13. Murillas J, Rimola A, Laguno M, de Lazzari E, Rascón J, Agüero F, et al. ESLD-HIV Working Group Investigators. The model for end-stage liver disease score is the best prognostic factor in human immunodeficiency virus 1-infected patients with end-stage liver disease: a prospective cohort study. Liver Transpl. 2009;15:1133–41.
14. Rullier A, Trimoulet P, Neau D, Bernard PH, Foucher J, Lacoste D, et al. Fibrosis is worse in HIV-HCV patients with low-level immunodepression referred for HCV treatment than in HCV-matched patients. Hum Pathol. 2004;35:1088–94.
15. Ragni MV, Moore CG, Soadwa K, Nalesnik MA, Zajko AB, Cortese-Hassett A, et al. HHH Study Group. Impact of HIV on liver fibrosis in men with hepatitis C infection and haemophilia. Haemophilia. 2011;17:103–11.
16. Resino S, Sánchez-Conde M, Berenguer J. Coinfection by human immunodeficiency virus and hepatitis C virus: noninvasive assessment and staging of fibrosis. Curr Opin Infect Dis. 2012;25:564–9.
17. Merchante N, Rivero-Juárez A, Téllez F, Merino D, José Ríos-Villegas M, Márquez-Solero M, et al. Liver stiffness predicts clinical outcome in human immunodeficiency virus/hepatitis C virus-coinfected patients with compensated liver cirrhosis. Hepatology. 2012;56:228–38.
18. Miro JM, Torre-Cisnero J, Moreno A, Tuset M, Quereda C, Laguno M, et al. [GESIDA/GESITRA-SEIMC, PNS and ONT consensus document on solid organ transplant (SOT) in HIV-infected patients in Spain (March, 2005)]. Enferm Infecc Microbiol Clin. 2005;23:353–62.
19. O'Grady J, Taylor C, Brook G. Guidelines for liver transplantation in patients with HIV infection (2005). HIV Med. 2005;6(Suppl 2):149–53.
20. Xia XJ, Liu BC, Su JS, Pei H, Chen H, Li L, et al. Preoperative CD4 count or CD4/CD8 ratio as a useful indicator for postoperative sepsis in HIV-infected patients undergoing abdominal operations. J Surg Res. 2012;174:e25–30.
21. Takatsuki M, Eguchi S, Soyama A, Kanematsu T, Nakao K, Shirasaka T, et al. Evaluation of portal hypertension and prognosis of patients with HIV-HCV co-infection through comtaminated blood product. Acta Hepatol Japonica (KANZO). 2012;53:586–90 (in Japanese).
22. Soyama A, Eguchi S, Takatsuki T, Hidaka M, Muraoka I, Kanematsu T. Analysis of hepatic functional reserve in HIV_HCV co-infected patients. Acta Hepatol Japonica (KANZO). 2012;53:403–8 (in Japanese).
23. López-Diéguez M, Montes ML, Pascual-Pareja JF, Quereda C, Von Wichmann MA, Berenguer J, et al. GESIDA 37/03-FIPSE 36465/03-NEAT IG5 Study Group. The natural history of liver cirrhosis in HIV-hepatitis C virus-coinfected patients. AIDS. 2011;25:899–904.
24. Schreibman I, Gaynor JJ, Jayaweera D, Pyrsopoulos N, Weppler D, Tzakis A, et al. Outcomes after orthotopic liver transplantation in 15 HIV-infected patients. Transplantation. 2007;84:697–705.
25. Duclos-Vallee JC, Feray C, Sebagh M, Sebagh M, Teicher E, Roque-Afonso AM, et al. Survival and recurrence of hepatitis C after liver transplantation in patients coinfected with human immunodeficiency virus and hepatitis C virus. Hepatology. 2008;47:407–17.
26. Miro JM, Montejo M, Castells L, Rafecas A, Moreno S, Agüero F, et al. Spanish OLT in HIV-Infected Patients Working Group investigators. Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. Am J Transplant. 2012;12:1866–76.
27. Anadol E, Beckebaum S, Radecke K, Paul A, Zoufaly A, Bickel M, et al. Orthotopic liver transplantation in human-immunodeficiency-virus-positive patients in Germany. AIDS Res Treat. 2012;2012:4–9.
28. Harbell J, Fung J, Nissen N, Olthoff K, Florman SS, Hanto DW, et al. Surgical complication in 275 HIV-infected liver and/or kidney transplantation recipients. Surgery. 2012;152:376–81.
29. Ragni MV, Devera ME, Roland ME, Wong M, Stosor V, Sherman KE, et al. Liver transplant outcomes in HIV(+) haemophilic men. Haemophilia. 2013;19:134–40.
30. O'Grady JG. Liver transplantation in human immunodeficiency virus/hepatitis C virus-coinfected patients: response needed! Liver Transpl. 2012;18:617–18.
31. Baccarani U, Adani GL, Bragantini F, Londero A, Comuzzi C, Rossetto A, et al. Long-term outcomes of orthotopic liver transplantation in human immunodeficiency virus-infected patients and comparison with human immunodeficiency virus-negative cases. Transplant Proc. 2011;43:1119–22.
32. Tsukada K, Sugawara Y, Kaneko J, Tamura S, Tachikawa N, Morisawa Y, et al. Living donor liver transplantations in HIV- and hepatitis C virus-coinfected hemophiliacs: experience in a single center. Transplantation. 2011;91:1261–4.
33. Terrault NA, Roland ME, Schiano T, Dove L, Wong MT, Poordad F, et al. Solid Organ Transplantation in HIV: Multi-Site Study Investigators. Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection. Liver Transpl. 2012;18:716–26.
34. García F, Plana M, Vidal C, Cruceta A, O'Brien WA, Pantaleo G, et al. Dynamics of viral load rebound and immunological changes after stopping effective antiretroviral therapy. AIDS. 1999;13:F79–86.
35. Neff GW, Bonham A, Tzakis AG, Ragni M, Jayaweera D, Schiff ER, et al. Orthotopic liver transplantation in patients with human immunodeficiency virus and end-stage liver disease. Liver Transpl. 2003;9:239–47.
36. Castells L, Escartín A, Bilbao I, Len O, Allende H, Vargas V, et al. Liver transplantation in HIV-HCV coinfected patients: a case-control study. Transplantation. 2007;83:354–8.
37. Frassetto LA, Browne M, Cheng A, Wolfe AR, Roland ME, Stock PG, et al. Immunosuppressant pharmacokinetics and dosing modifications in HIV-1 infected liver and kidney transplant recipients. Am J Transplant. 2007;7:2816–20.
38. Armstrong MJ, Corbett C, Rowe IA, Taylor GP, Neuberger JM. HTLV-1 in solid-organ transplantation: current challenges and future management strategies. Transplantation. 2012;94:1075–84.
39. Tricot L, Teicher E, Peytavin G, Conti F, Calmus Y, Barrou B, et al. Safety and efficacy of raltegravir in HIV-infected transplant patients cotreated with immunosuppressive drugs. Am J Transplant. 2009;9:1946–52.
40. Ragni MV, Belle SH. Impact of human immunodeficiency virus infection on progression to end-stage liver disease in individuals with hemophilia and hepatitis C virus infection. J Infect Dis. 2001;183:1112–15.
41. Sulkowski MS, Sherman KE, Dieterich DT, Bsharat M, Mahnke L, Rockstroh JK, et al. Combination therapy with telaprevir for chronic hepatitis C virus genotype 1 infection in patients with HIV: a randomized trial. Ann Intern Med. 2013;159:86–96.
42. Polard E, Camus C, Abault AY, Turlin B, Arvieux C, Messner M, et al. Retransplantation for acute liver failure due to combined antiviral agents in an HIV-HCV coinfected liver transplant recipient. Transplantation. 2005;80:1136–8.
43. Lin YL, Mettling C, Portales P, Reynes J, Clot J, Corbeau P. Cell surface CCR5 density determines the post-entry efficiency of R5 HIV-1 infection. Proc Natl Acad Sci U S A. 2002;99:15590–5.
44. Weissman D, Dybul M, Daucher MB, Davey RT Jr, Walker RE, Kovacs JA. Interleukin-2 up-regulates expression of the human immunodeficiency virus fusion coreceptor CCR5 by CD4+ lymphocytes in vivo. J Infect Dis. 2000;181:933–8.
45. Heredia A, Amoroso A, Davis C, Le N, Reardon E, Dominique JK, et al. Rapamycin causes down-regulation of CCR5 and

accumulation of anti-HIV beta-chemokines: an approach to suppress R5 strains of HIV-1. Proc Natl Acad Sci U S A. 2003;100: 10411–16.
46. Di Benedetto F, Di Sandro S, De Ruvo N, Montalti R, Ballarin R, Guerrini GP, et al. First report on a series of HIV patients undergoing rapamycin monotherapy after liver transplantation. Transplantation. 2010;89:733–8.
47. Klintmalm GB, Davis GL, Teperman L, Netto GJ, Washburn K, Rudich SM, et al. A randomized, multicenter study comparing steroid-free immunosuppression and standard immunosuppression for liver transplant recipients with chronic hepatitis C. Liver Transpl. 2011;17:1394–403.
48. Marubashi S, Umeshita K, Asahara T, Fujiwara K, Haga H, Hashimoto T, et al. Steroid-free living donor liver transplantation for HCV – a multicenter prospective cohort study in Japan. Clin Transplant. 2012;26:857–67.
49. Di Benedetto F, Tarantino G, Ercolani G, Baccarani U, Montalti R, De Ruvo N, et al. Multicenter Italian experience in liver transplantation for hepatocellular carcinoma in HIV-infected patients. Oncologist. 2013;18:592–9.
50. Baccarani U, Adani GL, Tavio M, Viale P. Liver transplantation for hepatocellular carcinoma: the impact of human immunodeficiency virus infection. Hepatology. 2011;53:2138–9.

