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ARTICLE

Evolving outcomes of surgery for retinal detachment in retinopathy of prematurity: the need for a national service in the United Kingdom

An audit of surgery for acute tractional retinal detachment complicating ROP in the UK.

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OBJECTIVES: To audit the structural and functional outcomes of surgery for acute tractional retinal detachment due to retinopathy or prematurity between 2004 and 2014 in Oxford UK.
METHODS: Consecutive operations were identified from a surgical log. Clinical data including demography, perioperative data, and retinal outcomes were extracted into a spreadsheet and compared against two international data sets referenced in the method section. Nonparametric tests (Fisher's exact, and the Mann–Whitney *U*-tests) were used for statistical analysis with a *p*-value < 0.05 considered significant.
RESULTS: Twenty-nine eyes of 19 babies underwent surgery. The mean age (SD) at final follow-up was 6.4 (3.7) years of age and comparable to the reference data sets. The mean birth weight and gestational age of babies matched the ETROP data set referenced in the method section. Anatomical success was obtained in 16/29 (55.2%) of eyes and more likely with stage 4 ROP than stage 5 disease ($p < 0.05$). Thirteen of 29 eyes (44.8%) obtained form vision post-operatively. All instances of macular retinal reattachment during follow up were verified with post-operative OCT.
CONCLUSIONS: Surgery for stage 5 ROP is not worthwhile. For stage 4 ROP it yielded better visual outcomes than ETROP but registration for visual impairment was not prevented. Innovation such as endoscopic vitrectomy could yield better outcomes. Earlier detection of vitreoretinal fibrosis could result in timelier referral. A formally funded national service is needed to ring-fence resource to avoid delays in access to surgery, which has a narrow surgical window.

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INTRODUCTION

Retinopathy of prematurity (ROP) is a disease of the immature retina first described by Terry who linked the epidemic of resulting blindness to excess oxygen administration in the neonatal intensive care unit [1]. The sequence of events resulting in blindness is circumferential extra-retinal neovascularisation at the junction of vascular-avascular retina that progresses to cicatrisation. The resulting acute and chronic changes described include acute tractional retinal detachment (a-TRD), exudation, pigmentary responses, macular fold, and foveal ectopia [2]. Peripheral retinal ablation as an outcome of an ROP screening programme reduces the risk of a-TRD. For advanced healthcare settings the risk was reduced from 21% in the 1980s to approximately 12% in the 2000s through refinement of criteria for laser ablation [3, 4]. The review by Hansen and Hartnett provides a comprehensive review of surgical approaches to manage a-TRD [5]. The purpose of this paper is to describe the evolution of the diagnostic approach and to audit long-term structure-function outcomes of conventional vitreoretinal surgery from 2004 over a 10-year period at a tertiary referral centre in the United Kingdom.

METHODS

Data

A log of all cases undergoing surgery for a-TRD after informed consent over a 10-year period from 2004 at Oxford University Hospitals NHS Foundation Trust was used to request notes for the purpose of audit, which was registered under the governance procedures at the Oxford University Hospitals Foundation NHS Trust. The study was performed in accordance with the principles of the Declaration of Helsinki. Where babies had been discharged to local units, a request for information was made to local ophthalmologists using secure NHS e-mail. Output from BadgerNet neonatal database was printed at referral and available online for babies admitted to Oxford to summarise medical complications of premature birth. The early treatment of retinopathy of prematurity study (ETROP) and
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recently published European data set by Karacorlu were used as the reference standards for the audit [6, 7]. Data collected and entered into a spreadsheet included: referral source, gestational age (GA) at birth, postmenstrual age (PMA) at several time points(referral, first consultation in Oxford, initial surgery for a-TRD, final follow-up), gender, occurrence of multiple births, post-code of the referring hospital, treatment with pre-operative laser or Anti-VEGF injection, intra-operative procedures, post-operative complications, follow-up duration, retinal anatomic status, Log MAR equivalent visual acuity (VA) at the final follow-up, and images acquired during the management pathway. Classification of ROP was according to the revised international classification [8]. Zone 1 or posterior zone 2 ROP was termed posterior ROP. Stage 4a and 4b represented partial retinal detachment with and without macular attachment respectively. Stage 5a and 5b represented open and closed funnel configuration of total retinal detachment.

Pre-operative management

Referring hospitals treated babies with primary laser or Anti-VEGF injection for posterior ROP and supplied Retcam (Natus Medical Inc, California, USA) images if available. All cases underwent pre-operative imaging in Oxford. The choice of en-face retinal imaging evolved during the study period and included video-indirect ophthalmoscopy (2004), Retcam (2008), and Optos (Optos PLC, Dunfermline, Scotland) (2012) [9]. Pre-operative fluorescein angiography was adopted as standard of care from September 2012 to identify residual peripheral non-perfusion requiring targeted additional photocoagulation of the retina to control plus disease. Intravitreal injection with Anti-VEGF agents were used selectively following informed consent. Drugs included Macugen (Bausch + Lomb, New Jersey, USA) bevacizumab (Genentech, California, USA) or Lucentis (Genentech, California, USA), injected in the neonatal unit under topical anaesthesia with prior irrigation with 5% Iodine.

