Autologous Transplantation of RPE for the Management of Acute Exudative AMD

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Surgical treatments for age-related macular degeneration (AMD) are based on the principle of reapposing foveal photoreceptors to healthy retinal pigment epithelium (RPE), when the subfoveal RPE has become compromised. In macular translocation surgery, this is achieved by rotating the neurosensory retina to relocate the fovea onto an area of unaffected RPE, followed by globe counter-rotation to correct for the induced torsion.[1]

Autologous transplantation of the RPE follows the same principle, but in reverse, so that healthy RPE is brought from the retinal periphery to the subfoveal location, without moving the neurosensory retina. The advantage of this procedure is that the retina is not rotated and it can be performed on the first eye, because there is little risk of torsional diplopia. The concept of translocating a full-thickness patch of RPE and choroid was first described by Aylward at Moorfields Eye Hospital in London.[2] These grafts, however, were small and harvested from within the macular area and did not sustain visual function at the 5-year follow-up.[3] Van Meurs in Netherlands described a modification to the technique and harvested larger grafts of full-thickness RPE and choroid from the globe equator (Figure 1).[4]

GRAFTS HARVESTED AT THE EQUATOR

We set up a prospective cohort study at Moorfields Eye Hospital to assess the technique using the larger grafts harvested from the equator.[5] The patients in the study all had a very poor visual prognosis and were ineligible for photodynamic therapy (PDT) (eg, RPE rip or lesion size >5,400 µm). In addition to visual acuity changes, we were particularly interested in knowing how consistently the grafts could reestablish

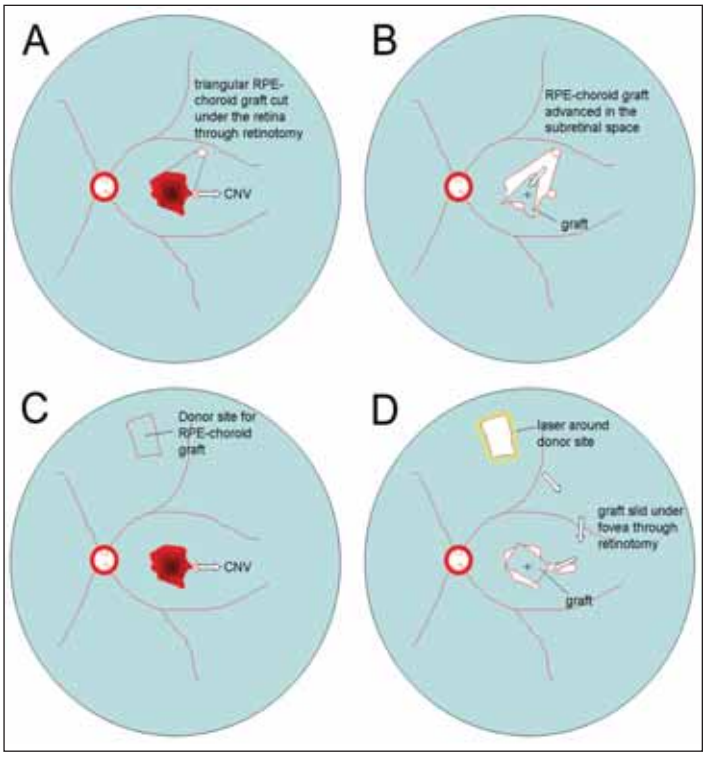

Figure 1. Two techniques of autologous RPE transplantation are shown. The technique described by Aylward begins with vitrectomy and removal of CNV through a temporal retinotomy (arrow) (A). A second retinotomy is made to insert vertically cutting scissors. Two linear cuts thus create a triangular island of RPE and choroid. The triangular wedge of tissue is advanced into the subfoveal position to cover the defect created by CNV excision (B). The technique described by van Meurs is similar with regard to CNV excision, but the patch graft of RPE and choroid is harvested through a superior peripheral retinotomy, and the overlying retina is discarded (C). The RPE-choroid graft is held by a specially designed instrument and reinserted into the subretinal space through the original retinotomy (arrows) (D). A laser is applied to the donor site to prevent retinal detachment.

their blood supply. We also wished to assess visual function all over the graft using microperimetry.

