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ARTICLE

Factors affecting anatomical and visual outcome after macular hole surgery: findings from a large prospective UK cohort

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Abstract
Objectives To reassess the definition of a large macular hole, factors predicting hole closure and post-surgery visual recovery.
Design Database study of 1483 primary macular hole operations. Eligible operations were primary MH operations treated with a vitrectomy and a gas or air tamponade. Excluded were eyes with a history of retinal detachment, high myopia, previous vitrectomy or trauma.
Results A higher proportion of operations were performed in eyes from females (71.1%) who were 'on average' younger ($p < 0.001$), with slightly larger holes ($p < 0.001$) than male patients. Sulfur hexafluoride gas was generally used for smaller holes ($p < 0.001$). From 1253 operations with a known surgical outcome, successful hole closure was achieved in 1199 (96%) and influenced by smaller holes and complete ILM peeling ($p < 0.001$), but not post-surgery positioning ($p = 0.072$). A minimum linear diameter of ~500 μm marked the threshold where the success rate started to decline. From the 1056 successfully closed operations eligible for visual outcome analysis, visual success (defined as visual acuity of 0.30 or better logMAR) was achieved in 488 (46.2%) eyes. At the multivariate level, the factors predicting visual success were better pre-operative VA, smaller hole size, shorter duration of symptoms and the absence of AMD.
Conclusions Females undergoing primary macular hole surgery tend to be younger and have larger holes than male patients. The definition of a large hole should be changed to around 500 μm, and patients should be operated on early to help achieve a good post-operative VA.

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Introduction

Idiopathic age related macular holes (MHs) are a common cause of significant visual impairment, with a prevalence of up to 1 in 200 in the over 60-year-old age group and are bilateral in up to 10% of patients [1]. Following the first report of successful treatment with vitrectomy and short acting gas tamponade in 1991, they are now routinely treated surgically, where the aim is to close the hole, which typically results in an improvement in vision [2]. Hole closure rates are high at over 90% but various factors are known to reduce the success rate, in particular the size of the hole. A number of surgical variations and adjunctive procedures have been described to improve hole closure rates including post-operative face down positioning, longer acting tamponade, surgical creation of ILM flaps, and other biological membranes and platelets [3, 4]. The benefit of these variations is unclear and the optimum MH size threshold to deploy them is also uncertain. Furthermore, although surgical hole closure is the chief

determinant of visual acuity postoperatively, the extent of visual improvement in surgically closed cases is variable with ~55% improving by at least 0.30 logMAR units, but only 35% achieving an acuity of 0.30 logMAR or better in a recent large UK audit [5]. Although several variables affecting post-operative vision have been described, their effect size has not been clearly defined. This is particularly important for those factors which could be potentially modifiable including hole duration, tamponade choice and post-operative posturing.

To identify and quantify the factors that affect MH closure, and the visual outcome in those that close, we examined the visual and anatomical outcomes in a cohort of 1483 MHs treated by vitrectomy and gas tamponade who had prospective data collection as part of a national speciality group study. Furthermore, we sought to redefine the threshold for a large macular hole, at which typical closure rates start to decline.

Methods

The data were extracted from the BEAVRS Vitreoretinal database with a data collection period from November 2015 to August 2018 [6]. The database is compliant with the Royal College of Ophthalmologists' National MH dataset [7].

The BEAVRS database is an online web application for the collection, and analysis, of anonymised vitreoretinal surgical data including MH. Under UK guidance the data collection is regarded as audit for the purposes of service evaluation and as such ethical approval is not required, but Caldicott approval was obtained from each participating Hospital Trust to allow data compilation. Data is entered prospectively immediately following surgery and again when follow-up is complete, at least 4 weeks post surgery or after all gas had dissolved. A variety of pre-operative, peri-operative and post-operative details are included. Minimum linear diameter is defined in the online collection tool with the measurement technique illustrated, and as per previously described [8]. Successful closure, defined as closure without a neurosensory retinal defect, or not of the macular hole was recorded by the operating surgeon after post-operative assessment.

Eligible operations were primary MH operations treated with a vitrectomy and a gas or air tamponade. Excluded from the analysis were MH associated with retinal detachment, high myopia (>6 dioptres of myopia) or trauma, previously vitrectomised eyes, and those in whom silicone oil was used. Acuity data recorded in Snellen were converted to a logMAR equivalent. LogMAR visual acuity values representing 'count fingers' and 'hand movements' were replaced with 1.98 and 2.28 respectively in numeric calculations [9, 10]. Operations with less than 4 weeks follow-up were not included in any post-operative VA analysis. Operations with a pre-operative VA equivalent to ≤0.30 logMAR or those that included air or oil tamponade were not included in the visual outcome modelling.

The probability of a post-operative visual acuity equivalent to ≤0.30 logMAR (6/12 or better) and anatomical closure were modelled separately using multivariable logistic regression. All covariates under consideration were investigated at the univariate level using χ^2 tests. Any covariate with a p value < 0.10 progressed to multivariable modelling where the full model was fitted and backward selection employed. A p value of < 0.05 plus assessment of Akaike Information Criterion and the area under the receiver operating curve were used for final covariate selection.

Robust standard errors where calculated using bootstrapping with 100 replications and clustering of the individual consultant responsible for the patient care, where the operations performed by the consultant surgeon were considered as a separate cluster to the operations performed by a trainee surgeon under their supervision.

