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Influence of donor criteria on postoperative graft function after orthotopic liver transplantation

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Abstract Evaluation of graft quality remains a major problem in liver transplantation. The aim of this retrospective analysis was to examine the impact of donor criteria on postoperative graft function. Between June 1986 and September 1993 324 liver transplantations were performed at our institution. Criteria for exclusion from analysis were postoperative thrombosis of graft vessels, retransplantation, death prior to the 5th postoperative day or missing donor criteria. For the eligible 255 transplantations the impact of the following donor criteria were examined: age (range 1–62 years, median 28 years), size/body weigt index, duration of intensive care, cause of death, circulatory condition, need for vasopressive support and liver function tests (bilirubin, GOT, GPT, GGT, LDH, ALP, prothrombin time (PT), creatinine, sodium). The following intraoperative factors were also assessed: type of protective solution, cold ischaemic time (CIT), anhepatic period and blood transfusions. Graft function during the first 5 postoperative days was categorized into four groups: (1) good function (GOT max < 1000 U/l, spontaneous PT > 50%, bile production > 100 ml/day); (2) fair function (GOT 1000–2500 U/l, clotting factor support < 2 days, bile < 100 ml/day); (3) poor function (GOT > 2500 U/l, clotting factor support > 2 days, bile < 20 ml/day); (4) primary non-function (retransplantation required within 7 days). A univariate analysis revealed duration of intensive care ($P = 0.001$), circulatory condition ($P = 0.005$), anhepatic period ($P = 0.0004$), blood transfusions ($P = 0.03$) and CIT ($P = 0.039$) as significant risk factors for postoperative graft function. Entering these factors in a multivariate regression model we identified creatinine ($P = 0.007$), duration of intensive care ($P = 0.009$) and the size/body weight index ($P = 0.03$) as donor-related factors of high significance. Analysis of the intraoperative data revealed the anhepatic period as the factor of highest significance ($P = 0.0004$) together with CIT ($P = 0.02$) and intraoperative blood transfusions ($P = 0.008$). A doubling of the number of days of intensive care resulted in a threefold increased risk of postoperative graft failure. Prolonged intensive care is a variable representing multiple risk factors. Accepting donors with a longer history of hypotension of

who show signs such as elevated creatinine should be carefully considered. In patients with expected surgical difficulties resulting in an extended anhepatic period and a higher blood loss, transplantation of organs retrieved from donors with a long duration of intensive care and a long CIT should be avoided.

Key words Orthotopic liver transplantation · Graft function Donor criteria

Introduction

The initial function of the transplanted liver is a major determinant of the postoperative course. Some of the factors that will affect this initial function include preoperative donor factors, factors during the donor operation, the method and duration of organ preservation and recipient factors during the intra- and immediate postoperative period.

Failure of the hepatic allograft continues to be a serious life-threatening risk for the recipient. Because no effective method of extracorporeal support is available for these patients, undergoing retransplantation is the only alternative that offers the potential for survival. Primary non-function (PNF) following orthotopic liver transplantation is characterized by rapidly rising transaminases, absence of bile production, severe coagulopathy, high lactate levels, aggressive ventilation support, need for circulatory assistance by catecholamines, hypoglycaemia and acute renal failure. Some ideas do exist about the cause of PNF in grafts related to donor and recipient factors [3, 5, 6, 8, 11], but a satisfactory predictor of PNF has not yet been found.

The purpose of this retrospective study was to examine the impact of donor cirteria on postoperative graft function and their potential for predicting the occurrence of PNF.

Patients and methods

From June 1986 to September 1993 324 orthotopic liver transplantations were performed at our institution. Excluded from analysis were grafts suffering from postoperative thrombosis of graft vessels, retransplanted patients, patients who died prior to the 5th postoperative day other than from PNF and recipients of grafts with missing donor criteria. The indication for liver transplantation in the remaining 255 patients was benign liver disease (187 cases, 73.3%) and malignancy (68 cases, 26.7%). For the eligible transplantations we examined the effect of the following donor criteria: age (range 1–62 years, median 28 years); size body weight index (Broca); duration of intensive care (0–2, 3–4, > 4 days); cause of death (CCT, ICB, other); circulatory condition (normal, hypotensive period); need of vasopressive support; liver function tests (bilirubin, GOT, GPT, LDH, ALP, GGT, prothrombin time (PT); kidney function (creatinine < or > 1 mg/dl, sodium). The effects of the following intraoperative factors were also studied: type of protective solution (EC, UW); cold ischaemic time (CIT, ≦ or > 10 h); anhepatic period (≦ or > 90 min) blood loss (< or > 10 blood units).