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原　著

HIV/HCV 重複感染患者の肝障害病期診断における acoustic radiation force impulse（ARFI）elastography の有用性

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要旨：【背景】HIV コントロールの改善により HIV/HCV 重複感染者の死因として肝疾患の割合が増加している．【目的】重複感染者における acoustic radiation force impulse（ARFI）elastography による肝疾患進行度評価の有用性を明らかにする．【方法】肝実質硬度をせん断弾性波の速度（Vs）として定量化し，他の肝機能評価項目との相関を検討．【結果】Vs 値は血小板数，脾容積，ヒアルロン酸，IV 型コラーゲン，アシアロシンチ LHL15 値と有意な相関あり．【考察】ARFI は肝線維化・予備能評価に有用であり，HIV/HCV 重複感染者に対する非侵襲的で正確な肝疾患進行度評価に応用可能と考えられた．

索引用語：HIV/HCV 重複感染，肝移植，ARFI elastography，腹部超音波検査

はじめに

1990 年代後半の anti-retroviral therapy（ART）の登場によって human immunodeficiency virus（HIV）のコントロールは改善し，HIV 感染例の死亡数は減少するとともに死因に大きな変化が見られた．HIV 感染者における acquired immunodeficiency syndrome（AIDS）以外の死亡で最も多いのは肝疾患であり，その原因の多くは hepatitis C virus（HCV）感染症であった（Weber ら[1)]）．本邦においても平成 22 年度厚生労働省調査で，HIV/HCV 重複感染患者における死因の 1/3 は肝疾患であることが報告された[2)]．本邦における HIV 感染者の 19.2% が HCV に重複感染しており，その原因のほとんどが過去の HIV/HCV 混入血液製剤の投与であるが，血液製剤による HIV 感染者の HCV 抗体陽性率は 97% と極めて高い[3)]．このような薬害による HIV/HCV 重複感染者に対する的確な病期分類は，救済医療としての面からも今後その重要性が増すと考えられる．

重複感染者では単独感染者に比して線維化の進行が早いと報告されているが[4)]，過去の血液製剤の使用による重複感染者では血友病を有しているため，肝生検による線維化評価は困難である．近年，非侵襲的な肝線維化評価の方法として acoustic radiation force impulse（ARFI）elastography の有用性が報告されている[5)]．ARFI とは収束超音波パルスで組織に微細な変形をおこし，パルスが止んで組織が元の形に戻る際に体表に対して水平に発生するせん断弾性波の速度（velocity of shear wave；Vs）を測定し，組織の硬度を定量

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化したものである．今回われわれは，HIV/HCV重複感染者に対して，ARFI elastographyによる肝線維化評価の有用性を明らかにする目的で検討を行った．またわれわれは，重複感染者においては一般肝機能検査などが正常でも肝予備能が低下している症例が少なからず存在することを報告した（曽山ら[6]）．ARFIの測定結果と予備能の関連についても検討を行った．

I 対象と方法

2009年9月から2013年6月までに当院で精査を行ったHIV/HCV重複感染患者37名のうち，ARFI elastographyを施行したChild分類A症例23例を対象とした．37例はいずれも原疾患に血友病を有し，過去の血液製剤の使用によってHIV/HCV重複感染をきたした症例であり，全例男性，年齢の中央値は40歳（30～63歳）であった．肝機能の内訳はChild Aが34例，Bが1例，Cが2例であった．対照として同時期に当院消化器内科で加療を行ったHCV単独感染症例18例，および健常群として同時期に当院でグラフト採取術を施行した生体肝移植ドナー10例と比較を行った．まずARFIを用いて肝線維化をVsとして数値化し（右肋間より右葉のVs値を5回測定し平均値を用いた），重複感染群，HCV単独感染群，健常群でVs値の比較を行った．次にHIV/HCV重複感染群においてVs値（肝右葉・左葉それぞれでVs値を5回ずつ測定してそれぞれの平均値を算出し，左右の値の平均値を肝全体のVs値として用いた）とALT，総ビリルビン値，血小板数，CTでの肝形態，脾容積，ヒアルロン酸，IV型コラーゲン，ICG15分停滞率，アシアロシンチLHL15値との相関を検討した．脾容積はAquilion™，64列（東芝メディカルシステムズ，日本）を用いて動脈相，門脈相，平衡相の3相で造影CTを撮影し，平衡相の脾容積をSYNAPSE VINCENT（富士フイルムメディカル，日本）を用いてvolumetryを行い測定した．また肝形態の評価は当院の放射線科医師が読影し，正常肝の他に脂肪肝，慢性肝炎，肝硬変の4つに分類した．統計学的検定には，統計解析ソフトystat 2008（医学図書出版，東京）を用い，2群間比較にはMann-Whitneyの順位和検定を，相関についてはSpearmanの順位相関を行った．

II 結 果

Vs値（以下中央値と範囲）はHIV/HCV重複感染群で1.27（0.98～2.61）m/s，HCV単独感染群で1.27（0.85～3.00）m/s，健常群で1.08（0.98～1.33）m/sであり，重複感染群は健常群に比べて有意に高値であった（$p=0.010$）が，重複感染群とHCV単独感染群，およびHCV単独感染群と健常群では有意差を認めなかった（それぞれ$p=0.436$，$p=0.059$，Figure 1）．またARFI施行時の年齢については，重複感染群が46（31～63）歳に対して単独感染群が61（33～76）歳と，重複感染群は単独感染群に比べて有意に若年であった（$p=0.008$，Figure 1）．

重複感染群におけるVs値と他の肝機能検査の比較では，ALT（$p=0.358$）や総ビリルビン値（$p=0.949$）では両群に相関を認めなかったが，血小板数（$r=0.737$，$p<0.001$），脾容積（$r=0.592$，$p=0.006$），ヒアルロン酸（$r=0.637$，$p=0.003$），IV型コラーゲン（$r=0.569$，$p=0.009$）はVs値と有意な相関を認めた（Figure 2）．またCTで正常肝を示したものは23例中6例のみで，その他の内訳は脂肪肝1例，慢性肝炎8例，肝硬変8例であった．CTによる形態評価とVs値の相関については，正常肝6例で1.24（1.11～2.12）m/s，その他の17例では1.87（1.14～3.04）m/sであり，両群に有意差を認めなかった（$p=0.058$）．肝予備能評価項目との比較検討では，ICG15分停滞率（$p=0.054$）とは相関を認めなかったものの，アシアロシンチLHL15（$r=0.503$，$p=0.024$）とは有意な相関を認めた（Figure 3）．

III 考 察

HIV/HCV重複感染者のChild A症例においては，健常者と比較してVs値が有意に高値であり，ARFI elastographyの線維化測定は正しく行われていると考えられた．またVs値は，肝線維化のマーカーとして知られるヒアルロン酸やIV型コラーゲン，門脈圧亢進症の所見である血小板数，脾容積と相関を認めた．今回の検討では血友病のため肝生検を行っておらず，組織学的な線維

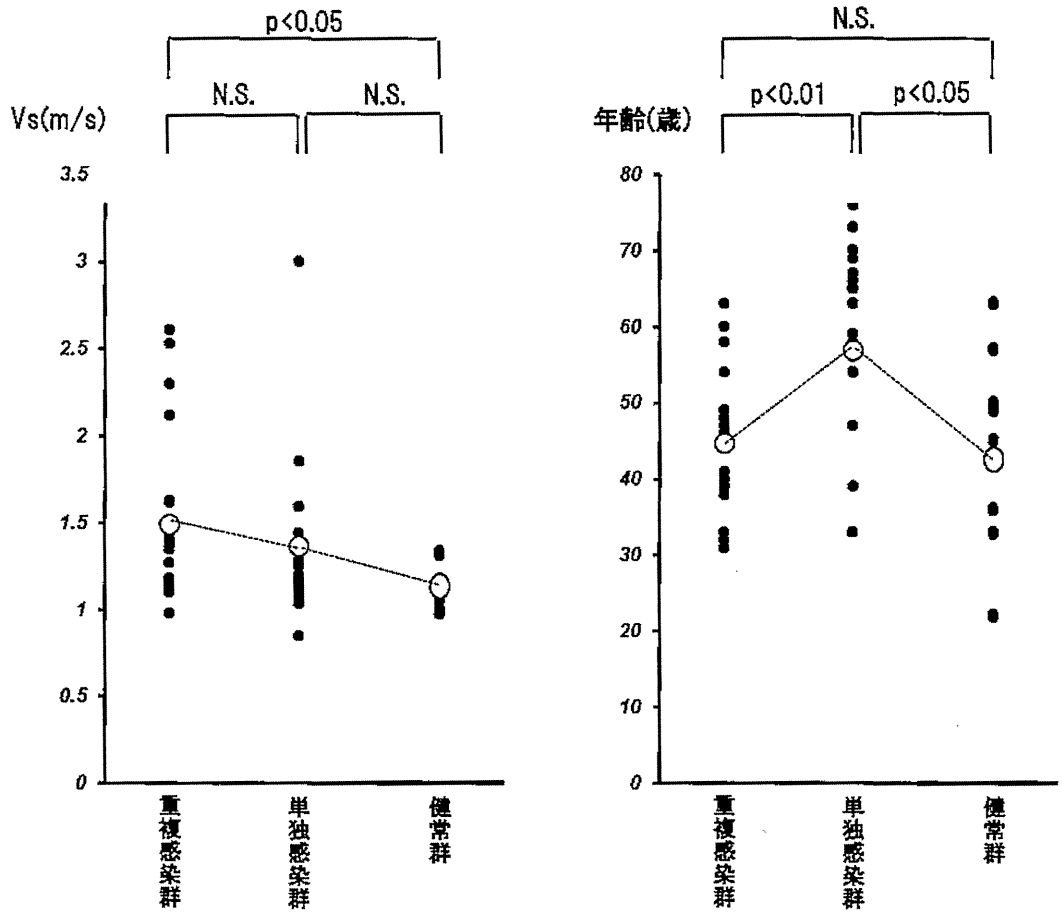

Figure 1. Comparison of Vs and age among HIV/HCV co-infected patients, HCV mono-infected patients, and healthy control (living donor liver transplantation (LDLT) donor).

化の評価はできていないが，HIV/HCV 重複感染者では Child A 症例であっても肝線維化が進行している症例を含んでいることを反映していると思われた．重複感染群と HCV 単独感染群との比較では Vs 値に有意差を認めなかったが，測定時の年齢については，重複感染群の方が有意に若年であった．視点を変えれば，重複感染においては若年者でも既に単独感染の高齢者と同等の線維化をきたしているということになる．重複感染者においては肝線維化の進行が HCV 単独感染群より早いことが諸家から報告されている[6]ことを念頭に，若年期から適切な治療のタイミングを逸しないように，綿密なフォローアップを行うことが重要である．

重複感染者においては HIV/HCV の相互作用や ART による薬剤性肝障害によって肝線維化の進行が早い事例が存在することに加えて，肝実質障害に比して門脈圧亢進症の進行が早い非硬変性門脈圧亢進症の病態を呈することもあり[7][8]，一般肝機能検査のみでは病勢を正確に評価できないケースを多数認める．今回の検討では Vs 値は ALT やビリルビン値などの一般肝機能検査とは相関を示さず，また CT で正常肝であった症例と異常を認めた症例間の Vs 値に有意差は認めなかった．ARFI により Vs 値を測定することは従来の一般肝機能検査とは違った角度から肝機能を評価することとなり，より正確な病期診断につながる可能性が示唆された．

今回の検討で興味深いのは，ARFI elastography の結果が，肝予備能評価と相関していたことである．重複感染者は現在全国各地でフォローアップされているが，肝臓病専門施設や地域中核病院から遠方に居住する患者では，定期的な肝予備能評価が行われていないことも少なくない．さ

