Updates, predictors & benefits of early diagnosis & management of acute kidney injury in post liver transplant patient

Essay

Submitted for partial fulfillment of master degree in intensive care

Presented by

Mohamed Yehia Sayed Ramadan
M.B, B.ch Ain shams university

Under the supervision of

Prof. Dr. Huda Omar Mahmoud
Professor of Anesthesia & pain management
Faculty of medicine Ain shams university

DR. Khaled Mostafa Khalaf
Lecturer of Anesthesia & pain management
Faculty of medicine Ain shams university

DR. Mostafa Kamal Abdelatif
Lecturer of Anesthesia & pain management
Faculty of medicine Ain shams university

Faculty of medicine
Ain-Shams University
2015

التحديثات والدلالات الصلبة وفائدة التشخيص والعلاج المبكر للاصابة الكلوية الحادة لمرضى زرع الكبد

رســالة

مقدمة توطئة للحصول علي درجة الماجستير
في الرعاية المركزة

مقدمــة من

الطبيب/ محمد يحيي سيد رمضان

بكالوريوس الطب والجراحة جامعة عين شمس

تحت إشراف

الأستاذ الدكتور/ هدى عمر محمود

أستاذ التخدير وعلاج الألم

كلية الطب - جامعة عين شمس

الأستاذ الدكتور/ خالد مصطفى خلف

مدرس التخدير وعلاج الألم

كلية الطب - جامعة عين شمس

دكتور/ مصطفى كمال عبد اللطيف

مدرس التخدير وعلاج الألم

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس
٢٠١٥

List of Contents

List of Table

INTRODUCTION

Liver transplantation, whether living donor (LDLT) or deceased donor (DDLT), is currently the treatment of choice for patients with advanced liver disease. While initially the focus was on acceptable short-term survival, currently the efforts are aimed at improving long term prognosis. Thus, focus is now on the quality of life after liver transplantation, as well as prediction and management of conditions related to morbidity and mortality in long-term survivors.

Renal insufficiency, whether acute or chronic, is a common complication after OLT ,with an incidence ranging from 12 to 64%,and represents a major cause of morbidity and mortality following OLT.3 The cumulative risk of renal failure has been reported to be as high as 20% at 5 years post-transplant. It occurs more frequently in those who have hepatorenal syndrome at the time of liver transplantation.

Acute renal dysfunction has been associated with an 8-fold increase in mortality risk, prolonged intensive care unit stay and a greater risk for infectious complications. In the subgroup of patients who develop acute renal failure and survive, 80% to 90% regain some degree of renal function, whereas the rest develop permanent renal dysfunction.

Chronic renal dysfunction, not only has implications in terms of an increased demand on resources, but is also significantly associated with a higher patient mortality rate.

Also, the incidence of chronic kidney disease post-transplant varies widely, from 10 to 83 percent, most likely owing to the lack of a standard definition of post-transplantation renal disease, differences in the types of transplantation studied, and variable periods of follow-up.

About 78 percent of the transplant recipients had a rise in creatinine or more than 0.5 mg/dL from baseline, considered mild in severity. About 46 percent had a moderate creatinine increase of 1.0 mg/dL or more, while 14 percent had a marked creatinine increase of 50 percent or more to above 2.0 mg/dL. “Even mild acute kidney injury defined as rise in serum creatinine of >0.5 mg/dL was associated with reduced patient and graft survival. This is a sensitive definition, which captures a large majority of liver transplant recipients, deserves attention and strategies for prevention.

However, the strictest definition of acute kidney injury is associated with the worst outcomes, including higher incidence of cardiovascular events and end-stage renal disease.

In this review, we discuss the various definitions, diagnostic tools, predictors of renal dysfunction after liver transplantation together with discussion of specific causes of renal dysfunction. This information will be useful in developing strategies for preventing the development or progression of renal dysfunction in liver transplant recipients, especially in view of the current availability of nonnephrotoxic immunosuppressive drugs.

AIM OF THE WORK

The aim of the present study is to identify the incidence, preoperative, intraoperative, and postoperative risk factors related to the development of renal dysfunction in post orthotopic liver transplantation and the impact of renal dysfunctions pre- and post- orthotopic liver transplantation on mortality.

