RECENT ADVANCES IN THE POSTOPERATIVE MANAGEMENT OF A LIVER TRANSPLANTED PATIENT

Essay

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By

Doaa A. Elwab Mohamed Torkie
(M.B., B.Ch.)

Under supervision of

Prof. Dr. Mohga Adel Samy
Professor of Anesthesiology,
National Cancer Institute, Cairo University

Prof. Dr. Ashraf Mounir Amin
Professor of Anesthesiology,
Faculty of Medicine, Cairo University

Dr. Dina Zakaria Mohamed
Lecturer of Anesthesiology
Faculty of Medicine, Cairo University

Faculty of Medicine
Cairo University
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Doaa Mohamed Torkie
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ABSTRACT

Indications of liver transplantation include: Hepatocellular diseases as liver cirrhosis and chronic hepatitis. Inborn errors of metabolism on Wilson's disease and alpha 1-antitrypsin deficiency. Chemically induced liver damage such as by aspirin, phenytoin and INH. Cholestatic diseases as sclerosing cholangitis and biliary cirrhosis. In addition to vascular diseases and primary tumour of the liver. Pre-operative evaluation of the recipient occur in 2 separate steps and includes careful assessment of whole body systems such as: Respiratory system by chest X-ray,arterial blood gases and pulmonary function tests. Cardiovascular system by ECG and echocardiography. Renal function and electrolyte balance. Metabolic function to exclude hypoglycemia or hypoalbuminemia. Central nervous system to exclude encephalopathy.

In addition to proper immunological and nutritional evaluation: Immediate pre-operative preparation include repetition of labs and reassessment of the patient in addition to proper coordination with the blood bank for possibility of the need for rapid infusion of large amounts of blood and its products. Intra-operatively anesthetic management is divided according to surgical steps into pre-anhepatic, anhepatic and neohepatic stages, each stage needs close monitoring and careful anesthetic management with special care of cardiovascular stability, electrolyte balance and management of coagulopathy. Post-operative care of the liver transplant recipient should be a multidisciplinary effort involving the transplant surgeon, an intinsivist, and experienced hepatologist. Daily rounds by the multidisciplinary team of physicians, nurses and supporting personnel are essential for developing a comprehensive daily and nursing care plan. This is important for avoiding and detecting postoperative complications and manage them early as possible as they can.

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INTRODUCTION

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Orthotopic liver transplantation (OLT) has become the first choice approach for the treatment of patients with end-stage liver diseases **(Starzl *et al.*, 1998)** and is the most effective treatment for many patients with acute or chronic liver failure resulting from a variety of causes.

Before transplantation, patients with advanced liver disease usually died within months to years. These patients now have the opportunity for extended survival with excellent quality of life after liver transplantation **(Belle *et al.*, 1997)**. Furthermore, the costs of liver transplants have steadily declined in recent years **(Best *et al.*, 2001)**.

However, despite great improvements in graft preservation, surgical skills, anesthetic techniques and perioperative management **(Ramos *et al.*, 2003; Porte *et al.*, 2004)**, OLT is still associated with severe bleeding and considerable transfusion requirements, which in turn greatly contribute to the perioperative morbidity and mortality **(Bontempo *et al.*, 1985).**

Despite continued advances in antiviral therapy and the medical management of chronic liver disease, liver transplantation remains the only prospect for long-term survival in patients with decompensated cirrhosis, unresectable primary hepatic malignancies, and fulminant hepatic failure in which spontaneous recovery is not anticipated.

Research into the possibility of liver transplantation (LT) started before the 1960s with the pivotal baseline work of Thomas Starzl in Chicago and Boston, where the initial LT techniques were researched in dogs. Starzl attempted the first human LT in 1963 in Denver, but a successful LT was not achieved until 1967.

In 1970, with an immunosuppressive regimen largely based on steroids and azathioprine, survival rates were dismal—approximately 15% at 1-year follow-up. LT did not become a clinical reality until the early 1980s, after the discovery of cyclosporine, which led to improvements in rejection rates.

In 1983, the US National Institutes of Health established, by consensus, that LT was to be considered out of the experimental realm and was to be clinically accepted as definitive therapy for end-stage liver disease (ESLD). Additional improvements in immuno-suppression that were instrumental in advancing the science included the discovery of monoclonal antibodies (i.e. muromonab-CD3 [OKT3]) in 1986.

The combination of improvements in rejection rates and in surgical technique led to an enormous expansion of the field during the 1980s, with expansion from 3 centers in 1982 to more than 120 centers today. In 1999, 4,500 procedures were performed, up from approximately 100 in 1982. Currently, more than 16,000 patients are on the liver waiting list, and slightly more than 6,600 liver transplants were performed in 2006 (United Network for Organ Sharing [UNOS] data as of June 19, 2007).

