MERITS OF INTRA-OPERATIVE PORTAL VENOUS PRESSURE MEASUREMENT IN LIVING-DONOR LIVER TRANSPLANTATION

THESIS

For Parial Fulfillment of M.D. Degree In General Surgery

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Abstract

The strong association between Small-for-size syndrome and portal

hyperperfusion in Living-donor liver transplantation has aroused the need for

prevention of graft overperfusion and portal hypertension aiming at improving

patient survival.

This can be achieved through intra-operative portal venous pressure

measurement and modulation of portal graft inflow accordingly.

The aim of this work is to illustrate the merits of intra-operative portal

venous pressure measurement in LDLT and to study the influence of portal venous

pressure and the effects of graft inflow modulation on postoperative graft function.

Key Words: Living-donor liver transplantation - portal venous pressure

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List Of Abbreviations

ALDLT	Adult living donor liver transplantation
ANA	Antinuclear antibody
APOLT	Auxiliary partial orthotopic liver transplantation
AT III	Anti thrombin III
CMV	Cytomegalovirus
CT	Computed tomography
DDLT	Deceased donor liver transplantation
DUS	Doppler ultrasonography
EBV	Epstein barr virus
ELTR	European Liver Transplant Registry
ERCP	Endoscopic Retrograde Cholangiopancreatography
ESLD	End stage liver disease
ESLV	Estimated standard liver volume
FAP	Familial amyloidotic polyneuropathy
FHF	Fulminant hepatic failure
FHVP	Free hepatic venous pressures
GIM	Graft inflow modulation
GRWR	Graft recipient weight ratio
GV	Graft volume
HAART	Highly active antiretroviral therapy
HAT	Hepatic artery thrombosis
HBO	Hyperbaric oxygen
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HE	Hepatic encephalopathy
HIV	Human immunodeficiency virus
HSPs	Heat shock proteins
HRS	Hepatorenal syndrome
HSV	Herpes simplex virus
HTK	Histidine -tryptophan-ketoglutarate
HU	High urgency
HVPG	Hepatic Venous Pressure Gradient
ICG	Indocyanine green
IMV	Inferior mesenteric vein

INR	International normalized ratio
IVC	Inferior vena cava
MELD	Model of end-stage liver disease
MRI	Magnetic resonance imaging
MHV	Middle hepatic vein
MRCP	Magentic resonance cholangiopancreatography
LDLT	Living donor liver transplantation
OLT	Orthotopic liver transplantation
PBC	Primary biliary cirrhosis
PELD	Pediatric End-Stage Liver Disease
PGE1	Prostaglandin E1
PNF	Primary non-function
PHP	Portal hyperperfusion
PSC	Primary sclerosing cholangitis
PVF	Portal venous flow
PVP	Portal venous pressure
PVT	Portal vein thrombosis
SAL	Splenic artery ligation
SBP	Spontaneous bacterial peritonitis
SFS	Small for size
SFSS	Small for size syndrome
SGS	Small grafts
SLV	Standard liver volume
TSAE	Trans-splenic artery embolization
UCSF	University of California, San Francisco
UNOS	United Network for Organ Sharing
US	Ultrasonography
WHVP	Wedged hepatic venous pressure
VEGF	Vascular endothelial growth factor

Introduction

Liver transplantation (LT) is now considered as the main therapeutic option for end stage liver disease (ESLD) (*Tanaka et al; 2005*).

The first human LT was attempted by Starzl in the united states in 1963, but a successful LT was not achieved until 1967 (*Manzarbeitia*, 2006).

Living donor liver transplantation (LDLT) is one of the innovative surgical techniques that has been developed in attempts to overcome the shortage of available cadaveric livers for transplantation. This modality now covers a wide range from newborn to advanced age (*Tanaka et al*; 2003).

In LDLT, part of the liver from a living donor is resected and transplanted into a recipient. In pediatric recipients, either left lateral segments or full left lobes usually suffice. For adults, right lobe grafts are necessary to ensure enough liver volume (*Manzarbeitia*, 2006).

Small-for size syndrome (SFSS) is a major concern in LDLT. It is a widely recognized clinical complication that may result from the transplantation of a too small functional mass of liver for a designated recipient. It is defined as "symptoms attributed to relative shortage of functional liver graft volume including parenchymal and non –parenchymal structure". Owing to the high metabolic demands of the adult recipients, it is believed that liver grafts in adult LDLT are almost always SFS grafts except those for low body weight patients (kiuchi et al; 2003).

