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Cold Ischemia Time vs Outcome of Human Liver Transplantation Using UW Solution

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LABORATORY experiments¹ and clinical trials¹⁻³ of University of Wisconsin (UW) solution have shown beyond a doubt the superior qualities of this preservation fluid. Successful liver replacement in dogs has been reported after as long as 2 days of refrigeration,⁴ but in the canine model there is a slow deterioration of graft quality that is evident at the end of 24 hours.⁵ The extent of the penalty (if any) for increasingly long periods of preservation of human livers is not known. The retrospective present study has examined this question.

METHODS

All cases of primary liver transplantation were examined from October 24, 1989 to May 19, 1990. Sufficient data were available for assessment in all but 31 cases, leaving 593 for analysis. There were 93 (15.7%) infants and children (≤ 18 years) and 500 (84.3%) adults. In each case, the time was determined from devascularization in the donor to reperfusion in the recipient. This cold ischemia time (CIT) was used to stratify the recipients as follows: group 1, <10 hours ($n = 223$); group 2, 10 to 14 hours ($n = 188$); group 3, 15 to 19 hours ($n = 101$); group 4, 20 to 24 hours ($n = 52$); and group 5, >25 hours ($n = 29$). Between these groups there were no significant differences in recipient age, sex, mix of diagnoses, acceptance of positive cytotoxic crossmatches or ABO incompatibilities, or severity of illness as documented with the four-tier plus UNO-Stat delineation of urgency.⁶ The donors for these grades of recipients were not different in respect to age, sex, liver function, cardiopulmonary status, and time of hospitalization for the disease or conditions that brought them to donor status.

During the first 5 months of the study, the UW solution was prepared from raw materials at the School of Pharmacy of the University of Pittsburgh. After this, it was provided by the Department of Medical Research of the Dupont Corporation (Waukegan, Ill). Throughout the study period, two factors dictated the conditions of UW solution use. First, the solution was a scarce resource that had to be used sparingly, usually with a limitation of no more than 2 L per donor. Second, host procurement teams that had no experience with and who had understandable suspicion of a new technique usually insisted upon the use of conventional cold lactated Ringer's or Euro-Collins-like solutions for the in situ aortic perfusion, which is inherent in the multiorgan procurement methods that were used.^{7,8} Consequently, almost all of the livers were chilled first in situ by core cooling with either lactated Ringer's or Euro-Collins solutions, and reperfused with the UW solution in what has been called the "mixed" technique. The preferred method of using UW solution for all phases of the procurement did not become feasible until the spring of 1989.

All of the surviving recipients were followed until July 1, 1990. The parameters used to assess the effect of CIT were patient and graft survival, and quality of graft function with particular reference to the first 2 postoperative weeks. When retransplantation became necessary, the reasons were classified as technical error, primary nonfunction, rejection, infection, or miscellaneous.

Table 1. Highest Liver Enzymes and Prothrombin Time Within 7 Days After Liver Transplantation

	Group 1	Group 2	Group 3	Group 4	Group 5
CIT (h)	<10	10.14.9	15-19.9	20-24.9	>25
n	223	188	101	52	29
SGOT (U/L)	1,169	1,333	1,410	1,099	1,403
SGPT (U/L)	824	930	931	800	939
PT (sec)	17.7	19.4	19.3	17.2	17.1

Abbreviations: SGOT, serum glutamate oxaloacetic acid; SGPT, serum glutamate pyruvic acid; PT, prothrombin time.

Statistical evaluation was by chi-square test, analysis of variance, simple regression analysis, and logistic regression analysis.

RESULTS

Graft Function

Liver function tests in the five groups of recipients were not significantly different at any time out to 1 year post-transplantation. The highest transaminases and prothrombin times in the first 7 days are shown in Table 1. Because livers lost by death or retransplantation no longer contributed to the averages, these figures represented a progressively culled group of satisfactorily performing organs.

Patient and Graft Survival

Overall patient survival at 3 months and 1 year was 92% and 77.2%, respectively. There was no difference in the five groups.

However, graft survival was better in the patients with shorter preservation times in groups 1 and 2 (Fig 1). This meant that the equivalent patient survival in the different groups depended on a higher rate of retransplantation in patients whose grafts were stored for longer times.

Reasons for Retransplantation

Primary nonfunction was the leading indication for retransplantation (67.2%), followed by technical or mechanical

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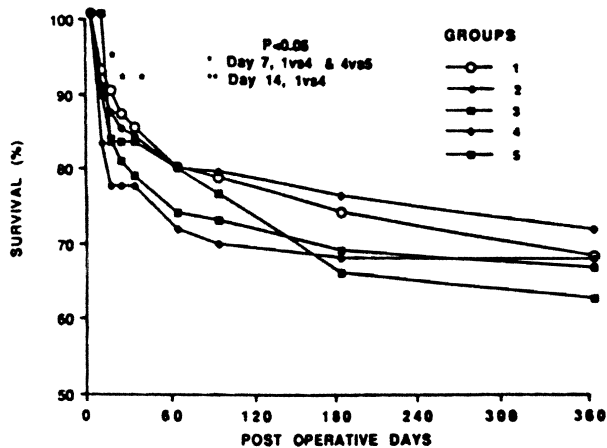


Fig 1. Graft survival (actual) of different CIT groups.

imperfections (20.7%), and rejection (10.3%). Primary nonfunction was significantly more frequent in groups 4 and 5 than in groups 1 to 3 ($P < .05$).

DISCUSSION AND CONCLUSIONS

It is not profound to suggest that static preservation has finite limits. Livers were shown in these studies to have entered the danger zone once 20 hours had passed. The rate of primary nonfunction increased beyond this time, but patient survival was protected by aggressive retrans-

plantation. What was equally evident was that the majority of livers were usable well beyond 20 hours. The liver with the longest CIT (>34 hours) functioned perfectly. There is no reliable way at present to test these organs on the back table for their safety and viability.

The folly of complete indifference to CIT is evident from this study. The conditions of testing may not have allowed the full value of UW to be seen since the potentially suboptimal policy was in effect at the time of preliminary flushing with electrolyte solutions. Since completion of this study, we have used the now freely available UW solution from the outset. However, the trend in the new cases is similar to that in the earlier experience.

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