Journal of Experimental and Clinical Medicine
http://dergipark.ulakbim.gov.tr/omujecm

Clinical Research

J. Exp. Clin. Med., 2015; 32(2): 55-57
doi: 10.5835/jecm.omu.32.02.002

Experience of liver transplantation in Uludag University: Preliminary results

Talat Ayyildiz[a*], Murat Kiyici[b], Tanju Basarir Ozkan[c], Gurkan Turker[d], Naile Bolca Topal[e], Remzi İscimen[d], Nalan Yildirim[e], Ekrem Kaya[f]

[a] *Department of Gastroenterology, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey*
[b] *Department of Gastroenterology, Faculty of Medicine, Uludag University, Bursa, Turkey*
[c] *Department of Pediatric Gastroenterology, Faculty of Medicine, Uludag University, Bursa, Turkey*
[d] *Department of Anesthesiology, Faculty of Medicine, Uludag University, Bursa, Turkey*
[e] *Department of Radiology, Faculty of Medicine, Uludag University, Bursa, Turkey*
[f] *Department of General Surgery, Faculty of Medicine, Uludag University, Bursa, Turkey*

ARTICLE INFO

Article History
Received 09 / 03 / 2014
Accepted 03 / 08 / 2014

*** Correspondence to:**
Talat Ayyildiz
Department of Gastroenterology,
Faculty of Medicine,
Ondokuz Mayis University,
Samsun, Turkey
e-mail: talatayy@gmail.com

Keywords:
Hepatitis B
Liver cirrhosis
Portal biliopathy
Transplantation

ABSTRACT

Liver transplantation (LT) is a viable treatment option for end-stage hepatic failure. Uludag University Liver Transplant Center has begun performing liver transplant operations in December 2007 and in this article, we review outcomes of 34 cases of LT performed until August 2010 including 30 cadaveric livers and 4 living donors. We achieved a 24-month survival rate of 84.2% in our center and LT surgeries continue with an acceptable success rate.

*This study is presented as a poster submission in Türkiye Organ Nakli Kuruluşları Koordinasyon Derneği VII. Kongresi, S17, 13, 14-17 Ekim, Eskişehir, 2010.

1. Introduction

Liver transplantation (LT) is the leading, life-saving treatment option for end-stage liver disease. Development of novel immunosuppressive drugs, improvements in postoperative intensive care services, selection of suitable patients and advances in surgical techniques as well as strategies for prevention of infections have led to increased survival rates after LT, allowing many centers to embark on LT (Agopian et al., 2013).

Turkey has a long history of LT. We aimed to share morbidity, mortality and survival results of 34 liver transplant surgeries undertaken by the Uludag University Liver Transplant Center (UULTC) team from December 2007 to August 2010.

2. Materials and methods

Data on the etiology, demographics, mortality and complications recorded for liver transplant surgeries which were performed at UULTC between the aforementioned dates for end-stage liver disease were reviewed retrospectively. Additionally, survival at 1, 3, 6, 12 and 24 months were analyzed. Kaplan-Meier statistical method was used to estimate life expectancy of patients.

Piggy-back technique was used as the surgical technique. Hepatitis B Virus (HBV)-specific immunoglobulin was used for patients with hepatic cirrhosis related to chronic HBV infection at a dose of 10.000 IU during the anhepatic phase followed by 200 IU daily for one week; there after,

2000 IU Hepatitis B immunoglobulin (HBIG) combined with lamivudine or alternative antivirals (for cases who were resistant to lamivudine) were given as maintenance therapy with anti-HBs antibody titers measured monthly to ensure a titer of 100 IU/L. A tacrolimus-based regimen was used as immunosuppressive therapy.

3. Results

Throughout the aforementioned period, 34 patients including 31 adults and three children had liver transplants.

