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EYE CHOOSE: An economic evaluation of surgical strategies for retinal detachment

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Abstract

aims

Rhegmatogenous retinal detachment (RRD) is a sight threatening condition requiring urgent surgical intervention. As the prevalence of RRD is increasing; it is important for decision-makers to understand the clinical and economic evidence for RRD repair. Three main procedures are commonly utilised to repair RRD; pars plana vitrectomy (PPV), scleral buckle (SB) and pneumatic retinopexy (PnR). This study compares the existing evidence and costs and benefits of each approach.

Methods

A systematic review and a random effects network meta-analysis (NMA) of randomised control trials (RCT) was conducted to sythesise data from existing studies on RRD surgery. Searches of key databases and clinical trials registries were performed. To assess the cost-effectiveness of the surgical options, an economic decision tree model was designed. The results were expressed as a cost per line of logMAR acuity and cost per good visual result gained.

Results

Fifteen RCTs were identified for inclusion. The NMA demonstrated that PnR had the greatest likelihood of better vision. There was significant uncertainty in the estimates due to limited evidence for PnR compared to other techniques. The economic model demonstrated a strong signal for the cost effectiveness of PnR, demonstrating more effectiveness at a lower cost. The results of the sensitivity analysis did not change this conclusion.

Conclusion

There is limited evidence for the use of different surgical techniques to manage RRD, including a lack of functional outcomes. However, the current evidence demonstrates that PnR could represent a cost effective approach to the management of retinal detachment.

Plain Language Summary

Background: Retinal detachment is an eye disease that can occur suddenly and needs to be treated as soon as possible. To prevent any loss of sight, surgery needs to be carried out. There are three different surgeries that can be carried out to repair a detached retina. They are: pars plana vitrectomy (PPV), scleral buckle (SB) and pneumatic retinopexy (PnR). This study aims to review all the information about which surgery works best. We also want to know which one gives the best value for money for the health service.

What we did: We reviewed all existing information about how well each of the three surgeries worked and combined all the information. We used this information to build an economic model to assess the cost-

effectiveness of each surgery.

What we found: We found 15 studies in our search. There was more information about some surgeries than others. From what we found there is a good possibility that PnR is a surgery that works well and is cost-effective.

What this means: More evidence comparing the different surgeries to each other would be useful. However, from what we found, PnR could be a good choice of surgery to repair a detached retina.

Introduction

Rhegmatogenous retinal detachment (RRD) is a sight threatening ophthalmic condition caused by a tear or hole in the retina, requiring urgent intervention. Recent studies estimate an annual incidence of 16 cases per 100,000 in the UK [1]. With increasing global prevalence of myopia and pseudophakia, this may further increase [2].

Three main surgical treatment options exist. The first is pars plana vitrectomy (PPV), a keyhole approach to remove the vitreous humour, mechanically drain sub-retinal fluid via a retinal break, and typically tamponade with a near-complete fill of gas or silicone oil. The second, scleral buckle (SB), is an external approach whereby a silicone component is secured to the sclera to alter its internal contour, facilitating physiological reattachment of the retina by the retinal pigment epithelium (RPE). The third technique, pneumatic retinopexy (PnR), involves injection of a small gas bubble without vitreous removal. With PnR, retinal reattachment is achieved by alignment of the bubble (by means of head posturing) against the retinal break, facilitating RPE-mediated retinal reattachment [3]. Currently, in the UK National Health Service (NHS), the vast majority of RRDs are treated using PPV (79.1%), followed by SB (12.1%), with PnR (8.7%) being least commonly utilised [4]. However, emerging evidence suggests better visual outcomes of PnR compared to PPV, [5] suggesting that wider use of PnR could be advantageous for patients and the healthcare system.

As pressures on health care services increase understanding the resource implications of different treatment options becomes increasingly important. Cost-effectiveness of different interventions can be evaluated using economic evaluation; an evaluation of the costs and consequences of interventions [6]. One method of economic evaluation, utilising best available published evidence of efficacy, is an economic decision model. This uses mathematical relationships to understand the consequences that would flow from each alternative under evaluation: in this case PPV, SB and PnR for the treatment of RRD. The aim of this study was to summarise existing evidence regarding the effectiveness of all three techniques using a systematic review and network meta-analysis (NMA), and use this data to populate an economic evaluation decision model. Thus, this study provides evidence on the relative costs, benefits and cost-effectiveness of each surgical approach, to aid decision makers involved in the management of RRD.