The covariates considered were the patient's age and gender, the pre-operative VA, the duration of symptoms, size of hole, vitreous attachment status, type of tamponade used during surgery, lens status, completion of internal limiting membrane peel, the presence of age-related macular degeneration (AMD), surgeon grade and the post-surgery posture positioning.

Continuous data were compared using the Student's t test with Welch adjustment for unequal variances or ANOVA. Comparisons of follow-up time were compared using non-parametric tests and categorical data by Chi-squared tests or univariate logistic regression. All analyses were conducted using STATA version 14, (StataCorp. 2009. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).
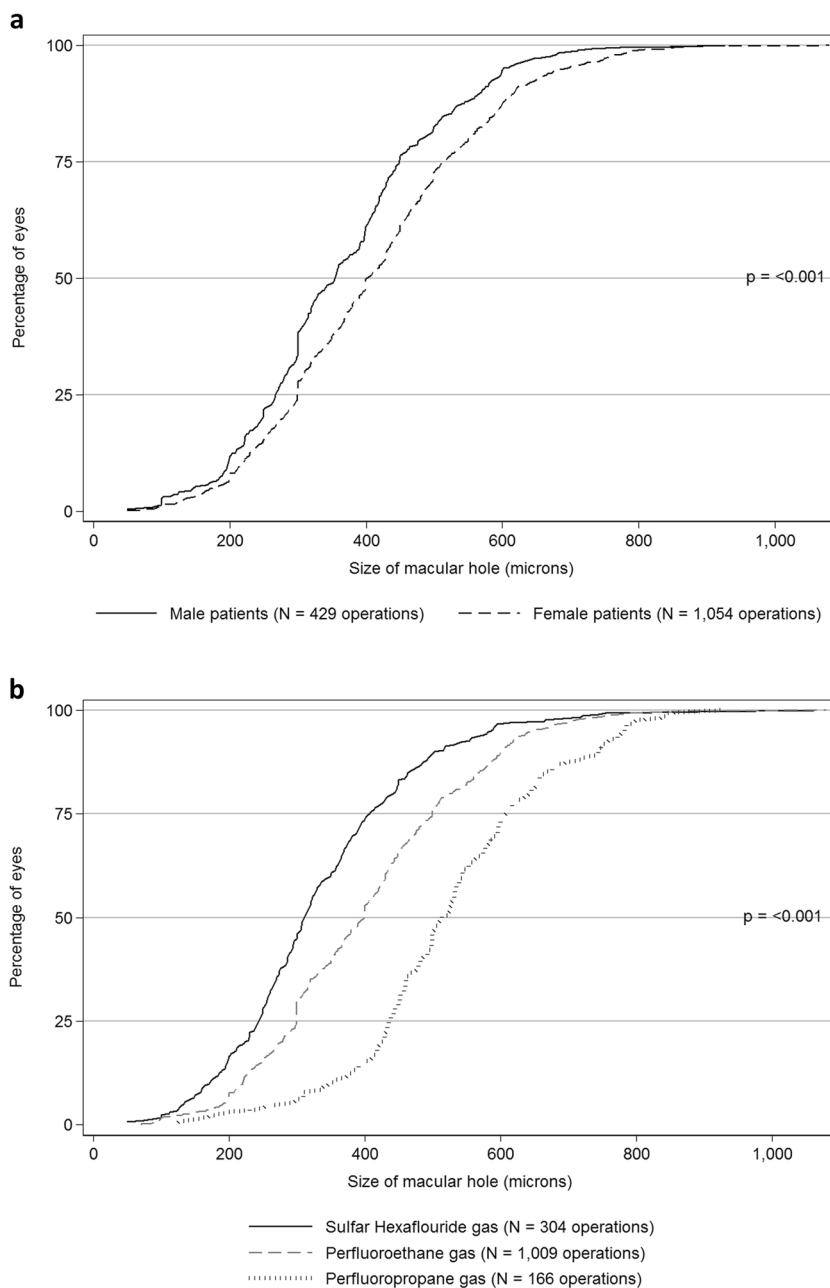
Results

From 1527 macular hole operations, 44 (2.9%) were excluded from the analysis; 24 operations were associated with previous retinal detachment, 9 in highly myopic eyes, 8 operations in vitrectomised eyes, 1 non-primary MH operation, 1 trauma operation and 1 operation that included silicone oil. There were therefore 1483 primary MH operations eligible for analysis where 735 (49.6%) operations were performed in left eyes and 748 (50.4%) in right eyes.

Thirty-five consultant surgeons performed 1245 (84.0%) operations and 238 operations were performed by trainee surgeons. The median number of operations performed by consultant surgeons was 30 (range; 1–132).

AMD was present in 58 (3.9%) eyes, amblyopia in 12 (0.8%) eyes, glaucoma in 23 (1.6%) eyes and unspecified 'other' in 44 (3.0%) eyes. The macular hole was associated with an epiretinal membrane in 220 (14.8%) eyes and 229 (15.4%) eyes had previously undergone cataract surgery.

