Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

Renal dysfunction in liver transplant patients: comparing patients transplanted for liver tumor or acute or chronic disease

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Keywords
acute liver failure, chronic liver disease, glomerular filtration rate, liver tumor, renal failure.

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Received: 1 December 2006
Revision requested: 29 December 2006
Accepted: 8 March 2007

doi:10.1111/j.1432-2277.2007.00482.x

Summary

Liver transplant patients are susceptible to renal dysfunction through a number of mechanisms. Our aim was to investigate if renal function differs among transplant indication groups. Consecutive liver transplantations (396) were divided in three groups: 277 with chronic liver disease (CLD), 90 with acute liver failure (ALF), and 29 with liver tumor. Data were recorded before and after transplantation. The glomerular filtration rate (GFR) was based on Cockcroft–Gault formula and renal function staged using the National Kidney Foundation guidelines. On the transplantation day, 4%, 15%, and 0% of patients in the CLD, ALF, and tumor groups, respectively, showed severely decreased GFR (≤29 ml/min/1.73 m^2). The percentage with moderately or severely decreased GFR (<60 ml/min/1.73 m^2) increased steadily in the CLD group (46% at 5 years) but decreased in the ALF group from the transplantation day (26% at 5 years). Of patients with moderately or severely decreased GFR at listing, 73% of the CLD and 35% of ALF patients continued to exhibit it at 1 year. The cumulative incidence of chronic renal failure was 16% at 10 years. MELD scores did not show notable correlation with post-transplant GFR. Renal dysfunction prior to transplantation often improved post-transplant in ALF patients, but was often irreversible in CLD patients. In CLD and tumor patients, renal function steadily deteriorated post-transplant.

Introduction

As the success rates of liver transplantations have improved in recent years, the role of late complications, such as renal dysfunction, has attracted greater notice. For both prognostic and therapeutic reasons, it is important to assess the level of renal function and the degree of irreversibility of potential renal dysfunction in liver transplant patients [1,2]. Pre-existing renal dysfunction may negatively affect the outcome after liver transplantation and may require a combined liver–kidney transplantation [2–5]. Furthermore, post-transplant renal dysfunction may require changes in immunosuppression therapy to avoid progression of the renal dysfunction [1].

Liver transplant patients are at the risk of developing renal dysfunction through a number of mechanisms before, during, and after transplantation [3–16]. Both the existence and duration of pretransplant renal dysfunction have been presented as independent predictors of renal insufficiency after liver transplantation [2,15,17–20]. However, the incidence, mechanism, and duration of renal insufficiency may differ widely between acute and chronic liver disease (CLD) and in liver tumor patients [13,21–22].

The aim of this study was to investigate renal function in adult liver transplant patients in Finland and to compare renal function between different liver transplant indication groups. Furthermore, we have investigated

more closely those patients who developed chronic renal failure (CRF) and end-stage renal disease (ESRD).

Patients and methods

Patients

All liver transplantations were carried out at a single centre (Transplantation and Liver Surgery Clinic, Helsinki University Central Hospital). The study population included all adult patients (17 years of age and older) who received their first liver transplant up to June 2004. Excluded from the population were patients with prior organ transplants (one patient with a prior kidney transplant) and patients who received combined liver-kidney transplants (eight patients). Included patients are referred to here as the 'total group.' The total group was further stratified into subgroups based on the indication category for their liver transplantation: CLD, acute liver failure (ALF), or liver tumor. Patients with both liver tumor and some degree of CLD were included only in the tumor group.

Collected data

Clinical and laboratory data were collected from the Finnish liver transplant registry. Missing parameters were filled out from patient records and the hospital's laboratory database. The time points were pretransplantation (at listing), the day of transplantation, the worst value during the first postoperative week, and yearly thereafter. There was at least 1 year of the follow-up. Other endpoints of follow-up were start of dialysis, kidney transplantation, re-transplantation, or the patient's death.

Laboratory parameters linked to renal function were collected, namely plasma creatinine and urea. Furthermore, data on age, waiting time, indication for liver transplantation and pretransplantation extra-corporeal support therapies were recorded. Extra-corporeal therapies included were hemodialysis and hemodiafiltration; from 2001, molecular adsorbent recirculating system dialysis was also included. Scores according to the model of end-stage liver disease (MELD) [23] were calculated at transplantation.

