

Analysis of critical issues in case management for liver retransplantation

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ABSTRACT

We report a case of a patient who underwent successful combined liver-kidney transplant after two prior liver transplantations. The topic of liver retransplantation is very controversial. Given the critical organ shortage, the question arises as to whether hepatic retransplantation should be offered liberally despite its greater cost, and inevitable denial of access to primary transplantation for the other patients on the waiting list. We suggest that careful selection of the retransplant candidates will improve outcomes and allow rational use of the limited organ supply. Analysis of the available literature allows us to identify the main predictors of morbidity and mortality for this patient population. It also enables development of a detailed plan for perioperative management. The role of transesophageal echocardiography (TEE) as a monitor in the complex liver transplant cases is also discussed. Our report is a significant contribution to the very limited data available on the subject of multiple liver retransplants.

Keywords: Liver Retransplantation; TEE in Liver Transplantation; Monitoring in Liver Retransplantation; Anesthetic Management Liver Retransplantation

1. INTRODUCTION

Liver transplantation is currently the life-saving therapeutic modality for treatment of the end-stage liver disease. With significant advances in antiviral therapy, postoperative immunosuppression and improved surgical technique today's 5 and 10 year survival rates after orthotopic liver transplant are over 70% and 65% respec-

tively [1]. However, the survival rates of retransplanted livers among different centers in the United States vary from 10.0% to 19.4% [2,3] and in the world from 5% to 22% [4,5].

Retransplantation carries greater surgical risks, longer ICU and hospital stay and significantly poorer outcome in terms of graft and patients survival. The 5 and 10 year survival rates range from 47% to 63% and 45% to 62% respectively [6,7]. The medical problems related to retransplantation are compounded by rising financial burden and multiple ethical issues. In an era of extreme organ shortage, the practice of liver retransplantation can deny access to transplantation to patients waiting for their first transplant. Additionally, the annual death rate per 1000 patient has been 2 to 3 times higher for recipients of multiple liver procedures versus recipients of primary transplants over the past 9 years [8].

Careful selection of patients for retransplantation and especially for the repeated retransplantation is extremely important. The decision regarding this high-risk surgery should be individualized and based on specific patient risk factors and the chances for long-term survival.

2. CASE PRESENTATION

The patient is a 29-year-old female with end stage liver disease caused by graft failure secondary to chronic rejection and recurrent autoimmune hepatitis. She had a history of two prior liver transplants, 16 and 12 years ago. She presented with clinical symptoms of ascites, severe portal hypertension and chronic kidney disease requiring hemodialysis. Her past medical history also included hypertension, diabetes, and depression. Her medications include novolog insulin, spironolactone, furosemide, prednisone, prograft and lactulose. Physical examination showed significant ascites and jaundice, normal airway, normal cardiac and pulmonary functions.

Her laboratory studies revealed: Hgb 8.2 mg/dl, total

bilirubin/direct bilirubin 54/23.9 mg/dl respectively, BUN 26 mg/dl, Creatinine 6.4 mg/dl, potassium 4.1 mEq/l, INR 4.8, PT 29 sec, PTT 56 sec, Platelets 39,000.

Transthoracic echocardiogram (TEE) demonstrated normal left ventricular function with an ejection fraction of 60% and mild tricuspid valve regurgitation. When an ABO compatible donor became available the patient was scheduled for a combined liver-kidney transplant.

Standard ASA monitors were placed. After pre-oxygenation, anesthesia was induced with midazolam 2 mg, fentanyl 150 mcg, propofol 150 mg, and cisatracurium 18 mg. The patient was intubated orally with 7.5 cuffed endotracheal tube. Subsequently, two large bore peripheral intravenous lines, an arterial line, and a right internal jugular 8.5 French introducer catheter were placed. Multiple attempts to float a Swan Ganz catheter were unsuccessful. A TEE probe was inserted. The examination revealed significant tricuspid valve regurgitation with dilatation of the right atrium. Right and left ventricular function was preserved. The calculated pulmonary artery pressure was 45/25 mm Hg (**Figure 1**).