Fig. 1 Cumulative frequency of macular hole diameter.
a Macular hole diameter and patients' gender, $N = 1{,}483$ primary macular hole operations. **b** Macular hole diameter and ocular tamponade, $N = 1{,}479$ primary macular hole operations. Four operations that used air tamponade not included.

a

Male patients (N = 429 operations) ——— Female patients (N = 1,054 operations) – – – –

b

Sulfar Hexaflouride gas (N = 304 operations) ———
Perfluoroethane gas (N = 1,009 operations) – – –
Perfluoropropane gas (N = 166 operations) ·········

The vitreous had detached from the fovea prior to surgery in 565 (38.1%) eyes, with complete posterior vitreous detachment present in 151 (10.2%) eyes (i.e. stage 4 holes), attached with traction in 374 (25.2%) eyes and not recorded for 393 (26.5%) eyes.

Demographics

A higher proportion of operations were performed in eyes from females (71.1%) who were 'on average' younger than the males undergoing surgery, (means in years; 68.9 for females vs. 71.7 for males, $p < 0.001$).

Female patients generally had slightly larger holes than male patients (means in μm; 414.8 for females vs. 366.3 for males, $p < 0.001$), Fig. 1a.

The duration of symptoms prior to the time of surgery was known for 732 (49.4%) operations and uncertain for 751 (50.6%) operations. When known the median duration was 3 months, with 6.8% having symptoms for greater than 12 months. There was no difference in the duration between

Table 1 Patient demographics.

	Males	Females	Overall	p value
N	429	1054	1483	–
Age at surgery (years)				
Median	72	69	70	<0.001
Mean	71.7	68.9	69.7	
Range	19–92	33–95	19–95	
Pre-operative logMAR equivalent VA				
Median	0.78	0.78	0.78	<0.001
Mean	0.86	0.95	0.92	
Range	0.18–HM	0.18–HM	0.18–HM	
Number with CF	23 (5.4%)	103 (9.8%)	126 (8.5%)	
Number with HM	1 (0.2%)	8 (0.8%)	9 (0.6%)	
Size of hole (μm)				
Median	355	402	394	<0.001
Mean	366.3	414.8	400.8	
Range	50–926	50–1080	50–1080	
Duration of symptoms (n, %)				
Duration known	189 (44.1)	543 (51.5)	732 (49.4)	0.009
Duration not known	240 (55.9)	511 (48.5)	751 (50.6)	
When known (months)				
Median	3	4	3	0.422
Mean	4.6	4.9	4.8	
Range	0–36	0–60	0–60	

the genders (mean duration months; 4.9 for females vs. 4.6 for males, $p = 0.4222$), Table 1.

Treatment

Vitrectomy was performed in all operations, 756 (51.0%) using a 23 gauge, 515 (34.7%) a 25 gauge, 65 (4.4%) a 27 gauge and for 147 (9.9%) operations the vitrectomy gauge was not recorded.

Internal limiting membrane peeling was completed for 1393 (93.9%) operations, incomplete for 30 (2.0%) operations and not recorded for 60 (4.1%) operations. Combined phacoemulsification was carried out in 851 (57.4%) operations, meaning 403 eyes were phakic at the completion of surgery.

The ocular tamponade used was sulfur hexafluoride gas in 304 (20.5%) operations, perfluoroethane gas in 1009 (68.0%) operations, perfluoropropane gas in 166 (11.2%) operations and air in 4 (0.3%) operations.

Hole size

Overall the size of the macular hole was approximately normally distributed around a mean of 400 μm and a standard deviation of 156 μm, although there is a suspicion of

measurement rounding around 300 μm, Supplementary Fig. 1. The macular hole size was <250 μm for 241 (16.3%) eyes, 250–400 μm for 508 (34.3%) eyes and >400 μm for 734 (49.5%) eyes.

The use of ocular tamponade was strongly associated with the size of the hole, where sulfur hexafluoride gas was generally used for smaller holes (mean 333.5 μm) than perfluoroethane gas (mean 401.5 μm) or perfluoropropane gas (mean 526.5 μm), this distribution difference was statistically significant ($p < 0.001$), Supplementary Table 1 and Fig. 1b.

Operative complications

A retinal break was recorded for 235 (15.8%) operations, with no statistical difference between the vitrectomy gauge used, the ocular tamponade used or if the hole was successfully closed postoperatively. Lens touch was recorded for 10 (0.7%) operations and unspecified 'other' operative complication for 31 (2.1%) operations.

Hole closure and hole size

Of the 1483 macular hole operations the anatomical outcome was known for 1253 (84.5%) operations, in which macular hole closure was achieved in 1199 (95.7%) operations.
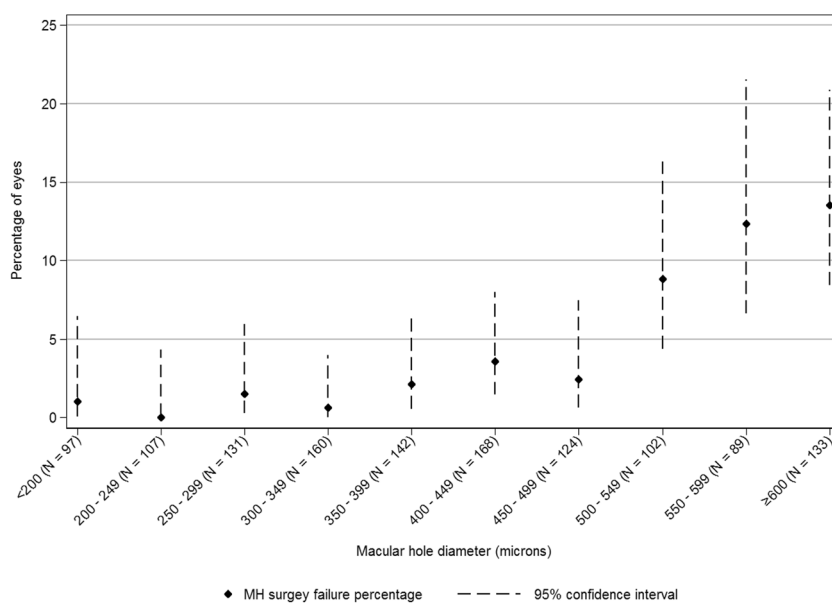
The mean MLD for the 230 cases where the outcome was unrecorded was 406 μm with 24.8% greater than 500 μm, compared with 400 μm and 24.3% greater than 500 μm for the remaining 1253 eyes.