Chapter one

ORTHOTOPIC LIVER TRANSPLANTATION

Liver transplantation is a treatment, used in appropriately selected patients, for acute and chronic liver failure due to any cause. It is not indicated if an acceptable alternative is available or if contraindications, such as some cases of malignancy, terminal conditions, or poor expected quality of outcome, are present ***(Burra et al., 2009)***.

The first liver transplant was performed in 1963; however, it was notuntil 1967 that the first successful transplant was performed by Starzl on an 18-month-old child who survived for 400 days ***(Burra et al., 2009)***.

In adults, Liver transplantation is indicated in any cause of acute and chronic liver cell failure when all other treatment modalities fail, major examples include chronic active hepatitis (HCV, HBV), primary biliary cirrhosis, primary sclerosing cholangitits, fulminanat hepatitis, autoimmune hepatits and neoplasms. Biliary atresia comprise 50% of the pediatric patients who require a liver transplant. Other disease states that progress to end-stage liver disease in pediatric patients include metabolic disorders and progressive intrahepatic cholestasis. Examples of metabolic derangements include Wilson disease, alpha1-antitrypsin deficiency, tyrosinemia, and hemochromatosis. Other metabolic disease states leading to hepatic dysfunction include Crigler-Najjar syndrome, glycogenosis, hyperoxaluria, metabolic

respiratory chain deficiencies, familial hypercholesterolemia, and methylmalonylaciduria ***(Burra et al., 2009)***.

When a patient is likely to require a liver transplant, the medical management is generally divided into pretransplant and posttransplant periods, with the posttransplant period further separated into early and late time frames ***(Burra et al., 2009)***.

➢ Anatomy of the liver:

The liver is a solid gastrointestinal organ that largely occupies the upper quadrant of the abdomen. The costal margin coincides with the lower margin and the superior surface is draped over by the diaphragm. Most of the right liver and most of the left liver is covered by the thoracic cage. The liver extends superiorly to the height of the fifth rib on the right and the sixth rib on the left. The posterior surface straddles the inferior vena cava (IVC). A wedge of liver extends to the left half of the abdomen across the epigastrium to lie above the anterior surface of the stomach and under the central and left diaphragm. The superior surface of the liver is convex and is molded to the diaphragm, whereas the inferior surface is mildly concave and extends to a sharp anterior border ***(Owen et al., 2006)***.

- **Surfaces of the liver**

The diaphragmatic surface is smooth and dome shaped where it is related to the concavity of the inferior surface of the diaphragm. Subphrenic recesses exist between diaphragm and

anterior and superior aspects of diaphragmatic surface of the liver. The hepatorenal recess is a posteriosuperior extension of the subhepatic space that is a gravity-dependant part of the peritoneal cavity in the supine position ***(Owen et al., 2006)***.

The visceral surface is covered with perioteneum except at the fossa for gallbladder and the portahepatis. The visceral surface bears multiple fissures and impressions from contact with other organs ***(Owen et al., 2006)***.

- **Ligaments of the liver**

The liver is attached to the anterior abdominal wall by the falciform ligament and, except for a small area of the liver against the diaphragm (the bare area), the liver is almost completely surrounded by visceral peritoneum. Additional folds of peritoneum connect the liver to the stomach (hypogastric ligament), the duodenum (hepatodudenal ligament), and the diaphragm (right and left triangular ligaments and anterior and posterior coronary ligaments) ***(Poge et al., 2005)***.

Important relations

Anteriorly, the liver is related to the diaphragm, right and left costal margins, right and left pleura, and lower margins of both lungs, xiphoid process and anterior abdominal wall in the subcostal angel ***(Owen et al., 2006)***.

Posteriorly, the liver is related to diaphragm, right kidney, hepatic flexure of the colon, duodenum, gallbladder,

IVC, esophagus, and fundus of the stomach ***(Owen et al., 2006)***.

- **The biliary duct and gallbladder**

  1- The common hepatic duct.

  2- The gallbladder.

  3- The cystic duct.

  4- The common bile duct ***(Owen et al., 2006)***.

