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(Short title: Visual acuity after cyclodiode)

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ABSTRACT

Purpose: To investigate the effect of diode laser cyclophotocoagulation for glaucoma on central visual function in patients with good visual acuity (VA).

Patients and Methods: Patients with pre-operative VA 20/60 or better who had undergone cyclodiode treatment according to a standard protocol were evaluated retrospectively. The primary outcome variable was a recorded loss of ≥2 Snellen lines of best corrected visual acuity (BCVA) during follow-up. Successful intraocular pressure (IOP) control was defined as being between 6 and 21 mmHg inclusive without oral acetazolamide or other glaucoma surgery.

Results: 49 eyes of 43 patients with a median pre-treatment acuity of 20/30 were included (range 20/16-20/60). After a mean duration of follow-up of 5.0 years, median VA was 20/60 with a ≥2 line loss recorded in 15 eyes (30.6%) (mean survival time 7.7 years). 67.3% (33/49) retained VA 20/60 or better, but VA deteriorated by 1 Snellen line or more in 31 (63.2%) and in 16.3% (8/49) final VA was <20/200.

In cases experiencing a 2 line loss in acuity, the main causes were glaucoma progression (9 cases) and macula oedema (4 cases). Visual loss was unrelated to total treatment dose (mean 99.7J), initial acuity or initial IOP level. IOP was controlled at final follow-up in 39/49 (79.6%) with no cases of hypotony.

Conclusions: The majority of these eyes with difficult to manage glaucoma retained their good visual acuity over long-term follow-up after undergoing diode laser cyclophotocoagulation. The proportion losing 2 Snellen lines is in line with that reported following trabeculectomy or tube surgery. These results suggest a possible role for the use of transscleral cyclodiode in selected eyes with significant visual potential. Further controlled prospective studies are required to better define this role.

Keywords: Diode laser, Cyclophotocoagulation, Cyclodiode, Glaucoma

INTRODUCTION

Transscleral cyclophotocoagulation is a well-established treatment for glaucoma that has not responded to other interventions and it is widely used in advanced cases with minimal visual potential[1]. There is concern, however, regarding the adverse effects of this type of destructive surgery on visual function. This concern has prevented its wider acceptance as a treatment in eyes with good residual visual acuity[2]. However, the majority of published data relate to the treatment of eyes with initially poor vision and few series include significant numbers of cases with good visual acuity (VA). In this study we describe the visual outcome in patients undergoing transscleral cyclodiode with pre-treatment acuity of 20/60 or better.

METHODS

The study involved a retrospective case note review of all patients who underwent cycloablation with the Oculight Sx semiconductor diode 810nm laser and the contact G-probe (Iris Medical Instruments, California, USA) at Queen's Medical Centre, Nottingham, UK between April 1994 and December 2006. The authors identified patients by a review of operating theatre records in which all cases undergoing surgery are recorded. We accessed the case notes and included all patients with pre-operative best corrected Snellen visual acuity (BCVA) of 20/60 or better on at least 2 consecutive occasions at the time of treatment.

Indications for cycloablation included medically uncontrollable glaucoma in subjects who declined, had not responded to, or were unlikely, in the

judgement of the surgeon responsible at the time, to respond to filtration surgery.

We performed cyclophotocoagulation under peribulbar, retrobulbar or general anaesthesia using a standard treatment protocol which we have previously described[3]. Briefly, this involves the application of 14 burns of 2 Watts power and 2 seconds duration, spaced half the width of the G-probe apart around 270° of the ciliary body, unless ocular co-morbidity (eg scleral thinning) dictates otherwise. Laser energy is focussed at a point corresponding to the pars plicata, 1-2 mm behind the limbus with the heel of the probe aligned at the limbus. In the contexts of congenital glaucoma, high myopia and distortion of limbal anatomy secondary to previous surgery, we identified the position of the ciliary body prior to treatment by transillumination and adjusted the probe position accordingly if necessary.

Post-operatively, we prescribed topical steroids four times daily for 2–4 weeks. We discontinued glaucoma medications during follow-up using clinical discretion based on the intraocular pressure (IOP) reduction achieved. The decision to repeat the treatment was dependent on the magnitude of the hypotensive response and the drug load necessary to achieve a satisfactory IOP.