The probability of successful macular hole closure was linked to the size of the hole, where for holes of <400 μm the failure rate was 1.1% (7/637), holes between 400 and 599 μm 3.1% (9/292), holes between 500 and 599 μm 10.5% (20/191) and for holes of ≥600 μm 13.5% (18/133), Fig. 2.

The receiver operating curve for failure and hole size had an area under the curve of 77.9% (95% CI; 75.5–80.2%) and the hole sizes that equated to the points where the sensitivity and specificity were both >70% were 464–500 μm, Supplementary Fig. 2.

Failed hole closure occurred in 17.9% (5/28) eyes with incomplete ILM peeling, 4.1% (48/1179) eyes with complete ILM peeling and in 2.2% (1/46) eyes with unknown ILM peeling status ($p < 0.001$). Macular hole closure was not influenced by the vitreous attachment status ($p = 0.215$), the type of tamponade used ($p = 0.125$), vitrectomy gauge size ($p = 0.476$) or post-surgery posturing position, with failure rates of 3.8% (37/982) and 6.3% (17/271) for prone versus not-prone positioning respectively ($p = 0.072$). For eyes with holes <500 μm the hole closure failure rates were 1.5% (11/726) and 2.5% (5/203) for prone versus not-prone

Fig. 2 Macular hole surgery failed closure rates. 95% confidence intervals shown for 50 micron increments of the hole diameter in microns, $N = 1,253$ primary macular hole operations with a known surgical outcome.

Visual acuity

The mean pre-operative acuity for all eyes was 0.92 logMAR, and the median was 0.78.

From the 1199 operations that were successfully closed, 121 (10.1%) operations are excluded from post-operative VA analysis due to less than 4 weeks follow-up. From 1078 operations the median post-operative VA was 0.42 logMAR (Snellen 6/16) (range; −0.30–HM). The post-operative VA was ≤0.30 logMAR (Snellen 6/12 or better) for 506 (46.9%) eyes and between 0.31 and 1.00 logMAR (Snellen >6/12–6/60) for 531 (49.3%) eyes.

From 621 eyes with a pre-operative VA equivalent to between 0.31 and 1.00 logMAR, 57.8% had a post-operative VA equivalent to ≤0.30 logMAR. The median follow-up was very similar for the different levels of post-operative VA, Supplementary table 3.

Any post-surgery improvement in vision was achieved for 1012 (93.9%) eyes and a gain in vision of ≥0.30 logMAR by 692 (64.2%) eyes.

Visual success

From the 1199 operations that were successfully closed, 121 (10.1%) operations are excluded from post-operative VA analysis due to less than 4 weeks follow-up. From 1078 operations 19 (1.8%) eyes were excluded from the visual

positioning respectively ($p = 0.359$), and for eyes with holes ≥500 μm the hole closure failure rates were 10.2% (26/256) and 17.6% (12/68) for prone versus not-prone positioning respectively ($p = 0.088$), Supplementary table 2.

success analysis as their pre-operative VA was ≤0.30 logMAR (Snellen 6/12). A further three eyes were excluded as the ocular tamponade used during surgery was air. Eligible for visual success analysis were 1056 primary macular hole operations, 488 (46.2%) of these eyes achieved a post-operative vision of 0.3 logMAR or better, and 568 (53.8%) eyes did not.

Visual success was more often achieved for male patients than female patients (53.0% vs. 43.5%, $p = 0.005$), in eyes with a better pre-operative VA ($p < 0.001$), for smaller holes ($p < 0.001$), for shorter duration of symptoms when the duration was known ($p < 0.001$), in eyes without AMD (47.3% vs. 19.5%, $p = < 0.001$), for operations that used sulfur hexafluoride gas or perfluoroethane gas instead of perflouropropane gas (53.6% vs. 46.6% vs. 33.1%, $p = 0.001$) and for operations with completed internal limiting membrane peeling instead of incomplete peeling or not recorded peeling status (46.9% vs. 23.8% vs. 41.0%, $p = 0.089$). No statistically significant differences in the visual success rates were observed for the grade of operating surgeon, lens status, vitreous attachment status or post-surgery posturing position, Table 2.

At the multivariate level, the factors influencing visual success were the pre-operative VA, hole size, duration of symptoms and the presence of AMD, Table 3. The model area under the receiver operator curve was 71.72%, Supplementary Fig. 3.

