

Factors affecting visual outcome of myopic choroidal neovascularization treated with verteporfin photodynamic therapy

Colin S. Tan^{1,2}, Milton C. Chew¹, Kai-Hung Lim¹, Tock-Han Lim^{1,2}

Foundation items: Dr. Tan receives travel support from Bayer. Dr. Lim receives travel support from Novartis, Bayer and Heidelberg Engineering.

¹National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore

²Fundus Image Reading Center, National Healthcare Group Eye Institute, Singapore

Correspondence to: Colin S. Tan. National Healthcare Group Eye Institute, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng 308433, Singapore. Colintan_eye@yahoo.com.sg

Received: 2013-01-18 Accepted: 2013-04-25

Abstract

• **AIM:** To evaluate the visual outcomes of choroidal neovascularization (CNV) secondary to pathological myopia and the impact of novel risk factors affecting the final visual outcome.

• **METHODS:** Interventional case series of 18 consecutive patients with pathological myopia treated with photodynamic therapy (PDT). Inclusion criteria were spherical equivalent $-6D$ or worse or features of pathological myopia on retinal examination. The main outcome measure was final best-corrected visual acuity (BCVA).

• **RESULTS:** Of 18 eyes, 13 (72.2%) avoided moderate visual loss (≥ 3 lines of LogMAR BCVA) and 5 eyes (27.8%) improved by at least 1 line after 1 year. Patients with LogMAR BCVA ≤ 0.3 (Snellen equivalent 20/40) at one year were younger than those with BCVA >0.3 (mean age 39.0 vs 61.6 years, $P=0.001$). A higher proportion of eyes with greatest linear dimension (GLD) of $\leq 1000\mu m$ avoided moderate visual loss (100% vs 50%, $P=0.026$). Among patients who were treated within 2 weeks of visual symptoms, 88.9% avoided the loss of 3 or more lines compared to 55.6% for those who presented later. The mean improvement in LogMAR BCVA of those with GLD $\leq 1000\mu m$ was +0.12 compared to a loss of 0.55 LogMAR units for those with GLD $>1000\mu m$ ($P=0.02$). Visual outcomes were not associated with gender or refractive error.

• **CONCLUSION:** Good visual outcome in myopic CNV is associated with younger age, smaller lesion size and earlier initiation of treatment. These factors are relevant for ophthalmologists considering treatment options for myopic CNV.

• **KEYWORDS:** myopic choroidal neovascularization; pathologic myopia; photodynamic therapy

DOI:10.3980/j.issn.2222-3959.2013.03.13

Tan CS, Chew MC, Lim KH, Lim TH. Factors affecting visual outcome of myopic choroidal neovascularization treated with verteporfin photodynamic therapy. *Int J Ophthalmol* 2013;6(3):327-330

INTRODUCTION

Myopia has a high prevalence among Asian populations, especially among the younger age groups, and its prevalence has been reported to be increasing^[1]. Myopic choroidal neovascularization (CNV) affects between 5%-10% of high myope, and if untreated, has a poor visual prognosis^[2-5]. While ophthalmologists currently use intravitreal anti vascular endothelial growth factor (anti-VEGF) injections to treat myopic CNV, there may be situations where such treatment is unavailable, or associated with a higher risk to the patient. For example, a patient with previous strokes may be at a higher risk for recurrent strokes or thromboembolic events, or a patient with only one good eye remaining may not be willing to accept the risk of blindness from endophthalmitis^[6-10,11-14]. In such cases, photodynamic therapy (PDT) may still play an important role. It is important, therefore, for clinicians to understand possible risk factors affecting visual outcome in patients with myopic CNV.

Earlier studies have identified risk factors such as older age that are associated with poor visual outcomes^[15,16]. It is possible that other risk factors, such as the time between the onset of symptoms and initiation of treatment, and laser spot size on PDT, may have an impact on the visual prognosis. It is believed that PDT may damage the underlying tissues, including the choroid, which affects long-term visual acuity.

Therefore a larger laser spot size used during PDT may have some impact on visual outcomes.

The objectives of our study are to evaluate the visual outcomes of myopic CNV in Asian patients, and to examine the impact of various risk factors on the final visual outcome.

SUBJECTS AND METHODS

Subjects We performed an interventional case series of 18 consecutive patients with pathologic myopia treated for myopic CNV at Tan Tock Seng Hospital, National Healthcare Group Eye Institute, Singapore. This review was approved by the Institutional Review Board of the National Healthcare Group, Singapore and conformed to the Tenets of the Declaration of Helsinki.

The inclusion criteria were spherical equivalent $\leq -6D$ or features of pathological myopia on retinal examination (Figure 1). Patients with co-existing ocular pathology, such as CNV secondary to age-related macular degeneration or other retinal diseases, were excluded. The presence of myopic CNV was confirmed using confocal scanning laser ophthalmoscopy fluorescein and indocyanine green angiography using the Heidelberg HRA2 (Heidelberg Engineering, Heidelberg, Germany).