Suggested clinical features of SFSS include massive ascites, gastro intestinal bleeding, recurrent infections, and renal dysfunction, as well as impaired liver function, enhanced cholestasis, delayed protein synthesis, and increased surgical

complications. However, these clinical features are neither specific nor inevitable in SFS grafts and have causative relationship with each other (*Tanaka et al*; 2002).

There is currently limited data on the pathogenesis of SFSS but recent studies have proved that the occurrence of this syndrome is determined, not only by reduced graft weight but also reduction of the functional graft volume. Aspects involved in the pathogenesis of SFS syndrome include graft-related factors such as functional and regenerative capacity, as well as recipient-related factors, such as over health status and severity of cirrhosis (*Felix et al*, 2005).

In cirrhotic patients, the close correlation between portal hypertension and severity of cirrhosis as assessed by liver biopsy or the Child-Pugh classification, has conceptually directed many researches to study the influence of portal venous pressure changes on graft function and survival after liver transplantation (*Patch et al; 1999*).

Portal hyperperfusion was found to be one of the most important factors aggravating the sinusoidal microcirculatory injury of the graft, thereby impairing postoperative liver regeneration, reducing the functional the graft volume and contributing to small –for size syndrome, which, consequently, exposes the recipient to high risk of postoperative graft dysfunction and, even graft loss (*Uemoto et al; 2004*).

From this stand point, clinical studies nowadays are mainly focusing on portal hyperperfusion as the basis for the "small-for-size syndrome". On the other hand, from the view point of pressure in the portal system, recent reports suggest that the essence of pathogenesis in SFS graft is not the increase of portal flow, but

the elevation of portal pressure. In other words, absence of pressure elevation even under "over perfusion" is a benign phenomenon (*Man et al*, 2003).

The strong association between the small for size syndrome and portal hyperperfusion in LDLT has aroused the need for prevention of graft overperfusion, aiming at minimizing the risk of SFSS and improving patient survival. This can be achieved through intraoperative portal venous pressure measurements and modulation of the graft inflow accordingly (*Tanaka et al*, 2003).

Several technical modifications are currently adopted for graft inflow modulation (GIM) recipients with Small-for –size grafts or elevated portal pressures. These include porto-systemic shunting operations, splenectomy, splenic artery ligation and early postoperative splenic artery embolization. This strategy can permit the use of the left lobe in adult to adult living donor transplantation (Masetti et al., 2004/Kiuchi et al., 2003).

Portosystemic shunting operations allow portosystemic decompression during the anhepatic phase and diversion of mesenteric blood from the graft during the critical period after portal vein declamping, thereby modulating the graft inflow. However, attention should be paid to the possibility of portal hypoperfusion and thrombus formation (*Kiuchi et al*, 2003/ *Troisi et al*, 2003).

Splenic artery ligation and splenectomy after graft reperfusion have also been used without a firm hemodynamic basis for graft inflow modulation. However, although splenectomy is done with an aim of portal pressure reduction, it has a potential risk of portal hypoperfusion in some cases and combined interruption of collaterals can lead to the opposite risk. Further more, it can lead to increased risk of bacterial infection. Splenic artery embolization in the early

postoperative period is another method of graft inflow modulation with good results reported (Yamamoto et al, 2002/ Takayama et al, 2002).

Intraoperative portal venous pressure measurement also has other merits e.g. diagnosis of significant portal vein stenosis by comparing pressures and distal to anastomosis, early prediction of abnormal splanchnic circulation (ASC) that is often caused by increased portal venous resistance and is often detected too late, when hepatic circulation is already irreversibly compromised (*Ardizonne et al*, 2003).

AIM OF THE WORK AND METHODS

The aim of the work is to illustrate the merits of the intra operative portal venous pressure management in living donor liver transplantation and to study the influence of portal venous pressure and the effects of the graft inflow modulation on the postoperative graft function.

Methods:

Twenty –five cases of living donor liver transplantation will be prospectively studied, the portal venous pressure of the recipient swill be measured intra operatively before and after the portal venous anastomosis, the portal inflow of the graft will be modulated if necessary , and the postoperative graft function will be followed up for 1-month period.

Evolution of Liver Transplantation

The field of liver transplantation has undergone remarkable advances in the decades. An essentially experimental procedure in the early 1980s, a liver transplant treatment of choice for patients with acute and chronic liver failure. I survival at 1 year posttransplant has increased from 30% in the early 1980s to than 85% at present (Charles et al; 2010).

¶.:محدوف

منستّق:الخط: مائل

منسّق:الخط: مائل، (العربية وغيرها) العربية مصر

> منسّق:الخط: مائل منسّق:الخط: مائل

The major reasons for this dramatic increase include refined surgical and preser techniques, better immunosuppressive protocols, more effective treatme infections, and improved care during the critical perioperative period. Howeve transplantation remains a major undertaking, with the potential for complic affecting every major organ system (Charles et al; 2010).

