対し，肝機能が低下する前にIFN＋リバビリン療法を行えるように肝移植後に高ビリルビン血症を認めた場合，肝生検を行い早期診断に努めるべきである．

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# RAPIDLY PROGRESSED FIBROSING CHOLESTATIC HEPATITIS AFTER LIVING DONOR LIVER TRANSPLANTATION FOR HCV-RELATED CIRRHOSIS—REPORT OF A CASE—

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Liver transplantation (LTx) for liver cirrhosis caused by hepatitis C virus is increasing in recent years. The problem of LTx for cirrhosis due to hepatitis C is the reactivation of hepatitis C virus after transplantation. Approximately 50-60% of patients will develop chronic active hepatitis within one year after transplantation. In addition, 20% of those patients develop liver cirrhosis within five years. Unlike hepatitis B, recurrent hepatitis C is usually mild and is characterized by gradual progress. On the other hand, fibrosing cholestatic hepatitis (FCH), a specific histologic manifestation of hepatitis B virus infection, is characterized by periportal fibrosis, hepatocyte ballooning, cholestasis and relatively scant inflammation. FCH will rapidly progress to liver cirrhosis for a short period of time. In recent years, FCH has been increasingly reported to occur after LTx for hepatitis C cirrhosis. Herein, we report a case of FCH after living-donor LTx for hepatitis C, which led to a rapid graft loss on POD 233.

特集／肝炎から肝がんまで

肝がんの治療

# 肝　移　植

吉住朋晴*　島田光生**　副島雄二*
内山秀昭*　武冨紹信*　前原喜彦*

## はじめに

肝癌はその背景にウイルス性肝炎あるいは肝硬変があるために，治療後の再発が高率であることはよく知られた事実である。肝移植は背景の肝硬変をも含めた治療であり，理論上はこれに優る治療法はないと言える。しかし，黎明期の肝癌に対する肝移植の成績は期待に反して不良で，慢性的な臓器不足の環境下で肝癌を治療の適応とするか否かで，議論が分かれたこともある。1996年にMazzaferroらの提唱したMilan基準により[1]，肝癌患者でも症例を選べば，肝移植後の成績は向上することが示された。

本邦においては1997年臓器移植法が施行されて以来，2004年4月までの脳死肝移植数は計24例にすぎない。一方，生体肝移植施行数は年間400例以上，通算でも3,000例を越え，成人間その中でも肝癌症例に対する生体肝移植が積極的に施行されるようになった。さらに，2004年1月からMilan基準を満たす肝癌に限り，肝癌に対する生体肝移植が保険適応となり，施行症例数は今後益々増加するものと思われる。

生体肝移植では，脳死肝移植における提供肝の公平分配という原則と異なり，ドナーとレシピエントが1対1の関係でかつ親族であるため，充分なインフォームドコンセントの下では，医療費の問題はあるものの，進行肝癌症例でも移植の対象となりうる[2]。拡大された適応の中で，肝癌の移植後再発は最も憂慮すべき問題である。各施設毎に移植の適応基準を設けてはいるものの，未だ除外症例の判断基準が確立されていないのが現状である。

本稿では，最近の報告をレビューするとともに，肝癌に対する生体肝移植の位置づけについて，概説する。

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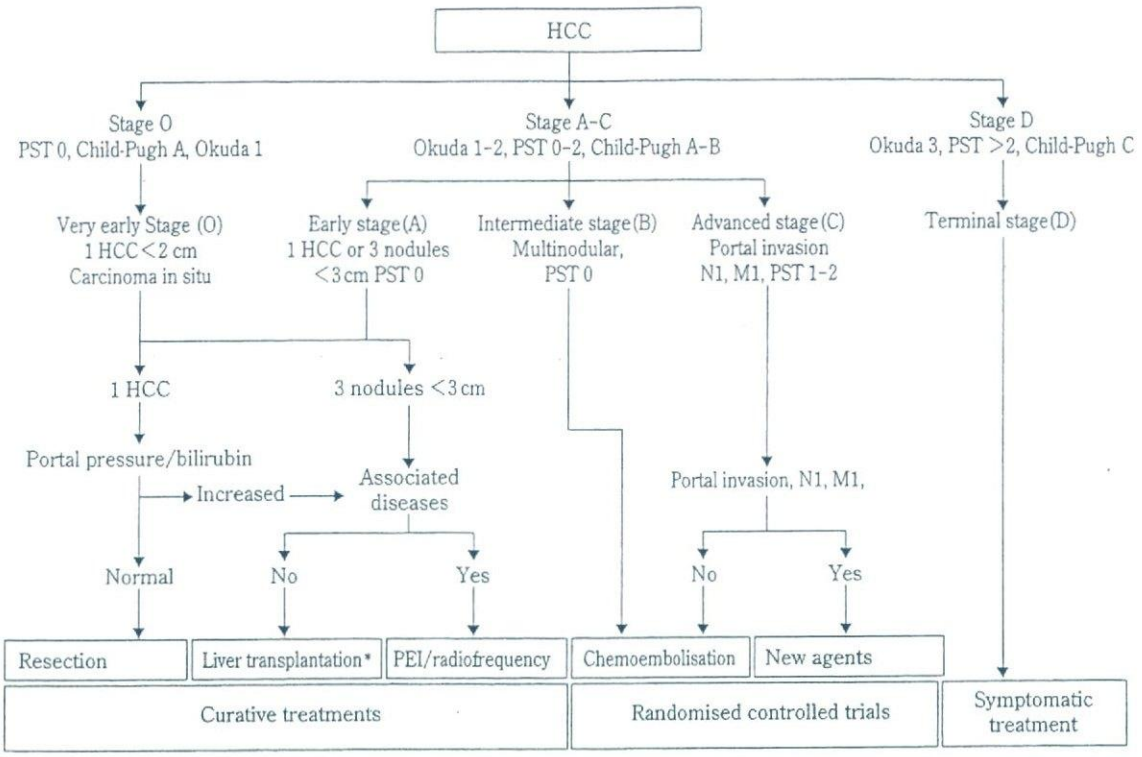
## Ⅰ．肝癌に対する肝移植：世界の現状

1988年O'Gradyらの報告によれば，肝癌症例の移植後5年生存率は30%以下[3]，以後1990年代初めまで施行された肝移植は主に進行肝癌を対象としたものであり，その成績は極めて不良であった。Mazzaferroらは前述のMilan基準（腫瘍径5cm以下の単発あるいは腫瘍径3cm以下で腫瘍数3個以下）を満たす症例に限定すると，移植後4年生存率は75%（無再発生存率83%）と，良好な成績が得られることを報告した[1]。現在のアメリカにおけるUNOSの基準でも，T2（腫瘍径2～5cmの単発あるいは腫瘍径3cm以下で腫瘍数3個以下）の肝癌には追加点を加えることでpriorityを与え，より早期に移植が受けられるシステムとなっている。2002年だけを見れば，実に23%の脳死肝グラフトがHCCの患者に移植された（2002年には腫瘍径2cm未満のT1症例にもpriorityあり）。現在のUNOSの統計では，2001年までの生存率しか得られていないため，新しいシステムでの解析結果が待たれる。

図1にBarcelonaグループのBruixらが推奨する肝癌治療のアルゴリズムを示す[4]。このアルゴリズムによると，肝癌の治療として肝機能がChild A・Bで単発3cm以下の腫瘍には肝切除を，それ以外のMilan基準合致例には肝移植を施行することで根治が得られるとしている。これまで切除可能な肝癌症例に対する肝移植と肝切除の無作為化比較試験はないが，切除可能肝癌においても肝移植が優れていることを示唆する報告が多い。待機期間が極めて重要な因子であり，Bruixらは待機期間が6ヵ月以内の場合に限り，肝移植の有用性を示唆している。また，最近同グループは待




PST：performance status test, N：nodules, M：metastases, PEI：percutaneous ethanol injection

図　1　Barcelona グループ，Bruix らの推奨する肝癌治療のアルゴリズム（Llovet JM ら[4]2003より抜粋）

機期間の drop out を可能な限り少なくするためにも，単発7 cm以下・5 cm以下3個・3 cm以下5個の腫瘍までは肝移植の適応を拡大できると提唱している[4]。

