mg/kg/day for 8 days together with PP. The titer of anti-A antibody decreased after the 9th POD but hyperbilirubinemia persisted. Her liver function gradually improved but she died on POD 22 because of cardiac failure.

Case 9: The patient was a 2-year-old girl with homozygous familial hypercholesterolemia. She received an ABO incompatible partial liver graft from her mother. Preoperative PP was performed because her anti-A antibody titer was high. On POD 3 the values of liver function parameters and anti-A antibody titer indicated humoral rejection. She was subjected to PP and DSG. DSG was administered at the dose of 3 mg/kg/day for 10 days together with PP. The titer of anti-A antibody decreased after POD 11. She suffered from biliary stenosis 6 months after LDLTx, but her liver function improved after percutaneous transhepatic biliary drainage.

Adverse events

As for adverse events, three recipients had leukopenia and/or thrombocytopenia and these were rescued by G-CSF or platelet transfusion (Table 2). Three recipients showed DSG-induced hepatotoxicity but their liver function tests improved within one week after withdrawal of the drug. None of the recipients died because of complications directly induced by DSG.

TABLE 2. *Adverse events observed during the anti-rejection therapy*

	n
Leukopenia	4
	(Use of G-CSF 2)
Thrombocytopenia	2
	(Platelet transfusion 1)
Drug induced toxicity	3

G-CSF, granulocyte colony stimulating factor.

Long-term follow-up

As for long-term follow-up, seven recipients are alive and six of them are symptom free at present (Table 3).

TABLE 3. *Long-term follow up*

No. of Case	Long term status	Period after LDLTx
1	symptom free	11y 5m (alive)
2	symptom free	11y 4m (alive)
3	symptom free	10y 5m (alive)
4	symptom free	9y 1m (alive)
5	symptom free	8y 10m (alive)
6	symptom free	8y 8m (alive)
7	recurrence of primary disease	7y5m (dead)
8	dead on 22 POD	-
9	biliary stenosis	1y (alive)

DISCUSSION

Steroid-resistant acute rejection is treated with DSG after living donor liver transplantation in our institution. Progressive graft rejection in a patient with a liver graft is life threatening and when steroids and/or other immunosuppressive agents fail to reverse the process retransplantation has been the only option. The cases described here show that DSG is effective for steroid-resistant acute rejection in living donor liver transplant recipients. DSG has been recognized as an effective immunosuppressive agent in kidney transplantation, particularly in Japan. The drug is mainly used as a prophylactic and/or rescue therapy for acute rejection. Particularly, in the case of rescue therapy for acute rejection after kidney transplantation, it was reported that therapy using DSG combined with MP was one-hundred percent effective while DSG alone was effective in more than 70% of the cases (Kenmochi et al. 1990). Moreover, it was reported that the efficacy of DSG and that of OKT3 against steroid resistant acute rejection were comparable (Ohkubo 1993).

In the field of liver transplantation there have been only a few reports that refer to the efficacy of DSG. Kato et al. (1997) reported 3 cases, including 2 ABO incompatible recipients, who were rescued by DSG after steroid-resistant acute cellular rejection. Groth et al. (1990) reported the reversal of acute rejection with DSG in a patient in whom previous treatment with steroid and

OKT-3 had failed. In our experience, DSG was effective for steroid-resistant acute cellular rejection in 6 out of 8 liver transplantation cases. But in one case with accelerated humoral rejection, DSG was not effective.

The precise mechanism of the immunological effect of DSG is not known but it is believed to inhibit a protein called heat shock protein 70, which is necessary for the translocation of transcription factors such as nuclear factor-kappa B (NF-kB) to the nucleus (Nadler et al. 1992). As a result, DSG inhibits not only the maturation of T lymphocytes but also the activation, differentiation and maturation of B lymphocytes, inhibiting thereby antibody production. Therefore, DSG is useful for sensitized or ABO incompatible recipients, relying on its ability to suppress humoral immunity. In the field of kidney transplantation, Okazaki et al. (1991) reported the efficacy of DSG in recipients after donor specific transfusion. In a study involving 44 ABO incompatible kidney recipients, in which DSG was used together with standard induction therapy, PP, splenectomy and local graft irradiation, the results of transplantation were excellent, i.e., graft survival was 83% at one year and 80% at three years (Takahashi et al. 1993). In liver transplantation, the efficacy of preformed lymphocytotoxic anti-donor antibodies on graft survival still remains controversial. Several hypotheses have been proposed as possible explanations for the discrepancies among various studies (Donaldson et al. 1995; Manez et al. 1995). These discrepancies relate, in particular, to the relatively small numbers of patients as well as to methodological differences and sensitivity of the assays in renal transplantation.

As for liver transplantation, the survival rate of ABO incompatible patients has been reported to be significantly worse than that of ABO compatible patients (Farges et al. 1995). The presence of preformed anti A and/or anti B antibodies in the recipient and the wide expression of these antigens on endothelial cells in vessels and parenchymal epithelial cells in the graft are indeed risk factors for a hyper acute rejection (Ernst et al. 1984). Therefore, liver transplantation from ABO mismatched donors has been justified only in emergency cases, especially in children, due to the shortage of appropriate donor grafts. However, in living donor liver transplantation we have to use ABO mismatched grafts even in elective cases. In the case of blood type mismatched grafts, we take a lot of measures in an effort to succeed such as pre- and post- transplant PP, splenectomy and strong immunosuppressive therapy (Kawagishi et al. 2001). In our institution we experienced 11 patients who received an ABO blood type incompatible graft. We used DSG in four cases of acute cellular rejection and in two the therapy proved successful. But one patient with accelerated humoral rejection could not overcome severe rejection despite DSG combined with PP, splenectomy and portal cannulation (Case 8). In recipients of kidney transplants, it was reported that DSG was effective even for accelerated acute rejection (Amemiya et al. 1990).

The adverse effects observed in kidney transplant patients included numbness of the face, lips and limbs, gastrointestinal toxicity, bone marrow suppression and the occurrence of infection (Amemiya et al. 1990). In our experience none of the side effects, such as leukopenia, thrombocytopenia and drug toxicity, persisted for a long period. Infectious complications were prevented with antibiotics and stringent screening for bacterial and viral infection.

In conclusion, DSG proved effective for steroid-resistant acute rejection in some LDLTx recipients without inducing severe adverse effects. But DSG was not effective in patients with accelerated humoral rejection.

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特集 生体肝移植をめぐる諸問題

生体肝移植の現状をめぐる諸問題
(5) 先天性肝疾患に対する肝移植

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Key words : 生体肝移植，先天性肝疾患，代謝異常症，胆道閉鎖症

要 旨

先天性肝疾患にはさまざまな疾患があるため，生体肝移植の適応，周術期，長期には各疾患に合わせた幅広い領域からより専門的な見地での管理が必要である．また，遺伝的な背景をもつことが多いことから，ドナーの選択にも遺伝子検索も含めた厳重な検査が要求されることもある．本稿では，本邦における先天性疾患に対する生体肝移植のうち，頻度の高かったものを中心に，胆道閉鎖症，ウィルソン病，家族性アミロイドポリノイロパチーなどについて，当科における経験もまじえて概説する．

はじめに

先天性肝疾患は代謝異常症が含まれるためさまざまな疾患がある(表)．小児のみならず成人発症の代謝異常症もあり，一般的な肝移植の管理とは別に，各疾患に合わせた処置が必要である．したがって小児科，小児外科，内科など幅広い領域からより専門的な見地で症例を検討しなくてはならないのも特徴である．また，遺伝的な背景をもつことが多いことから，ドナーの選択には遺伝子検索も含めた専門的な検査が要求されることもある．

本稿では当科の経験も含め概説する．

表 肝移植の適応となるおもな先天性疾患

胆汁うっ滞性疾患	
胆道閉鎖症	(992)
アラジール症候群	(39)
バイラー病	(23)
代謝性疾患	
ウィルソン病	(60)
家族性アミロイドポリノイロパチー	(42)
シトルリン血症	(30)
オルニチントランスカルバミラーゼ欠損症	(15)
糖原病	(11)
チロシン病	(10)
原発性高シュウ酸尿症	(8)
家族性高コレステロール血症ホモ型	(2)

( )内は2003年までの本邦における生体肝移植数〔日本肝移植研究会[1]による〕．

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Ⅰ．胆汁うっ滞性疾患

この項のポイント

- 胆汁うっ滞性疾患は胆道閉鎖症を筆頭にもっとも生体肝移植数の多い疾患である．

胆汁うっ滞性疾患は大きく肝外性と肝内性に分類されるが，肝移植の適応としてもっとも多いのは肝外性である胆道閉鎖症である．近年，ほかの疾患数の増加により移植数の割合は減少したが，総数では2003年末の時点でもっとも多い適応疾患である[1]．そのほかに，本邦で比較的多く肝移植されているアラジール症候群とバイラー病について述べる．

