Registry of post liver transplantation patients in Maadi Armed Forces Compound Hospital

Thesis

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Abstract

Objective:

Registry of post operative liver transplantation patients at Maadi Armed Forces Compound Hospital at the period for January 2008 to June 2010 (54 recipients) as regard survival, mortality, and complications and causes of each.

We found that the strong relation between the preoperative MELD and CHILDS classification and the outcome of patients postoperative.

The most common cause of mortality in our study was hemorrhage. The most common complication in our study was renal complications.

Our recommendations are good selection for donors and recipients, perfect surgical and post operative care and good control for infection.

Key words:

Liver transplantation, Immunosuppression, Liver recipient , donor , Blood transfusion ,MELD score ,CHILDS classification.

Acknowledgment

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Finally I am so grateful and thankful to my colleagues.

Ahmed Elbakry

Dedication

To:

My Mother, Father and Soul of my Brother

Who gave me too much

And received too little

&

My Cute Wife my lovely Kid *Mohamed*

Table of contents

LIST OF ABBREVIATIONS

ACE	*Angiotensin converting enzymes*
ACR	*Acute cellular rejection*
AFP	*Alpha feto protein*
AHT	*Arterial hypertension*
AIDS	*Acquired immunodeficiency syndrome*
AIH	*Autoimmune hepatitis*
ALF	*Acute liver failure*
ALT	*Alanine amino transferase*
ASCVD	*Atherosclerotic cardiovascular disease*
AST	*Aspartate amino trasnaminase*
ATG	*Antithymocyte globulin*
BAL	*Broncho alveolar lavage*
BCS	*Budd chiari syndrome*
CMV	*Cytomegalo virus*
CNI	*Calcineurin inhibitor*
CT	*Computed tomography*
CTL	*Cytotoxic T lymphocytes*
CTP	*Child-turcotte-pugh*
CyA	*Cyclosporine A*
D	*Donor*
DCD	*Donation after cardiac*
DDLT	*Deceased donor liver transplantation*
ESLD	*End stage liver disease*
FKBP	*FK binding protein*
GFR	*Glomerular filtration rate*
GRWR	*Graft to recipient body weight ratio*

HAT	*Hepatic artery thrombosis*
HBV	*Hepatitis B virus*
HCC	*Hepatocellular carcinoma*
HCIG	*Hepatitis C immunoglobulin*
HCMV	*Human cytomegalovirus*
HCV	*Hepatitis C virus*
IE	*Immediate early*
IFN	*Interferon*
IL	*Interleukin*
IMS	*Immunosuppression*
INR	*International normalized ratio*
IVC	*Inferior vena cava*
IVIG	*Intravenous immunoglobulin*
LDLT	*Live donor liver transplantation*
LRLT	*Live related liver transplantation*
LT	*Liver transplantation*
MELD	*Model for end stage liver disease*
MMF	*Mycophenolate mofetil*
MPA	*Myocphenolic acid*
MRCP	*Magnetic resonance cholangiopancreatography*
MRI	*Magnetic resonance imaging*
NAS	*Non alcoholic steato hepatitis*
OLT	*Orthotopic liver transplantation*
PBC	*Primary biliary cirrhosis*
PCR	*Polymerase chain reaction*
PELD	*Pediatric end stage liver disease*

PSC	*Primary sclerosing cholangitis*
PTDM	*Post transplantation diabetes mellitus*
R	*Recipient*
SOT	*Solid organ transplant*
TAC	*Tacrolimus*
TNF	*Tumor necrosis factor*
UCSF	*University of California San Francisco*
UNOS	*United network for organ sharing*

Introduction

Liver transplantation is now a well-established, definitive treatment for irreversible acute and chronic end-stage liver disease. The number of liver transplants has grown exponentially for the last 2 decades, and the list of indications for transplantation has been extended. Transplantation has significantly improved survival and quality of life of the recipients *(Krasko et al., 2003).*