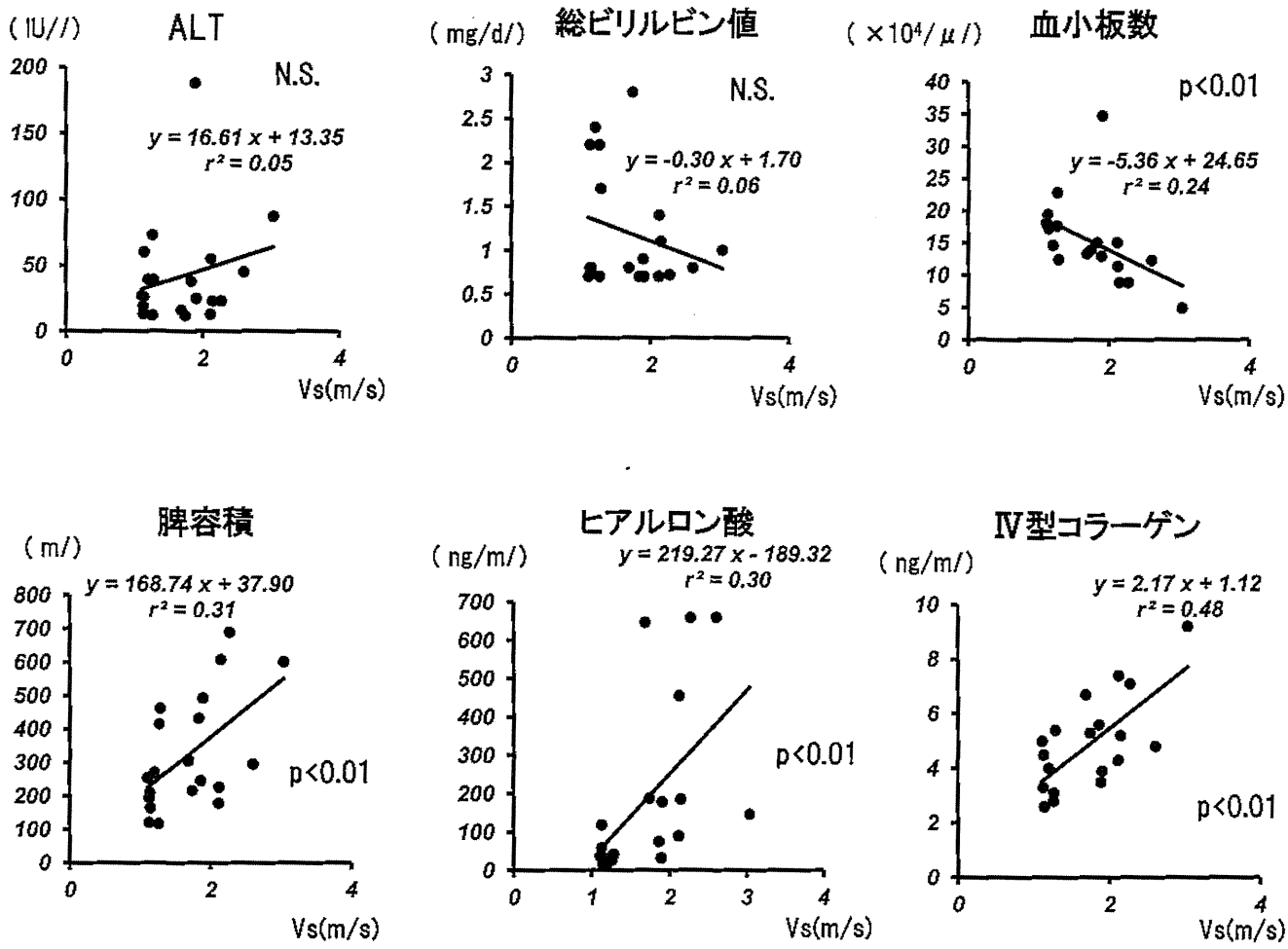

Figure 2. Correlation between Vs and other liver function (ALT, total bilirubin, and platelet counts), splenic volume, hyaluronic acid, type IV collagen.

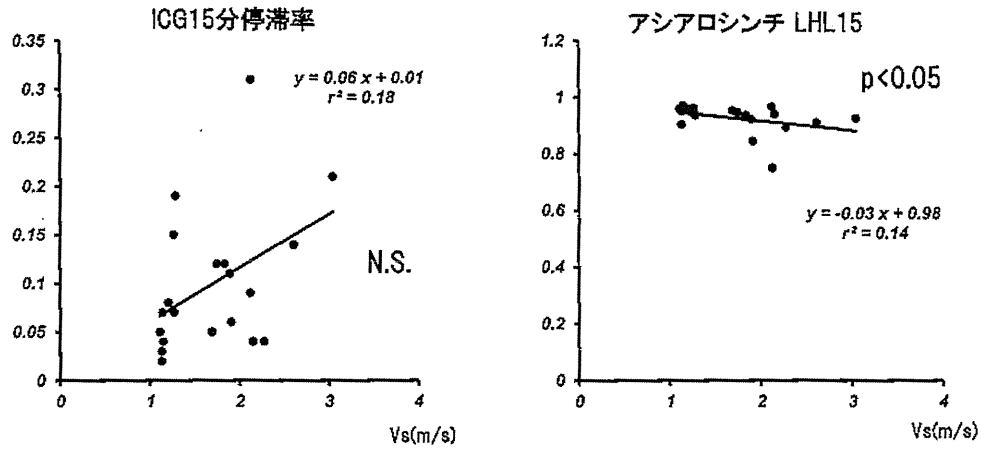

Figure 3. Correlation between Vs and hepatic functional reserve (indocyanine green retention rate and LHL15 in 99mTc-GSA scintigraphy).

らに本邦における重複感染の原因の大半は血友病に対する血液製剤使用にあり，凝固異常のため肝生検による病期診断が困難であるという点が，重複感染者の病期評価を困難にしている一因と思わ

れる．超音波検査はシンチグラムなどに比べて簡便で特別な装置を必要とせず，肝疾患専門施設以外でも導入しやすいと思われる．また凝固能の異常があっても繰り返し施行することが可能であり，病状の進行を経時的に評価することができる．このように従来の肝線維化・肝予備能の指標と有意な相関を示し，かつ非侵襲的なARFI elastographyは有用な診断ツールと考えられる．

前述の如く，HIV/HCV重複感染者における肝線維化の進行は多因子に影響される．ARFIにより肝線維化の程度を数値化し，その経時的測定値と，各種臨床データや服薬歴などとの相関を明らかにすることで，重複感染者における線維化進行のメカニズム解明につながる可能性がある．ひいては個々の症例が有する危険因子から，肝疾患の正確な予後予測へとつながることが期待される．

HIV/HCV重複感染者におけるelastographyを用いた肝線維化評価としては，transient elastography（FibroScan®，Echosens，フランス）の測定結果と組織学的な肝線維化進行度との有意な相関が報告されている[9][10]．FibroScanもARFIと同様にせん断波の速度を測定することにより肝硬度を評価する装置であるが[11]，FibroScanは低周波弾性波を用いて体表と垂直方向の弾性波伝搬速度を測定するため，腹水貯留例や高度肥満例においては測定が困難とされている[12]．またARFIではBモードも可能であり，ルーチンの観察を行った後に肝線維化を測定するといった使用法も可能であるという利点がある．ARFIとFibroScanの精度については，ウイルス性肝炎における検討ではほぼ同等とする報告が多い[5][13]．HIV/HCV重複感染者におけるARFIと組織学的線維化の相関についてはいまだ報告はなく，今後の検討が必要と思われる．

近年，HIV/HCV重複感染者に対する肝移植の成績が欧米を中心に報告されており，その成績は3年生存率が60%程度であった[14]．これはHCV単独感染よりやや不良であるが徐々に改善が見られている．近年ではRaltegravirのようにTacrolimusとの相互作用を認めない抗HIV薬も登場しており，今後移植後の免疫抑制剤の調整が容易となることでさらなる成績の改善が期待される[15][16]．

結　語

ARFI elastographyは，HIV/HCV重複感染者の肝線維化や肝予備能評価のツールとして，肝疾患病期診断に有用であり，肝移植も含めた適切な治療の選択の判断材料となると思われた．

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本論文内容に関連する著者の利益相反
：なし

文　献

1) Weber R, Sabin CA, Friis-Møller N, et al : Liver-related deaths in persons infected with the human immunodeficiency virus : the D : A : D study. Arch Intern Med 166 ; 1632-1641 : 2006
2) エイズ予防財団：血液凝固異常症全国調査厚生労働省委託事業：平成22年度報告書，2010
3) 平成16年度厚生労働省科学研究費補助金エイズ対策研究事業「HIV感染症に合併する肝疾患に関する研究」班：HIV・HCV重複感染時の診療ガイドライン，2005
4) Benhamou Y, Bochet M, Di Martino V, et al : Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus coinfected patients. The Multivirc Group. Hepatology 30 ; 1054-1058 : 1999
5) Sporea I, Bota S, Peck-Radosavljevic M, et al : Acoustic Radiation Force Impulse elastography for fibrosis evaluation in patients with chronic hepatitis C : an international multicenter study. Eur J Radiol 81 ; 4112-4118 : 2012
6) 曽山明彦，江口　晋，高槻光寿，他：HIV-HCV重複感染患者における肝予備能評価の重要性．肝臓　53 ; 403-408 : 2012
7) Kovari H, Ledergerber B, Peter U, et al : Association of noncirrhotic portal hypertension in HIV-infected persons and antiretroviral therapy with didanosine : a nested case-control study. Clin Infect Dis 49 ; 626-635 : 2009
8) Vispo E, Moreno A, Maida I, et al : Noncirrhotic portal hypertension in HIV-infected patients : unique clinical and pathological findings. AIDS 24 ; 1171-1176 : 2010

9) de Lédinghen V, Douvin C, Kettaneh A, et al : Diagnosis of hepatic fibrosis and cirrhosis by transient elastography in HIV/hepatitis C virus-coinfected patients. J Acquir Immune Defic Syndr 41 ; 175–179 : 2006
10) Sánchez-Conde M, Montes-Ramírez ML, Miralles P, et al : Comparison of transient elastography and liver biopsy for the assessment of liver fibrosis in HIV/hepatitis C virus-coinfected patients and correlation with noninvasive serum markers. J Viral Hepat 17 ; 280–286 : 2010
11) Sandrin L, Fourquet B, Hasquenoph JM, et al : Transient elastography : a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol 29 ; 1705–1713 : 2003
12) Fraquelli M, Rigamonti C, Casazza G, et al : Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut 56 ; 968–973 : 2007
13) Friedrich-Rust M, Wunder K, Kriener S, et al : Liver fibrosis in viral hepatitis : noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography. Radiology 252 ; 595–604 : 2009
14) Joshi D, O'Grady J, Taylor C, et al : Liver transplantation in human immunodeficiency virus-positive patients. Liver Transpl 17 ; 881–890 : 2011
15) Cousins D, Topping K, Lee V, et al : Successful tacrolimus treatment following renal transplant in a HIV-infected patient with raltegravir previously treated with a protease inhibitor based regimen. Drug Metabol Drug Interact 26 ; 139–141 : 2011
16) Bickel M, Anadol E, Vogel M, et al : Daily dosing of tacrolimus in patients treated with HIV-1 therapy containing a ritonavir-boosted protease inhibitor or raltegravir. J Antimicrob Chemother 65 ; 999–1004 : 2010

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Acoustic radiation force impulse elastography for liver disease staging in human immunodeficiency virus and hepatitis C virus co-infection

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Background : Survival of human immunodeficiency virus (HIV)-infected patients has improved due to the widespread use of anti-retroviral therapy. However, mortality has increased when HIV-infected patients are co-infected with hepatitis C virus (HCV), and the liver disease in such patients is rapidly progressive compared with that in HCV monoinfected patients. Therefore, accurate staging of the liver disease is critical when determining appropriate treatment. Aim : To clarify the efficacy of acoustic radiation force impulse (ARFI) elastography for the evaluation of liver fibrosis and hepatic functional reserve in HIV/HCV co-infected patients. Methods : The correlation of shear wave velocity (Vs), measured by ARFI elastography, with liver fibrosis or hepatic functional reserve was analyzed. Results : Vs was significantly correlated with platelet count, splenic volume, hyaluronic acid, type IV collagen, and LHL15 (receptor index : uptake ratio of the liver to the liver plus heart at 15min) in 99mTc-GSA (technetium-99m-diethylenetriaminepentaacetic acid-galactosyl human serum albumin) scintigraphy. Conclusion : ARFI elastography was useful for the staging of liver disease in HIV/HCV co-infected patients and it facilitated minimally invasive and accessible evaluation of fibrosis and functional reserve.