現在，最も有用とされているミラノ基準は画像診断的基準であり（腫瘍径，腫瘍数，肉眼的血管侵襲），必ずしも肝癌の biology を正確に反映しているとは言い難く，単に経験に基づいた推測（educated guesses）から行っているにすぎない。つまり，これまでの肝切除や肝移植後の最も重要な予後因子である組織学的血管侵襲がミラノ基準には反映されていない。Neuhaus らは5 cm以上の肝癌では，高分化肝癌に対し中あるいは低分化癌で血管侵襲が有意に多く，これらは予後因子となることを報告した[5]。組織学的血管侵襲は，腫瘍径5 cmまでの比較的小型の肝癌の30～50%に認められることが知られており，また，5 cm以上の肝癌でも組織学的血管侵襲が陰性であれば移植後の成績が極めて良いとの報告もある。肝癌の生検は肝移植前のルーチン検査ではなく，また needle tract 播種のリスク（1.6%）があるものの，肝移植後の1年死亡率が約10%という事実や，高悪性度の肝癌症例に移植が施行された場合の悲惨な結果を考え合わせると，肝癌の生検は術前検査として十分考慮に値する。Cillo ら Padova のグループは肝癌の分化度に注目したデータを最近報告した[6]。彼らは，腫瘍径及び腫瘍の個数は問わないものの，肝癌を疑った症例は全例で肝生検を施行し，低分化肝癌（G3）は移植の待機リストから除外した。その結果，高あるいは中分化肝癌48例中42%が組織学的 TNM stage Ⅲあるいは Ⅳ，また38%は Milan 基準逸脱例であったが，移植後5年生存率は75%，無再発生存率は92%であり，生存率は非担癌患者のそれと同等で，術前の Milan 基準逸脱例でも再発は認めなかったと報告した。同様に，Klintmalm らも腫瘍の分化度が独立した予後因子となることを報告している[7]。又，腫瘍生検により組織型のみならず，microarray による遺伝子発現など他の分子生物学的因子の評価も可能である。経験に基づく推測の時代（画像診断であるミラノ基準）に終焉を告げるためには，肝癌の biology と患者の genomics を探究し，それらを十分に利用することが特に重要である。

生体肝移植に関しては，Gondolesi らが施行した36症例中，53%が Milan 基準を逸脱する症例であったが，その成績はこれまでと遜色ないことを報告した（表1）。彼らは生体肝移植の利点を，UNOS の基準から逸脱した腫瘍径＞5 cmの症例

表 1　肝癌に対する肝移植の成績

| 筆者 | 症例数 | Milan基準逸脱例 | 生存率 | | 無再発生存率 | |
|---|---|---|---|---|---|---|
| | | | 1年 | 2年 | 1年 | 2年 |
| Mazzaferro et al. | 48 | 0 | | 75%<br>(4年) | | 83%<br>(4年) |
| Roayaie et al. | 43 | 43<br>(100%) | 90% | 66% | 82% | 59% |
| Cillo et al. | 48 | 18<br>(38%) | 94% | 79%<br>(3年) | 92% | 92%<br>(3年) |
| Gondolesi et al. | 36 | 19<br>(53%) | 75% | 60% | 82% | 74% |

でも待機期間を持たずにドナーが得られること，UNOS基準内の症例が待機期間中の腫瘍進展により移植が不可能になることを回避できること，としている[8]。

## Ⅱ．肝癌に対する肝移植：本邦での現状

本邦における肝癌に対する脳死肝移植の適応基準は，2001年からMilan基準が取り入れられたが，施行症例が年間数例に留まる現状では，待機中のドロップアウトは不可避で，実際2003年までに脳死肝移植を受け得たレシピエントは全て非担癌患者である。一方，生体肝移植においては肝移植研究会[9]及び藤堂ら[10]の報告によると，1990年10月から2002年12月までに2,164例の生体肝移植が施行され，そのうち肝癌（肝細胞癌と肝芽腫）は225例（10.4%）であった。18歳未満の小児例では1,127例中16例(1.4%)，成人例では1,037例中209例（20.2%）が肝癌症例であった。肝癌に対する移植施行症例数は，1999年より増加し始め，2001年に76例，2002年には90例となっている。粗生存率は74.2%，再発率は10.8%で，生存例中の再発は5.5%，死亡例での再発率は26.3%であった。死因は感染症が22例（38%），肝癌再発が16例（21%），その他が20例（34%）であった。再発のリスクファクターについて検討したところ，単変量解析では門脈浸潤，AFP値，術後化学療法の有無，肝静脈浸潤，腫瘍径，腫瘍の両葉への分布で差が認められ，多変量解析では，門脈浸潤，AFP値，腫瘍径，腫瘍の両葉への分布の4因子であった。これらの症例の生存率及び累積再発率は，Milan基準合致例で，逸脱例に対して有意に良好であった。Milan基準逸脱例の3年再発率は35%だったが，これも裏を返せば逸脱例でも65%では無再発生存が得られることを意味している。

京都大学は，成人肝癌68例に生体肝移植を施行し，3年生存率は56%，再発は8例に認め，うち6例が腫瘍死，75%が移植後8ヵ月以内に再発したと報告した。再発に影響を与えた因子としては，組織学的分化度・組織学的脈管浸潤・組織学的Milan基準逸脱をあげている。一方，組織学的Milan基準逸脱例でも短期間であれば70%は無再発だったこと，CLIPスコア別の3年生存率の比較では，肝移植症例において，いずれも非移植症例を上回っていたことに注目している[11]。

生体肝移植においては健常ドナーからの臓器提供が必要なため，適応基準をより厳格にすべきとの考えと，必然的に臓器提供は親族からに限定されるため，双方がリスクを十分理解した上でなら，より適応を拡大してもよいとの考えがある。現実的には，我が国のほとんどの施設での適応は，肝移植以外の治療法で腫瘍がコントロールできず，肝外転移及び主要血管への浸潤がない肝癌とされており，腫瘍径や腫瘍個数には制限を設けていない施設が多い。

図2に田中らの推奨する肝癌治療のアルゴリズムを示す[12]。Milan基準を満たすChild C症例で，肝移植が選択されている。これは，現在の本邦の肝癌に対する生体肝移植の保険適応と一致しているが，前述したBarcelonaグループはChild AあるいはBで，肝移植を推奨している。これには，脳死肝移植施行数などが関与していると考えられ，興味深い。一方，我々は田中のアルゴリズムより適応を拡大し，Child BあるいはCの症例でMilan基準を満たす症例では，肝移植を推奨している[2]。

## Ⅲ．当施設における肝癌症例に対する生体肝移植

九州大学第二外科では，2004年3月までに施行した生体肝移植142例中，肝癌症例は40例（28.2

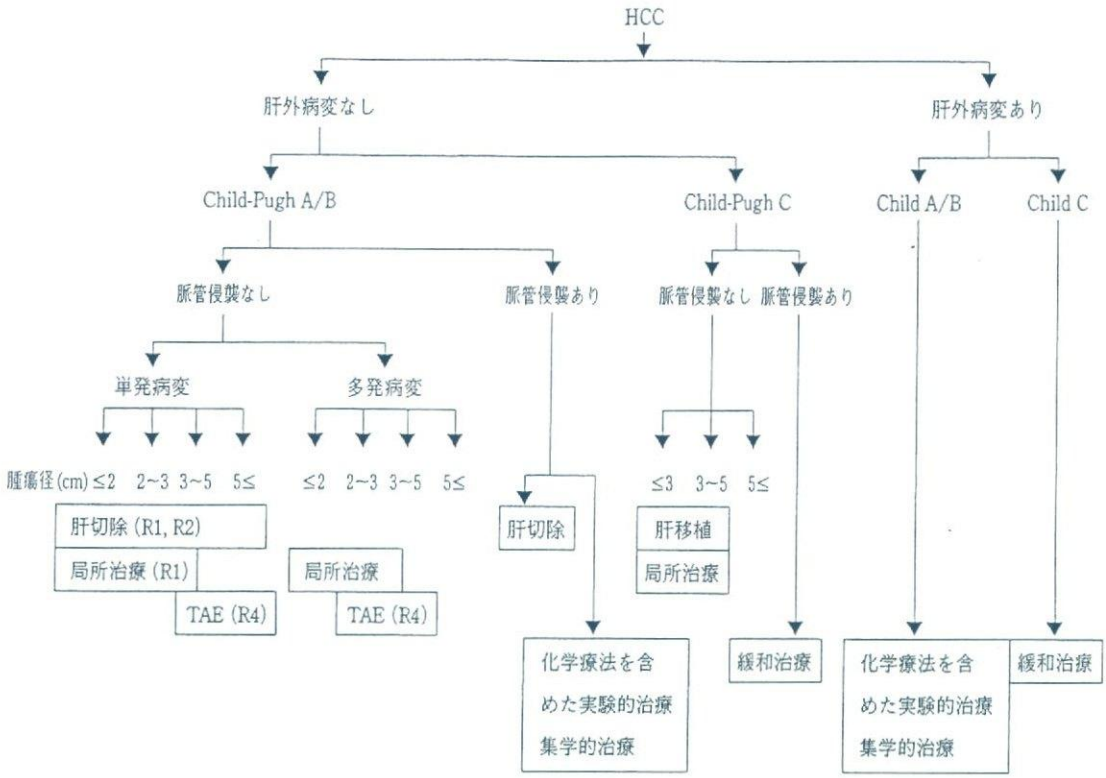
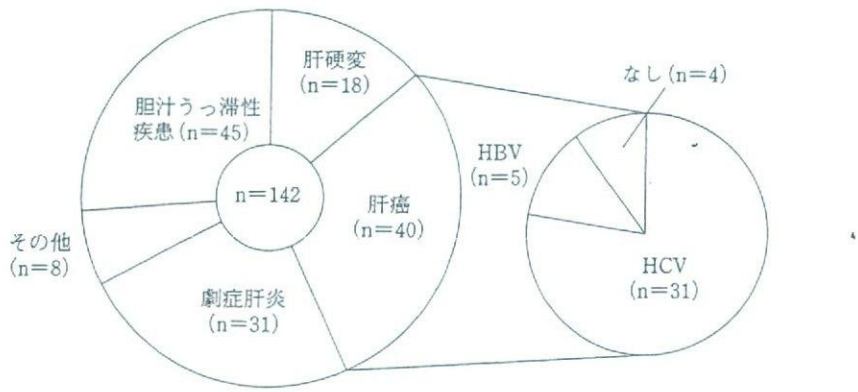


