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## Which ABO-matching rule should be the decisive factor in the choice between a highly urgent and an elective patient?

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**Abstract** ABO blood group matching policy between donor and recipient is a key element of organ allocation. Unequal distribution of the ABO blood groups in the population can lead to inequities in the distribution of organs to potential recipients. Furthermore, High Urgency liver transplant candidates might compromise the chances of transplantation for the elective patients. To compare the influence of the various ABO blood group matching policies on the transplantation rate of HU patients and on the subsequent donor liver availability for elective patients, a simulation study was undertaken. The study shows that in the Eurotransplant liver allocation program, a restricted ABO-compatible matching policy for HU liver patients offers the highest probability of acquiring a liver transplant, for both High

Urgency- and elective patients, irrespective of their ABO blood group. A simulation study once again proved to be an elegant tool for objectively analysing various options in a complex organ allocation algorithm.

**Keywords** Organ allocation · ABO blood group · Simulation study  
Liver transplantation

### Introduction

Many cadaveric donor liver allocation schemes incorporate mandatory exchange of livers for the treatment of so-called High Urgency (HU) patients suffering from either a de-novo acute liver failure or an acute life-threatening irreversible liver graft failure [4, 7, 8, 9]. Although the liver graft survival rate of these HU patients is lower than that of elective (non-HU) patients [1], the criterion of distributive equity is cited to justify and accept this prioritisation. The ABO blood group system is the primary immunological barrier in

transplantation. However, the four ABO blood groups are not proportionally distributed. Moreover, the classical ABO-blood group compatibility overcompensates this inequality, and, within an organ allocation area, the ABO blood group distribution of donors and potential transplant candidates are usually not similar. Therefore, ABO blood group matching policy between donor and recipient is a key element of organ allocation.

In view of the prevailing donor liver scarcity and various inequalities in the ABO blood group distribution, one should be cautious not to prioritise the HU category too highly. Even though HU liver transplant

candidates represent a minority of the new registrations for a liver transplantation (10%–20%) [3], the organ allocation policy on the HU level might compromise the chances of transplantation for the elective patients. In order to be able to compare the influence of various ABO blood group matching policies on the transplantation rate of the HU patients and on the subsequent donor liver availability for the elective patients, a simulation study was undertaken.

## Materials and methods

The inflow data of liver donors and liver transplant candidates (HU as well as elective) used in the simulation model were derived from data of the Eurotransplant organ exchange organisation, the participants of which are Austria, Belgium, Germany, Luxembourg, The Netherlands, from 1992 through 1996. The annual ratio of donor livers ( $n=860$ ) versus liver transplant candidates ( $n=1280$ ) was calculated as 2:3. The annual inflow ratio of HU patients ( $n=240$ ) versus elective patients ( $n=1040$ ) was 1:4. The ABO blood group distribution of the liver donors was as follows: 43% ABO-A; 6% ABO-AB; 11% ABO-B, and 40% ABO-O. The HU liver transplant candidates showed the following ABO blood group distribution: 43% ABO-A, 6% ABO-AB, 13% ABO-B, and 38% ABO-O.

The Eurotransplant Liver Allocation System dating from 1996 [4], offers the option of requesting an ABO-identical and/or ABO-compatible and/or ABO-incompatible donor liver for their HU liver transplant candidates. As soon as a liver becomes available, the liver allocation list is generated: the HU patients are sorted, first according to the acceptance of the donor's ABO blood group, then by the length of stay on the HU waiting list. For the elective liver transplant candidates, a complex centre rota system is used, where the centres are obliged to select a patient having the same ABO blood group as the donor (ABO-identical).

### HU liver simulation model

A discrete probabilistic dynamic model of the HU Eurotransplant Liver Allocation System was built, using the computer language PROSIM [2]. The following assumptions and simplifications were made: 1) liver donors and liver transplant candidates arrive homogeneously in time (homogeneous Poisson process); 2) if a suitable donor liver, i.e. in accordance with the ABO blood group matching policy, is available, the probability of acceptance of this donor liver for a HU liver transplant candidate is 100%; 3) if a HU liver transplant candidate is still on the HU waiting list 2.5 days after HU listing, the patient is removed from the list and is no longer considered a liver transplant candidate.