Thirty patients received cadaveric liver transplants and four patients received liver transplants from living donors. Median age of the patients was 47.0 years (2-65 years) of whom 70% were male and 30% were female. ABO blood type of the donor and recipient was identical in 30 patients and compatible in four patients. Human leukocyte antigen typing was not conducted as a routine test. Etiologies are shown in Table 1 along with the number and characteristics of the patients.

Table 1. Etiology of the Liver Disease

Etiology	Number of the patients	n (%)
Chronic HBV infection	12	35.2
Chronic HBV + Hepatocellular carcinoma	2	5.8
Chronic HCV + Hepatocellular carcinoma	1	2.9
Criptogenic liver cirrhosis	6	17.6
Chronic alcoholism	3	8.8
Autoimmune hepatitis	2	5.8
Wilson's Disease	3	8.8
Acute liver failure	2	5.8
Portal hypertensive biliopathy	1	2.9
Hepatoblastoma	1	2.9
Glycogen storage disease	1	2.9

Patients with liver cirrhosis associated with chronic HBV infection and cryptogenic liver cirrhosis represented most of the cases. Mean duration of cold ischemia was 8.8±0.8 hours. The Model for End-Stage Liver Disease and Pediatric End-Stage Liver Disease scores of patients were 20.5±1 and 18.3±3, respectively. Bile ducts were reconstructed using choledochocholedochostomy for 31 patients and Roux-en–Y hepaticojejunostomy for three patients. Perioperative mortality rate and overall mortality rate were 11.7% and 14.7% (n=5) respectively and causes of death included multi-system organ failure (MSOF) in two patients, portal venous thrombosis in one patient, catheter sepsis in one patient and acute rejection in one patient. A total of 28 comorbidities (both major and minor) developed in 18 patients (52%) (Table 2). Survival rates at 1, 3, 6, 12 and 24 months were 91.2%, 88.2%, 88.2%, 84.2% and 84.2% (Confidence interval: 7.308 (4.4-9.7), respectively.

4. Discussion

As known, the first successful human liver transplant was performed in 1967 by a surgical team led by Dr. Thomas Starzl (Starzl et al., 1968). Obviously, LT is the major treatment option for end-stage liver disease and fulminant hepatic failure. The number and success of liver transplants have increased owing to introduction of novel immunosuppressive agents in particular and subsequent

Table 2. Minor and major morbidities in recipients

Morbidity		Number (n)	n (%)
Biliary	Bile leakage	4	14.2
	Cholangitis	1	3.5
Vascular	Hepatic artery thrombosis	1	3.5
Drug toxicity	Cytopenia	5	17.8
Pneumonia		5	17.8
Intra-abdominal abscess		3	10.7
Diabetes mellitus		3	10.7
Intra-cerebral hemorrhage		1	3.5
Deep vein thrombosis		1	3.5
CMV infection		2	7.1
Intra-abdominal hemorrhage		2	7.1

discovery of antiviral therapies for patients with underlying HBV infection. In Turkey where patients with HBV-related hepatic failure account for the majority of individuals awaiting transplantation, liver transplants are performed successfully in many centers. The first cadaveric LT was performed in 1988 (Haberal et al., 1992a) and the first living donor liver transplant was reported in 1990 in Turkey (Haberal et al., 1992b). Our transplantation center has started performing liver transplants in 2007 and since then, surgical operations were carried out mostly with cadaveric livers in patients with different etiologies. The most common indications included liver cirrhosis in the setting of chronic HBV infection and cryptogenic liver cirrhosis. A remarkable achievement of our center was a successful liver transplantation which was performed in a patient with portal hypertensive biliopathy. Our search in English-language literature revealed that this was the second case of liver transplantation with a successful outcome among patients with portal hypertensive biliopathy (Filipponi et al., 2004; Oo et al., 2009).

Hepatitis B-related cirrhosis is the most common cause of liver transplantation in Asia (Iloeje et al., 2006). Following the recent introduction of HBIG and nucleoside analogues, five-year survival rates exceeding 75% have been achieved in individuals receiving liver transplants due to hepatitis B-related cirrhosis (Kim et al., 2004). Hepatic artery thrombosis (HAT) is the major vascular complication after liver transplantation and HAT rates of 1.5% to 25% were reported in different series (Vivarelli et al., 2004).

