

CLINICAL SCIENCE

Indocyanine green assisted retinal internal limiting membrane removal in stage 3 or 4 macular hole surgery

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Aims: To determine surgical outcome in primary idiopathic stage 3 or 4 macular holes with indocyanine green (ICG) assisted retinal internal limiting membrane (ILM) peeling.

Methods: A prospective, consecutive, interventional case series with 41 eyes of 40 patients was included. No patient defaulted follow up. Besides a standard macular hole surgery, all eyes received ICG assisted ILM removal of 3–4 disc diameters around macular holes. At the end of the surgery, 12% perfluoropropane gas was used. A face down posture for 2 weeks was required postoperatively.

Results: The mean follow up period was 15.1 months (range 6–24 months). Twenty (48.8%) eyes had stage 3 macular holes and 21 (51.2%) had stage 4 macular holes. The overall median duration of holes was 11 months. 19 (46.3%) were chronic macular holes of more than 12 months' duration. The anatomical success rates after one surgery was 87.8% (36 eyes), while that of chronic and non-chronic ones was 78.9% and 95.5%, respectively. The median preoperative and postoperative visual acuity was 20/200 (range 20/60 to counting fingers) and 20/100 (range 20/20 to 20/400), respectively. 24 (58.5%) eyes had improvement of two or more Snellen lines. The mean was 3.2 lines (range two to nine lines), with 3.6 lines and 2.7 lines for non-chronic and chronic holes, respectively. For all the 41 eyes, 16 (39%) eyes had a final visual acuity of 20/50 or better.

Conclusion: ICG assisted retinal ILM removal, in idiopathic primary chronic and non-chronic stage 3 or 4 macular hole surgery, appears to give a promising anatomical closure rate without compromising the visual result.

Since Kelly and Wendel first demonstrated the successful closure of macular hole with pars plana vitrectomy and fluid-gas exchange a decade ago, this surgery has been widely practised as the treatment of stage 2, 3, and 4 macular holes.^{1–3} Various adjuncts have also been studied in order to promote a glial scar formation that improved the closure rate of macular hole surgery. These adjuncts included intraoperative applications of transforming growth factor- β 2, autologous serum, autologous platelet concentrates, and laser photocoagulation to the retinal pigment epithelium in the bed of the macular hole.^{4–11}

The internal limiting membrane (ILM) forms the innermost layer of the retina and the outer boundary of the vitreous. It contains collagen fibrils, proteoglycans, basement membrane and the plasma membrane of Müller cells, and possibly other glial cells of the retina.¹² Histologically, ILM around macular holes also contains myofibrocytes, and contraction of these myofibrocytes has been suggested to cause enlargement of the macular hole and prevent its closure.¹³ Therefore, the removal of the ILM may be a surgical adjunct that can promote gliosis and the closure of macular hole.^{14–17} However, the visualisation of the thin and transparent ILM intraoperatively is often difficult and may preclude its complete removal without damaging other parts of the retina. Excessive unsuccessful attempts to remove the ILM during macular hole surgery may decrease the visual success.¹⁷ Indocyanine green (ICG) dye has been used to stain the ILM and facilitate its removal.^{18–20} In our previous study, we demonstrated that removal of ICG stained ILM around idiopathic macular hole was confirmed with histology and might contribute to macular hole closure.²⁰

None the less, the role of ILM peeling in macular hole surgery is not well defined yet. Without any adjunct, Ryan and Gilbert reported 94% anatomical success rate in 36 eyes with stage 2 macular holes.²¹ Similarly, a randomised controlled clinical trial of stage 2 macular hole reported a closure rate of

80% in 15 eyes.²² The anatomical closure rate of stage 3 or 4 macular holes reported in various randomised clinical trials without any adjunct varies from 53% to 81%.^{3 7 8 23} The mean anatomical closure rate of these four series was 66%. It appears that the anatomical closure rate of stage 3 or 4 macular holes is less favourable than that of stage 2 macular holes.

