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Impact of RIFLE classification in liver transplantation

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Abstract: Acute renal failure (ARF) is common after orthotopic liver transplantation (OLT). The aim of this study was to evaluate the prognostic value of RIFLE classification in the development of CKD, hemodialysis requirement, and mortality. Patients were categorized as risk (R), injury (I) or failure (F) according to renal function at day 1, 7 and 21. Final renal function was classified according to K/DIGO guidelines. We studied 708 OLT recipients, transplanted between September 1992 and March 2007; mean age 44 ± 12.6 yr, mean follow-up 3.6 yr (28.8% ≥5 yr). Renal dysfunction before OLT was known in 21.6%. According to the RIFLE classification, ARF occurred in 33.2%: 16.8% were R class, 8.5% I class and 7.9% F class. CKD developed in 45.6%, with stages 4 or 5d in 11.3%. Mortality for R, I and F classes were, respectively, 10.9%, 13.3% and 39.3%. Severity of ARF correlated with development of CKD: stage 3 was associated with all classes of ARF, stages 4 and 5d only with severe ARF. Hemodialysis requirement (23%) and mortality were only correlated with the most severe form of ARF (F class). In conclusion, RIFLE classification is a useful tool to stratify the severity of early ARF providing a prognostic indicator for the risk of CKD occurrence and death.

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Orthotopic liver transplantation (OLT) is a well-established treatment for patients with advanced cirrhosis, fulminant acute hepatitis and a therapeutic option for some malignancies or metabolic diseases (1). Despite recent advances, in immunosuppressive regimens, surgical techniques, anesthesia and post-surgical management of liver transplants, renal dysfunction is a common complication in these patients (2).

Acute renal failure (ARF) is common in OLT and associated with several causes including volume depletion, sepsis and calcineurin inhibitor toxicity (3, 4). The reported incidence ranges from 12% to 70% (2, 5–7), depending on the criteria used to define ARF. In addition, some studies have shown that acute renal failure is associated with increased morbidity and mortality (2, 7, 8).

The Acute Dialysis Quality Initiative – ADQI – workgroup developed a set of criteria for defining and classifying ARF, i.e., the RIFLE classification, in which ARF is classified according to the degree of renal impairment, as Risk of renal dysfunction (R), Injury to the kidney (I), Failure (F) or Loss (L) of kidney function and End stage kidney disease (E). Both L and E criteria were subsequently removed, remaining only as clinical outcomes (9).

Two studies involving 92 and 300 OLT recipients have analyzed ARF according to the RIFLE classification and have shown that ARF was associated with an increase in mortality and length of hospital stay (10, 11). Several studies on non-OLT recipients, using RIFLE, have also demonstrated that ARF is associated with high mortality and occurrence of chronic kidney disease (12).

This retrospective study was performed in a large group of OLT recipients submitted to transplantation over the last 15 yr. The main aim of this study is to evaluate the prognostic value of RIFLE classification in the development of chronic kidney disease. Furthermore, this study also aims at

determining its prognostic value in requirement of hemodialysis and mortality.

Patients and methods

Study design

This was a retrospective study of 708 OLT recipients transplanted in our unit, between September 1992 and March 2007, using the piggy back technique, with partial cava clamping.

Clinical data included the age of patients when the transplantation occurred, their gender, weight, the etiology of hepatic failure, presence of diabetes mellitus, hypertension, hepatitis B and C infection, requirement for acute renal replacement therapy and immunosuppression. MELD classification was introduced in February 2002, and it has been only used in clinical practice in Portugal since 2007, and we did not classify recipients according to this score.

We analyzed serum creatinine (Scr) values and the glomerular filtration rate (GFR), estimated by the Cockcroft–Gault equation, before transplantation and at days 1, 7, and 21 after transplantation. Renal dysfunction before transplantation was defined by GFR ≤ 60 mL/min or Scr ≥ 1.5 mg/dL. At each time point, the patients were categorized as R, I or F according to the RIFLE criteria (R if increased Scr $\times$ 1.5 and/or decreased GFR $>25\%$; I if doubled Scr and/or decreased GFR $>50\%$; F if increased Scr $\times$ 3 and/or decreased GFR $>75\%$ and/or Scr >4 mg/dL). We selected the worst value for renal function of these three time points. The urinary output was not included.