For an estimation of glomerular filtration rate (GFR), creatinine clearances were calculated at the same time points as the creatinine levels were measured and patients' weights were recorded. Creatinine clearance was calculated using the Cockcroft–Gault formula [24]. According to this formula, GFR = (140-age) × weight (kg)/a × plasma creatinine (μmol/l), where a is 0.8 for males and 0.95 for females. All clearance values were normalized to a standard body surface area of 1.73 m^2 by the formula of DuBois and DuBois [25]. For stage classification of the renal function, the clinical practice guidelines from the National Kidney Foundation [26] were used. Here, stage 1 is GFR ≥ 90 ml/min/1.73 m^2 (normal), stage 2 is GFR 60–89 (mild decrease), stage 3 is GFR 30–59 (moderate decrease), and stage 4 is GFR ≤ 29 (severe decrease). In this study, ESRD was defined as GFR < 15 or dialysis/kidney transplantation, and CRF as stage 4 or ESRD lasting at least six months.

Immunosuppression

All patients had calcineurin-inhibitor-based initial immunosuppression. Over 80% received cyclosporine-based therapy, combined with azathioprine and methylprednisolone. Only some patients, participating in controlled clinical trials, had tacrolimus-based initial immunosuppression. Furthermore, some immunologically unstable patients were converted from cyclosporine to tacrolimus. Cyclosporine and tacrolimus blood concentrations were recorded at the time points mentioned above. The initial target of cyclosporine concentration was 200–250 ng/ml, decreasing with time to maintain a level of 70–150 ng/ml; for tacrolimus, these values were 15–20 ng/ml and 5–10 ng/ml, respectively. The target blood concentrations of cyclosporine were somewhat higher during the 1980's than at later times, but patients transplanted during this period comprise only 9% of our total transplant population.

Statistical methods

The data were fed into a Microsoft Excel file and analyzed using StatView for Windows (SAS Institute, Inc., Cary, NC, USA) statistical software. The unpaired t-test or Mann–Whitney test as appropriate was used for comparing two groups; the Kruskal–Wallis test was used for comparing three groups. The paired t-test or Wilcoxon signed-rank test as appropriate was used to test differences within a group between values at listing, transplantation day, first week, and 1 year. Chi-square tests were used for categorical numbers. Cumulative incidences were assessed using Kaplan–Meier methodology. Correlations between laboratory parameters were calculated using the Spearman correlation. P values < 0.05 were considered statistically significant.

Results

A total of 396 patients fulfilled the criteria for the total group; of these, 277 (70%) were in the CLD group, 90 (23%) in the ALF group, and 29 (7%) in the tumor group. The demographic and clinical features of these groups are presented in Tables 1 and 2. Eight patients

(28%) in the tumor group also had Child B or C chronic liver disease, and 21 patients (72%) had either no or Child A liver disease.

In the total group, the 1-, 3-, 5-, and 10-year graft survivals were 84%, 79%, 73%, and 64%, respectively.

Renal function

Mean levels of creatinine, estimated GFR, and urea for the different groups at different time points are shown in Table 3.

During the first post-transplant week, the plasma creatinine level was significantly higher compared with the levels at the transplantation day and at 1 year in all groups ($P < 0.0001$), except in the tumor group. In the total, CLD, and tumor groups, there was a significant increase in plasma creatinine from pretransplant levels to the one-year level ($P < 0.001$). In the ALF group, the corresponding difference was not significant. According to the Kruskal–Wallis test, statistical differences in creatinine between subgroups were found only at the first-week time point ($P = 0.0002$). When comparing the CLD and ALF groups, a significant difference was also found at listing ($P = 0.02$).

The mean estimated GFR decreased significantly in all groups by 1 year post-transplant compared with pretransplant levels ($P < 0.01$). No statistical differences were found between subgroups at different time-points, according to the Kruskal–Wallis test.

The level of urea followed the same trend in all groups. There was a significant increase by 1 year post-transplant compared with pretransplant levels in the total, CLD, and tumor groups ($P < 0.01$). Significant differences between subgroups were found at listing ($P = 0.03$) and at transplantation day ($P = 0.02$), according to the Kruskal–Wallis test.

The mean blood concentrations of cyclosporine and tacrolimus decreased steadily in post-transplant follow-up. Mean (SD) concentrations (ng/ml) in the total group at 1-, 3-, 5- and 10 years were 184 (82), 159 (63), 143

Table 2. Liver transplantation diagnoses *n* (%) in the chronic liver disease, acute liver failure, and liver tumor groups.