1．胆道閉鎖症

胆道閉鎖症は，1万～1万5千人に1人の頻度で起こる原因不明の難病である．先天性の構造的奇形，後天的な炎症性硬化性病変などが考えられている．そのため，最近では「先天性」とつけないのが一般的である．肝外胆管の欠損形態から大きく三つに分類される．1968年に当科の葛西らがKasai手術を報告して以来[2]，その治療成績は飛躍的に向上したが，きわめて難治性の疾患であることには変わりがない．当院小児外科の成績では，1980年代以降に限ってみると約70%の症例が10年以上の生存を得ており[3]，20歳以上の長期生存例も40例を超えている[4]．しかし，進行する肝硬変，イレウス，脾機能亢進，食道静脈瘤，胆管炎などで入退院を繰り返す症例も存在する．一方，本邦での胆道閉鎖症に対する生体肝移植は約1,000例にのぼり，5年生存率も80%を超えている[1]．

最近では，顕性の黄疸がなくとも，難治性胆管炎や消化管出血などによる頻回の入退院を繰り返す症例，食道静脈瘤，瘙痒感などの症状がコントロール不可能な症例，成長発育障害を認める症例など，患児のQOLをも考慮した適応が考えられている．当科で生体肝移植術を受けた患者における検討でも，移植後の生存症例と死亡症例で術前の血清総ビリルビン値に有意差はないが，5歳未満に移植をした症例のほうが移植後の発育が良好であることから，胆道閉鎖症の移植適応並びに時期については，ビリルビン値にかかわらず患児のQOLを考慮したうえで肝移植することを提唱している[5]．

2．アラジール症候群

アラジール症候群は肝内の小葉間胆管の欠損による胆汁うっ滞と特徴的な顔貌，心血管系，椎体，眼球の異常などの臨床的特徴をもつ症候群である．特徴的な顔貌とは，広い前頭部，離れた両眼，小顎などである．心血管系の異常としては末梢肺動脈の狭窄がもっとも多いが手術適応となるものは少なく，ほかに心室中隔欠損，大動脈狭窄，ファロー四徴症などを伴うものがある．椎体では，蝶形の椎体，椎間の狭小化などで，眼球では後方角膜周囲混濁，網膜の色素沈着異常，虹彩の異常，近視などがある．末梢血検査では血清ビリルビン値，血清トリグリセリド値，アルカリフォスファターゼ(ALP)の高値などがある．常染色体優性で第20染色体短腕の欠損が報告されている．

予後は非常に良く，肝硬変症まで進行する例は数%であり，薬物療法が中心で，重症例には胆嚢空腸吻合による胆道ドレナージなどが施行される．しかし，著しい成長障害，門脈圧亢進症，肝硬変症による肝不全には肝移植が適応となる．肝移植に際しては，心血管系，腎臓などの異常に注意が必要である．肝移植成績は良好である[6]．

3．バイラー病

バイラー病は，進行性家族性肝内胆汁うっ滞

症とも呼ばれ，常染色体劣性遺伝である．瘙痒感，黄疸などの症状は10カ月から1歳頃に現れることが多い．血清ビリルビン値が40～50 mg/dlになることもまれではないが，血清コレステロール値は正常であることが多い．血清AST，ALT，ALPは高値である．胆道造影では肝内胆管は開存していることから，疾患の本態は毛細胆管レベルでの胆汁うっ滞であると考えられている．

予後は非常に悪く，ほとんどの症例は2～15歳の間に死亡する．まれに25歳まで生きたという報告がある．したがって，薬物療法などの保存的療法には限界があり，肝硬変，肝不全症例には肝移植しか完治の見込みはない．肝移植成績は良好である[7]．

Ⅱ．代謝異常症

この項のポイント

- 代謝異常症にはさまざまな疾患があり，ドナー選択も含め十分な術前検討を要する．

代謝異常症のうち肝移植適応となるのは，生命維持のために必要な代謝機能に異常がある疾患が対象となる．ここでは，本邦で行われた生体肝移植のうち，症例数の多かったものを中心に述べる．

1．ウィルソン病

ウィルソン病は，常染色体劣性の遺伝形式をとる銅代謝異常症である．臨床的には慢性活動性肝炎もしくは劇症肝炎で発症するが，5歳以下で臨床所見が出現するものはまれであり，多くは10歳代に発症する．神経学的症状としては，錐体外路への銅の沈着による振戦，精神発達遅延などである．診断としてはKayser-Fleischer輪，血清セルロプラスミンの低値，血清銅の低値，24時間尿中銅の高値であるが，肝臓乾燥組織中の銅含有量が250 μg/gを超えることがもっとも診断に有用である．治療としては，ペニシラミン-D，トリエンチンなどのキレート剤や銅の腸管からの吸収を抑制する亜鉛が用いられる．劇症肝炎になる症例は2：1で女性に多く，クームス試験陰性の溶血性貧血，血清と尿中の銅高値，血清セルロプラスミンの低値，肝逸脱酵素はほかの劇症肝炎に比し低値，Kayser-Fleischer輪は半数以下であるなどの特徴をもっている[8]．

肝移植適応となる病態は，劇症肝炎はもちろんであるが，内科的治療抵抗性の進行性肝障害，繰り返す消化管出血などである．肝障害の程度が軽微で神経症状のみ存在する症例は内科的治療で回復可能なため，肝移植の適応とはならない．肝移植後の長期成績は良好で，神経症状や腎尿細管障害も移植後回復することが多い．Kayser-Fleischer輪も3～4年で消失する．

2．家族性アミロイドポリノイロパチー

家族性アミロイドポリノイロパチーは，常染色体優性の全身性アミロイドーシスである．末梢神経障害または自律神経障害で発病し，最終的には心臓，腎臓を中心にすべての臓器が障害を受ける．この疾患のアミロイド前駆タンパクは肝臓で産生されるトランスサイレチンである．発症年齢は20歳代～40歳代が多い．初発症状は足底から始まる疼痛などの異常感覚，長期にわたる下痢または便秘，嘔気・嘔吐などである．末梢神経障害としては下肢を中心とする感覚障害，筋萎縮・筋力低下であり，自律神経障害としては起立性低血圧，消化管運動障害，膀胱直腸障害である．とくに消化管運動障害は1週間周期で高度な便秘と下痢を繰り返す特徴的な症状である．発病後5～6年で歩行不能，10年前後で臥床状態，その後，多臓器不全で

死に至る．

診断は生検によるアミロイドの証明と，免疫組織学的にアミロイドが抗トランスサイレチン抗体陽性であること，また，トランスサイレチンのアミノ酸変異を確認することである．肝移植が唯一有効な治療法である．

肝移植の適応としては，施設間にやや差があるものの罹病期間が5年以内，多発神経炎が下肢に限局または自律神経症状のみで重篤な心機能異常がない，などである[9]．肝移植後の経過は，術前の状態が軽度の者は2～3年で無症状になるが，術前に進行した排尿障害などは改善しない．本邦での移植後生存率は5年85%ほどである．また，肝移植前に心臓に沈着した変異型トランスサイレチンを核として，野生型トランスサイレチンが肝移植後に沈着し，心機能が障害される症例があり問題となっている．

3. シトルリン血症

シトルリン血症のうち成人型(II型)は日本人の若年男性に多いアルギノコハク酸合成酵素(ASS)の欠損による尿素サイクル酵素欠損症である．遺伝形式は常染色体劣性で，初発年齢は10歳代～60歳代と幅が広い．初発症状は突然の意識障害発作で，異常行動，不穏状態，傾眠傾向などであるが，これらの症状は再発を繰り返し，多くの症例で2年以内に高度な脳障害へと進行する．てんかんや統合失調症と診断されてしまう症例もある．診断は血中アンモニア，シトルリン値の上昇，肝生検組織によりASSの活性低下，責任遺伝子であるSLC25A13遺伝子異常の証明である．

治療としては，低タンパク食，ラクチュロース，安息香酸ナトリウム，カナマイシンなどの血中アンモニアを下げる療法が行われてきたが，多くの症例で脳症の進行は食い止められない．

本疾患は，発病後急激に脳症が進行し，しかも進行した脳症に対しては保存的療法，急性血液浄化療法による改善は期待できないことから，シトルリン血症と診断された時点で肝移植を早期に行うべきである[9]．肝移植後の予後は良好で，移植後速やかに血中アンモニア，シトルリン値は正常化し，脳症状も軽快する．

4. オルニチントランスカルバミラーゼ欠損症

オルニチントランスカルバミラーゼ欠損症(ornithine transcarbamylase deficiency；OTCD)は，尿素サイクル異常症のなかで一番頻度の高い疾患である．男の新生児型は生後数カ月以内に死亡し，生存例も重度の神経障害を残すといわれている．遅発型の発症年齢はさまざまであるが，繰り返す嘔吐，精神錯乱などで発症する．診断は高アンモニア血症，アロプリノール負荷後の尿中オロット酸排泄増加，血中グルタミン，グルタミン酸の上昇などである．