Primary surgery

Written informed consent was obtained from the parents of all babies before surgery and subsequent examinations under anaesthesia. Scleral incisions at 1 mm posterior to the limbus were made for a 20-gauge 4-port lens sparing approach assisted by chandelier illumination. A 4 mm sutured infusion was placed nasally where traction was minimal. The 20-gauge approach was maintained when narrower gauge instruments became available because of concern that longer sharp trocars designed for adult eyes could result in iatrogenic trauma to detached retina. Vitrectomy and bi-manual release of circumferential bands addressed ridge to ridge, and ridge to disc traction while a 5 mm encircling band was used to address ridge to Ora and ridge to lens vectors. Posterior hyaloid separation was not attempted. The plan for an iatrogenic retinal break was to abandon surgery if the fellow eye had visual potential but to proceed to retinectomy and oil tamponade if the fellow eye was blind. Surgery concluded with fluid air exchange to prevent vitreous incarceration or silicone oil injection. All ports and conjunctival incisions were sutured with 7/0 vicryl. Subconjunctival cefuroxime, Dexamethasone and Marcaine were administered. For stage 5 ROP, a vitreo-lensectomy with more extensive membrane dissection was performed.

Follow up assessment

All infants were routinely examined on day 1 after surgery, and 1–2 weeks later as in-patients. Anti-VEGF injections were given if there was recurrence of plus disease. Infants were reviewed in outpatients 1–2 months, 4–6 months and 6 monthly thereafter with care delivered in Oxford where possible or locally. Ammetropic and anisometropic amblyopia was managed by correction with contact lenses or spectacles and subsequent occlusion therapy. Binocular near vision was assessed using the near vision detection scale at 30 cm in the early post-operative period following a basic clinical assessment of fixation behaviour [10]. Forced Choice Preferential Looking (Keeler), Cardiff cards, Kay pictures, and crowded LogMAR (Sonkson) tests were used to quantify uniocular vision according to age and ability to perform a test. When developmental delay precluded such assessment, fixation behaviour was documented as fix and follow, Light perception (LP) or no light perception (NLP). Functional success was defined as the presence of form vision, which is anything better than light perception. All babies underwent indirect ophthalmoscopy with pupil dilation. Anatomic success was defined, for the purposes of audit, as complete retinal reattachment for stage 4 ROP, and posterior pole attachment for stage 5 as judged by post-operative indirect ophthalmoscopy at final follow up. Failure of primary surgery was defined as extension of retinal detachment occurring early (<6 months) or late (>6 months) from the date of surgery. Examination under anaesthesia was initially planned between 3 and 6 months post-operatively to divide the encircling band [5]. This protocol was modified to defer division of buckle if deemed safer in light of an early surgical failure; this takes into account vitreoretinal fibrosis in the peripheral retina. Additional vitreoretinal surgery was considered and performed when there was failure of primary surgery.

Imaging during follow-up

En-face fundal imaging was attempted at each follow-up using the systems already mentioned. This was complimented by Optical Coherence Tomography (OCT) using table-top devices, customised for use in children under anaesthesia. A time domain OCT system (Stratus; Carl Zeiss Meditec, Jena, Germany) was available in 2004 and replaced with the spectral domain device in 2011 (Spectralis; Heidelberg Engineering, Heidelberg, Germany) [11, 12]. A handheld platform was available on trial for a week in September 2008 and used in one baby following surgery (Envisu; Bioptigen/Leica, Morrisville, NC). Images were cropped using Microsoft Paint. Montages of images were created using PTGui software (New House Internet Services B.V., Rotterdam The Netherlands). Photoshop (Adobe Inc, California, USA) was used to assemble figures for illustration.

Statistical analysis

Fisher's exact, and the Mann–Whitney *U*-tests were used in Stata version 9.0 for statistical analyses (StataCorp, LP, College Station, TX). Statistical tests were 2 tailed, and significance was defined when p was <0.05.

RESULTS

Demographics

Twenty-nine eyes of 19 babies underwent surgery for a-TRD over a 10-year period. Seventeen (89.5%) infants were tertiary referrals of which 2 were from units within the Thames valley neonatal network. Of the 17 externally referred babies only 2 had imaging performed by the referring ophthalmologist. The mean gestational age (GA) (SD) and birth weight (SD) of the cohort was 25.2 (l6) weeks and 745.6 (168.3) grams. Mean postmenstrual age (PMA) at surgery was 48.1 (9.0) weeks. There were 10 females (52.63%), 5 babies (26.32%) were one of a set of twins, and the racial distribution was 17 (89.5%) white Caucasian and 2(10.5%) mixed race. Eleven babies (57.9%) underwent bilateral surgery. The mean PMA for unilateral surgery was older at 52.1 (11.7) compared with 45.1 (5.28) weeks for bilateral surgery ($p =$ 0.09). Of the nine eyes managed conservatively, two were because of resolution of ROP and seven were deemed inoperable and ended up blind at final follow-up. The mean time in days(range) in days from referral to surgery was 25.8 (0–87) split into referral to out-patient consultation (mean 6.3) and out-patient consultation to date for surgery (mean 20.5 days).