Study parameters included demographic details, BCVA, IOP, visual field loss, anti-glaucoma medications, diagnosis, details of prior ocular surgery and duration of follow up. We documented BCVA and IOP at the pre-operative assessment, postoperatively on day 1, at 1 week, 1 month, 3 months and each subsequent clinic visit (every 3-6 months). We defined final follow-up as the last recorded clinic visit in the time period of the study.

As the primary endpoint for the study we used a reduction in BCVA by two or more lines on two successive visits. We defined successful pressure control as a final IOP ≥6 mmHg and ≤21 mmHg irrespective of the need for topical anti-glaucoma medication but without the need for oral acetazolamide or further glaucoma surgery.

Visual field testing was performed by Humphrey threshold standard automated perimetry, Goldmann or Friedmann perimetry. For the purposes of this group of patients we classified visual field loss as advanced in the presence any of the following: a) Humphrey 24-2 mean deviation ≥ 15dB; b) deviation of ≥15dB affecting any part of the central 10 degrees on Humphrey 24-2; c) encroachment of the I4e isopter in the central 10 degrees of a Goldmann field; or d) any loss of the central 4 target points on Friedmann field.

We performed data analysis using SPSS V10 (SPSS Inc, Chicago, Il). We used the chi squared test for determining the statistical significance of differences between discrete variables (or Fisher's exact test when a cell value less than 5 was expected), Student's t test for parametric continuous data and Mann-Whitney for non-parametric continuous. We performed Kaplan-Meier survival analysis to investigate the loss of visual acuity following treatment.

RESULTS

Out of 351 patients recorded as undergoing cyclodiode treatment, we identified 51 eyes of 45 patients with initial visual acuity of 20/60 or better. Two patients were lost to follow-up within the first 12 months (one died and one after discharge back to the referring centre). For the remaining 49 eyes of 43 patients, the distribution of glaucoma types and other baseline characteristics are shown in table 1. Median pre treatment BCVA was 20/30 (figure 1).

Reliable visual fields prior to cyclodiode were available for 36/49 eyes (73.5%). Of these, 25 were automated Humphrey threshold fields, 8 were Goldmann and 3 were Friedmann fields. Mean deviation (SD) for the Humphrey fields was 13.8 (9.7) dB (range 1.6 to 30.4). Advanced loss was present in 19/36 (52.7%) of fields.

We performed a total of 85 treatment episodes on these 49 eyes using a power setting of 2 Watts for a duration of 2 seconds for all shots. We applied a mean of 14.4 shots with a mean energy of 57.6 Joules per treatment episode

We performed a mean of 1.73 treatment episodes per eye (range 1-6; median 1.0) with more than one episode given in 18/49 eyes (36.7%). During the course of treatment we applied a total mean energy of 99.7 Joules per eye (range 40-336; median 60J). .After the first treatment we followed subjects for a mean of 263 weeks (range 62-578), or 5.1 years.

IOP and glaucoma medication use at final follow-up is shown in table 2. IOP was controlled at final follow-up without oral acetazolamide in 39/49 (79.6%).

None of the 49 eyes developed sustained hypotony (IOP<6 mmHg) during follow-up although one eye developed transient hypotony after both treatment episodes which resolved by the end of the first post-operative month.

Median VA at final follow-up was 20/60 (figure 1). It improved in 8/49 eyes (16.3%), remained unchanged in 11/49 (22.5%) and deteriorated by 1 line or more in 30/49 (61.2%). Final visual acuity, after a mean of 5.0 years follow-up, was reduced to less than 20/200 in 8/49 eyes (16.3%).

A loss of 2 Snellen lines or more of acuity was measured in15/49 eyes (30.6%) in 15 different patients. The mean (SD) survival time using this primary endpoint was 399.7 (70.3) weeks (95%CI: 330.8-468.6) or 7.7 years (figure 2). During the first 12 months 18.3% (9/49) of eyes lost 2 or more lines of acuity.

There was no difference in the mean number of treatment episodes between those losing visual acuity (1.60) and those maintaining visual acuity (1.79) (p=0.69). Loss of visual acuity was also independent of the total energy applied (p=0.66), age (p=0.11), sex (p=0.14), pre-operative IOP (p=0.63), pre-operative VA (p=0.17) or advanced pre-operative visual field loss (p=0.22). Those that lost visual acuity had a similar final IOP (15.0 mmHg) to the remainder (16.1 mmHg) (p=0.55).