治療としては，高度の高アンモニア血症に対しては血液透析，薬物療法としては安息香酸ナトリウム，フェニール酢酸ナトリウム，栄養療法として低タンパク食などである．日本人の遅発型症例の20年生存率は男女とも40～50%であるが，初発時の血中アンモニア値が360 μmol/lを超える症例は予後が悪い[10]．肝移植の適応は，頻回の高アンモニア血症，知能発育遅延，薬物治療抵抗性などの症例である．肝移植後の成績は良好である．

5. 糖原病

糖原病には12種類あり，そのうち肝移植の適応となるのはおもにIV型とIA型の2種類である．III型も適応となることがある[11]．IV型は常染色体劣性で，栄養療法の効果は期待できず2～3歳で肝硬変へと移行する．また，アミ

ロペクチンが中枢神経，心臓，骨格筋に沈着し障害をもたらす．

肝移植の適応としては，肝硬変による肝不全時を基本とするが高度のアミロペクチン沈着前に行うことも重要である．ＩＡ型は常染色体劣性で，栄養療法に効果が認められる症例もある．しかし，てんかんを伴う重篤な低血糖になる症例では，肝移植が必要になる．また，ＩＡ型には肝内に腺腫を伴うことが多いが，癌化するリスクは不明なため，これ自体が肝移植の適応とはならない．

6．チロシン病

チロシン病は常染色体劣性の fumarylacetoacetate hydrolase 欠損症で，この酵素活性低下により診断される．新生児では劇症肝炎として発症し，慢性に経過する症例では１歳を過ぎたころに肝硬変となり，２歳以降には約３分の１の症例で多中心性の肝癌の発生を見る．ほかに精神障害，呼吸障害，腎障害も出現する．

肝移植適応は新生児劇症肝炎のほか，慢性に経過した２歳以降にも肝癌発生の頻度が高く，しかも多中心性で肝切除が困難であることから，肝移植を施行すべきと考えられている．肝移植後の成績は良好であるが，腎障害が遷延する症例がみられる[12]．

7．原発性高シュウ酸尿症

原発性高シュウ酸尿症（primary hyperoxaluria type Ⅰ）は，腎臓，骨，心臓などに過剰産生によるシュウ酸が沈着する常染色体劣性の遺伝性疾患である．肝臓の alanine-glyoxylate aminotransferase 欠損による．乳児期の腎不全が死因となることが多いため，腎機能が悪化する前に早期の肝移植が推奨されている[13]．腎機能障害が出ている症例に対しては，肝腎同時移植を施行し，良好な長期成績であったという報告があり，また，本邦での異時性生体肝腎移植も報告されている[14]．

8．家族性高コレステロール血症ホモ型

LDL レセプター欠損症である家族性高コレステロール血症ホモ型は，常染色体劣性で約100万人に１人の割合である．高コレステロール血症，腱黄色腫，冠動脈疾患を主症状とする．多くの症例は LDL アフェレシスで治療され，30歳以上の生存はまれである．欧米での肝移植の成績は良好であるが，本邦では当科においてヘテロの親からホモの子に肝移植した２例が最初であり，現在，薬物療法を併用し経過順調である[15]．

おわりに

このほかにもさまざまな先天性肝疾患が肝移植の適応になると考えられる．先天性疾患では遺伝的素因も大きく影響すると考えられることから，ドナーが近親者であることが多い本邦での生体肝移植では，長期にわたって原疾患の再発に厳重な監視が必要である．

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Summary

Living Donor Liver Transplantation for Congenital Liver Disease

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Congenital liver diseases, which are indicated for liver transplantation are represented as cholestatic and metabolic diseases. There are many liver diseases and we must treat them in a variety of ways. Particularly metabolic diseases often have genetic back ground, we must also check the genetic status of the donor before transplantation. In this article we describe congenital liver diseases for which we have performed living donor liver transplantation (LDLT) in Japan. Biliary atresia is the most frequent disease requiring LDLT and the number of these cases treated with LDLT in Japan totals 1,000. The most frequent indications for LDLT were failed Kasai operations and developmental retardation. However, the indications became wider when considering the quality of daily life for the patient. Other diseases such as Wilson's disease, familial amyloid polyneuropathy and citrullinemia are described. We also describe our experiences with two homozygous for familial hypercholesterolemia (FH) who received LDLT from their parents, who were heterozygous for FH.

Key words : congenital liver disease, biliary atresia, liver transplantation, living donor, indication

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ORIGINAL ARTICLE

Using a radial artery as an interpositional vascular graft in a living-donor liver transplantation for hepatocellular carcinoma

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Keywords
hepatocellular carcinoma, living-donor liver transplantation, radial artery graft.

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Summary

With increasing numbers of living-donor liver transplantations (LDLTs) for hepatocellular carcinoma (HCC), cases with some arterial troubles are encountered; because most HCC cases waiting for LDLT have undergone interventional treatments. In these patients, the reconstruction of the graft artery needs to be planned preoperatively. We report a 52-year-old male, with hepatitis C-related liver cirrhosis and advanced HCC, who for 4 years repeatedly underwent continuous intraarterial chemotherapy through an implanted reservoir port. A suitable artery was not available for arterial reconstruction and the patient underwent LDLT using an autologous radial artery conduit based on the infrarenal aorta. Postoperatively, the patient is well with normal liver function and efficient arterial flow. Autologous radial artery can be safely and successfully used as an aortic-based arterial conduit when HCC patients waiting for LDLT have undergone long-term repeated intraarterial chemotherapy.

Introduction

For living-donor liver transplantation (LDLT), successful hepatic artery reconstruction is essential and interpositional vascular grafts are needed in the case of an inadequate or thrombotic hepatic artery. There are several reports regarding vascular grafts in liver transplantation: including of the saphenous vein [1], iliac artery [2], inferior epigastric artery [3] and the cadaveric iliac artery [4]. On the contrary, with increasing numbers of LDLTs for hepatocellular carcinoma (HCC) [5], cases with some arterial troubles are being encountered more often because most HCC cases waiting for LDLT have undergone interventional treatments such as transcatheter arterial embolization (TAE), transcatheter arterial chemoembolization (TACE) and intraarterial chemotherapy through the implanted reservoir. In these patients, the reconstruction of the graft artery has to be planned preoperatively. We undertook LDLT using the radial artery as an interpositional vascular graft between the graft artery and the infrarenal aorta for an HCC patient who previously had repeated interventional treatments. Although it has routinely been used for coronary artery bypass grafting [6], there are few reports on its utility for the reconstruction of the hepatic artery in LDLT. Here, we report its versatility as an arterial conduit in LDLT.

Case report

A 52-year-old male was found positive for the hepatitis C antibody during a routine health examination in 1991. He was treated with interferon twice and has been followed ever since then because the initial treatment was not effective. In November 1999, three nodular HCC

lesions were diagnosed in liver segment 7 Couinaud's classification, 4 cm in diameter, and segments 2 and 6, both 0.5 cm, by computed tomography (CT) scan; and the patient twice underwent TAE. In May 2000, multiple HCCs were detected in liver segments 2, 3, 4, 5, 7 and 8 with diameters from 1.5 to 0.5 cm. A reservoir port was implanted and he underwent continuous intraarterial chemotherapy through it for 4 weeks. Since then, he has undergone several treatments of intraarterial chemotherapy. In July 2003, because the multiple HCCs could not be controlled by any treatment, and as he complained of liver dysfunction caused by the progression of liver cirrhosis and the HCCs, he was referred to our hospital to undergo LDLT.

Physical examination revealed him to be moderately well built with stable vital signs and with no hepatosplenomegaly or superficial lymph-node enlargement.

Serum total protein level was 6.7 g/dl with an albumin level of 2.9 g/dl. Serum liver function test results showed slightly elevated levels of aspartate transaminase (136 IU/l), alanine aminotransferase (54 IU/l) and gamma GTP (79 IU/l). The value of total bilirubin and direct bilirubim were 4.4 and 3.1 mg/dl respectively. Prothrombin time-international normalized ratio was 1.15. Hepatitis C virus (HCV) antibody, tested by EIA, was positive, and the value of HCV-RNA was 18.5 KI/ml, tested by RT-PCR method. Tumour marker levels of alpha fetoprotein and protein induced by vitamin K antagonist II (PIVKAII) were 39 131 ng/dl and 37 600 U/ml respectively.