Post-operative classification of ROP and treatment. There were 17 (58.6%) right eyes undergoing surgery. The zone of ROP was posterior in 20 (69%) of eyes. The proportion of stage 4a had reduced by the time surgery from 18/29 (62.1%) at time of first appointment in Oxford to 9/29 (31.0%) at surgery. The primary treatment of ROP was laser ablation of the peripheral retina in 27 eyes (93.1%) and injection with Lucentis in 1 eye (3.45%) with 1 eye recorded without ROP by the time screening had concluded. Rescue treatment was performed with Macugen (2 eyes) and Avastin (1 eye) following laser. Laser was used as rescue treatment in one eye undergoing primary treatment with Lucentis injection. Pre-operative Anti-VEGF injection was used in 5 (17.24%) eyes (2 Avastin, 3 Lucentis) and angiographically guided laser in 2 eyes to reduce the risk of intra-operative haemorrhage. Figure 1 illustrates this image guided approach used for case 16R. Optomap imaging shows antero-posterior disc to ridge traction, residual plus disease and retinal non-perfusion, which was then be targeted with precision for additional laser ablation and Anti-VEGF injection to control plus disease prior to surgery. Further intravitreal injection

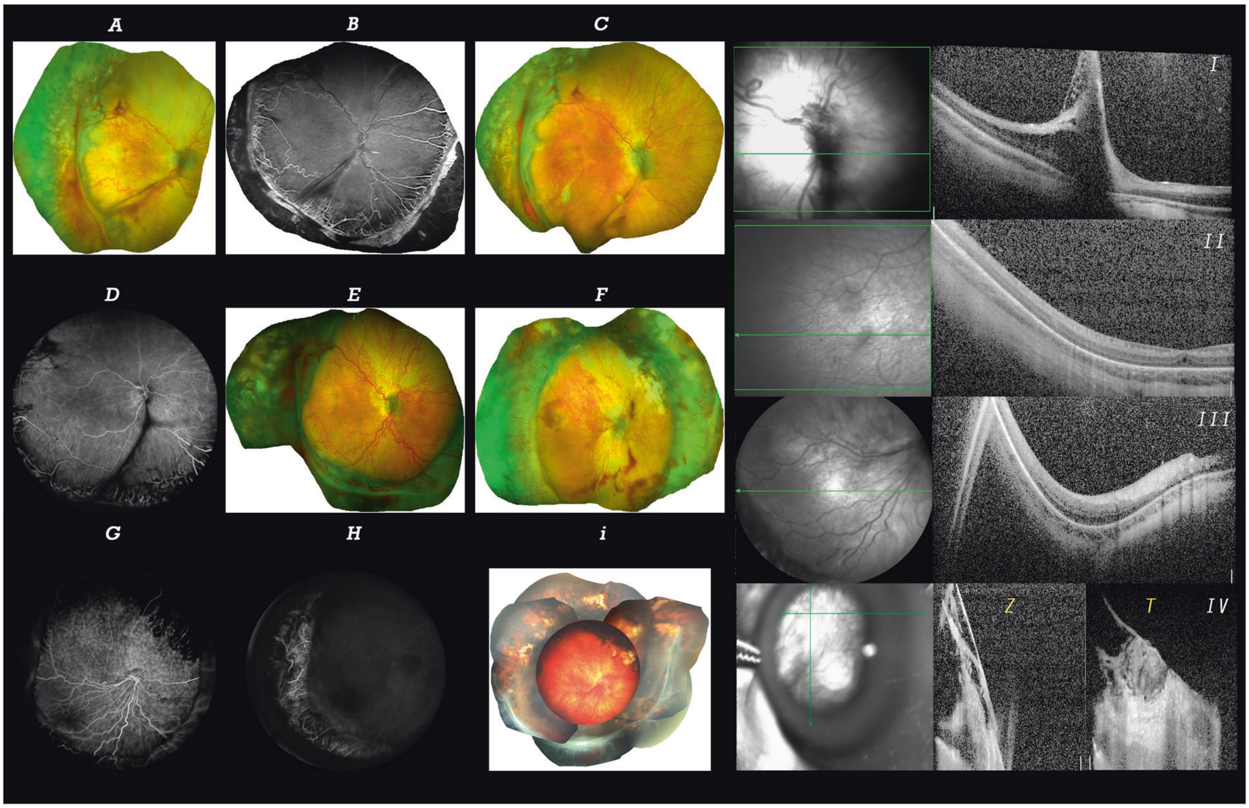

Fig. 1 Image guided management in eye 16R. Following primary laser retinal ablation there is persistence of plus disease (**A**). Non-Perfusion of the retina posterior to the ridge is seen using Fluorescein angiography (**B**), which also shows circumferential and ridge to disc traction (**B**). Pre-operative injection with anti-vegf injection and posterior to ridge laser photocoagulation of the retina controls the plus disease (**C**, **D**). There is early recurrence of plus disease a week post-operatively (**E**), which responds to repeat anti-vegf injection (**F**). Rotation of the macula occurs later as a consequence of maturation of residual peripheral scarring (**G**, **H**, **I**). OCT scans verify macular attachment (II, III) and show anterior peripheral scarring and retinoschisis (IV) that support the clinical decision to defer division of the scleral buckle.

was required to control post-operative recurrence of plus disease. Imaging showed how asymmetric inferior retinal fibrosis caused translation and rotation of the fovea post-operatively. The decision to cut the buckle post-operatively was deferred as OCT showed residual tractional schisis affecting the anterior retina.