Total group, $n = 396$	*n* (%)
Chronic liver disease group, $n = 277$ (70%)	
Primary biliary cirrhosis	95 (34)
Primary sclerosing cholangitis	62 (22)
Alcoholic cirrhosis	41 (15)
Cryptogenic cirrhosis	31 (11)
Cirrhosis posthepatitis (C)	8 (3)
Other	40 (15)
Acute liver failure group, $n = 90$ (23%)	
Unknown etiology	57 (63)
Other known	11 (12)
Acute Budd-Chiari	9 (10)
Other drug related	8 (9)
Toxic (nondrug)	4 (5)
Paracetamol	1 (1)
Liver tumor group, $n = 29$ (7%)	
Hepatocellular carcinoma and cirrhosis	13 (45)
Hepatocellular carcinoma and non-cirrhotic liver	10 (35)
Other liver malignancies	6 (20)

Table 1. Clinical and demographic characteristics of the total group and the CLD, ALF, and tumor groups.

	Total group	CLD group	ALF group	Tumor group
Patients	396	277	90	29
Age at transplantation (years), mean (SD)	48 (11)	49 (11)	46 (12)	52 (9)
Male/female, % (*n*)	42:58 (168:228)	42:58 (117:160)	34:66 (31:59)	69:31 (20:9)
Waiting time (days), mean (SD)	32 (49)	42 (55)	5 (6)	31 (33)
Preoperative dialysis* or MARS, % (*n*)	15% (58)	8% (21)	40% (36)	3% (1)
days on preoperative dialysis, mean (SD)	10 (17)	16 (26)	5 (5)	11 (-)
MELD score at transplantation, mean (SD)	20 (11)	18 (9)	31 (9)	10 (7)
Time period of liver transplantation, *n*				
1982–1994	130	95	24	11
1995–2000	142	94	39	9
2001–2004	124	88	27	9
Endpoints of follow-up, *n*				
Living	273	198	61	14
Dialysis	7†	6	1	0
Death	81	55	12	14
2. Liver transplantation	35	18	16	1

CLD, chronic liver disease; ALF, acute liver failure; MARS, molecular adsorbent recirculating system; MELD, model of end-stage liver disease.
*Hemodialysis or hemofiltration.
†Of these patients, three later received a liver transplant and two received a kidney transplant.

Table 3. Levels of creatinine (μmol/l), estimated GFR (ml/min/1.73 m^2) and urea (mmol/l) at different time-points for the total group and the chronic liver disease, acute liver failure, and liver tumor groups.

	At listing	LT day	1 week	1 year	3 years	5 years	10 years
Total group							
n	396	395	394	327	213	161	52
Creatinine, mean (SD)	100 (87)*	106 (81)*	166 (112)	109 (50)	112 (38)	115 (45)	102 (32)
Estimated GFR, mean (SD)	99 (50)*	94 (55)*		76 (29)	71 (28)	67 (24)	70 (23)
Urea, mean (SD)	7.9 (7.4)*	8.1 (6.3)*		9.5 (4.3)	9.0 (3.7)	9.4 (3.9)	8.7 (3.2)
Chronic liver disease group							
n	277	276	276	235	156	120	41
Creatinine, mean (SD)	91 (73)*	96 (60)*	155 (104)	108 (48)	111 (38)	116 (47)	100 (33)
Estimated GFR, mean (SD)	98 (46)*	91 (43)*		76 (30)	71 (27)	65 (23)	71 (23)
Urea, mean (SD)	8.1 (7.2)*	8.5 (6.3)*		9.6 (4.3)	8.9 (3.4)	9.6 (4.1)	8.8 (3.5)
Acute liver failure group							
n	90	90	88	71	47	34	9
Creatinine, mean (SD)	137 (122) N.S.	143 (126) N.S.	210 (131)	107 (55)	113 (38)	107 (33)	115 (32)
Estimated GFR, mean (SD)	97 (62)***	101 (86)***		76 (28)	71 (28)	75 (26)	64 (23)
Urea, mean (SD)	8.1 (8.3) N.S.	7.7 (6.7) N.S.		9.2 (4.6)	9.3 (4.5)	8.7 (2.5)	8.3 (2.0)
Liver tumor group							
n	29	29	29	21	10	7	2
Creatinine, mean (SD)	75 (20)**	80 (25)**	145 (93)	121 (45)	124 (42)	134 (39)	87 (11)
Estimated GFR, mean (SD)	111 (38)*	105 (35)*		75 (24)	77 (43)	60 (25)	70 (-)
Urea, mean (SD)	5.6 (4.3)***	5.7 (2.5)***		9.4 (2.6)	10.0 (3.5)	10.6 (5.0)	8.5 (2.1)