GFR was also calculated after six months, 12 months and yearly thereafter. At the end of the follow up, renal function was classified according to the K/DIGO Clinical Practice Guidelines, as chronic kidney disease (CKD) stage 3 if the GFR was 30–59 mL/min; CKD stage 4 if the GFR was 15–29 mL/min and CKD stage 5 if the GFR was <15 mL/min or dialysis (13), dependent on the last value of the GFR.

Biochemical analysis

Laboratorial data considered were Scr at day 1, 7, 21, month 6, month 12 and annually. Biochemical analysis was performed using standard laboratory methods.

Immunosuppression protocols

Different immunosuppressive protocols have been used over a period of 15 yr. An association of cyclosporine, azathioprine and prednisolone was used in the majority of recipients up to 2003. Since then, 82% of the recipients received tacrolimus plus MMF and prednisolone. Between the years 2001 and 2007, sirolimus was used in a limited number of recipients. The use of cyclosporine, tacrolimus or sirolimus was considered as a dichotomous variable (yes or no) Steroids were usually employed during the first months (20 mg/d), and were slowly decreased during a period up to 12 months. Induction protocols with ATG or basiliximab were rarely employed until 2007.

Statistical analysis

The data are presented as mean $\pm$ SD values for normally distributed variables or as frequencies for categorical variables. Independent variables were compared using the Mann-Whitney or chi-square tests. Correlations between variables were studied with the Spearman correlation test for univariate analysis, and by linear regression for multivariate analysis (confidence interval of 95%), with forward method. All tests were performed using the SPSS system 15.0 (SPSS Inc., Chicago, IL, USA) and a $p < 0.05$ was considered statistically significant.

Results

Table 1 shows clinical characteristics of our population. The major cause for OLT was familial amyloidotic polyneuropathy, Portuguese type, and alcoholic liver disease. In 31.5% of the cases, hypertension and diabetes were present before transplantation. Mean follow up was 3.6 yr (range 1 d to 15 yr), with 28.8% of the patients (n = 204/708) having more than a five-yr follow-up period and 6.5% (n = 46/708) of them with a follow-up period lasting more than 10 yr.

Table 1. Clinical characteristic of OLT recipients

Variable	All patients (n = 708)
Age (yr)	44 ± 12.6
Male gender	64% (453)
Diabetes	15% (106)
Arterial hypertension	16.5% (117)
Etiology	
Familial amyloidotic polyneuropathy	30.6% (217)
Alcoholic cirrhosis	20.2% (143)
VHB and VHC cirrhosis	18.2% (129)
Primary biliary cirrhosis	5% (35)
Others	26% (184)
Renal dysfunction pre-transplantation	21.6% (133)
Mean follow-up (yr)	3.6 ± 3.4

( ) Number of patients.

Table 2. Outcome data post-transplantation

Variable	All patients (n = 708)
Acute renal failure (RIFLE criteria)	33.2% (235)
Renal replacement therapy	10.3% (73)
Retransplantation	12.6% (89)
Immunosuppression	
With cyclosporine	46.4% (329)
With tacrolimus	44.7% (316)
With sirolimus	8.9% (63)
Development of chronic kidney disease	45,6% (323)
Stage 3	34.3% (243)
Stage 4	6.2% (44)
Stage 5d	5.1% (36)
Months to CKD (≥stage 3)	14.1 ± 21.7
Months to CKD stage 5d	14.1 ± 23.6
Mortality	21.8% (154)

( ) Number of patients.