Surgery and post-operative management. The most frequent planned surgical approach was vitrectomy and encirclement in 17 (58.6%) eyes, lensectomy-vitrectomy with (3) and without (3) encirclement in 6 (20.68%) eyes, segmental sponge buckle or vitrectomy alone in 4 (13.79%) and 2 (6.9%), respectively. Unplanned interventions were required in three eyes including lensectomy, retinectomy and silicone oil tamponade. Intra-operative complications occurred in 6 eyes (20.69%) and included cataract requiring lensectomy, intraocular haemorrhage (2), iatrogenic retinal break (l), and retina and lens touch in 1 eye each. Further surgery was performed in 5 eyes of 3 babies with 4 eyes treated for early failure and 1 eye for late failure.

Twenty six of the 29 eyes (89.6%) underwent primary (24) or secondary (2) scleral buckling. Of these 22 eyes were encircled and 4 underwent segmental buckling. Fourteen of 26 eyes (53.8%) have had buckles divided or removed. The mean duration between surgery and buckle intervention was 1.8 (1.4) years. Refraction data was available for 14 of the 26 eyes. The mean spherical equivalent after buckle removal was −19.3DS (14.3). Of the 12 eyes retaining buckles, it was deemed unsafe to divide the buckle in 5 eyes because of peripheral retinal traction (Fig. 1IV-Z, IV-H) and in the remaining eyes there was no clinical advantage conferred by removal of buckle. Refraction immediately following buckle division under anaesthetic was available for case 13 and there was a reduction of myopia by 4.00DS in the right eye and 5.00DS left eye.

Anatomical and visual outcome. The mean age at final follow-up was 6.6(3.5) years of age. Anatomical success was obtained in 16/29 (55.2%) of eyes. Form vision was documented in 12/29 (44.44%) eyes and known to be present but not recorded in 2 eyes and unknown in 2 eyes. Fourteen of 29 eyes (48.3%), therefore, obtained form vision following surgery. Final Anatomical success was significantly more likely when surgery was for stage 4 (16/22) (72.7%) rather than stage 5 disease 0/7(0%) ($p < 0.05$). Even when macular reattachment was proven with OCT, and intensive refractive rehabilitation used, the best near vision recorded for stage 5 ROP was grade 2 (light fixation) at 18 months following surgery. The best vision recorded was one eye with 0.9 Log MAR (6/48 Snellen equivalent); 4 others had Log MAR 1.0. All children were registered as visually impaired. OCT was used in 15 of the 19 babies in this report, with all instances of macular reattachment verified with post-operative OCT. All patients in the Oxford cohort were registered visually impaired.

Audit. Table 1 compares key metrics between the present study and the two reference standard studies. The sample of babies treated in Oxford matches ETROP demographically and with respect to the high proportion of babies undergoing peripheral retinal ablation for ROP prior to surgery. The groups are well matched for follow up. Stage 4a was less prevalent in the Oxford data set. Macular reattachment was equivalent to Karacorlu and marginally exceeded ETROP. The proportion of patients achieving form vision was greater than ETROP and the proportion achieving 6/60 or more greater than Karacorlu.

Table 1. Audit for benchmarking Oxford data against 2 reference standards: PL—perception of light; NPL—no perception of light.

Criteria for comparison	Oxford	ETROP	Karacorlu et al.
Subjects undergoing surgery	19	57	65
Mean birth weight (grams)	746	715	1212
Mean GA (weeks + days)	25 + 2	25 + 1	28+
Mean PMA at Surgery (weeks)	48.1	Not available	43.1
Mean follow-up[a] or mean age at final follow-up[b]	6.4[b]	6.0[a]	6.9[a]
Eyes undergoing surgery	29	75	88
Eyes available for analysis following surgery	29	70	88
Eyes with long-term follow up	29	59	88
Eyes with no prior retinal ablation prior to surgery	1	0	37
Eyes with stage 4a	10/29 (34%)	28/70 (40%)	19/88 (22%)
Eyes with stage 4b	12/29 (41%)	14/70 (20%)	38/88 (43%)
Eyes with stage 5	7/29 (24%)	13/70 (19%)	31/88 (35%)
Eyes with no staging for ROP	0	15 (21%)	0
Success post vitrectomy + -buckle	13/25 (52%)	17/50 (34%)	54/88 (61.3%)
Success post buckle	4/4 (100%)	6/9 (67%)	NA-Buckles not used
Macular attachment at final follow up	18/29 (62%)	25/59 (42%)	54/88 (61%)
Eyes with stage 5 with long-term macular reattachment	0	0	13
Eyes in which Form Vision measurable	13/29 (45%)	20/59 (34%)	45/88 (51%)
No form vision (PL or NPL)	14/29 (48%)	32/59 (54%)	34/88 (39%)
6/60 or better	5/29 (17%)	Not provided	8/88 (9%)
>6/60	1/29 (3%)	5/59 (8%)	Not provided
Eye in which vision not measured	0/29	7/59 (12%)	9/88 (10%)

[a]Interval between presenation and final follow up(reported in ETROP and Karacrlu) while.
[b]Interval between birth and final follow up (Oxford).