LT day, day of liver transplantation; 1 week indicates highest creatinine values recorded for each patient during their first post-transplant week. *$P < 0.0001$, **$P < 0.001$, ***$P < 0.01$; NS, not significant, when compared with 1-year levels. Estimated GFR tested by paired *t*-test, others by Mann–Whitney test.

(41) and 122 (35) for cyclosporine, and 10.7 (7.6), 9.2 (5.1) and 7.7 (3.9) (10 year level not available) for tacrolimus, respectively.

Frequency distribution of different stages of renal dysfunction

The relative frequency distributions of the different stages of renal dysfunction at different time-points are shown in Fig. 1. It must be pointed out here that patients in continuous post-transplant dialysis at the different time-points are not included in these results because their follow-up ended when dialysis was started. The incidence of stage 4 (severe) renal dysfunction at listing was 4.8% in the total group, and 2.2%, 14.6%, and 0.0% in the CLD, ALF, and tumor groups, respectively. In the post-transplant years, a steadily increasing proportion of patients in stages 3 or 4 (moderate or severe decrease) was seen in the total and CLD groups.

In the ALF group, there was a significant decrease ($P = 0.005$) in the incidence of stage 4 renal dysfunction at 1 year compared to at listing. A similar decrease was not seen in the other groups. In the tumor group, stage 4 renal dysfunction did not occur at listing or at 1 year, but, at 3 years, there was already an incidence of 10%, followed by 20% at 5 years.

CRF and ESRD after liver transplantation

In the total group, there were seven patients who developed ESRD. An additional 18 patients developed CRF, making the total amount of patients with CRF 25. The cumulative incidence of CRF rose from 1.8% at 1 year post-transplant to 9.7% at 5 years, and 15.7% at 10 years. The incidence of ESRD rose from 0.3% at 1 year post-transplant to 1.8% at 5 years, and 3.3% at 9 years. The mean time to ESRD was 5.6 years (range 0.2–9.6 years), and the mean time to CRF was 4.3 years (range 0–10 years). Of the seven ESRD patients, six belonged to the CLD group and one to the ALF group. Of the remaining 18 CRF patients, 14 belonged to the CLD, three to the ALF, and one to the liver tumor group.

The renal diagnoses in ESRD patients were clinically confirmed and also confirmed by renal biopsy in four cases. Four of the seven ESRD patients had presumed chronic calcineurin inhibitor toxicity (three supported by biopsy results), one had pre-existing IgA nephropathy (biopsy confirmed), one had polycystic kidney-degeneration along with antibiotics toxicity, and one had an uncertain diagnosis due to multiple predisposing factors (diabetes mellitus, hypertension, and calcineurin inhibitor toxicity). At the end of our follow-up, two of the ESRD patients remained in dialysis, two had received a kidney transplant, and three

