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Corneal transplantation: the fine line between donor shortage and tissue quality

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In the current issue of *BMJ Open Ophthalmology*, Downward *et al*,[1] on behalf of the UK National Health Service Blood and Ocular Tissue Advisory Group and Contributing Ophthalmologists, investigate long-term graft survival and rejection rates in patients who received corneas from donors who donated both corneas for Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy (PBK), defined as 'paired' donors. The aim was to assess, whether there was an association between recorded donor characteristics such as endothelial cell density (ECD), age and sex, and endothelial graft failure and rejection. A total of 1536 paired and 9302 unpaired corneal transplants were included. While for these endpoints, no clear differences were found between paired and unpaired patients in terms of endothelial graft failure and rejection rates, the authors were able to confirm a lower ECD in unpaired single eye donors. In addition, based on their results, they suggested that unpaired single cornea donors had slightly worse rates of rejection and failure for patients with PBK. They also reported that for Fuchs' endothelial corneal dystrophy, there was a small difference in outcomes between paired and unpaired donors (p=0.06).

The UK transplant registry is a highly valuable database which has, in the past, allowed a large number of unique large-scale register studies to be conducted investigating the outcomes of corneal transplantation.[2] Specifically, it provided evidence of the effect of donor and recipient factors including donor age,[3] ethnicity,[4] sex or H-Y incompatibility,[5] sequential corneal transplantation,[6] on transplant outcomes.

Endothelial cell count (usually measured in cells per mm^2 is currently considered the single most important indication of donor quality. Endothelial corneal cells do not divide postnatally and, therefore, are vital for graft survival. Corneal graft rejection and/or inflammation in the recipient are significant causes of endothelial graft failure,[7] however, the major cause of failure is endothelial cell decline. The lack of significant difference in failure between paired and unpaired donors, presented by Downward *et al*,[1] may reflect a homogeneous donor pool in the UK. It is of interest that graft survival has been reported to be poorer in UK compared with Italy for Descemet Membrane Endothelial Keratoplasty (DSAEK) even though rejection rates are higher in Italy.[8] Whether this reflects a difference in ECD and donor quality is unclear. Part of the difficulty in comparing and understanding graft outcomes in terms of donor factors between countries, lies in the differences in donor age and postmortem times between countries.[9] For example, as Downward *et al* reported, there is a skew to a higher donor age (61–104 years) in the UK for patients undergoing endothelial keratoplasty, which may be due to donor shortages. In response to this problem, England recently switched to an opt-out organ donation policy aiming to close the annual gap of approximately 1500 corneas, despite importing tissue from the USA and European Union (EU).[10] However, the effect of this step remains to be quantified, being temporarily masked by a relative donor shortage due to Brexit and the aftermath of the COVID-19 pandemic, which significantly affected eye bank donor cornea procurement on a global scale.[11]

In addition, compared with other eye bank systems, such as in USA or Italy, the postmortem times such as death to retrieval, retrieval to processing and processing to issue may be skewed to being longer in the UK. What is needed, therefore, are comparisons between graft survival controlling for donor age and ECD between countries.

An issue that requires resolution is finding a way of measuring ECD in both

donor eyes in the eye bank and directly in the patients, as currently there are discrepancies probably due to the use of different techniques. The findings reported in this issue should push eye banks to try to keep improving postmortem times, and also to push basic science research into looking for novel, alternative ways to measure the true heath of endothelial cells as well as improving their health to increase graft survival.

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