Table 2 shows the outcome data after the transplantation. Immunosuppression was based on calcineurin inhibitors in more than 90% of the recipients (cyclosporine on 46.4% of the patients and tacrolimus on 44.7% particularly after 2003). Only a few of the recipients were treated with sirolimus in the absence of tacrolimus or cyclosporine. Sirolimus was more frequently used in recipients with evidence of renal dysfunction pre-OLT (n = 21/133–15.8% vs. n = 42/575–7.3% without previous renal dysfunction; p = 0.0013), and in recipients with evidence of renal lesion within the first 24 h post-OLT (n = 18/63–28.5%).

In 21.6% of the patients (n = 133 patients), renal dysfunction was present before OLT, distributed as follows: 23% were familial amyloidotic polyneuropathy patients (n = 31 patients), 18.8% were alcoholic liver disease patients (n = 25), 18% were hepatitis patients (n = 24), 10.5% were primary biliary cirrhosis patients (n = 14), 9% were retransplanted patients (n = 12), 5.3% were fulminant hepatitis patients (n = 7), 3% were cryptogenic cirrhosis patients (n = 4), 3% were autoimmune hepatitis patients (n = 4), 3% were primary sclerosing cholangitis patients (n = 4), 2.3% were polycystic disease patients (n = 3), 1.5% were *amanita phalloides* intoxication patients (n = 2), 0.8% were hemocromatosis patients (n = 1), 0.8% were Budd Chiari patients (n = 1), and 0.8% were Wilson disease patients (n = 1).

Renal dysfunction prior to OLT was significantly correlated with the development of subsequent CKD, stage 3 ($r = 0.44$, $p < 0.0001$), stage 4 ($r = 0.15$, $p < 0.0001$), stage 5d ($r = 0.12$, $p = 0.003$), with dialysis requirement ($r = 0.20$, $p < 0.0001$) and with mortality ($r = 0.1$, $p = 0.001$). Hepatorenal syndrome occurred in 14 of these 133 patients (10.5%) and it was also correlated with mortality ($r = 0.1$, $p = 0.01$); eight of these 14 patients died, with a mean follow-up of three wk. Three patients recovered renal function with no need for renal replacement therapy, but the others (three patients) needed dialysis temporarily, eventually recovered renal function, within 22 d after OLT.

According to the RIFLE criteria, 33.2% of the recipients (n = 235) developed ARF during the first 21 d post-transplant, with a predominance of the R criteria patients (16.8% of recipients; n = 119). The mean time for R class development was 3.8 ± 3.4 d post-OLT. I criteria (8.5% n = 60) appeared with a mean time of 3.9 ± 3.8 d post-OLT and F criteria (7.9% n = 56) with a mean time of 2.8 ± 3.5 d post-OLT. The clinical data of these recipients are summarized in Table 3. The incidence and degree of ARF did not correlate with age, gender (except for a slight predominance of females in the F subgroup; $r = 0.1$, $p = 0.01$) or with the presence of diabetes. ARF was significantly more frequent in hypertension recipients and less frequent in recipients with familial amyloidotic polyneuropathy ($p < 0.005$). Recipients with viral cirrhosis did not have an increasing global incidence of ARF, although the R class occurred more frequently in these patients (R class – 25.5%, n = 33/129; $p = 0.005$). Viral hepatitis ($r = 0.1$, $p = 0.003$) particularly VHC cirrhosis ($r = 0.1$, $p = 0.005$) were risk factors for R criteria. Renal dysfunction pre-OLT was associated with an increasing incidence of more severe ARF (F class), but not with the classes I and R. The higher incidence of ARF (notably the F class) in OLT recipients under sirolimus probably only represents a more frequent use in recipients with initial evidence of increasing renal risk (renal dysfunction pre-OLT and changes in renal function in the first 24 h), as previously indicated.