Surgery was performed successfully in all 12 patients. Primary graft failure occurred in one, due to the development of a large hemorrhage beneath the graft immediately postoperative. Indocyanine green angiography in the remaining 11 patients confirmed good perfusion of the grafts by 2 weeks after surgery.

Vision was improved in three patients (25%) and one patient reached 20/30. The remainder showed variable degrees of vision loss, but remember that we selected only AMD patients with a particularly poor visual prognosis. Our results should therefore be compared to the natural history of AMD patients with subfoveal RPE rips, lesions too large for PDT and/or 4 to 6 disc areas of subretinal haemorrhage.

Complications in our pilot study included subretinal hemorrhage from the excision site of choroidal new vessels (CNV) in five patients and retinal detachments, due to proliferative vitreoretinopathy (PVR) in five patients. These complications were all managed successfully but required further surgery.

Our results, therefore, support the concept of autologous transplantation of the RPE and choroid in the management of AMD in selected cases. The finding that RPE harvested from the equator can support foveal photoreceptor function is highly significant for all forms of AMD and may have implications for the treatment of other degenerative conditions such as inherited retinal diseases affecting the subfoveal RPE.

THREE DIRECTIONS FOR THE FUTURE

Further research and development of AMD surgery should progress in three directions. First, it is essential to know how badly damaged foveal photoreceptors are before surgery. This is because surgery replaces the RPE on the assumption that it is the major cause of visual loss. A perfect RPE (or macular) translocation will not restore vision if the patient has no foveal photoreceptors. Although photoreceptor loss is probably slow and correlates to the duration of symptoms, we still need some means of assessing the detailed morphology of the outer nuclear layer before considering patients for surgery. This may be achieved with developments in optical coherence tomography or in vivo confocal microscopy imaging.

Second, subretinal hemorrhage is a problem and may be related to the fact that the choroid is one of the most vascular tissues in the body, and we are operating on it during an acute phase of angiogenesis. The new molecular treatments directed against vascular endothelial growth factor (VEGF) may be beneficial in reducing hemorrhage. In the future, many patients considered for AMD surgery are likely to be those who have lost vision despite intraocular anti-VEGF injections. Preoperative anti-VEGF administration may reduce the tendency for hemorrhage, particularly from the subfoveal bed of CNV excision. Finally, the problems of PVR are likely to be reduced with the development of improved surgical techniques, as has occurred in retinal detachment surgery over recent years.

Some ophthalmologists have questioned the role of surgery in AMD, now that new anti-VEGF treatments have become available. We currently have full published randomized control trial data for PDT and pegaptanib (Macugen; OSI/Eyetech, New York, NY and Pfizer, New York, NY), both of which show a slowing of vision loss in AMD, compared with nonintervention.[6,7] Clearly, developing a treatment that could improve vision compared with current treatments is still warranted. Initial results with ranibizumab (Lucentis; Genentech, San Francisco), however, appear significantly better. Preliminary data from the Minimally Classic/occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD (MARINA) study show 90% of treated AMD patients maintained or improved vision by year 2, compared to 53% in the control group. AMD surgery is likely to evolve in combination with these treatments and it is also important to remember that maintained vision still includes patients losing sight of up to 15 letters. Ultimately, one must identify patients who have a particularly poor prognosis for anti-VEGF treatments, and this might include those with a subfoveal RPE rip or large subretinal hemorrhage.[8]

Surgical complications currently present a limiting factor for autologous RPE transplantation, and the treatment options will undoubtedly expand as this is resolved with further research advancements and technical developments. ■

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