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Review Article

Liver transplantation for HIV/hepatitis C virus co-infected patients

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Since the introduction of antiretroviral therapy (ART) in the mid-1990s, AIDS-related death has been dramatically reduced, and hepatitis-C-virus (HCV)-related liver failure or hepatocellular carcinoma has currently become the leading cause of death in HIV/HCV co-infected patients. Liver transplantation may be one of the treatments of choices in such cases, but the indications for transplantation, perioperative management including both HIV and HCV treatments, immunosuppression and the prevention/treatment of infectious complications are all still topics of debate. With the improved understanding of the viral behaviors of both HIV and HCV and the development of novel strategies, especially to avoid drug interactions between ART and immunosuppression, liver transplantation has become a realistic treatment for HIV/HCV co-infected patients.

Key words: hepatitis C virus, HIV, liver transplantation

INTRODUCTION

IN JAPAN, IN the late 1980s, contaminated blood production of coagulation factor for hemophilia caused co-infection of HIV and hepatitis C virus (HCV). Actually, greater than 90% of HIV-infected patients have HCV as well.[1]

After antiretroviral therapy (ART) was introduced in the late 1990s, successful control of HIV was achieved in most cases and death due to AIDS was dramatically reduced, but HCV-related death due to liver failure or hepatocellular carcinoma became a serious problem, not only in Japan, but all over the world.[2–6] In such cases, liver transplantation (LT) is the only treatment option to achieve long-term survival, but several modifications of perioperative management are required. In this review, the outcome and the points of management of LT for HIV/HCV co-infected patients were reviewed.

REPORTED OUTCOME OF LT FOR HIV/HCV PATIENTS

THE REPORTED OUTCOMES of LT for HIV and HIV/HCV co-infected patients from Western countries after the introduction of ART are summarized in Table 1.[7–11] In general, most reports concluded that the results were worse than in the cases with HCV mono-infection, with a 3-year survival of approximately 60–70%. In Japan, the Tokyo group reported six cases of living donor liver transplantation (LDLT) between 2001 and 2004, of whom four died.[12] These unfavorable outcomes are likely related to the difficulties of determining the indications for LT and of perioperative management, including HIV/HCV treatment and the prevention and treatment of infectious complications. Terrault *et al.* reported that older donor age, combined kidney–liver transplantation, an anti-HCV positive donor and a body mass index of less than 21 kg/m^2 were independent predictors of graft loss.[10] After transplantation, several studies showed that acute cellular rejection was more frequent and severer in HIV/HCV co-infected patients than that in HCV mono-infected patients, possibly due to the difficulties in achieving optimal immunosuppression because of interactions between antiretroviral agents and immunosuppression.[10,11]

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Table 1 Outcome of liver transplantation for HIV/hepatitis C virus co-infection

Authors	Publication year	Country	*n*	Patient survival (%)		
				1 year	3 years	5 years
de Vera *et al.*[7]	2006	USA	27	67	56	33
Schreibman *et al.*[8]	2007	USA	15	73	73	–
Duclos-Vallee *et al.*[9]	2008	France	35	–	73	51
Terrault *et al.*[10]	2012	USA	89	76	60	–
Miro *et al.*[11]	2012	Spain	84	88	62	54

SPECIAL ISSUES REGARDING LT INDICATIONS FOR HIV/HCV CO-INFECTION

ART-related non-cirrhotic portal hypertension

IN HCV MONO-INFECTED patients, LT should be considered when the patients develop deteriorated liver function as indicated by a Child–Pugh classification of B or C. In HIV/HCV co-infected patients, liver failure due to HCV hepatitis was generally enhanced by ART-related hepatotoxicity, especially non-cirrhotic portal hypertension.[13–15] Accordingly, not only in cases with deteriorated liver function but also in class A cases, the patients can easily develop severe liver dysfunction suddenly,[16,17] so that all HIV/HCV co-infected patients should be carefully followed up so as not to miss the chance for LT. Also, Murillas *et al.* reported that Model for End-Stage Liver Disease (MELD) score is the best prognostic factor in HIV-infected patients,[18] so that HIV/HCV co-infected patients may be considered for LT before MELD score increase to achieve comparable results with HCV mono-infected patients. Several studies showed the aggressive fibrosis in HIV/HCV co-infected patients compared with HCV mono-infected patients,[19,20] but the mechanism of this aggressive fibrosis remains unclear. Recently, transient elastography or acoustic radiation force impulse imaging to check for liver stiffness has been introduced as an effective and non-invasive modality to determine patients' candidacy for LT.[21–23]

Count of CD4$^+$ T lymphocytes

Generally, the count of CD4$^+$ T lymphocytes has been required to be more than 200/μL to perform general elective surgeries in HIV-infected patients,[24] but in HIV/HCV co-infected patients, current studies show that a count of more than 100/μL is acceptable,[25,26] because patients generally have portal hypertension which can cause pancytopenia. In such patients, the ratio of CD4/CD8 is reported to be a feasible marker to predict postoperative complications including opportunistic infections. When the ratio is less than 0.15, the incidence of infectious complications is significantly higher.[27]

Preoperative infections

In regard to latent opportunistic infections that occur before LT, they are not absolute contraindications when they can be expected to be controlled.[28] Infections regarded as contraindications for LT included uncontrollable multidrug resistance HIV infection, chronic *Cryptosporidium enteritis*, progressive multifocal leukoencephalopathy and lymphoma.[29]

MANAGEMENT OF HIV/HCV IN LT

Management of HIV

THE NUMBER OF HIV RNA copies before LT is suggested as an independent risk factor of postoperative mortality, so that HIV should be controlled sufficiently before LT.[30] Accordingly, in the patients who are under consideration to receive LT, ART can be safely stopped before LT because HIV is generally well-controlled for a long period by ART. After LT, ART should be restarted as soon as possible because HIV RNA appears at 3–30 days after ART is stopped,[31] but the timing of restart of ART depends on the patient's condition, including liver function.[32] As long as the liver function has not fully recovered, or partial liver graft such as in LDLT has not sufficiently regenerated yet, ART cannot be started. Castells *et al.* reported in their case–control study that ART was started at a median of 8 days after LT (range, 4–28 days).[33] In principle, the ART administrated after LT should be the same as the pretransplant regimen, but the majority of ART drugs including protease inhibitor (PI) and non-nucleoside reverse transcriptase inhibitor (NNRTI) have interactions with calcineurin inhibitors

(CNI) or mammalian target of rapamycin (mTOR),[34] so that the monitoring of blood levels of immunosuppression is extremely important to avoid infectious complications or rejection. Currently, a novel HIV-1 integrase inhibitor, raltegravir (RAL), is expected to be a feasible drug because it has no interactions with CNI, unlike other drugs.[35,36]

Management of HCV

The treatment strategy for HCV in HIV/HCV co-infected patients is the same as in HCV mono-infected patients. Combination therapy of pegylated interferon (PEG IFN) and ribavirin is the standard treatment both before and after LT. The timing of the induction therapy after LT is controversial. A Tokyo group proposed early induction as a preemptive therapy before patients develop hepatitis,[37] while several other reports showed favorable results when the treatment was administrated only after the development of hepatitis was confirmed by liver biopsy.[38,39] Theoretically, the treatment should be started as soon as possible, because in HIV/HCV co-infected patients, HCV recurrence may be accelerated in an immunocompromised state.[30,40] The novel protease inhibitor, telaprevir, is currently introduced as an effective drug to achieve sustained viral response of 70%, even in genotype 1b, with PEG IFN/ribavirin in a non-transplant setting,[41] but this drug is metabolized via cytochrome P450 as a substrate, as are CNI and various protease inhibitors of ART for HIV. Close monitoring of the CNI trough level should be performed, and although triple therapy with telaprevir/PEG IFN/ribavirin is currently reported to be effective to prevent HCV recurrence after LT in HCV mono-infected cases, special attention should be paid when this regimen is adapted in HIV/HCV co-infected patients.

IMMUNOSUPPRESSION

AS PREVIOUSLY MENTIONED, many factors including ART, anti-HCV treatment and an HIV-related immunocompromised state make post-LT immunosuppressive treatment difficult. Many ART drugs, both PI and NNRTI, cause instability in the blood concentration of CNI through the cytochrome P3A4 (CYP3A4)-related metabolism. Most PI cause the overconcentration of CNI by inhibiting CYP3A4, while most NNRTI cause decreased levels of CNI by stimulating CYP3A4.[29,42] As mentioned earlier, RAL is introduced as a key drug in LT in HIV positive patients, because the metabolism of this drug is not related to CYP450, so it does not affect the blood concentration of CNI. Several reports have demonstrated both the *in vitro* and *in vivo* effectiveness of rapamycin in reducing HIV replication,[43–45] and Di Benedetto *et al.* found that rapamycin monotherapy was significantly beneficial in long-term immunosuppression maintenance and HIV control after LT.[46] Mycophenolate mofetil is expected to be an effective immunosuppressive drug because of its efficacy in reducing HIV infection by both virological and immunological mechanisms.[47–49] Using these drugs, a more effective regimen of immunosuppression with ART may be established.

In regard to the steroid, several studies proposed that a steroid-free regimen can be safely applied and effective in LT for HCV cirrhosis. Also, in HIV/HCV co-infected patients, steroid-free protocol may be beneficial to prevent both HIV and HCV recurrence after LT.[50,51]

CONCLUSIONS

LIVER TRANSPLANTATION FOR HIV/HCV co-infected patients remains challenging, but with recent developments in perioperative management and novel drugs for both HIV and HCV, the results are likely to be improved.

REFERENCES

1 Eguchi S, Soyama A, Hidaka M *et al.* Liver transplantation for patients with human immunodeficiency virus and hepatitis C virus coinfection with special reference to hemophiliac recipients in Japan. *Surg Today* 2011; **41**: 1325–31.
2 Weber R, Sabin CA, Friis-Moller N *et al.* Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med* 2006; **166**: 1632–41.
3 Rosenthal E, Pialoux G, Bernard N *et al.* Liver-related mortality in human-immunodeficiency-virus-infected patients between 1995 and 2003 in the French GERMIVIC Joint Study Group Network (MORTAVIC 2003 Study). *J Viral Hepat* 2007; **14**: 183–8.
4 Bica I, McGovern B, Dhar R *et al.* Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis* 2001; **32**: 492–7.
5 Darby SC, Ewart DW, Giangrande PL *et al.* Mortality from liver cancer and liver disease in haemophilic men and boys in UK given blood products contaminated with hepatitis C. UK Haemophilia Centre Directors' Organisation. *Lancet* 1997; **350** (9089): 1425–31.
6 Thio CL, Seaberg EC, Skolasky R *et al.* HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). *Lancet* 2002; **360** (9349): 1921–6.

