

# Liver Retransplantation in Adults: Overall Results and Determinant Factors Affecting the Outcome

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THE 1-year graft and patient survival rates following liver transplantation are continuously improving.<sup>1</sup> Advances in immunosuppression, improvements in organ preservation, technical refinements, and patient management have been determinant factors in this outcome.<sup>2</sup> However, few studies have attempted to analyze the role played by these and other factors in the outcome of liver retransplantation.<sup>3-5</sup>

Liver retransplantation is a life-saving operation, and retransplantation actually represents the only available alternative for patients with a failed initial graft. However, in the face of the organ shortage, and for the benefit of the patients, it would be useful to determine which factors, in the graft or in the recipient, are of importance in the outcome. This knowledge could help us in the selection of grafts' and patients' conditions with the higher success rate, by trying to avoid features linked with a significant lower success rate.<sup>6</sup>

Our study aimed to describe the actual results with liver retransplantation in adults, and to retrospectively identify which elements in the graft and the recipient were of importance in the outcome.

## MATERIALS AND METHODS

Between October 1987, the beginning of the systematic use of the University of Wisconsin preservation solution in our transplant program, and November 1990, 173 patients underwent a liver retransplant at our institution. Of these 173 patients, 151 had charts with complete information that could be analyzed in our study.

These 151 patients all had a second transplant (mean age 45 ± 13 years), 28 had a third transplant (mean 45 ± 13 years), and 6 had a fourth transplant (mean 42 ± 14 years). We will limit our analysis to the first and second transplants.

The initial liver diseases were: 104 cirrhosis (69%) (43 cryptogenic, 32 postnecrotic, 19 primary biliary cirrhosis, and 10 alcoholic), 16 fulminant hepatitis (10%), 12 primary sclerosing cholangitis (8%), and 19 other causes of liver failure (13%).

Causes of the initial graft failure were: 46 primary nonfunction (31%), 13 primary poor function (9%) (graft that never functioned

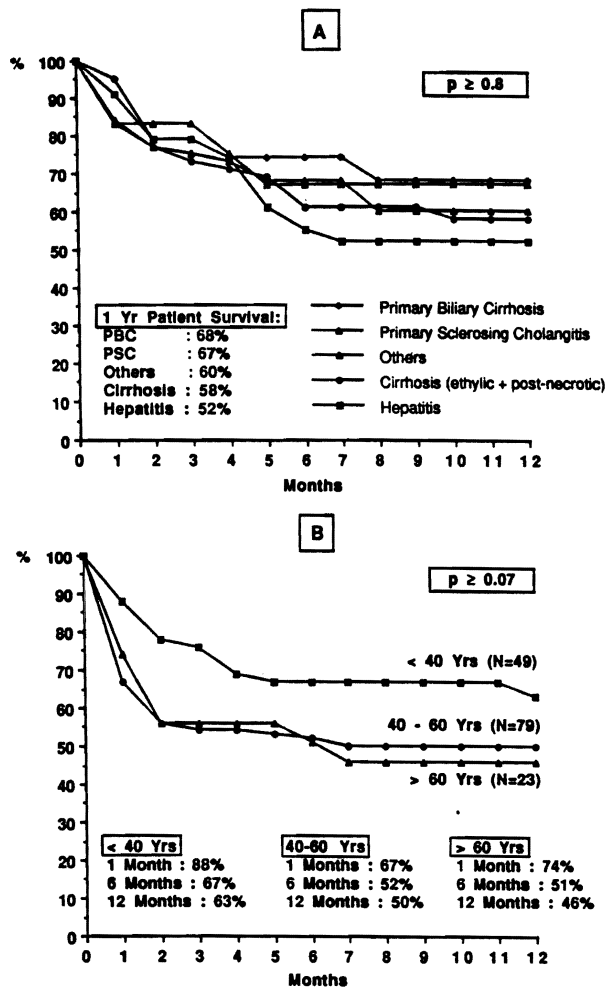


Fig 1. Actuarial patient survival curves according to the initial liver disease (A) and the age at the time of retransplantation (B).

properly without any identified reason), 40 rejections (26%), 27 thrombosis of the hepatic artery (18%), 5 venous thrombosis (3%), 8 recurrent hepatitis (5%), and 12 other (multifactorial) causes (8%). For the second transplant, the cold ischemia time was ≤8 hours in 37, 9 to 18 hours in 57, and >18 hours in 10. Recipients'