The purpose of this prospective study is to determine the anatomical and visual outcome in primary surgery for idiopathic stage 3 or 4 macular holes with ICG assisted retinal ILM peeling, with a minimal follow up period of 6 months.

METHODS

All consecutive patients aged 18 years or older with stage 3 or 4 primary idiopathic macular holes were recruited from the vitreoretinal services of several ophthalmic centres in Hong Kong. Patients with myopia greater than 6 dioptres, traumatic, and secondary macular holes were excluded. As described by Gass, stage 3 holes were full thickness macular holes with diameters equal to or greater than 400 μ m. Stage 4 holes were similar to those of stage 3 but the posterior hyaloid of the former was separated from the optic disc.²⁴ The stages of macular holes were confirmed intraoperatively. The size of a macular hole was assessed comparing it to a peripapillary retinal vein of 125 μ m in diameter.³

All the surgeries were performed by three of the authors (AK, DW, and WC). The surgical technique involved standard subtotal pars plana vitrectomy with removal of the posterior hyaloid. Any visible epiretinal membrane (ERM) was removed with intraocular forceps. Preparation of the ICG solution has been described previously.²⁰ A volume of 0.2 ml of the prepared ICG solution (concentration 0.25 mg/ml, 0.5 mg/ml, or 1.25 mg/ml) was gently injected over the disc and then the macula with the infusion temporarily stopped. Caution was paid to avoid direct injection over the macular hole. After 30 seconds, infusion was resumed and ICG in the vitreous cavity was

Table 1 Conversion table for Snellen best corrected visual acuity to line score

Snellen best corrected visual acuity	Line score
20/20	16
20/25	15
20/30	14
20/40	13
20/50	12
20/60	11
20/80	10
20/100	9
20/120	8
20/160	7
20/200	6
20/300	5
20/400	4
CF	3
HM	2
LP	1

CF = counting fingers, HM = hand movement, LP = light perception.

removed. The ILM would then be stained light green visually. On some occasion, repeated injection of ICG solution was required to complete subsequent ILM removal. Depending on the preference of the individual surgeon, a myringo-vitreoretinal (MVR) blade, a diamond dusted scraper, or an intraocular forceps was used to initiate a flap of ILM at the temporal raphe 1.5–2.0 disc diameters from the macular hole. An intraocular forceps then held the flap and ILM of 3–4 disc diameter was removed in a circular fashion around the macular hole. The ILM in close proximity to the macular hole was removed in a centripetal direction towards the macular hole. At the end of surgery, 12% perfluoropropane gas was used. Patients were required to maintain a face down posture for 2 weeks postoperatively.

Preoperative data including age and sex of the patient, duration of the macular hole, stage of the macular hole, size of the macular hole, lens status of the patient, and the preoperative best corrected Snellen visual acuity (BCVA) was recorded. Fundus photographs of each eye were taken. Fluorescein angiography was performed when indicated. Intraoperative data including any concurrent surgical procedures, degree of ILM staining by ICG, presence or absence of ERM, and any intraoperative complications was noted. Postoperative data including anatomical status of the macular hole and BCVA at 6 months postoperatively as well as at the last follow up was recorded. Fundus photographs of each eye were taken 6 months postoperatively. Fluorescein angiography was also performed in all patients to determine the possible toxicity as a result of the use of ICG.

Anatomical status of a macular hole was categorised in three defined end points (elevated/open, flat/open, flat/closed) as suggested by Tornambe *et al.*²⁵ A hole was considered closed as long as it was flat (flat/open, flat/closed). All postoperative complications due to the surgery were also recorded. The Snellen BCVA was converted to a line score for analysing the number of lines gained or lost after surgery (Table 1). The data were entered into SPSS for Windows (SPSS Inc, Chicago, IL, USA) for statistical analysis. A p value ≤ 0.05 was considered statistically significant.

