.

There is a science of deceased organ donation that is about to unfold that hopefully will be embraced by liver transplant surgeons again worldwide. It is the ex vivo repair of the deceased donor liver allograft.

Research grants should be secured to foster this approach to the expansion of recovering liver allografts from a deceased donor source. We are at the very beginning stages of that scientific effort. It will be a revealing testimony of liver transplantation when its history is examined in 2063--- was there a concerted effort to change the current practice and its reliance upon the living liver donor.

L57
DCD Liver Transplantation (LT) in the UK – A Valuable Source of Organs or the 'Thin Edge of the Wedge?'

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The burden of chronic liver disease continues to grow worldwide and the UK is no exception. Consequently, the indications for LT continue to expand with increasing numbers of patients listed (52% increase over the last 4 years in the UK) but a continuing shortage of donor livers. The LT waiting list mortality in the UK is currently 8-22%, comprising patients who die waiting for a transplant or are removed from the list because they become too ill. Besides the national campaigns to increase donor numbers, strategies for increasing the liver donor pool includes a UK wide split liver program and expanding the use of DCD organs. The long term outcome for LT from DCD donors has been considered inferior to organs from DBD donors. However, recent reports suggest comparable outcomes for DBD and DCD livers after transplantation. It is also becoming apparent that the outcome of DCD livers depends on a number of donor and recipient factors and technical factors in relation to the organ retrieval and implantation. Preoperative identification of factors associated with poor outcomes in DCD LT remains an important challenge. The period between extubation and asystole may help predict graft function. Less liver damage may occur if the donor progresses quickly to cardiac death, as opposed to maintaining a heartbeat in the presence of significant hypoxia or hypotension. Consistent with this, restrictions on recovery are now imposed by most UK centres based on donor time to death and the duration of hypoxia or hypotension. This FWIT starts when the systolic blood pressure has a sustained (i.e. at least 2 min) fall below 50 mmHg (or the haemoglobin oxygen saturation falls below 70%) and extends up to the onset of cold in situ perfusion. The duration of the FWIT is the important determinant of outcome. The expected lifetime of a LT candidate offered a DCD liver should be compared with the expected lifetime of that candidate if they were to turn down the DCD offer and continue to wait for a DBD liver. That is to say, even if graft and/or patient survival is lower with a DCD liver, it may be better than dying on the waiting list. Considering the current shortage of donor organs, every liver transplant candidate should be informed at the time of evaluation that the choice in the UK is frequently not between a marginal (including DCD) liver and a standard liver, but between a marginal (DCD) liver or no liver at all. Until an algorithm for the use of the DCD donor is determined, recommendations by transplant teams and decisions by LT candidates should be predicated on full disclosure of the known risks and potential benefits of DCD LT.

L58
Induction Therapy

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Three-fold increase in induction therapy was noticed over the last decade. The objectives for induction therapy is to augment immunosuppression, facilitate delay introduction of calcineurin inhibitors, allow minimization / avoidance strategies of steroids and /or calcineurin inhibitors, beside its important role in desensitization protocols and ABO incompatibility transplants.

Different agents utilized for induction therapy will be highlighted in some details.

The conclusion will stress on induction therapy evaluation and its impact on outcome.

I think that till the end of 2013 the final chapter of induction therapy is not yet written.

L59
Expansion of the Cadaveric Liver Donor Pool By Utilizing Partial Grafts

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Introduction: To examine the current techniques of split liver transplantation.

Technique: Split liver transplantation can be performed ex vivo or in situ using left-right or conventional (left lateral segment [LLS] and right trisegment [RTS]) splitting techniques. Each has its own set of advantages and disadvantages.

Ex vivo split: Ex vivo splitting requires decreased donor operating room time and results in acceptable patient and

graft survival. However, it involves inadvertent graft re-warming, biliary complications, bleeding from the liver's cut surface, and poorer outcomes in critically ill patients

In situ split: In situ splitting allows rapid identification of biliary and vascular structures, hemostasis during the parenchymal transection, and less warm and cold ischemia time. It also can facilitate graft sharing among transplant centers. Disadvantages include longer donor operating room time, the need for a stable donor, and the need for a skilled procurement team at the donor hospital.

Left-right split: Recipient selection for left-right split involves informed consent at the time of listing for transplant. The vessels should be tailored for the index patient, and the recipient should have minimal portal hypertension, if possible. Graft size and weight matching should be as follows: left recipient <60 kg and > 1% body weight; right recipient <80 kg and >1 % body weight.

Current issues with left-right split liver transplantation include whether it should be done ex vivo or in situ, the problem of venous outflow in the right lobe graft, small for size syndrome in the left lobe graft, and logistical considerations of the index patient.

Conventional split: In conventional in situ splitting, the decision to split is made in the operating room upon visualization of the liver. It uses standard operating room equipment, but requires an additional 1-2 hours prior to aortic cross-clamp. LLS grafts demonstrated long-term graft and patient survival equal to living-donor and whole-organ liver transplant outcomes with a slightly increased incidence of complications. RTS grafts demonstrated equal or better graft and patient survival compared to whole-organ grafts.

Conclusions: Whether performed ex vivo or in situ, split liver transplantation is a challenging operation that requires meticulous patient selection and meticulous surgical technique. Split liver grafts exhibit outcomes similar to cadaveric whole organs with only a slightly higher rate of complications. Split liver transplantation offers immediate expansion of the donor pool, and its routine use may decrease the dependency on living donation, thus overcoming the concerns of living donor safety.

L60
Collaborative Transplant Study (CTS) Results on Long-Term Outcome of Liver Transplantation

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Lecture

The Collaborative Transplant Study (CTS) has collected background clinical as well as outcome data on liver transplants since 1985. Data on nearly 80,000 liver transplantations have been recorded and are currently available for analysis. Analysis of the evolution of liver transplant results over time as well as interesting comparisons with kidney, heart, lung and pancreas transplantation are possible. Outcome analysis shows an impressive improvement of the success rate of liver transplantation. However, unlike the results of kidney transplantation, which have improved both in the short- and long-term, liver transplant results show a significant short-term improvement during the early post-transplant period only. The long-term attrition rate, best expressed as long-term half-live, has remained virtually unchanged for many years.

We will discuss how the introduction of the MELD score for donor liver allocation has had undesired effects in at least one country. Disease-specific survival rates as well as the influence of different immunosuppressive drug strategies and immunogenetic factors will be discussed as well.

L61
How to Expand Donor Pool in Liver Transplantation – US Experience

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Orthotopic Liver Transplantation (OLT) has become a therapy for the treatment of end stage liver diseases over the past 20 years. The demand has rapidly increased, creating a large gap between the number of patients awaiting OLT and the number of patients who actually receive OLT. In the eastern countries, Liver Donor Liver Transplantation (LDLT) has become the sole or major source of grafts offered to the patients whereas in the Western Continent Deceased Donor (DD) grafts have been the only source of OLT. As of late April 2013, United Network of Organ Sharing (UNOS) has reported 15854 patients awiting Liver Transplantation

in US. In 2012, total of 6256 liver transplantation has been performed in US with 6010 cadaveric and 246 live donations. Especially, since early-mid 2000's the number of LDLTs performed in US has dramatically decreased with 3 donor mortalities being reported in the literature, with computed donor risk being calculated as 0.5%.

The alternatives that has been introduced into the daily practice of Liver Transplantation can be outlined as such;

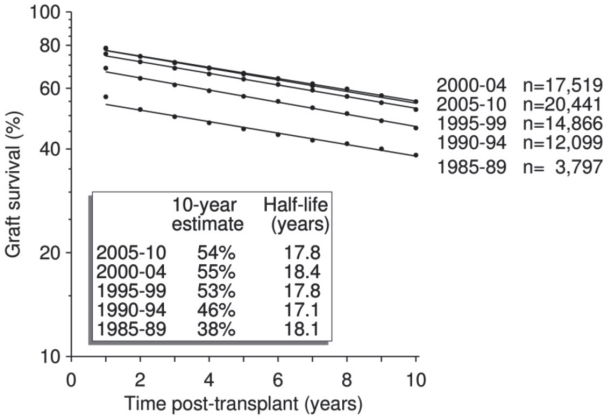
ECD: Extended Criteria Donors: Donor age >55, Donor Hospital Stay > 5 days, Cold Ischemia time >10hours, warm ischemia >40 min. Matching ECD allografts to appropriate recipients have been the main source establishing acceptable transplant outcomes as an alternative to higher waitlist mortality. ECD score of 2 or less is usually associated acceptable outcomes.

DCD: Donation after Cardiac Death: Previously called as non-heart beating donors. It consists of withdrawal of care in the operating room after adequate consent obtained from the family. In contrast to Brain Death Donors (DBD), among DCD donors , after extubation from the respirator, 5 minutes has to pass before the declaration of death. Warm ischemia time to the removal of the organs should be up to 20 minutes for better results. Graft survival is considered to be lower if the warm ischemia time is more than the allotted time. Biliary Complications can be as high as 35% in this group and its association with certain preservation solutions has been reported. Hepatic Artery Thrombosis (HAT) is also higher in this group. Careful donor and recipient match is the crucial part of this type of operation.

Advanced donor Age: Advanced age significantly decreased patient and graft survival in recipients with HCV. If the allograft is found to be suitable, may be appropriate in matched recipients. HCV receipients are recommended to match to an organ less than 55 year of age.

ABO Incompatibility: Not recommended unless in emergency situations for pediatric recipients. Blood type A2 can be given to O Blood type recipient.

Steotosis: Low and moderate steatosis can be considered as an important source and donor liver biopsies are encouraged.



Malignancy: History of Malignancy outside of the Central Nervous System (CNS) should not be used, previous CNS tumors may be acceptable.

HCV positivity: HCV–positive allograft can be accepted for HCV-Positive recipients. Survival is comparable with the use of HCV Negative allografts. Genotyping of the donor is currently is not done in routine practice.

Anti HBc positivity: Such donors can be accepted for non Hep B exposed receipients with the current HBIG and antiviral prophylaxis.

HIV: There is new literature suggesting that HIV positive donors can be accepted for HIV positive recipients.

Infections: Increased screening in endemic areas is important and donor cause of death should be identified before the procurement. West Nile and Rabies are the important CNS viral infections that need to be identified in the donor in advance.

SLT: Split Liver Transplantation; Splitting comes with its technical challenges and not all allografts are appropriate for splitting. Success rate is much higher in specialized centers with appropriate recipient match.

Facebook Phenomenon: Since May 1, 2012, Facebook users have been able to share their organ donor status with friends, family—and the world—as they do other basic information. The information is part of the site's new Timeline feature, which asks users to share stories and photographs. Since the launch, the results of the Facebook organ donation initiative have been phenomenal, boosting the nationwide increase in registered donors by a staggering 1,183 percent in its first week, a month later, the donor registration rates still were elevated.

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01

Evaluation of Pyrus Boissieriana Buhse Leaves Extract and Arbutin Effects on Nephrotoxicity Induced By Cyclosporine A in Rat

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Introduction: More than dozen frequently used immunosuppressive agents in liver transplantation with various target pathways are known and Cyclosporine (CsA) is a potent immunosuppressant drug which is widely used to prevent graft rejection after transplant. Overproduction of reactive oxygen species is one of the side effects of CsA that might cause severe damages primarily to the liver and kidneys. Also CsA treatments produce a significant increase in the serum urea and creatinine levels. Previous studies show that Pyrus boissieriana buhse leaves extract (Telka EXT) and Arbutin (ART) have antioxidant properties. We present the potential protective properties of ART in isolated rat that pretreatment by CsA.

Materials and Methods: Sixty four male wistar rats (250-300 g) divided into eight groups: Two doses of CsA (25 and 50 mg/kg), EXT (500 mg/kg), Arbutin (50 mg/kg), and distilled water (control). We analyzed serum urea and creatinine levels after the completion of treatment process.

Results: We report that the serum urea level in coadministration of ART and CsA at a dose of 50 mg / kg was significantly lower than its level in coadministration of EXT and CsA50 ($p = 0.01$). Urea level in administration of ART50 was lower than its level in coadministration of ART50 and CsA50 ($p = 0.003$). Although we found no statistically significant difference between the group which received only Arbutin and the control group ($p = 0.282$). Serum

Creatinine level was significantly higher in the administration of Arbutin 50 in comparison to the other groups ($p < 0.05$), but creatinine level in the groups that received only EXT was meaningfully lower than the rest ($p < 0.05$).

Conclusions: We conclude that EXT could diminish the side effects of CsA treatment by reduction of the serum urea and creatinine levels. These results suggest that EXT might be a potential adjunctive agent for the receiver CsA patients as an important parameter in liver transplantation.

02

Rapid Biosensor For Testing Acute Rejection After Liver Transplantation

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Introduction: Neutrophil activation is very important response to organ transplantation. Activation process may cause acute organ rejection. Rapid monitoring of inflammatory cells with membrane markers is an indicator for activation. Flow cytometry is current laboratory tool for testing activation. Sample preparation and measurement is a long, expensive and labor intensive method. Objective of this study is to design and manufacture alternative assays for testing cellular response to organ transplantation.

Materials and Methods: Twenty QCM crystals that were 12 MHz used for analysis. The electrode surface was pretreated sequentially with pure acetone, pure methanol and 0.5 M NaOH (30 minutes for each step) to obtain a clean, silver surface. After the pretreatment, the crystals were rinsed with deionised, distilled water in an ultrasonic washer and air-dried. cystamine molecule has two functional groups: the SH group is called a thiol, and the NH group is called an amine. With this property, the molecule was attached to the crystal surface by the thiol group. Glutaraldehyde was used as a spacer arm and has two functional groups. The amine groups on the cystamine molecules and aldehyde groups on the glutaraldehyde molecules were reacted and covalently bonded. During the immobilisation of ligands, the active regions of the ligand molecules participate in specific and rapid interactions with the analyte molecules. The spacer arm prevents steric interference during the interaction between the analyte and ligand molecules. A blood sample from a healthy donor was collected, and leucocytes were prepared at four different concentrations for testing the biosensor in vitro. In total, four different samples were prepared to test the biosensor in vitro. To prepare diluted samples of leucocytes, blood was centrifuged at 3000 rpm, and leucocytes were collected from the buffy coat and diluted to concentrations of 50%, 35%, or 10% in PBS.

Results: At the highest concentration of neutrophils the frequency value was much lower than that at the lowest concentration of neutrophils. This trend may occur because the activation of leukocytes is increased in samples with higher concentrations of neutrophils. AFM measurements of these samples showed that the antibodies were immobilised on the surface.

Conclusions: Neutrophils play an essential role in the inflammatory response. A rapid test for neutrophil activation would be a useful tool for acute rejection screening. The testing of the inflammatory response should be rapid, inexpensive and easy. In this study, surface modified QCM crystals were investigated for their use in measuring the inflammatory response. The results of this study suggested the use of frequency changes in surface-modified QCM crystals to measure the inflammatory response. The results presented here were supported by AFM surface topography measurements and SEM images.

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oral presentation

O3

Cytomegalovirus Reactivation After Liver Transplantation Under Preemptive Therapy Protocol

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Introduction: Cytomegalovirus (CMV) infection is the most common viral infection after orthotopic liver transplantation commonly occurs within 3 months after transplantation and may lead to severe CMV disease, which directly or indirectly reduces the graft and patient survival. There are two prophylaxis methods including universal prophylaxis and preemptive therapy. We conduct this study to find the prevalence of CMV infection in a group of Iranian liver recipients who received preemptive therapy and evaluate the effectiveness of this approach in prevention of CMV disease after liver transplantation. Besides, we are to find the risk factors associated with CMV infection after liver transplantation in our patients.

Materials and Methods: Patients who orthotopic liver transplantation in Imam Khomeini Hospital, Tehran University of Medical Sciences from 2006 to 2013 who survived for more than two weeks after liver transplantation were enrolled in the study. The data of recipients were recorded prospectively. After transplantation, all patients were examined for pp65-antigen weekly after liver transplantation until 90 days. CMV reactivation was concluded when a recipient had the PP65-antigenemia equal or greater than 1/50,000 leukocytes. In patients with CMV reactivation, preemptive therapy with intravenous Gancylovir 5 mg/kg twice a day was immediately started and continued for at least 21 days and until two consecutive CMV antigen became undetectable.

Results: From January 2006 until February 2013, 161 liver transplantations were performed in 155 patients. Ten patients who died in two weeks after liver transplantation were excluded. One-hundred and forty-five liver recipients were enrolled in the study. The overall mean age was 40±12.35 years (range=8-62) including 78 males (53.8%). The mean follow-up time was 27.1±19.7 months (range=5.2-80.6). Forty-six patients (31.7%) experienced CMV reactivation at mean of 56.4±67.3 days (range=12-445) post transplant. All CMV patients were sero-positive for CMV before transplant. The mean age of CMV Ag positive patients was 41.3±12 years (range=16-61) which was not significantly different compared with the control group (P=0.309). The number of females patients were significantly greater in the CMV Ag positive group compared with the control group (OR=2.3; P=0.02). The most common etiology of liver failure in the CMV group was autoimmune hepatitis following by cryptogenic and HBV related cirrhosis. There was no significant relationship between etiology of liver failure, pre and post transplant use of steroid, and rate of acute rejection and CMV reactivation (P=.357, P=.278, P=.595, and P=.297, respectively). Only one patient (2%) developed CMV disease at 22 days post transplant who was successfully treated. Six patients (13%) developed second episode of CMV reactivation at median of 43 days (range=10-176) after the first episode. All these six patients were also successfully with the same protocol.

Conclusions: The preemptive therapy with monitoring the PP65-antigenemia can be a safe and cost-effective approach against CMV in liver recipients. In our center, female patients are at the higher risk of developing CMV infection after liver transplantation.

O4
Efficacy of Allogeneic Mesenchymal Stem Cell Transplantation in Patients With Wilson Cirrhosis

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Introduction: Wilson's disease is an autosomal recessive genetically inherited disorder of copper metabolism, causing neurological, psychiatric and liver disorders. Cirrhosis due to Wilson's disease is the end stage of liver disease where transplantation can be the only cure. Many studies encourage use of allogeneic bone marrow (BM) derived mesenchymal stem cells (MSC) for genetic liver diseases. Mesenchymal stem cells (MSCs) are shown to differentiate to hepatocytes. Many experimental and a few clinical trials encourage the use of bone marrow derived allogeneic MSCs in human genetic liver diseases. Here we aimed to assess the differentiation capacities of MSCs to hepatocytes, the changes in regeneration and fibrosis rates in liver tissue before and after MSC transplantation.