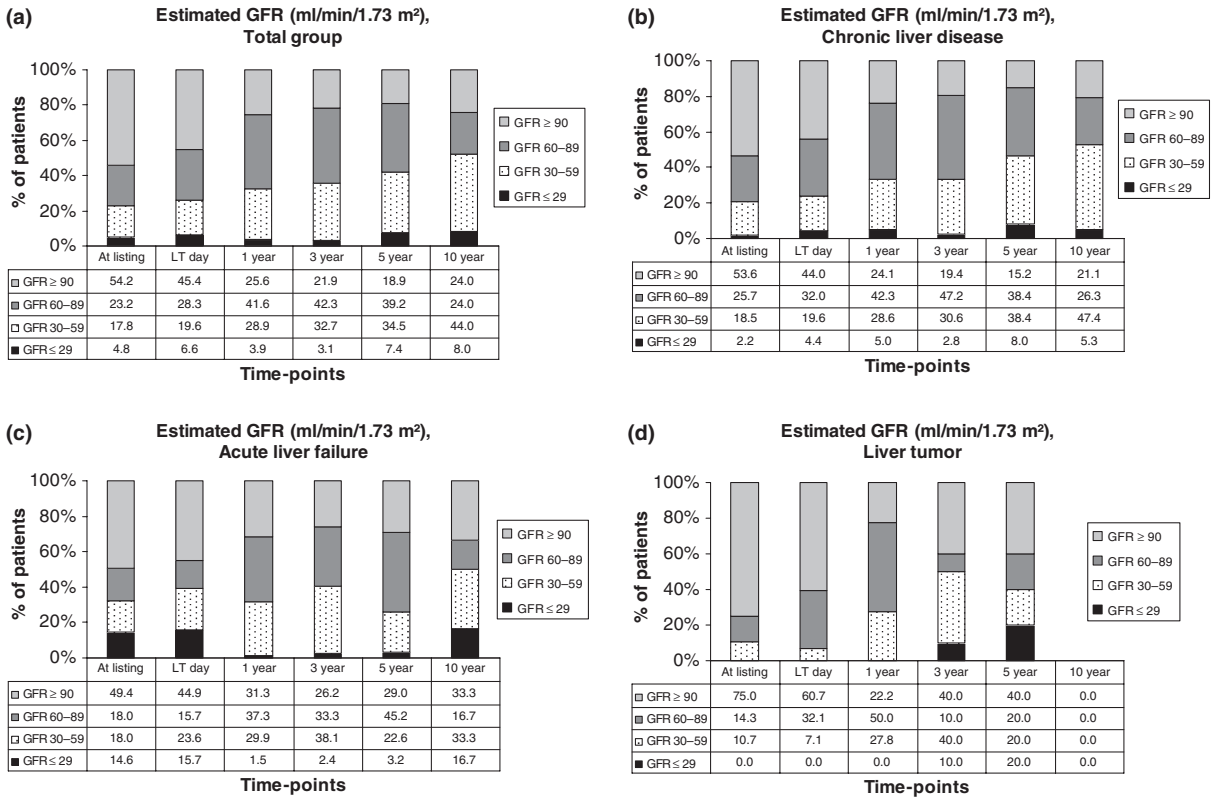

Figure 1 Relative frequency distribution of estimated GFR at different time-points among the total group (a), chronic liver disease (b), acute liver failure (c), and liver tumor (d) groups. Patients in continuous post-transplant dialysis were excluded. LT day, day of liver transplantation.

had died without kidney transplantation. Dialysis was begun in all patients before kidney transplantation.

Of the 25 patients who developed CRF, 36% (9/25 patients) had stage 3 renal dysfunction at listing, and 12% (3/25 patients) had stage 4 renal dysfunction at listing. At 1 year, 44% (11/25 patients) had stage 3 renal dysfunction, and 40% (10/25 patients) had stage 4 renal dysfunction.

Five of the 58 patients who were on pretransplant dialysis (Table 1) developed CRF post-transplant, making the relative risk of developing CRF 1.46 compared to patients without pretransplant dialysis. This increase, however, was not statistically significant according to the chi-square test.

Stratification of patients based on their estimated GFR at listing

All patients were stratified in two subgroups based on their estimated GFR at listing, either <60 (90 patients) or ≥60 (306 patients) ml/min/1.73 m^2. The mean levels of estimated GFR at different time-points for these subgroups are shown in Fig. 2a. After transplantation, the renal function decreased in patients with good pretransplant estimated GFR; in contrast, it improved among patients with poor pretransplant estimated GFR.

In the CLD and ALF groups, the number of patients with estimated GFR < 60 ml/min/1.73 m^2 at listing were 57/277 and 30/90, respectively. Post-transplant changes of the mean estimated GFR in both the CLD and ALF groups are also shown for subgroups according to pretransplant estimated GFR in Fig. 2b. Patients in the tumor group were excluded from this stratification because of too few patients.

Of the patients with poor pretransplant GFR, 73% (32/44 patients) remained with an estimated GFR < 60 ml/min/1.73 m^2 at 1 year in the CLD group, compared with 35% (8/23) in the ALF group at 1 year. The respective results at 5 years were 76% (19/25) in the CLD group and 15% (2/13) in the ALF group.