7 de Vera ME, Dvorchik I, Tom K *et al.* Survival of liver transplant patients coinfected with HIV and HCV is adversely impacted by recurrent hepatitis C. *Am J Transplant* 2006; **6**: 2983–93.
8 Schreibman I, Gaynor JJ, Jayaweera D *et al.* Outcomes after orthotopic liver transplantation in 15 HIV-infected patients. *Transplantation* 2007; **84**: 697–705.
9 Duclos-Vallee JC, Feray C, Sebagh M *et al.* Survival and recurrence of hepatitis C after liver transplantation in patients coinfected with human immunodeficiency virus and hepatitis C virus. *Hepatology* 2008; **47**: 407–17.
10 Terrault NA, Roland ME, Schiano T *et al.*, Solid Organ Transplantation in HIV: Multi-Site Study Investigators. Outcomes of liver transplant recipients with hepatitis C and human immunodeficiency virus coinfection. *Liver Transpl* 2012; **18**: 716–26.
11 Miro JM, Montejo M, Castells L *et al.*, Spanish OLT in HIV-Infected Patients Working Group Investigators. Outcome of HCV/HIV-coinfected liver transplant recipients: a prospective and multicenter cohort study. *Am J Transplant* 2012; **12**: 1866–76.
12 Tsukada K, Sugawara Y, Kaneko J *et al.* Living donor liver transplantations in HIV- and hepatitis C virus-coinfected hemophiliacs: experience in a single center. *Transplantation* 2011; **91**: 1261–4.
13 Vispo E, Moreno A, Maida I *et al.* Noncirrhotic portal hypertension in HIV-infected patients: unique clinical and pathological findings. *AIDS* 2010; **24**: 1171–6.
14 Mendizabal M, Craviotto S, Chen T, Silva MO, Reddy KR. Noncirrhotic portal hypertension: another cause of liver disease in HIV patients. *Ann Hepatol* 2009; **8**: 390–5.
15 Kovari H, Ledergerber B, Peter U *et al.*, Swiss HIV Cohort Study. Association of noncirrhotic portal hypertension in HIV-infected persons and antiretroviral therapy with didanosine: a nested case-control study. *Clin Infect Dis* 2009; **49**: 626–35.
16 Merchante N, Girón-González JA, González-Serrano M *et al.* Survival and prognostic factors of HIV-infected patients with HCV-related end-stage liver disease. *AIDS* 2006; **20**: 49–57.
17 Ragni MV, Eghtesad B, Schlesinger KW, Dvorchik I, Fung JJ. Pretransplant survival is shorter in HIV-positive than HIV-negative subjects with end-stage liver disease. *Liver Transpl* 2005; **11**: 1425–30.
18 Baccarani U, Adani GL, Bragantini F *et al.* Long-term outcomes of orthotopic liver transplantation in human immunodeficiency virus-infected patients and comparison with human immunodeficiency virus-negative cases. *Transplant Proc* 2011; **43**: 1119–22.
19 Rullier A, Trimoulet P, Neau D *et al.* Fibrosis is worse in HIV-HCV patients with low-level immunodepression referred for HCV treatment than in HCV-matched patients. *Hum Pathol* 2004; **35**: 1088–94.
20 Ragni MV, Moore CG, Soadwa K *et al.*, HHH Study Group. Impact of HIV on liver fibrosis in men with hepatitis C infection and haemophilia. *Haemophilia* 2011; **17**: 103–11.
21 Resino S, Sánchez-Conde M, Berenguer J. Coinfection by human immunodeficiency virus and hepatitis C virus: noninvasive assessment and staging of fibrosis. *Curr Opin Infect Dis* 2012; **25**: 564–9.
22 Merchante N, Rivero-Juárez A, Téllez F *et al.* Liver stiffness predicts clinical outcome in human immunodeficiency virus/hepatitis C virus-coinfected patients with compensated liver cirrhosis. *Hepatology* 2012; **56**: 228–38.
23 Sánchez-Conde M, Miralles P, Bellón JM *et al.* Use of transient elastography (FibroScan®) for the noninvasive assessment of portal hypertension in HIV/HCV-coinfected patients. *J Viral Hepat* 2011; **18**: 685–91.
24 Davison SP, Reisman NR, Pellegrino ED, Larson EE, Dermody M, Hutchison PJ. Perioperative guidelines for elective surgery in the human immunodeficiency virus-positive patient. *Plast Reconstr Surg* 2008; **121**: 1831–40.
25 Miro JM, Torre-Cisnero J, Moreno A *et al.* [GESIDA/GESITRA-SEIMC, PNS and ONT consensus document on solid organ transplant (SOT) in HIV-infected patients in Spain (March, 2005)]. *Enferm Infecc Microbiol Clin* 2005; **23**: 353–62.
26 O'Grady J, Taylor C, Brook G. Guidelines for liver transplantation in patients with HIV infection (2005). *HIV Med* 2005; **6** (Suppl 2): 149–53.
27 Xia XJ, Liu BC, Su JS *et al.* Preoperative CD4 count or CD4/CD8 ratio as a useful indicator for postoperative sepsis in HIV-infected patients undergoing abdominal operations. *J Surg Res* 2012; **174**: e25–30.
28 Grossi PA. Update in HIV infection in organ transplantation. *Curr Opin Organ Transplant* 2012; **17**: 586–93.
29 Joshi D, O'Grady J, Taylor C, Heaton N, Agarwal K. Liver transplantation in human immunodeficiency virus-positive patients. *Liver Transpl* 2011; **17**: 881–90.
30 Ragni MV, Belle SH. Impact of human immunodeficiency virus infection on progression to end-stage liver disease in individuals with hemophilia and hepatitis C virus infection. *J Infect Dis* 2001; **183**: 1112–5.
31 García F, Plana M, Vidal C *et al.* Dynamics of viral load rebound and immunological changes after stopping effective antiretroviral therapy. *AIDS* 1999; **13**: F79–86.
32 Neff GW, Bonham A, Tzakis AG *et al.* Orthotopic liver transplantation in patients with human immunodeficiency virus and end-stage liver disease. *Liver Transpl* 2003; **9**: 239–47.
33 Castells L, Escartín A, Bilbao I *et al.* Liver transplantation in HIV-HCV coinfected patients: a case-control study. *Transplantation* 2007; **83**: 354–8.
34 Frassetto LA, Browne M, Cheng A *et al.* Immunosuppressant pharmacokinetics and dosing modifications in HIV-1 infected liver and kidney transplant recipients. *Am J Transplant* 2007; **7**: 2816–20.
35 Armstrong MJ, Corbett C, Rowe IA, Taylor GP, Neuberger JM. HTLV-1 in solid-organ transplantation: current

challenges and future management strategies. *Transplantation* 2012; **94:** 1075–84.
36 Tricot L, Teicher E, Peytavin G *et al.* Safety and efficacy of raltegravir in HIV-infected transplant patients cotreated with immunosuppressive drugs. *Am J Transplant* 2009; **9:** 1946–52.
37 Sugawara Y, Tamura S, Yamashiki N *et al.* Preemptive antiviral treatment for hepatitis C virus after living donor liver transplantation. *Transplant Proc* 2012; **44:** 791–3.
38 Tanaka T, Selzner N, Therapondos G, Renner EL, Lilly LB. Virological response for recurrent hepatitis C improves long-term survival in liver transplant recipients. *Transpl Int* 2013; **26:** 42–9.
39 Ueda Y, Takada Y, Marusawa H, Egawa H, Uemoto S, Chiba T. Individualized extension of pegylated interferon plus ribavirin therapy for recurrent hepatitis C genotype 1b after living-donor liver transplantation. *Transplantation* 2010; **90:** 661–5.
40 Polard E, Camus C, Abault AY *et al.* Retransplantation for acute liver failure due to combined antiviral agents in an HIV-HCV coinfected liver transplant recipient. *Transplantation* 2005; **80:** 1136–8.
41 Barritt AS 4th, Fried MW. Maximizing opportunities and avoiding mistakes in triple therapy for hepatitis C virus. *Gastroenterology* 2012; **142:** 1314–23.
42 Sugawara Y, Tamura S, Kokudo N. Liver transplantation in HCV/HIV positive patients. *World J Gastrointest Surg* 2011; **3:** 21–8.
43 Lin YL, Mettling C, Portales P, Reynes J, Clot J, Corbeau P. Cell surface CCR5 density determines the post-entry efficiency of R5 HIV-1 infection. *Proc Natl Acad Sci U S A* 2002; **99:** 15590–5.
44 Weissman D, Dybul M, Daucher MB, Davey RT Jr, Walker RE, Kovacs JA. Interleukin-2 up-regulates expression of the human immunodeficiency virus fusion coreceptor CCR5 by CD4+ lymphocytes in vivo. *J Infect Dis* 2000; **181:** 933–8.
45 Heredia A, Amoroso A, Davis C *et al.* Rapamycin causes down-regulation of CCR5 and accumulation of anti-HIV beta-chemokines: an approach to suppress R5 strains of HIV-1. *Proc Natl Acad Sci U S A* 2003; **100:** 10411–6.
46 Di Benedetto F, Di Sandro S, De Ruvo N *et al.* First report on a series of HIV patients undergoing rapamycin monotherapy after liver transplantation. *Transplantation* 2010; **89:** 733–8.
47 Chapuis AG, Paolo Rizzardi G, D'Agostino C *et al.* Effects of mycophenolic acid on human immunodeficiency virus infection in vitro and in vivo. *Nat Med* 2000; **6:** 762–8.
48 García F, Plana M, Arnedo M *et al.* Effect of mycophenolate mofetil on immune response and plasma and lymphatic tissue viral load during and after interruption of highly active antiretroviral therapy for patients with chronic HIV infection: a randomized pilot study. *J Acquir Immune Defic Syndr* 2004; **36:** 823–30.
49 Coull JJ, Turner D, Melby T, Betts MR, Lanier R, Margolis DM. A pilot study of the use of mycophenolate mofetil as a component of therapy for multidrug-resistant HIV-1 infection. *J Acquir Immune Defic Syndr* 2001; **26:** 423–34.
50 Marubashi S, Umeshita K, Asahara T *et al.* Steroid-free living donor liver transplantation for HCV – a multicenter prospective cohort study in Japan. *Clin Transplant* 2012; **26:** 857–67.
51 Klintmalm GB, Davis GL, Teperman L *et al.* A randomized, multicenter study comparing steroid-free immunosuppression and standard immunosuppression for liver transplant recipients with chronic hepatitis C. *Liver Transpl* 2011; **17:** 1394–403.

