

The influence of an improved preservation solution on prognostic factors for graft survival in pediatric liver transplantation

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Abstract. We investigated the influence of Eurocollins (EC) and University of Wisconsin solution (UW) on prognostic factors for graft survival after pediatric liver transplantation. The 1-year graft survival was studied for 30 patients in which 38 transplantations were performed between 1982 and 1988. We preserved 19 grafts in EC and the other 19 grafts in UW solution. For grafts preserved in EC, the median preservation time was 5 h compared to 10.8 h for grafts preserved in UW solution ($P < 0.01$). Graft survival at 1 year was equivalent in both groups (63%). No significant differences were observed between the two groups for the following variables: patient diagnosis, child-pugh score, age, operative time, anhepatic phase, blood loss, morbidity, ICU stay, donor age and graft survival. Multivariate analysis indicated that in the EC group anhepatic phase, blood loss and preservation time were significant predictors of graft survival whereas in the UW group, none of these factors appeared to be significant. We concluded that UW was superior to EC solution in pediatric liver transplantations because it allowed longer preservation times, the length of the anhepatic phase was less important and the tolerance for blood loss seemed to be extended.

Key words: Liver preservation – UW/EC preservation solution – Prognostic factors – Graft survival

Until 1987, Eurocollins solution (EC) was the most frequently used solution for clinical liver transplantation. EC allowed preservation times up to a maximum of about 10 h [1, 2] making liver transplantation a non-elective procedure performed mostly during the night hours. Extending the preservation time of the liver beyond 9 h often caused delayed and poor graft function affecting the prognosis of the patient. The introduction of the University of Wisconsin solution (UW) by Belzer and his associates allowed for significantly longer preservation times with-

out negatively affecting the function of the graft [3]. Nowadays, preservation times of between 12 and 24 h are not exceptional making liver transplantation an elective procedure. Additionally, the results of liver transplantation have shown improvement with UW [4, 5]. The purpose of the present study was to examine whether the use of either the EC or UW solution had any effect on factors predicting graft survival after pediatric liver transplantation.

Patients and methods

Between March 1982 and March 1990, 38 transplantations were performed in 30 patients: 23 whole, 7 reduced and 8 segmental grafts were implanted. Of these, 19 grafts were preserved in the Eurocollins solution (EC group) whereas the other 19 grafts were preserved in the University of Wisconsin (UW) solution.

During this time period the same protocols for immunosuppressive therapy and infection prevention were employed except for 3 transplants. Immunosuppressive therapy was instituted by means of a quadruple regimen. Azathioprine was given in a dose of 3 mg/kg daily. Prednisolone was started in a dose of 4 mg/kg daily and quickly tapered down to a dose of 0.5 mg/kg. Cyclosporine A was started as soon as the creatinine clearance was above 50 ml/min (corrected for body surface). Dosages were adjusted according to the serum levels. During the first 4 weeks, we aimed at levels of 200–250 ng/l and thereafter at levels of 100–150 ng/l. Additionally, cyclophosphamide was given during the 1st postoperative week.

Infection prevention was performed by means of selective decontamination of the bowl (SDB). SDB was carried out by administering three oral non-absorbable antibiotics; polymixin E (100 mg qid), tobramycin (80 mg qid) and amphotericin B (500 mg qid). Since eliminating the gram negative bacteria and fungi takes some time, prophylactic parenteral antibiotics (tobramycin and cefotaxim) were given during the first 48 h after the transplantation.

For the EC and UW groups preservation times ranged from 3.5 to 7 h and from 3.3 to 18.5 h, respectively. The median preservation time for the EC group was 5 h and for the UW group, 10.8 h ($P < 0.01$).

In order to study the influence of the EC and UW solution on prognostic factors of graft survival, a logistic regression model was used. All patients were followed for at least 1 year after transplantation. The proportion of grafts surviving for 1 year was 0.63 for both groups. The following prognostic factors were considered: child-pugh score, recipient and donor age, operative time, preservation time, blood loss and anhepatic phase.