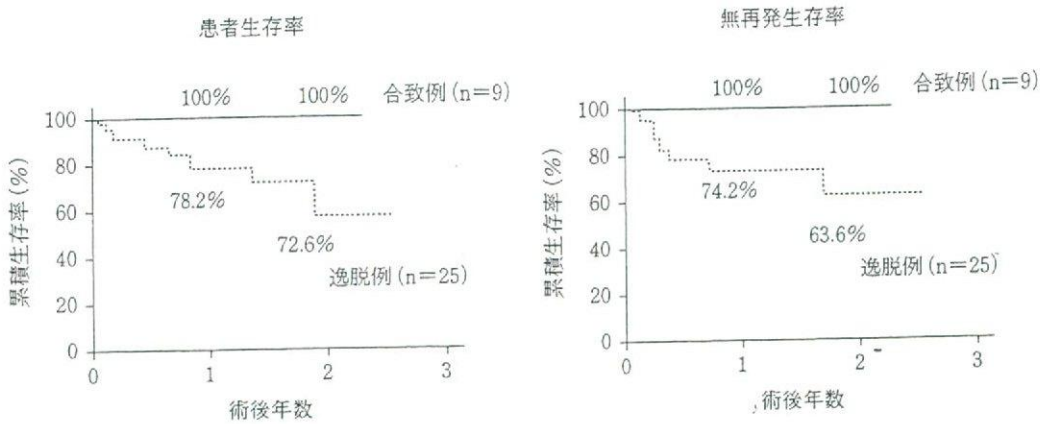

図　2　　田中らの推奨する肝癌治療のアルゴリズム（田中ら[12]2003より抜粋）




142例中で肝癌が40例を占め，最大であった。

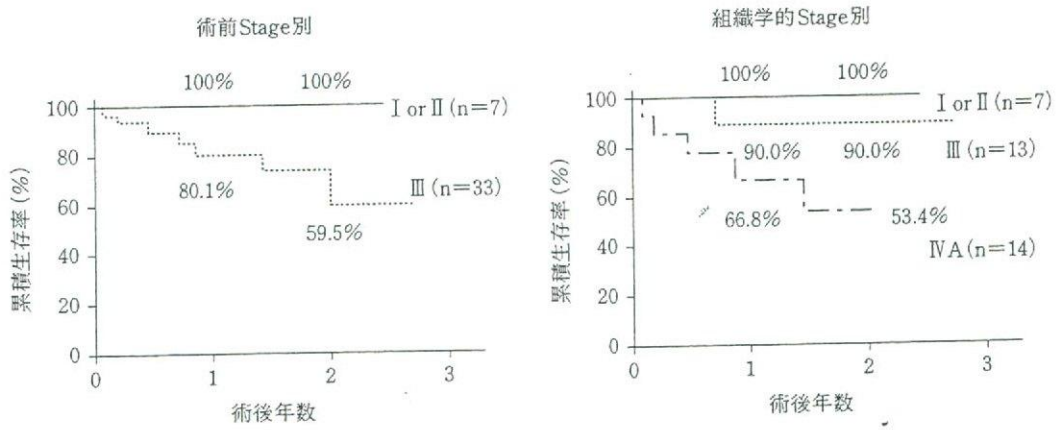
図　3　　九州大学における生体肝移植の適応疾患

%）であった。当科における肝癌への移植適応基準は，肝外病巣がなく，肝内主要血管への明らかな腫瘍の侵襲を認めず，肝臓移植以外に有効な治療法が現存しない。ただし，肝移植後の長期予後が他の治療法より明らかに上回ると予想される場合には，個々の症例につき検討し適応を判断する，としている。疾患別の内訳では，本施設の特色として肝癌が最多数で，背景にある肝硬変の原因としては，HCVが31例，HBVが5例，非B非Cが4例であった（図3）。術前Child分類ではChild Cが最多であったが，腫瘍が両葉・多発性に分布した症例などはChild Aでも適応となる場合があった。このため，癌の進行度別では，Stage Ⅲが大半を占めた。肝癌症例における1年生存率は86.2%，2年生存率は68.4%で，これは非担癌症例のそれと有意差を認めなかった。又，術後の免疫抑制剤による生存率の差は認めなかった。次に，生存率を背景因子別に詳細に検討した。組織学的検索まで終了した34例で，Milan基準合致例と逸脱例で生存率及び無再発生存率を比較したところ，




Milan 基準合致例では2年生存率100%と良好な成績であったが，逸脱例では成績が有意に悪化した。

図　4　　Milan 基準別の移植後生存率及び無再発生存率




術前 Stage Ⅰ，Ⅱ及び組織学的 Stage Ⅲまでの症例では，良好な成績が得られた。

図　5　　術前及び組織学的 Stage 別の移植後生存率

合致例では2年間でともに100%と良好な成績であったが，逸脱例では有意に生存率が悪化していた（図4）。術前 Stage Ⅰ・Ⅱ及び組織学的 Stage Ⅲ例までは，2年生存率90%以上が得られたが，組織学的 Stage ⅣA（組織学的血管浸潤例）では，生存率が有意に悪化した（図5）。

生体肝移植後の再発は7例（17.5%）に認め，うち骨転移の1例は放射線治療後，1例は腹膜播種の摘出術を施行し，生存中である。再発のリスクファクターは単変量解析にて，Milan 基準逸脱・腫瘍径5 cm以上・組織学的血管侵襲陽性・低分化肝癌・術前 PIVKA Ⅱ＞300mAU/ml であった。

以上から，組織学的 Stage Ⅲ（血管侵襲なし）までの肝癌では，移植後良好な成績が期待できるが，腫瘍径＞5 cm，術前 PIVKA Ⅱ高値例を呈する症例では，低分化あるいは組織学的血管侵襲の可能性を予想し，適応を慎重に選ぶ必要があると考えられた。

## ま　と　め

生体肝移植が主流となった本邦においては，提供肝の公平分配の必要がないため，今後も生体肝移植は肝癌に対する治療として確立されていくものと思われる。生体肝移植の脳死肝移植に対する利点として，医療側から見れば，スケジュールに沿った積極的な術前治療（systemic な化学療法及び局所療法）が可能な点があげられる。術前治療に対しては，逆に否定的な考えもあるが[8]，再発のハイリスク群が次第に明らかになってきた中，Milan 基準逸脱例や術前 PIVKA Ⅱ高値例では，治療による腫瘍の down-staging を行う必要があ

る[2)4)]。進行肝癌に対する術後のadjuvant chemotharapyの有効性も報告されており[13)]，そのレジュメ及び治療対照症例の選択法を確立することも課題となるであろう。

進行肝癌のみに話題が移りがちだが，特にB型肝炎ではHBIG・ラミブジンの使用により，背景に存在する肝炎までも，肝移植により同時に根治させることが可能となった。この場合，Child Aかつ Stage Ⅰあるいは Ⅱの肝切除も充分可能な比較的早期の肝癌症例においても，生体肝移植を患者側に提示・施行することも倫理的に許容されると考えられる。