Concerning the primary end-point of this study, RIFLE classification was a good predictor of CKD development at the end of the follow up. In fact, 55.5% (n = 66/119) of the recipients stratified to R class in the first 21 d post-transplant developed CKD (stage 3 in 43.7% of the patients, stage 4 in 8.4% and stage 5d in 3.4%) while 80% (n = 48/60) of the recipients classified as I class developed this same condition (stage 3 in 65% of the patients, stage 4 in 8.3% and stage 5d in 6.7%). The highest incidence of CKD (92.8%, n = 52/56) was found in the F class (57.1% developed CKD stage 3, and 12.5% stage 4; 23.2% of patients that developed F criteria were on regular hemodialysis at the time of the last follow-up). In both univariate and

Table 3. Clinical characteristic of OLT recipients with ARF according to the RIFLE classification compared with patients without ARF

Variables	Patients without ARF (n = 473)	Patients with ARF			
		R (n = 119)	I (n = 60)	F (n = 56)	Total (n = 235)
Age (yr)	43.6 ± 12.4	45.9 ± 13	45.5 ± 13	41.7 ± 12.8	44.8 ± 13
Male gender	65.8% (311)	65.5% (78)	61.7% (37)	48.2% (27)-*	60.4% (142)
Diabetes	14% (66)	21.4% (25)	17.2% (10)	10% (5)	17% (40)
Arterial HT	15% (71)	21.4% (25)	22.4% (13)	15.7% (8)	19.6% (46)**
Etiology					
FAP	34.2% (162)**	21.8% (26)	25% (15)	25% (14)	23.4% (55)
Alcoholic cirrhosis	18.2% (86)	23.5% (28)	28.3% (17)	21.4% (12)	24.2% (57)
HBV/HCV cirrhosis	16.7% (79)	27.7% (33)**	16.7% (10)	12.5% (7)	21.3% (50)*
PBC	4.7% (22)	2.5% (3)	10% (6)	7.3% (4)	5.5% (13)
RD pre-OLT	17.8% (84)	20.2% (24)	11.7% (7)	32.7% (18)*	20.9% (49)
ARF	0%	16.8%	8.5%	7.9%	33.2%
RRT	5.5% (26)	6.7% (8)	10% (6)	58.9% (33)**	20% (47)**
CKD development					
Stage 3	25.4% (120)	43.7% (52)*	65% (39)**	57.1% (32)**	52.4% (123)**
Stage 4	4.7% (22)	8.4% (10)	8.3% (5)	12.5% (7)*	9.4% (22)*
Stage 5d	3.2% (15)	3.4% (4)	6.7% (4)	23.2% (13)**	8.9% (21)**
Total	33.3%	55.5%*	80%**	92.8%**	70.6%
ISS					
With cyclosporine	46.5% (220)	48.8% (58)	50% (30)	37.5% (21)	46.4% (109)
With tacrolimus	45.9% (217)	44.5% (53)	35% (21)	44.6% (25)	42.1% (99)
With sirolimus	7.6% (36)	6.7% (8)	15% (9)	17.9% (10)	11.5% (27)**
Retransplantation	12.3% (58)	10.9% (13)	11.7% (7)	19.6% (11)	13.2% (31)
Mortality	23.5% (111)	10.9% (13)-**	13.3% (8)	39.3% (22)**	18.3% (43)

(-) inverse correlation; *p < 0.05; **p < 0.005.
() Number of patients; arterial HT, arterial hypertension; FAP, familial amyloidotic polyneuropathy; RD pre-OLT, renal dysfunction pre-orthotopic liver transplantation; ARF, acute renal failure; RRT, renal replacement therapy; ISS, immunosuppression.

multivariate analysis, ARF was correlated with development of all stages of CKD, the R and I criteria were correlated with the development of CKD stage 3 ($p = 0.02$ and $p < 0.001$, respectively), but not with the others stages of CKD, and F class was correlated with CKD stage 3, stage 4 and 5d ($p < 0.04$).