The Mann-Whitney test and chi-square test were used to test the differences between the EC and UW group for the following variables: recipient and donor age, anhepatic phase, child-pugh score,

Table 1. Characteristics of the liver recipient, liver donor and transplant procedure. Continuous variables are expressed as median values (ranges); discrete variables as frequencies (%)

	EC solution (<i>n</i> = 19) ^a	UW solution (<i>n</i> = 19)
1. Recipient age (years)	3.3 (0.17–16.0)	1.7 (0.3–16.0)
2. Donor age (years)	6.0 (0.58–20.0)	5.5 (0.3–44.0)
3. Anhepatic phase (min)	75.0 (40.0–310.0)	85.0 (55.0–175.0)
4. Child-Pugh score	9 (6–14)	11 (6–14)
5. Operative time (min)	370.0 (260.0–480.0)	328.0 (245.0–480.0)
6. Blood loss (cl)	960.0 (180.0–4410.0)	570.0 (140.0–3190.0)
7. ICU (days)	5.5 (1.0–88.0)	9.0 (1.0–62.0)
8. Complications (Yes)	15 (78.9%)	11 (57.9%)
9. Diagnosis ^b	10 (71.4%)	6 (37.5%)

^a No. of transplanted patients in EC and UW group was 14 and 16, respectively

^b Diagnosis: 1 = biliary atresia, 2 = others

Table 2. Significant predictors of graft survival after pediatric liver transplantation in the EC group

Predictors**	Estimated regression coefficients* EC Solution
Constant	4.50
Anhepatic fase	0.24
Blood loss	-0.66
Preservation time	-0.37

* $P < 0.05$

** Chi-square for testing the hypothesis that all regression coefficients are zero = 17.39, 7 degrees of freedom, $P < 0.05$

operative time, blood loss, ICU stay, complications and patient diagnosis. Values at $P < 0.05$ were considered to be significant.

Results

In order to make a comparative statement about prognostic factors we looked for possible differences between the EC and UW group in the distributions of characteristics relevant for graft survival. Details of the donor, recipient and operation characteristics are given in Table 1. Statistical analyses revealed that there were no significant differences between the EC and UW group with respect to these factors. Thus, both the type of patients, recipients, and the operation characteristics were similar and the groups were comparable. A logistic model was then used to examine the influence of prognostic factors on at least 1-year graft survival for the EC and UW group, separately. Variables entered into the model included blood loss, recipient and donor age, operative time, anhepatic phase, child-pugh score and cold ischemia time. By means of a backward stepwise selection procedure, those factors were selected which significantly effected graft survival. In the EC group, anhepatic phase, blood loss and preservation time were significant predictors of at least 1-year graft survival (Table 2) whereas none of the seven variables appeared to be significant predictors in the UW group.

Before using the three significant factors for predictive purposes, it was important to test the adequacy of the model. In the present study the number of transplantations was small enough to question the appropriateness of

using the chi-square statistic for interpreting the fitness of the model. Therefore, a different, though related, indication of the strength of the estimated regression coefficients in Table 2 was obtained by testing the null hypothesis that all regression coefficients were zero [6]. This hypothesis was rejected (chi square = 17.39, degrees of freedom 7, $P < 0.05$) which indicated that the relationship between anhepatic phase, blood loss and preservation time and the 1-year graft survival was statistically significant for grafts which were preserved in the EC solution.

Discussion

Although previous studies have shown the superiority of the UW over the EC solution for clinical liver transplantation [4], the significance of this new preservation solution on the prognosis of the graft was unknown. In this study the effect of the UW preservation solution on prognostic factors for graft survival after pediatric liver transplantation was investigated.

The EC and UW group were comparable on a variety of variables; recipient and donor age, anhepatic phase, child-pugh score, operative time, blood loss, ICU stay, complications and patient diagnosis. There was a significant difference between the preservation times for the EC and UW group. Logistic regression analysis revealed that in the EC group, anhepatic phase, blood loss and preservation time were significant predictors for (at least) 1-year graft survival. In the UW group, none of the variables entered into the regression model were significantly associated with graft survival.

These results clearly showed that the introduction of the UW solution allows a longer preservation time without negatively affecting graft prognosis. This results in more efficient transplant programs. There is more time for preoperative patient preparation. The length of the anhepatic phase is of less importance in the UW era compared to the EC era, providing more time for reconstructions or adaptations of the graft and hemostasis of the liver bed. Finally, the tolerance for blood loss appears to be extended in patients with livers preserved in the UW solution which may leave the patient in a stronger position for coping with preoperative disasters.

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