Discussion

Using prospective data from a cohort of over 1400 eyes this study has clarified and quantified factors that predict

Table 2 Univariate hypothesis testing of potential risk factors affecting visual success.

	No Visual success	Visual success	Overall	*p* value
N (row %)	568 (53.8)	488 (46.2)	1056	–
Grade of operating surgeon				
Consultant	467 (53.2)	410 (46.8)	877	0.437
Trainee	101 (56.4)	78 (43.6)	179	
Gender				
Male	143 (47.0)	161 (53.0)	304	0.005
Female	425 (56.5)	327 (43.5)	752	
Age at surgery (years)				
<80	521 (53.0)	462 (47.0)	983	0.060
≥80	47 (64.4)	26 (35.6)	73	
Pre-operative LogMAR (Snellen) VA				
>0.30–1.00 (>6/6–6/60)	261 (42.2)	357 (57.8)	618	<0.001
>1.00–<CF (>6/60 to <CF)	223 (66.2)	114 (33.8)	337	
CF—NPL	84 (83.2)	17 (16.8)	101	
Size of hole (µm)				
<300	97 (36.7)	167 (63.3)	264	<0.001
300–399	126 (47.7)	138 (52.3)	264	
400–499	146 (55.1)	119 (44.9)	265	
500–599	105 (67.7)	50 (32.3)	155	
≥600	94 (87.0)	14 (13.0)	108	
Duration of symptoms				
<4 months	134 (44.2)	169 (55.8)	303	<0.001
4 or 5 months	57 (59.4)	39 (40.6)	96	
≥6 months	105 (66.5)	53 (33.5)	158	
Unknown	272 (54.5)	227 (45.5)	499	
Vitreoretinal attachment				
Attached with traction	157 (56.9)	119 (43.1)	276	0.350
Detached from fovea	215 (50.6)	210 (49.4)	425	
Complete PVD	60 (53.6)	52 (46.4)	112	
Not recorded	136 (56.0)	107 (44.0)	243	
Lens status at time of surgery				
No cataract surgery	132 (53.4)	115 (46.6)	247	0.690
Pseudophakic	83 (50.9)	80 (49.1)	163	
Combined MH and cataract surgery	353 (54.6)	293 (45.4)	646	
Presence of AMD				
No	535 (52.7)	480 (47.3)	1015	<0.001
Yes	33 (80.5)	8 (19.5)	41	
Ocular tamponade used				
Perfluoroethane gas	391 (53.4)	341 (46.6)	732	0.001
Perfluoropropane gas	87 (66.9)	43 (33.1)	130	
Sulfur hexafluoride gas	90 (46.4)	104 (53.6)	194	
Internal limiting membrane peeling				
Complete	529 (53.1)	467 (46.9)	996	0.089
Incomplete	16 (76.2)	5 (23.8)	21	
Not recorded	23 (59.0)	16 (41.0)	39	
Post-surgery posturing				
Prone	453 (54.0)	386 (46.0)	839	0.793
Not prone	115 (53.0)	102 (47.0)	217	

macular hole closure and visual outcome. Our anatomical and visual results are consistent with previous large studies confirming high hole closure rates and visual success rates [5, 11–14]. Essex et al. recently presented their findings from Australia on over 2000 MHs [12]. Their study differs from ours in terms of hole size with generally smaller holes with a median hole size of 280 µm and 23% of holes being greater than 400 µm compared with a median of 394 µm and 57% greater than 400 µm in this study. To go along with this their pre-operative visual acuity was also better at a mean of 48.7 letters (~0.73 logMAR). Our study is unique in terms of previous database studies in having purely prospective data collection in a public sector healthcare setting and having size data on all holes.

The strongest predictor of hole closure was hole size. We found that hole closure remains fairly constant at around 97–98% until a size of around 500 µm in minimum linear diameter, and then reduces to around 90% for holes between 500 and 599 µm and 87% for holes greater than 600 µm (see Fig. 2). The presence of VMT was unrelated to hole closure rates or indeed hole size as others have found [15]. The completeness of ILM peeling was a significant factor predicting closure as has been clearly established [16]. Some degree of post-operative prone posturing was recommended in ~80% of patients but was unrelated to hole closure, although it is possible that this sample is too small to detect any true effect of post-surgery positioning. If an effect of positioning in large holes size truly does exist, it must be small. The rationale for using a size of 400 µm to define large for MH is unclear and appears to have been based on Gass's original work pre-dating surgery and relating to slit lamp biomicroscopy findings rather than OCT [17]. The 400-µm size point was continued in the classification suggested by the International vitreomacular traction study group in 2013 [18]. There is no doubt that MHs over 400 µm have a lower surgical success rate than those under 400, but the break point where this reduction occurs is unclear [19]. Our data suggests it is non-linear and Ch'ng et al. have recently suggested a size cut-off of 630 µm based on a study of 258 eyes over 400 µm in size undergoing surgery with C2F6 or C3F8 gas [20]. Examination of their ROC curve for anatomical closure using macular hole size as a predictor shows a fairly low profile covering a number of possible values and our larger series would suggest a lower cut-off point of 500 µm. Gupta et al. and Salter et al. similarly found a cut-off of around 500 µm albeit in far smaller studies [21, 22]. We would suggest that this cut-off point of 500 µm could be used as a new pragmatic size definition of large for the surgical treatment of MHs, where the surgical success rate starts to reduce. Several interventions have been suggested to improve closure rates in larger holes including ILM flaps, retinal massage, retinal expansion, amniotic membrane, blood or platelets and retinal free flaps [4, 23–28]. The exact size point at which these various options are chosen would depend however on any extra morbidity introduced by the technique.