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Surgical Technique

Hepaticoduodenostomy in Hepatectomy for Perihilarcholangiocarcinoma: A Preliminary Report

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Abstract

A Roux-en-Y anastomosis fashioned from the jejunum (i.e., hepaticojejunostomy) is usually used to reconstruct the biliary system in hepatectomy. In this study, we review our experience with hepaticoduodenostomy (HD) as an alternative to Roux-en-Y biliary anastomosis in patients undergoing hepatectomy for perihilarcholangiocarcinoma, report our preliminary findings in 2 patients, and speculate on future applications. Laparotomy was performed using a Kent retractor. Wide kocherization of the duodenum was done to provide a tension-free anastomosis to the hepatic duct. The Kent retractor was released transiently, and the anastomosis was confirmed to be free of tension. Hepatectomy and excision of the common bile duct were performed. In patients with short distances between the hepatic ducts, a hepaticoplasty was performed. A 10-Fr silicon drain with channels along the sides, approximately 20 mm in length, was used as an internal stent. HD was performed with a single-layer anastomosis with continuous sutures. No complication occurred after HD. Our initial experience suggests that HD may be a viable alternative to Roux-en-Y biliary anastomosis in patients undergoing hepatectomy for perihilarcholangiocarcinoma.

Keywords: Hepaticoduodenostomy; Hepatectomy; Perihilarcholangiocarcinoma

Introduction

A Roux-en Y anastomosis fashioned from the jejunum (i.e.,hepaticojejunostomy [HJ]) is usually used to reconstruct the biliary system in patients undergoing hepatectomy for perihilarcholangiocarcinoma [1]. Recently, reconstruction by hepaticoduodenostomy (HD) or choledochoduodenostomy has been recommended instead of reconstruction by HJ or choledochojejunostomy [2-14]. Complications such as biliary leakage and cholangitis are well documented after HJ and choledochojejunostomy [15-19]. Moreover, the biliary tree is difficult to access endoscopically in patients undergoing enteric reconstruction using a Roux-en-Y anastomosis to the jejunum [20]. HD offers the possible advantage of simple postoperative access to the biliary system by endoscopy and avoids the complications associated with HJ [2].

In this study, we review our experience with HD as an alternative to Roux-en-Y biliary anastomosis in patients undergoing hepatectomy for perihilarcholangiocarcinoma, report our preliminary findings in 2 patients, and speculate on future applications.

Case 1

A 74-year-old woman was admitted because of a dilated left intrahepatic bile duct. Previously, she had undergone a right colectomy because of colonic carcinoma. However, minor leakage of the anastomosis occurred, and reoperation (drainage) was performed. After that, ileus developed and reoperation was done again. Computed tomography revealed dilatation of the left intrahepatic bile duct and mild dilatation of the right posterior intrahepatic duct (Figure 1). Drip infusion cholangiography revealed only the right anterior intrahepatic duct and stenosis at the hepatic hilum (Figure 2). Perihilarcholangiocarcinoma was diagnosed.

Surgical procedures

Laparotomy was performed using a Kent retractor. Severe adhesions of the jejunum were detected, precluding the use of a Roux-en-Y anastomosis fashioned from the jejunum. After kocherization of the duodenum to provide a tension-free anastomosis to the hepatic

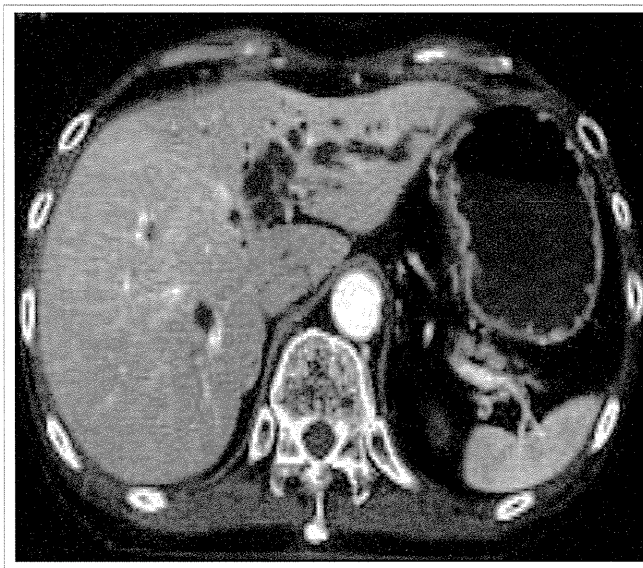

Figure 1: Computed tomography revealed dilatation of the left intrahepatic bile duct and mild dilatation of the right posterior intrahepatic duct.

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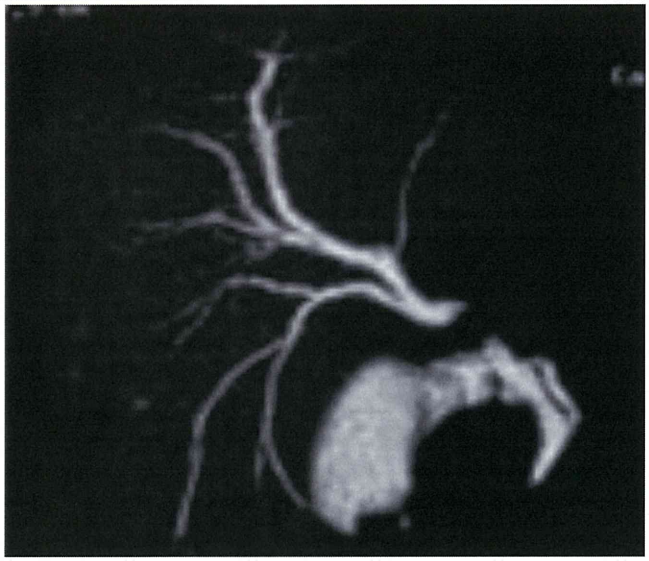

Figure 2: Drip infusion cholangiography revealed only the right anterior intrahepatic duct and stenosis at the hepatic hilum.

duct, an extended left hepatectomy with excision of the common bile duct and lymph-node dissection was performed. Intraoperative pathological examinations revealed that the stumps of the right intrahepatic bile ducts were negative for carcinoma. There were triple lumens of the right anterior bile ducts and double lumens of the right posterior bile ducts. Hepaticoplasty (i.e., the adjacent walls of the hepatic ducts were sutured together with single stitches using 6-0 polydioxane [PDS, Ethicon, NJ, USA] to obtain a single lumen for biliary anastomosis) was performed to make double lumens of the right anterior bile ducts and a single lumen of the right posterior bile duct. Unexpectedly, the duodenum was distant from the hepatic ducts. To provide a tension-free anastomosis, wide kocherization of the duodenum was performed again, and the right gastroepiploic artery and vein were cut. The Kent retractor was released transiently, and the anastomosis was confirmed to be tension-free. As an internal stent, a 10-Fr silicon drain with channels along the sides (BLAKE Silicone Drain, Ethicon, NJ, USA),approximately 20 mm in length, was used [21]. Before completing suture of the posterior row, the stent was inserted into each lumen. Five stents were placed within the hepatic duct and duodenal lumen to serve as the internal stents for the anastomosis. The stent was fixed to the anterior row of stitches with 5-0 polydioxane sutures. Three anastomoses of the intrahepaticbile ducts to the duodenum were established by means of a single-layer anastomosis with continuous sutures (5-0 polydioxane) (Figure 3). Fixation of the greater omentum to the peritoneum was not necessary to prevent delayed gastric emptying [22,23] because the stomach could not come in contact with the cut surface of the liver, a potential cause of adhesion.

The postoperative course was uneventful, and the patient was discharged on postoperative day 12. After discharge, upper gastrointestinal endoscopy revealed no duodeno gastric bile reflux.

Case 2

A 76-year-old man with dilatation of the left intrahepatic duct was admitted. Previously, he had undergone a distal gastrectomy (BillrothII reconstruction) because of gastric carcinoma. Computed tomography and magnetic resonance cholangiopancreatography revealed the dilated left intrahepatic bile duct (Figure 4,5). Perihilarcholangiocarcinoma was diagnosed.

Surgical procedures

Laparotomy was performed using a Kent retractor. Adhesions of the jejunum were detected. Wide kocherization of the duodenal stump was performed to provide a tension-free anastomosis. The Kent retractor was released transiently, and the anastomosis was confirmed to be free of tension. An extended left hepatectomy with excision of the common bile duct and lymph-node dissection was performed. Intraoperative pathological examinations revealed that the stump of the right hepatic duct was negative for carcinoma. Because the right hepatic duct had a single lumen, hepaticoplasty was unnecessary. HD was performed using a single-layer anastomosis with continuous sutures (5-0 polydioxane). After completing suture of the posterior row, the stent was inserted into the hepatic duct. As internal stents, 10-Fr silicon drains with channels along the sides, approximately 20 mm in length, were used. The stent was fixed to the anterior row of stitches with 5-0 polydioxane sutures. Anastomosis of the right hepatic duct to the duodenal stump was established

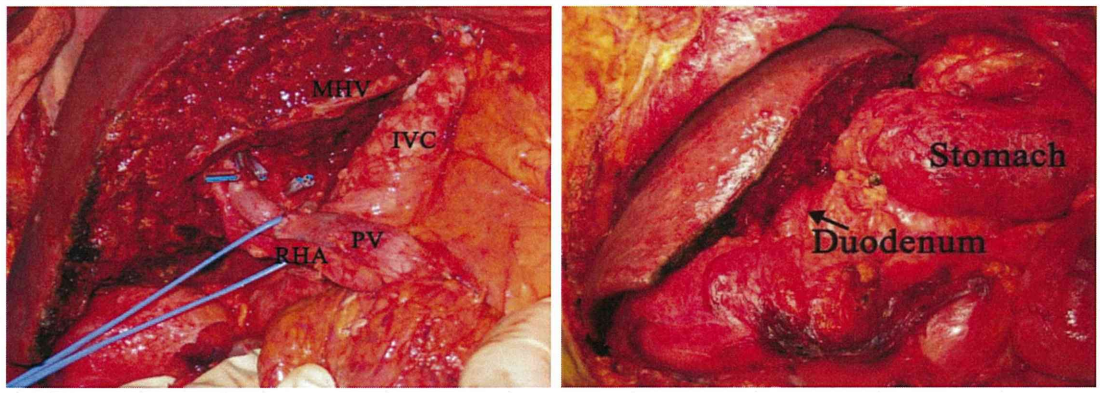

Figure 3: Before completing suture of the posterior row, the stent was inserted into each lumen. Five stents were placed within the hepatic duct and duodenal lumen to serve as the internal stents for the anastomosis. The stent was fixed to the anterior row of stitches with 5-0 polydioxane sutures. MHV: middle hepatic vein, IVC: inferior vena cava, PV: portal vein, RHA: right hepatic artery (**a**). Three anastomoses of the intrahepaticbile ducts to the duodenum were established by means of a single-layer anastomosis with continuous sutures(**b**).