Materials and Methods: Study was approved by Ministry of Health Ethical Committee and sponsored by TUBITAK. 6 male, 4 female patients with liver cirrhosis due to Wilson's disease were recruited (mean age: 33.3). Bone marrows were collected from healthy sex mismatch volunteer donors and sent to Acıbadem Labcell© İstanbul for MSC expansion under GMP (Good Manufacturing Practice) circumstances. Patients were transplanted 1x106 cells/kg, fifty million MSCs via hepatic artery, and the rest via peripheral vein. Patients did not receive any immunosuppressant regimes. Liver biopsies were performed before and 6 months after MSC transplantation. Histopathologic examinations were performed; liver tissue copper amounts were assessed. Also sex mismatch cells were tracked by FISH (fluorescent in situ hybridization) method in biopsy samples. Serum and 24

hour urine copper, serum seruloplasmin levels, biochemical and hematologic parameters were monthly monitored for one year. Periodic USG and MR screenings were obtained.

Results: No side effects due to allogeneic MSC transplantation were seen in neither acute nor chronic post-transplant periods and the procedure was very well tolerated by the patients. When compared with before transplantation, there was no significant change in patients' liver histopathologic scores and laboratory values. FISH analysis revealed female cells in 5 male patients' post-transplant 6th month liver biopsy specimens. Transplanted cells which belong to opposite sex donors' were absent in 4 female and 1 male patients' control biopsy specimens.

Conclusions: By this study, for the first time in literature bone marrow derived allogeneic MSCs which were transplanted via hepatic artery were shown to differentiate to liver tissue cells. MSC transplantation seems to be a good alternative candidate for liver transplantation in near future.

O5
Deceased Organ Donation and Transplantation Activity in The Kingdom of Saudi Arabia: A Decade of Perspective in The 21st Century

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Introduction: Organ transplantation is the best existing method for the treatment of end-stage organ failure. However, the need for viable organ supply limits its progress; thus, we studied the algorithm of process for deceased heart beating donors with the rate of adapting the critical pathways of organ donation from possible to potential to eligible to consent and to actual deceased donors (DD) in the kingdom.

Materials and Methods: A retrospective study comparing the nationwide figures and composition of the Critical Pathway of DD cases in a decade from 2001-2005 vs. 2006-2010 to Saudi Center for Organ Transplantation (SCOT).

Results: The Study showed a remarkable increase in the total number of Possible Deceased Donor cases from 1827 of 2001-2005 to 2651 (+45%) of 2006-2010. The mean possible case per year in relation to the number of population for the first half of the decade is 16 PMP as compared to 22 PMP in the last 5 years of the decade. The rate of conversion from possible to potential is 63% (1151 and 1674 respectively). Moreover, Eligible Donors ascends its number from 956 to 1336 (+39%) of which 270 (28% with 2.2 PMP) and 511 (38% with 4.1PMP) respectively were consented for organ donation. The Actual DD for the year 2001-2005 was 248 and 453 for the year 2006-2010. As a result, the number of Utilized DD organs increased from 244 to 441(+81%) cases.

Conclusions: There is a notable increase in the number of Possible DD reported and consented in the second half of the decade. There is also a significant increase in the Actual DD. In relation to this, the various strategies being implemented to promote organ donation in every region of the kingdom are relatively effective in applying the critical pathways of deceased organ donation.

O6
Biliary Complications After Liver Transplantation

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Introduction: Biliary complications (BC) are the mos common reason for morbidity and mortality after liver transplantation (LT). Although previous studies reported 50% mortality and 23-30%morbidity rates, advancements in surgical technique, immunosuppression and organ preservation enabled to decrease these rates to 5-32% for morbidity and 19% for mortality. In this bulletin we present BC after LT in our institution.

Materials and Methods: Between 1997 and 2013 490 LT in 484 patients were performed. Mean age was 43.5, 336(69.4%) patients were male and 148(30.6%) were female. The most common etiology of end-stage liver disease was Hepatitis B and D. Bilio-biliary, bilio-enteric and combined bilio-biliary/bilio-enteric anastomoses were performed in 307(62.6%), 180(36.7%) and 3(0.7%) patients.

Results: Thirty (6.1%) patients had BC, 25(83.3%) were male and 5(16.7%) were female. Living donor transplantation was performed in 17 (56.7%) patients and cadaveric LT was performed in 13(43.3%) patients. Anastomoses were bilio-biliary in 24(80%) patients, bilio-enteric in 5(16.7%) and combined in 1(3%) patients. Indcation of the LT was

Hepatitis B and D in all patients. Biliary complications were anastomotic stricture in 10 (33.3%) patients, bile leakage in 7(23.3%) patients, non-anastomotic stricture in 6(20%) patients, minimal dilatation in biliary tract in 6(20%) patients and bile stone in 1(3.3%) patient. Immunosuppression was achieved with calcineurin inhibitors based medication in all patients. Eleven (36.7%) patients had cholangitis at the time of diagnosis. Magnetic resonance cholangiopancreatography (MRCP), percutaneous cholangiography (PTC) and endoscopic retrograde cholangiopancreatography (ERCP) were diagnostic tests. In treatment, PTC and ERCP were used. Mortality was seen in 6 (20%) patients (5 biliary sepsis, 1 chronic rejection).

Conclusions: Biliary complications can be minimized with appropriate surgical technique and close postoperative follow-up. Most of the patients can be treated with interventional methods.

O7
De Novo Malignancy Following Liver Transplantation

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Introduction: The aim of this study is to evaluate the incidence of De Novo malignancies including skin cancers in patients with liver transplantation in Shiraz organ transplant center. Patients who undergo solid organ transplant are at high risk for development of hepatic and extrahepatic malignancies. Environmental factors, genetic predisposition, and immunosupression are among the predisposing factors for De Novo malignancies.

Materials and Methods: A total of 1550 orthotopic liver transplants from deceased and living donors performed from 1992 to march 2012 were analyzed. The immunosuppressive regimen included of calcineurin inhibitors with steroids with or without mycophenolate mofetil.

Results: Among 1550 patients, 30 (1.93%) cases developed malignancies. 19 patients (63.3%) developed PTLD, in whom 17 patients were pediatric (<18 years of age). Among PTLD patients, 5 expired in spite of diagnosis and treatment. Other malignancies were as follows: 3 cases of gastric adenocarcinoma, 2 cases of Kaposi sarcoma, 1 thyroid cancer, 1 Lumbosacral multiple myeloma, 1 intestinal adenocarcinoma, 1 pancreatic head adenocarcinoma, 1 testicular cancer and 1 retinal carcinoma.

Conclusions: PTLD is the most common cancer among our patients after liver transplantation which involved mostly children. Interestingly, there was no skin cancer in our patients, while skin cancers constitute the most common malignancy following liver transplantation in other centers. More studies are necessary to identify the cause of this discordance.

O8
Outflow Reconstruction in Adult Living Donor Liver Transplant; Taking The Right Lobe Graft Without The Middle Hepatic Vein

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Introduction: The difficulty and challenge of harvesting a right lobe graft without MHV drainage is reconstructing the outflow tract of the hepatic veins. Unlike the whole graft transplant operation, venous reconstruction in right lobe LDLT is perhaps more tricky and a perfect anastomosis is more difficult to construct. With the inclusion or the reconstruction of the MHV, early graft function is satisfactory. The inclusion of the MHV or not in the donor's right lobectomy should be based on sound criteria to provide adequate functional liver mass for the recipient, while keeping the risk to the donor to a minimum.

Objective: To investigate the safety of different modalities of venous outflow reconstruction in right lobe LDLT grafts without MHV (including MHV tributaries; Segments V,

VIII, and accessory veins) and establishing criteria for such reconstructions. Besides, comparing patients with single hepatic vein anastmosis, and patients who required complex venous reconstruction regarding operative details and outcomes.

Materials and Methods: This is both a prospective and retrospective study conducted in two centers: National Liver Institute: 40 cases of Living Donor Liver Transplant; Menoufiya University-Egypt from January 2009 to January 2011. The results were finalized, analyzed in Royal Free Hospital under Professor Brian Davidson's supervision: Liver transplant Department, Royal Free Hospital, University College London (UCL), London, UK, under UK/Egyptian Joint PhD Supervision Scheme. 40 cases underwent Rt. lobe LDLT without MHV; Group A (Venous Outflow Reconstruction patients with more than one HV anast.) (n=16), Group B (Patients with single HV anast.) (n=24) Both groups were compared regarding; indications for reconstruction, complications, and operative details. Besides, describing different modalities used for venous outflow reconstruction.

Results: No deaths occurred in any of the donors. 40 cases underwent LDLT without MHV (with the exception of two cases). 24 cases had single RHV anastmosis, 16 cases had more than one single hepatic vein, 14 cases out of them had two vein anastmosis. Out of these 16 cases, there were 6 cases who had different modalities of vein grafts and venoplasty, and they are doing well till now. There was a significant increase in operative details (cold ischemia, warm ischemia time, and hepatic venous anastmosis time) in Group A than in Group B; with means of 68.75, 57.875, 34.68 versus 51.25, 43.33, and 17.70 respectively. When the comparison came to the complications and outcomes in terms of laboratory findings (total Bilirubin on three days levels and one month levels), overall hospital stay, three months survival and one year survival there were not significant differences between both groups.

Conclusions: In summary, HV reconstruction in right-lobe LDLT is technically challenging. A custom-made strategy in individuals may be necessary depending on whether significant MHV tributaries and major SHVs are present. In our institute, we believe that Adult

O9

Does Fibrin Glue Sealant Decrease The Rate of Anastomotic Leak After Biliary Anastomosis in Liver Transplantation? Results of Our Initial Experience

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Introduction: Fibrin sealing are used to prevent postoperative hemorrhage and biliary leakage after liver resection. We performed preliminary evaluation of the effect of topical fibrin glue applied externally to all biliary anastomosis in liver transplantation.

Material and Methods: Between January 2011 to June 2013, fibrin glue was used in 10 patients underwent deceased donor liver transplantation (DDLT). Duct to duct anastomoses was performed in 9 of 10 patients and hepaticojejunostomy was performed in 1 patient. Biliary anastomosis was performed with 5.0 polydioxanone suture and interrupted technique. Fibrin glue injection was simply applied over the anastomosis. Biliary leakage was diagnosed when the drain fluid/serum bilirubin ratio was >5.

Results: Median age of recipients was 46.9 (28-65) and female predominance (n=8) was marked. Median MELD score of patients was 19.7 (16-26). DDLT was performed for HBV related cirrhosis (n=5), primary biliary cirrhosis (n=1), congenital hepatic fibrosis (n=1), cryptogenic cirrhosis (n=1), Wilson disease (n=1) and HBV related fulminant hepatic failure (n=1). Median age of donors was 46.6 (13-79). Three of 10 donors were considered as a marginal donor. Median operation time was 583.5 minute (360-765 min.). Median cold ischemia period of the graft was 591.5 minute (440-790 min.) and median warm ischemia period of the graft was 145.5 minute (60-360 min.). Median blood transfusion was 10.1 units (1-29 units) and median fresh frozen plasma transfusion was 11.2 units (7-27 units). Biliary leakage was observed in one patient. Leak was detected 18 days after DDLT for fulminant hepatic failure. Revision with hepaticojejunostomy was performed. Median intensive care unit stay was 4.5 days (3-7 days), and median hospital stay was 26.4 days (18-40 days). There were no peri-operative deaths. Median follow-up period was 13.5 months (1 to 30 months).

Conclusions: Fibrin sealants are effectively used as an adjunct to achieve hemostasis during liver resections. The limited evidence regarding to use of fibrin sealants for the prevention from anastomotic leaks has been published. Our initial results showed that fibrin glue would be effective in preventing biliary leakage after DDLT.

O10

Liver Donation and Transplantation in Saudi Arabia

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Introduction: The aim of the study is to evaluate and analyze the result of the liver donation and transplantation.

Materials and Methods: A retrospective study was done during the year 2004 to 2010 from the 616 living donors (LD) and deceased donors (DD). Data includes donor\'s characteristics and acceptance rate for DD offered livers, recipient's status post transplant follow up period and patient survival.

Results: A total of 612 cases from DD were consented for liver donation and 402 (65.7%) cases were retrieved with 331 (82.34%) from them were able to transplant with donor mean age of 33.2 years. As to LR donors, mostly were son, mother and father related with a mean age of 26.6 years with male/female ratio of 3/1 for a total of 285 transplants. The mean follow up period was 745 days and the mean stay in hospital post transplant was 28.2 days with 11 cases having a primary non-functioning graft. At the end of the follow up period, there were 532 (88%) active patients and 58 (10%) died. 491 (80%) of the active patients are doing well at home and only 41 (7%) at the hospital. The patient survival at three and five years was 87.2% and 77.1% respectively.

Conclusions: The outcome of the liver transplantation in the kingdom is comparable to international levels, though the need to increase the acceptance rate and the use of procured liver requires more effort in the management of deceased donors. Both LR and DD transplant should be enhanced to meet the ever-increasing demand of organ transplantation.

O11

High Serum Sodium Level in Deceased Donor Liver Transplant.Successful Management of 2 Liver Transplant Recipients

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Introduction: Hypernatremia is quite common in deceased liver donors. It has been suggested that donor hypernatremia results in exacerbation of reperfusion mediated injury in recipient. Uncorrected hypernatremia has been associated with poor graft functions or patient survival in at least four studies.. But there are few studies that indicate high serum sodium level in donor has little effect in outcome of liver transplant recipient. In our case report we came across with serum sodium as high as 198 meq/l in donor. In addition, a literature review revealed no previous reports of dealing with hypernatremia as high as 198 meq/l in donor.

Case Report: Here we report two cases of deceased donor with very high serum sodium level. . In Case 1, donor was brought in emergency with complaint of drowsiness and weakness. Brain CT without contrast indicated cerebellar tumor with brainstem compression. Serum sodium level was 198 meq/l. Recipient was a case of alcoholic liver cirrhosis and hepatocellular carcinoma. In Case 2, donor was a case of basal ganglia hemorrhage with mass effect and midline deviation. Serum sodium was 172 meq/l. Recipient was a case of HBV related end stage liver disease. In both cases standard operative techniques were used. Anesthesia protocol was followed as usual. Postoperative care was done accordingly. There was uneventful recovery in both cases. Graft performance was measured from liver functions tests specially ALT and serum bilirubin level. At the same time serum creatinine was also assessed throughout hospital stay. Both patients remained stable till discharge and are in contact with the hospital for their routine follow up.

Discussion: In previous studies, deceased donors having serum sodium 170 meq/l were discussed. Management of these two cases indicates that hypernatremia as high as 198 meq/l in deceased donor, has almost no effect in outcome of liver transplant recipient. With the rising demand for liver transplantation and the shortage of organs, adaptation of extended criteria including donor hypernatremia will increase the donor pool. More research on this topic is recommended.

O12

Recurrent Disease After Living Donor Liver Transplantation: Risk Factors, Management And Outcome

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Introduction: The threat to the success of liver transplantation is the recurrence of the original disease. Although the initial concern about recurrent disease mainly related to viral hepatitis, recurrence of nonviral liver disease has been shown to lead to graft failure. This study aimed to analyze the factors responsible for disease recurrence after LDLT and the effect of disease recurrence, and its management on the outcome of LT.

Materials and Methods: After exclusion of (6 months mortality), 45 alive transplanted patients were enrolled in the current analysis in the follow up duration from 6 months to 60 months. Univariate analysis and then multiple analysis were done to detect the relationship between (demographic, preoperative, intraoperative and postoperative data) and overall recurrence, and between recurrence variables, and total survival in the follow up period after LDLT.

Results: Sixty nine patients underwent LDLT in our institute from the start of LDLT program at 28 April 2003 until the end of December 2009. The present retrospective study included fourty five patients in the follow up duration from 6 months to 60 months. The fourty five patients were classified according to age into pediatrics <18 years, and adults >18 years. The pediatric group were fourteen patients (31.1%), and the incidence of recurrence of primary disease was 1/14(7.1%), this case was Budd Chiari syndrome. The all pediatric mortality was 4/14((28.6%). The adult group were thirty one patients(68.8%), and the incidence of recurrence was 15/31(48.4%) of patients. On univariate analysis, there was no statistically significant predictors of recurrence regarding (demographic, Preoperative, intraoperative and postoperative data). The survival of all, non recurrent, and recurrent adults was (83.9%), (93.7%), and (73.3%) respectively.

Conclusions: Recurrence of primary disease after LDLT is confirmed in our study with the least incidence in children and the highest in adult HCV patients. Similarly, it was higher in the following patients (males, with CMV infections, with co-morbidity, with post operative complications and patients with acute rejection). Recurrence of primary disease after liver transplantation decreases post transplantation Survival. However the effective management of recurrence improves post transplantion survival.

O13

The Levels Of Postoperative Cognitive Function in Living Liver Donors

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Introduction: Postoperative cognitive dysfunction (POCD), which tends to happen soon after surgery, is a problem that can persist for several weeks or months. Sometimes it may be permanent. POCD is a serious complication and it is reported that POCD increases rates of mortality. Living liver donor hepatectomy is performed under general anesthesia and takes a long time. Microembolies cause ischemic tissue damage that may occur during manipulation of the liver which may lead to the development of POCD. The aim of the study was to investigate the levels of preoperative and postoperative cognitive function in living liver donors.

Materials and Methods: After approval by the ethics committee of Inonu University and written informed patient consent, 102 living liver donors were enrolled in this prospective study. Preoperatively Standardized Mini-Mental test, Stroop test, Beck Depression inventory and Trail Making tests were performed by a psychiatrist. In the operation room, electrocardiogram, arterial oxygen saturation, noninvasive blood pressure monitoring were obtained in all patients. BIS monitor was used to assess the depth of anesthesia. The same anesthetic technique was

performed in all patients. Mean arterial pressure (MAP), heart rate, SpO2 and bispectral index values were recorded during the operation. Surgical technique (right/left lobe), pringle maneuver application time, amount of bleeding and blood replacement, the duration of surgery and anesthesia, hypotensive episodes (MAP<65 mmHg) were recorded. Postoperatively, 0.05 mg/kg morphine was given intravenously for analgesia. The patients were extubated at the end of the surgery. The patients were observed in the recovery unit for half an hour and then sent to the surgical intensive care unit. Preoperative tests were repeated one week after surgery. Postoperative complications and the recipients' prognosis were recorded.

Results: Postoperative Trail Making A test score significantly decreased compared with the preoperative period ($p<0.05$). Number of errors of Postoperative Trail Making B test increased significantly than the preoperative level ($p<0.05$). Postoperative Stroop black/white and color words reading time significantly prolonged compared with the preoperative period ($p<0.001$). The time difference between telling the color of color words and reading the color words was longer in the preoperative period than postoperative period ($p=0.016$). The number of incorrect answers, while telling color of color words in the preoperative period were significantly higher than post-operative period ($p =0.044$). In the postoperative period, infection occured in 19 donors, bleeding in two, prolonged hyperbilirubinemia in 7 donors. Two donors reexplored postoperatively.