A CT scan of the abdomen revealed multiple HCCs in liver segments 2, 3, 4, 5, 7 and 8 with diameters from 5 to 1 cm. Abdominal angiography revealed a complete obstruction of the common hepatic artery and the blood supply to the right hepatic lobe was fed from a collateral artery from the gastroduodenal artery (Fig. 1a). Celiac arterial angiography revealed stenosis of the celiac axis and the splenic, and irregularities of left gastric arteries; the blood supply to the spleen was fed from collateral arteries from the celiac axis (Fig. 1b).

We decided to use the radial artery as an interpositional vascular graft between the graft artery and the aorta. A clinical assessment of the patient's nondominant (left) arm was performed preoperatively using a modified Allen's test. In addition, pulsatile flow in the digital artery of the thumb was confirmed using a Doppler probe, while the radial artery was compressed. With a diagnosis of multiple hepatocellular carcinoma associated with liver cirrhosis, LDLT using his son's right lobe was performed on 19 August 2003. The left radial artery was procured by a cardiothoracic surgeon, highly experienced in this procedure, using previously described techniques [7] (Fig. 2a). The radial artery graft had a diameter of 4 mm and was shortened to a length of 15 cm. Cross clamping

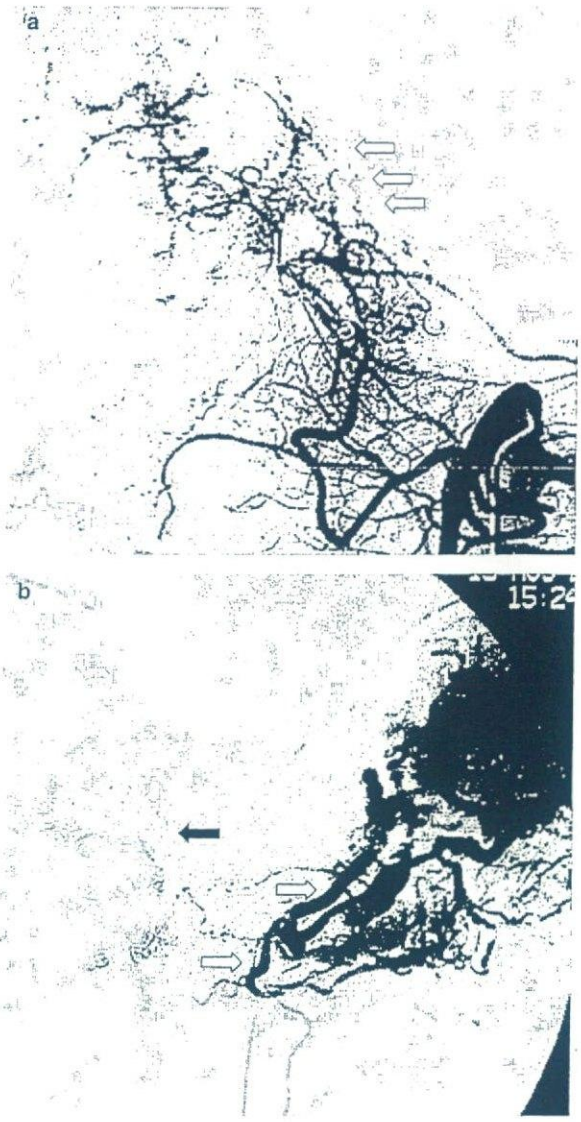

Figure 1 (a) Abdominal angiography demonstrates a complete obstruction of the common hepatic artery and the blood supply of the right hepatic lobe is fed from a collateral artery from the gastroduodenal artery, indicated by white arrows. (b) Celiac arterial angiography reveals stenosis of the celiac axis and the splenic artery, and irregularities of the left gastric arteries. The blood supply to the spleen was fed from collateral arteries from the celiac axis. A white arrow indicates collateral arteries from the celiac axis, black arrows indicate irregularities of the left gastric arteries.

was applied at the infrarenal portion of the aorta and an aortotomy was created with 4-mm aortic punch. Both ends of the radial artery were spatulated and the proximal anastomosis of the graft was carried out with 6-0 polypropylene running suture using parachute technique under 2.5 loupe magnification (Fig. 2a). The radial artery

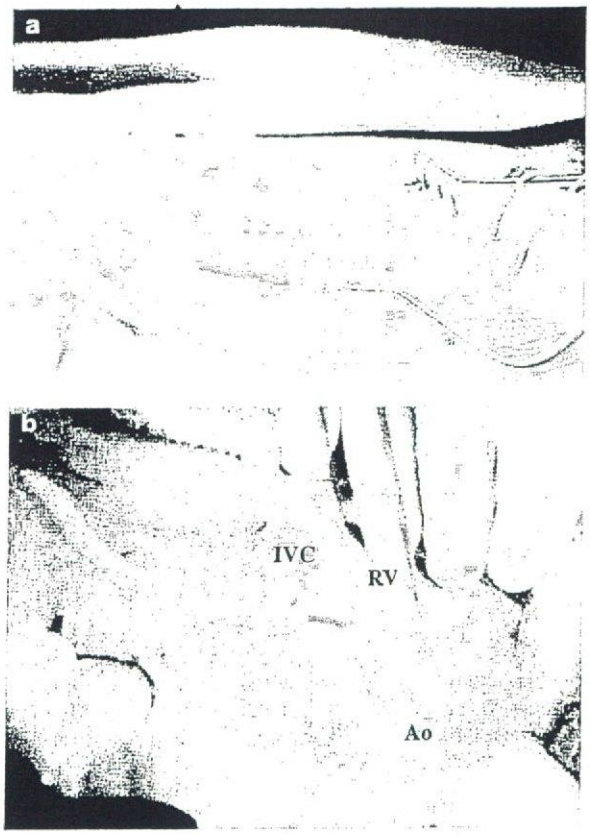

Figure 2 (a) Procurement of the left radial artery. (b) The radial artery graft is anastomosed to the infrarenal aorta. IVC, inferior vena cava; Ao, aorta; RV, renal vein.

graft was then anastomosed to the allograft hepatic artery using an interrupted 8-0 polypropylene suture under microscopic procedures. Good arterial inflow was then demonstrated by Doppler duplex ultrasound.

The patient had a good postoperative course and the patency of the radial artery graft has been very good. He was discharged on the 23rd postoperative day without any complications. He is currently well and free of disease, 3 months after the operation.

Discussion

In recent years, progress has been achieved in the radical treatment of HCC with several therapeutic modalities, including liver resection, percutaneous ethanol injection (PEI) and radiofrequency cytoablation (RFA) [8]. However, HCC patients with repeated recurrence, tumour progression, and advanced liver dysfunction have been increasing and are unable to undergo such radical treatment; most undergo TACE or intraarterial infusion chemotherapy through implanted reservoirs to prolong survival [9]. On the contrary, liver transplantation is an excellent treatment for HCC patients because this procedure is able to cure not only the tumour but also the underlying cirrhosis. It is reported that in 56 HCC patients who underwent LDLT most had received treatments for HCC, including TACE in 39 cases, PEI or RFA in 24 cases and liver resection in eight cases [5]. Increasingly, HCC patients are waiting for LDLT; some recipients do not have an adequate artery to reconstruct it to the graft hepatic artery such as a hepatic, gastric or splenic artery because these arteries are often injured by repeated interventional therapies.

In this case, we needed an interpositional artery graft with a length of >15 cm because we had to reconstruct the artery graft to the infrarenal aorta and the graft's hepatic artery. The saphenous vein [1], iliac artery [2], inferior epigastric artery [3] and the cadaveric iliac artery [4] have been described as interpositional arterial grafts. However, these grafts would not have sufficient length or diameter except for the saphenous vein graft. However, there have been several reports of complications of pseudoaneurysms of saphenous vein grafts after coronary bypass [10,11] and it was believed that an autologous arterial conduit would provide better long-term patency.

This is supported in the cardiac surgery literature with reports of <50% patency of vein grafts at 10 years and intraluminal disease in those grafts that were patent. In all angiographic studies, the patency rate for arterial grafts is consistently greater than for vein grafts at any point after coronary surgery [12]. The unsatisfactory patency of saphenous vein grafts compared with that of internal mammary artery grafts in these studies has stimulated a revival in the usage of the radial artery as a coronary artery bypass graft, based on the belief that it should improve long-term results from coronary operations. Carpentier *et al.* [13] first described an arterial conduit in myocardial revascularization in 1971 and the radial artery is now frequently used with excellent long-term patency rates [7,14,15]. A recent report showed an 83% angiographic patency rate of radial artery grafts at 5 years [16]. The excellent long-term patency of radial artery grafts in myocardial revascularization prompted us to use a radial artery graft for the interpositional artery graft in LDLT for this patient. Advances in minimal traumatic arterial-harvesting techniques have limited postoperative morbidity and virtually eliminated ischaemic complications. Because there are some possible complications of the donor arm such as developing of ischaemia or motor dysfunction and there are minor complications of stitch abscesses, skin dehiscence, superficial infection, and small haematomas or seromas, it is important to note that a radial artery graft should be harvested by a surgeon with experience in this technique [17].