Table 3 Visual success model output, model AUC = 71.72%.

	Odds ratio	Coefficient	p value	95% CI for the odds ratio	Median follow-up (months)
Constant	3.112	1.134	<0.001	2.076–4.678	N/A
Pre-operative logMAR (Snellen) VA					
>0.30–1.00 (>6/6–6/60)	REF	REF	N/A	N/A	2.7
>1.00 to <CF (>6/60 to <CF)	0.513	−0.667	<0.001	0.354–0.743	2.8
CF—NPL	0.224	−1.497	0.001	0.092– 0.543	2.0
Size of hole (μm)					
<300	REF	REF	N/A	N/A	2.5
300–399	0.647	−0.436	0.039	0.428–0.978	2.8
400–499	0.571	−0.560	0.036	0.339–0.963	2.8
500–599	0.375	−0.980	<0.001	0.223–0.631	2.8
≥600	0.139	−1.976	<0.001	0.058–0.333	2.9
Duration of symptoms					
<4 months	REF	REF	N/A	N/A	2.9
4 or 5 months	0.546	−0.604	0.117	0.257–1.164	3.1
≥6 months	0.493	−0.707	0.018	0.275–0.885	2.8
Not known	0.669	−0.403	0.073	0.431–1.038	2.6
Presence of AMD					
No	REF	REF	N/A	N/A	2.7
Yes	0.206	−1.579	<0.001	0.104–0.409	2.9

The cohort consisted of a consecutive series of eyes with data entered prospectively by a group of 35 surgeons from across the UK, using an approved and validated online data collection methodology. As expected, females formed ~70% of the cohort and interestingly, they had a significantly greater hole size than the males. This has not been found before as far as we are aware, although Forsaa et al. found a similar but non-significant trend in a series of 152 primary MH [29]. Macular hole size has been shown to be related to foveal floor size which is associated with foveal avascular zone (FAZ) size [30–33]. Interestingly female gender is associated with larger FAZ size as well as a thinner foveal floor thickness which might explain our findings [34, 35].

Most of the surgery was carried out using 23 or 25 gauge transconjunctival vitrectomy with retinal break formation rate in line with previous studies and with no difference between the gauges. It should be noted that all surgeries were carried out using cannulated sclerostomy systems which have been shown to reduce entry site breaks [36, 37]. Perfluoroethane (C2F6) was used in almost 70% of the cases, with a strong tendency for SF6 to be used in smaller holes and C3F8 to be used in those with the largest holes. Despite this surgeon rationale we found no evidence that gas type was related to hole closure nor visual success on multivariate analysis.

The factors that were most closely associated with visual success were pre-operative VA and hole size, as others have reported, however we also found two other factors which have been less clear in the literature to date [12, 21]. The duration of the macular hole prior to surgery was an important predictor, halving the chances of visual success in those with durations longer than 4 months, and similar to the effect size of hole dimensions and pre-operative VA. Other studies have reported similar findings, although it has not been extensively investigated and importantly, unlike hole size and pre-operative VA, it is potentially modifiable [12, 14, 38–40]. The duration we measured was cumulative hole duration at the time of surgery. The patient may have gone through several steps to reach this stage, including diagnosis by their primary care physician or optician, referral to a general ophthalmologist and then onward referral to retinal specialist before finally undergoing surgery. Minimising time to surgery will improve outcome. Finally, the presence of AMD significantly affected the post-operative vision as might be expected, but not age alone, as other have found [12, 14]. This is important as older patients with MHs can achieve good visual results if AMD is not present. Closure was also unaffected by age.

Cataract is the most common complication of macular hole surgery, and many surgeons advocate combined clear

lens extraction and vitrectomy [41, 42]. The rate of combined phacovitrectomy in this series was high at 57% compared with only 13% in the study by Essex et al. [12]. We did not find any evidence of any difference in anatomical or visual outcomes in the eyes that had combined surgery compared with eyes that were left phakic. This may be because the follow-up was relatively short, and phakic patients had not developed visually significant cataract. Although combined surgery is more convenient for patients, and reduces costs for the health care provider, we found no evidence that it affects outcomes.

Limitations for this study include no patient identifier to use patients as a cluster variable in the modelling; however, we believe that <10% of the sample would have had bilateral MH surgery. The BEAVRS audit database does not include a surgeon identifier for the trainee surgeon, although not many centres will have more than one trainee surgeon, and vitreoretinal surgery trainees are supervised by the consultant who is responsible for the patient care. The duration of symptoms was not known for ~50% of operations, although this is a reflection of clinical practice as the patient will not always be able to state how long they have had symptoms. There is a suspicion of measurement rounding of the hole size at around 300 μm, although this value corresponds to the lowest risk of failed hole closure failure and poor post-surgery vision. The multivariate modelling should be viewed as provisional given the relatively small sample, possible measurement rounding and high rate of missing duration of symptom data. Overall 15% of eyes did not have anatomical outcome data recorded and were excluded, but with MLD being the main predictor for anatomical success and their similarity in size to the 85% with outcome data included, we think it is unlikely that this would confound our results. We did not include details of the extent of ILM peeling nor the experience of the consultant surgeons who took part both of which may have had effects on outcome. Finally, the sample is relatively small for the number of comparisons that have been conducted which does increase the chance of type I errors.