According to KDIGO definitions, 45.6% (n = 323) of all recipients developed CKD stages 3 to 5d, with 11.3% of them attaining stage 4 or 5d. Stage 3 (34.3% of all OLT recipients, n = 243) was diagnosed at a mean of 11.4 ± 17.1 month post-transplantation, stage 4 (6.2% of OLT recipients, n = 44) at 22.3 ± 27.7 month, and stage 5d (5.1% of OLT recipients, n = 36) at a mean of 14.1 ± 26.3 month (Table 2). CKD was common even in patients without ARF, with 7.9% (n = 37/473) of recipients developing stage 4 or 5d, and an additional 25.4% (n = 120/473) developing stage 3. In the subgroup of the 204 OLT recipients who survived for more than five yr, 51.2% (n = 106/204) of them developed CKD stage 3 to 5d, with 9.8% (n = 20/204) presenting advanced CKD (stage 4 or 5d). If we further extend the analysis to the 46 recipients who were followed up for a period of 10 or more years, only 30.4% of them will have no evidence of CKD (n = 14/46), while stage 3 will be observed in 56.6% (n = 26/46), and stage 4 or 5 in 13% (n = 6/46) Incidence of CKD was higher in recipients with evidence of ARF (Table 3), and the degree of ARF was correlated with the development of all stages of CKD ($p < 0.01$). This incidence of CKD progressively increased along with the degree of acute renal failure, with 35.7% (n = 20/56) of recipients included in the F class developing CKD stage 4 or 5d during the study period, and the majority of the remaining recipients developing CKD stage 3. According to multivariate analysis, risk factors for CKD development were age, renal dysfunction prior to OLT, ARF, F class, and hemodialysis requirement. There was no impact on CKD development whenever CNI were or not used, probably due to the fact that almost all patients were under CNI. If we analyzed CKD according to the GFR, we find that permanent renal dysfunction, GFR < 45mL/min, was, on univariate analysis, positively correlated with the use of Azathioprine ($r = 0.13$; $p = 0.001$), CyA ($r = 0.12$; $p = 0.003$) and sirolimus ($r = 0.16$; $p < 0.001$) and was inversely correlated with the use of tacrolimus ($r = -0.12$; $p = 0.002$) and MMF ($r = -0.16$; $p < 0.001$). On multivariate analysis, permanent renal dysfunction was positively correlated with sirolimus (CI 0.05 to 0.31; $p = 0.008$)

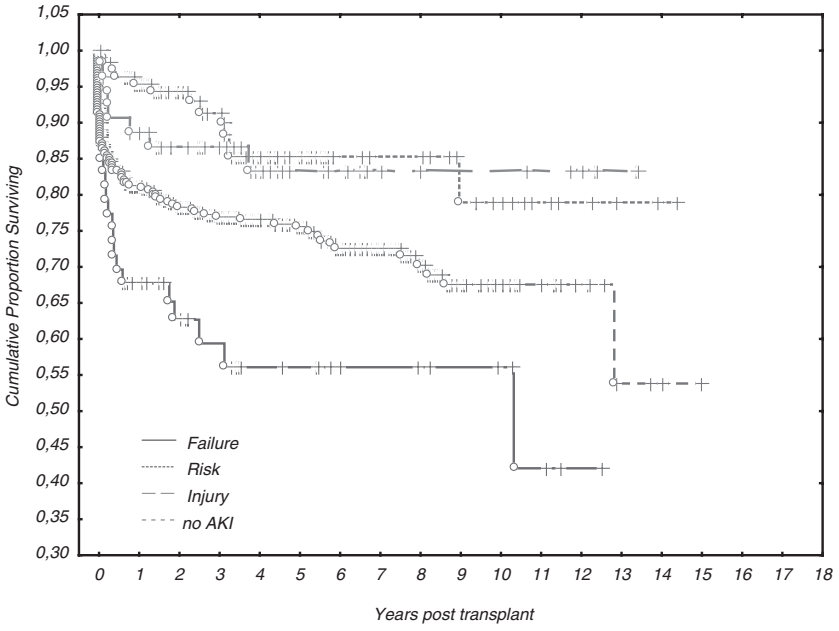

Fig. 1. Kaplan–Meier survival for OLT recipients according to RIFLE classification (failure, injury, risk and no ARF lesion); p = 0.0002. There is a significant difference between Failure and no AKI lesion.

and inversely correlated with the use of MMF (CI −0.2 to −0.07; p < 0.001).

