ORIGINAL RESEARCH

Survival in Patients with Neovascular Glaucoma Following Tube Shunt Implant or Cyclodestructive Procedure

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Abstract

Purpose: The study purpose was to assess patient survival after tube shunt implant or cyclodestructive procedure for neovascular glaucoma and to determine whether specific preoperative factors are predictive of survival.

Materials and methods: A retrospective chart review was performed on patients with neovascular glaucoma who underwent tube shunt implant and/or cyclodestructive procedure between January 2002 and December 2019 at the Minneapolis Veterans Affairs Health Care System. Patient survival was compared to the age and gender-matched Minnesota population. Cox regression analyses were performed to evaluate preoperative parameters and survival.

Results: Tube shunt alone was implanted in 30 eyes, cyclodestruction alone was performed in nine eyes, and two eyes underwent both (n = 41 eyes, 39 patients). The postoperative 5-year survival rate was 62% in neovascular glaucoma patients compared to 80% in controls. Survival did not differ significantly based on neovascular glaucoma etiology. Preoperative best-corrected visual acuity of the neovascular glaucoma-affected eye ($p = 0.05$) and Charlson Comorbidity Index ($p = 0.02$) were associated with survival, but preoperative maximum intraocular pressure, hemoglobin A1c, and creatinine were not. The mean intraocular pressure at 6 months postprocedure was 14 mm Hg for tube shunt and 27 mm Hg for cyclodestruction ($p = 0.03$).

Conclusion: Neovascular glaucoma patients have reduced survival, but the majority survived at least 5-year postprocedure. Ophthalmologists should consider patient survival and factors predictive of survival when planning procedures for neovascular glaucoma.

Clinical significance: Our findings provide an updated perspective on survival in the setting of neovascular glaucoma and can help ophthalmologists provide patient-centered and holistic care.

Keywords: Cyclodestruction, Glaucoma drainage implants, Neovascular glaucoma, Retrospective cohort study, Survival analysis.

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Introduction

Neovascular glaucoma (NVG) is a form of secondary glaucoma characterized by neovascularization and associated connective tissue growth at the peripheral iris, typically secondary to retinal ischemia and hypoxia.[1] Intraocular pressure (IOP) becomes elevated when abnormal blood vessels and related connective tissues occlude the iridocorneal angle.[2] NVG can be difficult to manage effectively. Medical treatment alone often is not sufficient and surgical intervention may be required to reduce IOP.[2]

Systemic health should be assessed when planning surgical glaucoma intervention since patients with NVG are likely to have cardiovascular risk factors or coagulopathy. In patients with central retinal vein occlusion, systemic hypertension is one of the risk factors for NVG development.[3] Furthermore, researchers have reported a correlation between increased risk of ischemic stroke and NVG.[4] Previous studies in New Zealand show increased mortality due to underlying systemic vascular pathology in NVG patients after ocular drainage device implantation.[5] Although postoperative survival of NVG patients with glaucoma procedures prior to April 2001 improved compared to a study performed 20 years prior by the same group,[6] survival rates of the NVG cohort remained substantially lower than controls.

It is unclear whether the survival of NVG patients in this New Zealand population is generalizable to other populations. Also, the survival of NVG patients as a whole may have changed since 2001 as a result of advances in treating systemic vascular disease. In the study described herein, we assess survival after tube shunt implantation or cyclodestructive procedure for NVG performed at the Minneapolis Veterans Affairs Health Care System (MVAHCS), and we determine whether specific preoperative clinical factors are associated with survival.

