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

THESIS

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

BY


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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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| | |
|---|---|
| **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.

منسّق:يسار: 2.54 سم، يمين: 2.54 سم، العرض: 21.59 سم، الارتفاع: 27.94 سم، مسافة رأس الصفحة اعتباراً من الحافة: 1.27 سم، مسافة تذييل الصفحة اعتباراً من الحافة: 1.27 سم



# 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 transp now the 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 el al; 2010 ).***

محذوف: ¶ .

منسّق:الخط: مائل

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

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 compli affecting every major organ system ***( Charles el al; 2010 ).***

منسّق:الخط: مائل

منسّق:الخط: مائل

The history of liver transplantation began with experimental transplants perfor dogs in the late 1950s. The first liver transplant attempted in humans was in 1 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 el 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 s dramatically improved, and liver transplantation was soon being recognized as a

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

The number of liver transplantations performed per year rose at an exponenti
both in Europe and in the American continent. Finally, this growth was limited
increasing shortage of donors, leading to prolonged waiting times and high m
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, anatomic
resections, respecting the vascular perfusion of the remaining segments, co
performed. Very early it was realised that this would open the road for reduc
liver transplantation, split-liver transplantation and even living donation ***( Br
DC et al; 2008 ).***

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

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 ).***

محذوف: .

محذوف: *(*Broering *et al; 2003).*

منسّق:الخط: مائل

منسّق:الخط: مائل

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

منسّق:الخط: 12 نقطة، غامق، مائل

منسّق:بلا تسطير

**تغيير رمز** الحقل

منسّق:بلا تسطير

منسّق:بلا تسطير

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

محذوف: ¶

محذوف: .

منسّق: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

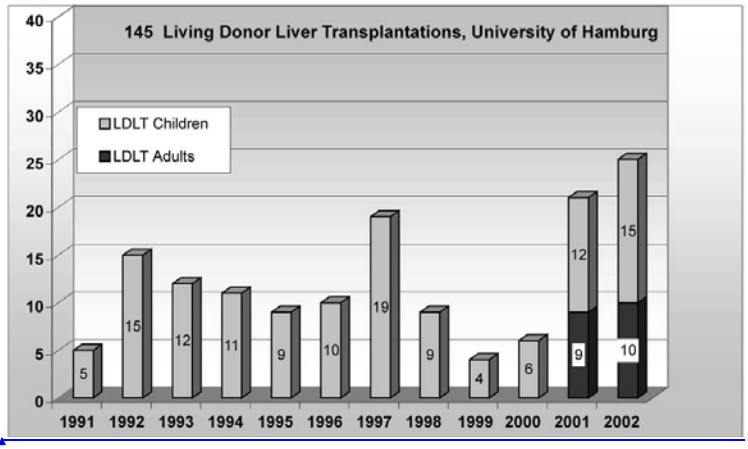


**Fig. 1**. Evolution of living donor liver transplantation at University of Hamburg, G ***(Broering et al; 2003).***

منسّق:بلا، اليسار 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

Despite initial heavy criticism in the Western world, living donation soon pro be 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 Goyet et al; 1997 ).***

**محذوف:** .

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

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