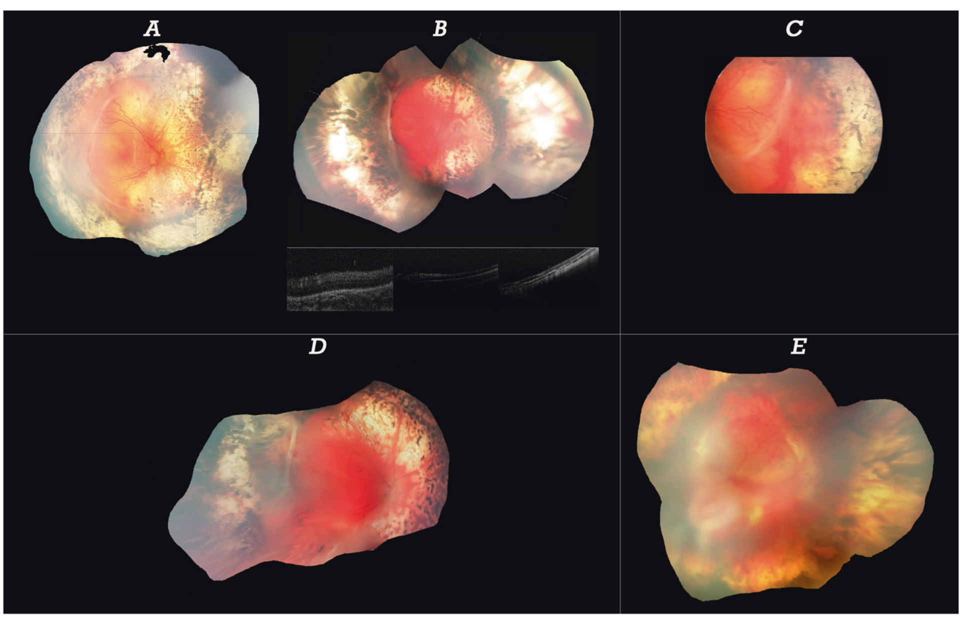

Fig. 2 Case 5. Following surgery for bilateral stage 4b ROP (**A**, **C**) the macula successfully reattached only in the right eye (**B**), but detached again when the encircling band was divided 3 months following surgery (**D**).

Case studies

Early bilateral failure: Case 5. This infant underwent bilateral vitrectomy and encirclement at 44 + 2 weeks PMA for bilateral stage 4b ROP, which was more advanced OS (Fig. 2A, C), By 51 + 1 weeks PMA clinical and OCT confirmation of retinal attachment was confirmed OD but the retina had failed to reattach OS (Fig. 2B, E). The encircling band was divided at 3 months following surgery and the silicone oil left in-situ. The macula re-detached 2 weeks later (Fig. 2D), and revision surgery consisted of repeat encirclement with further limited membrane dissection. Following silicone oil removal and subsequent division of buckle, the outcome at final follow' up is PL vision without reattachment of the macular retina and glaucoma as a late complication.

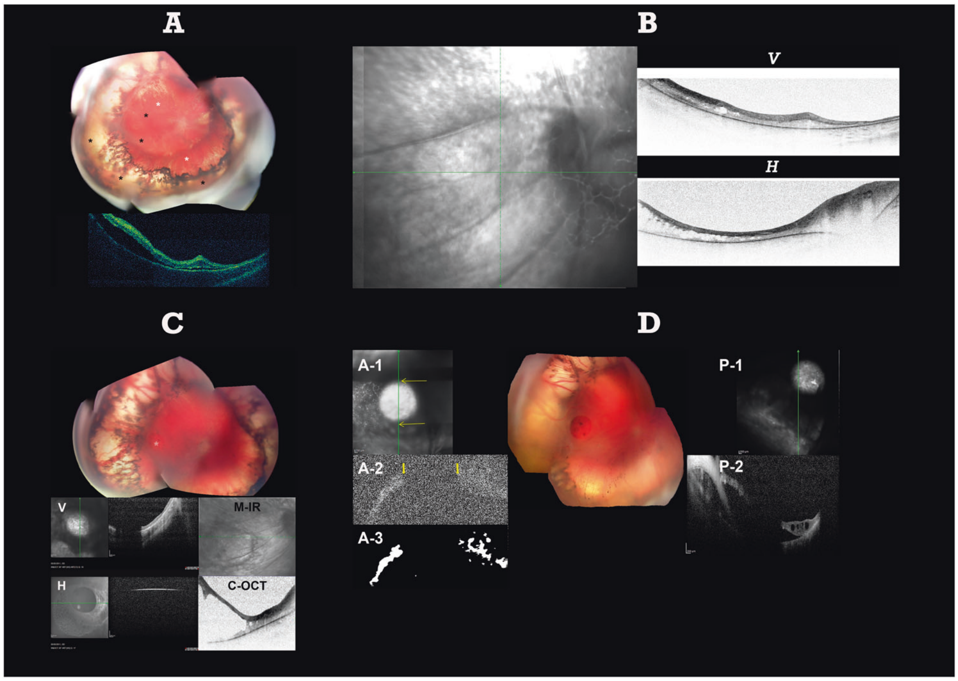

Fig. 3 Case 8. The retina was variably attached (white stars, **A**) with pockets of subretinal fluid remaining (black stars, **A**) and a pale disc 3 months following surgery for stage 5a ROP. Horizontal and vertical OCT scans across the macula (**B**–**H**, **V**) confirmed complete macular reattachment 3 months later with residual retinoschisis. A suspected hole (**C**) in the temporal retina was shown by a vertically focused OCT scan (**C**–**H**) to represent thinning of an enlarging schisis cavity. An anterior focused OCT scan, enhanced with image analysis (**D** A-3), shows that the defect (yellow arrows: **D** A-1, A-2) was a full-thickness hole associated with resulting retinal detachment (**D** P-2).