In conclusion in a large prospective database study we have defined the factors that predict hole closure and visual outcome in macular hole surgery. We have found that hole closure remains fairly constant at around 97–98% until a size of around 500 μm in minimum linear diameter, and then reduces with increasing hole size, suggesting this could be used as a new definition of large in future studies and clinical practice. In terms of visual success in those holes that closed, we found that better pre-operative VA, smaller hole size, shorter duration of symptoms and the absence of AMD were significant predictors in multivariate analysis.

Summary

What was known before

- Macular holes are a common indication for vitrectomy but the factors affecting hole closure and visual outcome are ill defined.
- Hole size is known to be important in predicting visual outcome and closure but the effect size uncertain. Similarly, the effect of hole duration has been unclear.
- The size of the hole has previously been defined as large if greater than 400 μm in minimum linear diameter, but this has not been based on surgical outcomes.

What this study adds

- Macular hole closure was high at over 97% until a size of around 500 μm where it reduced to less than 90%, which could be adopted as a new size threshold for a large macular hole.
- The factors predicting visual success were better pre-operative VA, smaller hole size, shorter duration of symptoms and the absence of AMD.
- Minimising time from symptom onset to surgery maximises visual success especially in holes of less than 4 months duration.

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Compliance with ethical standards

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References

1. Meuer SM, Myers CE, Klein BE, Swift MK, Huang Y, Gangaputra S, et al. The epidemiology of vitreoretinal interface abnormalities as detected by spectral-domain optical coherence tomography: the beaver dam eye study. Ophthalmology. 2015;122:787–95.
2. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes. Results of a pilot study. Arch Ophthalmol. 1991;109: 654–9.
3. Madi HA, Masri I, Steel DH. Optimal management of idiopathic macular holes. Clin Ophthalmol. 2016;10:97–116.
4. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. Ophthalmology. 2010;117:2018–25.
5. Jackson TL, Donachie PHJ, Sparrow JM, Johnston RL. United Kingdom National Ophthalmology Database study of vitreoretinal surgery: report 2, macular hole. Ophthalmology. 2013;120: 629–34.
6. BEAVRS datasets system. http://outcomes.beavrs.org/. Accessed 8 Jun 2019.
7. Royal College of Ophthalmologists macular hole surgery dataset https://www.rcophth.ac.uk/wp-content/uploads/2015/02/2015_PROF_311_Macular-hole-surgery-dataset.pdf. Accessed 8 Jun 2019.
8. Steel DH, Downey L, Greiner K, Heimann H, Jackson TL, Koshy Z, et al. The design and validation of an optical coherence tomography-based classification system for focal vitreomacular traction. Eye. 2016;30:314–24.
9. Lange C, Felten N, Junker B, Schulze-Bonsel K, Bach M. Resolving the clinical acuity categories "hand motion" and "counting fingers" using the Freiburg Visual Acuity Test (FrACT). Graefes Arch Clin Exp Ophthalmol. 2009;247:137–42.
10. Schulze-Bonsel K, Felten N, Burau H, Hansen L, Bach M. Visual acuities "hand motion" and "counting fingers" can be quantified with the Feiburg visual acuity test. Invest Ophthalmol Vis Sci. 2006;47:1236–40.
11. Vaziri K, Schwartz SG, Kishor KS, Fortun JA, Moshfeghi AA, Smiddy WE, et al. Rates of reoperation and retinal detachment after macular hole surgery. Ophthalmology. 2016;123:26–31.
12. Essex RW, Hunyor AP, Moreno-Betancur M, Yek JTO, Kingston ZS, Campbell WG. Australian and New Zealand Society of Retinal Specialists Macular Hole Study Group,et al. The visual outcomes of macular hole surgery: a registry-based study by the Australian and New Zealand Society of Retinal Specialists. Ophthalmol Retin. 2018;2:1143–51.
13. Essex RW, Kingston ZS, Moreno-Betancur M, Shadbolt B, Hunyor AP, Campbell WG. Australian and New Zealand Society of Retinal Specialists Macular Hole Study Group,et al. The effect of postoperative face-down positioning and of long- versus short-acting gas in macular hole surgery: results of a registry-based study. Ophthalmology . 2016;123:1129–36.
14. Tognetto D, Grandin R, Sanguinetti G, Minutola D, Di Nicola M, Di Mascio R, et al. Internal limiting membrane removal during macular hole surgery: results of a multicenter retrospective study. Ophthalmology. 2006;113:1401–10.
15. Philippakis E, Amouyal F, Couturier A, Boulanger-Scemama E, Gaudric A, Tadayoni R. Size and vitreomacular attachment of primary full-thickness macular holes. Br J Ophthalmol. 2017;101:951–4.
16. Spiteri Cornish K, Lois N, Scott N, Burr J, Cook J, Boachie C, et al. Vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with no peeling for idiopathic full-thickness macular hole (FTMH). Cochrane Database Syst Rev. 2013: CD009306.
17. Johnson RN, Gass JD. Idiopathic macular holes. Observations, stages of formation, and implications for surgical intervention. Ophthalmology. 1988;95:917–24.
18. Duker JS, Kaiser PK, Binder S, de Smet MD, Gaudric A, Reichel E, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology 2013;120:2611–9.
19. Williamson TH, Lee E. Idiopathic macular hole: analysis of visual outcomes and the use of indocyanine green or brilliant blue for internal limiting membrane peel. Graefes Arch Clin Exp Ophthalmol. 2014;252:395–400.
20. Ch'ng SW, Patton N, Ahmed M, Ivanova T, Baumann C, Charles S, et al. The manchester large macular hole study: is it time to reclassify large macular holes? Am J Ophthalmol. 2018;195: 36–42.
21. Gupta B, Laidlaw DA, Williamson TH, Shah SP, Wong R, Wren S. Predicting visual success in macular hole surgery. Br J Ophthalmol. 2009;93:1488–91.
22. Salter AB, Folgar FA, Weissbrot J, Wald KJ. Macular hole surgery prognostic success rates based on macular hole size. Ophthalmic Surg Lasers Imaging. 2012;43:184–9.
23. Ohana O, Barak A, Schwartz S. Internal aspiration under perfluorocarbon liquid for the management of large macular holes. Retina. 2017;37:2145–50.
24. Paques M, Chastang C, Mathis A, Sahel J, Massin P, Dosquet C. Platelets in Macular Hole Surgery Group,et al. Effect of autologous platelet concentrate in surgery for idiopathic macular hole: results of a multicenter, double-masked, randomized trial. Ophthalmology. 1999;106:932–8.
25. Grewal DS, Mahmoud TH. Autologous neurosensory retinal free flap for closure of refractory myopic macular holes. JAMA Ophthalmol. 2016;134:229–30.
26. Rizzo S, Caporossi T, Tartaro R, Finocchio L, Franco F, Barca F, et al. A human amniotic membrane plug to promote retinal breaks repair and recurrent macular hole closure. Retina. 2018. https://doi.org/10.1097/IAE.0000000000002320.
27. Wong R, Howard C, Orobona GD. Retina expansion technique for macular hole apposition report 2: efficacy, closure rate, and risks of a macular detachment technique to close large full-thickness macular holes. Retina. 2018;38:660–3.