In 8 cases loss of visual acuity was solely attributed to glaucoma progression and it was a contributory factor in one further case (table 2). Of these 9 cases loss of acuity occurred in spite of IOP consistently below 21 mmHg during follow-up in 4 cases, with a mean final IOP of 14 mmHg. All had advanced disc cupping and/or visual field loss affecting the central 10 degrees. In the

other 5 eyes IOP was not consistently controlled following cyclodiode treatment. In one case rapid loss of visual acuity from 20/60 to 20/600 occurred 6 days after treatment. This was attributed to optic nerve “snuff out” caused by an IOP of 50mmHg.

Visual loss was attributed partly or entirely to macula oedema in 4 cases. One had a history of proliferative diabetic retinopathy, one was aphakic and one had a history of previous vitreous loss during cataract surgery. These 3 eyes underwent a single standard treatment session of 56 Joules and the reduction in visual acuity was delayed between 6 and 12 months post treatment. In the fourth case the macula oedema developed a week after the second treatment episode.

One case was due to a rhegmatogenous retinal detachment (RD) which developed 10 weeks after cyclodiode in an eye with uveitic glaucoma. This patient had already had a spontaneous RD in the fellow eye.

One case with no identified risk factors developed a vitreous haemorrhage 5 days after cyclodiode in an eye with primary open-angle glaucoma (POAG). By the time that this had cleared spontaneously a dense cataract had formed reducing acuity to counting fingers. The patient declined cataract surgery.

DISCUSSION

Cycloablation is a recognised therapeutic approach in the management of complex and refractory glaucoma and appears to be an effective method of achieving a sustained reduction in IOP[1]. Advantages over the main

alternatives - filtration or drainage device surgery - include technical ease of the procedure, quicker recovery and none of the risks specific to intraocular surgery. However, cyclodestructive procedures have been linked to subsequent loss of visual acuity in a substantial proportion of those treated[4,5]. As a result, this approach has generally been reserved for patients who have previously undergone multiple glaucoma operations, are poor surgical candidates or who already have limited visual potential[2,6].

Resistance to the wider application of laser cyclotherapy is based for the most part on series of cases with visual acuity significantly compromised by the glaucoma itself or, in the case of secondary glaucomas, its underlying cause such as retinal vascular disease or uveitis. Published data on the long-term prognosis for vision following cyclodiode treatment applied to patients with significant baseline visual acuity are few (table 3)[7-11].

In this cohort of patients, the largest we have identified to date with visual acuity initially 20/60 or better, acuity was found to have declined from a median of 20/30 to 20/60. A two or more line reduction in Snellen acuity was seen in 30.6% of eyes and was reduced to less than 20/200 in 16.3%. The most frequent cause of visual loss was further progression of glaucoma which was an attributable cause in half the cases. In a number of these, this occurred despite a significant and sustained response to treatment. The only other cause linked to more than one case of visual loss was cystoid macula oedema which was a contributory factor in 3. Notably in 2 of these cases, neither of whom had an intact posterior capsule, cystoid did not develop until 6 months or more following treatment. In a further case it could be argued

that cyclodiode therapy might have led to worsening of diabetic macula oedema.

In no case did persistent hypotony develop, a finding which is consistent with our previous reported experience using the relatively conservative, standardised treatment protocol employed in these patients. Macular pucker, which has previously been reported as a cause of visual loss following laser cyclotherapy[8], was not seen clinically, although neither OCT nor fluorescein angiography were used.

Clearly it is difficult to attribute the deterioration in vision in the patients in this cohort in part or wholly to the cyclodiode treatment. Some loss may have been coincidental reflecting the natural course of the underlying disease and some might have occurred whatever surgical intervention had been applied. Nevertheless loss of 2 lines of visual acuity in 30% over a mean 5 year follow-up period is concerning. However, other treatment options also carry a significant risk to vision. In the recent tube versus trabeculectomy (TVT) study, patients with medically uncontrolled glaucoma who had previously undergone cataract and/or filtration surgery were randomised to insertion of a glaucoma drainage device or augmented trabeculectomy[12]. Mean baseline visual acuity was equivalent to that in our cohort before cyclodiode. A 2 or more Snellen line reduction in acuity was observed in 32% in the tube arm and 33% in the trabeculectomy group after 12 months. Even after excluding cataract as a cause the figures were 27% and 24% respectively. The equivalent one year figure for our cohort was 18% despite inclusion of a large number of patients with chronic uveitis, aphakia and other secondary glaucomas which were excluded from the TVT study. Similarly, in the

Advanced Glaucoma Intervention Study, 40% of medically uncontrolled patents treated with either trabeculectomy or laser trabeculoplasty had a 3-line reduction in visual acuity during 5 years follow-up[13]. Loss of visual acuity is, therefore, by no means the preserve of any single surgical modality.