Conclusions: In this study, POCD was not observed based on Standardized Mini Mental test and Trail Making tests. Stroop black/white and color words reading time significantly prolonged after a week. This suggests, there could be a little bit frontal lobe impairment in donors and could result attentional problems in the postoperative period. However, we believe further studies are needed to investigate whether these problems are permanent and clinically significant.

O14

Prevention of Posttransplant Lymphoproliferative Disease in Pediatric Patients With Liver Transplantation

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Introduction: To study the effect of utilizing intravenous Ganciclovir followed by oral Valcyte on the rate of posttransplant lymphoproliferative disease (PTLD) in pediatric liver transplant recipients. Post-transplant lymphoproliferative disorders are caused by monoclonal or polyclonal proliferations of lymphocytes in patients with solid organ transplant. According to our previous report, this rate was 0.9% in pediatric patients receiving first liver grafts and immunosuppressed with Tacrolimus.

Materials and Methods: All pediatric patients who received liver transplant from March 2009 to March 2012 entered the study. The patients were divided into two groups: The first group (control) including 87 patients transplanted between March 2009 and December 2010, didn't receive prophylactic Ganciclovir and the second group (test) including 117 patients transplanted between December 2010 and March 2012, received prophylactic Ganciclovir according to our protocol. In this interventional study, all patients in test group received Ganciclovir at the first month after transplantation. Intravenous form was used in hospital admission period and changed to oral Valcyte after discharging. EBV and CMV serology tests were checked weekly in the second month and every two weeks thereafter. The oral Valcyte was continued for two weeks after a negative result.

Immunosupression was based on Tacrolimus and Prednisolone, while Mycophenolate mofetil was added if more immunosupression was necessary.

For statistical analysis, we used SPSS 15 program. Chi-square test and Fisher's exact test was used to examine the effect of prophylactic Ganciclovir on reduction in the rate of PTLD and reduction in the mortality caused by PTLD, respectively.

Results: The follow-up period was 20 to 41 months in control group and 6 to 21 months in test group. PTLD occurred in 12 cases in control group (10.25%) and 5 cases

in test group (5.74%). This difference was not statistically significant (0.249). In spite of treatment, mortality occurred in 5 cases in PTLD cases (41.7%) in the control group while no mortality was seen in the test group (0%), but this difference was not statistically significant (0.245).

Conclusions: Although both PTLD and mortality rates are decreased using prophylactic Ganciclovir, these differences have not been significant. This may be due to small number of PTLD cases in the study, and larger studies with greater number of the patients or multicenter trials are proposed.

O15

521 Liver Transplant Recipients With a Minimum Follow-Up Of 6 Months: A Single Center Experience

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Liver transplantation is the only curative treatment for end-stage liver disease. We present the outcomes of 521 liver transplant recipients at our center. 544 liver transplants were performed between December 2006 and January 2013. Living donor grafts were used in 399 first transplants (77%), 287 of which were right lobe grafts. 23 patients required a re-transplantation Mean recipient age was 48 years (range: 18-71 years) for adults and 54 months (range: 5-17 months) for children. Mean MELD score was 17 and mean PELD score was 16. Viral hepatitis B (36%) was the most common cause for liver transplantation in adults. Cholestatic liver disease was the most common cause in pediatric recipients. 21 transplantations were performed due to fulminant hepatic failure. Four patients died during the operation and 39 patients died in the early postoperative period. Median hospital and intensive care unit stay were 15 and 2 days, respectively. Mean follow-up was 23 months (range: 6-79 months). Hepatic artery thrombosis (1.4%), portal vein thrombosis (2.2%), biliary leak (10.3%) and biliary stricture (14%) were the main surgical complications observed. Overall survival was 82%. Our results are acceptable for a high volume transplantation center. Close follow-up and a multidisciplinary approach are key to success

O16

Low Grwr Graft With Portal Flow Modulation - Way To Increase Donor Pool And Donor Safety?

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Introduction: Low GRWR grafts are known to associated with high rates of graft failure and small for size syndrome. Now a days portal flow is believed to be main causative factor for small for size syndrome. We present our experience of using smaller graft with portal flow modulation if portal flow is greater than 250 ml/min/100 gm of graft weight.

Materials and Methods: 450 living donor liver transplants was done during period of January 2010 to june 2013 .55 grafts with grwr less than 0.8 was used and consisit of study group. We used splenic artery ligation or spleenectomy as portal flow modulation if portal flow after reperfusion was greater than 250 ml/min/100 gm.To eliminate huge difference in sample size 130 patient were selected randomly as control group. small for size syndrome was defined according to clavian and kyushi university definations. parameters like MELD ,etiology,portal vein flow,age,sex were compared as a causative factors for small for size syndrome between two groups.statistical study were used using spss version 21.

Results: 6 patients out of 55 developed small for size syndrome in grwr < 0.8 group. There was 28 left lobe graft and 27 right lobe graft.While 16 out of 130 control group fulfilled definition of small for size syndrome. There was no statistical significant difference in graft dysfunction between low grwr group and high grwr group. In univariate and multivariate analysis Grwr was not associated with graft dysfunction. In multivariate analysis hcv etiology,Meld score and portal flow achieved statistical significance as factors associated with graft dysfunction.($p<0.05$).There was no early mortality or 30 days graft loss in low GRWR group. However Lower GRWR was significantly associated with prolong ascites.

Conclusions: Lower GRWR graft with portal flow modulation in case of high portal flow is effective way to increase donor pool and donor safety with low risk of small for size syndrome. portal flow and not GRWR predicts occurrence of small for size syndrome.

O17
Dual Hepatic Artery Reconstruction in Living Donor Liver Transplantation in Pediatric Patients

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Introduction: Hepatic artery (HA) reconstruction is one of the most crucial procedures when performing living donor liver transplantation (LDLT), especially in pediatric patients. Hepatic artery thrombosis (HAT) is the most feared complications of all as it can result in early graft loss and mortality. The liver grafts can at times have multiple hepatic arterial branches (HA). The size discrepancy between graft and recipient along with presence of multiple HAs in graft makes HA reconstruction even more challenging. Hence, discrete decision of reconstructing one or both the hepatic arteries is required. We herein report the criteria for reconstructing single or dual HAs and its outcome in pediatric LDLT.

Material and Methods: From 2002 to 2010, 101 of 103 pediatric patients undergoing LDLT received a left of left lateral segment liver grafts. The study population of was divided in to Group 1 (n= 21): 2 HA stumps with 2 HAs reconstruction, Group 2 (n=22): 2 HA stumps with 1 HA reconstruction and Group 3 (n=60): 1 HA stump with 1 HA reconstruction. The criteria for reconstruction of only one the two HAs were, that the selected artery was a dominant one on pre-operative radiological assessment, it was thicker of the two arteries on intra-operative assessment, good blood backflow was observed intra-operatively, from the remaining arterial stump post reconstruction of dominant one and intra-operative arterial Doppler confirmed arterial inflow signals in all segments of the liver graft post reconstruction of the dominant artery. If any of these criteria were not met, dual HA reconstruction was done. The incidence of hepatic artery related complications, biliary complications and patient survival were analyzed between the three groups.

Results: The operative time in Group 1 was more as compared to Groups 2 and 3 (p=0.01). The incidence of hepatic arterial related complications and biliary complications were similar in all the 3 groups, p=0.91 and p=0.24 respectively.

Conclusions: In accordance with the aforementioned criteria, we recommended to reconstruct only single HA in pediatric patients undergoing LDLT, with 2 arterial stumps. This makes the reconstruction much less technically demanding with comparable outcome.

O18
Pediatric Liver Transplantation: Istanbul Sisli Memorial Hospital Experience

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Liver transplantation is the only treatment of the end-stage liver disease. We present the outcomes of our 144 pediatric liver transplant cases. We performed 148 pediatric liver transplants between December 2006 and April 2013. The 92% of the cases were transplanted from living donors. Mean age was 4,5 years (0,31-17,95 years of age). Biliary Atresia (26,3%) and Progressive Familial Intrahepatic Cholestasis (19,4%) were the most common causes of the end stage liver disease. Nine (6,25%) of the transplantations were performed due to fulminant hepatic failure. Median hospital and intensive care unit stay were 18 and 4 days, respectively. Mean follow-up period was 23 months. The main complications were gastrointestinal bleeding (12,5%), portal vein thrombosis (6,9%), biliary leak (6,2%), biliary stricture (4,1%), and intestinal perforation (3,4%). Overall survival rate was 87%. Living donor liver transplantation is a life saving and safe procedure in the situation of low pediatric organ donation.

O19

Pregnancy and Delivery After Liver Transplantation: Presentation of 7 Cases

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Introduction: Over the last decades, liver transplantation has been the prominent treatment option in patients with end-stage liver failure. Patients who underwent liver transplantation can maintain their usual activities of daily living with a professional care and multidisciplinary follow-up. In this bulletin, we present 7 patients who had an uneventful gestation and delivery after liver transplantation.

Materials and Methods: Between 2002 and 2010, 7 patients at fertility age became pregnant after liver transplantation in our clinic. Mean age was 28. Etiology of end-stage liver disease was chronic Hepatitis B and D in 4 patients, Wilson's disease in 1 patient, Budd–Chiari syndrome in 1 patient and 1 patient had cryptogenic cirrhosis.

Results: Liver transplantation was performed from living donors in 5 patients and cadaveric donors in 2 patients. Postoperative follow-up was performed with routine office visits in our transplantation policlinic by a multidisciplinary team including supervisor liver transplantation physician, senior transplantation surgeons and gastroenterologists. Along with the gestation and delivery period, patients have been followed closely; immunosuppressive medications have been rearranged and an obstetrician has joined the team. All the patients had an uneventful gestation period and birth without any complications or malformations in the newborns.

Conclusions: Patients who underwent liver transplantation at fertility age can have a usual pregnancy and delivery period with a close follow up performed by a multidisciplinary team.

O20

Long Term Outcomes In Pediatric Intestinal And Multivisceral Transplantation

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Over the past half century there has been a dramatic change in the management of patients with intestinal failure. Most of the initially improved survival was the result of implemantation and availability of total parenteral nutrition (TPN). This required significant resouces because of hospital admissions in the beginning. Then with the development of convenient home-based infusions most patients did well as an outpatient. After many years of evolution, intestinal transplantation is now offered to patients who succumb to the inevitable complications of TPN in the form of infection, catheter-associated thrombosis, hepatic disease, renal disease, persistent gastrointestinal dysfunction and metabolic derangement. Pediatric intestinal failure is a devastating condition, with intestinal and multivisceral transplantation providing an alternative for patients with life-threatening complications of TPN. Recent improvements in immunosuppression, prophylaxis, surgical technique, monitoring and diagnosis of rejection have helped improve the quality of life, graft and patient survival. We reviewed about 188 patients with intestinal/multivisceral transplant between 1994-2013. Some single centers report of five-year patient and graft survival, 80% and 60% respectively. However, evidence suggests generally that five-year patient and graft survival rates after intestinal transplantation are closer to 58% and 40% respectively. Intestinal/multivisceral transplantation is one of the main treatment options in selected group of pediatric patients with intestinal failure.

O21

Liver Transplantation in Acute Liver Failure: The İstanbul Faculty of Medicine Experience

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Introduction: To analyze the current results of transplantation in acute liver failure at the Istanbul Faculty of Medicine.

Materials and Methods: The charts of the 26 patients (8 males, 18 females; median (range) age: 15(2-62) years) who underwent liver transplantation for acute liver failure between 2008-2012 were evaluated retrospectively.

Results: The identified etiologic factors were : toxic agents (6; mushrooms 5, herbal tea 1), Wilson's disease (4), autoimmune hepatitis (3), fulminant Budd-Chiari syndrome (2), acute hepatitis B infection (2), acute hepatitis A infection (1); 8 cases were cryptogenic. Organs from cadaveric donors were transplanted to 20 patients (3 left lateral sections from split livers); 6 patients underwent living donor transplantation (3 right lobes and 3 left lateral sections). One patient (4%) died of multiple organ failure, with a functioning graft on the second postoperative day. Bacterial infection was the most common early complication (20/25; 80%), followed by postoperative delirium (3/25; 12%) (treated with short courses of psychotropic agents) and severe acute rejection (2/25; 8%) (treated with pulse steroids). Acute renal failure (required hemodialysis but recovered without sequel), thrombotic thrombocytopenic purpura (treated successfully with plasmapheresis), tracheal stenosis due to prolonged intubation (treated with a removable stent), nonanastomotic hepatic artery stenosis due to kinking (in the second postoperative month; intimal dissection and thrombosis occurred during angioplasty. Recanalization was achieved with medical treatment but an asymptomatic left hepatic duct stricture developed.), recurrent autoimmune hepatitis (in the second postoperative month; treated successfully with modification of the immunosuppressive protocol) and stricture of the choledochocholedochostomy (treated with endoscopic stenting) occurred in one patient each. One patient died on the 18th postoperative month due to a fungal infection precipitated by steroid-resistant rejection treatment. Overall survival was 24/26 (92%).

Conclusions: Improved cadaveric organ sharing, use of split grafts when possible, and transplantation from living donors in appropriate situations yield a high survival rate, despite high early morbidity, in acute liver failure patients whose condition deteriorates despite intensive care treatment.

P1

Role of MR Venography in Planning Venous Outflow Reconstruction in Living Donor Liver Transplant

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Introduction: Preoperative mapping of the hepatic venous system is indispensable to the success of living related liver transplantation. The function of a new liver in the recipient and its regeneration depend on the inflow and outflow of the graft, respectively, and therefore the supplying and draining vessels are to be left intact. MR imaging of the liver has evolved in recent years mainly due to the development of fast imaging techniques that provide superior-quality, high-resolution images in a breath hold. A comprehensive MR imaging examination has the potential to serve as the sole preoperative imaging modality for a living adult-to-adult liver donor. Introduction: To evaluate whether the hepatic veins can be visualized with a rapid noninvasive technique, and if so, whether the obtained images could be helpful in the planning for venous outflow reconstruction in living donor liver transplant.

Materials and Methods: 40 donors of LDLT had MR Venography as a mandatory step in our routine preoperative scanning procedure. The following findings were recorded: (1) tributaries of the middle hepatic veins (MHV) including segments V, VIII veins; (2) the presence of accessory inferior right hepatic vein (IRHV), or superficial right hepatic vein (SRHV); (3) the variable entering patterns of the RHV, MHV, and IRHV into IVC and (4) the diameter of the veins at their point of connection to the major veins. A comparison of the findings from the preoperative MR venography and the operative findings was made.

Results: 30 cases out of 40 were with the same number of actual intra-operative hepatic veins in comparison with the pre-operative MRI Venography findings, and 10 cases with different intra-operative findings. Out of these 10, there were 4 cases only with Vessels diameter of more than 5mm (which were actually anastmosed) and 6 cases with Vessels diameter of less than 5mm (were not anastmosed) due to very tiny vessel diameter. The real discrepancy between preoperative estimates derived with MRI Venography and the intra-operative findings were only 4 cases (10%). Besides, we can also see that all of the six cases who needed the use of variable types of venous grafts for reconstruction were accurately determined on pre-operative MRI Venography. So that, the accuracy of pre-operative MRI Venography was at least 90%.

Conclusions: In summary, we conclude that MRI is a fast and safe non-invasive method to study parenchyma and vasculature of the pre-transplant human donor liver with minimal interference with the transplant procedure. The hepatic veins with their confluence can easily be visualized thus allowing planning donor liver resection procedures.

P2

Transfusion-Related Acute Lung Injury (Trali) After Orthotopic Liver Transplantation (Olt): Report of 3 Cases

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Introduction: TRALI is known as the leading cause of transfusion-related mortality that occurs within 6 h of transfusion and is defined as acute hypoxemia (PaO2/FIO2 <300 mmHg), bilateral pulmonary infiltrates on chest radiograph and no evidence of left atrial hypertension. The majority of patients recover within 72 to 96 h but some patients may remain hypoxic with persistent pulmonary infiltrates up to 7 days.

Case Reports: They were 3 cases of cirrhosis that OLT from deceased donor was performed for them between May 2011 and December 2012. The patients had no significant pulmonary complications before operation. They had difficult hepatic dissection besides massive bleeding intraoperative, so received massive transfusion [under guide of thromboelastography (TEG)] and had long operation time, therefore were sent intubated to intensive care unit (ICU). Postoperative, they suffered from respiratory distress, hypoxemia, agitation and bilateral infiltration on chest radiograph while transesophageal echocardiograghy (TEE) showed normal cardiac function in the patients. However, they were inevitably under low tidal volume assist/control mechanical ventilation for a few days. No-1: A 35 year-old man, known case of HBV cirrhosis that received 30 units packed red blood cells (PRBCs), 20 units fresh frozen plasma (FFP) and 10 units platelets intraoperative. After

operation he was under mechanical ventilation for 6 days and weaned successfully. Control chest radiograph showed a little plural effusion and finally patient discharged with good condition on 22th day postoperative. No-2: A 44 year-old obese man with a body mass index (BMI) of 35 kg/m2 and cryptogenic cirrhosis that received 15 units PRBCs, 5 units FFP, 5 units platelets and 2 g fibrinogen concentrate during OLT . Postoperative, he was under mechanical ventilation for 3 days and had a successful weaning and normal control chest X-ray. He had a progressive rehabilitation till 20th day that was afflicted by pulmonary thromboembolism so we started medical treatment plus mechanical ventilation for him, but he expired on 24th day postoperative. No-3: A 55 year-old man with cryptogenic cirrhosis that received 10 units PRBCs, 6 units FFP, 4 units platelets and 3 g fibrinogen concentrate intraoperative. After transplantation he was under mechanical ventilation and simultaneous suffered from renal insufficiency and mild coagolopathy, but he was weaned successfully on 4th day and then stayed in the department and discharged with good condition on 25th day.

Conclusions: Blood transfusion has remained a critical feature in OLT and TRALI is the dominant and serious hazard of transfusion. It seems necessary to Improve prevention methods for transfusion like TEG besides continued effort toward recognition and prevention of complication associated with blood components administration especially TRALI.