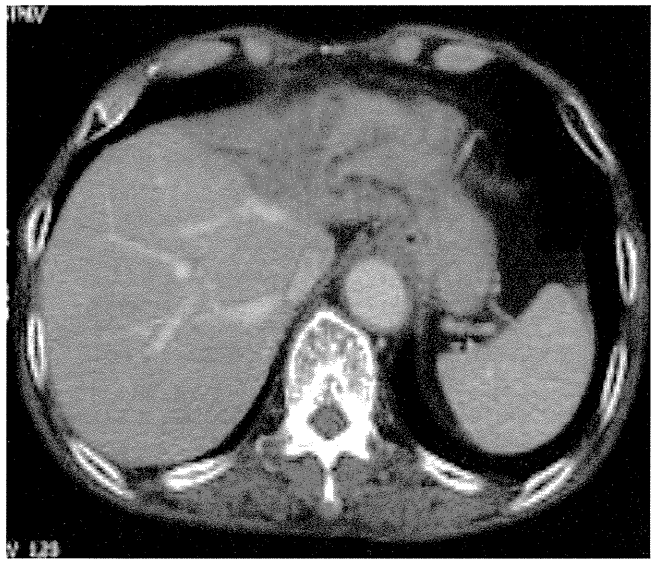

Figure 4: Computed tomography revealed the dilated left intrahepatic bile duct.

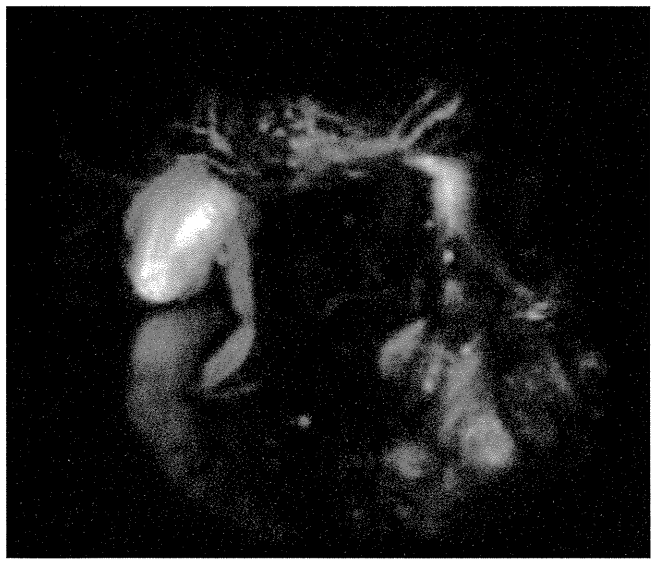

Figure 5: Magnetic resonance cholangiopancreatography revealed the dilated left intrahepatic bile duct.

(Figure 6). Fixation of the greater omentum to the peritoneum was not necessary to prevent delayed gastric emptying [22,23] because the residual stomach did not come in contact with the cut surface of the liver, a potential cause of adhesion.

The postoperative course was uneventful, and the patient was discharged on postoperative day 10. After discharge, upper gastrointestinal endoscopy revealed no duodenogastric bile reflux.

Discussion

Biliary reconstruction using the duodenum has been successfully performed in liver transplantation and the treatment of biliary obstruction, common bile duct stones, biliary injury, choledochal cysts, and biliary atresia [2-14]. We decided to perform HD instead of HJ in the 2 patients described here, because it was technically difficult to perform HJ. No complication occurred after HD. One disadvantage of HD is that, if an anastomotic leak does occur, the leakage volume can be much greater than with HJ because the leak would contain both gastric and pancreatic juices rather than bile alone in contrast to HJ. A second advantage of HD is that it is unnecessary to create a Roux-en-Yjejunal limb, associated with a higher incidence of adhesive bowel obstruction than HD.A third advantage of HD is that the biliary system can be easily accessed by endoscopy, which is not feasible with HJ.

One drawback of HD is anastomotic tension, which is higher than that of choledochoduodenostomy, especially in patients with perihilarcholangiocarcinoma. We performed wide kocherization of the duodenum and confirmed that the anastomosis was tension-free by releasing the Kent retractor transiently. Wide kocherization of the duodenum was an important factor in creating a tension-free anastomosis.

Shimotakahara [7] compared HD with HJ after excision of primary choledocal cysts in children. Complications after cyst excision occurred in 5 of the 12 patients in the HD group (42%). Four patients had bilious gastritis and 1 had temporary liver dysfunction. In the HJ group, 2 of the 28 patients (7.1%) had postoperative complications. Both patients had adhesive bowel obstruction, and 1additionally had cholangitis. Liem [14] reported that cholangitis occurred at a rate of 5.3% and bilious gastritis at a rate of 14.3% after laparoscopic cyst excision and HD for choledochal cysts in children. Moraca [5] compare dlong-term biliary function between HD and HJ in patients who underwent treatment of major bile-duct injuries during cholecystectomy. On long-term follow-up, no patient had cholangitis, jaundice, or liver failure in either group. Bennet [8] reported that preliminary experience suggested that choledochoduodenostomy is a safe technique for cadaveric liver transplantation. Campsen [2] documented the outcomes of 7 patients who underwent living donor transplantation with HD as the primary type of biliary anastomosis. There were no deaths or re-transplants during the follow-up period. One patient had cholangitis that responded to intravenous antibiotics and endoscopic removal of the stent. Various complications have occurred after HD or HJ, including bilious gastritis, temporary liver dysfunction, bowel obstruction, and cholangitis. Bilious gastritis occurred after HD in some children with choledocal cysts, but has not been reported after HD in adults. The severest complication is bowel obstruction or cholangitis. One advantage of HD is that the creation of a Roux-en Yjejunal limb and one anastomosis, associated with a higher incidence of adhesive bowel obstruction than HD, is unnecessary. After biliary reconstruction using the duodenum, cholangitis results from anastomotic stenosis and not reflux of the duodenal contents into the biliary tree [24]. The prevention of anastomotic stenosis is prerequisite to the prophylaxis of cholangitis.

In this study, we used a 10-Fr silicon drain with channels for internal biliary stenting of HD. We previously compared two types of stents in patients who underwent surgery for perihilarcholangiocarcinoma. In one group, a 10-Fr silicon drain with channels along the sides was used as a stent for HJ (channel stent group), while in the other a 5-Fr silicon drain with an internal lumen and side holes was used (intraluminal stent group). Leakage developed in 4 patients (36.4%) in the intraluminal stent group versus 2 (20.0%) in the channel stent group. Cholangitis developed in 3 patients with leakage (27.3%) in the intraluminal stent group versus no patient in the channel stent group.

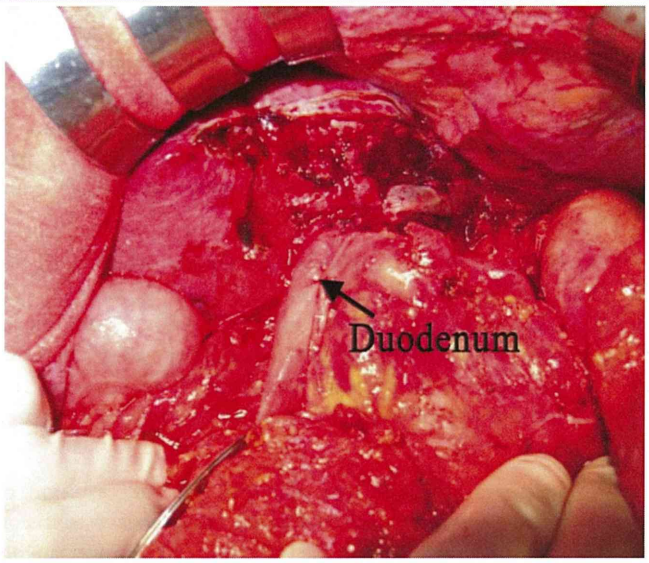

Figure 6: Anastomosis of the right hepatic duct to the duodenal stump was established.

Our results suggested that the use of a 10-Fr stent helps to maintain a 10-Fr intraluminal diameter of the anastomosis, even in the presence of biliary leakage. A 10-Fr stent may thus prevent cholangitis due to anastomotic stenosis [21]. No complication occurred after operation in the present study.

Hakamada [25] reported that cholangiocarcinoma developed in 7.4% of patients a mean interval of 18 years after transduodenalsphincteroplasty. Maeda [26] documented the development of bile duct cancer 21 years after choledochoduodenostomy. Tocchi [27] estimated that the incidences of cholangiocarcinomas after sphincteroplasty, choledochoduodenostomy, and hepaticojejunostomy were 4.8, 7.6, and 1.9%, respectively, occurring at intervals of 11 to 18 years. Therefore, cholangiocarcinoma as a delayed complication of transduodenalsphincteroplasty and choledochoenteric anastomosis has become a serious issue.

In conclusion, we reviewed our experience with HD as an alternative to Roux-en-Y biliary anastomosis in patients undergoing hepatectomy for perihilarcholangiocarcinoma, reported our preliminary findings in 2 patients, and speculated on future applications. No complication occurred after operation in this study. We emphasize that wide kocherization of the duodenum is necessary to provide a tension-free anastomosis, which should be confirmed after transiently releasing the Kent retractor. HD may be a reasonable alternative to Roux-en-Y biliary anastomosis in patients undergoing hepatectomy for perihilarcholangiocarcinoma. Additional studies and longer follow-up are needed, however, to confirm these findings and to accurately assess the rates and types of complications associated with HD. Further studies in larger numbers of patients are needed before HD can be designated a standard of care.