RESULTS

Preoperative demographics

Forty one eyes of 40 consecutive eligible patients with follow up of at least 6 months were recruited and all were included in the final analysis. No patient was lost to follow up. Short term result of nine cases has been briefly reported.²⁰ There were 25 (62.5%) females and 15 (37.5%) males. The mean age of the patients was 63.5 years (range 35–81 years). There were two

patients aged 40 years or less and detailed history and examination were obtained to exclude other causes of macular hole like trauma and high myopia. The mean follow up duration was 15.1 months (range 6–24 months). Except one pseudophakic eye, all the other 40 eyes were phakic before surgery. Twenty (48.8%) eyes had stage 3 macular holes and 21 (51.2%) had stage 4 macular holes. Chronic macular hole was defined as that of more than 12 months' duration. There were 19 (46.3%) chronic macular holes. The median duration of the macular hole was 11 months (range 2–120 months). The median size of the macular hole was 500 μ m (range 250–800 μ m). The median preoperative visual acuity was 20/200 (range 20/60 to counting fingers).

Intraoperative data

Macular hole surgery was performed in 20 right eyes and 21 left eyes. The number of eyes with 0.25 mg/ml, 0.5 mg/ml and 1.25 mg/ml concentration of ICG used was 11 (26.8%), 13 (31.7%), and 17 (41.5%), respectively. In all the 41 eyes, there was good staining of the ILM by ICG and surgeons were able to visualise the ILM clearly for complete removal. Combined macular hole surgery together with phacoemulsification and implantation of intraocular lens was performed in 20 (48.8%) eyes, before the procedure of ICG assisted ILM removal. The ICG occasionally also stained the anterior vitreous behind the posterior capsule, which could be safely removed by a vitreous cutter with the cutting port faced away from the posterior capsule.

Anatomical and visual results

Thirty six (87.8%) of the 41 eyes had successful anatomical closure of the macular hole after one surgery. These include 20 (90.9%) flat/closed holes and one (4.5%) flat/open hole in the non-chronic group, and 13 (68.4%) flat/closed holes and two (10.5%) flat/open holes in the chronic group. Four of the five elevated/open holes were chronic macular holes. Three of these open holes were reoperated, in which two underwent repeat pars plana vitrectomy with injection of silicone oil and one with repeat pars plana vitrectomy and gas/fluid exchange. The two reoperated holes with silicone oil subsequently closed. At the last follow up, 38 (92.7%) of the 41 eyes achieved anatomical closure of the macular hole. These included 35 (85.4%) closed macular holes and three (7.3%) flat macular holes. The anatomical success rates after one surgery for chronic and non-chronic macular holes was 78.9% and 95.5%, respectively. This difference was not statistically significant (Fisher's exact test, $p = 0.16$).

At the last follow up, 24 (58.5%) of the 41 eyes had improvement of two or more lines of visual acuity after surgery. Fifteen (36.6%) eyes had a final visual acuity within one line of the preoperative visual acuity. Two eyes (4.9%) lost two lines after surgery: one eye had an open macular hole with development of cataract and the other eye had postoperative rhegmatogenous retinal detachment 3 months after operation with macular involvement due to a sclerotomy related break. Despite the retinal detachment, the macular hole remained closed (flat/closed) and the retina was reattached after another operation of pars plana vitrectomy, cryopexy, and gas/fluid exchange. The final visual acuity of this patient was 20/400.

For all the 41 eyes, the median postoperative visual acuity at the last follow up was 20/100 (range 20/20 to 20/400). The mean improvement in visual acuity was 3.2 lines (range two to nine lines). Improvement in visual acuity was more marked in stage 3 than in stage 4 macular holes with mean improvement of 4.0 and 2.5 lines, respectively. However, this difference did not reach the level of statistical significance (two tailed t test, $p = 0.16$).