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Conflict of interest: None

Materials and Methods

Data from the Veterans Health Administration's Corporate Data Warehouse[7] were obtained by querying the Veterans Affairs Informatics and Computing Infrastructure.[8] The study population consists of all MVAHCS (Minneapolis, Minnesota) patients with neovascular glaucoma who underwent tube shunt implant and/or cyclodestructive procedure, including cyclophotocoagulation (CPC) and cyclocryotherapy, between January 2002 and December 2019. Specific inclusion criteria were: (1) one of the following International Classification of Diseases (ICD) codes for rubeosis iridis or secondary glaucoma associated with a MVAHCS medical encounter between January 2002 and December 2019: ICD-9 364.42, 365.63, 365.89, 365.9 or ICD-10 H21.1X9, H40.50X0, H40.50X1, H40.50X2, H40.50X3, H40.50X4, H40.51X0, H40.51X1, H40.51X2, H40.51X3, H40.51X4, H40.52X0, H40.52X1, H40.52X2, H40.52X3, H40.52X4, H40.53X0, H40.53X1, H40.53X2, H40.53X3, H40.53X4, H40.89, H40.9; (2) one of the following Current Procedural Terminology (CPT) codes 66,179, 66,180, 66,183, 66,184, 66,185, 66,710, 66,711 listed between January 2002 and December 2019; and (3) a diagnosis of neovascular glaucoma based on chart review.

The final evaluation of patient survival was conducted on March 1, 2021. Data from ophthalmology clinic visits before and after the procedure were collected from the MVAHCS medical record. All visual acuity measurements were converted to logarithm of minimal angle of resolution (logMAR) for statistical analysis. The etiology of NVG was determined by the attending physician as documented in the chart. The procedure performed, the date of the procedure, other systemic diseases, pertinent laboratory values, and death date (if applicable) were recorded. If an eye underwent more than one procedure for NVG treatment, only the first procedure performed was included in the statistical analysis. For the two patients with bilateral NVG, only the first eye treated was included in the statistical analysis. For comparison of IOP reduction after tube shunt vs cyclodestructive procedure, subjects without preoperative IOP and 6 months postoperative IOP were excluded.

The survival of the patient group was compared with those of the Minnesota population of the same age and gender-based on the Minnesota Life Tables.[9] Survival of patients whose NVG was secondary to diabetic retinopathy (DR) were compared with those caused by other etiologies using Log Rank survival analysis and Kaplan-Meier curve. Cox regression survival analyses were carried out to evaluate whether specific preoperative ophthalmic or systemic parameters were correlated with survival. All other between-group comparisons of variables (IOP reduction of tube shunt vs cyclodestruction) were conducted using an independent samples *t*-test. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 19.0.0 (Armonk, NY: IBM Corp).

The MVAHCS Institutional Review Board (IRB) deemed this study to be IRB-exempt under Category 4 (iii), and thus this study was overseen by the MVAHCS Research and Development Committee. This study adhered to the tenets of the Declaration of Helsinki and was conducted in accordance with the Health Insurance Portability and Accountability Act.

Results

Table 1 shows the clinical characteristics of the NVG study subjects. A total of 39 patients and 41 eyes were included in the study since two patients had bilateral NVG. Tube shunt was implanted in 30 (73.2%) eyes and cyclodestruction was performed in nine eyes (22%). Two eyes (4.9%) underwent both procedures. Ahmed tube implantation was performed in 22 eyes and Baerveldt tube implantation was performed in 10 eyes. The mean (median) age at the first operation was 70.2 (70) years.

The mean American Society of Anesthesiologists (ASA) score within a year of the NVG procedure for the study population was 3.06, indicative of severe systemic disease in the study cohort. Correspondingly, diagnoses of various cardiovascular diseases were found in 38 patients (97.4%), and 33 patients had a diagnosis of diabetes mellitus (84.6%) (Table 1). The predominant underlying etiologies for NVG were DR in 20 eyes (48.8%) and central retinal vein occlusion in 14 eyes (34.1%).

The integrated electronic health record for our patient population includes the comprehensive death data compiled by the United States Veterans Affairs Health Care System, which precluded loss to follow-up. At a 5-year follow-up after the procedure, the survival rate of the NVG patients was 62% compared to 80% in the age and gender-matched Minnesota population (Fig. 1). As of