28. Charles S, Randolph JC, Neekhra A, Salisbury CD, Littlejohn N, Calzada JI. Arcuate retinotomy for the repair of large macular holes. Ophthalmic Surg Lasers Imaging Retin. 2013;44:69–72.

29. Forsaa VA, Lindtjørn B, Kvaløy JT, Frøystein T, Krohn J. Epidemiology and morphology of full-thickness macular holes. Acta Ophthalmol. 2018;96:397–404.

30. Shin JY, Chu YK, Hong YT, Kwon OW, Byeon SH. Determination of macular hole size in relation to individual variabilities of fovea morphology. Eye. 2015;29:1051–9.

31. Ghassemi F, Mirshahi R, Bazvand F, Fadakar K, Faghihi H, Sabour S. The quantitative measurements of foveal avascular zone using optical coherence tomography angiography in normal volunteers. J Curr Ophthalmol. 2017;29:293–9.

32. Chui TY, Van Nasdale DA, Elsner AE, Burns SA. The association between the foveal avascular zone and retinal thickness. Investig Ophthalmol Vis Sci. 2014;55:6870–6787.

33. Wu LZ, Huang ZS, Wu DZ, Chan E. Characteristics of the capillary-free zone in the normal human macula. Jpn J Ophthalmol. 1985;29:406–11.

34. Shahlaee A, Pefkianaki M, Hsu J, Ho AC. Measurement of foveal avascular zone dimensions and its reliability in healthy eyes using optical coherence tomography angiography. Am J Ophthalmol. 2016;16:50–5.

35. Tick S, Rossant F, Ghorbel I, Gaudric A, Sahel JA, Chaumet-Riffaud P, et al. Foveal shape and structure in a normal population. Investig Ophthalmol Vis Sci. 2011;52:5105–10.

36. Issa SA, Connor A, Habib M, Steel DH. Comparison of retinal breaks observed during 23 gauge transconjunctival vitrectomy versus conventional 20 gauge surgery for proliferative diabetic retinopathy. Clin Ophthalmol. 2011;5:109–14.

37. Jalil A, Ho WO, Charles S, Dhawahir-Scala F, Patton N. Iatrogenic retinal breaks in 20-G versus 23-G pars plana vitrectomy. Graefes Arch Clin Exp Ophthalmol. 2013;251:1463–7.

38. Kanovský R, Jurecka T, Gelnarová E. Analysis of prognostic factors of anatomical and functional results of idiopathic macular hole surgery. Cesk Slov Oftalmol. 2009;65:91–6.

39. Chang E, Garg P, Capone A Jr. Outcomes and predictive factors in bilateral macular holes. Ophthalmology 2013;120:1814–9.

40. Jaycock PD, Bunce C, Xing W, Thomas D, Poon W, Gazzard G, et al. Outcomes of macular hole surgery: implications for surgical management and clinical governance. Eye. 2005;19:879–84.

41. Simcock PR, Scalia S. Phacovitrectomy without prone posture for full thickness macular holes. Br J Ophthalmol. 2001;85:1316–9.

42. Steel DH. Phacovitrectomy: expanding indications. J Cataract Refract Surg. 2007;33:933–6.