最後に，これまでは治療不可能と考えられていた肝癌も，症例によっては肝移植により根治させることが可能となってきた。C型肝炎再発への対策など，肝移植に取り組む医療従事者が今後克服すべき課題は多いが，最も憂慮しなければならないのは，肝癌の治療法としての肝移植が，未だ多くの肝臓専門医に認知されていない現状である。Milan基準内の肝癌であれば保険適応となった追い風を，肝移植関係者は最大限利用して啓蒙活動をする必要があるだろう。

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# Alternatives to the Double Vena Cava Method in Partial Liver Transplantation

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**Minimizing graft congestion in partial liver transplantation is important, especially when the graft weight is marginal for the recipient metabolic demand. We prefer the double vena cava technique for reconstructing middle hepatic vein tributaries with thick, short hepatic veins because the technique can reduce the warm ischemic time of the graft and make a wide anastomosis. This technique requires a cryopreserved superior or inferior vena cava. We devised an alternative double vena cava method using iliac or femoral vein grafts and applied it to two right liver transplantation patients. There was no postoperative hepatic venous outflow block in either patient. In conclusion, application of this technique, even in the absence of a suitable vena cava, can help to minimize graft congestion. (*Liver Transpl 2005;11:101–103.*)**

Adequate outflow is indispensable for graft function. Hepatic vein reconstruction for adequate outflow, however, is technically demanding in partial liver transplantation because of eventual twisting or compression by the regenerated liver graft.[1] The double vena cava (VC) technique is indicated in a right liver graft if the graft includes major short hepatic veins.[2] Application of this technique, however, depends on the availability of a VC graft. Here we introduce two alternative methods to the double VC technique using venous grafts of smaller diameter.

## Patients and Methods

From January 1996 to June 2004, 221 adult patients underwent living donor liver transplantation (LDLT) using a right liver graft at our hospital. The mean follow-up period was 850 days. The indications for LDLT in these patients included hepatitis C virus cirrhosis (n=54), primary biliary cirrhosis (n=50), hepatitis B virus cirrhosis (n=38), fulminant hepatic failure (n=25), cryptogenic cirrhosis (n=17), biliary atresia (n=14), metabolic disorder (n=6), primary sclerosing cholangitis (n=9), and autoimmune hepatitis (n=8). Details regarding the selection criteria and evaluation are described elsewhere.[3,4] All donors and patients provided written informed consent.

### Homologous Vein Graft Preparation

Vein grafts were provided by the University of Tokyo Tissue Bank. The preservation and thawing methods have been previously described.[5] In brief, the vein grafts were obtained in a sterile manner from cadavers within 24 hours after cardiac arrest after obtaining informed consent. The specimens were frozen slowly in a programmable freezer at a rate of 1°C/min to -40°C and stored in liquid nitrogen until use. The cryopreservation medium consisted of Rosewell Park Memorial Institute 1640 solution (Whittaker Co., Sydney, Australia), 10% dimethylsulfoxide (Sigma, St. Louis, MO), and .5 g/L cefazolin sodium (Fujisawa, Tokyo, Japan).

For use, the packed vein grafts were placed at room temperature for 7 minutes and immersed gently in 37°C sterile saline for 30 minutes. Thereafter, the vein grafts were picked up from the bag and placed into the Alloflow (Lifenet, Virginia Beach, VA). Finally, they were rinsed with 1 liter of lactated ringer's solution (Lactec G, Ohtsuka Pharmaceutical, Tokyo, Japan).

### Right Liver Harvesting

The right liver was harvested as described previously.[4] Briefly, in a basin, the graft was flushed with 1 liter of University of Wisconsin solution through a cannula inserted into the right portal vein. When the graft included major short hepatic veins, including inferior or middle right hepatic veins in the graft, the double VC technique was applied as described previously.[6] Briefly, a cryopreserved VC graft was prepared in a basin. A side hole was made in the wall of the VC, which was anastomosed with the hepatic veins in the graft. With this technique, all hepatic vein trunks of the recipient were sutured at their roots. Then, the inferior VC of the recipient was partially clamped and incised approximately 5 cm longi-

Abbreviations: LDLT, living donor liver transplantation; VC, vena cava.

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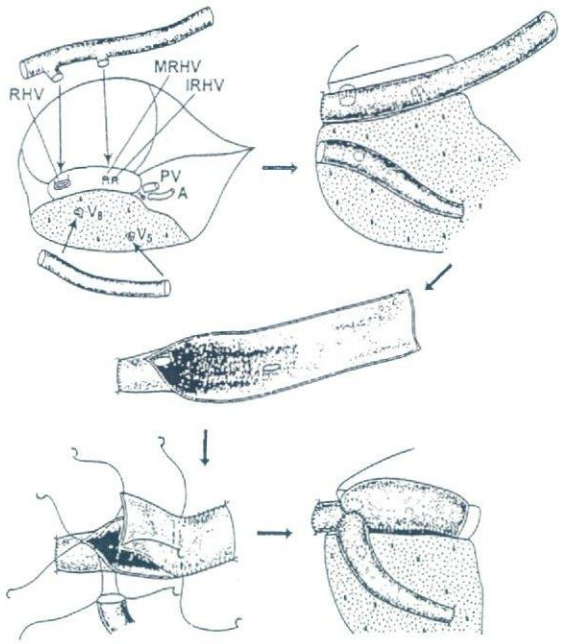


**Figure 1. A Method Using Two Iliac Veins. One iliac vein was used to reconstruct a V8 and a V5. The other vein graft was folded at its caudal end. Abbreviations: RHV, right hepatic vein; MRHV, middle right hepatic vein; IRHV, inferior right hepatic vein; V5, drainage vein from segment V; V8, drainage vein from segment VIII; PV, portal vein; A, hepatic artery.**

tudinally. The VC graft was similarly incised longitudinally, then anastomosed side-to-side with the inferior VC of the recipient. When a VC graft was not available, iliac or femoral vein grafts were used.

## Results

Of 105 right liver grafts, 35 had major short hepatic veins. Of these 35 patients, 2 received two iliac veins and two femoral veins, respectively, as an alternative to VC grafts for the double VC technique.

### Patient 1

The patient was a 61-year-old male with hepatitis C virus cirrhosis with a 2 cm diameter nodule of hepatocellular carcinoma. The right liver graft was harvested from his 56-year-old wife. The graft had a middle and inferior right hepatic vein. A VC graft was not available and two iliac veins (76 mm and 55 mm in length, respectively) were used for venous reconstruction at the bench (Figure 1).

One iliac vein was used for reconstruction of the middle hepatic vein tributaries (V5 and V8). The other iliac vein graft was used as an alternative to a VC graft. Its cranial end was closed. Two branches were anastomosed to the orifice of the right hepatic vein and orifices of the middle and inferior right hepatic veins together. The vein graft was 10 mm in diameter, which was too small for direct side-to-side anastomosis with the recipient's inferior VC. The iliac vein was incised longitudinally and the caudal side was folded. The two iliac veins were finally anastomosed side to end.

On the recipient side, all stumps of the hepatic veins were closed at their roots. The recipient inferior VC was semiclamped and incised longitudinally 5 cm in length. The folded iliac vein was incised similarly and sutured side-to-side. Cold and warm ischemic times were 140 minutes and 55 minutes, respectively. The postoperative course was uneventful. There were no vascular complications and Doppler ultrasonography 6 months after transplantation revealed well-maintained flow of all reconstructed veins.

### Patient 2

A 44-year-old man underwent LDLT for alcoholic liver cirrhosis. The donor was his 42-year-old wife. A right liver graft with middle hepatic vein trunk was indicated.[7] The weight of the graft was 454 g, which corresponded to 36% of the recipient standard liver volume,[8] leading us to perform venous reconstruction at the bench. Two cryopreserved femoral vein grafts (each 100 mm long) were available.

Five hepatic vein orifices appeared on the inferior VC sulcus of the harvested graft (Figure 2). Two fem-

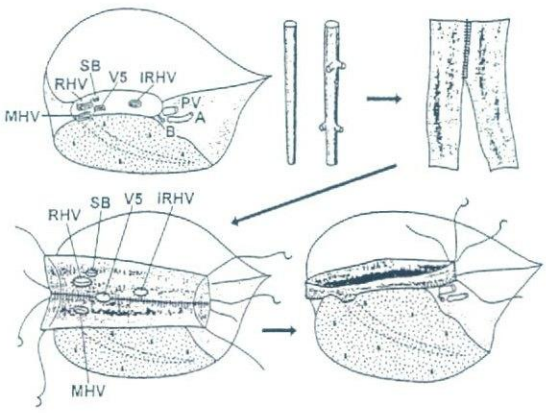


**Figure 2. A Method Using Two Femoral Veins. One large rectangular sheet was made, which was sutured to five vein orifices. Abbreviations: MHV, middle hepatic vein; RHV, right hepatic vein; SB, superficial branch; IRHV, inferior right hepatic vein; V5, drainage vein from segment V; B, bile duct; PV, portal vein; A, hepatic artery.**

oral veins were cut longitudinally and the two sheets were made into one sheet using interrupted sutures. The V5 orifice was sutured to the medial side of both sheets. Small holes were made on the sheet for anastomosis with the other four stumps of the short hepatic veins. The cranial and caudal ends of the sheet were then sutured to make a new "vena cava." On the recipient side, the inferior VC was cut longitudinally and sutured to the graft-side VC. Cold and warm ischemic times of the graft were 181 minutes and 85 minutes, respectively. Doppler ultrasonography revealed a well-maintained venous flow for 3 months after the operation. The postoperative course was uneventful except for surgical drainage of bile leakage on the fifteenth postoperative day.