Finally, the development of newer immunosuppressants, such as tacrolimus and interleukin (IL)–2 receptor blockers, has paved the way for further growth in this field. All these advances have produced excellent results, with current 1-year patient survival rates of 85-90% and 5-year survival rates of 65-75%. Future advances may include the development of xenotransplantation, which was pioneered by Starzl in 1992, and the development of cloning techniques and their impact on organ availability.

Most liver transplants are performed using a whole liver from a deceased cadaveric donor. During transplantation, the donor liver is placed in the orthotopic position, hence the term *orthotopic liver transplantation*. However, because of the unique anatomical organization of the liver, donor organs can be divided and the separate parts transplanted into two recipients (split liver transplantation) **(Keeffe, 2001)**. Using this technique, a portion of the left lobe of an adult donor organ can be transplanted into a child and the remaining portion used to transplant the liver into an adult. Under ideal circumstances, a deceased donor organ also can be split and transplanted into two adult recipients. The same surgical techniques can be used to facilitate transplantation using living donors, where only a portion of the donor liver is removed for transplantation **(Malago *et al.*, 2002; Gridelli *et al.*, 2003; Renz *et al.*, 2004)**.

Living donor transplantation for children, using a portion of the left lobe, is a well-established procedure. Living donor transplantation for adults, in which the donor right lobe typically is transplanted, also is performed at many transplant centers, although donor safety remains an ongoing concern **(Trotter *et al.*, 2002; Surman, 2002)**.

Perioperative complications are typically higher with these various techniques; however, long-term patient survival seems comparable to that of deceased whole liver transplantation **(Settmacher *et al.*, 2004)**.

Liver transplantation is a complex, time-consuming operation that requires vascular reconstruction of the hepatic artery, the portal vein, and the hepatic venous drainage to the inferior vena cava. Biliary reconstruction usually is accomplished using an end-to-end anastomosis of the proximal donor bile duct to the distal recipient duct; however, in recipients with diseased ducts, the donor duct is usually anastomosed to the jejunum using a Roux-en-Y loop. A number of complications can be anticipated with liver transplantation, including perioperative and surgical complications, immunologic and infectious disorders, and a variety of medical complications. The dramatic increase in transplants over the past two decades seems to have had a favorable impact on chronic liver disease mortality in the United States. Nevertheless, many issues remain, including specific indications and contraindications to liver transplantation, the optimum timing of the operation, and the most appropriate use of scarce donor organs, the postoperative care of liver transplant recipient is one of the most exciting challenge in clinical medicine and critical care field **(Evans, 1997)**.

CHAPTER 1

INDICATIONS OF LIVER TRANSPLANTATION

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I. **Hepatocellular diseases:**
   a. Chronic Hepatitis with Cirrhosis:
      i. Chronic Viral Hepatitis:
         1. Hepatitis B: transmitted via blood or sexual contact, perinatally, or via percutaneous contamination.
         2. Hepatitis C: transmitted via blood and possibly sexual contact.
      ii. Autoimmune Hepatitis: a chronic disorder caused by a cell-mediated immune response attacking normal cells of the liver.
   b. Laennec's Cirrhosis: results from excessive ingestion of alcohol.
   c. Cryptogenic Cirrhosis: cirrhosis of indeterminate origin.

II. Inborn Errors of Metabolism:
   a. $Alpha_1$ Antitrypsin Deficiency: $alpha_1$ antitrypsin is an inhibitor of trypsin, an enzyme secreted in inactive form by the pancreas, which breaks down proteins when it is activated in the duodenum. In adults, $alpha_1$ antitrypsin deficiency can manifest itself as cirrhosis and may be associated with the development of hepatocarcinoma.
   b. Wilson's disease: Due to a genetic mutation resulting in impaired hepatic excretion of Copper; Copper accumulates in the liver causing hepatitis and cirrhosis.

c. Hemochromatosis: This is a genetic disorder resulting in altered absorption of iron form the intestine. Excess iron accumulates in the hepatocytes. If this disease goes undiagnosed and untreated, cirrhosis may result.

III. **Chemically Induced Liver Damage may be caused by:**

a. Aspirin.
b. Phenytoin (Epanutin).
c. Acetaminophen (Paracetamol).
d. Isoniazid (INH).
e. Cocaine.
f. Ketoconazole (Diflucan).
g. Carbamazepine (Tegretol).
h. Amanita Phalloides poisoning (wild mushroom ingestion).
i. Others (niacin, nitrofurantoin, vaiproate, dapsone, azathioprine, total parenteral nutrition, certain herbs, etc).

IV. **Cholestatic Diseases:**

a. Sclerosing Cholangitis: an inflammatory process involving hardening and thickening of the tissues along the lumina of the intra- and extrahepatic bile ducts.
b. Primary Biliary Cirrhosis (PBC): a chronic inflammatory process with unknown cause, resulting in fibrosis of the small intrahepatic bile ductules.
c. Secondary Biliary Cirrhosis: occurs due to chronic obstruction of extrahepatic ducts, which could include the common bile duct and its major branches. This may result from several primary causes, some of which could include gallstone, chronic pancreatitis, or primary sclerosing cholangitis.