However the liver is an organ that actively interacts with all body systems, so that the patient who receives a liver graft faces a huge set of physiological changes. During and in the immediate postoperative period, the liver is subjected to a wide variety of potentially damaging factors, including hypotension, hypoxia, ischemia and hepatotoxic drugs; in addition, donor-related factors (hepatic steatosis, use of vasoactive drugs, hemodynamic changes), surgical-related aspects (intra- or postoperative hemorrhage, vascular or biliary complications) or immune responses (rejection) might lead to a very different outcome. In summary, the postoperative outcome of each patient varies greatly depending on the patient's preoperative state, the quality of the donated organ, and the complexity of the surgery *(Murray and Carithers, 2005).*

The complications occur both immediately post-transplantation and in the long-term. The main complications in the immediate postoperative period are related to the function of the graft (dysfunction and rejection), the surgical technique, infections (bacterial, fungal, and viral), and systemic problems (pulmonary, renal, or neurological). In the long term, the complications are typically a consequence of the prolonged immunosuppressive therapy, and include diabetes mellitus, systemic arterial hypertension, de novo neoplasia, and organ toxicities, particularly

nephrotoxicity *(Munoz, et al., 2000).*Establishing the correct diagnosis is essential for all the complications given the potential implications of different therapies on the graft function and patient outcome. The differential diagnosis is difficult though due to the similarities of clinical manifestations and laboratory abnormalities of most liver transplant complications *(Moreno and Berenguer, 2006)*.

Aim of the work

This study is a registry of post operative liver transplantation patients as regard survival, mortality, and incidence of complications in Maadi Armed Forces Compound Hospital.

Chapter 1

Indications &pre-transplantation work-up

History

Liver transplantation is now a well-established, definitive treatment for irreversible acute and chronic end-stage liver disease. The number of liver transplants has grown exponentially for the last 2 decades, and the list of indications for transplantation has been extended. Transplantation has significantly improved survival and quality of life of the recipients ***(Krasko et al., 2003)***.

The initial experiments on dog models by Welch in 1955 and Cannon in 1956 were unsuccessful; mortality was 100%. Because immunosuppression was not used, success was unlikely. By 1958, the focus of research changed to immunology, liver regeneration, and hepatotropic growth factors. Technical improvements were also made ***(Krasko et al., 2003)***.

Early in 1960, the introduction of immunosuppressants, 6-mercaptopurine and azathioprine combined with prednisone, began the era of successful organ transplantation. Dr. Thomas Starzl performed the first three human liver transplantations at the University of Colorado in 1963, but did not achieve 1-year survival until 1967. Over the next 15 years, relatively few liver transplantations were performed, and the 1-year survival rate was only 30% until the late 1970s and early 1980s when the implementation of cyclosporine-based immunosuppression led to doubling of the 1-year survival rate ***(Yu and Keeffe, 2003).***

In 1983 these improved outcomes led to the decision at a National Institutes of Health Consensus Development Conference that liver transplantation was no longer experimental and deserved broader application in clinical practice. This meeting initiated the modern era of liver transplantation and resulted in the establishment of liver

transplantation centers across the United States and around the world ***(Ahmed and Keeffe, 2007)***.

Liver transplantation then underwent a period of maturation fueled by significant advances in the surgical techniques of liver transplantation, improvements in immunosuppressive drug regimens to manage rejection, and implementation of effective strategies to prevent posttransplantation infections, all of which have led to further improvement in outcomes during the subsequent 20 years. Current 1-year patient and graft survival rates in the United States are 87.6% and 82.4%, respectively ***(UNOS, 2006).***

Liver transplantation in Egypt

The 1st trial was reported as a success of the first living-related liver transplantation in Africa. Left lateral lobe of the mother was transplanted orthotopically to her 6 year old child suffering from liver cirrhosis complicating glycogen storage disease. The operation was performed in the national liverinstitute by prof. Habib in 1991. It was the 74th LDLT in the world ***(Habib, et al., 1993).***

In 2001 the regulations made by the Egyptian medical sy*ndicate* was the initiation for witnessing LDLT programs in Egypt with the breakthrough done in Dar Al-Fouad Hospital by strating the program of LDLT (August 2001) followed by Wadi El-Neel Hospital (October 2001) and the national Liver Institute (April 2003) ***(Khalaf, et al., 2005)***.

