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Marginal donors for patients on regular waiting lists for liver transplantation

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Abstract The use of marginal donors is well accepted by most centers for emergency situations, but there is debate on their use for patients on regular waiting lists. We report our experience of the 1-year survival for patients on waiting lists (n = 147, 1-year survival = 32 %), patients transplanted from good donors (n = 60, 1-year survival = 84 %), and patients transplanted from marginal donors (n = 15, 1-year survival = 56 %). We concluded that liver transplantation from marginal donors (a) is a safe procedure (b) has a 1-year survival that is significantly better than that on a waiting list (c) is ethically justified especially in countries with donor shortages, and (d) may allow transplantation of "special" high risk and poor long-term outcome patients.

Key words Liver waiting list · Marginal donor · Donor shortage · Donor selection criteria · Liver transplantation

Introduction

Worldwide the waiting lists for solid organ transplants are steadily but constantly lengthening because of the enlarging spectrum of indications and the increasing number of patients with end-stage organ failure. Unfortunately, the number of donors does not match that of recipients, and a large number of patients awaiting transplantation die while on a waiting list [1]. This has lead to a broadening of donor acceptance criteria, and in the 1990s the term "marginal donor" entered the transplant terminology. Originally, the term was used to indicate only donors over 55 years of age [2, 3], but it is now used to indicate all donors with relevant alterations to one or more data relative to "classical" acceptance criteria [4–6]. Results from large series in terms of graft and patient survival after transplantation with these organs seem encouraging [7, 8], and it seems probable that in the future these organs will be used to transplant patients on regular waiting lists. In a retrospective study we analyzed data from 75 consecutive donor-recipient pairs transplanted in our center in an effort to identify the relations between donor quality and recipient outcome.

Patients and methods

Data from 75 consecutive donor-recipient liver pairs were analyzed to define if and how donor conditions influence 1-year graft survival after liver transplantation. Organs were allocated by the Nord Italia Transplant Program (NITp) on the basis of a national liver transplant waiting list. The policy of the transplant center of the Catholic University of Rome in the past excluded the possibility of accepting donors over 55 years of age, non-heart-beating donors, or overweight donors, so no donors with these characteristics are present in the donor group. The donor parameters we chose to analyze to discriminate "good" and "marginal" donors were the following: systolic pressure, urinary output, bilirubin levels, ALT/AST levels, prothrombin time, serum sodium level, PaO_2, and intensive care unit stay (Table 1). According to these criteria two groups were defined: Group I, good donors (GD: n = 60), in which all hemodynamic parameters and chemistry data were within the normal range or that presented a single minor alteration in one (i.e., < 2 times the standard deviation from the normal range) and group II, marginal donors (MD: n = 15), that presented one single major alteration (i.e., > 2 times the standard deviation from the normal range of the parameter studied) or multiple minor alterations.

The outcome of recipients was compared in relation to donor status (good donors group vs marginal donors group) by Kaplan Meier life table analysis at 1–12 months. For the statistical evaluation the Cox Mantel test and the log rank test were used.

Table 1 Donor parameters used to discriminate good and marginal donors

	Minor alteration	Major alteration
Systolic blood pressure (mmHg)	< 70 for 1 h	< 50 for 1 h
Urinary output	Oliguria	Anuria
Bilirubin (mg/dl)	Up to 2	> 2
ALT and/or AST (IU/dl)	Up to 150	> 150
Prothrombin time (%)	Down to 50 %	< 50 %
Na + (mEq/l)	Up to 160	> 160
PaO_2 (mmHg)	< 80	< 60
ICU stay (days)	3–7	> 7