Materials and methods

Systematic Review

Search Methods and Inclusion Criteria

The systematic search (MEDLINE, Embase, CENTRAL and clinical trials registries) sought to identify randomised controlled trials (RCT) comparing PPV, PnR or SB. It built upon the search strategies for two existing Cochrane Reviews that compared PPV and SB, and PnR and SB, respectively [7, 8], with an updated search to identify studies published from 2019 onwards. There was no published systematic review comparing PPV and PnR, so a literature search was performed from inception of each database to the end of 2022 (search strategies: appendix1).

Only studies with a randomised controlled design comparing two or more of the three surgical techniques (PPV, SB or PnR) for the management of RRD in adults (over 18 years) were included. Exclusion criteria included non-randomised study designs and any comparison including combination techniques (where 2 or more surgical techniques were combined). No specific inclusion or exclusion criteria were applied regarding complexity of the RRD. The outcomes study were chosen in conjunction with the study PPI steering group, who comprised of those who have lived experience of being treated for a retinal detachement.

Data screening, extraction and quality assessment

Studies were initially screened by title and abstract. The full text of potentially eligible studies were then screened. Those selected for inclusion had data extracted into a pre-specified template designed to extract the key outcomes and study characteristics. The key outcomes were vision, primary anatomical success (i.e., successful retinal re-attachment on first surgical attempt), post-surgical complications and cataract development. To assess the quality of the included studies, the Cochrane Risk of Bias tool was applied to each (ROB 1) [9]. For eligible studies, the full text, data extraction and quality were assessed independently by two reviewers (AK and SW), with a third reviewer (RJH) acting as mediator for any disagreements.

Network meta-analysis

A random effects NMA was carried out using WinBUGS software [10]. Data included in the NMA were the mean logMAR scores, standard deviations (SDs) and number of participants for each measure. Outcomes relating to vision were expressed in two ways: continuous and binary. For the continuous outcome, vision was converted to the logMAR scale (if not already reported as such) [11]. The results were represented using a mean logMAR score to assess the difference in logMAR scores between the arms. The binary visual outcome referred to whether 0.3 logMAR (used to represent a ‘good’ visual result - approximating UK driving standards) was achieved in the affected eye. The logMAR mean and SD were used to calculate a risk ratio (RR) for each surgical intervention meeting this visual standard, based on the assumption of normal distribution of visual outcomes (statistical, clinical and surgical assumptions appendix 2). Likewise, for primary anatomical success, the likelihood of achieving this was extracted and calculated as a RR, as was the risk of post-operative cataract development.

For complication data, a wide range of individually occurring complications were extracted from the studies. To estimate meaningful data that could be included in the decision model, the reported complications were categorised by severity. The categorisation was based on a published classification of RRD complications, derived from a Delphi process, whereby retinal surgeons graded potential post-surgical complications by severity (1 being the least severe, 10 being the most severe) [12]. By discussion and agreement, we (AK and

RJH) allocated each reported complication a numerical grade. Complications graded 1–4 were considered self-limiting, and were not included in the analysis. Complications graded 5–6 were considered ‘minor’ and those graded 7 or greater were considered ‘major’. This distinction was used to generate a RR for one or more minor or major complications for each of the surgical techniques (as well as to apportion cost to complications in the economic model).

Economic decision model

A cost effectiveness analysis (CEA) was carried out using a decision tree format based in Microsoft Excel [13]. Two measures of benefit were considered: incremental cost per additional logMAR line achieved (the continuous outcome) and incremental cost per additional case achieving good vision (the binary outcome). The evaluation was carried out from the UK NHS perspective with a 1 year time horizon, with costs expressed in GBP (2022 price year). This time horizon was selected as the principal costs and effects of a RRD and its repair are incurred during this period (diagram of economic decision model: appendix 3). No discounting was applied as costs and benefits were valued within 1 year.

Costs and effectiveness estimates

Surgical costs were derived from published NHS reference costs 2021/22 [14], and medication costs were derived from the British National Formulary (BNF) (breakdown of unit costs: appendix 4) [15]. For individual complications, the management of each was costed (with expert clinical opinion from the study team and hospital finance professionals) and a weighted average was used to calculate a cost estimation for a minor or major complication.