The mean line of improvement for eyes with non-chronic macular holes was better than those chronic ones, with 3.6

lines compared with 2.7 lines. However this difference was not statistically significant (two tailed *t* test, $p = 0.41$). Fourteen (63.6%) of the 22 non-chronic macular holes had improvement of two or more lines, whereas six (36.6%) of the 19 chronic macular holes had improvement of two or more lines. This difference was not statistically significant (χ^2 test, $p = 0.48$). For all the 41 eyes, 16 (39%) eyes had a final visual acuity of 20/50 or better. The rate was 45.5% (10 in 22 eyes) and 31.6% (six in 19 eyes) in non-chronic and chronic macular holes, respectively. There is no statistical difference in the number of eyes achieving a final visual acuity of 20/50 or better between the non-chronic and chronic groups (χ^2 test, $p=0.36$).

For the 20 phakic postoperative eyes, 17 (85%) of them subsequently developed nuclear sclerotic cataract with 12 of them received cataract surgery. The mean improvement in visual acuity for the 20 eyes with combined cataract surgery and the 12 eyes with subsequent cataract surgery 3.0 and 4.7 lines, respectively. There was no statistical difference in the line of improvement between the two groups (two tailed *t* test, $p = 0.20$). Six (50%) of the 12 eyes with subsequent cataract surgery had a final visual acuity of 20/50 or better whereas eight (40%) of the 20 eyes with combined macular hole and cataract surgery had a final visual acuity of 20/50. There was no association between combined or subsequent cataract surgery in achieving a final visual acuity of 20/50 or better (χ^2 test, $p = 0.58$). No clinical or angiographic cystoid macular oedema, as well as reopening of macular holes was found after cataract surgery, no matter it was a combined or consecutive one.

The mean improvement in visual acuity for the 0.25 mg/ml, 0.5 mg/ml, and 1.25 mg/ml concentration of ICG used were 2.6, 3.1, and 3.8 lines respectively. There is no statistical difference in the line of improvement between the three groups (one way ANOVA, $p=0.65$). The number of cases with final visual acuity of 20/50 or better for the 0.25 mg/ml, 0.5 mg/ml, and 1.25 mg/ml concentration of ICG used were three (27.2%), five (38.5%), and eight (47.1%) respectively. There is no statistical difference in the number of eyes achieving a final visual acuity of 20/50 or better between the three groups (χ^2 test, $p=0.58$).

The mean loss of visual acuity for open macular hole was 0.7 lines compared to mean improvement of 3.5 lines for holes with anatomical success. There was statistical significance in the difference between the lines of improvement for the two groups (two tailed *t* test, $p = 0.004$).

Besides the development of cataract, there was one case with rhegmatogenous retinal detachment that was detailed previously, and another case with vitreous haemorrhage that resolved spontaneously 5 weeks after the operation. The final visual acuity of this patient was 20/100 with a closed hole. There was no direct intraoperative or postoperative complication related to ICG assisted ILM peeling. No ICG related toxicity was detected on fluorescein angiograms. There was also no clinical toxicity like new retinal edema or RPE change during the follow up period.

DISCUSSION

In this study of 41 eyes with idiopathic stage 3 or 4 macular holes of median duration of 11 months, we achieved a primary anatomical closure rate of 89.7% with the use of ICG assisted retinal ILM removal. The primary anatomical success rates for chronic and non-chronic macular holes was 78.9% and 95.5%, respectively. Our anatomical success rate is similar to other reports in which ILM peeling, with or without ICG staining, was performed as an adjunct in macular hole surgery, although there were differences of methodology among ours and other series.^{14–19}

Without the use of ICG, Park *et al* reported an anatomical success rate of 91% in their retrospective study of 58 eyes, which included stage 2 holes.¹⁴ Mester and Kuhn reported

anatomical success rate of 96% among 46 eyes, which included stage 2 and traumatic macular holes.¹⁵ Brooks retrospectively reported anatomical success of 100% among 64 eyes with stage 3 or 4 macular holes.¹⁶ Smiddy *et al* reported an overall success rate of 93% in their series of 193 eyes, in which stage 2 holes and reoperative cases were included.¹⁷ In these four studies, staining of ILM was not performed before its peeling.