## Discussion

In adult-to-adult LDLT, right liver is frequently used. When the graft weight is marginal for recipient metabolic demand, the tributaries of the middle hepatic or short hepatic veins must be aggressively reconstructed. When the right liver graft has multiple short hepatic veins, the double VC method should be considered to decrease warm ischemic time. A large anastomosis should be made in a partial liver graft, which will regenerate and might compress the anastomotic site.[2] For this purpose, the double VC method is preferred, which secures a large outflow orifice. We describe two alternative techniques when VC grafts are not available.

The major concern in venous reconstruction using cryopreserved vein grafts is vein graft obstruction or the possibility of narrowing over the long term. We recently reported satisfying short-term results of hepatic vein reconstruction using cryopreserved grafts with a median follow-up of 9 months.[2] Millis et al.,[9] however, reported 51% complication rate after using a cryopreserved vascular graft. Kuang et al.[10] reported complications, including aneurysm, thrombosis, and stricture, in 8 of 9 cryopreserved vein grafts that were used for portal vein and hepatic arterial interposition. To date, we have not experienced any complications using cryopreserved vascular grafts, but the previous discouraging results indicate that long-term follow-up is necessary to confirm the practicality.

In right liver transplantation, the present techniques can be used to expand the chance for performing double VC reconstruction, which will contribute to satisfactory outflow.

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# Advances in Adult Living Donor Liver Transplantation: A Review Based on Reports From the 10th Anniversary of the Adult-to-Adult Living Donor Liver Transplantation Meeting in Tokyo

*Yasuhiko Sugawara and Masatoshi Makuuchi*

**In 1993, the Shinshu Group performed the first successful adult-to-adult living donor liver transplantation (LDLT). During the first 10 years of LDLT, many technical innovations have been reported. The major limitation of LDLT for adult recipients is the size of the graft. To overcome the problem, several graft types were designed, including left liver graft with caudate lobe, right liver, modified right liver, and right lateral sector and dual grafts. The necessity and criteria of reconstruction of middle hepatic vein is still on debate in right liver graft without trunk of middle hepatic vein. Biliary reconstruction remains a significant source of morbidity in LDLT. Donor safety must always be the primary consideration in LDLT and the selection criteria and management of the living donor must continue to be refined. On February 21, 2004, the 10th anniversary of the adult-to-adult LDLT meeting was held in Tokyo to review the accumulated experience and the presented information is summarized. (*Liver Transpl 2004;10:715–720.*)**

Living donor liver transplantation (LDLT) was first introduced among the pediatric population in 1989,[1] and the first successful case in the total occurred in 1990.[2] On November 2, 1993, the Shinshu Group performed the first successful adult-to-adult LDLT.[3] The patient, who was a 53-year-old woman with primary biliary cirrhosis, received a left liver graft from her son. The number of LDLT procedures for adult patients has increased rapidly since then. By June 2002, there were 433 adult LDLT cases recorded in the European Liver Transplantation Registry[4] with 3-year graft and patient survival rates of 65% and 68%, respectively.

According to the United Network for Organ Sharing,[5] 731 adult LDLT cases had been performed in the United States by October 2001. The 3-year graft survival was 47% between 1998 and 1999 (n = 156), but it improved significantly to 61% between July 1999 and June 2000 (n = 285). According to the Japanese Liver Transplantation Society,[6] 1063 adult LDLT procedures were performed in Japan by the end of 2002. All of the donors were related to the patients; most of them were within the third degree of consanguinity. During the same period, only 10 adult patients underwent liver transplantation using grafts from deceased donors. Death of one living donor was reported from Japan. The donor was a woman in her 40s with complicated mild hypertension and fatty liver preoperatively. Right liver resection was performed, and estimated remnant liver volume was 29% of the total. Postoperatively the donor progressed to liver failure and received a whole liver from a familial amyloid polyneuropathy patient 5 months after her donation. However, she expired 8 months after the donation. The 5-year survival rates were 83% in children and 69% in adults. The lesser outcome in adults compared to that in children ($P < .0001$) indicates that problems remain in adult LDLT.

During the first 10 years of LDLT, many technical innovations have been reported. Now appears to be a good time to review the accumulated experience. On February 21, 2004, the 10th anniversary of the adult-to-adult LDLT meeting was held in Tokyo. The presented information is summarized below.

## Donor Safety

Selection and evaluation of a living liver donor for adult recipients is a complex process that involves optimizing graft size in relation to the safety of donors and recipi-

**Abbreviations:** LDLT, living donor liver transplantation; MHV, middle hepatic vein; HBV, hepatitis B virus; HCV, hepatitis C virus; RHV, right hepatic vein.

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ents, technical details of liver procurement, and ethical problems of using nonrelated live donors. As in most countries, including the United States and Japan, no legal restrictions exist in for living donation, local ethics committees confirm whether the candidates are appropriate potential donors. Voluntarism is the primary selection criterion and medical evaluation can only be started after confirmation of the voluntary nature of the donation.

Volumetric study using computed tomography scans is mandatory. For patients with advanced liver disease, a graft volume of greater than 40% of the recipient standard liver volume is necessary,[7] while for the living donor the remnant liver mass must be more than 30% of the whole liver.[8] The term "standard liver volume"[9] has become a key concept in LDLT. Estimated liver volume on computed tomography in healthy volunteers is proportional to body surface area and is calculated using the following formula:

$$\text{liver volume (mL)} = 706.2 \times \text{body surface area } (m^2) + 2.4$$

Donor safety must always be the primary consideration in LDLT. At least 3 cases of donor death have been reported in the United States[10] and 1 in Japan. Therefore, the selection criteria and management of the living donor must continue to be refined. Cherqui et al. reported on laparoscopic left lateral segmentectomy in a living donor for pediatric liver transplantation.[11] This laparoscopic technique was used in 8 donors, and early graft function was satisfactory in all cases. Unfortunately, 2 patients were complicated with hepatic arterial thrombosis, and 1 of them died. The application of laparoscopic donor hepatectomy for adult liver transplantation requires further technical advances but should be possible in the near future.

## Small-for-Size Graft Problem

The major limitation of LDLT for adult recipients is the size of the graft that can be procured from a living donor, because a small-for-size graft might not meet the metabolic demands of an adult recipient.

## Left Liver Graft

In the initial adult LDLT procedures, only a left liver graft was used. In 1998, the Shinshu group reported satisfactory results using a left liver graft in 13 patients.[12] The donor was selected if, based on computed tomography volume examination, the calculated size of the liver graft was larger than 30% of the recipient's standard liver volume. By January, 2004, the group had performed 95 adult LDLTs using left liver grafts. The 5-year graft and patient survival rates were 81% and 82%, respectively. Graft survival did not appear to be related to the graft volume / patient standard liver volume ratio. One-year graft survival was 83%, 83%, and 100% in patients who received grafts with graft volume / patient standard liver volume ratios ranging from 30% to 39%, 40% to 49%, and more than 50%, respectively. Their data indicate that left liver graft provides satisfactory results for appropriately selected recipients.

Miyagawa et al[13] reported on LDLT using the left liver grafts including the left-side caudate lobe (the Spiegel lobe and the left side of the paracaval portion of the caudate lobe). Takayama et al.[14] designed a similar procedure with direct anastomosis to the vena cava of the hepatic vein from the caudate lobe. The caudate lobe corresponds to only 3% to 4% of the whole liver volume. In conjunction with a left liver graft, however, the caudate lobe increases the graft weight by 8% to 12%.

Fifty-six percent of the patients in the University of Tokyo program received a left liver or left liver with caudate lobe graft with patient and graft 5-year-survival rates of 82% and 84%, respectively.[15] The strategy for selection of left or right liver graft, is influenced by the patient's preoperative condition,[16] as patients with advanced liver disease require a larger liver mass. The model for end-stage liver disease score[17] could become a satisfactory criterion for differentiating between high- and low-risk patients and therefore to determine the type of graft to use.