P3
A Comprehensive Review of Immunosuppression Used For Liver Transplantation

Since liver transplantation was approved for the treatment of end stage liver disease, calcineurin inhibitors (CNI's) have played a critical role in the preservation of allograft function. Unfortunately, these medications cause a variety of Side effects such as diabetes, hypertension and nephrotoxicity which in turn result in significant morbidity and reduced quality of life. A variety of newer immunosuppressants have been evaluated over the last decade in an attempt to either substitute for CNI's or use with reduced dose CNI's while still preserving allograft function However, current data does not recommend complete cessation of CNI's due to unacceptably high rates of allograft rejection. As these medications have their own unique adverse effects, a careful assessment on their risks and benefits is essential, particularly when additive or synergistic effects with CNI's may occur. Furthermore, the impact of these newermedications on the risk of hepatitis C recurrence and progression remains to be elucidated. Controlled trials are urgently required to assist transplant physicians with choosing the optimum immunosuppressive regimen for their patients. This review will discuss commonly used immunosuppressants prescribed in liver transplantation, emerging therapies and where appropriate, the impact of these medications on the recurrence of hepatitis C after liver transplantation.

P4
Establishing a New Liver Transplantation Program in The Middle East Region: Twelve Years of Experience

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Introduction: In 2001, a liver transplantation program was commenced at Tehran University of Medical Sciences as the first one in the capital city of Tehran and the second center in Iran. We are willing to report our experiences after 12 years of study in one of the well-established centers in the Middle East region. In addition, we want to find factors associated with improved outcomes, emphasis on how a liver transplantation program can be established, and move toward better outcomes.

Patients and Methods: One-hundred and seventy two deceased donor orthotopic liver transplantations were performed between 1/2002-2/2013. This period was divided into four phases based on technical advances and number of transplants performed per year: 2002 to 2005 (n=9), 2006 to 2009 (n=41), 2010 to 2011 (n=49), and 2012 to 2013 (n=73). The prospectively recorded data of the liver recipients were assessed during different phases.

Results: Viral hepatitis was the most underlying liver disease (26%) followed by autoimmune hepatitis (23%) and cryptogenic cirrhosis (23%). The number of liver transplantations increased to more than 50 per year. In the end of phase two, after 50 liver orthotopic liver tranplantations, the learning curve was completed. Mean cold ischemia time (800 vs. 289 minutes, P<0.001), operative time (600 vs. 313 minutes, P<0.001) and transfusions of intraoperative platelet (8.75 vs. 0.53 units, P<0.001), packed red blood cell (11.4 vs. 5 units, P<0.001), and fresh frozen plasma (12.7 vs. 0.4 units, P<0.001) were decreased significantly over the time. Post transplant complications were not significantly differed from two to phase four: acute rejection (29% vs. 35%, P=0.73), hepatic artery thrombosis (12% vs. 4%, P=0.78) , and infection (49% vs. 45%, P=0.42). Overall, the most cause common of death was sepsis followed by intraoperative and postoperative bleeding. The short- and long-term patient survival rates increased significantly: 3-month patient survival rate improved from 44% to 95% (P<0.001) and 1-year patient survival improved from 33% to 88% (P<0.001).

Conclusions: Important factors to develop a new liver transplantation program and improve the outcomes are forming a cooperative multidisciplinary team, managerial coordination of different units, overcoming the learning curve and continuous modification of anesthesia and surgical techniques. In addition, comprehensive unified written protocols for every detail of pre, peri, and post transplant medical and surgical care can lead to better outcomes even after completing the learning curve.

P5

CT Volumetry; Is it an Efficient and a Reliable Tool for Predicting LDLT Graft Weight and Volume?

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Introduction: The literature provides differing information about the congruity between volumetric data of hepatic tissue determined preoperatively by using CT and data determined intraoperatively. Volumetric analysis of the liver using computed tomography (CT) datasets has become an important component of the preoperative assessment before major hepatectomy and for living related liver donation. CT images allow determination of the volume of liver tissue required by the recipient and the volume remaining with the donor. In this regard, CT volumetry is necessary for preoperative documentation because the volume of the left lateral segment is quite variable.

Objectives: To determine the relative accuracy of computed tomographic (CT) volumetry for estimation of right-lobe graft weight in living donor liver transplantation by comparing it with actual intraoperative findings.

Materials and Methods: Over the period from January 2009 to January 2011, 40 patients underwent live donor liver transplant using a right lobe liver graft without MHV in the National Liver Institute, Menoufiya University, Egypt. These cases had a contrast material-enhanced CT examination of the abdomen was included in the evaluation and was required for the analysis of morphologic characteristics, the vascular status of the liver, and the evaluation of the hepatic parenchyma. The hepatic venous phase was used for preoperative CT volumetric measurement of the donor liver because, in this phase, the determining hepatic veins are depicted with maximum contrast. The intraoperative graft weight was measured in 40 live liver donors who underwent graft hepatectomy.

Results: Mean of Calculated wt. of graft = 952.35 (n = 40), mean of Actual graft wt = 871.25 (n = 40) with no significant difference. 32 cases out of 40, the calculated weight of the graft is almost the same as or even greater than the actual one which means that we can guarantee donor safety, in the same time, we can also ensure adequacy of the graft for

the recipient provided that all the graft to recipient weight ratio (GRWR) were above 0.8, in our series it ranged from a minimum of 0.84 to 1.9 (mean 1.09525+ 0.21). In 8 cases the actual graft weight is more than the calculated one, the percentile difference between both for such cases ranged from (0.53 to 16.66 %) with a median of 1.615 and only two cases (5%) were out of the range (15.78, 16.66). This was also confirmed by comparing the medians of the calculated graft to recipient weight ratio (GRWR) and the actual GRWR (which were 1.1, 1.09 respectively) with no significant difference at all.

Conclusions: Our results demonstrate that the CT Volumetry is an efficient and a reliable tool for assessing LDLT graft weight and volume prediction. The size of the right lobe graft for LDLT can be precisely calculated from preoperative CT Volumetry with confidence and accuracy up to 95%, as it could offer a precise virtual model of individualized graft volumes for each potential live liver donor.

P6

The Diagnostic Significance of Hepatic Parenchymal Retention Index Parameter Determined By Hepatobiliary Scintigraphy in Liver Transplant Recipients

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Introduction: Hepatobiliary scintigraphy with Tc-99m iminodiacetic acid derivatives is a non-invasive, objective, and quantitative technique to evaluate the function and integrity of the hepatobiliary tree in liver transplant recipients. This method easily identifies many structural complications as well as functional complications related to hepatic perfusion, tracer uptake, and excretion. The aim of this study was to evaluate the value of hepatic parenchymal retention index parameter determined by hepatobiliary scintigraphy in the early diagnosis of functional complications in liver transplant recipients.

Materials and Methods: One hundred liver transplant recipients (64men, 36 women of overall mean age 29.12 ± 14.2 years) were studied. Hepatobiliary scintigraphy was performed at 7-10 days after the transplantation immediately after intravenous injection of 1.85 MBq/kg of Tc-99m mebrofenin. A large field-of-view dual-head gamma camera was used for image acquisition. To test graft perfusion data were recorded every one second for one minute, to evaluate parenchymal function, data were recorded every 30 seconds for 40 minutes. The images were evaluated visually and quantitatively. The quantitative parameters used werehepatocyte extraction fraction and hepatic parenchymal retention index. Scintigraphic findings were then correlated with biopsy results.

Results: In the visual analysis, all grafts (100%) showed normal perfusion and normal hepatocyte extraction. In the quantitative analysis, hepatocyte extraction fraction values were within the normal range in all cases (mean value: 96.2 ± 2.3%). According to the results of hepatic parenchymal retention, patients were divided into 3 groups. Group 1 consisted of 75 recipients, in whom hepatocyte excretion was seen as normal. In these patients, hepatic parenchymal retention index values were within the normal range (mean: 18.14± 4.30%). Group 2 included 15 patients, whose liver grafts showed severely decreased hepatocyte excretion. In this group, hepatic parenchymal retention index values elevated severely (mean: 82.64 ± 8.23 %). Group 3 included 10 patients, in whom hepatocyte excretion decreased mildly-moderately and hepatic parenchymal retention index increased mildly-moderately (mean: 43.60 ± 9.80 %). The hepatic parenchymal retention index values were then statistically compared and significant differences were found among these 3 groups ($p<0.001$). When the scintigraphic findings were compared with biopsy results, it was revealed that acute rejection in all Group 2 recipients and mild-moderate hepatocyte damage/cholestasis in all Group 3 patients.

Conclusions: In the light of these findings, we conclude that, hepatic parenchymal retention index parameter determined by hepatobiliary scintigraphy may be valuable in the early diagnosis of functional complications in liver transplant recipients.

P7
Fibrosingcholestatic Hepatitis Following Methotrexate Therapy For Rheumatoid Arthritis

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Introduction: Fibrosing cholestatic hepatitis (FCH) is a variant of viral hepatitis reported in hepatitis B virus or hepatitis C virus infected liver, renal or bone transplantation recipients and in leukemia and lymphoma patients after conventional cytotoxic chemotherapy. FCH constitutes a well-described form of fulminant hepatitis having extensive fibrosis and severe cholestasis as its most characteristic pathological findings. Here, we report a case of a 55-year-old female patient diagnosed with rheumatoid arthritis (RA) who developed this condition following methotrexate therapy.

Case Report: This is a case of a 55-year-old female with a RA history and a past medical history of hepatitis B. The RA was diagnosed at September 2012. Methotrexate (15 mg per week) and prednisolone (10 mg per day) treatment was started after diagnosis. Patient was administered to our hospital with jaundice and weakness at April 2013. A complete serological study was performed demonstrating hepatitis B reactivation (HBsAg, HBeAb and HBcAbIgG positive). Elevation of liver transaminase levels, bilirubin levels and bleeding tests were determined (GOT: 1323 UI/mL; GPT: 2272 UI/mL; total bilirubin: 20 mg/dL; direct bilirubin: 10.7 mg/dL; INR: 1.24). Despite treatment with lamuvidine, the hepatitis progressed towards acute hepatic failure (GOT: 849 UI/mL; GPT: 1310 UI/mL; total bilirubin: 34.2 mg/dL; direct bilirubin: 15.7 mg/dL; INR: 1.4).After six cycle of plasmapheresis therapy (with 10 unites of fresh frozen plasma), slight improvement in liver function test was observed at the 3rd week of admission (GOT: 375 UI/mL; GPT: 299 UI/mL; total bilirubin: 16.4 mg/dL; direct bilirubin: 8.4 mg/dL; INR: 1.43). However, elevation on ammonia levels and INR levels were remarked in the 4th week of admission. Abdominal sonography was revealed moderate abdominal ascites without splenomegaly or hepatomegaly. In the 5th week of admission, moderate encephalopathy was developed and deceased donor liver transplantation was performed. The patient was re-operated for bile leak at 18th postoperative days. Patient was discharged at 40 days after liver transplantation. Microscopically lobules were markedly disarrayed because of fibrous expansion of portal tracts, showing prominent ground glass appearance of hepatocytes, and marked canalicular or intracytoplasmic cholestasis. Portal inflammation was mild to moderate, and cholangiolar proliferation was prominent.

Conclusions: Although the ultimate physiopathological mechanism in this condition remains elusive, the extremely high levels of viral replication, the massive HBcAgand HBsAg expression in the liver and the nonsignificant inflammatory component suggest a direct HBV cytopathologic effect. Additional immunosuppression is generally considered as a stimulating factor for FCH. Antiviral therapy with intensive liver support is mainstay of FCH treatment. In the case of liver failure related to FCH, liver transplantation is the only treatment option.

P8
Lung Metastasis of Fatty Hepatocellular Carcinoma After Liver Transplantation: Differantial Diagnosis With Lipoid Pneumonia

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Introduction: Hepatocellular carcinoma (HCC) is the most common primary malignant tumor in the liver. It is three times more common in men than in women. Several typical histologic patterns of hepatocellular carcinoma have been described by the World Health Organization; the most common is the trabecular pattern. We present a rare case of HCC with prominent fatty change that metastasis to lung 10 months after liver transplantation.

Case Report: We report the case of 57-year-old woman who received a right lateral segment liver transplant from his daughter who was 25 years old and started to use tacrolimus and mikofenolat mefotil based immunosuppression regimen. The patient has been reviewed because of elevated serum hepatitis B surface antigen (HBsAg) for 17 years and has chronic liver disease symptoms for two years. She has been followed by another hospital. Multipl solid nodules in liver has been recognized in routine control and the biopsy of this nodule was reported as HCC. She underwent arterial chemoembolization in two times for HCC. Then she was referred to Başkent University for liver transplantation. In

the histopathologic examination of nativ liver, HCC with necrosis depending on chemoembolization and cirrhosis were noted. Fatty change was only focal in tumor cells. Ten months after transplantation, she was presented with persistant cough and computed tomograpy of the chest revealed a solid lung mass in her right inferior lobe and lobectomy was performed. In the histopathological examination of lobectomy, HCC with prominent fatty changes was detected.

Conclusions: HCC with prominent fatty change is extremely rare and the histological picture is different from the usual HCC, so it may cause some diagnostic difficulties especially in metastatic lesions. In metastasis to lung, fat droplets in the tumor cell cytoplasm may confused with the accumulation of aspirated oils in lipoid pneomonia, especially in small needle biopsies. We presented this case because of its rarity and having some difficulties in differential diagnosis in liver transplant recipients.

P9

Synchronous Post-Transplant Lymphoproliferative Disease and Inflammatory Myofibroblastic Tumor of The Lung in Liver Transplanted Patient: A Case Report

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Introduction: Inflammatory myofibroblastic tumor (IMT) is a rare benign tumor, accounting for 0.7% of all lung tumors. The tumor occurs most commonly in children and young adults and its aetiology is still not completely understood. We report a case who had a liver transplantation four years ago and presented with post-transplant lymphoproliferative disease and inflammatory myofibroblastic tumor involving lung.

Case Report: Six months old boy was referred to the Transplant Department at Başkent University, with biliary atresia presented with jaundince to thrive since he was born. In our institution, he received a left lateral segment liver transplant at the age of 9 months from his mother who was 23 years old and started to use tacrolimus based immunosuppression regimen. Eleven months later, when he presented with longstanding diarrhea, upper gastrointestinal system endoscopy and colonoscopy was performed, and ulcerations with malign appearance were seen both in his antrum and colon. Endoscopic biopsies were taken and the histological diagnosis was posttransplant lymphoproliferative disease (PTLD). Expression of EBV-encoded RNA (EBER) was found as positive in these biopsies. He had started to receive chemotherapy, including cyclophosphamide for the treatment of PTLD. Because of having fewer and cough at the time of second chemoterapy, computed tomograpy of the chest was performed and it revealed a solid lung mass in the left inferior lobe. The transthorasic biopsy was performed and the histological diagnosis was reported as inflammatory myofibroblastic tumor of the lung. The child has remained well during 3 years of follow-up with no evidence of recurrence both of PTLD and inflammatory myofibroblastic tumor.

Conclusions: IMTs of the lung are extremely rare and their aetiology is currently unknown. It has been hypothesized that an initial infection may lead to an IMT, such as mycoplasma, nocardia, actinomycetes, Epstein-Barr and human herpes virus. In our case the presence of synchronous IMT and PTLD may explain the possible cause, because both of the tumor may appear as a cause of EBV infection, as mentioned in some of reports in the literature.

P10

Giant Hepatic Hemangioma: An Indication For Liver Transplantation

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Introduction: Hemangiomas are the most common benign tumor of the liver with an estimated prevalence of 0.4% to 20%. They are usually smaller than 4 cm in diameter and remain asymptomatic. Those with a diameter more than 5 cm are termed giant hemangioma. Here we present a case of giant hepatic hemangioma that causes liver failure and cured by liver transplantation.

Case Report: Six years ago, a 57 year old woman was referred to the hospital because of a history of abdominal distention. The physical examination of the woman revealed a mass with the diameter of 17 cm that was extending through the abdominal region. This tumor was diagnosed as giant hemanjioma with the abdominal ultrasonography (USG) and computed tomography. She was treated with chemoembolution at that time. Ten months after chemoembolution, she was admitted to our hospital for second opinion. Abdominal USG revealed liver hemangioma which was occupying the left lobule and was

found to increased in size (21 cm in diameter). Laparatomy was performed for the resection of the hemangioma, but during the laparotomy, intraoperative biyopsy revealed a cirrhotic prossess in the non-tumoral liver paranchyma. Thus the operation was ended without the resection of the tumor. After two years, liver transplantation was performed to patient from living related donor. Tacrolimus based regimen was started as an immunosupressive therapy. Five years after liver transplantation the patient is doing well without allograft failure.

Conclusions: A liver hemangioma is a benign, usually small tumor comprised of blood vessels, which is often discovered coincidentally and do not require treatment. However, giant hemangiomas may give rise to symptoms requiring treatment such as interferon, radiation, arterial embolization, surgical resection or rarely liver transplantation. Here we report a rare case of giant hemangioma, occupying almost all the liver paranchyme and cured by liver transplantation.

PI1
Cutaneous Disorders in Liver Transplant Recipients

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Introduction: Liver transplantation is often the only remaining therapy for patients with end stage liver cirrhosis, acute liver failure and some metabolic and congenital hepatic diseases. Several factors are known to predict skin complications in liver transplant recipients, especially immunosuppressive regimen, age, sex, viral infections and sun exposure. The aim of this study was to analyze the incidence and risk factors of skin complications in liver transplant recipients.

Materials and Methods: Patients who had skin biopsies were selected among 408 liver transplant recipients from January 1990 to December 2012 in Başkent University. Demographic and clinical findings of these patients, including age, gender, primary liver disease, immunosuppressive therapy and the time between transplantation and cutaneous lesions were examined.

Results: There were 38 patients who had skin biopsy after liver transplantation. The mean age at transplantation was 30.5 years. The primary liver disease was hepatocellular carcinoma seconder to viral hepatitis in 15 patients, Wilson disease in 7 patients, criptogenic cirrhosis in 3, familial hypercholesterolemia in 3 patients, and 1 each patients of Byler disease, Caroli disease, tyrosinemia, Budd-Chiari sendrom, congenital hepatic fibrosis, alcholic cirrhosis, and biliar atresia. The primary disease in 2 patients were unknown. The histologic diagnosis included infectious diseases (n=4); xanthomatous lesions (n=4); vasculopathic lesions (n=4); melanocytic lesions (n=4); precancerous and cancerous lesions (n=3), benign adnexial tumors (n=2); skin atrophy (n=2); calcinosis cutis (n=2), keratinous cyst (n=2) and miscalenous lesions (n=11)

Conclusions: We presented the cutaneous manifestations in liver transplant recipients. The most common skin lesion in these patients were infectious, xanthomatous and melanocytic lesions. Precancerous and cancerous lesions came after these lesions, so our study indicates that the risk for skin malignancy after liver transplantation is lower than the malignancy risk for other solid organ transplants, particularly kidney.