Late failure: Case 8. This infant underwent vitreo-lensectomy, membrane peeling and encirclement at 62 + 2 weeks PMA for stage 5a ROP OD (see online video 1). Three months following surgery at 75 + 2 weeks PMA most of the subretinal fluid had reabsorbed but the optic disc was pale and retina thin (Fig. 3A). At 93 + 2 weeks PMA, 6 months following surgery there was complete macular reattachment at the posterior pole but with residual retinoschisis (Fig. 3B), A suspected break (White star, C) was confirmed to be a component of an enlarging retinoschisis cavity at 12 months following surgery, progressing to full thickness break and retinal detachment 6 months later (Fig. 3C, D). The best vision developing with intensive refractive rehabilitation was fixation of light, which was lost with onset of late retinal detachment. Further surgery was attempted but the retina would not flatten under air. Retinectomy and long-term oil tamponade was not deemed to be in the patient's best interest.

Post-operative heterotopia and tractional retinoschisis: Case 14. Figure 4 illustrates a more exaggerated superior rotational macular heterotopia in left eye of case 14. This patient was suspected of post-operative retinal detachment based on B-scan assessment. OCT however, verified a schisis that has remained stable and not affected vision, which is functionally hard to associate with the marked structural disruption that has occurred.

DISCUSSION

The incidence of a-TRD following treatment of acute ROP varies considerably but is in line with ETROP at about 10% for developed economies. There is a very narrow surgical window for a-TRD when there is early fibrosis and lower surgical risk. This study provides further confirmation that when fibrosis is advanced, resulting in stage 5 disease, that anatomical and functional outcomes are poor; no babies obtained a successful outcome in this study, which is consistent with the findings of the ETROP study. Case 8R is an excellent example, confirming that even when retinal reattachment is achieved and confirmed with OCT in stage 5 disease, that structural damage is too advanced to permit form vision. The results of the present study and the reference standards show that surgery for progressive 4a has the best outcomes. The paradigm of minimal vitrectomy to deal with antero-posterior and circumferential traction, while using encirclement to deal with anterior ridge to lens traction in the best cases, results in the ability to develop form vision that can allow near vision able to support sighted education. The best distance vision outcomes were around 6/60 Snellen equivalent and required registration of children as visually impaired. The barriers to developing better vision in babies developing a-TRD are macular detachment, foveal heterotopia, high myopia, anisometropia during the sensitive period of visual development. Timelier referral and access to surgery is required to avoid progression to 4b macular detachment. The visual outcome in case 14 underscores the remarkable impact on vision conferred by any form of macular reattachment when brain structure and function has been minimally compromised because of prematurity. In the UK, babies move between as many as four and five hospitals during the neonatal period. This can make the detection of subtle progression of disease challenging if the subjective nature of indirect ophthalmoscopy is relied upon as the only means of detecting and documenting disease progression. The availability of high-quality imaging is one way of detecting such change without babies needing to be moved and is one factor that could improve access to timelier surgery. During the study period only two referring units had the ability to monitor babies and provide feedback. Case 2L was the first illustration of the value of pre-operative OCT in reducing the potential for false-negative diagnosis of stage 4a disease [13]. In the present study there were 22 eyes with stage 4 ROP of which 8(36.4%) underwent pre-operative OCT. The mitigating circumstance precluding OCT in every case was the complexity of using table-top OCT devices. Advances in OCT instrumentation including handheld devices and customised mobile table-top devices such as Heidelberg Flex