The history of liver transplantation began with experimental transplants perform dogs in the late 1950s. The first liver transplant attempted in humans was in 19 Thomas Starzl. The recipient was a 3-year-old boy with biliary atresia unfortunately died of hemorrhage. The first successful liver transplant was in again by Starzl. Yet, for the next 10 years, liver transplants remained esse experimental, with survival rates well below 50%. Still, advances in the s procedure and in anesthetic management continued to be made during that *Charles et al; 2010*).

:محذوف

منسّق:الخط: مائل منسّق:الخط: دون غامق، مائل، لون الخط: أسود

The major breakthrough for the field came in the early 1980s, with the introd and clinical use of the immunosuppressive agent cyclosporine. Patient start dramatically improved, and liver transplantation was soon being recognized as a

therapeutic option. Results continued to improve through the 1980s, due to on improvements in immunosuppression, critical care management, surgical tech and preservation solutions (Charles el al; 2010).

(Broering et al; 2003).

:محدوف

منستّى:الخط: مائل منستّى:الخط: مائل

منسّق:الخط: 10 نقطة، دون غامق، دون مائل، بلاً تسطير، لون الخط: تلقائي

منستّى:الخط: 12 نقطة، غامق، مائل

The number of liver transplantations performed per year rose at an exponentia both in Europe and in the American continent. Finally, this growth was limited increasing shortage of donors, leading to prolonged waiting times and high me on the waiting list. At the same time, the development of the knowledge of seg anatomy of the liver and in particular the systematic description by Co contributed very much to liver surgery. Based on this knowledge, anatomica resections, respecting the vascular perfusion of the remaining segments, coperformed. Very early it was realised that this would open the road for reduci liver transplantation, split-liver transplantation and even living donation (Br. DC et al; 2008).

منسّق:بلا تسطير **تغيير رمز** الحقل

منسّق:بلا تسطير منسّق:بلا تسطير

منسّق:الخط: دون غامق، دون مائل

In 1984, the first successful reduced-size liver transplantation of a child with 1 the liver of a deceased donor, was reported by Bismuth. In 1988, both the tea Hanover and of Paris managed to divide a liver into two grafts, allowing suc split-liver transplantation in two recipients (Bismuth et al; 1989).

لِّي:الخط: دون غامق، دون مائل، لون

٩ :محذوف

:محذوف

The practical feasibility of split-liver transplantation as well as the increased sa conventional liver surgery suddenly opened up the idea of removing part of th from a living donor to transplant it in a pediatric recipient. First cases were perf in 1989 in Australia and South America and finally a first series was produced close institutional control by Broelsch et al. in Chicago. The procedure was take in Europe (Figure 1) and further developed in Japan, where it encountered : success (Singer et al; 1990).

ق:الخط: دون غامق، دون مائل، لون

الخط: أسود

منسّق:الخط: 14 نقطة، لون الخط: أسود، خط اللغة العربية وغيرها: 14 نقطة، عدم إجراء تدقيق نحوي أو تدقيق إملائي

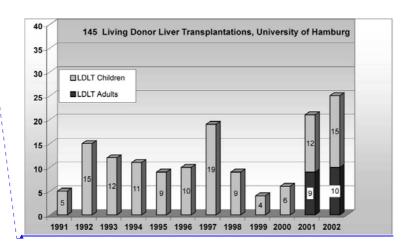


Fig. 1. Evolution of living donor liver transplantation at University of Hamburg, G (Broering et al; 2003).

منسّق:بلا، السار لليمين، مسافة قبل: 1 نقطة، بعد: 0 نقطة، تباعد الأسطر: سطر ونصف، عدم ضبط المسافة بين النص اللاتيني والآسيوي، عدم ضبط المسافة بين النص والأرقام الآسيوية، النقش: بلا تظليل

:محذوف

منستّق:الخط: دون غامق، دون مائل، لون الخط: أسود Despite initial heavy criticism in the Western world, living donation soon probe an inevitable development if one was to run a successful paediatric trar program. Indeed, in centres performing both split-liver transplantation and donor liver transplantation (LDLT), mortality of children on the waiting list almost zero (*De Govet et al: 1997*).

The success in paediatric liver transplantation and the shortage of organs provid necessary incentive to attempt living donation for adults. The emerging awarer the importance of graft volume and the suboptimal results with smaller grafts surgeons move to developing right lobe liver donation for transplanting adults (al; 1997).

منسّق:الخط: 14 نقطة، بلا تسطير، لون الخط: تلقائي