Concerning the secondary aim of this study, renal replacement therapy was required for 73 recipients (10.3%), 37 patients required it only temporarily, and it was correlated in both uni- and multivariate analysis with ARF (r = 0.21, p < 0.0001; p < 0.001). Dialysis was required for 6.8% of R class patients, for 10.2% of I class patients and for 62.3% of F class patients (p < 0.0001). The mortality for the three groups R, I and F was, respectively, 10.9%, 13.3% and 39.3% versus 23.5% in OLT recipients without ARF. Mortality was higher in F class, in both univariate and multivariate analysis (r = 0.12, p = 0.001 and CI 0.06 to 0.28, β = 0.11, p = 0.003, respectively). The R criteria was inversely correlated with mortality (r = −0.12, p = 0.002 and CI −0.2 to −0.03, β −0.1, =0.006). Results on survival estimates using Kaplan–Meier formulation are presented in Fig. 1. As expected, there was a statistically decreased survival in F class patients.

Discussion

Changes in renal function are common after liver transplantation, both at an early stage with appearance of ARF, and latter with development of CKD. In our study of 708 OLT recipients both these observations are clearly demonstrated, but we further show that the presence of ARF (identified in 33.2% of recipients), and particularly the severity of early ARF (defined by standardized criteria) are associated with the development of CKD in the long term, allowing a very early identification of patients at risk.

Using RIFLE classification, the majority of ARF cases are classified as R class, followed by I class and F class. ARF of any severity (criteria R, I and F) correlated with subsequent development of chronic renal disease with GFR < 60 mL/min (CKD stage 3 or higher), while F class, the worst in terms of severity, was also associated with the appearance of CKD stage 4 and 5d and an increased mortality rate. The presence of mild to moderate ARF (R and I criteria) was not associated with an increased mortality or with the development of advanced renal failure, at least over the follow-up period. Interestingly, recipients with R class presented in fact a significantly lower mortality when compared to recipients without ARF. Both the R group and those without ARF have a similar follow-up procedure (data not shown), and except for a higher percentage of recipients with viral hepatitis and lower proportion of recipients with familial amyloidotic polyneuropathy, there are no apparent differences between the two groups, for which we have no explanation at the moment. However, we did not study the causes of mortality. Future studies are needed to clarify risk factors for ARF. The identification of these risk factors may lead to a development of measures to decrease ARF after OLT, and consequently reduce the severity of renal injury (F class), thus decreasing the development of CKD and mortality.

It is important to note that renal dysfunction pre-OLT was only correlated with the F criteria (failure) and was not correlated with less severe

degrees of ARF (R and I criteria) In addition, F class was associated with dialysis requirement and with a higher mortality. We may argue the fact that patients with renal dysfunction pre-OLT may be more susceptible to renal insult with severe complications, as renal failure, development of chronic renal disease and higher mortality. The higher mortality in this group of patients is in agreement with the findings of previous studies (14, 15).

Ultimately advanced CKD, stages 4 and 5d, developed in 11.3% of recipients, with 5.1% developing end stage renal disease (stage 5d). Less severe degrees of renal failure (stage 3) developed in 34.3% of all recipients, a figure that increases to 42.2% in patients followed for a period of more than five yr, when 9.8% of surviving recipients will have advanced renal failure (stage 4 or 5d). After a 10-yr follow-up period, only 30.4% of surviving recipients will not have evidence of CKD, and 13% will have advanced CKD (stage 4 or 5d). Although the incidence of advanced CKD in our study is similar to that previously described, the incidence of lesser degrees of CKD (stage 3) according to the K/DIGO definitions have only recently been described in detail (16). In our study the incidence of stage 3 is very high, ranging from 34.3%, in the entire cohort, to 42.2% in those with a follow-up period of more than five yr, and 56.6% for those followed for 10 or more years. The recent report found an incidence of CKD stage 3 of 47% in stable recipients with a follow-up period of at least five yr (16). Also CKD post-OLT is probably progressive once stage 3 has been attained. Taken together, these results demonstrate that in the next few years the proportion of OLT patients presenting with advanced renal disease will continue to increase, resulting in considerable morbidity and mortality.