The earlier use of laser cyclotherapy in eyes with good residual visual acuity appears to be gaining support[10,11]. Ansari et al presented a retrospective subgroup of 23 eyes with POAG and mean pre treatment visual acuity in the range 20/20 to 20/120) who underwent a single application of transscleral cyclodiode between 60 and 160 Joules (mean 120J)[11]. Mean visual acuity did not deteriorate although the final visual acuity was worse in 3 cases (13%), 2 of which were due to cataract progression.

In another retrospective study of 21 eyes with pre-laser visual acuity 20/80 or better which had previously mostly undergone filtration surgery, cycloablation was applied either by diode or Nd:YAG laser[10]. Although 17 of the 21 patients required additional laser and/or surgical treatment to further lower IOP, visual acuity remained within one line of the pre-treatment level in 81%.

A prospective study in Ghana even examined the effect of cyclodiode as a primary surgical treatment in one eye of patients with POAG[9]. Although a reduction in visual acuity was observed in 18 (23%) after a mean follow-up of 13.2 months, there was no significant difference in acuity between the fellow eyes treated medically and the diode treated eye. In the 19 eyes with pre-treatment visual acuity 20/60 or better, only 1 had a decrease in visual acuity.

Our study's main limitations are its retrospective nature and the absence of a control group to distinguish the adverse effects of the treatment from the

natural history of the underlying disease. While undertaking cyclodiode treatment in eyes with uncontrolled glaucoma but with good visual acuity comes with a significant risk of visual loss, that risk does not appear to be any greater than for other, more conventional surgical interventions. This needs testing in a randomised study.

In the absence of such comparative data, this study indicates that cyclodiode treatment can be used effectively in eyes with good visual acuity and may be a useful alternative surgical treatment in patients with difficult to manage glaucoma.

Table 1. Baseline characteristics

	Category	**Cases (n=43)**
Age (years), mean ± SD	--	64.7 ± 17.0
Gender, n (%)	Male	19 (44.2)
	Female	24 (55.8)
Race, n (%)	White	40 (93.0)
	Other	3 (7.0)
		Eyes (n=49)
Pre-operative VA, median (range)	--	20/30 (20/16-20/60)
IOP (mmHg), mean ± SD (range)	--	28.0 ±7.2 (16-50)
Glaucoma drops, mean (range)		2.3 (0-5)
Oral acetazolamide, n (%)		35 (71.4)
Phakic status, n (%)	Phakic	9 (18.4)
	Pseudophakic	28 (57.1)
	Aphakic	12 (24.5)
Prior ocular surgery, n (%)	Filtration	25 (51.0)
	Congenital cataract	10 (20.4)
	Vitreo-retinal	5 (10.2)
	PK	2 (4.1)
Glaucoma type, n (%)	POAG	16[a](32.7)
	Uveitic	12[b](24.5)
	Aphakic	10[c](20.4)
	PACG	5[d](10.2)
	Other	6[e](12.2)

Abbreviations: POAG (primary open-angle glaucoma), PACG (primary angle-closure glaucoma), SD (standard deviation), VA (visual acuity), PK (penetrating keratoplasty). [a]Includes 1 eye with juvenile onset open-angle glaucoma. [b]Includes 6 eyes with Fuch's heterochromic cyclitis; 1 also aphakic. [c]5 aphakic after congenital cataract surgery. [d]Includes 1 eye with aqueous misdirection. [e]2 secondary to anterior chamber lens implant; 2 with pseudoexfoliation, 1 each following retinal detachment surgery, PK, trauma, rubeosis iridis.

Table 2. IOP and glaucoma medication use at final follow-up after cyclodiode

	Outcome
IOP (mmHg), mean ± SD (range)	15.3 ±5.8 (6-37)
IOP ≤ 21 mmHg, n (%)	44 (89.8)
IOP ≤ 16 mmHg, n (%)	36 (73.5)
No. Drops, mean (range)	1.9 (0-4)
Acetazolamide, n (%)	8 (16.3)

Table 3. Details of cases losing 2 or more lines of visual acuity following cyclodiode treatment.