Correlations of estimated GFR at different time-points

Correlations of estimated GFR at listing with that at 1 year were 0.540 ($P < 0.0001$) in the total group, 0.626 ($P < 0.0001$) in the CLD group, 0.352 ($P = 0.004$) in the ALF group and 0.489 ($P = 0.03$) in the tumor group, respectively. The corresponding correlations for estimated GFR at listing with that at 3 years were 0.512 ($P < 0.0001$), 0.621 ($P < 0.0001$), 0.271 (not significant)

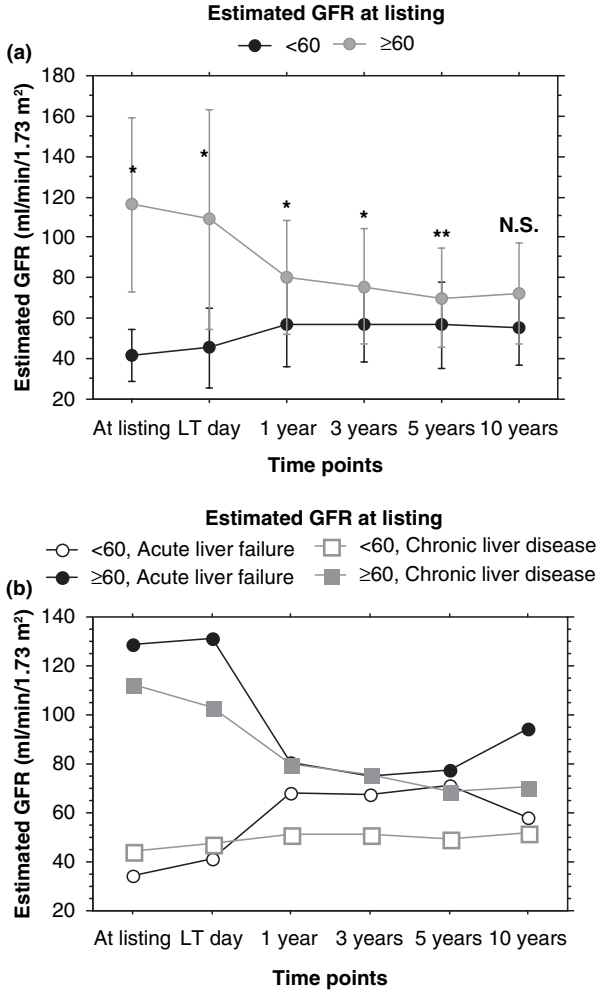

Figure 2 Stratification of the total group (a) and the CLD and ALF groups separately (b), based on the estimated GFR at listing (< or ≥ 60 ml/min/1.73 m^2), and the subsequent mean estimated GFR after liver transplantation. Vertical lines represent ±1 standard deviation. CLD, chronic liver disease; ALF, acute liver failure; LT day, day of liver transplantation; NS, not significant. *$P < 0.0001$, **$P = 0.003$.

and 0.721 ($P = 0.03$) in the respective groups. Further, correlations at 1 year with at 3 years were 0.862 ($P < 0.0001$), 0.862 ($P < 0.0001$), 0.852 ($P < 0.0001$) and 0.988 ($P = 0.003$). These results show that the estimated GFR at listing had the strongest correlation with the estimated GFR at 1 year in the CLD group compared to other subgroups.

Estimated GFR according to time period of transplantation

Patients were stratified into three equally large subgroups according to time period of their liver transplantation, as

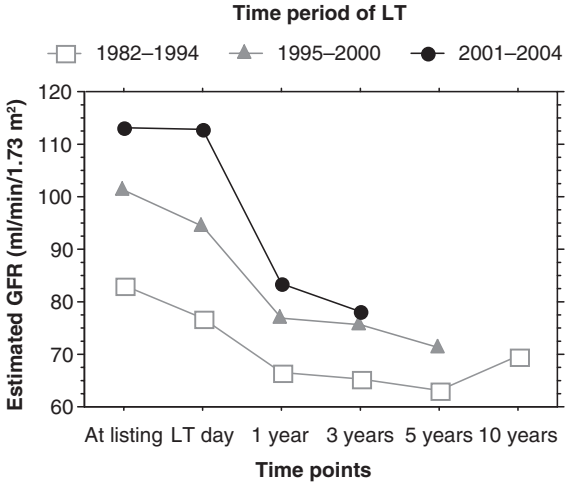

Figure 3 Mean estimated GFR at different time-points for the total group according to time period of transplantation. LT, liver transplantation.

presented in Table 1. The mean estimated GFR of these subgroups is given in Fig. 3. According to the Kruskal–Wallis test, mean estimated GFR was significantly lower in earlier time periods than later ones (at listing and at transplantation day $P < 0.0001$, at 1 year $P = 0.0004$, at 3 years $P = 0.029$, at 5 and 10 years not computable). However, the steepness of loss of function post-transplant was greatest in the later time periods, namely the subgroups with better pretransplant estimated GFR.