PI2
Anesthetic Management in Pediatric Orthotopic Liver Transplantation For Fulminant Hepatic Failure and End-Stage Liver Disease

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Introduction: Orthotopic liver transplantation (OLT) is the only curative therapeutic option in children with end-stage liver disease (ESLD) or severe fulminant hepatic failure (FHF). However, these two groups of patients have certain differences in terms of development of collateral vessels and previous surgeries, which are more common in ESLD. Despite these differences the impact of these two conditions on the perioperative management of these two groups is not clear.

The purpose of this retrospective study was to assess the anesthetic management along with short-term morbidity and mortality in a series of pediatrics patients who underwent OLT for FHF or ESLD in a university hospital.

Materials and Methods: After obtaining approval from the Institutional Review Board, we retrospectively analyzed the records of children who underwent OLT from May 2002

to May 2012. The patients were categorized into two groups according to the reason for OLT: Group FHF (n=22) and group ESLD (n=19). Perioperative data related to anesthetic management and intraoperative events were collected along with information related to postoperative course and survival to hospital discharge. The patients fulfilled the King's College Hospital Criteria for liver transplantation in FHF.

The information gathered from the subjects' records included demographic features of gender, age, and weight; comorbidities; etiology of the liver failure; perioperative laboratory values; arterial blood gas analyses; use and volume of crystalloid, colloid, packed red blood cells, fresh frozen plasma, platelets, cell-saver, and 20% human albumin; anhepatic phase duration; vasopressors; anesthesia duration; and urine output. We also noted the lengths of stay (LOS) in ICU and hospital as well as the mortality rates.

Results: The mean age and weight for groups FHF and ESLD were 8.6 ± 2.7 years versus 10.8 ± 3.8 years (p=0.04) and 29.2 ± 11.9 kg versus 33.7 ± 16.9 kg (p=0.46), respectively. There were no differences between the two groups regarding the length of anhepatic phase (65±21min vs73±18 min,p=0.13) and operation time (9.1±1.6h versus 9.5±1.8h, p=0.23). The source of the donor liver was cadaveric in 4.5% of patients in group FHF and 21.1% in group ESLD (p=0.10). When compared with the patients in group FHF, those in group ESLD more commonly had a Glasgow coma score of 7 or less (32% vs 6%, p=0.04). The amounts of 20% human albumin, packed red blood cells, and fresh frozen plasma that were administered intraoperatively were not significantly different between the groups (p>0.05 for all). Patients in group FHF received more crystalloid solution intraoperatively than those in group ESLD (66±40 ml/kg versus 105±52 ml/kg, p=0.01). The groups were not significantly different in terms of intraoperative urine output and vasopressor requirements (p>0.05 for both). Compared with those patients in group FHF, those in group ESLD were more frequently extubated in the operating room (31.8% versus 89.5% p<0.001). Postoperative duration of mechanical ventilation (2.78±4.02 day vs 2.85±10.21 day, p=0.05), and the mortality rates at 1 year after OLT (7.3% vs 0%, p=0.09) were similar between the two groups.

Conclusions: Our results suggest that during pediatric OLT, those children with FHF require more intraoperative fluids and more frequent postoperative mechanical ventilation than those with ESLD. The higher rate of mechanical ventilation need after OLT for FHF has important clinical implications in terms of effective use of scarce intensive care resources.

P13
De Novo Non-Skin Solid Organ Neoplasia After Liver Transplantation

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Introduction: De novo neoplasia is a frequent and serious complication in liver transplant recepients. Non-skin solid organ malignancies are not as common as skin related malignancies after liver transplantation (LT). The aim of this study is to investigate the incidence and the type of tumor, time of appearance and evaluation of de novo non-skin solid organ neoplasies (DNSN) after LT at our hospital.

Materials and Methods: We analysed 408 patients who had LT between January 1990 and December 2012 at Başkent University Hospital retrospectively. Clinical and pathological findings of these patients including age, gender, immunosupressive regimen, clinical symptoms, radiological findings, time between LT and development of neoplasies were examined.

Results: Only 4 of 408 (0.98%) liver transplant recepients had DNSN . The mean age of these 2 male and 2 female patients at the time of tumor diagnosis is 52,25 ± 9,94 years. The mean time between LT and tumor diagnosis is 55.75±15,45 months. The etiology of LT were billiary cirrhosis, HBV and HDV related chronic liver failure, congenital hepatic fibrosis and hepatocellular carcinoma. There were two conjunctival neoplasia cases; one with squamos cell carcinoma in unilateral eye and other is squamos cell carcinoma insitu in bilateral eyes. There was just one thyroid papillary carcinoma and bilateral serous adenocarcinoma of ovary. They had different immunsuppresive regimens including tacrolimus, mycophenolate mofetil, prednisolone and cyclosporin. Only one of 4 patients has died 11 months after the diagnosis of malignancy.

Conclusions: The incidence of DNSN is too low in our liver transplantation cases. De novo neoplasms of thyroid, conjunctiva and ovary are reported rarely in the literature. Given their relative infrequency in large case series, these cancers are likely accepted as sporadic and not directly related to liver transplantation.

P14

Liver Transplantation for Progressive Familial Intrahepatic Cholestasis With Infantile Hemangioendothelioma: A Case Report

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Introduction: Hepatic tumors in children are relatively rare, accounting of %1-4 of all pediatric solid tumors and infantile hemangioendothelioma (IHE) is the most common type of vascular tumors in infancy. There is female predominance and most of the patients are diagnosed during the first months of life. The natural course of disease varies, from spontan regression to heart failure and even death. Progressive familial intrahepatic cholestasis (PFIC) refers to a heterogeneous group of autosomal recessive disorders of childhood that disrupt bile formation and present with cholestasis. The signs of PFIC appears in the first years of life and leads to death from liver failure. Thus the liver transplantation is the only treatment option for these patients.

Case Report: We report a 7 months male patient, with glucose 6 phosphate dehydrogenase defficiency (G6PDD) and PFIC-2 leading to chronic liver failure and underwent orthotopic liver transplantation (OLT). On gross examination of his native liver; 0.5 cm nodule was recognised on posterior of right lobe, 2 cm away from capsule and was diagnosed as IHE histopathologically. Besides this nodule all the parenchyme showed submassive hepatocyte loss and diffuse hepatocanalicular cholestasis . The size of IHE nodule in our case was too small to make an abdominal mass and it was not recognised by abdominal sonography or computed tomography (CT) before transplantation. There were symptoms and signs like jaundice, anemia hepatomegaly, intraabdominal massive fluid, high AFP and liver enzymes in serum but all were explained by the PFIC-2 and G6PDD. For 3.5 years he was followed and didn't have any rejection episodes.

Conclusions: We report this case because of rarity of PFIC-2 with IHE synchronously and review the literature focusing on IHE.

P15

Invasive Fungal Infections in Liver Transplant Recepients

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Introduction: Invasive fungal infections (IFIs) have been reported to have high rates of mortality in transplant recipients. The aim of this study is two folds, first to evaluate the incidence of IFIs among liver transplant recepients; second to find out the possible risk factors of the development of IFIs.

Materials and Methods: A retrospective analysis was made of the recorded data in 408 patients received liver transplantation between January 1990 to December 2012 at Başkent University. Demographic and clinical findings of these patients including age, gender, primary liver disease, immunsupressive treatment, blood drug level and the time between the transplant surgery and the occurence of the fungal infections were examined.

Results: Only 10 of 408 liver transplant patients (2.5%) were developed IFIs. Of the total 10 patients, 8 were male and two of them were women. The mean age of these patients was 45.5±21.9 years. Six of ten patients had the diagnosis of diabetes mellitus before liver transplantation. In addition, three of ten patients had CMV infections before the diagnosis of IFIs. Diagnosis of the fungal infections was made by the positive blood or bronchoalveolar lavage cultures and with the biopsies. The mean time between transplantation and the development of IFIs was 32±19.2 days. Aspergillus was the most common cause of invasive fungal infections (n=8), followed by candida (n=1) and criptococcus neoformans (n=1). Pulmonary involvement was dominant in nearly all patients (n=9), and only one patient had disseminated fungal infection (criptococcosis). The only one of these ten patients response to therapy, while the remaining patients died because of IFIs.

Conclusions: Only ten of our liver transplant patients (2.5%) had fungal infections and we suggested that the most predisposing factor of IFIs in transplant patients were found to be diabetes mellitus and CMV infection, In addition to immunosupressive therapy. As reported in the literature, Aspergillus was found to be the most common pathogen also among our cases. This study pointed out that because of its high mortality rate, it is very important to follow up transplant patients carefully for the development of IFIs.

P16
Role of Bronchoalveolar Lavage in Diagnosis of Fungal Infections in Liver Transplant Recepients

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Introduction: Bronchoscopy with bronchoalveolar lavage (BAL) is useful tool in the diagnosis of pulmonary infections in immunocompromised patients such as liver transplant patients. Several factors might predict pulmonary infections in liver transplant recipients, especially immunosuppressive regimen, age, and accompanying systemic disease. The aim of this study was to analyze the effectiveness of BAL in establishing the diagnosis of pulmonary infections in liver transplant recipients.

Materials and Methods: Patients who underwent BAL were selected among 408 liver transplant recipients from January 1990 to December 2012 in Başkent University. Clinical findings of these patients, including age, immunosuppressive therapies, clinical symptom, thorax computed tomography results, bronchoscopic findings, culture results of BAL fluid, total blood count, treatment regimen, age at transplantation and the time between transplantation and BAL were examined. Conventional cytology and BAL culture was performed.

Results: There were 18 patients who underwent BAL after liver transplantation. The mean age of these patients was 49.5±18 years. Of the total 18 patients, 16 were male, two of them were woman. Eight of 18 patients had the diagnosis of diabetes mellitus before liver transplantation. Immunosupressive regimen of 9 patients was tacrolimus while 6 patients received cyclosporine and 3 patients received sirolimus. Only 5 of 18 patients (27.8%) showed fungal microorganism in bronchoalveolar lavage material. Three of them were Aspergillus fumigatus and two of them were Candida albicans. The only one of these five patients response to therapy, while the remaining patients died because of invasive fungal infections.

Conclusions: Solid organ transplant recipients are at high risk of infectious complications and the most common manifestations of these infections is pulmonary fungal infection. These infections are associated with a considerable morbidity and mortality, so the rapid diagnosis is notably important. As an extremely useful tool, flexible bronchoscopy with bronchoalveolar lavage (BAL) is simple, safe, fast and reliable method for detecting fungal infections in liver transplant recipients.

P17
Liver Transplantation in Two Children With Primary Oxalosis

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Introduction: Primary hyperoxaluria (oxalosis) is an inherited metabolic disorder caused by a deficiency of the liver-spesific enzym, peroxisomal alanine: glyoxylate aminotransferase characterized by increased production and urinary excretion of oxalate and glycolate that leads to urolithiasis, nephrocalcinosis and, renal failure. In addition, oxalate accumulation in extrarenal all tissues such as the bone, joints, soft tissues, eye, cardiovascular system can be seen. The disease presents in childhood or adolescence with reccurrent urolithiasis and progressive renal failure. Because metabolic defect is located in the liver, liver-kidney transplantation, either combined or sequential is the only curative option in severe cases. We report two children with primary oxalosis.

Case Reports: Case 1: A-8-year-old girl presented with reccurrent urinary tract infection. Computed tomography and ultrasonography of her kidney revealed medullary nefrocalcinosis and urolithiasis. Analysis of the removed ureteric stones showed mainly Weddellite type of calcium oxalate. Serum oxalate and glycolate levels and daily urine oxalate excretion were elevated. End stage renal failure was developed after 1 year and the patient was started on continuous ambulatory peritoneal dialysis. At the age of 10, she received liver transplatation from her mother and she received renal transplantation from her mother after 4 months of liver transplantation. Case 2: A-2-month-old boy was diagnosed as primary oxalosis at external hospital. End stage renal failure was developed and the patient was started on continuous ambulatory peritoneal dialysis. At the age of 3, he received liver transplantation from his father. Two months later, he was hospitalized for kidney transplantation from his father. While at this time, he had convulsion attack. Glasgow Coma Scale was found as three. Computed tomography of head revealed intracranial haemorrhage. Even though all of medical interventions, the patient was died.

Conclusions: Because of continuing enzyme defect and oxalate accumulation, only transplantation of kidney is

insufficient treatment. Liver-kidney transplantation, either combined or sequential is the only curative surgery. The patients must be follow up clinically for accumulation of oxalate after transplantation by serum oxalate and glycolate levels, daily urine oxalate excretion levels.

P18
A Case of Cerebral Tuberculosis After Liver Transplantation and Review of The Literature

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Introduction: Tuberculosis is a major public health problem that leads to an important cause of morbidity and mortality at worldwide level. The risk of active tuberculosis is high in solid organ recipients. When we evaluate, the clinical presentations of tuberculosis, pulmonary localizations are the most frequent type but extrapulmonary localizations are rarely seen. Among extrapulmonary sites, intracranial tuberculosis is extremely rare and only few case reports are reported in the literature.

Case Report: Here we report a case of 27 years old, male patient who received cadaveric liver transplantation due to HBV related chronic liver failure. One month after the liver transplantation, neurological symptoms were developed, following he had tonic clonic convulsion attacks. In serebral stereotactic needle biopsy of left temporal region, in addition to gliozis, rare lymphocyte infiltration, epitheloid hystiocytes and acid fast resistant bacillus had been noted. The case was diagnosed as granulomatous inflamation which was pointing out to the tuberculosis. In addition to antituberculosis therapy, patient had also been taken antiviral therapy for profilaxis. During his therapy, the reactivation of HBV was noted and the recurrent disease of HBV, viral hepatitis was diagnosed in the serial liver biopsies. Ten months after transplantation he has died because of liver failure.

Conclusions: We reported this unusual case of cerebral tuberculosis after liver transplantation in order to discuss the influence of chronic infection such as tuberculosis on the reactivation of HBV and therefore the development of the liver allograft failure due to recurrent disease.

P19
Pathological Findings of The Liver Allografts Evaluated at Autopsy

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Introduction: An autopsy is a specialized surgical procedure to determine the cause and the manner of the death. Autopsies are also used in clinical medicine for the evaluation of any disease or injury that may be present. The number of autopsies performed for medical purposes has been decreasing since 1950s. The reduction in autopsies is negatively affecting to detection of early causes which can lead to disease. The survival of patients undergoing liver transplantation has increased in the last years because of improvements including selection of candidates, surgical procedures and postoperative management of patients. Analyses of the causes of death after liver transplantation are important to to improve liver transplant recipient survival. The aim of this study was to review the pathological findings as determined by autopsy of the liver allografts.

Materials and Methods: We analysed 408 patients who had liver transplantation between January 1990 and December 2012 retrospectively. Thirteen of 408 patient was underwent postmortem examination. Clinicopathologic findings including age at the death , causes of deaths and main pathological findings were evaluated.

Results: The study group of 13 patients whom underwent liver transplantation had a mean age of 29 years at the time of death. The mean survival time was 260.69 ±586.78 days for all these patients. Ten of 13 (76.9%) were died 90 days after liver transplantation. Remaining 2 patients were died after the first year of the transplantation.The causes of the deaths were due to infection (6 cases), respiratuar distress (2 cases), multiorgan failure (1 cases), primary graft failure (1 cases), massive intraabdominal bleeding (1 cases) and hepatic encephalopathy (1 cases). The causes of the infection were bacterial sepsis in 3 cases and invasive fungal infection in other 3 cases. The main pathological findings was hepatic infarction in 9 cases. Bridging fibrosis (3 cases) and hematoma (1 cases) were obtained in remaining cases. Our results emphasize that infections are the main cause of the death and hepatic infarction is the main histopathologic findings among these 13 patients within the first year of transplantation.

Conclusions: We consider that post-mortem examination have important role in order to determine the primary graft failure and the other causes that increased mortality in liver transplantation patients such as infections.Autopsies can provide understanding the main causes and the manner of the death to expanding lifespan in the future.

P20

Karyomegalic Tubulointerstitial Nephritis After Liver Transplantation- A Case Report

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Introduction: Karyomegalic tubulointerstitial nephritis is a rare entity which can lead to progressive renal failure. The pathogenesis of this disorder is unknown; however, a mitotic block linked to certain MHC genotypes has been proposed. Other potential etiologies include heavy metal or ochratoxin exposure and viral infections. Here, we report a 16-year-old liver allograft recipient who presented with progressive decline of renal function in the third year of the liver transplantation.

Case Report: A 16-year-old female who had liver transplantation at 2003 because of Wilson chirrosis, developed calcium-phosfate imbalance 3 years after her transplantation. Patient had only one episode of acute rejection during past 3 years. During follow-up, because of the elevated creatinine levels and the developing of glycosuria, a kidney biopsy was performed. The biopsy noted many tubular cells with striking nuclear enlargement with bizarre nuclear shapes. In addition, patchy fibrosis with tubular atrophy and a moderate chronic inflammatory infiltrate was observed in the biopsy. These findings were interpreted as karyomegalic nephropaty. EBV, Polyomavirus and CMV viral markers were negative in the biopsy. There was no exposure history to lead, cadmium, mercury or chromium but the patient's copper level in the liver biopsy found highly elevated (112ug/gr). The patient denied a family history of kidney disease. Electrolyte replacement was applied and routinely controls are suggested.The patient is still at routine control with mildly elevated creatinine level (1,83mg/dl) and without liver allograft faliure.

Conclusions: Karyomegalic interstital nephritis is a rarely seen important condition. The clinicians should be alert for karyomegalic intestitial nephritis especially in patients with liver failure. Because, in the absence of viral infections and the other environmental factors, karyomegalic tubulointerstitial nephritis may be induced by altered copper metabolism.

P21

Liver Transplantation for Metastatic Neuroendocrine Carcinoma : A Case Report

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Introduction: Patients with neuroendocrine tumors (NET) often present with synchronous liver metastases or develop hepatic metastases in the course of the disease.

Case Report: We report a case of liver transplantation (LT) in a 37 years old female patient with hepatic metastases originating from neuroendocrine carcinoma of pancreas. She had distal pancreotectomy and splenectomy 6 months before LT and diagnosed as well differentiated neuronedocrine carcinoma histopathologically. At the same time multiple metastatic nodules which were infiltrating nearly the whole liver was noted in the abdominal CT and the biopsy of these metastatic nodules revealed the same diagnosis with the pancreas tumor. Thus LT became the only therapy option for the patient. After LT she had only one rejection episode during follow-up and neither reccurence nor metastasis was found during 6 years follow-up.