## Extended Right Liver Graft

Use of right liver grafts has had a large impact on the results of adult LDLT. The Hong Kong group was the first to transplant a right liver graft including reconstruction of the middle hepatic vein (MHV) in 1996,[18] terming it an extended right liver graft. The outcome of the initial 8 donors and recipients were not without complications. One recipient died, and the recipients as well as the donors experienced high morbidity. The next 92 patients subsequently received extended right liver grafts with the following innovations: elimination of veno-venous bypass from the routine protocol, preservation of segment IV venous drainage in the donor, venoplasty of MHV and right hepatic vein into a single orifice for better venous return and easy vein reconstruction in recipients,[19] and preservation of blood supply to the right hepatic ducts. Over time, the mortality rate of the recipients decreased from 16% in the initial 50 cases to 0% in 50 more recent patients.

## Right Liver Graft

In 1998, the University of Colorado group[20] introduced the right liver graft without reconstruction of the MHV trunk in adult LDLT. From January 1997 until

July 2003, the group performed 80 adult LDLTs. In the first 10 cases, in which the MHV branches of the graft were not preserved, 3 grafts were lost. Based on the group's preliminary experience, the resection line of the graft in the donor was moved to the left to preserve the MHV branches and their connections with the right hepatic vein (RHV).[21] The new transsection line was set between the right border of the MHV and the left margin of the gallbladder bed. In the subsequent 70 cases, no graft loss due to venous congestion was experienced.

## Right Lateral Sector Graft

The small graft problem related to the left liver graft has been overcome by the use of a right liver graft. Right hepatectomy, however, imposes an increased surgical risk on the donor, due to the reduced residual liver volume. Fan and associates[8] concluded that safe donation was possible only when the estimated residual liver volume was over 30%. A recent report indicated that in 25% of the potential donors the right liver had an estimated volume of more than 70% of the whole.[22] Thus, based on these volumetric considerations, right hepatectomy is not possible for some potential donors.

The University of Tokyo group was the first to design the right lateral sector graft, consisting of segments VI and VII.[23] The indication for harvesting this type of graft includes a right liver of over 70% of the estimated total donor liver volume, while the estimated volume of the 2 right lateral sectors is greater than that of the left liver. In addition, this graft needs to be larger than 40% of the recipient's standard liver volume. Between January, 2000, and April, 2001, 6 of 32 adult-to-adult LDLTs with a right lateral sector graft[24] were performed at our institution. The postoperative course was uneventful in all donors. All recipients survived the operation. Three patients experienced bile leakage from the dissection plane of the graft. By January, 2004, 16 adult patients had received right lateral sector grafts, and 15 patients were still alive, with normal graft function.

From a technical point of view, careful attention must be paid to transecting the bile duct of the right lateral sector. When the right lateral duct enters the common bile duct separately (caudal right lateral duct), the duct is divided at its origin. Otherwise, after the right portal branch is dissected first and pulled cranially, the right lateral duct is dissected as far as possible from surrounding connective tissues.

## Dual Grafts

Lee et al. were the first to devise dual grafts from two living donors.[25] Most commonly, both donors donate the left liver or left lateral segments, although various combinations of graft types can be used.[26] The first left liver graft is orthotopically implanted at the original left position. The second left liver graft is rotated 180 degrees and positioned heterotopically in the right upper quadrant fossa. Modifications in the surgical technique are needed for implantation of the second graft. Because the bile duct is now located behind the portal vein and the hepatic artery, bile duct reconstruction is necessary before reconstruction of the vessels. An interposition vein graft might be necessary for the reconstruction of the hepatic or portal vein, because the second left liver graft is too small to bridge the distance between the hepatic and portal veins. By the end of 2003, this technique was used in 93 patients with satisfactory results. Also, the Kyoto group has implanted dual grafts in 1 adult patient.[27] However, the procedure has limited appeal due to the high requirements of economic and medical resources: 3 operating rooms and 3 surgical teams are required simultaneously. Therefore, liver transplantation using dual grafts is clearly technically demanding and not widely performed around the world.

## MHV Reconstruction in Right Liver Graft

A right liver graft without the MHV trunk can cause severe congestion of the right paramedian sector. However, a strategy to prevent such congestion or the necessity to reconstruct the MHV has not been discussed in detail.

### Cons

In the meeting, Igal Kam et al. reported that only 2 of 70 patients who received a right liver graft without the MHV trunk required reconstruction of the MHV tributaries. Their research stated that, in general, the MHV can be ligated during the procurement of right liver graft, as connecting the MHV to the vena cava is unnecessary. They emphasized that reconstruction of the MHV is mainly indicated when right hepatic vein of the graft is small. This policy might[50] affect the selection of the potential recipients of the right hemiliver graft. Whole liver grafts from deceased donors can be used for poor-risk patients, while hemiliver grafts from living donors can be used for good-risk patients who can tolerate lesser parenchymal liver mass.

### Pros

In contrast, Lee et al. aggressively reconstructed the MHV tributaries in right liver grafts without the MHV trunk and named this type of graft a modified right liver graft.[28] As it is difficult to predict the degree of right paramedian sector congestion, they recommended rou-

tine reconstruction of MHV tributary veins. Ghobrial et al.[29] also recommended reconstruction of the MHV tributary veins when RHV in graft was less than 1.5 cm in diameter. From July, 1997, to February, 1998, 2 of 5 right lobe grafts without MHV drainage reconstruction were complicated with severe congestion of the paramedian sector. Since then, 42 adult recipients, who received right liver grafts with fairly sized MHV tributaries, underwent reconstruction of these veins.[30] All MHV tributaries with a size of >5 mm were preserved during donor hepatectomy and were reconstructed with the autogenous interposition vein grafts of the recipient during bench surgery.

### Indications

It remains unclear whether all modified right liver grafts require MHV drainage. Sano et al.[31] proposed clear criteria for MHV reconstruction. During the donor operation, hepatic venous congestion in the right paramedian sector was investigated after transsection of the liver parenchyma. First, liver surface discoloration in the right paramedian sector was observed after 5 minutes of simultaneous clamping of MHV tributaries and the right hepatic artery. Next, intra-operative Doppler ultrasonography was performed after declamping only the hepatic artery. If the portal flow of the paramedian sector was found to be hepatofugal, the area was considered congested. If the congestive area was significant, as determined by the clamping test and ultrasonography, bench reconstruction of MHV tributaries was performed. Using these criteria, we performed MHV reconstruction in 18 of 30 grafts, resulting in an uneventful functional recovery of all grafts.[32] The necessity of short hepatic vein reconstruction can be determined using the same criteria.

### Biliary Reconstruction

Biliary reconstruction remains a significant source of morbidity in liver transplantation, with a complication rate of 6% to 47%. Complications include anastomotic leakage and stenosis, problems related with T or stent tubes, and rarely, nonanastomotic strictures or intrahepatic bilomas. These complications can lead to cholangitis, sepsis, and eventually retransplantation and death. Therefore, due to the diminished functional reserve of the hemiliver graft, it might lead to serious complications in adult LDLT.

Initially, the type of biliary anastomosis commonly used in LDLT was the hepaticojejunostomy. Kiuchi and colleagues[33] were the first to report preliminary results of duct-to-duct biliary reconstruction in adult LDLT. Now duct-to-duct biliary reconstruction is enthusiastically performed in a growing number of programs.[34-39] The reports advocate the advantages of duct-to-duct biliary reconstruction over hepaticojejunostomy, such as an aseptic surgical field and shorter duration for reconstruction. The physiologic bilioenteric circulation and bowel continuity can also be preserved, preventing delayed peristalsis. Duct-to-duct reconstruction allows easy endoscopic access to the biliary tree for diagnostic and therapeutic instrumentation and management. For the management of biliary stenosis, the duct-to-duct anastomosis is usually converted to the hepaticojejunostomy. However, the Kyoto group[40] recently reported that 13 of 14 patients were successfully treated with an internal stent. The endoscopic approach appears to be a therapeutic alternative to reoperation. However, the follow-up period in these patients is still short. Long-term postoperative observation is necessary to confirm the safety and feasibility of this procedure.

### Viral Hepatitis and Hepatocellular Carcinoma

#### Hepatitis B Virus

The results of liver transplantation in patients with hepatitis B (HBV) have improved significantly as a result of the rapid evolution in strategies for postoperative prophylaxis. Hepatitis B immunoglobulin, which is costly, was the first effective prophylactic agent. Lamivudine monotherapy prevents emergence of viral mutants. Now, combination therapy with hepatitis B immunoglobulin and lamivudine has become a widely adopted approach. Other nucleotide analogs, such as adefovir, are promising alternative agents.