- **Functional anatomy of the liver**

The functional anatomy of the liver is composed of eight segments, each of which is supplied by a single portal triad (also called a pedicle) composed of a portal vein, hepatic artery, and bile duct. These segments are further organized into four sectors that are separated by scissurae containing the three main hepatic veins. The four sectors are even further organized into the right and left liver. This system was originally described in 1957 by Woodsmith and Goldburne as well as Couinaud and defines hepatic anatomy as it is most relevant to surgery of the liver ***(Owen et al., 2006)***.

- **Blood supply of the liver**

The liver, like the lung, has a dual blood supply, a dominant venous source and a lesser arterial one. The portal vein brings 75-85% of the blood to the liver. The portal vein carries virtually all of the nutrients absorbed by the alimentary

tract (except lipids, which bypass the liver in the lymphatic system) to the sinusoids of the liver. Arterial blood from the hepatic artery accounting for only 20-25% of blood received by the liver ***(Poge et al., 2005)***.

➢ Physiology of the liver:

The liver is a large, chemically reactant pool of cells that have a high rates of metabolism, sharing substrates and energy from one metabolic system to another, and performing myriad other metabolic functions ***(Poge et al., 2005)***.

These functions are summarized in the following table:

Table (1): Functions of the liver

Principle functions of the liver
1- Bile acid metabolism.
2- Bilirubin metabolism
3- Amino acid and protein metabolism.
4- Cabohydrate metabolism.
5- Lipid and lipoprotein metabolism.
6- Hormone metabolism.
7- Vitamin metabolism.
8- Trace elements and the liver.
9- Biotransformation and detoxification function.
10- Alcohol degradation.
11- Acid-base balance

(Poge et al., 2005)

- **Physiology of the Hepatic blood flow:**

  - **Hepatic vascular system**

The liver has high blood flow and low vascular resistance. About 1050 ml of blood flows from the portal vein into the liver sinusoids each minute, and an additional 300 ml flows into the sinusoids from the hepatic artery, the total averaging about 1350 ml / min. This amounts to 27% of the resting cardiac output ***(Poge et al., 2005)***.

- **Regulation of the hepatic blood flow:**

Although the liver as a whole receives 25% of the cardiac output, regional blood flow within the organ is such that certain areas are highly prone to ischemia. The hepatic circulation is regulated by both intrinsic (regional microvascular) and extrinsic (neural and hormonal) mechanisms ***(Poge et al., 2005)***.

➢ Pharmacology:

A liver transplant will be rejected by the recipient unless immunosuppressive drugs are used. In adult liver transplant recipients receive corticosteroids plus a calcineurin inhibitor such as tacrolimus or ciclosporin plus a purine antagonist such as mycophenolate mofetil ***(Gonwa et al., 2004)***. In pediatric liver transplantation steroid-sparing protocols are becoming popular because of the numerous side effects including

diabetes, hypertension, dyslipidemia and affection of the linear body growth, in addition Pediatric patients eliminate calcineurin inhibitors faster than adults and require larger doses, up to 50% to 100% more than adult doses on a per-kilogram basis ***(Gonwa et al., 2004)***.

IMMUNOSUPPRESSION

In transplantation, the major classes of immunosuppressive drugs are: (1) glucocorticoids, (2) calcineurin inhibitors, (3) antiproliferative antimetabolic agents, and (4) biologics (antibodies). These drugs have achieved a high degree of clinical success in treating conditions such as acute immune rejection of organ transplants and severe autoimmune diseases. However, such therapies require lifelong use and nonspecifically suppress the entire immune system, exposing patients to considerably higher risks of infection and cancer. The calcineurin inhibitors and glucocorticoids are nephrotoxic and diabetogenic, respectively, thus restricting their usefulness in a variety of clinical settings ***(Gonwa et al., 2004)***.

Finally newer small molecules and antibodies have expanded the arsenal of immunosuppressives. In particular, mTOR (mammalian target of rapamycin) inhibitors (sirolimus, everolimus) and anti-CD25 (interleukin [IL]-2receptor) antibodies (basiliximab, daclizumab) target growth factor pathways, substantially limiting clonal expansion and potentially promoting tolerance ***(Gonwa et al., 2004)***.