Unal et al. (2013) reported an incidence of 6.8% for complicating hepatic artery thrombosis and 25.8% for biliary leakage after 278 living donor liver transplantations. They have shown that hepatic artery thrombosis is still a major concern in terms of morbidity, graft failure and mortality. In our center, liver transplantations from living donors are performed infrequently. We might possibly expect to see an increase in the rate of complications with increased liver transplantations from living donors.

Bile leak after LT has been reported with incidences varying from 2% to 25%. It occurs more frequently in the pediatric population and liver transplantations from living donors (Moreno and Berenguer, 2006). In our series, bile leak incidence was 14.2%.

Hepatocellular carcinoma (HCC) in the setting of chronic HBV or hepatitis C virus (HCV) infection is the third leading cause of cancer-related deaths worldwide and it is associated with a very short survival time (4-8 months) after

the initial diagnosis due to late-onset of symptoms (Lai et al., 2001). Karakayali et al. (2008) performed orthotopic liver transplantation (OLT) in 99 HCC patients and reported fatal outcome in two patients, tumor recurrence in four patients, hepatic artery thrombosis in two patients and biliary leakage in one patient over a follow-up period of 24.3±12.5 months. Patient- and disease-free survival rates were 93.5% and 90%, respectively.

Earlier detection of patients with HCC by advanced laboratory and radiological methods would provide the opportunity to utilize other treatment modalities including liver transplantation. In this context, we might expect to see an increase in the number of liver transplants for HCC in the coming years worldwide and also in our center. The mortality and morbidity associated with liver transplantation are considerable.

Infectious complications associated with lifelong immunosuppression after transplantation account for significant morbidity. Infections may result from agents preexisting in the transplanted organ, blood transfusions, bacteria found in the environment of recipients or activation of latent viruses. Also, long-term intubation and comorbid conditions such as renal failure or diabetes mellitus increase the risk of perioperative infections. Bacterial agents including Pseudomonas and Klebsiella spp. are isolated frequently in such cases (Pomposelli et al., 2014). Pneumonia, intra-abdominal abscess and cytomegalovirus (CMV) infections occurred in our study patients.

CMV infection leads to shortened survival due to its unfavorable effects including the likelihood of predisposing patients to acute and chronic allograft rejection, accelerated course of hepatitis C recurrence and increased occurrence of other opportunistic infections (Bruminhent and Razonable, 2014). Thus, CMV infection which was also observed in our patients, appears to be a factor that should always be kept in mind.

Immunosuppressive drugs may be associated with cytopenic effects similar to those seen in our patients. Obviously, close monitoring for drug levels and interactions with other drugs is of paramount importance.

Taking into account the duration of our follow-up period, liver transplants performed in our center and their outcomes were consistent with those reported by experienced centers (Jain et al., 2000) and this is encouraging for us to achieve continued successful transplant results.

REFERENCES

Agopian, V.G., Petrowsky, H., Kaldas, F.M., Zarrinpar, A., Farmer, D.G., Yersiz, H., Holt, C., Harlander-Locke, M., Hong, J.C., Rana, A.R., Venick, R., McDiarmid, S.V., Goldstein, L.I., Durazo, F., Saab, S., Han, S., Xia, V., Hiatt, J.R., Busuttil, R.W., 2013. The evolution of liver transplantation during 3 decades: Analysis of 5347 consecutive liver transplants at a single center. Ann Surg. 258, 409-421. doi: 10.1097/SLA.0b013e3182a15db4.

Bruminhent, J., Razonable, R.R., 2014. Management of cytomegalovirus infection and disease in liver transplant recipients. World J. Hepatol. 6, 370-383. doi:10.4254/wjh.v6.i6.370.