	VA drop	Glaucoma type	Total dose: shots/Joules	Details of loss of visual acuity
1	20/60-20/100	POAG	15/60	Glaucoma progression despite IOP control
2	20/16-20/40	POAG	14/56	Glaucoma progression despite IOP control
3	20/60-20/200	RD surgery	14/56	Glaucoma progression despite IOP control
4	20/60-HM	POAG	20/80	Glaucoma progression despite IOP control
5	20/60-LP	PXF	56/224	Glaucoma progression – poor IOP control
6	20/30-NLP	POAG	56/224	Glaucoma progression – poor IOP control
7	20/60-NLP	Rubeotic	70/280	Glaucoma progression – poor IOP control
8	20/60-HM	PK	26/104	ON infarct after 6 days – poor IOP control
9	20/60-20/400	AM	31/124	CMO 1 month after 2nd dose + glaucoma progression with poor IOP control
10	20/30-20/60	Aphakic	14/56	CMO after 6 months
11	20/30-CF	AC IOL	14/56	CMO after 12 months. Later corneal oedema.
12	20/30-20/80	POAG	14/56	Diabetic maculopathy after 12 months
13	20/60-CF	POAG	15/60	Cataract – declined surgery
14	20/20-CF	Uveitic	28/112	RD 10 weeks after 2nd dose
15	20/30-20/80	POAG	14/56	Dry AMD

VA (visual acuity); CF (counting fingers); HM (hand movement perception); LP (light perception); NLP (no light perception); POAG (primary open-angle glaucoma); PXF (pseudoexfoliative glaucoma); RD (retinal detachment); IOP (intraocular pressure); AM (aqueous misdirection); CMO (cystoid macula oedema); AMD (age-related macula degeneration).

Table 4. Reported frequency of a two-line reduction in visual acuity

Author	**No. eyes**	**Visual Acuity**	**Mean follow-up (months)**	**% worse**
Rotchford (this data)	49	≥20/60	60.0	30.6%
Egbert[9]	19	≥20/60	13.2	5%*
Wilensky[10]	21	≥20/80	40.7	28.6%
Ansari[11]	23	≥20/120	12.1	13.0%*
Bloom[8]	68**	≥20/200	21.7	10.3%*
Schuman[7]	36	≥20/200	>12	47.2%

* Degree of decrease in visual acuity not defined

** 25 eyes had visual acuity at least 20/60

Figure 1. Snellen visual acuity distribution pre cyclodiode and at final follow-up. Abbreviations: CF (counting fingers), HM (hand movements), LP (light perception), NLP (no light perception).

Figure 2. Kaplan-Meier plot showing survival time to loss of 2 or more lines of Snellen visual acuity.

References

1. Vernon SA, Koppens JM, Menon GJ, Negi AK. Diode laser cycloablation in adult glaucoma: long-term results of a standard protocol and review of current literature. *Clin Experiment Ophthalmol* 2006;34:411-20.
2. Pastor SA, Singh K, Lee DA et al. Cyclophotocoagulation: a report by the American Academy of Ophthalmology. *Ophthalmology* 2001;108:2130-8.
3. Spencer AF, Vernon SA. "Cyclodiode": results of a standard protocol. *Br J Ophthalmol*. 1999;83;311-6.
4. Youn J, Cox TA, Allingham RR, Shields MB. Factors associated with visual acuity loss after noncontact transscleral Nd:YAG cyclophotocoagulation. *J Glaucoma*. 1996;5:390-4.
5. Kosoko O, Gaasterland DE, Pollack IP, Enger CL. Long-term outcome of initial ciliary ablation with contact diode laser transscleral cyclophotocoagulation for severe glaucoma. The Diode Laser Ciliary Ablation Study Group. *Ophthalmology.* 1996;103:1294-302.
6. American Academy of Ophthalmology. Primary open-angle glaucoma, Preferred Practice Pattern. San Francisco: *American Academy of Ophthalmology*. 2005. www.aao.org/ppp (accessed Jan 2006)
7. Schuman JS, Bellows AR, Shingleton BJ et al. Contact transscleral Nd:YAG laser cyclophotocoagulation. Midterm results. *Ophthalmology*. 1992;99:1089-94.

8. Bloom PA, Tsai JC, Sharma K et al. "Cyclodiode". Trans-scleral diode laser cyclophotocoagulation in the treatment of advanced refractory glaucoma. *Ophthalmology*. 1997; 104:1508-19.