Surgery was planned with the use of veno-venous bypass and TEE.

An outflow 21 French heparin coated bypass cannula was placed in left femoral vein and inflow 19 French cannula was placed in internal jugular vein under ultrasound guidance. The bypass flow through the case was 1.6 - 1.7 L/min. Cell saver and Belmont rapid infuser were utilized during the surgery. Inferior vena cava cross clamp time was 27 minutes. There were moderate hemodynamic changes after reperfusion necessitating vasopressin and norepinephrine infusions. The patient was coagulopathic requiring 45 units of PRBC, 20 liters of cell saver blood, 37 units of FFP, 5 units of cryoprecipitate and 5 units of platelets.

Thromboelastography was utilized to guide the treatment of the coagulopathy. Surgery lasted 10 hours and

the patient was transferred to the ICU intubated in stable condition. The postoperative course was uncomplicated, except for the need for several hemodialysis sessions. She was extubated on postoperative day 2. The patient was discharged from the ICU after 5 days and left the hospital 2 weeks after surgery. Ten months after the transplant the patient is doing well.

3. DISCUSSION

Transplantation is often the best option for patients faced with organ failure. Although the results following primary transplantation have improved, allograft loss is a problem confronted by many patients and their physicians. While retransplantation offers hope for good health and better survival, previous studies have demonstrated inferior outcomes after repeat liver transplantation [1,7].

In a time of extremely limited organ supply, retransplantation remains to be very controversial on ethical, economic and medical grounds. Therefore, it is particularly important to identify the group of patients who will definitely benefit from retransplantation, and to delineate major donor risk factors that potentially can lead to poor outcomes and coordinate the work of the multiple services involved in these high-risk procedures. The key to the growing success of liver retransplantation is in careful selection and strategic planning of this operation.

It is very important to be aware of the multiple risk factors affecting the outcome of the procedure. In the past, technical complications were the main indication for early retransplantation, while chronic rejection was the most important cause for late retransplantation. At the present time, the scarcity of donor organs necessitates the acceptance of suboptimal donor grafts for primary transplantation. This practice, in turn, contributes to the fact that primary graft dysfunction has become the leading indica-

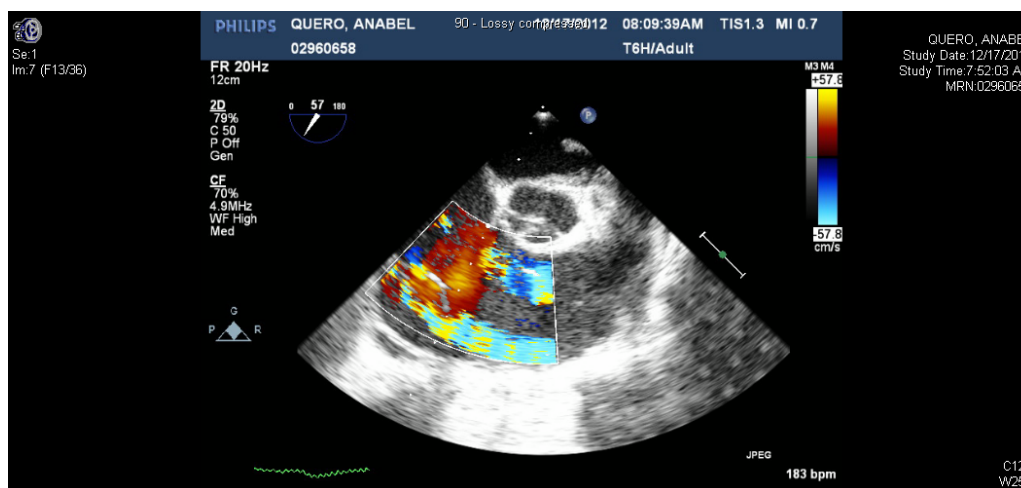


Figure 1. Mid esophageal right ventricle inflow-outflow view. Tricuspid regurgitation.

tion for liver retransplantation within the first year after primary transplantation. Also, the use of more potent immunosuppression has decreased chronic rejection but has increased recurrent hepatitis C in grafts as the primary cause for retransplantation one year after primary surgery [9].