Kadonosono *et al* stained the ILM with ICG using a specially designed cannula with viscomaterial as the carrying medium.¹⁸ In their series of 13 eyes with stage 3 or stage 4 macular holes, 92% attained anatomical closure. Da Mata *et al* reported a primary closure rate of 88% in 24 patients with stage 3 or 4 macular holes with ICG assisted ILM peeling, although the follow up period was rather short (range 23–195 days), serum was also used and traumatic holes were included.¹⁹ By analysing the prospective studies of ours and Kadonosono *et al*, the mean primary anatomical success rate of ICG assisted ILM removal in idiopathic stage 3 or 4 macular holes of the two series was 90.9%.¹⁸ The result is encouraging, as the mean primary anatomical closure rate of stage 3 or 4 macular holes reported in four randomised clinical trials without any adjunct was 66% (range 53–81%).^{3,7,8,23} By including only the three more recent studies published in 1997–9, the mean primary anatomical closure rate was still 70.3% (range 61–81%).^{3,7,8} Although some surgeons reported very high anatomical success rate in their own series without any adjunct, a recent series reported a primary closure rate of 56% in stage 3 or 4 macular hole surgery.²⁶

The mean line of improvement in visual acuity in our current study series was 3.2 lines, with 58.5% of eyes having an improvement of two or more lines after surgery. Our results are similar to the studies involving ILM peeling by Park *et al*¹⁴ and Smiddy *et al*.¹⁷ They demonstrated an improvement of two or more lines after surgery in 62% and 72%, respectively. Similar data were not available from the series of Brooks,¹⁶ while the chronicity of holes in the series of Mester and Kuhn as well as Kadonosono *et al* was not reported.^{15,18} The visual results in our study may seem less favourable when compared with the series by Da Mata *et al*, in which they reported a 96% visual improvement with a mean improvement of five lines.¹⁹ In their series, visual improvement was defined as gain of one or more lines, rather than the commonly used definition of gain of at least two lines. They also used a conversion scale of 20 lines instead of 16 lines as in our study. Additionally, chronic macular holes were present in 46.3% of cases in our study compared to only 25% in theirs.

In terms of final visual acuity of 20/50 or better, this was attained by 39% (16 eyes) of our 41 eyes. This result is comparable to the rate of 42% (24 out of 57) reported by one of the four randomised clinical trials without any adjunct.⁷ In those series with ICG assisted ILM peeling, Kadonosono *et al* and Da Mata *et al* reported a rate of 53.8% and 37.5%, respectively.^{18,19} For those series with ILM peeling without ICG staining, Park *et al* and Smiddy *et al* reported a rate of 53% and 56%, respectively.^{14,17} The slight difference in the rate between ours and other series may be due to the different duration and stages of macular hole included as well as a high rate of chronic macular hole (46.3%) in our series.

Potential retinal and retinal pigment epithelial damages related to ICG assisted ILM peeling have been reported.^{27–29} Gandorfer *et al* suggested that in their experience, visual outcome of eyes received ICG assisted ILM peeling was less favourable than those received conventional macular hole surgery.²⁷ Additionally, asymptomatic paracentral scotomata detected by microperimetry and potential ICG toxicity causing retinal pigment epithelium atrophy have been reported after macular hole surgery.^{28,29} However in our series, RPE atrophy related to ICG toxicity was not found.

Chronic macular holes have been suggested to be more difficult to close with a less favourable postoperative visual outcome than those of shorter duration.^{30,31} In our study, the anatomical success rates for chronic macular holes and non-chronic ones was 78.9% and 95.5%, respectively. This difference is not statistically significant (Fisher's exact test, $p = 0.16$). The anatomical closure rate in our series seems encouraging compared to those reported rate of 62.7%, 81.8%, and 70.8% in chronic macular hole surgery with or without other adjuncts.³¹⁻³³ In our series, 52.6% (10 out of 19) of eyes with chronic macular holes attained two or more lines of improvement, with 31.6% (six in 19 eyes) had final visual acuity of 20/50 or better. These visual results are very similar to those reported.³¹⁻³³ The role of ILM peeling in chronic macular hole surgery needs further evaluation.