Effectiveness estimates were derived from the NMA. For complications, there was insufficient evidence to produce NMA estimates due to the limited numbers of events in the data. For major complications an assumption of no difference between the arms was made. For minor complications, evidence from one-way meta-analyses were used.

Sensitivity analysis

To assess the uncertainty in the cost effectiveness estimates both deterministic and probabilistic sensitivity analyses were carried out. A deterministic sensitivity analysis (DSA) was used to assess the uncertainty of the individual parameters, by varying individual parameters to assess their individual impact on conclusions. A probabilistic sensitivity analysis (PSA) evaluated the uncertainty in the cost effectiveness ratio associated with the joint uncertainty in all model parameters for which there was evidence of imprecision in the parameter mean estimates. The covariance in effect estimates from WinBUGS was estimated from the CODA data (convergence diagnosis and output analysis) and the covariance was implemented in the PSA using Cholesky decomposition.

Results

Studies Identified

The search yielded 4,915 titles and abstracts, with 15 studies identified for inclusion (a PRISMA diagram included in appendix 5 demonstrates the selection process). Of these 15, 1 compared all 3 techniques, 9 compared PPV and SB, 4 compared PnR and SB and 1 compared PPV and PnR. The study which compared all 3 techniques was an abstract that did not report any useable data for meta-analysis [16]. The studies are summarised in Table 1.

The results of the quality appraisal found the studies to be of mixed quality. Most were a mix of low/uncertain risk of bias, but 5 were assessed as being at a high risk of bias in at least one domain. (results of the ROB 1 assessment: appendix 6).

Included Studies			
PPV vs SB	**SB vs PnR**	**PPV vs PnR**	**PPV vs PnR vs SB**
Moradian (2016) [17]	Mulvihill (1996) [25]	Hillier (2019) [5]	Betran-Loustaunau (1997) [16]
Ahmadieh (2005) [18]	Kryl (2021) [26]		
Azad (2007) [19]	Morescalchi (2021) [27]		
Zhao (2020) [20]	Tornambe (1989) [28]		
Heimann (Phakic) (2007) [21]			
Heimann (Pseudophakic) (2007) [21]			
Koriyama (2007) [22]			
Sharma (2005) [23]			
Brazitikos, (2005) [24]			

1.Pars Plana Vitrectomy, 2.Scleral Buckle, 3.Pneumatic Retinopexy.

Table 1. Studies included in the systematic review.

Network meta-analysis

Risk ratio (RR) estimates were produced for the binary visual outcome, primary anatomical success and risk of cataract formation from the NMA. For vision, PnR was slightly more effective than SB and PPV, with the lowest average LogMAR score. The likelihood of reaching 0.3 logMAR in the affected eye was highest for PnR. The likelihood for primary anatomical success was highest for PPV, as was the likelihood of developing cataract. There was considerable uncertainty in some of the results, most notably in wide confidence intervals for the likelihood to reach 0.3 logMAR and likelihood of cataract development for PnR vs SB (which had a relatively small number of conflicting

LogMAR acuities for each technique			
	PPV	**SB**	**PnR**
LogMAR acuity (mean) (SD)	0.55 (0.1)	0.53 (0.14)	0.47 (0.19)
Risk Ratios of Different Events			
	SB vs PPV	**PnR vs PPV**	**PnR vs SB**
Likelihood to reach 0.3 logMAR (RR) (CIs)	1.36 (0.80-2.00)	1.93 (0.90–3.51)	1.46 (0.72–2.50)
Likelihood of primary anatomical success (RR) (CIs)	0.94 (0.82–1.02)	0.85 (0.61–1.01)	0.91 (0.70–1.08)
Likelihood of developing cataract (RR) (CIs)	0.25 (0.01–0.82)	0.23(0.01–1.04)	1.69 (0.062–7.52)

studies).

PPV (Pars Plana Vitrectomy), SB (Scleral Buckle), PnR (Pneumatic Retinopexy), RR (risk ratio), CI (credible interval), SD (standard deviation)

Table 2. Mean acuity values for each technique and risk ratios for events between comparators.

Economic Decision Model

The base case results for the continuous outcomes are described in Table 3 below.