Although retransplantation in general has poorer outcomes in terms of survival, multiple studies have shown that patients having elective retransplantation exhibited survival curves indistinguishable from those of the single transplant group [1,10,11]. In spite of a trend towards longer hospital stay and higher charges in the retransplant patients, retransplantation is fully justifiable when performed electively [12]. Outcomes are worse for emergency retransplants, especially those performed within 8 to 30 days of the initial transplantation [13]. However, despite its inferior results, hepatic retransplantation can not be abandoned just for practical and ethical reasons. Prognostic modeling allowing prediction of mortality risk and long-term survival of patients after retransplantation is extremely important. Analysis of prognostic factors confirmed by several studies identified a significant correlation between mortality and patient age, serum creatinine level, urgency of the operation, and ICU recipient status before retransplantation [14,15]. Younger patients with normal creatinine coming for elective procedures more than a year after previous transplants have better survival chances [1,12,15]. It is a difficult decision to identify the optimal time for retransplantation in the case of chronic progressive graft rejection. In this setting, there might be a place for living related liver transplantation. Living related transplant shortens the waiting time, allows for better preparation of the recipient, and provides an optimal graft with the shortest possible ischemia time [16].

There are several other measures proposed to improve the results of retransplantation of the high-risk patients. One of them is to match the severity of the patient's condition with the quality of the graft. It is a well-established fact that the recipients of good quality grafts have better survival chance compared to those who received extended criteria grafts [17]. Another area of improvement in retransplantation identified in the literature is refinement of surgical techniques. The success rate of retransplantation has increased as a growing number of surgeons have gained expertise in doing this procedure [18].

Ethical issues related to retransplantation are also very important. When a patient receives a repeat transplant, many people think it is unjust to give them priority over someone who has never had one before. While the number of liver transplants performed in United States has reached over 6000 per year, the demand for donor organs exceeds the supply. As a result, around 1800 deaths per

year occur on the waiting list. Currently, only 554 out of 16,026 patients nationally listed as candidates are listed for retransplantation [19]. Statistically, these numbers are very small, but still can raise many ethical concerns for the transplant teams, candidates for transplant, and family members.

Although the primary goal of organ retransplantation is the optimal health of the patients, it is realistic to analyze the financial considerations behind the procedure. The high cost of retransplantation has been well documented [7]. The cost of retransplantation is usually twice that of primary one. Even finances are a driving force in our society; the question arises if it is ethically correct to place monetary value on human life.

In our case, weighing the risks versus benefits for this particular patient, the team decided that young age, late graft failure and the non-urgent nature of the operation would increase the chances of a favorable outcome.

Repeat retransplantation of a patient with chronic kidney failure necessitated to combine liver-kidney transplant which presented additional risks. In this setting, the appropriate choice of the invasive monitoring becomes extremely important. Our current standard of care for perioperative hemodynamic monitoring during liver transplantation remains an arterial line and a pulmonary artery catheter (PAC). However, perioperative transesophageal echocardiogram (TEE) has been shown to be helpful in managing fluid therapy, monitoring myocardial function, and identifying intraoperative complications [20,21].

In our case, TEE monitoring was imperative as the presence of the significant tricuspid valve regurgitation (TR) prevented successful placement of the PAC. The primary advantage of TEE is real-time assessment of cardiac function, quantitative and qualitative determination of right and left ventricular filling and ejection fraction. Right and left ventricular dysfunction can be exacerbated during liver transplantation by large fluid shifts that occur during clamping and unclamping of the major vascular structures such as the inferior vena cava and the portal vein. Patients are at particular risk of right ventricular failure during and after the reperfusion phase of the operation. In the presence of TR, this risk is significantly increased. Unlike the PAC, the TEE as an imaging modality can detect new wall motion abnormalities, shunting, as well as pulmonary and intracardiac emboli [22,23]. Previous concerns about possible trauma to esophageal varices during TEE placement were largely unfounded. A large retrospective cohort study demonstrated no major bleeding complications, even in higher risk patients [24].