Studies of ILM peeling in macular hole surgery have reported a few complications similar to those of macular hole surgery without adjunct.¹⁴⁻²⁰ Common ones include cataract, retinal tear, retinal detachment, visual field loss, and phototoxicity. Although minimal superficial retinal haemorrhages are commonly encountered as ILM is peeled, they are usually self limiting and do not cause any significant problem. However, Brooks reported that three (2.5%) eyes developed postoperative hyphaema that required repeat vitrectomy or anterior chamber washout.¹⁶ In our study, there was one (3.4%) case of postoperative vitreous haemorrhage that resolved by itself. The underlying cause might be bleeding from these superficial retinal vessels. Good intraoperative haemostasis and adequate fill of gas at the end of surgery to avoid hypotony may reduce this complication.

There were limitations of our study. There was variation of the concentration of ICG used, although all of them were on the low side and the volume used was small compared to the vitreous volume. Additionally, not all patients uniformly received combined vitreous and cataract surgery and some patients were planned for post-vitrectomy cataract surgery. Standardised EDTRS visual acuity measurement was also not used.

In summary, ICG assisted retinal ILM removal, in idiopathic primary chronic and non-chronic stage 3 or 4 macular hole surgery, appears to give a promising anatomical closure rate without compromising the visual result.

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REFERENCES

- Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes: results of a pilot study. *Arch Ophthalmol* 1991;**109**:654-9.
- Wendel RT, Patel AC, Kelly NE, et al. Vitreous surgery for macular holes. *Ophthalmology* 1993;**100**:1671-6.
- Freeman WR, Azen SP, Kim JW, et al. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes. Results of a multicenter randomized clinical trial. The Vitrectomy for Treatment of Macular Hole Study Group. *Arch Ophthalmol* 1997;**115**:11-21.
- Glaser BM, Michels RG, Kuppermann BD, et al. Transforming growth factor- β 2 for the treatment of full-thickness macular holes: a prospective randomized study. *Ophthalmology* 1992;**99**:1162-72.
- Lansing MB, Glaser BM, Liss H, et al. The effect of pars plana vitrectomy and transforming growth factor-beta 2 without epiretinal membrane peeling on full-thickness macular holes. *Ophthalmology* 1993;**100**:868-71.
- Liggett PE, Skolik DSA, Horio B, et al. Human autologous serum for the treatment of full-thickness macular holes: a preliminary study. *Ophthalmology* 1995;**102**:1071-6.
- Thompson JT, Smiddy WE, Williams GA, et al. Comparison of recombinant transforming growth factor-beta-2 and placebo as an adjunctive agent for macular hole surgery. *Ophthalmology* 1998;**105**:700-6.
- Paques M, Chastang C, Mathis A, et al. Effect of autologous platelet concentrate in surgery for idiopathic macular hole: results of a multicenter, double-masked, randomized trial. Platelets in Macular Hole Surgery Group. *Ophthalmology* 1999;**106**:932-8.
- Ohana E, Blumenkranz MS. Treatment of reopened macular hole after vitrectomy by laser and outpatient fluid-gas exchange. *Ophthalmology* 1998;**105**:1398-403.
- Ikuno Y, Kamei M, Saito Y, et al. Photocoagulation and fluid-gas exchange to treat persistent macular holes after prior vitrectomy. *Ophthalmology* 1998;**105**:1411-8.
- Min W-K, Lee J-H, Ham D-I. Macular hole surgery in conjunction with endolaser photocoagulation. *Am J Ophthalmol* 1999;**127**:306-11.