The HBV prophylactic regimen at Queen Mary Hospital in Hong Kong consists of lamivudine monotherapy,[41,42] while adefovir is reserved for breakthrough reinfection after transplantation. Lo et al. performed 180 liver transplants for HBV-positive patients (120 LDLT and 60 grafts from deceased donors). The 5-year cumulative mutant-free survival was 86%. In contrast, the Tokyo University group[43] presented satisfactory results of LDLT for HBV (n = 20) using hepatitis B immunoglobulin monotherapy. The use of lamivudine was limited to the perioperative period to avoid generating mutants.

One recent report of active production of HBV-antibodies after liver transplantation suggests the possibility of adoptive transfer of immunity against HBV through a liver graft from an immune donor.[44] Active immunization with standard hepatitis B vaccines was recently reported, with conflicting results.[45]

#### Hepatitis C Virus

Early experience suggested rapid and severe recurrence of hepatitis C (HCV) following adult LDLT.

Ghobrial et al.[46] reported that the time interval to HCV recurrence (n = 11) was significantly shorter in LDLT patients than in patients who received grafts from deceased donors (n = 510). The University of Colorado group[47] reported that serum alanine aminotransferase and total bilirubin levels increased more rapidly after the operation in LDLT patients (n = 24) than in cadaveric graft recipients (n = 41). In addition, LDLT patients had greater serum aspartate aminotransferase levels at 1, 3, and 6 months, compared with a matched group of cadaveric controls.[48]

Gaglio et al.[49] reported that the overall incidence of severe sequelae of hepatitis C recurrence—either cholestatic hepatitis, grade III-IV inflammation, and/or hepatitis C–induced graft failure requiring retransplantation—were not different between cadaveric grafts (n = 45) and those grafts from living liver donors (n = 23). However, the morbidity of cholestatic hepatitis C was more severe in LDLT patients (0% vs. 17%, respectively; $P = .001$). These preliminary reports indicate that more intensive antiviral therapy might be necessary for recipients of living donor grafts. All of these reports, however, have some limitations, which include small numbers of patients, lack of standard virologic evaluation, and short-term follow-up. The results must be confirmed in larger, multicenter studies.

### Hepatocellular Carcinoma

LDLT is an established therapeutic option for patients with hepatocellular carcinoma. From 1990 to the end of 2002, LDLT for hepatocellar carcinoma was performed in 225 cases in Japan.

Prof. Furukawa from the Hokkaido University reported in the Tokyo meeting that 160 patients were alive, with a recurrence rate of 5%, while 65 patients were dead, with a recurrence rate of 32%. Multivariate analysis revealed that alpha-fetoprotein levels, tumor size, and invasion of hepatic and portal veins are significant predictors for outcome. When the subjects were categorized into two groups (patients meeting the Milan criteria, and those beyond), difference both in patient and recurrence-free survival reached significance (76% vs. 52%, respectively; $P = .001$; and 76% vs. 50%,respectively; $P = .001$).

## Conclusions

During the 10-year period, many technical innovations have been developed for LDLT, contributing to a better patient outcome. LDLT was originally devised and performed in countries where organs from deceased donors are extremely scarce. The contributions made by Asian countries with regard to the design of several graft types, including left liver graft with caudate lobe, right liver, modified right liver, and right lateral sector grafts, are noteworthy. A recent review by Grewal,[50] however, has failed to acknowledge the significant Asian contribution to LDLT.

In LDLT, the physical and psychological sacrifice by the donor is significant and is associated with high expectations regarding a good outcome for themselves and the recipient. We should not be satisfied with the present outcome and need to strive to achieve 0% donor mortality.[15] Firm criteria for graft selection and further technical advances will be helpful in reaching this goal.

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# Refinement of Venous Reconstruction Using Cryopreserved Veins in Right Liver Grafts

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**Short and direct vein anastomosis is generally performed in living donor liver transplantation using a right liver graft. The graft will regenerate, however, and might thus compress the anastomosis. We formulated a strategy for outflow reconstruction in right liver graft. When reconstruction of multiple short hepatic veins was necessary, a cryopreserved inferior vena cava graft was anastomosed with the hepatic veins of the graft in a basin. When there were no major short hepatic veins in the graft, a rectangular-shaped vein graft was used to make a single orifice using the middle and right hepatic veins in the graft. When there were no tributaries of the middle hepatic vein to be reconstructed, a diamond-shaped vein patch was anastomosed on the anterior wall of the right hepatic vein orifice of the graft. These techniques were satisfactorily applied in 40 patients with no torsion or tension at the anastomotic site of the hepatic venous reconstruction or other complications in outflow. The present strategy seemed to be technically feasible for outflow reconstruction in a right liver graft. (*Liver Transpl 2004;10: 541–547.*)**

Living donor liver transplantation (LDLT) is now widely performed to compensate for the critical cadaveric organ shortage in adult patients.[1] The significant increase might be due to the introduction of right liver graft for adult patients.[2]

An extended right liver graft (ERLG)[3] which includes the trunk of the middle hepatic vein (MHV), was devised by Fan and colleagues. Although the extent of the donor hepatectomy might be increased, this method is beneficial with regard to venous drainage of the graft because the MHV is a major draining vein of the right paramedian sector, and its role in the left paramedian sector is limited.[4] A right liver graft without the MHV trunk (RLG) is now more commonly used. This type of graft, however, can cause severe congestion of the right paramedian sector (segments V and VIII). MHV drainage into the recipient's venous system can be reconstructed using vein grafts[5] to provide a functioning liver mass comparable to an extended right liver.[6]

Vein reconstruction in a right liver graft is technically challenging.[7] The different strategy may be devised according to the existence of thick MHV tributaries or inferior right hepatic vein (IRHV). Additionally, the average right liver graft is only half size for the recipient, and regenerates in all directions after LDLT. As a result, the graft might compress the venous anastomotic site. In the present manuscript, we formulated a strategy for vein reconstruction tolerable to the compression.

## Material and Methods

### Patients

From January 2002 to April 2003, 62 adult patients underwent LDLT at our hospital. Of these, 40 patients (31 men, 9 women) received a right liver graft and were the subjects of the present study. The age ranged from 20 to 66 years (median age = 52 years). The indications for LDLT in these patients included hepatitis C virus–cirrhosis (n=12), hepatitis B virus–cirrhosis (n=8), primary biliary cirrhosis (n=6), cryptogenic cirrhosis (n=5), fulminant hepatic failure (n=4), biliary atresia (n=2), Wilson's disease (n=1), citrullinemia (n=1), and primary sclerosing cholangitis (n=1).

### Donors

The donors were 20 men and 20 women. The age ranged from 20 to 61 years (median age = 36 years). Their relation to the patients included children (n=20), siblings (n=10),

**Abbreviations:** AST, aspartate aminotransferase; CT, computed tomography; ERLG, extended right liver graft; IRHV, inferior right hepatic vein; IVC, inferior vena cava; LDLT, living donor liver transplantation; LHV, left hepatic vein; MHV, middle hepatic vein; MRHV, middle right hepatic vein; RLG, right liver graft without the MHV trunk; RHV, right hepatic vein; SHV, short hepatic vein; VC, vena cava.

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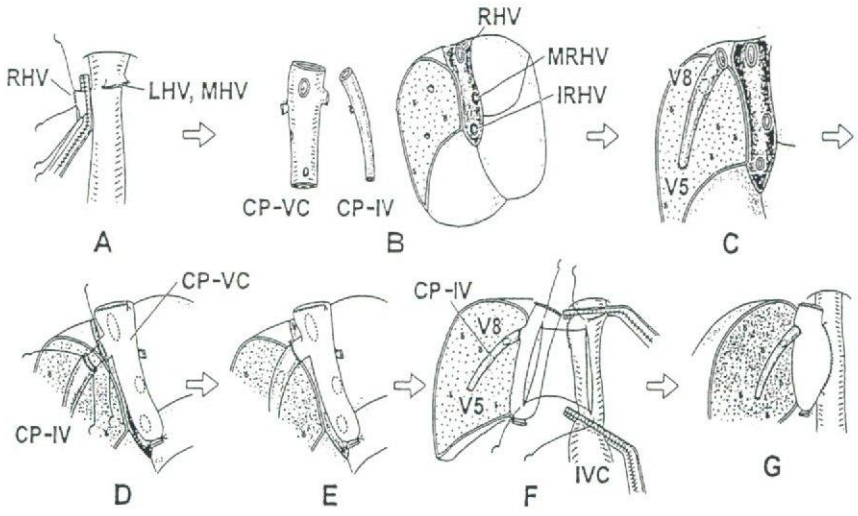


**Figure 1. Schematic view of double vena cava technique. (A) All hepatic vein trunks of the recipient (LHV, MHV, RHV) were sutured at their roots. (B) Three side holes were created in the wall of the cryopreserved vena cava graft (CP-VC) for anastomosis with the right hepatic vein and the short hepatic veins (IRHV or MRHV) of the graft. (C, D) Another cryopreserved vein graft (CP-IV) can be used for middle hepatic vein reconstruction. (E) The stump of venous branch was anastomosed with jumping vein graft for the middle hepatic vein reconstruction. (F, G) Side-to-side anastomosis between the recipient inferior vena cava and CP-VC with continuous sutures was performed.**

spouses (n=5), parent (n=4), and nephew (n=1). Right liver volume was preoperatively estimated by computed tomography (CT). Candidates in whom the right liver comprised more than 70% of the whole liver were rejected as prospective donors. An estimated graft volume to recipient standard liver volume[8] ratio of 40% was the lower limit for right liver transplantation.