Liver transplantation is acknowledged as the treatment of choice for patients with early, unresectable HCC and the Milan criteria have been widely accepted for selection of HCC patients for transplantation [18,19]. On the contrary, Kaihara *et al.* [5] reported that the 20 HCC patients beyond the Milan criteria showed tumour-free survival of approximately 50% at 2 years after LDLT. These results demonstrated the considerable possibility that even HCC patients, who had been excluded by the Milan criteria, can survive for long periods after transplantation. In our institution, all HCC patients have the extent of tumour involvement evaluated with abdominal, chest and brain CT scans, and by bone scintigraphy within the 2 months before transplantation; but condition, number and size of the tumours are not criteria for exclusion. The present patient underwent LDLT for HCC beyond the Milan criteria. However, as he would get the opportunity for long-term survival, long-term arterial graft patency would be necessary.

In conclusion, we believe that this report is the first documented use of an autologous radial artery for interpositional artery graft in LDLT for HCC patients. Although the radial artery is not a first-line arterial conduit, it can safely and successfully be used when a suitable recipient's artery is unavailable and the use of a saphenous vein or other conduits is believed to be undesirable. Autologous radial artery grafts should be added to the transplant surgeon's armamentarium as needed for interpositional artery graft in LDLT patients who have undergone repeated intraarterial chemotherapy for HCC.

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Impact of Right Lobe with Middle Hepatic Vein Graft in Living-Donor Liver Transplantation

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Technical improvements in adult-to-adult living-donor liver transplantation (LDLT) have led to the use of right-lobe grafts to overcome the problems encountered with 'small-for-size grafts'. The major controversy remains that the venous drainage from anterior segment substantially depends on tributaries of the middle hepatic vein (MHV), and deprivation of such tributaries may critically influence the postoperative graft function. Right-lobe grafts with MHV could resolve the potential problem of congestion in anterior segment. From December 2000 to January 2004, we performed 217 right-lobe LDLTs for adult patients. Of these, 40 patients received a right lobe with MHV graft (18.4%). The overall cumulative 3-year graft survival rate of a right lobe with (n = 40) and without MHV (n = 177) was 86.2% and 74.8% (p = NS). The proximal side of the MHV and the drainage vein of segment IV to the MHV (the left medial superior vein) were preserved in 24 patients. All of them needed venous interposition graft for anastomosis. All patients had a patent right hepatic vein (RHV) and MHV anastomosis during the follow-up period. We adopted the right lobe with MHV graft in 40 LDLT cases. Vein graft is essential for safe MHV anastomosis in cases which preserve proximal side of the MHV.

Key words: Hepatic vein reconstruction, liver transplantation, living donor, right-lobe graft

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Introduction

The accumulating results of living-donor liver transplantation (LDLT) are comparable to those of cadaveric transplantation (1). Experience of and technical improvements in left-lobe donation have led to the use of right-lobe grafts in adult-to-adult LDLT to overcome the problems encountered with 'small-for-size grafts'. We have reported that the use of 'small-for-size grafts' (<1.0% of recipient body weight) leads to lower graft survival, probably through enhanced parenchymal cell injury and reduced metabolic and synthetic capacity (2).

The major controversy about right-lobe LDLT remains that the venous drainage from the anterior segment depends substantially on tributaries of the middle hepatic vein (MHV), and deprivation of such tributaries may influence the postoperative graft regeneration (3). We have reported that the regeneration of the posterior segment was significantly greater than that of the anterior segment. Despite deprivation of MHV tributaries, a graft will regenerate to meet the metabolic demand (4). However, some patients substantially suffered from complications related to 'small-for-size graft'. In some right-lobe grafts, regional volume of the MHV might be dominated over the right hepatic vein (RHV), and the functional liver volume could be reduced in such type of the grafts. To maximize the benefit of right-lobe graft, several technical modifications have been reported, such as additional venous reconstruction of segment V and VIII (5–8).

The application of right lobe with MHV graft could resolve the potential problem of congestion in the anterior segment (6). However, sufficient drainage veins of the remnant donor liver might not be certified due to the presence of tributaries from segment IV to the MHV (left medial superior vein) (9). Preservation of the drainage veins of segment IV to the MHV in the donor might be important for surgical innovation in right lobe with MHV LDLT.

Recent developments in imaging studies have made it possible to visualize the distribution of the hepatic vessels without hepatic dissection (10). Preoperative three-dimensional (3D) computed tomography (CT) volumetry and computer-assisted volumetric analysis according to the hepatic venous anatomy (MeVis, Germany) were adopted as a noninvasive and objective evaluation for application of a right lobe with MHV graft (11). The computer-assisted preoperative donor risk analysis is helpful for providing volumetric calculations, relating the volume of the compromised areas to total graft or remnant liver. We describe the surgical techniques and outcome in 40 cases of

hepatic vein reconstruction in LDLT using right lobe with MHV grafts, while preserving the significant drainage veins of segment IV to the MHV remaining in the donor.

Patients and Methods

During the period from June 1990 to January 2004, 966 LDLTs were performed in 922 patients at Kyoto University Hospital. Right-lobe LDLT was first carried out in February 1998, and we have since carried out 345 right-lobe LDLTs. Since the initiation of the right lobe with MHV graft procedure for adult patients (>18 years old) in December 2000, we have performed a total of 217 cases of right-lobe LDLTs for adult patients in the same period. Of these, 40 patients received a right lobe with MHV graft (18.4%). Nineteen cases of right-lobe LDLT with additional vein reconstruction of the anterior segment were excluded from the study.

The patients were 29 males and 11 females, with a median age of 49.7 years (range: 18.8–65.7), and a median weight of 64.3 kg (range: 37.1–99.0). Median model for end-stage liver disease (MELD) score was 19.0 (range: 4.0–37.0). The indication for transplantation was hepatocellular carcinoma with hepatitis C virus (HCV) cirrhosis in 17 patients; hepatocellular carcinoma with hepatitis B virus (HBV) cirrhosis in 4; liver cirrhosis in 9 (HCV in 6, HBV in 1 and alcoholic in 2); biliary atresia in 3; fulminant hepatic failure in 2; primary biliary cirrhosis in 2; glycogen storage disease in 1; retransplantation in 1 and a metastatic neuroendocrine tumor (pancreatic polypeptide-secreting tumor) in 1. Six patients received blood-type incompatible grafts (Table 1).

Immunosuppression consisted of tacrolimus and low-dose steroids (12). Patients who received blood-type incompatible transplants had preoperative plasma exchange or double-filtration plasmapheresis in order to reduce the anti-ABH antibody titer. Prostaglandin E1, cyclophosphamide and additional steroids were administered from the portal vein or hepatic artery postoperatively (13).

Donor evaluation

Potential donors were evaluated through the use of liver function tests, determination of blood type, HLA typing and determination of anatomical variation and graft size using 3D CT volumetry. The potential indication for right lobe with MHV grafting was a graft-to-recipient weight ratio (GRWR) of less than 1.0% with right-lobe graft, as determined by preoperative 3D CT volumetry. If the regional volume of the MHV dominated over the RHV and the remnant liver volume in the donor was shown to be over 35% of the whole liver volume, then the entire MHV could be included with the graft. If not, the proximal side of the MHV, which is the concourse of the segment IV drainage vein (left medial superior vein), should be left in the donor to reduce the risk of venous congestion in segment IV. The MHV dominance in right lobe was defined as follows:

regional volume of vein 5 + vein 8/right-lobe volume × 100 > 40%.

Donor operation

Before parenchymal transection, the right lobe was mobilized and the sizeable right inferior hepatic vein (RIHV; >5 mm) was preserved with a caval cuff for reconstruction. After careful definition of biliary anatomy in the hepatic hilum using intraoperative cholangiography, the right hepatic duct was transected. The right portal vein and the right hepatic artery were temporally clamped to clarify the parenchymal transection line.

The surface markings of the donor liver consisted of a line from a point to the middle of the gallbladder fossa anteriorly and inferiorly/dorsally to the left side of the RHV entry to the vena cava. An 8-mm Penrose drain was passed between the RHV superiorly and the portal bifurcation inferiorly to maintain the cutting plane during parenchymal dissection (hanging maneuver technique) (14).