Conclusions: Metastatic tumors of the liver have been considered to be a poor indication of LT. But neuroendocrine tumors have biologically less agressive nature throughout the life span. LT appears to be a therapeutic approach which should be considered for selected patients with unresectable metastatic hepatic disease originating especially from endocrine tumors of pancreas.

P22
Liver Transplantation for Pediatric Patients With The Diagnosis of Hepatoblastoma

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Introduction: The current role of liver transplantation in treating malignant tumors of the liver is uncertain, except for selective histologic types. Hepatoblastoma is the most common malignant liver tumor of early childhood accounting for 60%-85% of all hepatic tumors in children. More than 60% of lesions that appear unresectable on initial imaging will shrink with chemotherapy and become resectable. However, approximately 20% of tumors remain unresectable after chemotherapy and the liver transplantation is the only curative option in these cases. The aim of this study was to review the clinicopathological findings in 5 children who underwent liver transplantation for hepatoblastoma.

Materials and Methods: We analysed retrospectively 408 patients who had liver transplantation between January 1990 and December 2012. Only five of 187 (2.6%) pediatric liver transplant patients underwent liver transplantation with the diagnosis of hepatoblastoma. Clinicopathologic findings of these cases including age, gender, chemoterapeutic regimen, stage and histopathologic subtypes of the hepatoblastoma were recorded.

Results: The study group included 2 female and 3 male patients of mean age at the transplantation of 44.2 ±27.8 months (range, 14-75 months). All of these 5 cases treated first of all with the cisplatin. In addition to cisplatin 2 of 5 cases also admitted to adriamycine and 3 of them also received doxorubicin. After chemoterapy, radiological examinations showed no regression of the tumor.Thus, all of these cases were accepted as unresectable tumor and underwent liver transplantation. Histopathological study of the native livers of all 5 cases showed pure epithelial type (fetal and embryonal) hepatoblastoma in 3 cases, mixt epithelial and mesenchimal type hepatoblastoma in remaining 2 patients. The mean follow-up time for all patients was 30.17±29 months (range,3-71 months). During follow-up neither acute nor chronic rejection was found in any case. But, one patient had developed post-transplant lenfoproliferative disease (PTLD) after 2 years of the liver transplantation and he was died because of the PTLD. Two of 5 patients were died because of the hepatoblastoma and remaining 2 of 5 patients are still alive without liver failure.

Conclusions: Chemotherapy and/or resection of the tumor may be curable for some hepatoblastoma patients but some cases do not have any chance with these treatment modalities. Such cases were accepted as unresectable and the only treatment left for these cases is liver transplantation.

P23
Fine Needle Aspiration Biopsies of Thyroid in Liver Transplant Recepients

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Introduction: Liver transplant (LT) recipients are at high risk for the development of post-transplant malignancies but there are only solitary reports of thyroid carcinomas in the literature.

Materials and Methods: We analysed 408 patients who had LT between January 1990 and December 2012 at Başkent University Hospital retrospectively. We examined clinical and pathological findings including age, gender, immunosupressive regimens, clinical symptoms, radiological findings and thyroid hormone levels of patients who had fine needle aspiration biopsies (FNAB) before and after LT.

Results: Only 7 of 408 (1.71%) LT recepients had FNAB of thyroid ; 4 before, 3 after LT. The mean age of these patients at the time of LT is 52.75±9.46 years. The etiology of LT were: Wilson disease, congenital hepatic fibrosis, primary billiary chirrosis, hepatocellular carcinoma (HCC) and cholangiocellular carcinoma, HBV and HCV related HCC (2 patients) and criptogenic chronic liver failure. All of 4 pretransplant FNAB and 2 of 3 posttransplant FNAB diagnosed as benign and just 1 of 3 postransplant FNAB (0.24% of all LT) diagnosed as malign according to Bethesda classification. This case was underwent to total thyroidectomy and multifocal papillary thyroid carcinoma was noted in the thyroidectomy specimen. On the follow up of this patient , neither reccurence nor metastasis was noted during 10 years.

Conclusions: The incidence of FNAB and carcinoma of thyroid in our transplantation cases are too low. Because of the high incidence of thyroid dysfunction in transplant

patients, screening of thyroid function and taking FNAB from these cases should be a part of follow-up. Our results suggest that although frequency of thyroid nodules is increased in transplant patients, prevalance of thyroid cancer is low among liver transplant patients in contrast to renal transplant patients.

P24
Hepatic Angiosarcoma And Liver Transplantation: A Report of Two Cases With Diagnostic Difficulties

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Introduction: Angiosarcoma is a rare primary malignant tumor of the liver. The prognosis of hepatic angiosarcoma (HA) is extremely poor with an average life expectancy of 6 months following diagnosis. The diagnosis of HA is challenging because of nondiagnostic liver biopsy or specious history and radiologic presentation. We report two cases with HA wich were diagnosed in the native liver after liver transplantation (LT).

Case 1: A 38-year-old male with complaints of abdominal pain, weakness and weight loss and with history of chronic hepatitis B virus infection for four years, was referred to hospital. Hepatosplenomegaly, ascites, and jaundice were noted in the phisical examination. The serum alpha-fetoprotein levels were in normal limits. Radiological examination and liver function tests showed decompensated cirrhotic liver. Therefore the patient underwent LT. The gross examination revealed a multinodular and sponge-like apparence with cystic spaces full of with blood in the native liver specimen. A diffuse infiltrative vascular neoplasm was seen microscopically. Neoplastic cells had high grade nuclei, but not high mitotic activity. The tumor was diagnosed as HA. The patient was lost of followup after discharged from hospital, postoperative 14th days.

Case 2: A 43-year-old male with complaint of abdominal pain, with findings of hepatomegaly, ascites, jaundice, and pleural effusion had end-stage-liver function tests and high serum levels of CA19.9, normal serum levels of CEA and alpha-fetoprotein. Radiological examination revealed multiple nodules in both lobes of the liver, and the patient was underwent to liver tru-cut biopsy. Epithelioid hemangioendothelioma was diagnosed in the biopsy specimen that composed of single tissue core. The patient underwent LT after 3 days of the diagnosis. The gross examination of the native liver showed that multiple nodular lesions involving both lobes of the liver. An infiltrative vascular neoplasm with nodular growing pattern was noted microscopically. The neoplasm had more complex dissecting proliferation of thin-walled vascular channels, compared to the tumor was seen in the first biyopsy specimen. Contrary to the first biyopsy, hepatectomy specimen had some criteria of malignancy histopathologically; the findings of lymphovascular invasion, and presence of atypical cells with necrosis. Thus the final diagnosis was given as HA. Eight months after LT, a recurrence of the HA was noted in allograft liver by tru-cut biopsy. The patient was died of HA in 18th month, after LT.

Conclusions: Diagnosis of HA is a challenging issue for LT because of the multinodular appearance in both of liver cirrhosis and HA on radiological examination. The multinodular pattern of HA may be mistaken for the nodularity of cirrhosis. Thus, in order to eliminate the unexpected malignancy multiple liver biopsies must be done before the LT. Because, the efficacity of LT on the life expectancy of the patients with HA is controversial yet.

P25
Can Routine Laboratory Findings Predict Potential Complications After Liver Transplantation?

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Introduction: After liver transplantation, some complications such as acute or chronic rejection, recurrence of primary disease, thrombus of hepatic artery or vein, and biliary complications seem to be inevitable and may cause morbidity and/or mortality for the patients. Currently, liver biopsy, along with laboratory findings and diagnostic images are required to elucidate the cause of liver dysfunction in these circumstances. This study was performed because there are few studies investigating the relationship between histopathological diagnosis and routine laboratory data in transplanted patients.

Materials and Methods: We retrospectively studied 113 patients who had undergone liver transplantation between January 2002 to April 2012. Liver biopsies were taken in

45 of 113 patients. Patients were divided into the following groups according to their histopatological diagnoses: rejection (42.4%), recurrence of primary disease (27.9%) and non-specific changes (26.7%). The relationship of histopatholigical diagnoses with age, sex, underlying disease and post-biopsy laboratory data (including liver function tests and complete blood count) were compared between the groups.

Results: Autoimmune hepatitis, cryptogenic cirrhosis and viral hepatitis, in order, were the most common underlying diseases necessitating transplantation. The mean age (±SD) of biopsied patients (25 women and 20 men) was 39.6 (±9.86) years and the most frequent pre-transplantation diagnosis was viral hepatitis (18.0%). The mean age of patients with recurrence of viral hepatitis was 50.70 (±5.80) years which was significantly higher than rejection group (35.4±14 years) and group with non-specific changes (36.50 ±15.60) (P = .001). As expected, most recurrences of primary liver disease were observed in patients infected by HCV (P =.002). The patients with rejection showed higher platelets counts in comparison to the non-rejection groups
(P = .011). Other laboratory findings revealed no significant difference among the groups.

Conclusions: According to this study, there is a correlation between age and recurrence of viral hepatitis, and also between rise in platelets count and possibility of rejection. However, the clinical application of the latter finding requires further investigation in future studies with larger sample sizes.

P26
A Clinicopathologic Study of 19 Renal Biopsies From 10 Patients With Liver Transplantation

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Introduction: The ever-growing number and increasing survival of liver transplantation (LT) allow better recognition of its associated renal injuries. Renal injury is a common problem after LT. Studies evaluating renal pathology Post-LT are sparse and sample sizes are small. Renal injury is traditionally attributed to calcineurin inhibitor (CNI) toxicity. This view was recently challenged. Many investigators have concluded that the cause of renal impairment may be multifactorial, and interconnected. Herein, we performed a clinicopathologic study of patients having renal biopsies after LT by reviewing 19 percutaneous renal biopsies from 10 patient in our institute.

Material and Methods: A retrospective clinicopathologic study of all renal biopsies from patients with LT archived to the Department of Pathology, Başkent University Ankara Hospital during the period January 1990 to December 2012 was performed. Clinical data on presentation and follow up were retrieved from hospital records and physicians.

Results: In the 22-year period, 408 patients received LT in the Transplantation Surgery Center of Başkent University. Nineteen percutaneous renal biopsies were accessed from 10 liver transplant recipients (2 cadaveric donor, 8 living related donor), in the Department of Pathology. The male to female ratio was 7:3 and the mean age at transplantation was 41 years (10-62 years). The mean interval of renal biopsy after LT was 20 months (range 2–166 months). Evidence of increased serum creatinine level (7 cases) and proteinuria (4 cases) were the most observed clinical presentations among our patients. The predominant glomerulopathy in these patients was membranoproliferative glomerulonephritis (MPGN) (n = 3). One patient had MPGN due to relapsing HCV hepatitis after LT. Two cases of IgA nephropathy, and one case of karyomegalic nephropathy were also recorded. In addition to glomerulonephritis, evidence of tubulointerstitial nephritis (TIN) was also found in four patients. One patient showed only TIN. Only two patients had findings of chronic CIT. Three of the patients also had renal transplantion befor or during LT. Seven of 10 patients died at mean 34 months (1–66 months) after LT. Of the remaining three patients with a mean follow up of 127 months (range, 67–193 months) were still alive with a functioning transplant liver.

Conclusions: The occurrence of chronic kidney disease before and after liver transplantation has a major impact on mortality. Additional studies are needed to understand better the natural history of chronic kidney disease among liver transplant recipients. Strategies need to be put in place for the early detection of these individuals and then preventive measures introduced to retard the progression of chronic kidney disease.

P27

24 Years Post Cadaveric Liver Transplant, Is it Time To Withdraw Cyclosporine?!

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Introduction: Today, the 1-year expected survival rate is over 85% and 5-year survival rates of 65-75%. The introduction of cyclosporine markedly improved patient outcomes Introduction: To present 1st cadaveric liver transplant patient with long term follow in Libya, to discuss possibility of cyclosporine withdrawal

Materials and Methods: medical chart of the patient was reviewed, co morbidities were evaluated, and demographic data were collected

Results: The patient is female Egyptian, born in 1950, married, she was known post hepatitis liver cirrhosis, for which she received treatment with standard interferon, cadaveric liver transplantation was in Germany in June 1989, she was started cyclosporine in a dose of 250mg/bd, an now on 50mg with C0 of 40ng/l. She is hypertensive and diabetic

Conclusions: Management of modifiable post-LT factors including diabetes, hypertension and renal insufficiency may impact long-term mortality. Immunosuppressive weaning affects long term survival, an its withdrawal is the future decision.

P28

Post Transplant Burkitt Lymphoma Is A More Aggressive and Distinct Form of Post-Transplant Lymphoproliferative Disorder

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Introduction: Although the literature reports a low incidence of Burkitt Lymphoma (BL) as a post-transplant lymphoproliferative disorder (PTLD), this entity appears to be different from other monomorphic PTLDs (M-PTLDs), both in its aggressive clinical presentation and its distinct pathologic profile.

Case Report: Our case was a eleven-year old boy who was referred to the Transplant Department at Başkent University of Ankara at the age of 2 years, with "progressive familial intrahepatic cholestasis byler's disease" presented with jaundice to develope since he was born. In our institution, he received liver transplant at the age of 26 months from his paternal uncle, and started to use tacrolimus based immunosuppressive regimen. The patient was EBV seronegative before liver transplantation. During his routine controls EBV-PCR got positive a month after his transplantation. Two months after liver transplantation he was treated with antiviral therapy (ganciclovir) for positive CMV antigenemia. Two acute rejection episodes, were treated with steroids. Seventeen months after liver transplantation, the computed tomography showed multiple portal masses and diagnosed as Burkitt lymphoma with liver allograft needle-guided biopsy. Bone marrow biopsy was also positive for tumor involvement. The tumor displayed the typical histological features of Burkitt's Lymphoma and was markedly positive with insitu hybridisation for EBV. After the diagnosis of PTLD, the chemotherapeutic regimen consisted of etoposide 30mg, adriamycin 6,5mg, cyclophosphamide 60mg and prednisolone 4x7,5 mg has given. He is in complete remission, approximately 76 months after completion of the therapy.

Conclusions: There are only isolated case reports of Burkitt's lymphoma presenting as PTLD in the literature. Because of the aggressive progression and the high turn over of tumor proliferation, it is important to start chemotherapy immadiately after the diagnosis of Burkitt lymphoma for the best outcome. Therefore it is very important and life-saving to diagnose Burkitt lymphoma as quickly as possible. Thus because of the close relationship between EBV and PTLD,

we recommend a viral monitoring of EBV during follow-up of especially in pediatric LTx patients to prevent dramatic outcomes because of the possible development of PTLD.

P29
T-Cell Acute Lymphoblastic Leukaemia After Liver Transplantation

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) of T-cell origin are quite uncommon, and the vast majority represent neoplasms of mature, post-thymic T- or natural killer cells. Here, we report a rare case of T-cell acute lymphoblastic leukaemia (T-ALL), which occurred in an 3-year-old child who had undergone liver transplantation for the reason of hepatoblastoma.

Case Report: Three-years old male patient whom had liver transplantation because of hepatoblastoma had neither liver allograft failure nor rejection episode during fallow-up of twenty-two months. Twenty-two months after liver transplantation patient came to the hospital with the complaint of severe cough. Thoracal CT scan which was taken for this reason showed a large mediastinal mass measuring 9x7.2x7cm. The needle-guided biopsy of the mass noted a diffuse infiltration of blastic cells which was accepted as T-ALL infiltration. The patient recieved methotrexate and, prednisolone for the T-ALL treatment, and he was died two months after the diagnosis due to chemotherapy-related sepsis.

Conclusions: This case highlights the challenge for classifying rare neoplasms occurring in recipients of solid organ transplants that are currently not recognized to lie within the spectrum of PTLD. Given the long interval between the liver transplantation and the development of T-ALL, a coincidental occurrence of the leukaemia cannot be ruled out. However, the potential roles of immunosuppressive therapy and other co-morbid conditions of the individual as possible risk factors for the pathogenesis of T-ALL must be always taken in consideration.

P30
Single-Center Analysis of Biopsy-Confirmed Posttransplant Lymphoproliferative Disorder: Incidence, Clinicopathological Characteristics and Prognostic Factors

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Introduction: Post-transplant lymphoproliferative disorders (PTLD) are a heterogeneous set of complications of organ transplantation associated with poor patient prognosis. Here we present the clinicopathological features of a single center series of 26 cases.

Materials and Methods: All of the 2224 solid organ transplant recipients who underwent transplantation between 1985 and 2013 in Baskent University were included in this study. Demographic and clinical findings of these patients baseline immunosupressive therapy, and the time between transplantation and the development of PTLD were examined in all cases. Among cases whom have been diagnosed as having PTLD were (re)-classified according to the WHO 2008 classifications of lymphomas. Three main pathologic subsets / stages of evolution are recognised: early, polymorphic, and monomorphic lesions. The grading of PTLD and the association of PTLD with EBV were compared. The causes of death were also evaluated.

Results: Of 2224 solid organ transplant recipients, 26 cases(1.16%), developed heterogeneous types of PTLDs. The cumulative incidences of PTLDs during this period were 0.86% (15 / 1740) for kidney transplant recipients and 2.69% (11 / 408) for liver transplant recipients. PTLDs had not developed in 76 heart transplant recipients. Mean interval between the first transplantation and the diagnosis of PTLD was 64,6 ±70 months (range, 4-248 months). Among 26 cases only 7 patients developed PTLD with in the 1st year of transplantation. The mean age at the time of PTLD diagnosis was 27.3 ± 18 years (range, 1-52 years) and eight patients (30.8%) were younger than 19 years at the time of PTLD diagnosis. There was a male predominance (16 cases 61.5%) among patients with PTLD. The gastrointestinal tract was the organ system most commonly involved (9/26, 34.6%) in our cases. The second highest PTLD involvement was found in lymph nodes in 5 cases. Only 3 cases showed PTLD involvement in the allograft. Of 26 cases 23 of them showed monomorphic PTLD, while only 1 case showed polymorphic PTLD and remaining 2 cases showed early

lesion. Total of 26 cases 8 of them died 37.9±49.9 months (range 0.3-131 months) after the PTLD diagnosis because of the complication of transplantation and/or the PTLD.

Conclusions: Immunophenotyping PTLD's is essential because of the significant differences in prognosis and therapy between B-cell and NK / T cell lymphomas. Sampling of several lesions in cases with multiple site involvement is also essential because early, monomorphic and polimorphic lesions can be synchronously present in different sites. In conclusion, even with treatment the mortality rate is high in patients with PTLD. Thus in order to decrease the incidence of PTLD and related mortality, the risk factors should be evaluated and the new approaches must be derive for prophylaxis, diagnosis and treatment.

P31
Preoperative Pleural Fluid Assessment Among Liver Transplantation Candidates

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Introduction: The aim of this study is to assess the pleural effusion frequency retrospectively and to define characteristics of pleural fluid, among patients referred to our center as liver trasplantation candidates.