We examined graft function within the first 5 postoperative days by categorizing the grafts into four groups: (1) good function (GOT < 1000 U/l, spontaneous PT > 50%, bile > 100 ml/day; (2) fair function (GOT 1000–2500 U/l, clotting factor support < 2 days, bile < 100 ml/day); (3) poor function (GOT > 2500 U/l, clotting factor support > 2 days, bile < 20 ml/day); (4) PNF (retransplantation necessary within 7 days because of further deterioration of liver function and the beginning of multiorgan failure).

For statistical analysis we first entered all these factors in a univariate model. All factors that reached significance in this model were then applied in a stepwise polychotomous logistic regression analysis to identify the independence and relative importance of each of these variables.

Results

Initial analysis showed that 58% (148 patients) had good graft function, 22.7% (58 patients) had fair function, 10.2% (26 patients) had poor function and 9% (23 patients) had PNF. In the univariate analysis the following donor criteria and intraoperative data values showed significance: intensive care duration ($P = 0.001$); sodium ($P = 0.015$); circulatory condition ($P = 0.048$); anhepatic period ($P = 0.0004$); blood loss ($P = 0.03$); CIT ($P = 0.039$). Entering all the above variables in a stepwise logistic regression analysis identified the following significances: intensive care duration ($P = 0.0095$); creatinine ($P = 0.0074$); size/body weight index ($P = 0.034$); anhepatic period ($P = 0.0004$); blood loss ($P = 0.011$); CIT ($P = 0.02$). Regarding the correlation of intensive care duration as a variable of great significance with other values, LDH ($P = 0.002$), GGT ($P = 0.002$), ALP ($P = 0.008$) and creatinine ($P = 0.021$) were found to influence each other. Donor age was not a significant risk factor.

To identify a possible limit of acceptable treatment duration we divided the risk factor intensive care duration into three groups (0–2, 3–4, > 4 days) and applied a regression analysis to determine the relative risk (PR) for

PNF of a transplanted liver with the following results: 0–2 vs 3 or > 4 days donor treatment increased the risk by a factor of 2.6, and 0–2 days vs > 4 days showed a RR of 6.7. The RRs for an unfavourable transplantation outcome for the other significant variables were as follows: creatinine, RR 2.23; CIT, RR 1.93; blood loss, RR 2.35; anhepatic period RR 1.87.

Discussion

PNF of transplanted livers has been reported to occur in 2–23% of cases, and is a devastating complication which carries a high mortality without retransplantation [1, 3, 5–9, 11, 12]. Of 255 first liver transplants, 23 patients (9%) developed PNF at our centre. Our study showed that prolonged intensive care was one of the most important factors in predicting the postoperative function of the liver graft. Every additional day of a donor in the ICU worsens the prognosis of the graft. Although our findings are in accord with the results of other studies [7, 11, 10] intensive care duration was a multifactorial variable. Probably the worse results from longer intensive care were due to suboptimal donor management during hospitalization. Over-hydration may be a cause of liver distension and subsequent graft dysfunction [14]. As parenchymal changes are not always macroscopically visible we now perform a liver biopsy routinely during each donor procurement to obtain microscopic information about fatty infiltration and water content before the start of the transplantation. Although fatty infiltration cannot always be observed by the procurement team, over-weigt of the donor (according to the Broca index) showed a detrimental effect on transplantation outcome. The kidney as an organ which shows early circulatory disturbances is also a good prognostic factor in the assessment of an organ donor.

Nevertheless previous studies have shown the safety of longer CIT in UW-preserved grafts [2, 4, 13]. A CIT of over 10 h turned out to be associated with a higher incidence of PNF. A second warm ischaemic time (defined as an anhepatic period) of over 90 min turned out to be the factor associated with the worst prognosis in our model. Together with the identified risk factor intraoperative blood loss, we should therefore pay particular attention to patients with expected surgical difficulties and resulting higher blood loss. In these patients we do not recommend the use of organs retrieved from donors with a long intensive care duration or expected long CIT.

In conclusion, it is clear that donor and recipient status should be regarded in an undivided way in order to avoid the coincidence of prognostically miserable factors.

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