MELD score as a predictor of post-transplant renal dysfunction.

The highest mean MELD scores were in the ALF group and the lowest in the tumor group (Table 1). Correlation of MELD score with estimated GFR at 1 year was −0.220 ($P < 0.0001$) in the total group, −0.341 ($P < 0.0001$) in the CLD group, −0.001 (not significant) in the ALF group and −0.081 (not significant) in the tumor group. The corresponding correlations for MELD scores with estimated GFR at 5 years were −0.072 (not significant), −0.264 ($P = 0.005$), 0.135 (not significant) and 0.107 (not significant) in the respective groups.

We further stratified patients into two groups based on their MELD scores, either ≤25 (269 patients) or >25 (127 patients). The mean levels of estimated GFR at different time-points for these two subgroups are shown in Fig. 4. The mean estimated GFR was higher pretransplant in the group with MELD ≤ 25, but the differences decreased by 1 year post-transplant. A significant difference between groups in the post-transplant period was found only at 3 years ($P = 0.03$).

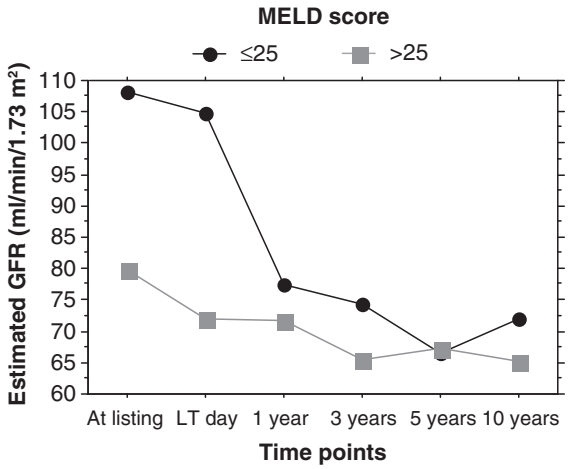

Figure 4 Stratification of the total group based on MELD score at LT day (≤ or >25), and subsequent mean estimated GFR at different time-points. LT, liver transplantation; MELD, Model of end-stage liver disease.

Discussion

It is well recognized that CRF and ESRD occur in liver transplant patients [16,19,27–28]. In our study, the cumulative incidence of CRF was 9.7% at 5 years after transplantation and 15.7% at 10 years, which is almost half of that recorded by Ojo *et al.* [19] in their review of 36 849 liver transplant patients in the United States. Ojo *et al.* [19] reported a cumulative incidence of CRF of 18% at 5 years. In addition, the cumulative incidence of ESRD in our study, specifically 1.8% at 5 years and 3.3% at 9 years, was somewhat lower than those reported in previous studies [16,27–28]. One explanation for these different results may be that ours was a single-center study, while the results reported by Ojo *et al.* [19] were based on a national registry that included a wide range of different centers. Another reason may be that we included only first transplants. Furthermore, during the follow-up, chronic patients developed CRF more often (7%, 20/277 patients) than acute patients (4%, 4/90 patients), and our liver transplant population included more acute patients (23%) compared with most national registries with about 10% of acute patients [29]. The relative number of acute patients in our transplant population was higher because of the extremely low number of patients with viral hepatitis or alcoholic liver disease. Moreover, the leading diagnoses in the CLD group in our population were primary biliary cirrhosis and primary sclerosing cholangitis (together 56%), while alcoholic liver disease and hepatitis C together constituted only 18% of diagnoses in this group. This is not true for most transplant centers [29], and due to this fact our results on the CLD group might not be directly generalized for other series.