There are some limitations to our study. First of all, it is a retrospective study with all the limitations of such studies, including a time span of 15 yr, a period during which recipient's recruitment and clinical protocols were undoubtedly subjected to various changes. The immunosuppression strategy was based on cyclosporine in early years, and based on tacrolimus after 2003. We noticed no influence of the type of calcineurin inhibitor used on the appearance of ARF. Tacrolimus and MMF may have a protective effect on renal dysfunction, although this apparent benefit may only result from the shorter follow-up of patients treated with these two immunosuppressants. Sirolimus was more frequently used in recipients with early evidence of renal dysfunction (either prior to or immediately after OLT) and also with more frequent evidence of severe ARF. However, a delayed recovery of renal function, like the one described in renal allografts with acute tubular necrosis, cannot be excluded (17).

Secondly, the number of FAP patients is very high and not comparable to the majority of liver centers. Nevertheless, our FAP patients, according to the RIFLE criteria, had less ARF events ($p < 0.005$) than the others and, according to the K/DIGO definition, had less renal dysfunction prior to OLT ($p = 0.01$) and had less CKD when compared to the others patients ($p < 0.0001$). We analyzed the data excluding FAP patients and the results were very similar to those presented in the manuscript and, therefore, FAP patients don't represent any bias to the results.

Thirdly, the recipient's selection was not based on the MELD score. In fact the MELD score was introduced only after 2002 and in Portugal only after 2007, and our study period goes back to 1992. A retrospective scoring would be inaccurate, therefore we did not attempt it, as we were not studying the causes of ARF, but instead the prognostic importance of its presence and degree.

Fourthly, changes in renal function (pre- and post-OLT) were based on Scr values, a further limitation, as malnutrition, reduced muscular mass and lack of hepatic function may contribute for false lower Scr levels (2). However, we believe that by estimating GFR on the basis of age, weight and creatinine we can partially surpass such limitation. Nevertheless, we cannot exclude that the number of patients with previous renal dysfunction may have been underestimated. Despite this limitation, recipients with renal dysfunction pre-OLT had severe ARF more frequently (and not class R or I), indicating the reliability of our approach. Notwithstanding, an estimation of GFR was applied to all patients.

Finally, we did not use urine output to stratify ARF. This approach has been validated by others (12), and we decided to take this approach as reliable records from the earlier recipients were unavailable and diuretics were used.

Altogether our results indicate that in the early post-transplant period, aggressive clinical care must be employed to prevent the development of severe ARF (F criteria), as soon as the first evidence of renal lesion appears. The presence of mild changes in renal function within the first days after the transplant (i.e., the R criteria) may rapidly progress to severe ARF, with considerable morbidity and mortality, as we have shown. However, our data also indicate that in the long term, if the ARF does not progress, mortality does not increase (in fact is lower than the control group), although increased incidence of CKD will be present, particularly stage 3.

Conclusions

In conclusion, RIFLE classification is a simple and a useful tool to stratify the severity of ARF providing a valuable prognostic indicator of the risk of developing chronic renal dysfunction and death. The R and I criteria predict in the long term a GFR < 60 mL/min, and the F criteria is a strong predictor of mortality and advanced CKD. As a consequence of our study, it is clear that the presence of early degrees of acute kidney injury (criteria R and I) require aggressive treatment as they anticipate the appearance of F criteria and in the long term they are associated with moderate CKD. By employing such strategy, taking every effort not to allow progression of the early acute renal lesion, we may be able in the long term to reverse the increased incidence of chronic renal failure and improve the survival rate of OLT recipients.

Conflict of interest statement

The results presented in this paper have not been published previously in whole or part, except in abstract form.

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