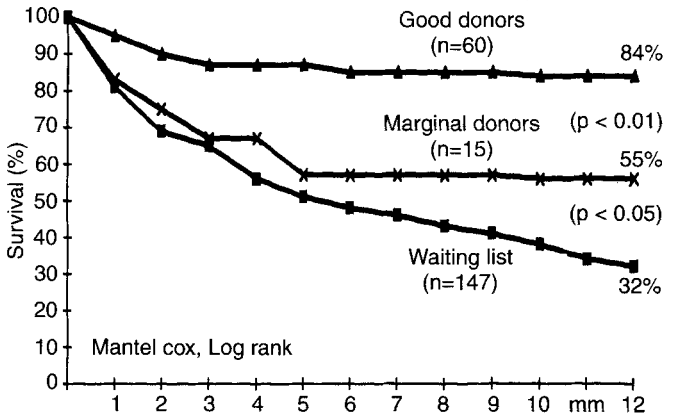

Fig. 1 One to 12-months survival by Kaplan-Meier life table analysis for patients transplanted with good donors *(triangle)*, marginal donors *(cross)*, and on the waiting list *(square)*

Results

One-year survival was 32 % for patients on the waiting list ($n = 147$) and 76 % for patients who underwent liver transplantation ($n = 75$). The difference in the 1-year survival rate was significant ($P < 0.01$). The difference in 1-year graft survival between patients who received livers from good donors (84 %, $n = 60$) and patients who received livers from marginal donors (56 %, $n = 15$) was also significant. The P values were: Cox Mantel $P = 0.038$, log rank $p = 0.047$ (Fig. 1).

Discussion

Liver transplantation is the current therapeutic choice for end-stage liver failure, but the number of donors available does not match number of patients on the waiting lists. In Italy, among European countries, the problem is more critical because of the lower number of donors per million inhabitants (7 vs 15 in France, vs 17 in the United Kingdom, vs 25 in Spain, vs 14 in Eurotransplant, and vs 17 in Northern Europe).

The use of marginal donors is well accepted by most centers for emergency situations (i.e., fulminant liver failure or retransplantation), but there is still debate on their use for patients on regular waiting lists. This is understandable when one considers that the 1-year survival figures of 70–80 % (with variability due to center effect, patient age, disease pattern and immunosuppressive protocols) for regular donors are 10–20 % less for marginal donors (older age, alterations in liver tests, overweight, prolonged ischemia time). It must be kept in mind, however, that in Italy the 1-year mortality on the waiting list reaches almost 70 %.

In a recent analysis of donor acceptance policies conducted in 80 centers registered with the European Liver Transplant Group [5] 38 % of marginal donors were accepted (33–50 % in relation to different countries) for patients on regular waiting lists, 20 % were accepted only with additional information (e.g., histological reports), 17 % were accepted only for emergencies, and 23 % were refused.

The definition of "marginal donors" in our series was very restrictive since donors over 55 years of age and those who were overweight were not accepted. The indexes used to define the two groups were chosen on the basis of previous reports on the quantification of liver damage and prediction of survival after transplantation, showing these parameters to be precisely discriminative among survival curves [9, 10]. It is possible that the donors that we defined as marginal may not be so classified by others with even less strict selection criteria [8]. However, the strict criteria we used made the difference in the 1-year patient survival between recipients of good or marginal donors even more evident. This difference can only be amplified even further when the acceptance criteria are widened.

The systematic use of marginal or nonoptimal donors could present three main effects: (a) the donor pool will be enlarged at least by 15–25 %; (b) the overall survival after liver transplantation will probably decrease more or less by 5–10 %; (c) a 10–15 % difference in the 1-year survival will be evident between transplants from regular and marginal donors. On the other hand, current survival data of patients transplanted from marginal donors are much better than those observed in selected groups of patients who are transplanted over the age of 65 years, who have hepatic tumors, or who have multiple organ failure. These patients are considered by most transplant centers to be at higher risk, as are also patients who are likely to present with a recurrence of pre-existing disease (hepatitis or liver cancer). Marginal donors could be used to transplant these patients considering the odds of an already biased survival rate.

In conclusion, our data demonstrated an advantage in the enlargement of the donor pool by using marginal donors, but the specific decision on who should be assigned a nonoptimal liver remains an open question.

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