References

1. Sano T, Shimada K, Sakamoto Y, Esaki M, Kosuge T. Changing trends in surgical outcomes after major hepatobiliary resection for hilar cholangiocarcinoma: a single-center experience over 25 years. J Hepatobiliary Pancreat Surg. 2007; 14: 455-462.
2. Campsen J, Zimmerman MA, Mandell MS, Wachs M, Bak T, Forman L, et al. Hepaticoduodenostomy is an alternative to Roux-en-Y hepaticojejunostomy for biliary reconstruction in live donor liver transplantation. Transplantation. 2009; 87: 1842-1845.
3. Cole FR, Pisillo CJ. Choledochoduodenostomy: an evaluation of its indications. Int Surg. 1966; 46: 108-112.
4. Todani T, Watanabe Y, Mizuguchi T, Fujii T, Toki A. Hepaticoduodenostomy at the hepatic hilum after excision of choledochal cyst. Am J Surg. 1981; 142: 584-587.
5. Moraca RJ, Lee FT, Ryan JA Jr, Traverso LW. Long-term biliary function after reconstruction of major bile duct injuries with hepaticoduodenostomy or hepaticojejunostomy. Arch Surg. 2002; 137: 889-893.
6. Srivengadesh G, Kate V, Ananthakrishnan N. Evaluation of long-term results of choledochoduodenostomy for benign biliary obstruction. Trop Gastroenterol 2003; 24: 205-207.
7. Shimotakahara A, Yamataka A, Yanai T, Kobayashi H, Okazaki T, Lane GJ, et al. Roux-en-Y hepaticojejunostomy or hepaticoduodenostomy for biliary reconstruction during the surgical treatment of choledochal cyst: which is better? Pediatr Surg Int. 2005; 21: 5-7.
8. Bennet W, Zimmerman MA, Campsen J, Mandell MS, Bak T, Wachs M, et al. Choledochoduodenostomy is a safe alternative to Roux-en-Y choledochojejunostomy for biliary reconstruction in liver transplantation. World J Surg. 2009; 33: 1022-1025.
9. Degenshein GA. Choledochoduodenostomy: an 18 year study of 175 consecutive cases. Surgery. 1974; 76: 319-324.
10. Bhandarkar DS, Shah RS. Laparoscopic choledochoduodenostomy for retained bile duct stone. J Postgrad Med. 2005; 51: 156-157.
11. de Aretxabala X, Bahamondes JC. Choledochoduodenostomy for common bile duct stones. World J Surg. 1998; 22: 1171-1174.
12. Onken JE, Pappas T, Baillie J. Long term results of choledochoduodenostomy in the treatment of choledocholithiasis. Gastrointest Endosc. 1992; 38: 403-405.
13. Ramirez P, Parrilla P, Bueno FS, Abad JM, Muelas MS, Candel MF, et al. Choledochoduodenostomy and sphincterotomy in the treatment of choledocholithiasis. Br J Surg. 1994; 81: 121-123.
14. Liem NT, Dung le A, Son TN. Laparoscopic complete cyst excision and hepaticoduodenostomy for choledochal cyst: early results in 74 cases. J Laparoendosc Adv Surg Tech A. 2009; 19: S87-90.
15. Bourgeois N, Deviere J, Yeaton P, Bourgeois F, Adler M, Van De Stadt J, et al. Diagnostic and therapeutic endoscopic retrograde cholangiography after liver transplantation. Gastrointest Endosc. 1995; 42: 527-534.
16. Sossenheimer M, Slivka A, Carr-Locke D. Management of extrahepatic biliary disease after orthotopic liver transplantation: review of the literature and results of a multicenter survey. Endoscopy. 1996; 28: 565-571.
17. Colonna JO 2nd, Shaked A, Gomes AS, Colquhoun SD, Jurim O, McDiarmid SV, et al. Biliary strictures complicating liver transplantation. Incidence, pathogenesis, management, and outcome. Ann Surg. 1992; 216: 344-350.
18. Greif F, Bronsther OL, Van Thiel DH, Casavilla A, Iwatsuki S, Tzakis A, et al. The incidence, timing, and management of biliary tract complications after orthotopic liver transplantation. Ann Surg. 1994; 219: 40-45.
19. Lerut J, Gordon RD, Iwatsuki S, Esquivel CO, Todo S, Tzakis A, et al. Biliary tract complications in human orthotopic liver transplantation. Transplantation. 1987; 43: 47-51.
20. Ryozawa S, Iwamoto S, Iwano H, Ishigaki N, Taba K, Sakaida I. ERCP using double-balloon endoscopes in patients with Roux-en-Y anastomosis. J Hepatobiliary Pancreat Surg. 2009; 16: 613-617.
21. Yoshida H, Mamada Y, Taniai N, Mizuguchi Y, Kakinuma D, Ishikawa Y, et al. Silicon drain with channels along the sides for internal biliary stenting of hepaticojejunostomy in hepatic hilar malignancies. J Gastroenterol Hepatol

2009; 24: 752-756.

22. Yoshida H, Mamada Y, Taniai N, Mizuguchi Y, Shimizu T, Kakinuma D, et al. Fixation of the greater omentum for prevention of delayed gastric emptying after left hepatectomy with lymphadenectomy for cholangiocarcinoma. J Hepatobiliary Pancreat Surg. 2007; 14: 392-396.

23. Yoshida H, Mamada Y, Taniai N, Mizuguchi Y, Shimizu T, Takahashi T, et al. Fixation of the greater omentum for prevention of delayed gastric emptying after left-sided hepatectomy: a randomized controlled trial. Hepatogastroenterology. 2005; 52: 1334-1337.

24. Escudero-Fabre A, Escallon A Jr, Sack J, Halpern NB, Aldrete JS. Choledochoduodenostomy. Analysis of 71 cases followed for 5 to 15 years. Ann Surg. 1991; 213: 635-642.

25. Hakamada K, Sasaki M, Endoh M, Itoh T, Morita T, Konn M. Late development of bile duct cancer after sphincteroplasty: a ten- to twenty-two-year follow-up study. Surgery. 1997; 121: 488-492.

26. Maeda A, Yokoi S, Kunou T, Saeki S, Murata T, Niinomi N, et al. Bile duct cancer developing 21 years after choledochoduodenostomy. Dig Surg. 2003; 20: 331-334.

27. Tocchi A, Mazzoni G, Liotta G, Lepre L, Cassini D, Miccini M. Late development of bile duct cancer in patients who had biliary-enteric drainage for benign disease: a follow-up study of more than 1,000 patients. Ann Surg. 2001; 234: 210-214.

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Ⅲ　各　論

6. 脾
a) 巨脾摘出の注意点*

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はじめに

脾機能亢進症の治療法としては，脾臓摘出術（脾摘）が脾機能亢進の改善と，門脈圧を下げる目的で施行されているが，近年より低侵襲の治療を目的に腹腔鏡下脾摘[1~4]が普及し，従来の開腹手術に比べ低侵襲の脾摘が可能となった．

本稿では，巨脾の摘出における手技と注意点を述べる．

Ⅰ．術前準備

脾摘後重症感染症（overwhelming postsplenectomy infection：OPSI）は，肺炎球菌が最多の原因菌で，脾摘前には肺炎球菌ワクチンの投与が必要である．

血小板数が5万/μl以下の場合には安全性を考慮して部分的脾動脈塞栓術（partial splenic embolizaion：PSE）[5~10]を施行するのもよい．血小板数はPSEの12～24時間後に上昇し始め，ピークは1～2週間後である．1～2週間またなくても，ある程度血小板数が上昇すれば脾摘は可能となる．しかし，PSE後は脾臓の癒着が高度となり脾摘に難渋する場合があるので，血小板の輸血準備をして手術を施行する場合もある．侵襲面を考慮してChild-Pugh score 10点以上（Child-Pugh分類C）は原則的に脾摘の適応外としている．PSEなどで肝予備能が改善後に施行する場合もある．

画像診断

術前に上部消化管内視鏡を施行し，食道胃静脈瘤の有無をチェックする必要がある．巨脾の場合，脾動脈が屈曲蛇行しており脾動脈瘤が合併する場合もあるので，術前画像で脾動脈走行を入念にチェックする．また門脈圧亢進症に起因する巨脾の場合，側副血行路が発達している場合が多く，その走行を十分に把握しておかなければいけない．

Ⅱ．手　術　法

従来は巨脾例ではworking spaceの確保に難渋するため，開腹による脾摘を選択することが多かった．しかし近年は，低侵襲治療である腹腔鏡下脾摘が行われるようになってきた[1~4]．腹腔鏡下手術では拡大視効果で，より丁寧な手術が可能となる．また細いデバイスを挿入するので，基本的には腹腔鏡で観察可能な部分の処理は可能である．

上腹部正中に8cm弱の切開を入れ，片手を挿入（hand-assist）し腹腔鏡下手術を行う腹腔鏡補助下脾摘では，術中脾の脱転や脾出血時の圧迫止血が容易となる．巨脾であるため最終的には摘出時にある程度の皮膚切開創が必要となるため，最初から上腹部に正中切開を入れることは利にか

キーワード：脾機能亢進症，治療，巨脾

* Surgical treatment of huge spleen

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なっている．

ここでは各手術法について述べる．

Ⅲ．手　　技

❶開　　腹

a．皮膚切開

巨脾の場合は，十分な視野を得るために皮膚の大きな切開が必要になる．一般的に上腹部正中切開に左腹部の横切開，肋間切り上げを加えたL字切開が適している．吊り上げ鉤を使用し，より良好な視野展開が重要である．

また同時に施行する手技によって，皮膚切開の追加が必要となる．肝切除や肝移植の場合には，右の横切開，肋間切り上げ，食道離断術[11]やHassab手術[12]の場合には，食道胃周囲の血行遮断などのため右腹直筋右縁までの横切開追加で，より良好な視野が得られる．

b．腹腔内操作

まず胃結腸間より網嚢内に入り，脾結腸間膜（左側）に向かって大網を切離する．網嚢の開放により脾門部の観察が可能となる．巨脾の場合には，脾動脈結紮の先行により出血量の軽減と脾臓の緊満を改善することができる．術前にチェックした画像をもとに脾動脈を露出し結紮する．しかし良好な視野が得られない場合は無理をせずに，脾動脈結紮は視野が確保された後に行うべきである．

まず脾動脈結紮を行う．しかし視野が不良の場合は無理をせずに後で行う．

次に胃脾間膜内にある左胃大網動静脈，短胃動静脈を結紮切離する．食道胃周囲の血行遮断を行う場合は胃側，脾摘のみの場合は胃と脾臓の中間点で切離する．中間点で切離すると出血時にも処理が容易となる．胃脾間膜の切離は可及的に頭側まで行う．しかし視野展開が不良の場合は中断し，次の処理にとりかかる．この時点で脾門部の視野はさらに良好となるため脾動脈結紮（確保）を行う．

そして，脾結腸間膜を切離し脾の下極を脱転していく．ここに側副血行路を認めることが多いので，慎重に操作をすすめなければいけない．脾を左外側の腹膜より脱転する際に視野が不良の場合には，吊り上げ鉤でさらに牽引しながら肋間を切り上げて十分な視野展開を行う．左外側の腹膜からの剝離を可及的に脾上極まで施行し脱転する．この際に脾を内側尾側腹側方向へ牽引することが重要であるが，脾の損傷に留意し愛護的に牽引する．脾の損傷部は縫合ではなく圧迫止血で対処する．縫合を試みることにより損傷部がさらに広がることが多い．最終的には脾臓を摘出すれば止血されるので，圧迫止血にとどめておくことが重要である．

脾臓を牽引時には愛護的に．脾臓を損傷したら圧迫止血で対処する．

脾が十分に脱転遊離したら脾門部の処理に戻る．膵尾部との境界に留意して脾静脈の処理を行って摘出する．

手順にこだわらず視野の良好な部分から処理することが重要である．

側副血行路の発達した症例では術中に食道胃周囲の血行遮断（Hassab手術）[12]，食道静脈瘤合併例では食道離断術[11]を併施することがある．側副血行路の血行遮断は結紮だけでは早期に再開通するので，その拡張した静脈を摘出すべきである．しかし悪性疾患でのリンパ節郭清とは違い血行遮断が目的であることを忘れてはならない．側副血行路は高い門脈圧を反映しているため，損傷時には大量出血となるので留意しなければいけない．

❷腹 腔 鏡

巨脾の場合は腹腔鏡補助下（または開腹）にコンバートする可能性があるので，対応できるように手術器具を準備しておく．

a．体位，トロッカーポジション

開脚して仰臥位で行うが，左側をベッドアップするとより良好な視野が得られる．巨脾の場合はhand-assistにコンバートできるように上腹部正中に約8 cmの切開予定線をマーキングしておく．臍部より腹腔鏡用に12 mmトロッカーを挿入し，心窩部に5 mmトロッカーを正中マーキング部に合わせて挿入する．また巨脾の程度で位置はかわるが，左下腹部（ほぼ臍部の左方）に12 mmトロッカー，その左方に5 mmトロッカー，その他に右上腹部に5 mmトロッカーを追加することもある．腹腔鏡で観察して巨脾の程度に応じてトロッカーを挿入する必要がある．

巨脾の程度に応じて症例ごとにトロッカーの位置を選択する．

術者は患者右側または尾側に適時移動して手術を行う．