Controversy

Should the allocation of cadaveric kidneys for transplantation be based on HLA matching?

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In 1996 the European centres participating in the Eurotransplant organization agreed to the implementation of a new allocation system for kidneys of postmortem donors (Eurotransplant Kidney Allocation System, ETKAS). The proposed procedure was based on the following five criteria: HLA mismatch grade, waiting time, mismatch probability (a correction factor increasing the chances for patients with uncommon HLA phenotypes and for homozygous or immunized patients), local transplants (kidneys are shipped only if the HLA match is at least two match grades better than the best compatible local patient), and import–export balance per centre. In the course of time several changes have been made in the original procedure, but the basic principles are still used for the exchange of kidneys within Eurotransplant.

The brief report of Gillich et al. [1] in the current issue of the journal raises the question of whether the exchange based on HLA matching is still offering an advantage. In a single-centre study the transplant team in Bonn compared the fate of 77 pairs of kidneys of which one was transplanted locally and the other was offered to Eurotransplant for exchange to another centre. For the locally used kidney no attempt to match for HLA antigens with the recipient was made. Consequently, the mean mismatch grade of the local kidney transplants was almost twice that of the exchanged kidneys. Despite this difference in HLA matching, 1-year and 5-year graft survival rates of the kidney pairs did not differ. As expected cold ischaemia time of the locally used kidneys was considerably shorter. The results suggest that HLA matching is not a conditio sine qua non for a successful renal transplantation and that, with current immunosuppressive protocols, ischaemia time has become a more decisive factor.

The results are of interest because the study was systematically performed by a single centre and paired kidneys from the same donor were compared. As the authors acknowledge it also has its limitations. The number of patients is relatively small and the waiting times of the recipients in both groups differ. Also, the immunosuppressive protocols used were most likely not similar in the different centres. They advise to perform larger studies to settle this question.

In fact, such data are already available. Three large surveys show that the longer ischaemia times that result from kidney exchange virtually abolish the beneficial effects of HLA matching. Peter Morris et al. [2] analysed the factors that played a part in the long-term survival of almost 3000 cadaveric kidneys transplanted in the UK. They found that kidneys matched for all HLA-A, HLA-B, and HLA-DR antigens (000 mismatches) had a significantly better graft survival, and this held also for kidneys with so-called favourable matches (010, 100, and 110 mismatches). However, in the group of favourable matches this beneficial effect on graft survival was completely neutralized by a significant, untoward effect of prolonged ischaemia due to the kidney exchange. An earlier, even larger study from the USA on the economic implications of HLA matching in cadaveric renal transplantation had reached a similar conclusion [3]. This study comprised 27,000 patients. Graft survival at 3 years was significantly better for HLA-identical kidneys and costs were lower. On the other hand, graft survival decreased and costs increased with longer ischaemia times. The authors concluded that the additional costs of longer cold-ischaemia times would be greater than the benefits of optimizing HLA matching through a national allocation programme. In a recently published third study [4], the survival of shipped and locally transplanted kidneys was studied in a manner comparable to the study of Gillich et al. [1]. In contrast to the study from Bonn, it was not a single centre comparison of paired kidneys, but on the other hand it comprised more than 5000 pairs of kidneys, one kidney being exchanged and the other...
used locally. Overall graft survival rates were similar for both groups, but after adjustment for the degree of HLA mismatching and other relevant risk factors it appeared that shipped kidneys had lower graft survival rates. In recipients of shipped kidneys with HLA mismatches, a 17% increase in the risk of graft failure in the first year after transplantation was found as compared to locally transplanted kidneys. Adjustment for the duration of cold ischaemia attenuated this untoward effect of shipment. Similar to the study of Morris et al. [2] the graft survival rates of kidneys with no HLA mismatches were not influenced by shipment. The authors conclude that the benefit of HLA matching in shipped kidneys with one or more mismatches is offset by the longer duration of cold ischaemia time resulting from the shipment.

All these data suggest that the exchange of kidneys with more than zero mismatches does not offer an advantage. Abandoning of this practice would have no detrimental effect on graft survival. These findings call for a revision of the allocation system currently used within Eurotransplant, especially with regard to the HLA matching criteria. Exchange should be limited to kidneys with no HLA mismatches and to kidneys for which a highly sensitized recipient with a negative crossmatch is present on the waiting list. This latter group of patients should be included, because their chances to receive a suitable kidney would otherwise be negligible. For patients who do not fulfil these criteria, HLA matching should be abandoned as a selection criterion. Those donor kidneys should preferably be transplanted locally, as advocated by the transplant team from Bonn. This is the best guarantee for a short ischaemia time. Furthermore, the costs of shipment can be avoided. The costs of the transplantation itself will decrease as predicted by the USA study [3]. Lastly, the possibility to use kidneys in the local centre may serve as an incentive for the procurement of kidneys.

References


Editor’s note

Please see also Original Article by Gillich et al., pp. 884–886.