Combined liver and kidney transplantation

L. Bäckman, MD, PhD
Department of Transplantation and Liver Surgery. Sahlgenska University Hospital. Sweden

INTRODUCTION

Liver failure, acute or chronic is commonly associated with some degree of renal dysfunction. In selected patients with an irreversible renal failure a combined kidney and liver transplantation may therefore be indicated. Hepatorenal syndrome is a controversial diagnosis that most commonly reverses after liver transplantation (Ltx). The diagnosis of hepatorenal syndrome is made after the exclusion of a coexisting renal disease.

The evaluation of a liver transplant recipient with renal failure should include urinalysis, estimation of the glomerular filtration rate (GFR), and quantification of proteinuria, blood urea nitrogen measurement, creatinine measurement, ultrasound of the kidneys and preferrably also a kidney biopsy. The latter should be done with caution because of the considerable risk of bleeding caused by the coagulopathy. The diagnosis of hepatorenal syndrome is thus made by exlusion.

Serum creatinine levels are misleading in the evaluation of renal function in liver transplant candidates and in order to get an accurate determination of the renal function it is neccesary to measure the GFR[1]. This is also true after liver transplantation where renal dysfunction is becomming an increasing problem. High levels of bilirubin can interfere with the measurement of creatinine in deeply jaundiced patients resulting in lower creatinine levels. Secondly, the severe nutritional depletion and deranged protein metabolism associated with liver and renal failure may produce a situation where the creatinine level reflects the lowered muscular mass and protein stores rather than the renal function. The same is also true with creatinine clearence estimates

RESULTS AND DISCUSSION

There are a limited number of reports and the number of patients is relatively small[2-8]. Therefore it is difficult to make conclusions and recommendations based on these reports. Several papers also include combined liver and kidney transplants preformed over longer periods of time[2,3]. Patient selection is, as always an important factor when analyzing the outcome. An obvious indication for a combined kidney and liver transpantation is polycystic liver and kidney disease. The need for kidney transplantation in those patients in need for Ltx was however reported to be low, 1/14[4].

From a surgical - technical point a combined liver and kidney transplantation is usually not more complicated than a Ltx, however the procedure is of course more time consuming than a regular Ltx. The liver is transplanted first followed by the kidney from the same donor. The risk of intraoperative and post operative bleeding must be considered and the risk of acute tubular necrosis post-transplant. This risk should theoretically not be higher than after any kidney transplantation but some sort of kidney assisting device i.e., contious venous-venous hemofiltration should be used during the Ltx in order to optimize the fluid and electrolyte balance i.e, potassium and circulatory status. Post-transplant a non-nephrotoxic immunosuppressive regimen, or a regimen with low nephrotoxic potential should preferrably be used[9].

The survival rates seem to be comparable with patients undergoing Ltx. It was however recommended that the indication for simultaneous organ transplantation should be considered earlier than for transplantation involving only one organ[5]. In a pediatric study the 5 year survival rates after combined kidney and liver transplantation were comparable to patients undergoing Ltx alone (67% *versus* 69%, respectively)[3].

The most striking result is the relatively low number of kidney rejection episodes after combined liver and kidney transplantation. The incidence of acute rejection was reported to be 30% for the liver and 15% for the kidney, respectively[5]. It was therefore suggested that the liver immunologically protected the kidney from being rejected[2,6]. It was also reported on successful kidney transplants in patients against a positive cross match and multispecific HLA antibodies after a combined liver and kidey transplantation[6,10]. In a follow-up on 18 patients undergoing combined liver and kidney transplantation 8 had lymphocytotoxic antibodies and 5 had positive cross-matches pre-transplant. The 1-year patient survival was excellent (95%) and the long-term survi-

val was not impaired in patients with a positive cross-match[6].

The exact mechanism behind this effect is unknown. It was suggested that the liver graft neutralized or inactivated the multispecific antibodies[10]. When the cross-match was repeated during the Ltx the cross-match became negative after portal reperfusion. In a case report from our center the long-term kidney and liver function was excellent in a sensitized patient undergoing a combined liver and kidney transplantation[10]. This patient, a 50 year old woman with chronic glomerulonephritis received her 4th kidney transplant in combination with a livergraft from the same donor against a positive cross-match. The indication for Ltx was end stage liver disease secondary to chronic hepatitis C. Her current immunosuppression consits of Prograf (1 mg bid) and CellCept (250 mg qd) and off steroids completely, with a GFR of 35 ml/min and a creatinine level of 125. She is also back to full time work.

In conclusion, combined liver and kidney transplantation is the treatment of choice in patients with end-stage liver disease and irreversible renal failure. The results are similar to isolated liver transplantation but the number of acute rejection episodes in the kidney seems to be less. A kidney transplantation may be performed against a positive cross-match in sensitized patient when done after a liver transplantation from the same donor. The liver seems to imunologically protect the transplanted kidney by unknown mechanisms.

REFERENCES

1. Bäckman L, Olausson M, Mjörnstedt L, Herlenius G, Friman S: Renal Function after Liver Transplantation. *Transplant Proc* 2001 (in press).
2. Margreiter R, Streurer W, Spechtenhauser B, Konigsranier A. Kidney transplantation together with another solid organ from the same donor- a singel center progress report. *Clin Nephrol* 53: 38-433, 2000.
3. Grewal HP, Brady L, Cronin DC, Loss GE, Siegel CT, Oswald K, Fisher JS, Bruce DC, Aronsson AJ, Woodle ES, Millis JM, Thistletwaite JR, Newell KA: Combined liver and kidney transplantation in children. *Transplantation* 15: 70, 2000.
4. Pirenne J, Aerts R, Yoong K, Gunson B, Koshiba T, Fourneau I, Mayer D, Buckels J, Mirza D, Roskams T, Elías E, Nevens F, Fevery J, McMaster P: Liver transplantation for polycystic liver disease. Liver Transpl 7: 238-245, 2001.
5. Kleim V, Ringe B, Frei U, Pichlmayr R: Single-center experience of combined liver and kidney transplantation. *Clin Transplant* 9: 39-44, 1995.
6. Lang M, Kahl A, Bechstein W, Neumann U, Knoop M, Frei U, Neuhaus P: Combined liver-kidney transplantation: long-term follow up in 18 patients. *Transplant Int* 11: 155-159, 1998.
7. Hiesse C, Samuel D, Bensadoun H, Blanchet P, Castaing D, Adam R, Chraibi A, Charpentier B, Bismuth H: Combined liver and kidney transplantation in patients with chronic nephritis associated with end-stage liver disease. *Nephrol Dial Transplant* 6: 129-133, 1995.
8. Jeyarajaah DR, Gonwa TA, McBride M, Testa G, Abbasolglu O, Husberg BS, Levy MF, Goldstein RM, Klintmalm GB: Hepatorenal syndrome: combined liver kidney transplants versus isolated liver transplants. *Transplantation* 64: 1760-1765, 1997.
9. Bäckman L, Morales JM: Is non-nephrotoxic immunosupression a possibility. *Transplantation* 69: 27-30, 2000.
10. Mjörnstedt L, Friman S, Bäckman L, Rydberg L, Olausson M: Combined liver and kidney transplantation against a positive cross match in a patient with multispecific HLA-antibodies. *Transplant Proc* 29: 3164-3165, 1997.