Filipponi, F., Urbani, L., Catalano, G., Iaria, G., Biancofiore, G., Cioni, R., Campatelli, A., Mosca, F., Campani, D., Romagnoli, P., 2004. Portal biliopathy treated by liver transplantation. Transplantation. 77, 326-327.

Haberal, M., Tokyay, R., Telatar, H., Buyukpamukcu, N., Simsek, H., Kayhan, B., Arslan, G., Bilgin, N., Ekici, E., Uzunalimoglu, B.l., 1992a. Living related and cadaver donor liver transplantation. Transplant. Proc. 24, 1967.

Haberal, M., Buyukpamukcu, N., Telatar, H., Bilgin, N., Arslan, G., Simsek, H., Ekici, E., Karamehmetoglu, M., 1992b. Segmental living liver transplantation in children and adults. Transplant. Proc. 24, 2687.

Iloeje, U.H., Yang, H.I., Su, J., Jen, C.L., You, S.L., Chen, C.J., 2006. Predicting cirrhosis risk based on the level of circulating hepatitis B viral load. Gastroenterology. 130, 678-686.

Jain, A., Reyes, J., Kashyap, R., Dodson, S.F., Demetris, A.J., Ruppert, K., Abu-Elmagd, K., Marsh, W., Madariaga, J., Mazariegos, G., Geller, D., Bonham, C.A., Gayowski, T., Cacciarelli, T., Fontes, P., Starzl, T.E., Fung, J.J., 2000. Long-term survival after liver transplantation in 4,000 consecutive patients at a single center. Ann. Surg. 232, 490-500.

Karakayali, H., Sevmis, S., Moray, G., Yilmaz, U., Ozcay, F, Savas, N.A., Arslan, G., M. Haberal, M., 2008. Liver transplantation in patients with hepatocellular carcinoma: One Center's Experience. Transplantation Proceedings. 40, 213-218. doi:10.1016/j.transproceed.2007.11.006.

Kim, W.R., Poterucha, J.J., Kremers, W.K., Ishitani, M.B., Dickson, E.R., 2004. Outcome of liver transplantation for hepatitis B in the United States. Liver Transpl. 10, 968-974.

Lai, K.M., Millan, M., Razavi, M., Keeffe, E.B., Prapong, W., Fisher, G.A., Esquivel, C.O., So, S.K., 2001. Center experience in liver transplantation for hepatocellular carcinoma associated with cirrhosis. Transplant. Proc. 33, 1490-1491.

Moreno, R., Berenguer, M., 2006. Post-liver transplantation medical complications. Ann. Hepatol. 5, 77-85.

Oo, Y.H., Olliff, S., Haydon, G., Thorburn, D., 2009. Symptomatic portal biliopathy: A single centre experience from the UK. Eur. J. Gastroenterol. Hepatol. 21, 206-213. doi: 10.1097/MEG.0b013e3283060ee8.

Pomposelli, J.J., Simpson, M.A., Simon, C.J., Pomfret, E.A., 2014. Liver transplantation. In from transplantation. Forsythe J.L.R., eds. Elsevier limited, Edinburgh, pp. 127-148.

Starzl, T.E., Groth, C.G., Brettschneider, L., Moon, J.B., Fulginiti, V.A., Cotton, E.K., Porter, K.A., 1968. Extended survival in 3 cases of orthotopic homotransplantation of the human liver. Surgery. 63, 549.

Unal, B., Gonultas, F., Aydin, C., Otan, E., Kayaalp, C., Yilmaz, S., 2013. Hepatic artery thrombosis-related risk factors after living Donor Liver Transplantation: Single-Center Experience from Turkey. Transplant. Proc. 45, 974-977. doi.org/10.1016/j.transproceed.2013.02.070.

Vivarelli, M., Cucchetti, A., La Barba,G., Bellusci, R., De Vivo, A., Nardo, B., Cavallari, A., Pinna, A.D., 2004. Ischemic arterial complications after liver transplantation in the adult: Multivariate analysis of risk factors. Arch. Surg. 139, 1069-1074.