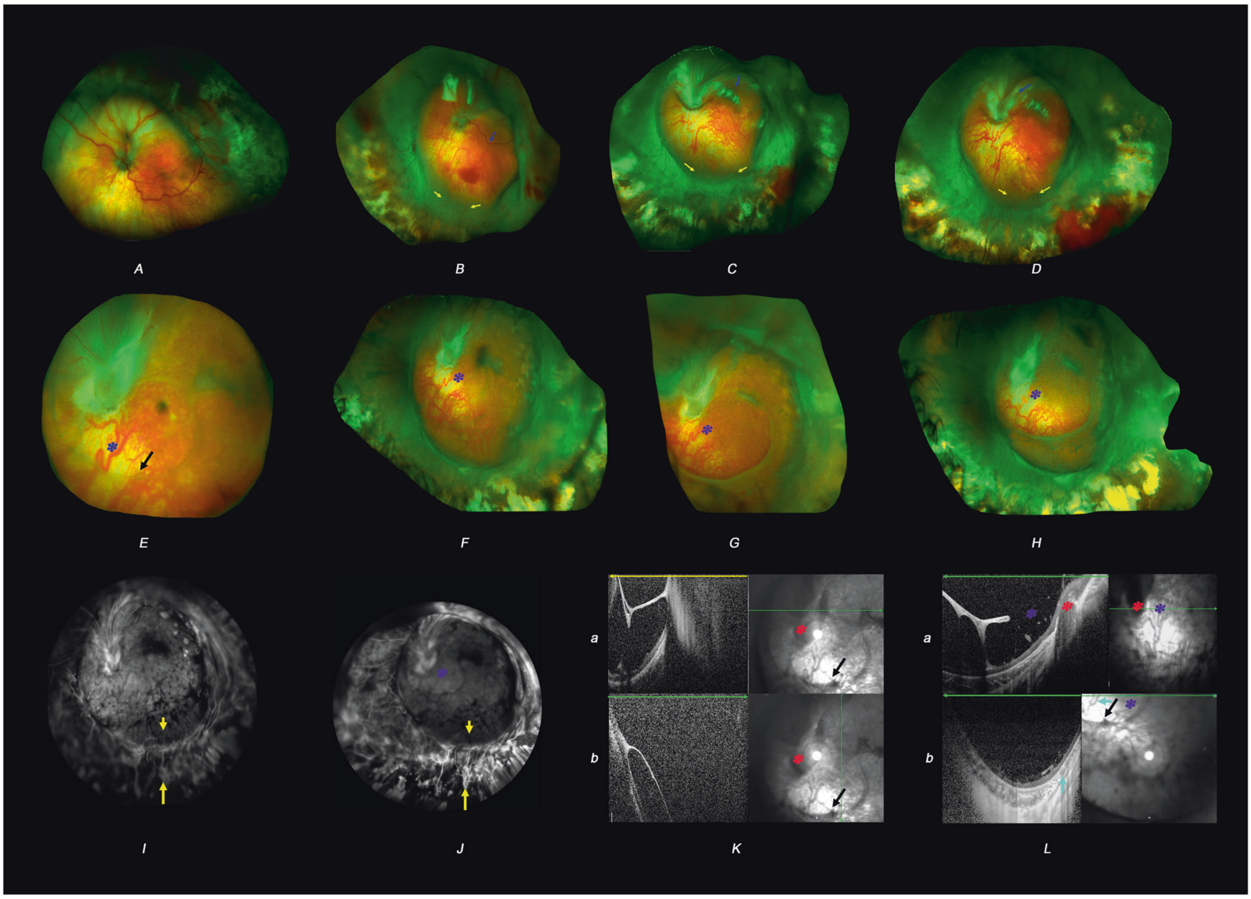

Fig. 4 **Case 14.** Following vitrectomy and encirclement, the macula reattaches nicely (**A**) but then there is marked progressive counter-clockwise rotation of the retina about the disc (blue arrow **B**–**D**) with the peripheral stretched retina draping over the buckle shown by the retinal blood vessels in the Optos pseudocolour images and Spectralis angiogram (yellow arrows **B**–**D**, **I**, **J**). The retina between the disc (red star **K**, **L**) and the buckle becomes schitic and develops a round inner retinal break (purple star in **E**–**H**, **J**, **L**) centred on a prominent choroidal vessel with a small inflection of retinal tissue (black arrow **E**, **K**, **L**). This area was interpreted as a retinal detachment on B-Scan when visual symptoms were investigated using B-Scan. The OCT findings at EUA led to a conservative management plan and there has been no decline in visual function since.

should allow universal OCT grading of stage 4 ROP with the aim of increasing the proportion of surgical cases favouring stage 4a disease [14, 15]. This cohort of surgery for a-TRD is also the first in which anatomical success has been verified by OCT in all cases. OCT is also clinically useful in helping if encircling bands should be divided or not. Classical teaching advocated division of buckle at 3 months following surgery [2–5]. The first case in which this was done resulted in recurrent retinal detachment shortly after. Deferral of buckle division to a later time point has not been accompanied by any further cases of late retinal detachment. There is the potential for long-term sight threatening complications such as buckle erosion, in eyes where encircling bands have been retained. However, no such complications have emerged over a mean follow up of 6.5 years. The mean age at which surgery was performed 48.1 weeks in the present study and higher than one of the reference standards. This reflects the relatively large number of late presentations where unilateral surgery was carried out in the less advanced eye. Service development in the UK should aim to develop a pathway that allows earlier detection and access to surgery—a nationally commissioned service is suggested given the small annual caseload and complexity that this study has alluded to. An increase in the proportion of referring centres that could capture high-quality widefield retinal images should facilitate liaison for accurate diagnosis and timelier referral. Increasing use of non-contact widefield imaging with the Optomap system for larger infants has the potential to monitor infants treated with primary laser and Anti-VEGF without the need for examinations under anaesthesia to accurately monitor for cicatrisation. Access to surgery needs ring fencing of post-operative intensive care beds, paediatric anaesthetic provision and beds for extended post-operative recovery at the referring unit if needed. Only one case in the present studied developed a-TRD following primary treatment of ROP with Anti-VEGF injection. More cases are likely in the future if the trend continues in the UK [16]. The configuration of a-TRD is said to be different following primary treatment anti-VEGF injection [17]. The typical configuration is either a focal temporal or a "volcano" style elevation as occurred for eyes 5R and 5L. Following Anti-VEGF injection, the elevation is a posterior circumferential or a pre-papillary configuration for which segmentation is advocated with 27-gauge instrumentation [18]. Endoscopic vitrectomy for managing peripheral tractional vectors has the potential to overcome the complications of encirclement including extreme high myopia and would also allow for a larger number of unilateral cases to be considered for surgery where high ammetropia post-operatively would exclude encirclement as a surgical option [19]. In summary, between 2004 and 2014 a framework for a national service was developed. Surgical treatment of a-TRD using standard approaches at the time combining scleral buckle and vitrectomy, resulted in 29 eyes having surgery; 16/29 (55%) were attached at the last follow-up; 14/29 (48.3%) had form vision. This compares favourably with ETROP, but there is potential to improve outcomes. This audit demonstrates that Surgery for stage 5 has not proved worthwhile. The present study shows that image guided management offers a way to improve diagnosis and optimise referral for surgery. The techniques reported in the present study have limitations and potential for complications that endoscopic surgery could overcome. Developing a strategy for urgent referral, coordinating a national approach to transfer, and monitoring long-term follow-up in a rigorous and prospective manner is the goal of the new de-facto national centre based at GOSH that should allow for improvements in key performance indicators presented in this study.