Materials and Methods: 135 patients (43 women, 92 men) were included in the study and the mean age was 40 years (min. 16, max.66 years). Demographic features and respiratory symptoms were noted. Chest X-ray of each patient included in the study was examined to evaluate pleural effusion.

Results: 16 patients had respiratory symptoms at the time of first admission to the hospital (11.9%) and abnormal radiologic findings were found in 49 patients(36.3%). Elevated right hemidiaphragm was the most common radiographic abnormality (n=32). Pleural effusion (n=22, 16.2%), atelectasis (n=21, 15.5%), hilar enlargement (n=18, 13.3%) and left hemidiaphragm elevation (n=9, 6.6%) were other radiographic findings respectively. Of the 22 patients with pleural effusion, 17 had right sided (77.2%), 4 had bilateral (18.1%) and one patient had left sided (4.5%) pleural fluid. 10 of the patients underwent thoracentesis and the results of the pleural fluid analysis were compatible with transudate in 9 patients and exudate in 1 patient.

Conclusions: About one-third of the liver transplantation candidates inclued in this study was diagnosed with any lung disease during routine preoperative assessment tests. Pleural effusion was detected about half of these patients and most of the cases had right side localized transudative pleural effusion. Preoperative pleural effusion is a frequent problem in liver transplantation candidates.

P32
Early Pulmonary Complications of Liver Transplantation

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Introduction: Pulmonary complications are one of the leading problems after liver transplantation. The aim of this study is to investigate postoperative early pulmonary complications among adult orthotopic liver transplant recipients.

Materials and Methods: 135 patients (43 women, 92 men) whose medical data can be reached retrospectively were included in the study and the mean age was 40 years (min. 16 /max. 66 years). Postoperative chest X-ray of each patient was evaluated to check for pulmonary complications.

Results: 77 of the 135 patients , whose chest X ray was performed in the early preoperative stage, had radiographic findings of pulmonary complications. Pleural effusion was the most common radiographic finding (n=50, 37%), respectively atelectasis (n=25, 18.5%), consolidation (n=6, 4.4%) and bronchiectasis (n=1, 0.7%) were other detected abnormalities. Pleural effusion was right sided in 25 cases, bilateral in 20 cases, left sided in 2 cases and accompanied by atelectasis in 3 cases. 40 patients underwent thoracentesis(80%). Pleural fluid analysis results were compatible with transudate in 22 cases (55%) and exudate in 18 cases (45%). From 40 thoracentesis specimen sent for

pleural fluid culture, 33 were negative (82.5%) and 7 were positive (17.5%)

Conclusions: Early postoperative pulmonary complications were detected in more than a half of liver transplantation recipients. Besides radiologic follow-up, interventional radiologic procedures were also utilised for management of pulmonary problems. First month follow-up is important for early management of pulmonary complications in these cases.

P33

Plasma Disappearance Rate of Indocyanine Green as a Diagnostic Tool for Early Complications and Graft Outcome After Orthotopic Liver Transplantation

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Introduction: Plasma disappearance rate of indocyanine green (PDR-ICG) has been used to assess early detection of graft dysfunction and complications after orthotopic liver transplantation (OLT). However, there are few data regarding the value of PDR-ICG measured by a noninvasive technique to predict early complications and graft outcome after OLT. The aim of this study was to evaluate the role of PDR-ICG measurement in predicting early complications and graft outcome after OLT.

Materials and Methods: We retrospectively analyzed the records of 18 patients who underwent OLT from June 2012 to April 2013 at our center. PDR-ICG was measured within the first 24 hours following OLT with a digital sensor after patients were injected with 0.5 mg/kg indocyanine green. Preoperative, intraoperative, and postoperative variables of liver transplant recipients were collected. Postoperative complications were defined as primary nonfunction of the graft, acute cellular rejection, arterial/portal complications, hemorrhagic shock and death within 30 days.

Results: The mean age at transplantation was 20.3 ± 22.3 yrs (55.6% female) and mean Model for End-Stage Liver Disease (MELD) score was 27.7 ± 7.1. Early postoperative complications of 18 patients included 1 death and 5 patients were classified as having grade 2 dysfunction after OLT. The PDR-ICG in patients with grade 2 dysfunction was significantly lower than in patients with grade 1 dysfunction (22.9 ± 8.9 vs 36.9 ± 9.4%/min, p=0.01).

Conclusions: Lower values of PDR-ICG measured in the early postoperative period after orthotopic liver transplantation may help as a diagnostic tool for graft dysfunction.

P34

Living Donor Liver Transplantation Post Transarterial Embolization in Hepatitis C Related Hepatocellular Carcinoma: Long-Term Outcomes

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Introduction: Transarterial embolization (TAE) is a well-established modality of treatment for downstaging hepatocellular carcinoma (HCC) cases prior to liver transplantation. Hepatitis C virus (HCV) related HCC is difficult to manage even with liver transplantation because of the almost universal recurrence of HCV post transplantation and the risk of the transplanted liver undergoing subsequent fibrosis. Hence to address this issue, we evaluated the impact of TAE in HCV related HCC patients undergoing living donor liver transplantation (LDLT). The long-term outcomes of these cases are analyzed in this study.

Materials and Methods: We retrospectively evaluated the outcome in those post LDLT patients with HCV related HCC who received TAE intervention and those who did not. The demographic, clinical and pre-operative surgical factors were compared among the 2 groups. The waiting time pre LDLT as well as the overall patient survival and the HCC recurrence free survival were compared between the 2 groups. The tumors were downstaged in the TAE group to fit the UCSF criteria. The prognostic risk factors for HCC recurrence post LDLT were analyzed using the univariate and multivariate analysis.

Results: Over an 8 year period (2002 to 2010), a total of 62 patients having HCV related HCC underwent LDLT at Kaohsiung Chung Gung Memorial Hospital, Taiwan. For the entire cohort study, the mean duration of follow-

up was 4.37 ± 2.29 years. The 2 groups were well matched except for the Childs C score, which was more in non-TAE group (p=0.007). The median waiting time for LDLT in TAE group was 11.91 months (range, 6.67- 31.23 months) which was significantly more than that in the non-TAE group, which was 3 months (range, 2-3.33), p=0.029. Post TAE 27 patients were within UCSF criteria and 3 were within UCSF but outside Milans criteria. There were 19 cases overall, having rapid progression of fibrosis (>0.8 fibrosis score/year). The overall survival in the TAE group, both at 5 and10 years was 92%, and in the non-TAE group was 96.9% and 48.4% respectively. The recurrence rate was 15.6% (5/32), in the non TAE group and was 0% (0/30), in the TAE group; p=0.019.

Conclusions: Pre LDLT, TAE was effective in downstaging tumor as well as in lowering the HCC recurrence rate in patients having HCV related HCC and fitting the UCSF criteria.

P35

Acinetobacter Infection After Liver Transplantation Clinical Features and Effect Survival

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Introduction: Despite advances in surgical technique and postoperative care, infectious complications associated with high mortality rates. Acinetobacter types around the globe has become an increasingly important nosocomial pathogens which cause infection. Liver transplant patients with Acinetobacter types can lead to peritonitis, bacteremia, pneumonia, urinary tract infection, which has a wide range of infection.

Materials and Metods: Between January 2001 and May 2013 in our clinic 355 patients have liver transplantation patients retrspektif age, etiology, Child score, duration of stay in the intensive care unit, surgical complications, presence and type of catheter, and which is taken from the cultures and antibiograms were antibiotic treatments. Multidrug-resistant Acinetobacter types were identified as resistant to all antibiotics except colistin

Results: Because of Acinetobacter types total 11 patients (3%) acinetobacter infections refractory to every kind of antibiyotics produced in 88 different cultures. Acinetobacter baumannii and Acinetobacter Iwoffiii ,Acinetobacter types were identified. Cause of bile duct infection (8 patients, 45 times), lung (1 patient, 4 times), intra-abdominal drain (4 patients, 15 times), blood culture (11 times in 4 patients), urinary tract (3 patients, 13 times). Age, length of stay in intensive care, Child-Pugh score, and etiology of patients infected with Acinetobacter important risk factors for morbidity and mortality were not. However, mortality among the patients infected with Acinetobacter types, respectively, when we compared with other patients mortality (27%, 11.5%), (p> 0.05) were found to be significantly higher

Conclusions: Acinetobacter types infection after liver transplantation in patients with significantly worse prognosis. Everything has been a major problem in center multidrug- resistant Acinetobacter types

P36

Acute Renal Injury Rate in Liver Transplant Patients and Its Effect on Patient's Survival

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Introduction: Acute renal injury is a common complication in liver transplant patients. Acute kidney injury is due to nephrotoxic drugs used after liver transplant, infections and hemorrhage. Though it is generally reversible it has effects on grafts and patients survival. In this retrospective observational study carried out at a single centre, effects of acute renal disease on liver recipient's survival were investigated.

Materials and Methods: Liver transplant, live donor & cadaver, patients between Jan 2002- May 2013 were icluded in this study. The acute kidney disease diagnosis and staging was made based on nephrology department evaluation and daily serum creatinine levels. Patients with acute kidney injury history prior to liver transplant and those undergoing transplantation for the second time were excluded from the study.

Results: 310 liver transplant patients were included in the study. There were 165 male and the remaining 145 were female patients. The patients' average was 28 (6 months- 62

years age range). Kidney functions were evaluated by the nephrology department 1 week, 3 months and 1 year after liver transplant. Acute kidney disease rates in these patinets was 5%, 8% and 12% respectively. Four patients developed chronic kidney failure during the follow up period. When patients that developed acute renal failure and those that didn't have this condition were compared mortality rate was higher, 18% in acute renal failure patients. Mortality rate was 11% in patients that had no acute renal failure.

Conclusions: Acute renal injury is quite common after liver trabsplant and has an important effect on mortality.

P37

Analyzing Quality of Life, Depression and Sexual Functions of The Patients in Liver Transplantation Waiting List of One Center

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Introduction: The only alternative treatment in patients developing liver failure is liver transplantation (LT). According to the 2013 statistics of Ministary of Health, the number of patients waiting for a LT is 2065 and under current circumstances, the average waiting period for a suitable donor is approximately five years. 15 -18 % of these patients lose their life while waiting for transplantation. In addition to liver failure, limitations in daily activities and depression-anxiety are commonly found in these patients. Aim of our study was to find out and analyze life quality, depression symptoms and existence of sexual functional disorders of patients waiting for a LT from a cadaveric.

Materials and Methods: By November 2012, 63 patients, who were in the list of Republic of Turkey, National Organ and Tissue Transplantation Coordination Center and who were registered in Baskent University Hospital and were regularly followed by gastroenterology, were included into the study. Face to face interviews were conducted. Gastrointestinal life quality evaluation form (GIQLI), Beck depression scale (BDI) and Arizona Sexual Experience Scale (ASEX) were applied to the 48 patients who approved the study.

Results: 30 of the patients were male and 18 of them were female and the average age was 46,06±13,8. The average measurement of BDI that were applied to the patients was found as 18,4±11,3. According to BDI, the patients were found to be suffering from medium depressive symptoms. The Average value of GIQLI results was 86,18±21,6. These average values actually show that life qualities of the patients have deteriorated. According to ASEX, average value for men was found as 16,3±5,58 and they were found to have sexual functional disorders at medium-high level. In women, this value was 10,05±8,21 and they were found to have sexual functional disorders at mild-medium level.

Conclusions: Depression and sexual functional problems are commonly found in chronic liver patients and their life qualities deteriorate significantly. We think that psychological support that should be given to these patients in organ waiting period will increase their life quality. Also, in order to decrease the waiting time of these patients, the society should be educated in organ donation and cadaveric organ donations must be increased.

P38

Postoperative Gastrointestinal Bleeding After Orthotopic Liver Transplantation: A Single-Center Experience

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Introduction: The overall incidence, etiology, and timing of posttransplantation gastrointestinal bleeding are described in a limited number of publications. They are rare but life-threatening conditions. In this study, we examined the causes and treatment of postoperative gastrointestinal bleeding after orthotopic liver transplantation (OLT).

Material and Methods: Clinical data of 335 patients who underwent OLT at our institution from September 2001 to December 2012 were analyzed retrospectively. The experiences in diagnosis and treatment of postoperative gastrointestinal bleeding after OLT were reviewed.

Results: Gastrointestinal bleeding occurred in 13 patients (3.8%) after OLT. The 5(38,4%) patients were adult and 8(61,6%) patients were pediatric. The sites of the bleeding was; jejuno-jejunal anastomosis bleeding in 5 cases, peptic ulcer in 3 cases, erosive gastritis in 3 cases, gastric and

esophageal varices in 1 case, and hemobilia in 1 case. These 13 patients with gastrointestinal bleeding were managed with conservative treatment, endoscopic treatment, radiological interventional embolism, or exploratory laparotomy. No patients passed away due to gastrointestinal bleeding. During the follow up period 5 patients passed away (Causes of death: n= 5 sepsis, n=1 reccurence of HCC).

Conclusions: Gastrointestinal bleeding after liver transplantation and its incidence, etiology, and timing are not well described in the literature. Bleeding may occur from different sites after OLT. Diagnosis and management of gastrointestinal bleeding requires a multidisciplinary team approach involving surgeons, hepatologists, advanced and experienced endoscopists and interventional radiologists.

P39

Is High Resistive Index And Peak Arterial Systolic Velocity A Sign Of Acute Rejection After Liver Transplantation?

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Introduction: Acute rejection is major disorders in the postoperative setting after orthotopic liver transplantation (OLT). An immediate diagnosis and successful therapy are essential for graft survival. In this study, we want to compare doppler sonography findings and patological findings.

Materials and Methods: We retrospectively analyzed the datas of patients who underwent OLT between January 2006 and February 2012, for identify patients with acute cellular rejection. We have 2 groups. Group 1(n=58) is acute rejection group and group 2(n=58) is patients without graft rejection. Analyzed parameters included resistive index (R/I), peak arterial systolic velocity (PASV) in the hepatic artery, laboratory values, histopathologic grade and therapy as well as graft and patient survival. All patients were treated with the same immunsupration protocol after LT. No protocol liver biopsy specimens were obtained, and biopsies were performed only for investigation of biochemical abnormalities (elevated serum transaminase or bilirubin levels).

Results: In group 1, 31 patients were pediatric and 27 patients were adult. The median age of the patients was 14,5 (range;1-64). In group 2, 34 patients were pediatric and 24 patients were adult. The median age of the patients was 16 (range; 1-64). In group 1, the mean R/I was 0,65±0,09 and the mean PASV was 85,6±32,8. In group 2; mean R/I was 0,66±0,07 and the mean PASV was 81,2±26,7. There is no significant difference in R/I and PASV between the two groups (p=0,716 and p= 0,423 respectively).There was no vascular problems after transplantation.

Conclusions: Even if doppler sonography revealed normal finding in patients have elevated serum transaminase and bilirubin levels; acute rejection can be still found. To elimate acute rejection liver biopsy is mandatory.

P40

Post- Kasai Liver Transplantation; Difficulties and Postoperative Problems

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Introduction: Biliary atresia(BA); is a congenital obliterative cholangiopathy and is the major cause of obstructive jaundice in neonates. Its etiology is unknown. Introduction of the Kasai operation (hepatic portoenterostomy) contributed to a dramatic improvement in the long-term survival in patients with BA and this procedure is now accepted as the standard surgical technique. Indications for liver transplantation(LT) in patients with post-Kasai BA include liver cirrhosis, liver failure, gastrointestinal bleeding due to portal hypertension, growth retardation, progressive intrapulmonary shunting, hepatopulmonary syndrome and repeated cholangitis, either singly or in combination. In the present study, we want to present our experience about post-Kasai LT.

Materials and Methods: The data of 22 pediatric patients who underwent liver transplant after kasai operation from 2001 to november 2012 at our center were analized retrospectively. All patients were treatedwith the same immunsupration protocol after LT.

Results: We performed 167 pediatric liver transplantation at our center and 30(17,9%) of them were due to BA. Twenty two patients had portoenterostomy operation, before transplantation. One of them were deceased donor LT and 21 of them were living related LT. The mean operation

time was 9±1,9 hours. During the transplantation, average need for blood transfusion was 450ml. In the early period after the transplantations; abdominal bleedings was seen in 4 patients, intestinal perforation was seen in 3 patients, chylous ascites was seen in 1 patient, biliary leak was seen in 4 patients and biliary stricture was seen in 4 patients. There was not any donor mortality or major morbidity.

Conclusions: For the management of patients with BA post-Kasai in the modern era, LT should be used for those patients who develop complications or failure of the Kasai operation.

P41
Postoperative Intraabdominal Bleeding After Liver Transplantation

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Introduction: In this study, we examined the incidence and management of postoperative abdominal bleeding after orthotopic liver transplantation (OLT) and to identify risk factors for abdominal bleeding.

Materials and Methods: We retrospectively reviewed the medical records of 335 patients who underwent OLT at our institution from September 2001 to December 2012 to identify subjects with posttransplantation abdominal bleeding, defined as any hemorrhage requiring laparotomy within the first month.

Results: 42 (13,5%) patients showed abdominal bleeding, requiring laparotomy within the first month, occurring at a mean of 4,9 days (range, day 1 to 21 days). 11(23,8%) of them were cadaveric LT and 32(76,2%) of them were living related LT. The 26(62%) patients were male and 16(38%) patients were female. The bleeding sites requiring laparotomy were the inferior vena cava (n=12), liver graft cut surface (n=9), abdominal wall (n=5), greater omentum (n=5), hepatic artery (n=3) diaphragm (n=2), , portal vein anastomosis site (n=2), hilar plate (n=3) and abdominal drain insertion site (n=1), İn all patients, active bleeding was controlled with surgical ligation or vascular reconstruction. No patients passed away due to abdominal bleeding.

Conclusions: The risk of bleeding because of coagulopathy, anticoagulant treatement and iatrogenic injury is high during the early posttransplantation period. This can be minimized by meticulous surgical dissection and bleeding control. Also it is important to differentiate the patients who need a surgical intervation and who can be followed by medical treatments.

P42
Posttransplant Malignancies in Liver Transplant Recipients

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Introduction: The overall incidence of malignancy in the transplant recipient has been estimated to be as high as 20% in the 10-year period after transplantation. In the present study, we present our experience with de novo malignancies encountered after both deceased and living donor liver transplantations.

Materials and Methods: We retrospectively reviewed the medical records of 335 patients who underwent OLT at our institution from September 2001 to December 2012 to identify subjects with de novo malignancy in orthotopic liver transplantation recipients.