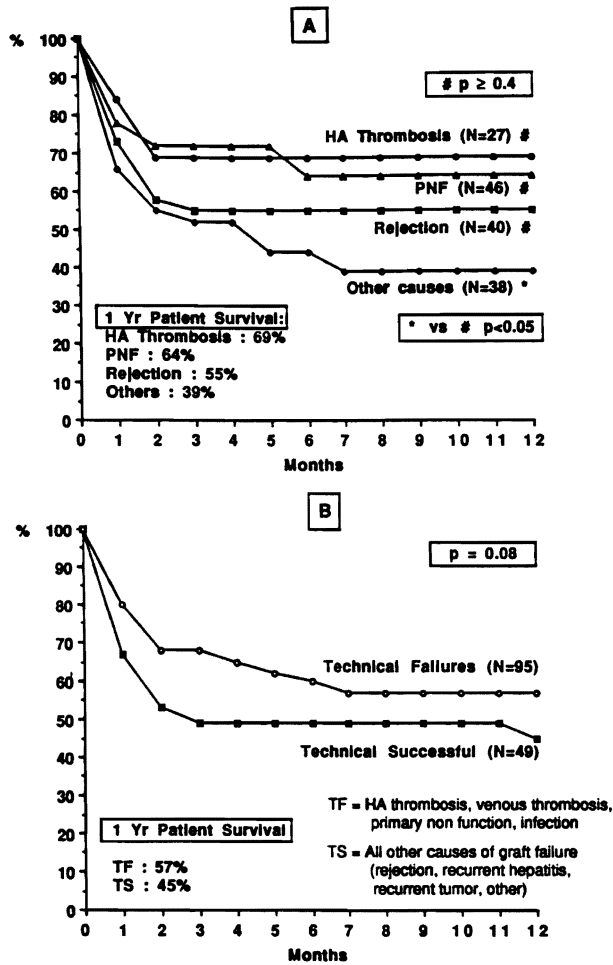
Table 1. Results of the Cox Regression Analysis for Values Significantly Affecting Patient and Graft Survival Rates

Levels	Relative Risk	P Value
<b>Graft Survival</b>		
Preservation time >18 hours (≤18 hours)	4.02	.0001
Immunosuppression FK 506 (CyA)	0.45	.0009
<b>Patient Survival</b>		
Preservation time >18 hours (≤18 hours)	4.42	.0001
Immunosuppression FK 506 (CyA)	0.43	.0008

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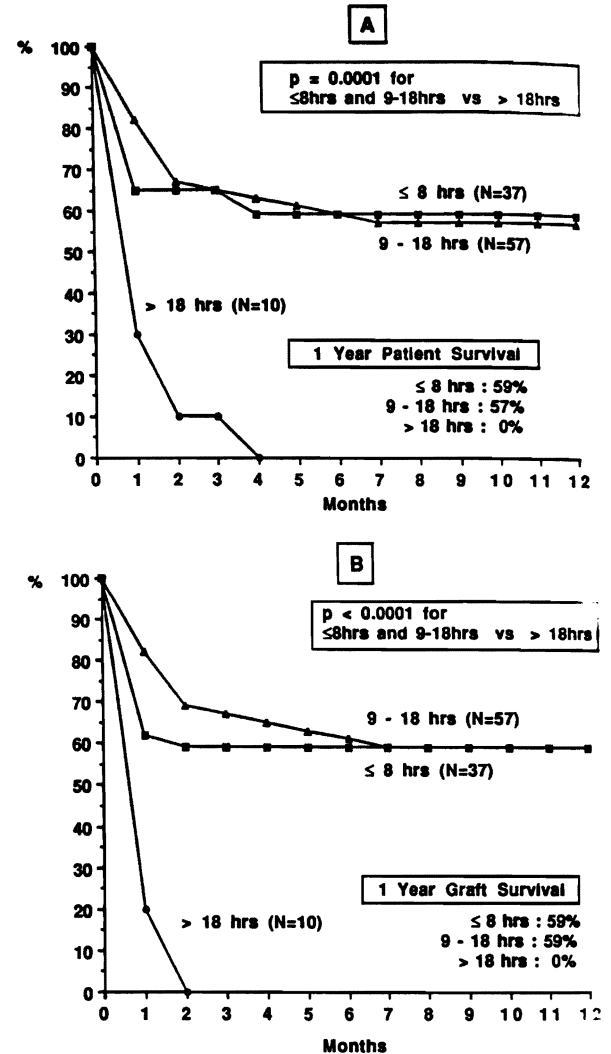


**Fig 2.** Actuarial patient survival curves according to the diagnosis of primary graft failure for each diagnosis (A) and for technical vs nontechnical failures (B).

age was <40 years in 49 cases, 40 to 60 years in 79 cases, and >60 years in 23 cases.

For the first graft, 9% of the transplants were performed in emergency (patient in the intensive care unit), 63% in semiemergency (patient hospitalized waiting for a transplant), and 16% in elective situations (patient at home). For the second graft, 62% were done in emergency, 23% in semiemergency, and 3% in elective conditions.

We started to use FK 506 in combination with steroids as an alternative to cyclosporine (CyA) in 1989. In our study group, 106 (70%) patients were treated with CyA, prednisone, and azathioprine for their first transplant, and 45 (30%) with FK 506 and prednisone. For the second transplant, 91 (60%) patients received CyA, prednisone, and azathioprine, and 60 (40%) received FK 506 in combination with prednisone. Patients on CyA were given 4 mg/kg per day IV and then 8 mg/kg orally in two divided doses. Patients on FK 506 received a continuous IV infusion at 0.1 mg/kg per day, and later changed to oral administration at 0.15 mg/kg every 12 hours.