Four ABO blood group matching policies on HU liver allocation level were studied: 1) ABO-identity [ABO-id]; 2) ABO-compatibility (no hierarchical distinction between ABO-identity and ABO-compatibility) [ABO-co]; 3) prioritised ABO-compatibility (i.e. priority of ABO identity over ABO compatibility) [ABO-cp]; and 4) restricted ABO-compatibility (i.e. ABO-O donor only for ABO-O and ABO-B patients, not for ABO-A or ABO-AB patients; no hierarchical distinction between ABO-identity and ABO-compatibility) [ABO-cr]. The option 'ABO-incompatibility' was ultimately not simulated. In view of the poor outcome of an ABO-incompatible liver graft (29% graft survival at one year), this option was discontinued in the ET Liver Allocation System while the simulation model was built.

The HU liver simulation model was run for 30 cycles of 183 days. The end points were the number and percentage of HU

patients that underwent transplantation within 60h (2.5 days) after HU listing, and the donor liver availability for the elective liver transplant candidates. The results were expressed as an average value per cycle, and, separately, for each of the four recipient ABO blood groups. Statistical analysis was carried out using the chi-square test.

## Results

### HU patients

The effect of the various simulated allocation policies on the transplant rates of HU transplant candidates, per recipient's ABO blood group, is shown in Figs. 1, 2, 3, 4. For HU patients with the ABO blood group O, transplant rates were comparable, regardless of the ABO matching policies applied in the simulation. On average, 50% of the HU patients underwent transplantation within 24h and about 86% at 60h. The ABO-compatible matching policies (ABO-co & ABO-cp) resulted in higher transplant rates for HU patients with ABO blood group A, compared to the policies ABO-id and ABO-cr. The difference was statistically significant at 24h. The ABO-identical matching policy was deleterious for the transplant rate of ABO-B and ABO-AB HU patients; the chance of a transplant within 2.5 days was lower than 50%, with a corresponding risk of increased mortality on the waiting list. The highest cumulative quantity of HU patients to undergo transplantation at 2.5 days was achieved when the classical ABO-compatibility matching policy (ABO-co) was applied ( $n=112.6$ /cycle), whereas the ABO identical matching policy (ABO-id) resulted in the lowest cumulative number ( $n=96.6$ /cycle).

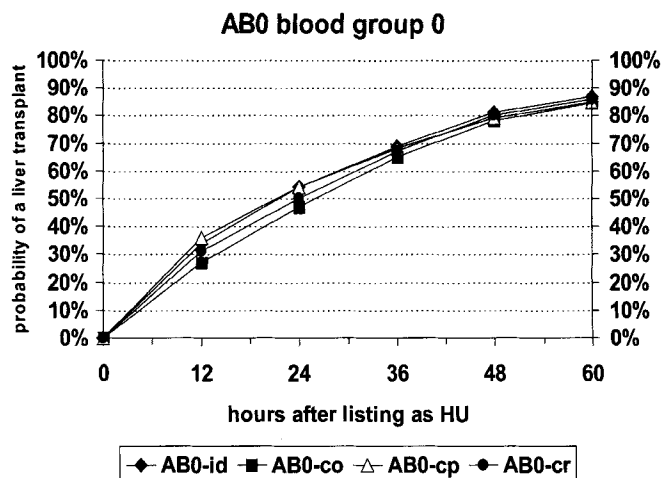


Fig. 1. Impact of HU ABO matching policies on the chances of a transplantation for HU patients with the blood group ABO-O

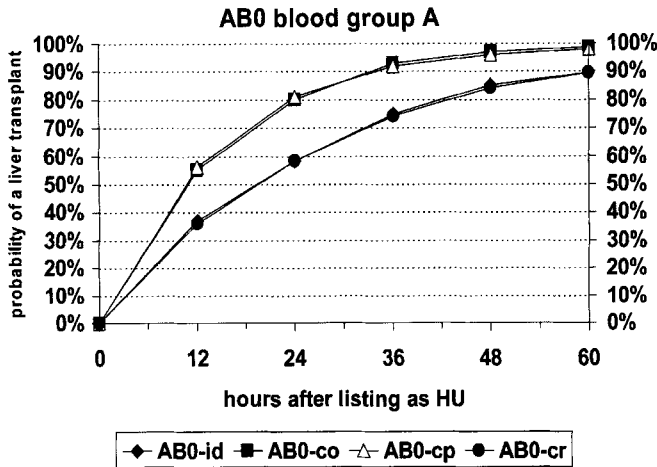


Fig. 2. Impact of HU ABO matching policies on the chances of a transplantation for HU patients with the blood group AB0-A