The initial parenchymal transection line should be same as the standard right-lobe donation. When encountering the MHV or V5 peripherally, the cutting line was modified to the left side of the MHV. Parenchymal transection was continued until the junction of the MHV and left hepatic vein without inflow occlusion. The MHV was transected distal to the common trunk with the left hepatic vein. When the hepatic vein from segment IV (left medial superior vein) had a significant drainage region in the remnant liver as determined by 3D CT volumetry, the proximal side of the MHV and the drainage vein of segment IV to the MHV were preserved in the donor (right lobe with partial MHV graft). Perfusion of the graft was done through

Table 1: Characteristics of 217 Right-Lobe Living-Donor Liver Transplantation With or Without Middle Hepatic Vein

	With MHV (n = 40)	Without MHV (n = 177)	p-value
Donor demographics			
Age (years)	41.3 ± 11.8 (range: 21–61)	40.1 ± 11.4 (range: 19–64)	NS
Weight (kg)	58.5 ± 10.5 (range: 40–80)	63.6 ± 10.9 (range: 42–107)	NS
Operation time (min)	432 ± 74.8 (range: 308–528)	402 ± 82.1 (range: 198–660)	NS
Blood loss (g)	243 ± 217 (range: 25–1030)	239 ± 241 (range: 5–2300)	NS
Blood-type combination (identical: compatible: incompatible)	29:5:6	109:34:34	NS
Recipient demographics			
Sex	Male, 29; female, 11	Male, 83; female, 94	
Age (years)	50.1 ± 12.8 (range: 18–66)	42.9 ± 15.2 (range: 16–69)	NS
Weight (kg)	64.3 ± 13.8 (range: 37.1–99.0)	60.0 ± 11.4 (range: 28.3–96.0)	NS
MELD score*	18.8 ± 7.1 (range: 6–37)	20.5 ± 9.2 (range: 6–54)	NS
Operation profiles			
Cold ischemic time (min)	128 ± 83 (range: 30–372)	99 ± 85 (range: 30–372)	NS
Warm ischemic time (min)	59 ± 16 (range: 27–100)	45 ± 16 (range: 22–114)	<0.001
Operation time (min)	781 ± 200 (range: 400–1415)	730 ± 178 (range: 337–1291)	NS
Blood loss (g)	5977 ± 6776 (range: 320–33 000)	7088 ± 9768 (range: 350–60 000)	NS
Graft weight (g)	678.9 ± 165.2 (range: 445–1270)	699.3 ± 120.9 (range: 425–1080)	NS
GRWR** (%)	1.10 ± 0.26 (range: 0.70–1.70)	1.20 ± 0.28 (range: 0.60–2.40)	NS

*Model for end-stage liver disease.
**Graft-to-recipient weight ratio.

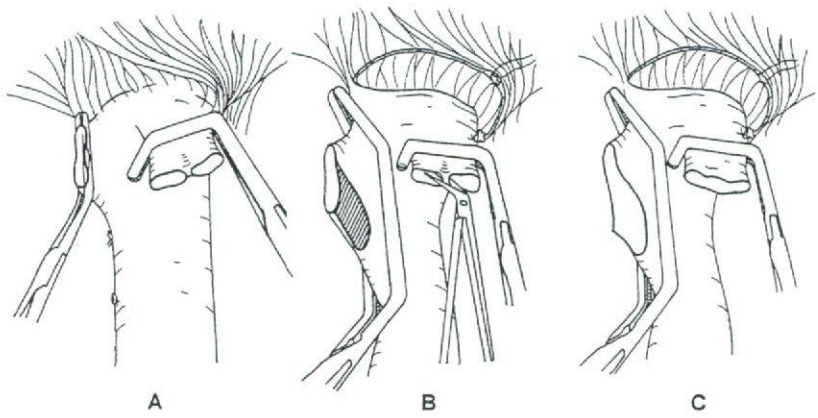


Figure 1: Skeltonization of the inferior vena cava and the hepatic veins to allow adequate spacing for the hepatic vein anastomosis (A,B). The orifice of the RHV was enlarged with a downward incision and an anterior wall excision making an oval orifice to obtain sufficient outflow (B,C).

the right portal vein with a histidine-triptophan-ketoglutarate solution (Dr. Franz Köhler Chemie, Alsbach-Hähnlein, Germany).

Back-table operation

In the case of a right lobe with partial MHV graft, the stump of the MHV was too short to be anastomosed directly to the recipient MHV, and the MHV orifice was not always close enough to the RHV to make a common cuff plasty. The vein graft, i.e. the recipient's portal branch, left portal vein or inferior mesenteric vein or donor's ovarian vein, was prepared according to the size of MHV and was anastomosed as an interposition graft to the MHV stump on the back table (6-0 polypropylene, Prolene, Ethicon, Japan).

Recipient operation

After a total hepatectomy, the top vena cava was freed from its diaphragmatic attachments, by dividing the phrenic veins, and was skeltonized to allow adequate spacing for the hepatic vein anastomosis (Figure 1). During the anhepatic period, a portosystemic shunt was made between the right portal branch and the inferior vena cava (IVC) to prevent portal hypertension in the patients without collaterality. The orifice of the RHV was enlarged with a downward incision and an anterior wall excision making an oval orifice to obtain sufficient outflow. Anastomosis of the RHV was accomplished in an end-to-end fashion with a continuous suture (5-0 Prolene). Significant RIHV was anastomosed to the sidewall of the IVC, the recipient RIHV or the stump of the portosystemic shunt. The interposition vein graft was anastomosed to the recipient's MHV with an interrupted suture in the anterior wall. The patch graft technique was used with an interrupted suture if tension was seen in the anterior wall of the MHV anastomosis. Portal and arterial reconstructions were carried out according to our previous report (15). Biliary reconstruction was carried out with duct-to-duct anastomosis in 36 cases, and with Roux-en-Y hepaticojejunostomy in four cases with 6-0 polydioxanone suture.

Statistical analysis was performed using the generalized Wilcoxon test. Actuarial survival rate was calculated with the nonparametric Kaplan-Meier method and was compared with the Wilcoxon test throughout the study. p-values < 0.02 were considered significant.

The study was approved by the international review board and informed consent was obtained in all the cases.

Results

Donor outcome

A comparison was made between right lobe with MHV grafts from living donors ($n = 40$) and graft cases without MHV ($n = 177$).

The median right lobe with MHV graft donor operation time was 420 min (range: 308–528), and median blood loss was 195 g (range: 25–1030). No blood transfusion was given during the donor operation. Four (10%) out of 40 donors experienced complications that required treatment, including two cases of biliary leakage, one of biliary stricture and one of liver failure. Biliary leakage was successfully resolved with percutaneous aspiration. Biliary stricture was treated by reexploration surgery. The liver failure was caused by unsuspected nonalcoholic steatohepatitis and small remnant liver volume. The donor underwent domino liver transplantation, but died from sepsis 9 months after the initial operation (16).

Of 177 donors of a right lobe without MHV graft in our center, duration of the donor operation was 402 ± 82.1 min and blood loss was 239 ± 241 g. There was no significant difference in duration of surgery or blood loss in the donors between right lobe with or without MHV graft operation. Nineteen (10.7%) out of 177 donors experienced complications that required treatment: 14 cases of biliary leakage; 1 of pulmonary embolization; 3 of wound infection and 1 of wound hernia. Nine donors with biliary leakage required endoscopic nasobiliary tube drainage (17).

To evaluate the impact of right-lobe donation, postoperative liver function tests in the donors were analyzed in relation to the type of graft carried out. However, asparate aminotransferase (AST) and serum bilirubin levels showed no significant difference between right-lobe donation either with or without MHV graft (Figure 2).

Recipient outcome

The median recipient operation time for right lobe with MHV graft was 753 min (range: 400–1415), and the median blood loss was 4100 g (range: 320–33 000). The median cold and warm ischemic time was 103 (range: 30–372) and 57 min (range: 27–100). The median graft weight was 675 g (range: 445–1270), and the median GRWR was 1.10% (range: 0.70–1.70%).

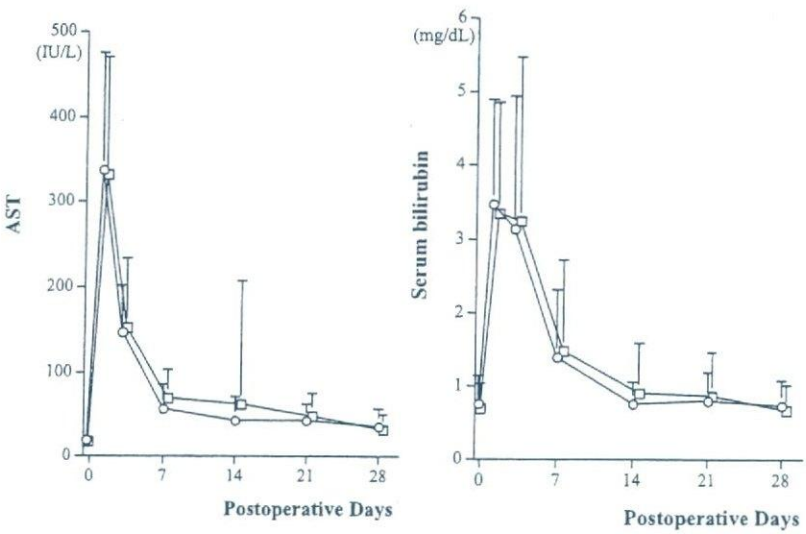


Figure 2: Postoperative liver function tests in the donors. ○: Right lobe with middle hepatic vein graft; □: Right lobe without middle hepatic vein graft.