It is known that none of the commonly used laboratory parameters accurately reflect renal function [2,30]. Also, creatinine-based equations for the GFR estimation have been shown to be inaccurate, especially in cirrhotic patients [2,30–36]. Direct measurement of GFR, on the other hand, using parameters like inulin clearance, is impractical and expensive, and was not used at our center. For the estimation of GFR, we employed the Cockcroft–Gault equation because of its wide use in clinical practice. In our study, mean creatinine and GFR did not markedly change after the first year of transplantation. The relative frequency distributions were better at showing the renal dysfunction development after transplantation. Approximately 23% of patients presented with moderate (stage 3) or severe (stage 4) renal dysfunction before transplantation. After transplantation, there was a clear trend of annually increasing incidences of moderate or severe renal dysfunction, namely 36% at 3 years and 42% at 5 years. These results are similar to those reported by Ojo *et al.* [19] and van Laarhoven *et al.* [37]. Both studies reported similar pretransplant incidences of up to 27% of moderate or severe renal dysfunction. Pawarode *et al.* [18] reported somewhat higher pretransplant incidences from their center, up to 36%.

The most noticeable difference in renal function among the three liver transplant indication groups was found in the first-week levels of creatinine. At that time point, ALF patients presented with worse creatinine levels compared with CLD or tumor patients. In the later postoperative period, no significant differences were found among the subgroups at different time-points; however, the frequency distribution of GFR again gives a more informative picture of the situation. As many as 15% of the patients in the ALF group had severe renal dysfunction at listing, compared with only 2% in the CLD group. In the years after transplantation, the relative frequency of patients with moderate or severe renal dysfunction increased steadily in the CLD group. In the ALF group, fewer patients developed severe renal dysfunction. Patients in the tumor group had rather good renal function before transplantation; however, even in this group, some deterioration of the renal function was seen in the years after liver transplantation.

Mai and Gonwa [1] emphasized in a recent review that it is important to assess the degree of irreversibility of a patient's renal dysfunction in the selection of patients best suited to combined liver-kidney transplantation. However, it is often difficult to predict if and in which patients renal function will recover, and in which patient the dysfunction will remain or even progress to ESRD [1,5]. In this regard, our study shows a clear difference

between patients with ALF and CLD. Of our ALF patients with moderate or severe renal dysfunction at listing, 65% recovered to the extent that their estimated GFR was ≥60 ml/min/1.73 m^2 at 1 year, which was also reflected in the total group as an improvement in the renal function for those patients with poor pretransplant renal function (seen in Fig. 2). These results agree with the results from previous studies, suggesting that patients with ALF often suffer from the reversible hepatorenal syndrome [2,4,11,15,38]. In the CLD group, however, only 27% of the patients with moderate or severe renal dysfunction at listing recovered to the same extent by 1 year post-transplant. Our results, therefore, suggest that renal dysfunction in CLD patients is generally more irreversible, while even severe renal dysfunction in ALF patients is likely to improve to some extent after transplantation.

As in previous studies [16,27–28], the GFR at 1 year had a better correlation with later renal function than the pretransplant GFR in the total group. In addition, of the patients who developed CRF, only 48% had moderate or severe renal dysfunction at listing, while up to 84% had that level of renal dysfunction at 1 year. However, in the CLD group, pretransplant GFR correlated rather well with GFR at both 1 and 3 years. This finding further supports the suggestion that there is a higher degree of irreversibility of pre-liver-transplantation renal dysfunction in patients with CLD. MELD scores at transplantation did not clearly correlate with the post-transplant renal function in this study. The only correlation was seen between the pretansplant MELD score and the estimated GFR at 1 year in the CLD group.

All patients received calcineurin-inhibitor-based immunosuppression, and four patients developed ESRD resulting from chronic calcineurin inhibitor toxicity. The policy of immunosuppression maintenance in patients with post-transplant renal dysfunction, at our center, was in mild cases to reduce doses of calcineurin-inhibitors, on an individual basis, as low as immunologically possible, and observe whether the renal function improved. In more severe cases, we aimed to withdraw calcineurin-inhibitors, either increasing or adding other immunosuppressive medication, which was successful in some patients. Although the mean levels of calcineurin inhibitor blood concentrations decreased steadily during the post-transplant follow-up, it is still possible that these reduced levels over a time of many years were nephrotoxic.

Conclusion

Prior to liver transplantation, the renal function was more often decreased in patients with ALF compared with patients with CLD or liver tumor. However, the renal function improved in patients with ALF by their first post-transplant year and remained quite stable thereafter, but steadily deteriorated in patients with CLD. Pretransplantation renal dysfunction was also more often irreversible in patients with CLD.

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