In a report by one of the big centers in Egypt whose objective was to evaluate the outcome of donors after right lobe liver donation on 50 LDL resections performed between 2001 and 2004, there was no mortality. The overall complication rate was 68 % (34 donors).major complications included intra operative bleeding in one, biliary leak in two, and pneumonia in three donors. Minor complications included mild pleural effusion in 13donors, transient ascites in 10, mild depression in 7, intra-abdominal collections in 3, and wound infection in 1 donor.

Residual liver volume did not affect the complication rate none requried re-operation. Return to pre-donation activity occurred within 6 to 8 weeks.no liver impairment occurred during follow up ***(Esmat, et al., 2005)***.

Another study in Wadi El-Neel Hospital included 11 patients transplanted for HCC nine patients were alive, all of them being disease free during follow-up periods ranging from 6 to 30 months. Two subjects died: one of HCC recurrence at 1 year post transplantation, and another of a pulmonary embolism on day 7. AFP levels decreased to normal values in 4 cases; this confirms the efficacy of LRLT for treatment of HCC superimposed on liver cirrhosis ***(El-Meteini, et al., 2005)***.

Another study performed on liver transplant programs in Egypt until February 2004 reported that out of 73 recepients, 50 (68.5%) survived after a median follow-up period of 305 days (range 15-826 days). They reported single donor mortality. Hepatitis C virus cirrhosis, whether alone or mixed with schistosomiasis, was the main indication for LDLT ***(Khalaf, et al., 2005)***.

Indications

The list of indications of liver transplantation is as wide as the spectrum of liver diseases itself, Generally any form of end stage liver that is irreversible and curable with liver transplantation is an indication for transplantation ***(UNOS, 2007)***.

I- Acute liver failure

ALF, also called “fulminant hepatic failure,” and the more indolent variant, subfulminant hepatic failure, are characterized by the development of liver failure manifested by coagulopathy, jaundice, and encephalopathy leading to coma in the absence of chronic liver disease. ALF accounts for 5% to 6% of all liver transplantations ***(UNOS, 2006).***

Acetaminophen hepatotoxicity is the leading cause of ALF, whereas idiosyncratic drug-induced liver injury is the major cause of subfulminant hepatic failure. Patients who have ALF can recover spontaneously, but those who have subfulminant hepatic failure have 100% mortality without transplantation ***(Yu and Keeffe, 2003).***

Other causes of fulminant hepatic failure include acute hepatitis A or B, Wilson's disease, autoimmune hepatitis, herbal supplement toxicity, cardiogenic liver failure, Budd–Chiari syndrome, pregnancy related complications, diffuse liver metastases, and unknown causes ***(Khan, et al., 2006)***.

Indications for liver transplantation in patients who have ALF are based on selection criteria described by O'Grady and colleagues at King's College Hospital and by Bernuau and colleagues at Villejuif Hospital. It is recommended that patients who have ALF who fail to meet the O'Grady listing criteria still be considered for liver transplantation, because spontaneous recovery is not guaranteed. Timely referral for liver transplantation is of paramount importance, because death from sepsis and cerebral edema may occur within days of the onset of stage 3 or 4 hepatic encephalopathy ***(Murray, et al., 2005).***

Criteria of King's College, London ***(Ahmed and Keeffe, 2007)***.

Acetaminophen patients:

pH < 7.3, or INR > 6.5 and serum creatinine level > 3.4 mg/dL

Nonacetaminophen patients:

INR > 6.5 or Any three of the following variables:

1. Age < 10 or > 40 years
2. Etiology: non-A, non-B hepatitis; halothane hepatitis; idiosyncratic drug reaction