The number and diameter of thick MHV tributaries draining the right paramedian sector were evaluated on CT. The tributaries were classified as V8, which drained the cranial part of the portal trunk of the right paramedian sector, and V5, which drained the corresponding caudal part. When the donor was under 50 years of age and the remnant left liver was estimated to be more than 35% of the whole liver, extended right liver graft (ERLG) harvesting was considered. Otherwise, a right liver graft without the middle hepatic vein trunk (RLG) graft harvesting was indicated. Details regarding the selection criteria and evaluation are described elsewhere.[9]

### Homologous Vein Graft Preparation

Vein grafts were provided by the University of Tokyo Tissue Bank. The preservation and thawing methods were described previously.[10] In brief, the vein grafts were obtained from cadavers or nonheart beating donors within 24 hours after cardiac arrest after obtaining informed consent. The specimens were packed in a sterile bag and frozen slowly in a programmable freezer at a rate of 1°C/min to -40°C. They can be semipermanently stored in liquid nitrogen until use.

### Surgical Procedure

The right liver was harvested as described previously.[9] In a basin, the graft was flushed with 1 liter of University of Wisconsin solution through a cannula inserted into the right portal vein. When there were major short hepatic veins, including inferior or middle right hepatic veins in the graft, the double vena cava (VC) technique was applied. The method was refined from our previous method.[11] A cryopreserved VC graft was prepared for venoplasty in a basin (Fig. 1). A side hole was made in the wall of the VC, which was anastomosed with the hepatic veins in the graft. When direct anastomosis was difficult for a distance between the orifice of the middle hepatic vein (MHV) tributaries and VC graft, an iliac branch of the VC vein graft was used for the interposition. If the iliac branch was not available, another cryopreserved vein graft was used for interposition. With this technique, there was no need to preserve any hepatic vein trunks of the recipient, which were sutured at their roots. Then, the inferior vena cava (IVC) of the recipient was partially clamped and incised longitudinally approximately 5 cm. The VC graft was similarly incised longitudinally, and then anastomosed side-to-side with the IVC of the recipient.

When there were no major short hepatic veins in the graft or a VC graft was not available, a rectangular-shaped patch method was applied (Fig. 2). The orifices of right hepatic vein (RHV), MHV, or MHV tributaries received venoplasty with a cryopreserved vein graft or recipient left portal vein. They were cut in a rectangular shape and placed on the orifices of the MHV and RHV of the graft. The vein grafts were sutured to the right side of the MHV orifice and the left side of the RHV orifice in a basin. When the distance between the orifice of V8/V5 and that of RHV was too great in RLG, and not appropriate for this technique, another vein graft was substituted as an MHV. Then, a rectangular-shaped vein patch was placed between the right side wall of the interposition graft

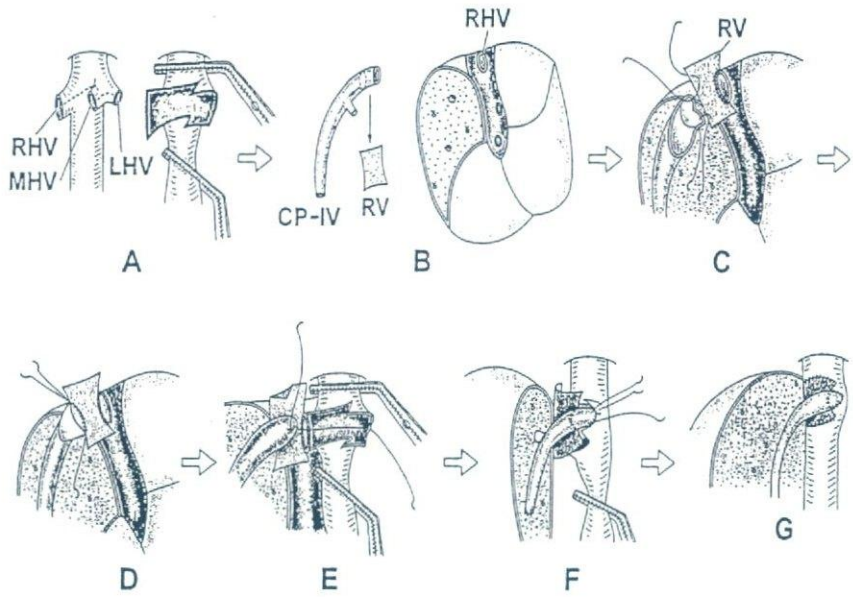


**Figure 2. Schematic view of rectangular shaped patch method. (A) All hepatic vein trunks of the recipient (LHV, MHV, RHV) were cut and one wide single orifice was made. (B) The cryopreserved vein graft (CP-IV) was used for interposition graft for MHV reconstruction. A proximal part of the CP-IV was cut and used for patching between the orifice of graft RHV and the interposition graft (RV). (C, D) The RV patch was anastomosed with the left side of the RHV orifice of the graft. The posterior wall of the CP-IV was cut longitudinally, which was anastomosed with another edge of the RV patch. (E) The right side of the RHV orifice of the graft was anastomosed with the edge of the common hepatic vein of the recipient. (F,G) The anterior wall of the CP-V, RV patch and the edge of common hepatic vein of the recipient were sutured together to make a reservoir of outflow between the liver graft and recipient vena cava.**

and the left side of the RHV orifice. In the recipient, a wide orifice was created by dividing three hepatic veins. The recipient IVC was cross-clamped above and beneath the roots of the hepatic veins. Anastomosis was started between the right edge of the recipient's common hepatic vein and the right side of the graft RHV orifice. Next, the left edge of the recipient's common hepatic vein and the left side of the graft MHV orifice were put together. Then, the caudal edges of the graft veins and recipient venous wall were sutured and the cranial edges were closed.

When the graft had no major MHV tributaries to be preserved, a diamond-shaped patch method was applied (Fig. 4). The method was refined from our previous method.[12] The anterior wall of the RHV orifice of the graft was cut short to widen the orifice while in the basin. An iliac vein graft or left portal branch of the recipient was anastomosed to the anterior

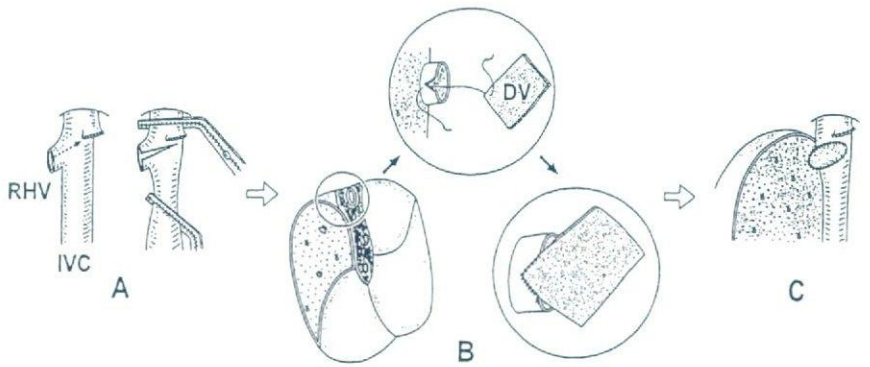


Figure 3. Schematic view of diamond-shaped patch method. (A) The anterior wall of the recipient right hepatic vein (RHV) was cut approximately 2 cm under cross-clamping of inferior vena cava (IVC). (B) The anterior wall of the RHV orifice of the graft was shortly (5 mm) cut for widening the area of orifice. The diamond shaped venous patch (DV) was anastomosed to the orifice of the RHV. (C) End-to-end anastomosis was done between the recipient and graft RHV with continuous sutures.