- Bron AJ, Tripathi RC, Tripathi BJ. *Wolff's anatomy of the eye and orbit*. 8th ed. Spain: Chapman and Hall Medical, 1997:487-8.
- Yoo HS, Brooks HL Jr, Capone A Jr, et al. Ultrastructural features of tissue removed during idiopathic macular hole surgery. *Am J Ophthalmol* 1996;**122**:67-75.
- Park DW, Sipperley JO, Sneed SR, et al. Macular hole surgery with internal-limiting membrane peeling and intravitreal air. *Ophthalmology* 1999;**106**:1392-8.
- Mester V, Kuhn F. Internal limiting membrane removal in the management of full-thickness macular holes. *Am J Ophthalmol* 2000;**129**:769-77.
- Brooks HL Jr. Macular hole surgery with and without internal limiting membrane peeling. *Ophthalmology* 2000;**107**:1939-49.
- Smiddy WE, Feuer W, Cordahi G. Internal limiting membrane peeling in macular hole surgery. *Ophthalmology* 2001;**108**:1471-8.
- Kadonosono K, Itoh N, Uchio E, et al. Staining of internal limiting membrane in macular hole surgery. *Arch Ophthalmol* 2000;**118**:1116-8.
- Da Mata AP, Burk SE, Riemann CD, et al. Indocyanine green-assisted peeling of the retinal internal limiting membrane during vitrectomy surgery for macular hole repair. *Ophthalmology* 2001;**108**:1187-92.
- Kwok AK, Li WW, Pang CP, et al. Indocyanine green staining and removal of internal limiting membrane in macular hole surgery: histology and outcome. *Am J Ophthalmol* 2001;**132**:178-83.
- Ryan EH, Gilbert HD. Results of surgical treatment of recent-onset full-thickness idiopathic macular holes. *Arch Ophthalmol* 1994;**112**:1545-53.
- Kim JW, Freeman WR, Azen SP, et al. Prospective randomized trial of vitrectomy or observation for stage 2 macular holes. Vitrectomy for Macular Hole Study Group. *Am J Ophthalmol* 1996;**121**:605-14.
- Smiddy WE, Glaser BM, Thompson JT, et al. Transforming growth factor-beta 2 significantly enhances the ability to flatten the rim of subretinal fluid surrounding macular holes. Preliminary anatomic results of a multicenter prospective randomized study. *Retina* 1993;**13**:296-301.
- Gass JD. Reappraisal of biomicroscopic classification of stages of development of a macular hole. *Am J Ophthalmol* 1995;**119**:752-9.
- Tornambe PE, Poliner LS, Cohen RG. Definition of macular hole surgery end points: elevated/open, flat/open, flat/closed. *Retina* 1998;**18**:286-7.
- Ip MS, Baker BJ, Duker JS, et al. Anatomical outcomes of surgery for idiopathic macular hole as determined by optical coherence tomography. *Arch Ophthalmol* 2002;**120**:29-35.
- Gandorfer A, Haritoglou C, Gass CA, et al. Indocyanine green-assisted peeling of the internal limiting membrane may cause retinal damage. *Am J Ophthalmol* 2001;**132**:43-3.
- Haritoglou C, Gass CA, Schaumberger M, et al. Macular changes after peeling of the internal limiting membrane in macular hole surgery. *Am J Ophthalmol* 2001;**132**:363-8.
- Engelbrecht NE, Freeman J, Sternberg P, et al. Retinal pigment epithelial changes after macular hole surgery with indocyanine green-assisted internal limiting membrane peeling. *Am J Ophthalmol* 2002;**133**:89-94.
- Margherio AR. Macular hole surgery in 2000. *Curr Opin Ophthalmol* 2000;**11**:186-90.
- Thompson JT, Sjaarda RN, Lansing MB. The results of vitreous surgery for chronic macular holes. *Retina* 1997;**17**:493-501.
- Roth DB, Smiddy WE, Feuer W. Vitreous surgery for chronic macular holes. *Ophthalmology* 1997;**104**:2047-52.
- Scott RA, Ezra E, West JF, et al. Visual and anatomical results of surgery for long standing macular holes. *Br J Ophthalmol* 2000;**84**:150-3.