Methods During the period these patients were studied (2005-2007), PDT was the standard of care for patients with myopic CNV and anti-VEGF injections were not commonly in use in our institution. Patients were treated by a single ophthalmologist (THL) and received full-fluence PDT with Verteporfin (Novartis AG, Basel, Switzerland), using the guidelines of the VIP study and Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) study^[17, 18]. Patients were followed up by retinal specialists for at least 12 months, with the best-corrected visual acuity (BCVA) and clinical findings monitored at each visit.

Patients were asked for the exact duration of symptoms during the initial consultation. The time between the onset of symptoms and the first treatment of the myopic CNV lesion was correlated with the final visual outcomes. In cases where the exact onset was unclear, the patient was excluded from analysis.

Statistical Analysis Statistical analysis was performed using SPSS for Windows version 16 (SPSS Inc., Chicago, USA), with P values <0.05 taken as significant. Chi-square tests were used to compare proportions, and t tests used to compare means.

RESULTS

There were 7 males (38.9%) and 11 females (61.1%) with a mean age 56.6 years ($SD \pm 14.0$) and mean spherical equivalent of $-11.5D$ (range, -6.0 to $-19.9D$, $SD \pm 3.89$). The right eye was affected in 8 patients (44.4%), and the left eye was

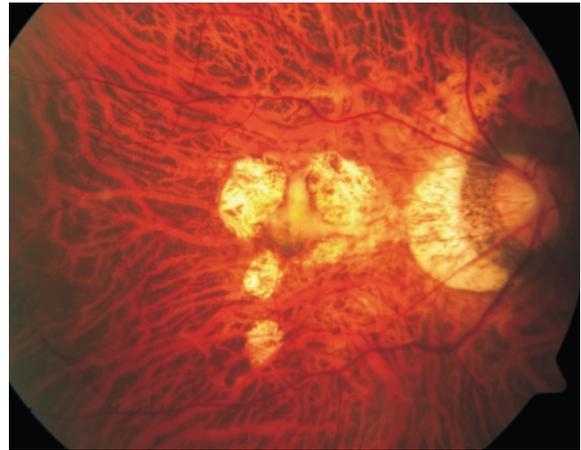


Figure 1 Color fundus photograph of a myope showing myopic CNV at the macula.

affected in 10 patients (55.6%). All patients were treated with PDT. The mean number of PDT treatments was 1.7 (range, 1-4).

The mean initial BCVA was 0.57 ± 0.39 . At 12 months, 13 of 18 eyes (72.2%) avoided moderate visual loss (loss of ≥ 3 lines of VA) and 5 eyes (27.8%) improved by at least 1 line. Patients with LogMAR VA ≤ 0.3 (Snellen equivalent 20/40) at one year were younger compared to those with VA >0.3 (mean age 39.0 years vs 61.6 years, $P=0.001$). Of those aged 50 years or younger, 75.0% had VA 20/40 or better at 1 year compared to only 7.1% of those older than 50 years ($P=0.004$). A higher proportion of eyes with greatest linear dimension (GLD) of $\leq 1000\mu m$ avoided moderate visual loss compared to those with GLD $>1000\mu m$ (100% vs 50%, $P=0.026$) and 57.1% had final VA 20/40 or better compared to 0% for those with GLD $>1000\mu m$ ($P=0.006$). Among patients with GLD $\leq 1000\mu m$, there was a mean improvement in LogMAR VA of +0.12 units, whereas those with GLD $>1000\mu m$ experienced a loss of vision (mean -0.55 units) for those ($P=0.02$).

Among patients who were treated within 2 weeks of the onset of visual symptoms, 88.9% avoided the loss of 3 or more lines compared to 55.6% for those who presented later. At 1 year, the mean LogMAR VA for those treated early was 0.57 compared to 1.08 for those treated after 2 weeks ($P=0.065$). Visual outcomes were not associated with gender, initial BCVA, or number of treatments.

DISCUSSION

In this study, we have identified several important risk factors which affect the visual outcomes of patients with myopic CNV who are treated with PDT. Specifically, younger age, a smaller laser spot size for PDT and a shorter duration to treatment are associated with a better visual outcome.