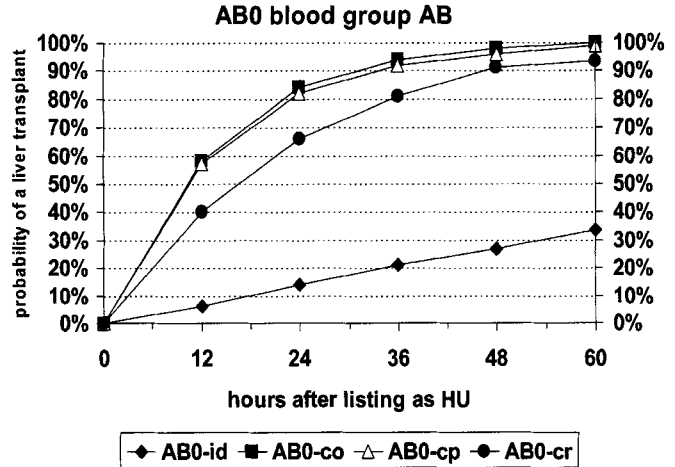


Fig. 4. Impact of HU ABO matching policies on the chances of a transplantation for HU patients with the blood group AB0-AB

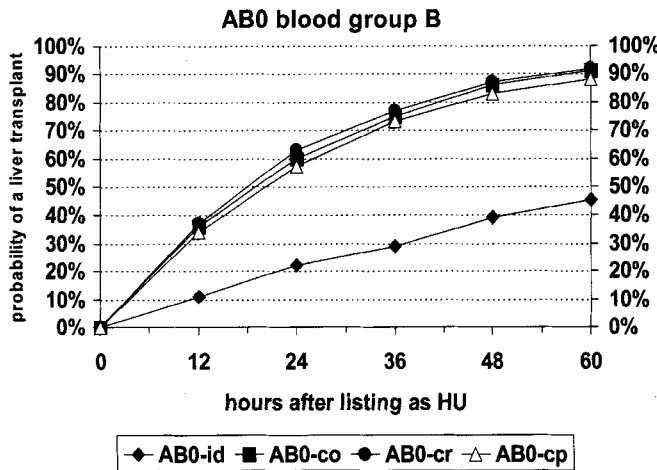


Fig. 3. Impact of HU ABO matching policies on the chances of a transplantation for HU patients with the blood group AB0-B

option ‘ABO-cr’ was applied, compared to the HU liver ABO matching policy ‘ABO-id’. These differences, however, were not significant.

**Discussion**

ABO blood groups play a key role in organ allocation strategies. However, there is an unequal distribution of the ABO blood groups in the population, which is overcompensated by the biologically effective ABO blood group compatibility, leaving the AB0-O blood group – the universal donor – to be the most vulnerable. Additionally, ABO blood group distribution of donors

**Elective recipients**

The AB0-co and AB0-cp blood group matching strategies significantly lowered the number of AB0-identical donor livers available for elective liver transplant candidates with AB0 blood group O (Fig. 5). The lower number of donor livers available when the policy ‘ABO-cr’ was applied at the HU level, was not statistically significant, compared with the policy ‘ABO-id’. All compatible ABO blood group matching policies, i.e. AB0-co, AB0-cp and AB0-cr, resulted in a higher number of donor livers for elective liver transplant candidates with AB0 blood group B and AB, though not significant. For elective patients with AB0 blood group A, more donor livers were available when the HU liver ABO matching policies AB0-co and AB0-cp were applied, and less donor livers were available when the