9. Egbert PR, Fiadoyor S, Budenz DL, Dadzie P, Byrd S. Diode laser transscleral cyclophotocoagulation as a primary surgical treatment for primary open-angle glaucoma. *Arch Ophthalmol*. 2001;119:345-50.

10. Wilensky JT, Kammer J. Long-term visual outcome of transscleral laser cyclotherapy in eyes with ambulatory vision. Ophthalmology. 2004;111:1389-92.

11. Ansari E, Gandhewar J. Long-term efficacy and visual acuity following transscleral diode laser photocoagulation in cases of refractory and non-refractory glaucoma. *Eye*. 2007;21:936-40.

12. Gedde SJ, Schiffman JC, Feuer WJ et al. Treatment outcomes in the tube versus trabeculectomy study after one year of follow-up. *Am J Ophthalmol*. 2007;143:9-22.

13. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes within race. Seven-year results. *Ophthalmol*. 1998;105:1146-64.

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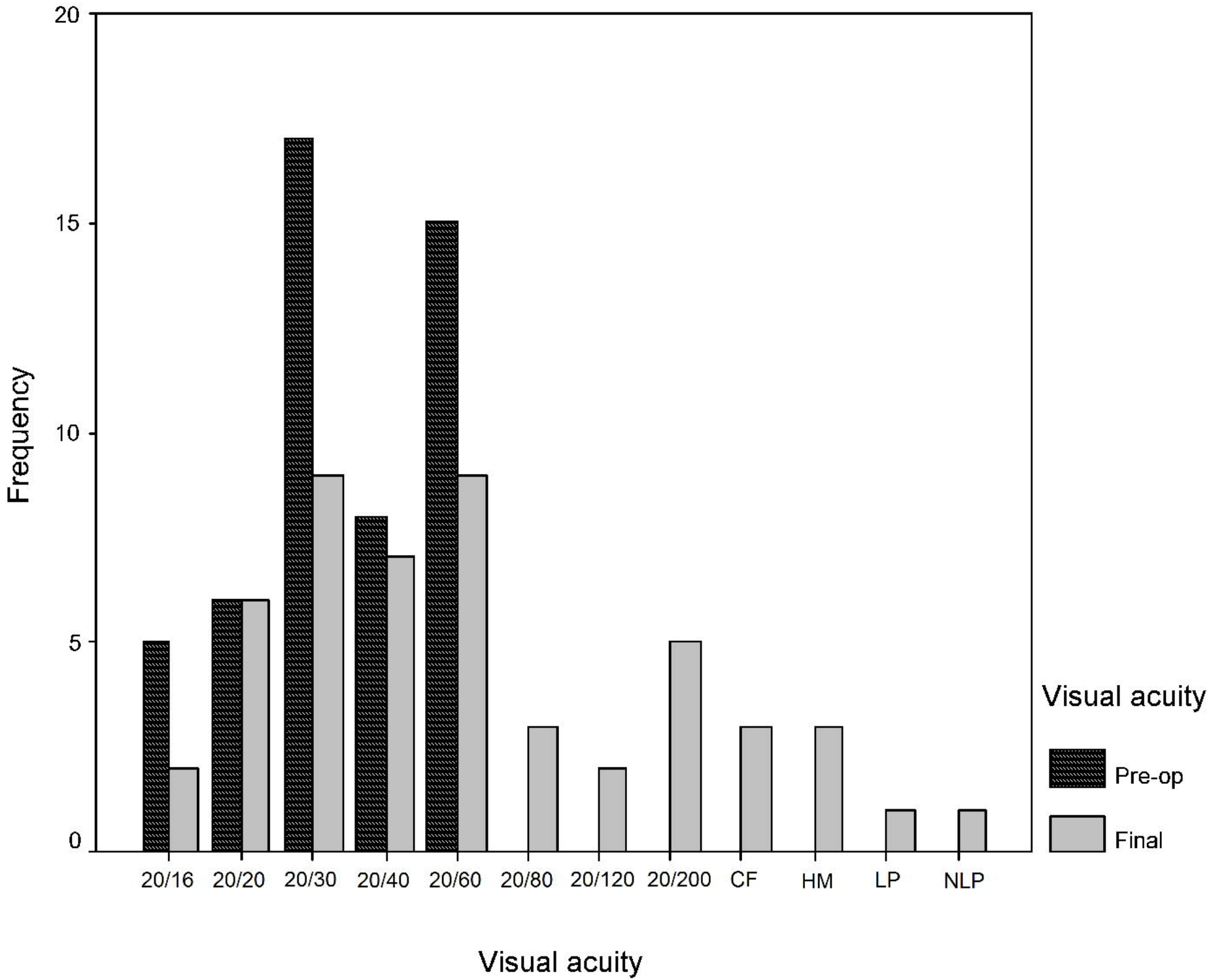
20
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10
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Frequency
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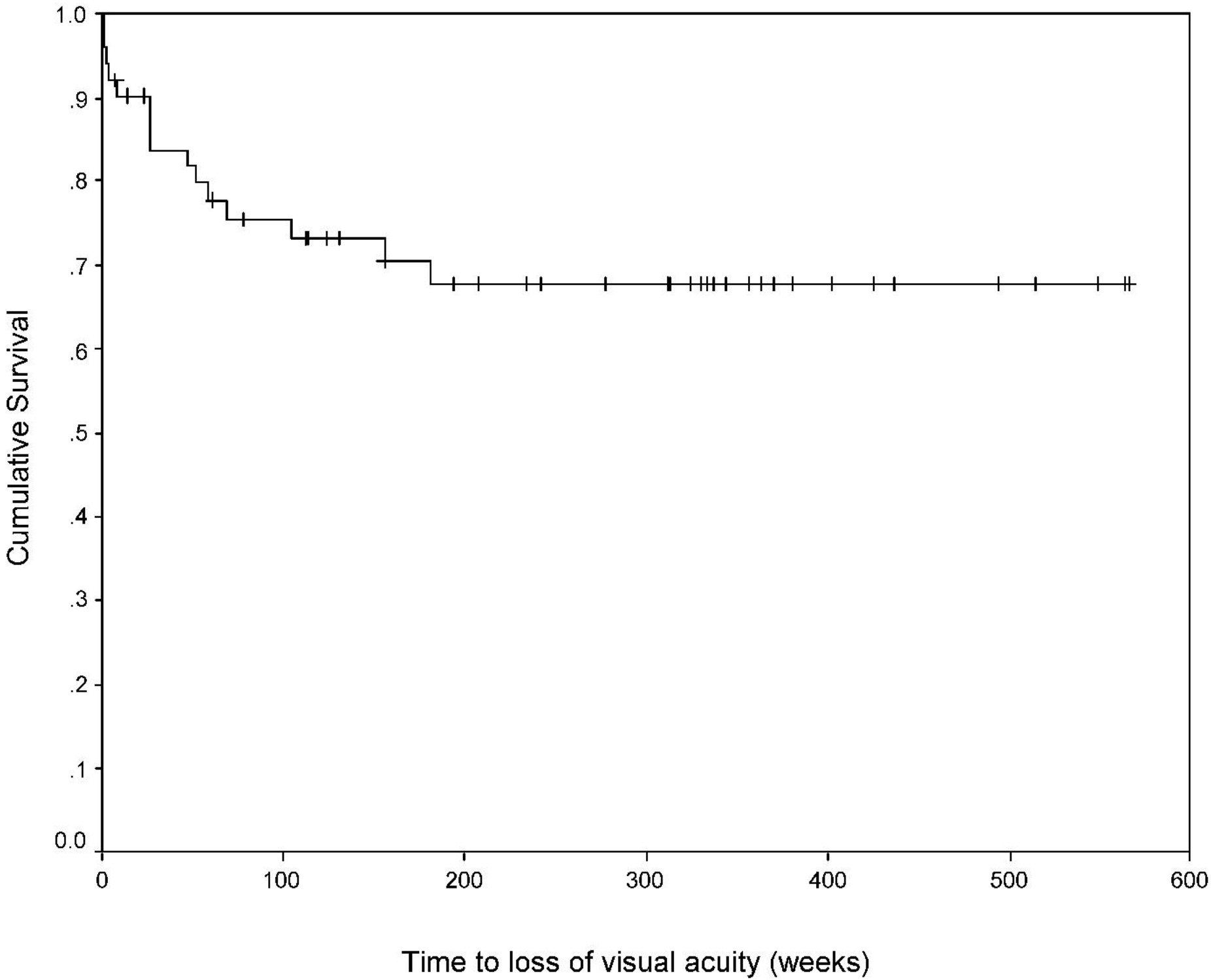
Visual acuity


1.0
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Cumulative Survival
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400
500
600
Time to loss of visual acuity (weeks)