An interesting observation in our study is that early treatment (within 2 weeks of onset of visual symptoms) was associated

with better mean VA at 1 year and a lower percentage who lost 3 or more lines of VA. If this factor can be confirmed in larger randomized controlled studies, it would suggest that patients should be advised to seek treatment earlier in order to mitigate the damage to the retina, and ophthalmologists should also consider initiating treatment as early as possible. Earlier studies have shown that a smaller lesion size on presentation is associated with a better visual outcome^[15,16]. This may be due to the reduction in damage to the choroid caused by photodynamic therapy, which results in chorioretinal atrophy and choroidal thinning. It is also possible that smaller lesions are due to earlier presentation by the patient, before the lesion has grown in size to involve the fovea. The impact of lesion size on long term visual outcomes will need to be examined in larger studies in future. A younger age has previously been shown to affect the visual outcomes in myopic CNV^[19]. While age is not a modifiable risk factor, this remains important in view of the large difference in clinical outcome in our series: 75.0% of younger patients had final VA of 20/40 or better compared to only 7.1% of those who were older. These results suggest that it is important to take age into account when counseling patients on the likely visual prognosis of their disease. In this series, all patients were treated with PDT, which has been shown to prevent severe visual loss in patients with myopic CNV. While we recognize that studies have reported that treatment of myopic CNV with intravitreal injections of anti-VEGF drugs may result in better clinical outcomes^[20-27], it is important to note that the use of anti-VEGF drugs are associated with systemic and ocular side effects, including the risk of stroke or endophthalmitis^[6-10,11-14]. Some patients are at greater risk of thromboembolic events and may be unwilling to accept the risks associated with these drugs, or the risk of endophthalmitis associated with intravitreal injections. In such patients, PDT may be an option that ophthalmologists will need to consider. It is therefore important for ophthalmologists to understand the factors that are associated with better visual outcomes when PDT is used. Potential limitations of this study include the relatively small number of patients, which may mask the effects of possible risk factors, and its retrospective nature. However, with the advent of anti-VEGF drugs, it is unlikely that large scale studies of PDT treatment of myopic CNV will be performed, and hence results from smaller studies remain relevant. In conclusion, this study has identified possible risk factors affecting the visual outcome in patients with myopic CNV, specifically the time to presentation, patient age, and the size of the lesion. These should be taken into account when assessing the long term visual prognosis of patients with

myopic CNV.

REFERENCES

- 1 Vitale S, Sperduto RD, Ferris FL, III. Increased prevalence of myopia in the United States between 1971-1972 and 1999-2004. *Arch Ophthalmol* 2009;127(12):1632-1639
- 2 Yoshida T, Ohno-Matsui K, Ohtake Y, Takashima T, Futagami S, Baba T, Yasuzumi K, Tokoro T, Mochizuki M. Long-term visual prognosis of choroidal neovascularization in high myopia: a comparison between age groups. *Ophthalmology* 2002;109(4):712-719
- 3 Yoshida T, Ohno-Matsui K, Yasuzumi K, Kojima A, Shimada N, Futagami S, Tokoro T, Mochizuki M. Myopic choroidal neovascularization: a 10-year follow-up. *Ophthalmology* 2003;110(7):1297-1305
- 4 Hampton GR, Kohlen D, Bird AC. Visual prognosis of disciform degeneration in myopia. *Ophthalmology* 1983;90(8):923-926
- 5 Hotchkiss ML, Fine SL. Pathologic myopia and choroidal neovascularization. *Am J Ophthalmol* 1981;91(2):177-183
- 6 Day S, Acquah K, Mruthyunjaya P, Grossman DS, Lee PP, Sloan FA. Ocular complications after anti-vascular endothelial growth factor therapy in Medicare patients with age-related macular degeneration. *Am J Ophthalmol* 2011;152(2):266-272
- 7 Martin DF, Maguire MG, Fine SL, Ying GS, Jaffe GJ, Grunwald JE, Toth C, Redford M, Ferris FL, III. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology* 2012;119(7):1388-1398
- 8 Chakravarthy U, Harding SP, Rogers CA, Downes SM, Lotery AJ, Wordsworth S, Reeves BC. Ranibizumab versus bevacizumab to treat neovascular age-related macular degeneration: one-year findings from the IVAN randomized trial. *Ophthalmology* 2012;119(7):1399-1411
- 9 Sharma S, Johnson D, Abouammoh M, Hollands S, Brissette A. Rate of serious adverse effects in a series of bevacizumab and ranibizumab injections. *Can J Ophthalmol* 2012;47(3):275-279
- 10 Wu L, Martinez-Castellanos MA, Quiroz-Mercado H, Arevalo JF, Berrocal MH, Farah ME, Maia M, Roca JA, Rodriguez FJ. Twelve-month safety of intravitreal injections of bevacizumab (Avastin): results of the Pan-American Collaborative Retina Study Group (PACORES). *Graefes Arch Clin Exp Ophthalmol* 2008;246(1):81-87
- 11 Shah CP, Garg SJ, Vander JF, Brown GC, Kaiser RS, Haller JA. Outcomes and risk factors associated with endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents. *Ophthalmology* 2011;118(10):2028-2034
- 12 Moshfeghi AA, Rosenfeld PJ, Flynn HW, Jr., Schwartz SG, Davis JL, Murray TG, Smiddy WE, Berrocal AM, Dubovy SR, Lee WH, Albin TA, Lalwani GA, Kovach JL, Puliafito CA. Endophthalmitis after intravitreal vascular endothelial growth factor antagonists: a six-year experience at a university referral center. *Retina* 2011;31(4):662-668
- 13 Goldberg RA, Flynn HW, Jr., Isom RF, Miller D, Gonzalez S. An outbreak of streptococcus endophthalmitis after intravitreal injection of bevacizumab. *Am J Ophthalmol* 2012;153(2):204-208
- 14 Pilli S, Kotsolis A, Spaide RF, Slakter J, Freund KB, Sorenson J, Klancnik J, Cooney M. Endophthalmitis associated with intravitreal anti-vascular endothelial growth factor therapy injections in an office setting. *Am J Ophthalmol* 2008;145(5):879-882
- 15 Hayashi K, Ohno-Matsui K, Shimada N, Moriyama M, Hayashi W, Wang J, Yoshida T, Tokoro T, Mochizuki M. Long-term Results of