**Fig 3.** Actuarial patient (A) and graft (B) survival curves according to the length of cold ischemia time of the graft.

We first performed a Cox proportional hazard regression analysis using BMDP statistical software (Los Angeles, Calif.). The following parameters were considered: initial liver disease, cause of first transplant failure, interval between first and second transplant ( $\leq 72$  vs  $> 72$  hours; ie, emergency vs semiemergency or elective retransplantation), recipient age ( $\leq 40$  vs 40 to 60 vs  $> 60$  years), preservation time of the graft ( $\leq 8$  vs 9 to 18 vs  $> 18$  hours), and immunosuppression (CyA vs FK 506). We then analyzed patient and graft outcome according to the same factors but using an univariate analysis.

## RESULTS

The overall 1-year actuarial patient survival rate for all 151 retransplants was 55%.

In the Cox model, two factors appeared to significantly

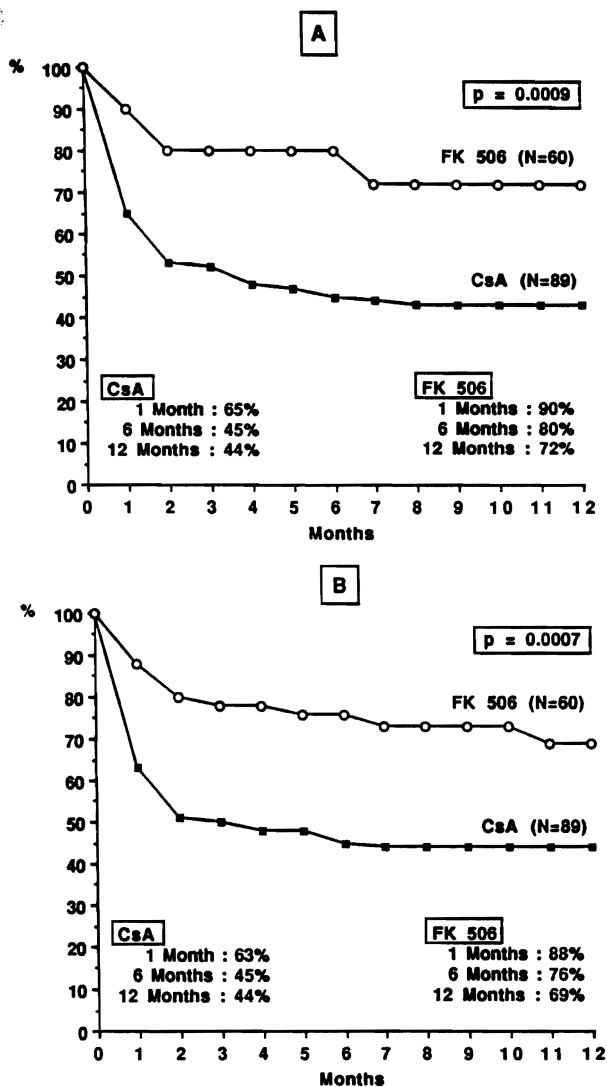


Fig 4. Actuarial patient (A) and graft (B) survival curves according to the use of FK 506 vs CyA as an immunosuppression.

influence patient and graft survival rates: the cold ischemia time of the graft and the use of FK 506 (Table 1). Grafts preserved  $\leq 18$  hours had a better outcome than those preserved for a longer period of time. The use of FK 506

improved graft and patient outcome when compared to CyA. The age of the patient, the initial liver disease, the time between the first and second transplant, and the cause of first graft failure did not significantly ( $P \geq .07$ ) affect either patient or graft survival.

The results of the univariate analysis are illustrated in Figs 1 through 4.

#### CONCLUSION

Our overall 1-year patient survival rate after a second liver transplant was 55%, a result comparable to others reported in the literature.<sup>4,7,8</sup> However, in the FK 506-treated group, the 1-year patient survival rate reached 72%. The initial liver disease, the cause of the first graft failure, the length of time between the first and second transplant, and the age of the patient did not significantly modify patient or graft outcome in our study, both in the univariate and multivariate analysis. We did not find that the time elapsed between the first and the second transplant, namely the degree of emergency of the retransplant, did significantly affect the outcome, as was previously suggested.<sup>5</sup> The preservation time was of importance only when exceeding 18 hours. In the univariate analysis, retransplants performed after hepatic artery thrombosis, primary nonfunction, or rejection of the initial graft had a similar outcome, but the prognosis of retransplantation significantly differed from these results when the initial liver transplant failed due to primary poor function, venous thrombosis, recurrent hepatitis, or other multifactorial causes.

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