Our unique experience with a repeat combined liver-kidney transplant opens a new perspective in the approach to the problem of liver retransplantation. Careful

patient selection, individualized monitoring, management plans, and strong team work contribute to making this high-risk procedure successful.

REFERENCES

- [1] Azoulay, D., Linhares, M.M., Huguet, E., Delvart, V., Castaing, D. and Adam, R. (2002) Decision for retransplantation of liver: An experience and cost based analysis. *Annals of Surgery*, **236**, 713-721. <http://dx.doi.org/10.1097/00000658-200212000-00003>
- [2] Jain, A., Reyes, J., Kashyap, R., Dodson, S.F., Demetris, A.J., Ruppert, K., Abu-Elmagd, K. and Gayowski, T. (2000) Long-term survival after liver transplantation in 4,000 consecutive patients at a single center. *Annals of Surgery*, **232**, 490-500. <http://dx.doi.org/10.1097/00000658-200010000-00004>
- [3] Kashyap, R., Jain, A., Reyes, J., Demetris, A.J., Elmagd, K.A. and Dodson, S.F. (2001) Causes of retransplantation after primary liver transplantation in 4000 consecutive patients: 2-19 years follow-up. *Transplantation Proceedings*, **33**, 1486-1487. [http://dx.doi.org/10.1016/S0041-1345\(00\)02563-X](http://dx.doi.org/10.1016/S0041-1345(00)02563-X)
- [4] Bramhall, S.R., Minford, E., Gunson, B. and Buckels, J.A. (2001) Liver transplantation in the UK. *World Journal of Gastroenterology*, **7**, 602-61
- [5] Pfitzmann, R., Benschmidt, B., Langrehr, J.M., Schumacher, G., Neuhaus, R. and Neusaus, P. (2007) Trends and experiences in liver transplantation over 15 years. *Liver Transplantation*, **13**, 248-257. <http://dx.doi.org/10.1002/lt.20904>
- [6] Markmann, J.F., Markowitz, J.S., Yersiz, H., Morrissey, M., Farmer, D.G. and Farmer, D.A. (1997) Long-term survival after retransplantation of the liver. *Annals of Surgery*, **226**, 408-420. <http://dx.doi.org/10.1097/00000658-199710000-00002>
- [7] Postma, R., Haagsma, E.B., Peeters, P.M., Van den Berg, A.P. and Slooff, M.J. (2004) Retransplantation of the liver in adults: outcome and predictive factors for survival. *Transplant International*, **17**, 234-240. <http://dx.doi.org/10.1111/j.1432-2277.2004.tb00436.x>
- [8] Enestvedt, C.K., Malik, S., Reese, P.P., Maskin, A., Yoo, P.S., Fayek, S.A., Abt, P., Olthoff, K.M. and Shaked, A. (2013) Biliary complications adversely affect patient and graft survival after liver retransplantation. *Liver Transplantation*, **19**, 965-972. <http://dx.doi.org/10.1002/lt.23696>
- [9] Bilbao, I., Figueras, J., Grande, L., Cleries, M., Jaurrieta, E., Visa, J. and Margarit, C. (2003) Risk factors for death following liver retransplantation. *Transplantation Proceedings*, **35**, 1871-1873. [http://dx.doi.org/10.1016/S0041-1345\(03\)00585-2](http://dx.doi.org/10.1016/S0041-1345(03)00585-2)
- [10] Mora, N.P., Klintmalm, G.B., Cofer, J.B., Poplawski, S.S., Goldstein, R.M., Gonwa, T.A. and Husberg, B.S. (1990). Results after liver retransplantation (RETx): A comparative study between "elective" vs "non-elective" RETx. *Transplantation Proceedings*, **22**, 1509-1511.
- [11] D'Alessandro, A.M., Ploeg, R.J., Knechtle, S.J., Pirsch, J.D., Stegall, M.D., Hoffman, R. and Sollinger, H.W. (1993) Retransplantation of the liver: A seven-year experience. *Transplantation*, **55**, 1083-1087. <http://dx.doi.org/10.1097/00007890-199305000-00028>