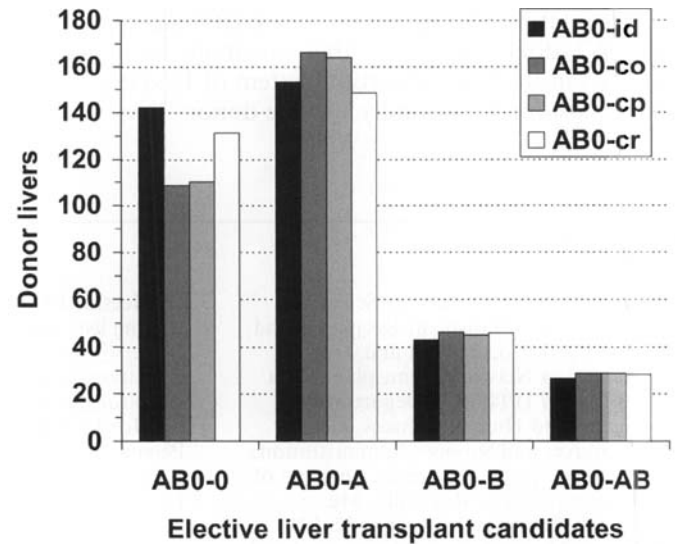


Fig. 5. Impact of HU ABO matching policies on the number of donor livers available for transplantation for elective liver transplant candidates

and potential transplant candidates is not always balanced within the local or even regional allocation area. As a consequence, the ABO-matching strategy between donor and recipient in an organ allocation program should be selected carefully.

The current simulation studies show, that in the Eurotransplant liver allocation program, a restricted ABO-compatible matching policy for HU liver patients offers the best chances of acquiring a liver transplant, for both HU as well as elective patients, irrespectively of their ABO blood group. ABO-identity matching was deleterious for HU ABO-B and ABO-AB patients, while classical ABO-compatible and prioritised ABO-compatible matching were detrimental for ABO-O elective patients. In the restricted ABO-compatible matching regime, the losses of ABO-O donor livers (to HU ABO-B patients) and of ABO-A donor livers (to HU ABO-AB patients) were marginal for the elective ABO-O and ABO-A patients respectively; the gain in probability of acquiring an HU liver transplantation for the HU ABO-B and ABO-AB, however, was significant. Evidently, there was a corresponding increase of the ABO-identical liver donor pool for the elective ABO-B and ABO-AB patients, however, this increase did not exceed five donor livers and/or transplants per six months. Altogether, the HU restrictive ABO-compatible matching policy was felt to be an ethically acceptable compromise supported by the principle of medical justice, in view of the life-threatening situation of the HU ABO-B and ABO-AB patients.

In addition, new developments in the field of liver transplantation could help to safeguard, to a better extent, the available ABO blood group O donors for the (elective) transplant candidates with ABO blood group O. Firstly, ABO-O liver patients can undergo transplantation safely with an (ABO-incompatible) ABO-A2 donor liver [6]; this possibility is officially included in the liver allocation system of UNOS [<http://www.unos.org/>]. Secondly, living-donor liver trans-

plantation, mainly living-related, can reduce the drainage of the cadaveric liver donor pool, albeit predominantly for paediatric patients [12]. Finally, the usage of a cadaveric donor liver is maximised with split-liver transplantation, grafting the left part in a paediatric recipient, and the remaining right lobe in an adult recipient [11]. Nonetheless, it is clear that split-liver transplantation, too, calls for strict regulation in terms of ABO blood group matching. Of course, one could advocate the mandatory splitting of each ABO-O donor liver, but the practical feasibility of such a policy has never been tested, not even in a single liver transplant program.

Quite surprisingly, the probability of HU ABO-O patients receiving a graft was largely independent of either HU ABO-matching scheme. So, allocating ABO-O donor livers exclusively to HU ABO-O patients would not improve their transplantation rate. In our view, this might be explained by the current ratios between liver donors, liver transplant candidates, and their corresponding ABO distribution. As a consequence, if major changes were to occur in donor availability, in the number of HU and/or of elective patients, or in the ABO blood group distribution of any of these three categories, the existing ABO-matching policy should be re-matched appropriately.

Simulation studies once again proved to be elegant tools for objectively analysing various options in a complex organ allocation algorithm. This has been previously demonstrated with the implementation of a new Eurotransplant Kidney Allocation System in 1996 [13, 14], and its subsequent adaptations. Similar simulation studies in the field of liver transplantation were also performed by Pritsker et al. in the frame of the organ exchange organisation UNOS [10]. However, when applying simulation studies, one should be cautious to make appropriate assumptions and simplifications. If this is done carefully, the predictions of the simulation will be met in the real situation [5].

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