SUMMARY

What was known before:

- Surgery for a-TRD in ROP was not supported in the mid 1990's because of poor outcome and not recommended by the first UK guideline. Centres outside the UK have reported surgery with improving outcomes with advances in surgical techniques.

What this study adds:

- Compared to a matched reference standard data set, improved outcomes are reported beyond the learning curve in this first large-scale effort to manage a-TRD in ROP in the UK. Imaging guided management is shown to facilitate surgical decisions. Key performance indicators have been benchmarked to improve outcomes as further innovation is incorporated into the service.

REFERENCES

1. Terry T. Fibroblastic overgrowth of persistent tunica vasculosa lentis in infants bom prematurely: II. report of cases-clinical aspects. Trans Am Ophthalmol Soc. 1942;40:262–81.
2. Aaberg T, Ben-Sira I, Charles S, Clarkson J, Cohen BZ, Flynn J, et al. An international classification of retinopathy of prematurity: II. the classification of retinal detachment. Arch Ophthalmol. 1987;105:906–12.
3. Palmer M. Retinopathy of prematurity. Arch Ophthalmol. 1988;106:471–9.
4. Hardy RJ, Good WV, Dobson V, Palmer EA, Tung B, Phelps DL. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol. 2003;121:1684–96.
5. Hansen ED, Hartnett ME. A review of treatment for retinopathy of prematurity. Exp Rev Ophthalmol. 2019;14:73–87.
6. Repka MX, Tung B, Good WV, Shapiro M, Capone A, Baker JD, et al. Outcome of eyes developing retinal detachment during the early treatment for retinopathy of prematurity study. Arch Ophthalmol. 2011;129:1175–9.
7. Karacorlu M, Hocaoglu M, Muslubas IS, Arf S. Long-term functional results following vitrectomy for advanced retinopathy of prematurity. Br J Ophthalmol. 2017;101:730–4.
8. International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol (Chic, Ill: 1960). 2005;123:991.
9. Patel CK, Fung TH, Muqit MM, Mordant DJ, Brett J, Smith L, et al. Non-contact ultra-widefield imaging of retinopathy of prematurity using the Optos dual wavelength scanning laser ophthalmoscope. Eye. 2013;27:589–96.
10. Sonkson PM. The assessment of 'vision for development' in severely visually handicapped babies. Acta Ophthalmol. 1983;61:82–90.
11. Patel CK, Chen SD, Farmery AD. Optical coherence tomography under general anesthesia in a child with nystagmus. Am J Ophthalmol. 2004;137:1127–9.
12. Fung T, Muqit M, Mordant D, Smith L, Patel C. Modification of spectralis HRA+OCT for intraoperative multi-modality imaging in pediatric retinal diseases. Investig Ophthalmol Vis Sci. 2013;54:1496–96.
13. Patel CK. Optical coherence tomography in the management of acute retinopathy of prematurity. Am J Ophthalmol. 2006;141:582–4.
14. Chen X, Prakalapakorn SG, Freedman SF, Vajzovic L, Toth CA. Differentiating retinal detachment and retinoschisis using handheld optical coherence tomography in stage 4 retinopathy of prematurity. JAMA Ophthalmol. 2020;138:81–5.
15. Kothari N, Chu A, Huang JM, Lin F, Lin BR, Manoharan N et al. Arm-mounted optical coherence tomography angiography in extremely low birth weight neonates with retinopathy of prematurity. Am J Ophthalmol. 2020; 100624. https://doi.org/10.1016/j.ajoc.2020.100624.
16. Adams GG, Bunce C, Xing W, Butler L, Long V, Reddy A, et al. Treatment trends for retinopathy of prematurity in the uk: active surveillance study of infants at risk. BMJ Open. 2017;7:e013366.
17. Yonekawa Y, Wu WC, Nitulescu CE, Chan RP, Thanos A, Thomas BJ, et al. Progressive retinal detachment in infants with retinopathy of prematurity treated with intravitreal bevacizumab or ranibizumab. Retina. 2018;38:1079–83.
18. Yonekawa Y, Thanos A, Abbey AM, Thomas BJ, Todorich B, Faia LJ, et al. Hybrid 25-and 27-gauge vitrectomy for complex vitreoretinal surgery. Ophthalmic surgery, lasers imaging. Retina. 2016;47:352–5.
19. Nagiel A, Yang U, Reid MW, Anulao KJ, Say EA, Wong SC, et al. Visual and anatomic outcomes of pediatric endoscopic vitrectomy in 326 cases. Retina. 2020;40:2083–90.

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