- [12] Bellido, C.B., Martinez, J.M.A., Gomez, L.M.M., Artacho, G.S., Diez-Canedo, J.S., Pulido, L.B., Acevedo, J.M.P. and Bravo, M.A.G. (2010) Indications for and Survival after liver retransplantation. *Transplantation Proceedings*, **42**, 637-640. <http://dx.doi.org/10.1016/j.transproceed.2010.02.017>
- [13] Magee, J.C., Barr, M.L., Basadonna, G.P., Johnson, M.R., Mahadevan, S., McBride, M.A., Schaubel, D.E. and Leichtman, A.B. (2007) Repeat organ transplantation in the United States, 1996-2005. *American Journal of Transplantation*, **7**, 1424-1433. <http://dx.doi.org/10.1111/j.1600-6143.2007.01786.x>
- [14] Biggins, S.W., Beldecos, A., Rabkin, S. and Rosen, H.R. (2002) Retransplantation for hepatic allograft failure: Prognostic modeling and ethical consideration. *Liver Transplantation*, **8**, 313-322. <http://dx.doi.org/10.1053/jlts.2002.31746>
- [15] Linhares, M.M., Delcio, M., Adauto, C.F., Tarcisio, T., Alberto, G. and Denis, C. (2006) Liver retransplantation: A model for determining long-term survival. *Transplantation*, **81**, 1016-1021. <http://dx.doi.org/10.1097/01.tp.0000203798.96491.2f>
- [16] European Liver Transplant Registry. (2000) <http://www.eltr.org>
- [17] Mirza, D.F., Gunson, B.K. and Da Silva, R.F. (1994) Policies in Europe on "marginal quality" donor livers. *Lancet*, **344**, 1480-1483. [http://dx.doi.org/10.1016/S0140-6736\(94\)90294-1](http://dx.doi.org/10.1016/S0140-6736(94)90294-1)
- [18] Lerut, J.P., Bourlier, P. and de Ville de Goyet, J. (1995) Improvement of technique for adult orthotopic liver transplantation. *Hepatology*, **30**, 395-400.
- [19] OPTN/SRTR 2010 Annual Report. (2010) <http://optn.transplant.hrsa.gov/ar2010>
- [20] Wax, D.B., Torres, A., Scher, C. and Lebowitz, A.B. (2008) Transesophageal echocardiography utilization in high-volume liver transplant centers in the United States. *Journal of Cardiothoracic and Vascular Anesthesia*, **22**, 811-813. <http://dx.doi.org/10.1053/j.jvca.2008.07.007>
- [21] Yoo, M.C., West, J.M., Eason, D. and Vanatta, J.M. (2012) The advantages and disadvantages of perioperative transesophageal echocardiography during liver transplantation. *Anesthesia and Clinical Research*, **S4**, 003.
- [22] Warnaar, N., Molenaar, I.Q., Colquhoun, S.D., Sloof, J.H., Sherwani, S., De Wolf, A.M. and Porte, R.J. (2007) Intraoperative pulmonary embolism and intracardiac thrombosis complicating liver transplantation: A systemic review. *Journal of Thrombosis and Haemostasis*, **6**, 297-302.
- [23] Sakai, T., Matsusaki, T., Dai, F., Tanaka, K.A., Donaldson, J.B., Hilmi, I.A., Marsh, J.W., Planinsic, R.M. and Humar, A. (2012) Pulmonary thromboembolism during adult liver transplantation: incidence, clinical presentation, outcome, risk factors, and diagnostic predictors. *British Journal of Anesthesia*, **3**, 469-477.

<http://dx.doi.org/10.1093/bja/aer392>

- [24] Spier, B.J., Larue, S., Teelin, T., Leff, J. and Swize, L.R. (2009) Review of complications in a series of patients with known gastro-esophageal varices undergoing trans-

esophageal echocardiography. *Journal of the American Society of Echocardiography*, **22**, 396-400.

<http://dx.doi.org/10.1016/j.echo.2009.01.002>