Visual outcomes of myopic choroidal neovascularization

- Photodynamic Therapy for Choroidal Neovascularization in Japanese Patients with Pathologic Myopia. *Am J Ophthalmol* 2010;151(1):137–147
- 16 Hayashi K, Ohno–Matsui K, Teramukai S, Shimada N, Moriyama M, Hara W, Yoshida T, Tokoro T, Mochizuki M. Photodynamic therapy with verteporfin for choroidal neovascularization of pathologic myopia in Japanese patients: comparison with nontreated controls. *Am J Ophthalmol* 2008;145(3):518–526
- 17 Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. 1–year results of a randomized clinical trial—VIP report no. 1. *Ophthalmology* 2001;108(5):841–852
- 18 Photodynamic therapy of subfoveal choroidal neovascularization in age–related macular degeneration with verteporfin: one–year results of 2 randomized clinical trials–TAP report. Treatment of age–related macular degeneration with photodynamic therapy (TAP) Study Group. *Arch Ophthalmol* 1999;117(10):1329–1345
- 19 Pece A, Vadalà M, Isola V, Matranga D. Photodynamic therapy with verteporfin for juxtafoveal choroidal neovascularization in pathologic myopia: a long–term follow–up study. *Am J Ophthalmol* 2007;143 (3): 449–454
- 20 Hayashi K, Ohno–Matsui K, Teramukai S, Shimada N, Moriyama M, Hayashi W, Yoshida T, Tokoro T, Mochizuki M. Comparison of visual outcome and regression pattern of myopic choroidal neovascularization after intravitreal bevacizumab or after photodynamic therapy. *Am J Ophthalmol* 2009;148(3):396–408
- 21 Yoon JU, Byun YJ, Koh HJ. Intravitreal anti–VEGF versus photodynamic therapy with verteporfin for treatment of myopic choroidal neovascularization. *Retina* 2010;30(3):418–424
- 22 Ruiz–Moreno JM, Montero JA, Amat–Peral P. Myopic choroidal neovascularization treated by intravitreal bevacizumab: comparison of two different initial doses. *Graefes Arch Clin Exp Ophthalmol* 2011;249 (4): 595–599
- 23 Voykov B, Gelisken F, Inhoffen W, Voelker M, Bartz–Schmidt KU, Ziemssen F. Bevacizumab for choroidal neovascularization secondary to pathologic myopia: Is there a decline of the treatment efficacy after 2 years? *Graefes Arch Clin Exp Ophthalmol* 2010;248(4):543–550
- 24 Nakanishi H, Tsujikawa A, Yodoi Y, Ojima Y, Otani A, Tamura H, Yamashiro K, Ooto S, Yoshimura N. Prognostic factors for visual outcomes 2–years after intravitreal bevacizumab for myopic choroidal neovascularization. *Eye* 2011;25(3):375–381
- 25 Ikuno Y, Sayanagi K, Soga K, Sawa M, Tsujikawa M, Gomi F, Tano Y. Intravitreal bevacizumab for choroidal neovascularization attributable to pathological myopia: one–year results. *Am J Ophthalmol* 2009;147 (1): 94–100
- 26 Chan WM, Lai TY, Liu DT, Lam DS. Intravitreal bevacizumab (Avastin) for myopic choroidal neovascularisation: 1–year results of a prospective pilot study. *Br J Ophthalmol* 2009;93(2):150–154
- 27 Lai TY, Chan WM, Liu DT, Lam DS. Intravitreal ranibizumab for the primary treatment of choroidal neovascularization secondary to pathologic myopia. *Retina* 2009;29(6):750–756