Among 177 recipients of a right lobe without MHV graft, duration of the recipient operation was 730 ± 178 min and blood loss was 7088 ± 9768 g. The graft weight and GRWR range was 699.3 ± 120.9 g and 1.20 ± 0.28%. The cold and warm ischemic time was 99 ± 85 and 45 ± 16 min, respectively. There was no significant difference in duration of surgery, blood loss and GRWR in the recipients between right lobe either with or without MHV graft. However, the warm ischemic time was significantly longer in the right lobe with MHV graft group ($p < 0.001$).

With regard to liver function tests, there was no significant difference in AST or prothrombin levels between the two groups. Although preoperative serum bilirubin level was significantly lower in the right lobe with MHV graft group ($p < 0.02$), serum bilirubin clearance was much delayed and persistent hyperbilirubinemia was observed in the right lobe without MHV graft group (Figure 3).

Venous reconstruction

With regard to the patients who had right lobe with MHV graft, a direct MHV anastomosis was possible in 12 patients in an end-to-end fashion (30.0%). Of these cases, the common cuff technique of the MHV and RHV in the graft after venoplasty, as reported by Lo et al. (18), was indicated in four. The proximal side of the MHV and the drainage vein of segment IV to the MHV (left medial superior vein) were preserved in 24 donors and a venous interposition graft was necessary in these cases: native portal vein in 19 cases; native inferior mesenteric vein in 2; donor's ovarian vein in 2 and native portal vein patch graft in 1. A Y-shaped portal vein graft was adopted in 13 cases, an I-shaped vein graft in 10 and a patch graft in 1, according to the distance between graft and recipient MHV (Figure 4).

Fourteen RIHV were reconstructed in 13 patients (46.4%). All patients had a patent RHV and MHV anastomosis confirmed by routine Doppler ultrasonography and/or CT/magnetic resonance imaging (MRI) at least 1 month after transplantation. There were no complications related to the hepatic vein anastomosis during the follow-up.

One patient had portal vein thrombosis 19 days after LDLT, and this was successfully treated by reexploration surgery. Two patients developed biliary leakage, which was resolved by percutaneous aspiration. Four cases developed biliary stricture, and this was treated with endosopic retrograde biliary drainage (19). Causes of death were sepsis in one patient, intraabdominal bleeding in one, multiple organ failure secondary to small intestinal perforation in one and severe pneumonia in one. The overall cumulative 3-year graft survival rate of right lobe with MHV graft was 86.2%, with a median follow-up of 18 months (range: 6–36). The cumulative 3-year graft survival rate of 143 right lobe without MHV graft for the same period was 74.8% (Figure 5; $p = 0.38$, NS).

Discussion

Right-lobe LDLT can provide an adequate graft size to compensate for the metabolic demands in most adult recipients, and the clinical outcome has improved in our series (5). One of the controversies in right-lobe LDLT is the potential congestion in the graft anterior segment due to the deprivation of the MHV tributaries. Techniques of venous reconstruction and the graft selection remain an open question.

Our standard technique of harvesting the right-lobe graft requires the transection of the MHV tributaries from the anterior segment to leave the entire MHV in the donor (20,21). To prevent congestion in the anterior segment, several technical modifications were reported. Fang et al. have adopted an extended right-lobe graft with the MHV

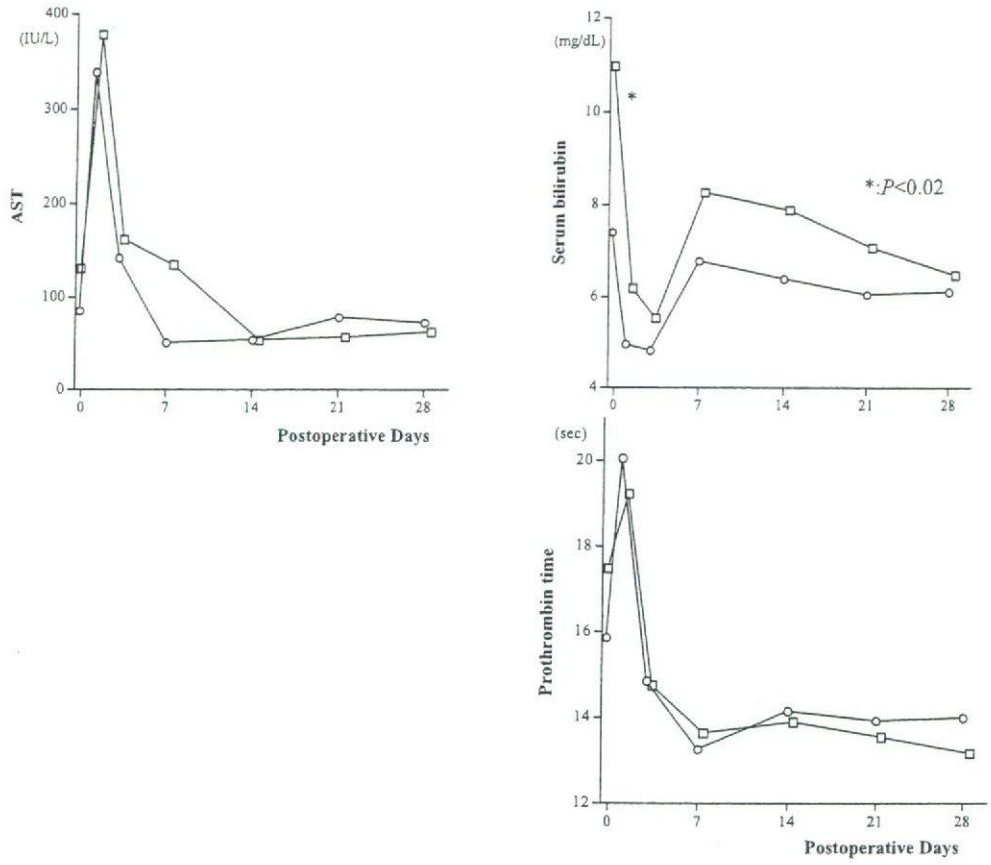
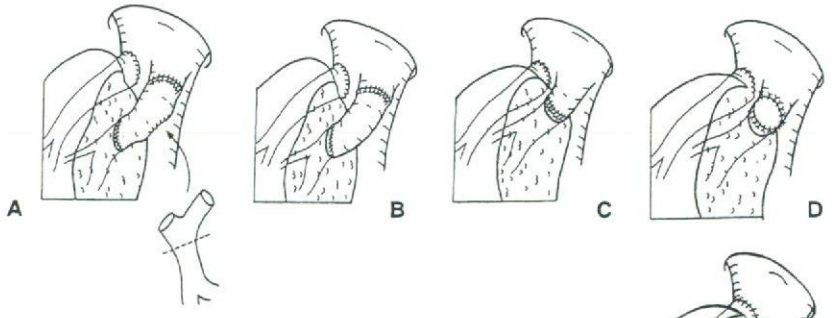


Figure 3: Postoperative liver function tests in the recipients. ○: Right lobe with middle hepatic vein graft; □: Right lobe without middle hepatic vein graft.



- A. Y-shaped portal vein graft (n=13)
- B. I-shaped vein graft (n=10)
- C. Direct anastomosis (n=12)
- D. Patch graft (n=1)
- E. Venoplasty (n=4)

Figure 4: The type of middle hepatic vein anastomosis with/without the use of interposition vein graft. (A) Y-shaped portal vein graft (n = 13), (B) I-shaped vein graft (n = 10), (C) direct anastomosis (n = 12), (D) patch graft (n = 1); and (E) venoplasty (n = 4).

(6,22), and reconstruction of the MHV with an interposition vein graft has also been adopted by the Toronto group (23). Reconstruction of the segment V/VIII branches using jump grafts has been reported both with and without the intraoperative MHV clamp test to confirm graft congestion in some centers (8,24). However, additional venous reconstruction of the anterior segment did not significantly reduce graft congestion defined on MRI despite the patency of reconstructed drainage veins in our previous series (25).

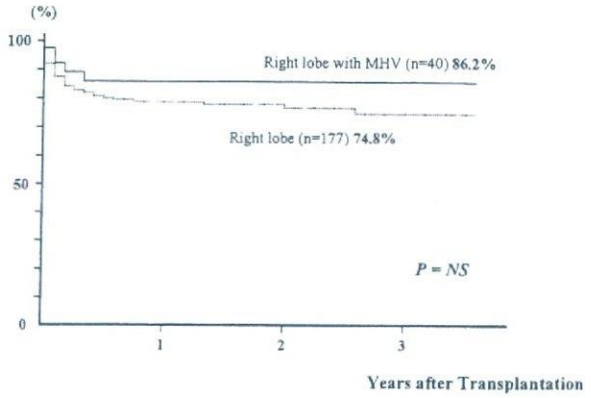


Figure 5: The overall cumulative graft survival rate in right lobe with/without middle hepatic vein.