Pneumatic Retinopexy	**Cost (£)**	**Effectiveness**	**Lines on chart read**	**Incremental cost**	**Incremental LogMAR**	**Incremental Lines on chart**	**ICER**
	1466	**0.47**	**5.32**				
Pars Plana Vitrectomy	3380	0.55	4.55	1915	0.0773	-0.77	**Dominated**
Scleral Buckle	3394	0.53	4.71	1928	0.0617	-0.62	**Dominated**
ICER (incremental cost-effectiveness ratio)							

Table 3

Base case results for the logMAR outcomes. The lowest cost intervention is PnR, with SB and PPV having a similar cost. The disparity in logMAR acuities are small, with the greatest difference being equivalent to approximately four letters. PnR is less costly and more effective than both PPV and SB, making it the dominant intervention in the base case. The base case results for the binary outcomes are shown in table 4.

Pneumatic Retinopexy	Cost (£)	Likelihood of a good visual result	Incremental cost	Incremental likelihood of a good visual result	ICER (£ per additional good visual result)
	1466	**0.61**			
Pars Plana Vitrectomy	3380	0.32	1915	-0.29	**Dominated**
Scleral Buckle	3394	0.43	1928	-0.18	**Dominated**
ICER (incremental cost-effectiveness ratio)					

Table 4. Base case results for the likelihood of a good visual result.

In the binary model, again PnR has the lowest cost. PPV and SB have a similar cost, with SB being slightly more costly. PnR has the highest chance of achieving a good visual result compared with PPV and SB, and is therefore the dominant intervention.

Sensitivity Analysis

In the one-way sensitivity analysis (OWSA) key parameters such as the likelihood of anatomical success and development of cataract were increased and decreased by a margin of 20% around the mean values from the NMA. In addition, to assess the impact of certain PnR cases potentially requiring an additional laser treatment, a scenario analysis whereby the PnR cost incorporated 10% of participants requiring a 2nd laser session was included. None of the changes in the parameters in the OWSA significantly impacted the cost effectiveness outcomes of the study tornado diagrams: appendix 7.

The results of the PSA for the continuous model are expressed as the probabilities of being cost effective at different willingness to pay thresholds for an additional line of visual acuity (table 5 and appendices 8 & 9). PnR has a substantially higher probability of being considered cost-effective over a range of threshold values than either of the alternatives. The outcomes are presented in a cost effectiveness acceptability curve (CEAC) (appendix 10) and in cost effectiveness planes (appendix 11).

Additional Line of LogMAR acuity					
Procedure	Prob of being CE at WTP of **£0** per correct decision	Prob of being CE at WTP of **£500** per correct decision	Prob of being CE at WTP of **£1000** per correct decision	Prob of being CE at WTP of **£3000** per correct decision	Prob of being CE at WTP of **£5000** per correct decision
Pars Plana Vitrectomy	0%	0%	1%	11%	15%
Scleral Buckle	0%	0%	0%	6%	9%
Pneumatic Retinopexy	100%	100%	99%	83%	76%

Prob (probability), CE (cost effective), WTP (willingness to pay)

Table 5. Probabilistic Sensitivity Analysis of the continuous outcomes.

Discussion

This study carried out a robust synthesis of evidence regarding surgical management of RRD. Based on this contemporary data, the economic decision model assessed the costs and benefits of each approach. Overall, there is a paucity of evidence on the effectiveness of the different techniques. For example, for the comparison of PnR with PPV there was evidence from a single trial [5]. The quality of the evidence was mixed, with particular limitations in selection and reporting bias. However, there were better visual outcomes from PnR and higher primary anatomical success from PPV.

When comparing the surgical options, PnR is consistently less costly than the alternatives. PnR dominates in the base case of both continuous and binary visual acuity models, being less costly regardless of which effectiveness outcome was used. Sensitivity analyses demonstrated that these conclusions did not change based on variance of the individual parameters and the probabilistic analysis of general uncertainty.