Results: Fourteen patients (4.1%) developed de novo post-LT malignancies. De novo malignancies included post-LT lymphoproliferative disorders (PTLD) in 7 patients who were treated with chemotherapy; thyroid papillary carcinoma in 1 patient who was treated with total thyroidectomy and radioactive iodine therapy; squamous cell carcinoma in 2 patients who were with surgical resection; gastric stromal tumor in 1 patient who was treated with surgical resection; ovarian carcinomas in 1 patient who was treated with radical surgical resection and chemotherapy but passed away within 1 year of diagnosis; lung cancer in 1 patient who was treated with chemotherapy but he had bone metastasis and passed away within 1 year of diagnosis; and neuroblastoma in patient who was treated with chemotherapy. In all patients the immunosuppression therapy were changed.

Conclusions: Transplant recipients generally have advanced stage cancers at the time of diagnosis with a

poor prognosis. Since some neoplasms are common early detection of cancer is important to decrease cancer related mortality and morbidity.

P43

The Relationship Between Locoregional Treatments Applied to Patients With Hepatocellular Carsinoma and Post-Transplant Recurrence

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Introduction: Locaregional treatments (LRTs) are used both to form a transplantation bridge in hepatocellular carcinoma and to downstage tumor phase in tumors that have exceeded the limits of transplantation. The aim of this study was to assess the relationship between controversial locaregional treatments, and post transplantation recurrence rate.

Materials and Methods: The patients who were diagnosed with hepatocellular cancer on cirrhosis basis and underwent liver transplantation were retrospectively evaluated in terms of HCC recurrence. Depending on the application of LRT before transplantation, the patients were divided into two groups as LRT+ and LRT-.

Results: In our center, 50 patients were retrospectively evaluated between January 2000 and May 2013. Seven of the patients were female and the other 43 patients were male. The mean age of the patients was 49.58±18.6. The mean follow-up period after transplantation was 120,81. 42 % of the patients had LRT at least once before transplantation. Nine patients (18 %), of which five of them were with LRT+ and four of them were with LRT-, had recurrence in 44,55 months. When Ki-square test was used, in patients with LRT+ and LRT-, post-transplantation recurrence rate was not different. (p=0,98).

Conclusions: In our patients, it was observed that LRTs that were applied before liver transplantation had no effect on the development of recurrence after transplantation.

P44

Liver Transplantation in a Child With an Uncommon Cooccurrence of Biliary Atresia and Bilateral Vesicoureteral Reflux

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Introduction: Biliary atresia (BA) is a well-known entity with an incidence of 0,8-1 per 10,000 live birth. BA can present with multiple congenital anomalies, in about 20% cases, such as polysplenia, situs inversus, intestinal atresias, and cardiovascular anomalies. But, the cooccurrence of vesicoureteral reflux (VUR) and BA is very uncommon. We report the clinicopathologic findings of a patient with BA associated VUR who underwent to the liver transplantation and nephroureterectomy in the same operation.

Case Report: A twenty two-months-old female child born of non-consanguineous marriage was reported to be icteric from first day of her life. She had antenatal history of bilateral hydronephrosis. Hepatobiliary scintigraphy showed that, there was no passage to the intestine. Liver biopsy revealed findings of BA. According to the results of the analysis, she underwent the Kasai operation when she was two-months-old. She was referred to our hospital when she was nineteen-months-old because of the complaints of jaundice, itching and increasing abdominal distension. On examination, the child had icterus, club¬bing, abdominal distantion, hepatomegaly, splenomegaly and ascites. Laboratory analysis revealed anemia, thrombocytopenia, direct hyperbilirubinemia, raised liver transaminases, hypoalbumine¬mia and prolonged prothrombin time. Renal scintigraphy showed decreased cortical uptake (acute pyelonephritis?) and bigger than the normal left kidney and atrophic right kidney. There was also bilateral VUR (grade 5 at right, grade 4 at left). She underwent both of the liver transplantation and right nephroureterectomy in the same operation at the age of 22 months. Histopathological evaluation revealed that cirrhosis with bile ductular and hepatocanalicular cholestasis widely in native liver. 6g weighing atrophic kidney with multiple parancimal cysts on cut surface and highly dilated ureter on gross examination of the nephroureterectomy specimen. Microscopic examination of the nephrectomy specimen showed diffuse sclerosis of glomeruli, diffuse interstitial inflamation and fibrosis with granulomas which was thought to developed secondery to the opaque material that is likely Tamm Horsfall protein. In addition chronic pyelonephritis ureteropelvic dilatation was diagnosed in pelvicaliceal system. In following few days after the operation the patient died from extrahepatic hematoma because of persistent thrombocytopenia.

Conclusions: A child having BA must be remain under investigation for associated anomalies include VUR that must be treated as early as possible because of its ability of rapid progress to chronic pyelonephritis and end-stage renal failure.

P45
Liver Transplantation To Giant Primary Hepatic Neuroendocrine Tumor

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Introduction: Neuroendocrine tumors (NET) comprise a heterogeneous group of rare neoplasms. Liver metastatic or primer hepatic NETs are amenable to various therapeutic modalities including liver transplantation (LT).

Case Report: 45 years old woman, from another country, suffers from dyspepsia, weight loss and early satiety. She underwent blood analysis, it revealed, gamaglutamyl transferase and alkaline phosphatase as high as 1172 and 369 respectively. She was cachectic and gross hepatomegaly detected in physical examination. Computerized tomography of the abdomen revealed 12x18cm in right and 8x6cm tumor in the left liver lobe. Intrahepatic bile ducts were dilated and there was moderate amount of ascites in the abdomen. The tumor had been accepted as unresectable from another center. She admitted to our center. Liver biopsy was performed and sample was consisted with NET type I, Ki67 1%. Histology revealed trabeculated pattern coexisting PGP 9.5 cytokeratin-19 and CD56 positivity and chromografin low positivity. Also CEA, HCC, Insulin, Gastrin, TTF-1 and CDX-2 staining were negative. The pathology yielded primary liver NET or metastasis of pancreatic NET. PET CT was performed and no tumor other than liver was founded. Endoscopic ultrasound (EUS) was performed, but did not find any pathology. We considered her for living donor liver transplantation based on unresectable primer liver NET, no extrahepatic disease and well-differentiated tumor (Ki67 < 10%) reasons. After her older brother was prepared for living donor liver transplantation, right lob liver transplantation was succesfully performed. Liver specimen revealed same with the pre-surgical biopsy. No lymph node metastasis was found in the hilum of the liver. She has been doing very well free of metastasis 4 years after surgery. Conclusion: The use of LT for NET is controversial. As organs are in short supply, it is important to select patients who are most likely to benefit from this demanding procedure. Beyond the consensual criteria, i.e., it has been shown that the use of stringent criteria to select patients for LT could achieve spectacular overall and disease-free survival rates.

P46
Surgical Outcome of Living Donor Hepatectomy: Single-Center Experience

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Living donor hepatectomy (LDH) for living related liver transplantatio (LRLT) has begun an accepted and widely used worldwide.

Introduction: To assess surgical outcome of living donor hepatectomies as a single center experience.

Materials and Methods: Totally 22 living liver hepatectomies were performed at Gazi University Transplantation Center/Ankara/Turkey since 2006. All data retrospectively collected from hospital charts. Donor evaluation's first step; full blood and viral load, blood group analyses have it done. If there is not any problem all recipients have gone through surgery team, gastroenterology, pulmonary, cardiologic and psychiatric evaluation as second step. Then, all had 3D celiac CT scan for evaluation of the hepatic vascular anatomy as third step. If necessary liver biopsy was performed otherwise liver transplantation committee gathered and gave the final decision about both donor and recipient. We perform intraoperative cholangiography for all donors to evaluate biliar tree during the surgery. In all cases we used xiphoid extended either left or right subcostal incision for donor hepatectomy.

Results: There were 13 female, 9 male as donor. Donors' origin was 12 parents, 4 siblings, 2 spouses, 1 aunt, 1nephiew and 2 others. Mean age of the donor was 32 ±7,5 years (between 23-48 years). Mean BMI of the donor was 27,2± 1,9 (median 27). Eleven out of 22 right hepatectomy, 8 out of 22 left and 2 left-lateral hepatectomy was performed. The mean remnant liver left at the donor liver percentage for right hepatectomy was 33,8±4 (median 35) and median graft-to-recipient body weight ratio of the right lobe was 1,7% (between 0,9-1,5%). The mean intraoperative blood transfusion was 1,3 ±1,4 U (0-6 U ES). Donors' average hospital stay 9±3 days (6-17 days, median 9 days) found. We have not seen any late surgical complications. Only 1 early surgical complications (bleeding, 4,7%) in grade III Clavien system detected in the study group. Patient re-explored and was found that blood was coming from left gastric artery stump. Stump succesfully repaired again without any problem. This patient discharged at D7 after surgery. We have not seen any vascular complication at the post-hepatectomy period.

Conclusions: Donor hepatectomy for living liver transplantation is a safe procedure. We believe that, donor

safety should be the first priority of all living liver donor programs and it is efficient way of treatment method whom are at the waiting list.

P47
Hepatic Diseases in Pediatric Renal Transplant Recipients

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Introduction: Hepatic dysfunction may occurs common in kidney transplant recipients. We aimed to evaluate associated risk factors that affects liver functions in children who underwent kidney transplantation.

Materials and Methods: Eighty-nine renal transplant recipients (F/M:44/45) aged 3-20 years (median: 13) were enrolled the study. Patients with hepatic disfunctions after the first month of the renal transplantation were evaluated retrospectively. Information about age at transplantation, number of transplant, graft survival, deceased or living donor transplant, immunosuppressive drugs, and causes of renal failure, systemic diseases were recorded. Serum electrolytes, kreatinin, AST, ALT, GGT, protombin time, PTT, INR levels and viral markers (hepatitis A, B, C, EBV, CMV, parvovirus) were evaluated. Abnormalities of liver function tests were recorded

Results: Abnormal liver function tests were detected in 38patients (%42.6) . Eighteen of these patients were female and 20 were male. Median age was found as 11 (3-17). Four of these patients had chronic liver disease secondary to hepatic fibrosis, one patient had cystinosis, two patients had glycogen storage disease. When viral markers were evaluated, one patient had positive HBsAg after the transplantation. That patient underwent liver and kidney transplantation because of oxalosis. One patient admitted to hospital because of weakness and vomiting after the fourth year of transplantation and AntiHBcIgM was found positive. Thirty three of 38 patients had positive AntiHBs and 5 had negative AntiHBs. These patients were not able to generate antibodies despite being vaccinated. There was no positive AntiHAV IgM and AntiHCV result. Seven patients had positive EBV-PCR and 4 of them had positive EBV IgM. Eight patients had positive CMV-PCR and 5 of them had positive CMV IgM. Parvovirus hepatitis was detected 2 of the patients during the follow up. Seven patients had drug related hepatic toxicity.

Conclusions: Consequently hepatic dysfunctions in patients who underwent kidney transplantation is a common situation. We found that the causes of the hepatic dysfunctions in these patients are associated with viral infections and drug toxicity. Thus viral markers should be assessed frequently and regularly and these patients need close follow up.

P48
Chylous Ascites After Living Donor Liver Transplantation, Effectively Treated With Octreotide in a Child

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Introduction: Chylous ascites is a rare complication after liver transplantation.We reported a patient with chylous ascites due to liver transplantation and management of this rare complication.

Materials and Methods: Eleven months old girl underwent living related liver transplantation for biliary atresia. Ascites was observed after initiating of enteral feeding on postoperatively seventh day. Biochemical analysis of the fluid was compatible with chylous ascites.Besides diuretics and octreotide (60-100 mcg/hour IV infusion rate) therapy, total parenteral nutrition was initiated. Octerotide infusion replaced by subcutane injection in dose 2x100 mcg because of hyperglycemia on the 3rd day of therapy. After three weeks, chylous ascites resolved and enteral feeding was begun. Ultrasonography revealed minimal fluid in abdomen and she was discharged with subcutaneous octreotide injections. She was rehospitalized with fever, pneumonia and abdominal distention after one week . Percutaneus drainage revealed milky ascitic fluid. The chylous fluid disappeared within two weeks under total parenteral nutrition and fasting,combined with octreotide theraphy. Ascitic fluid did not recur during

following period with enteral feeding. Octerotide was ceased after two weeks. She is following without any complaints for the last six months.

Conclusions: Chylous ascites after liver transplantation can be effectively managed by fasting, total parenteral nutrition and octreotide .

P49

Immune Trombocytopenic Purpura in a Liver Transplant Patient

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Introduction: Thrombocytopenia is common in liver transplant patients especially in early posttransplantation period. The aim of this report is, idiopathic immune thrombocytopenic purpura as a reason of late onset thrombocytopenia should be kept in mind in liver transplant patients.

Case Report: Ten years-old boy, diagnosed as progressive familial intrahepatic cholestasis underwent living related liver transplantation on January 2010. Three and half years post transplantation , he presented with multiple cutaneous ecchymosis on his legs and arms. He was receiving only tacrolimus in the last two years. His platelet count was 2700 cells/ml and direct coombs was positive. Bone marrow aspiration showed increased megakaryocytes. Idiopathic immune thrombocytopenic purpura was considered as a diagnose. The patient was treated with three dose intravenous immunoglobuline and platelets improved 2700 to 144700. His serum CMV, EBV and parvovirus B19 DNAs were negative. Tacrolimus serum level was kept in 6-7 ng/ml. His platelet count has been stable for last one month.

Conclusions: Immunoglobulin infusion is effective therapy in liver transplant patients with idiopathic immune thrombocytopenic purpura.

P50

Development of Anaphylaxis To Cow's Milk As Early As The First Week of Orthotopic Liver Transplantation

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Introduction: Food allergy is not a rare condition in post-transplant children. This report is the earliest transplant acquired food allergy case who developed anaphylaxis to cow's milk under tacrolimus and steroid therapy.

Case Report: Nine month-old girl underwent living related liver transplantation for biliary atresia. Before transplantation she was breasfed and fed with minimal complementary nutrients. After transplantation she had been received total parenteral nutrition for a week. On seventh day posttransplantation, she was fed with cow's milk based formula. Ten minutes after feeding, stridor and flushing developed under tacrolimus and steroid treatments. She was treated with intramuscular adrenaline. Scin prick test and spesific Ig E level suggested cow's milk allergy. Cow's milk and dairy products were eliminated from mother's and patient's diet and hydrolized Formula was recommended. At the age 28 month she developed tolerance to cow's milk.

Conclusions: Medical staffs and families should be aware about development of food allergies in the early post-transplant period, despite the high dose immunsupressive therapy.

P51
Organ Discard In Shiraz Transplant Center

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Introduction: One of the challenges in organ retrieval is the organ which is harvested but is not suitable for transplantation. This can impose additional costs and waste the valuable time of transplant team. The aim of this study is to estimate the frequency of unused livers and the reasons for organ discard.

Materials and Methods: Between May 2010 and January 2013, a total of 605 livers were retrieved from deceased donors in our country. These organs were harvested by trained surgeons and transported to our hospital by plane or car. Core needle biopsy of the organs was done and decision to use or reject the grafts was done by the senior transplant surgeon according to pathology report, ischemic time, recipient condition, and graft appearance.

Results: Among 605 grafts, 75 (12.4%) livers were unsuitable for transplantation. The most common underlying causes of brain death were as follows: cerebrovascular accidents in 43, cardiac events in 12 and trauma in 15 cases. Male to female ratio was 40/35 and mean age of the patients was 51±12 (range 16 to 67). The cause of organ rejection were severe steatosis (>40%), necrosis and severe fibrosis in 61 (81.3%), 8 (10.7%) and 6 (8%) cases, respectively.

Conclusions: Old age, cerebrovascular accidents, and severe steatosis were among the most common reasons for organ discard in this study.

P52
Five-Year Experience With Liver Transplantation in Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma is one of the few indications for liver transplantation in malignancies. There are different policies for liver transplantation of patients with hepatocellular carcinoma in different centers, but the most accepted criteria is Milan criteria. This study is designed to present our experience in liver transplantation of patients with hepatocellular carcinoma.

Materials and Methods: Between 2008 and 2013, a total of 90 patients including 73 males and 17 females with hepatocellular carcinoma underwent liver transplantation. All the patients had cirrhotic livers and child class B or C who were not candidate for liver resection. 83 patients received whole organ while 7 cases underwent living related liver transplantation. The hepatectomy technique was piggy-back in 39 patients and standard in 51 patients.The underlying cause of cirrhosis was HBV, HCV and cryptogenic in 50 (55%), 8 (9%), and 17(18%) patients, respectively. All the patients were followed for tumor recurrence with intermittent serum αFP measurement and abdominal sonography. The follow-up period was 2-60 months (26 ± 22).

Results: Outcome analysis showed that among 90 patients with HCC, 13 cases (14.4%) expired during the follow-up period in whom 3 cases died during hospital admission. Eight patients (9%) showed tumor recurrence

Conclusions: Hepatocellular carcinoma is one of the common indications for liver transplantation in our center. The initial results show considerable survival benefits in the affected patients.

P53
Split Liver Transplantation: Our Experience in Shiraz Organ Transplant Center

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Introduction: Orthotopic liver transplantation (OLT) is becoming the only treatment modality for patients with end-stage liver diseases. Because of the limited organ pool, other ways like splitting of the donated liver should be keep 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 increased incidence of waiting list mortality in this group. 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.

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

Results: One year survival of the recipients was 92%, and 5 year survival was 72%. Pediatric patient survival and graft survival after 1 and 5 years were91% and 72% and 85% and 75%, respectively. Adult patient survival and graft survival after 1 and 5 years were 92% and 71% and88% and 77%, respectively.The most common cause of liver cirrhosis were cryptogenic, biliary atresia, and autoimmune hepatitis.

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

P54
Multivisceral Transplantation

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Introduction: Multivisceral transplantations were initially done in animal models to understand the immunological effects and then in human beings as salvage procedure for unresectable complex abdominal malignancies. With advancement in surgical techniques, availability of better immunosuppressive drugs and development of better postoperative management protocols, outcomes have been improved after these complex surgical procedures. The aim of this study is to analyze and report results of multivisceral, modified multivisceral and small bowel transplantations done at our center.

Materials and Methods: In this study medical records of all patients of multivisceral, modified multivisceral and small bowel transplants were retrospectively analyzed.

Results: Most common indications in our series were unresectable carcinoma of pancreas followed by short bowel syndrome. Ten patients are alive with a median follow up of 8.7±7.5 months (range, 3-32 months). Eight patients (out of 18 cases) in our series died in post operative course. The most common cause of post transplantation death was septicemia.

Conclusions: Multivisceral and small bowel transplants are promising treatments for complex abdominal pathologies.