Based on our previous study, graft congestion in the anterior segment could be well tolerated and improved through intrahepatic anastomosis when the portal and arterial inflow and the RHV outflow were preserved (5,25). Although the regeneration of the posterior segment was shown to be superior to that of the anterior segment, the lack of anterior segment regeneration was resolved by a compensatory regeneration of posterior segment and the graft congestion in the anterior segment did not affect the overall graft regeneration (4). After the initiation of right lobe with MHV graft, however, we experienced some patients who suffered from complications related to 'small-for-size graft'.

Our recent study revealed that right lobe with MHV graft showed no congestion on MRI imaging (26). However, it remains open to question whether or not right lobe with MHV graft should be indicated in all adult recipients. Nakamura et al. suggested that 26.5% of the MHV had proper branches that internally drained from the anterior segment (27). Kinkhabwala et al. reported that 26% of the accessory venous reconstruction from the anterior segment was necessary in right-lobe LDLT (28). We agree with these results that the reconstruction of MHV tributaries was not always necessary and should be indicated according to the preoperative imaging study.

A graft without MHV reconstruction would be given a 'functional liver volume' that corresponded to area drained by the RHV (and RIHV if reconstructed), while a graft with MHV reconstruction would have the anterior segments included in the right-lobe calculation with 3D volumetry. In our preliminary study of 3D CT volumetry in right-lobe LDLT series, the regional volume of V5 and V8 in right lobe was 29.4 ± 11.1% (range: 12.4–56.7%) and 18.0% of the grafts showed MHV dominant (n = 52; data not shown). The importance of drainage vein in the anterior segment could be emphasized in the MHV dominant graft. Moreover, the tolerability of congestion in anterior segment and the compensate regeneration of posterior segment might not be guaranteed in the MHV dominant right-lobe graft. We recommend right lobe with MHV graft or additional vein reconstruction of the anterior segment in the MHV dominant right-lobe graft.

Recently, the Kaohsiung group provided an adequate algorithm for determining the extent of donor hepatectomy in right-lobe LDLT either with or without MHV. The decision to take MHV with the graft was made based on the donor-to-recipient body weight ratio and the size of the MHV tributaries from the anterior segment (29). The initial indication for right lobe with MHV graft in our institution was the GRWR < 1.0% using right-lobe graft. Figure 6 shows our current algorithm for the graft selection after the initial experience of 40 right lobes with MHV LDLTs. The graft selection should be made according to the RHV/MHV dominance, GRWR and remnant liver volume. It is important for avoiding the possibility of anterior segment congestion having information of the MHV dominant before an operation with 3D volumetry. If the graft selection is inconclusive, further discussion should be necessary to secure the recipient benefit as well as donor safety considering the graft quality and metabolic load of the recipient.

The inflow modulation of in 'small-for-size graft' might be an another important issue. Our study showed that elevated portal vein pressure (>20 mmHg) is strongly associated with poor patient survival attributable to 'small-for-size syndrome'. Further elucidation of the pathogenesis behind this phenomenon and efforts to modify portal vein pressure will be a key to improving results (30). Moreover, our recent study suggested that partial diversion of portal flow to systemic circulation and splenic artery ligation might be effective for avoiding injuries that occur in 'small-for-size graft' (31). The same technical modification was adopted in some centers in order to avoid graft congestion and failure by portal overperfusion (32,33). The decrease of portal vein pressure may be able to be used as an effective method to attenuate the 'small-for-size syndrome'. Further discussion about portocaval shunt and splenic artery ligation should be necessary to make a conclusion for the graft selection in right-lobe LDLT.

In determining whether a donor can provide adequate liver volume at acceptable risks, it is important to know not just the remnant liver volume but also the anatomical factors that may affect the functional capacity of the donor remnant liver. It was reported that 9.5% of patients had a left medial superior vein originating from the MHV and draining predominantly the left medial superior segment (27). The impairment of regeneration and functional recovery of segment IV after right lobectomy with MHV has been reported, while the overall regeneration of the remnant liver was not affected by the MVH harvesting in right-lobe LDLT (34).

The mean regional volume of the left medial superior vein in 3D CT evaluation was 159.3 ± 28.8 mL and the

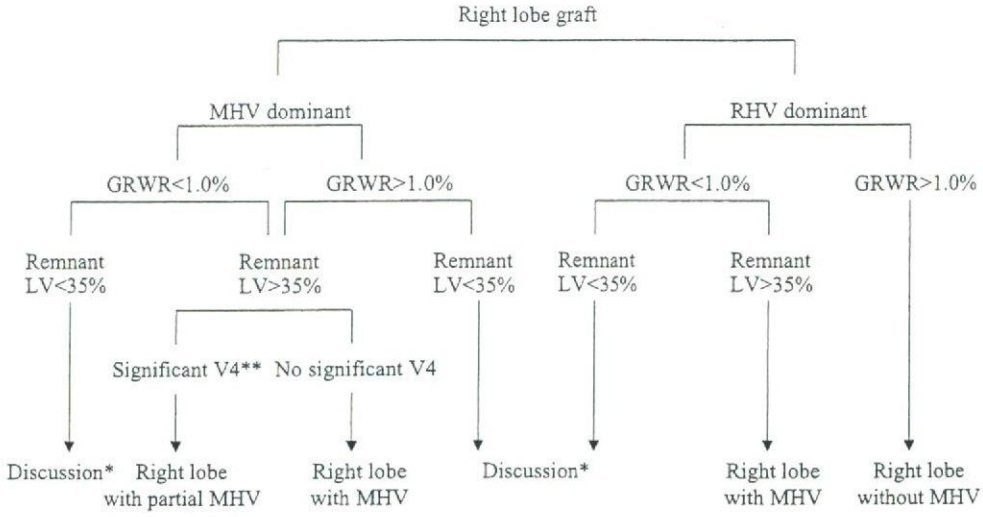


Figure 6: Algorithm for the graft selection. RHV: right hepatic vein; MHV: middle hepatic vein; GRWR: graft-to-recipient weight ratio; LV: liver volume. RHV dominant: regional volume of vein 5 + vein 8/right-lobe volume × 100 < 40% MHV dominant: regional volume of vein 5 + vein 8/right-lobe volume × 100 > 40% *Discussion for; additional vein reconstruction of V5/8, dual graft, auxiliary liver transplantation, ligation of splenic artery and/or partial portocaval shunt, exclude from potential donor candidate **V4: drainage vein of segment IV to the MHV (left medial superior vein).

percentage of the regional volume of left medial superior vein in remnant liver was 40.5 ± 8.0% (range: 27.9–49.9%) in our series (n = 52, data not shown). To obtain more evidence of the segment IV drainage vein and RIHV, a further study of '3D volumetric analysis' is now underway in order to clarify the exact role of these drainage veins. Evaluation of the regional volume of the left medial superior vein is important for the donor safety.

If the regional volume of the left medial superior vein was significant, then the proximal side of the MHV and the left medial superior vein were preserved in the donor, given that the MHV was divided at the side proximal to the left medial superior vein. If the remnant liver volume was revealed to be less than 35% of the whole liver volume, the potential donor was excluded and another donor candidate or option was considered, such as auxiliary liver transplantation, dual liver transplantation and additional vein of the anterior segment reconstruction (35–37).

Manner of the MHV reconstruction is controversial. It was reported that 7.6% of MHV anastomoses were found to be occluded intraoperatively even in an experienced center (22). Direct end-to-end MHV reconstruction was possible in 40.0% of the patients with entire MHV graft. Skeltonization of the IVC and the hepatic veins are important to allow adequate spacing for the hepatic vein anastomosis. In the case of a MHV divided proximal to the left medial superior vein, vein graft should be used to prevent torsion and tension in the anastomosis, as the MHV is considered too short for safe anastomosis. Recently, the common cuff of the MHV and RHV in the graft after venoplasty has been reported (18). While it is an excellent technique, reconstruction of the outflow of the RHV and distal part of the MHV into a single opening may not be possible if their orifices are far apart, and both may need to be implanted separately into the recipient IVC.

In conclusion, we adopted right lobe with MHV graft in 40 LDLT cases. Although no significant differences were revealed in the donor and recipient liver function tests nor in patient survival between right-lobe LDLT with or without MHV, right lobe with MHV graft should be indicated in very selected patients according to algorithm for the graft selection paying special attention to donor safety. It is hoped that as experience increases and refinements are made to the technique, improved outcomes in right-lobe LDLT will be seen.

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