Comparison with existing literature

Three other systematic reviews have synthesised the evidence comparing different methods of RRD repair. Considering the two Cochrane reviews which formed the basis of the evidence synthesis for this review, Znaor et al (2019) [7] found a similar rate of primary success, visual outcomes and complications (PPV had a higher rate of cataract formation) when comparing PPV to SB, albeit with low to moderate certainty evidence. This aligns with the results of the EYE CHOOSE study. Sena et al (2021) could not synthesise the evidence regarding visual results as they were too heterogenous. A further systematic review compared all three interventions (though ultimately did not include PnR in the meta-analysis) and concluded there was similar visual acuity for PPV and SB, with no evidence of a difference in primary anatomical success [29]. This study expands upon these earlier reviews as it includes more contemporary data. Further, the NMA approach allowed a simultaneous comparison of the three surgical approaches, with data from all studies contributing to the estimates of effectiveness.

Other economic modelling studies have compared the costs and benefits of surgical approaches for RRD. For example, Chang (2014) concluded that RRD repair is cost effective compared to a 'do nothing' approach, and that in this context, all techniques are to be considered cost effective [30]. To conclude that all treatments are cost-effective is misleading as their analysis failed to consider the relative merits of each form of surgery. Nevertheless, their finding is consistent with the approach adopted in EYE CHOOSE whereby 'no treatment' was excluded as a comparator.

A more recent economic evaluation study comparing RRD repair techniques was carried out by Felfeli et al (2023) [31] using a microsimulation approach to simulate a cohort of 100,000 adult patients. Their study concluded that SB was dominant and that PnR was unlikely to be cost effective. An important driver of their conclusion was a high disparity in primary anatomical success between PPV and SB, compared to PnR, based on the previous version of the Cochrane systematic review published in 2015 [32]. Updated literature from the 2021 Cochrane review [8] and the single published RCT comparing PPV and PnR [5] that contributed to the NMA reported herein found that PPV was most likely to achieve primary anatomical success, but the disparity with PnR was much smaller. Further, the authors make an assumption that primary anatomical failures would have no chance of achieving an excellent visual outcome, an assumption that does not accurately reflect clinical outcomes for secondary anatomical success that are apparent in clinical practice and reported in the literature.

Strengths, limitations & future research

This study was the first to undertake a NMA of the effectiveness of PPV, SB and PnR for the management of RRD and use the results in an economic decision model. This model, based on the contemporary evidence, provides clinicians and policy makers with valuable information to support informed decision making with regards treatment modalities in RRD.

There are limitations with regard to this work, primarily due to a paucity of evidence for several outcomes in the existing body of literature. A lack of studies including PnR as a comparator increases the uncertainty of comparisons made in the NMA, as compared to the PPV and SB arms, which have more available RCT data. As such, some parameters of the model had to be based on estimates and assumptions. For example, complication data was reported in a highly non-standardised manner. To promote inclusion of studies, no restrictions on the morphology or severity of the RRD configurations were made. Rather, as our data was limited to studies with RCT methodology, an assumption was made that each would be internally balanced in this regard. A further limitation of this study is a lack of published trial data on key patient-centric outcomes including health related quality of life measures for retinal detachment (such as relevant utility values) that could allow the results to be expressed in a cost utility framework. There is a also a paucity if secondary or functional visual outcomes (e.g. metamorphopsia and aniseikonia) across all three surgical groups. A review of functional outcomes by Muni (2022) suggests that PnR (and potentially SB) may offer secondary functional advantages over PPV in RRD.

Future research should ideally compare all three techniques directly, allowing for more robust comparisons with greater certainty to be drawn from the evidence base. Such trial methodologies should include standardised complication reporting, and incorporate health related quality of life and secondary functional

outcomes [33]. This would be particularly informative with regard to acute recovery, allowing factors such as recovery time, posturing, and impact on daily activities and emotional well-being to be evaluated.

Conclusion

This study provides a synthesis of contemporary RCT evidence and an economic decision model for RRD surgery. PnR is a potentially cost-effective treatment providing good visual results at a lower cost than PPV and SB. Future research should directly compare all three surgical interventions with incorporation of patient centred outcomes.

Declarations

Conflict of Interest:

The authors declare that they have no conflict of interest

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Author Contribution

Statement: RJH was the clinical lead for all workstreams and the primary investigator for the project. AK led the systematic review and economic evaluation and was the co-primary investigator for the project. MB led the qualitative evaluation and advised on the workstreams based on its findings. SR provided senior evidence synthesis and economic evaluation support. LV provided senior economic evaluation support. SW designed the search strategy and provided additional support for the systematic review. All authors have read and commented on the draft manuscript.

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