Table 1: Characteristics of neovascular glaucoma subjects

Number of subjects	39
Male (%)	38 (97.4)
Deceased at the time of the study (%)	16 (41.0)
Both eyes underwent procedure (%)	2 (5.1)
Number of eyes	41
Tube surgery only (%)	30 (73.2)
Cyclodestruction only* (%)	9 (22.0)
Both tube surgery and cyclophotocoagulation (%)	2 (4.9)
Mean age at first procedure, years (range)	70.2 (47–88)
Mean age at first tube surgery, years (range)	69.2 (47–88)
Mean age at first cyclodestruction, years (range)	75.1 (52–88)
Etiology of neovascular glaucoma	Number of eyes (%)
Diabetes mellitus	20 (48.8)
Central retinal vein occlusion	14 (34.1)
Central retinal arterial occlusion	3 (7.3)
Ocular ischemic syndrome	3 (7.3)
Viral	1 (2.4)
Major medial disease	Number of subjects (%)
Cardiovascular	38 (97.4)
Diabetes mellitus	33 (84.6)
Chronic kidney disease/kidney failure	12 (30.8)
Obstructive sleep apnea	14 (35.9)
Chronic obstructive pulmonary disease	4 (10.3)
Cancer	8 (20.5)
Rectum	1
Kidney	1
Prostate	3
Esophagus/tongue	1
Bladder	1
Thyroid	1

*Cyclocryotherapy in one subject and cyclophotocoagulation in the others

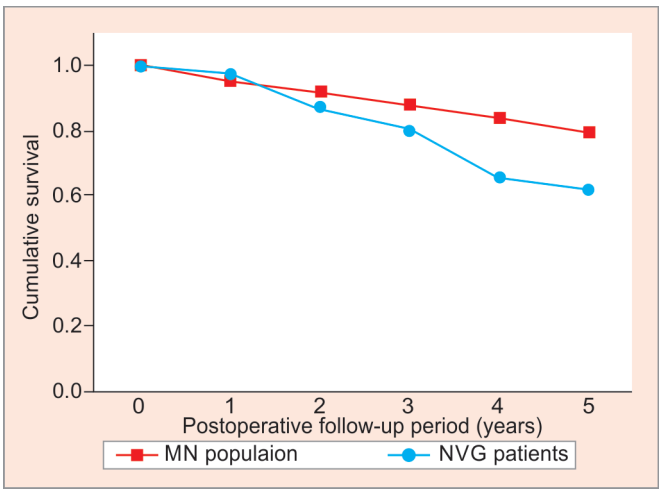

Fig. 1: Survival rate of neovascular glaucoma (NVG) patients following tube shunt implant or cyclodestructive procedure compared to the age and gender-matched Minnesota (MN) population

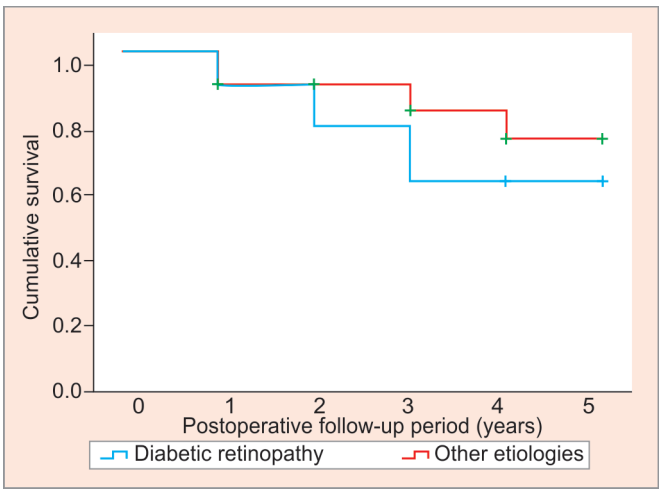

Fig. 2: Survival rate of neovascular glaucoma (NVG) patients with NVG caused by diabetic retinopathy compared with those with other NVG etiologies following tube shunt implant or cyclodestructive procedure ($p = 0.315$)

Table 2: Cox proportional hazards regression analysis of survival in 5 years after surgery for neovascular glaucoma

Preoperative variable	*Hazard ratio (95% CI)*	*p-value*
Best-corrected visual acuity of affected eye	3.44 (0.99–11.90)	0.05*
Best-corrected visual acuity of better-seeing eye	0.75 (0.17–3.38)	0.71
Maximum intraocular pressure of affected eye	1.02 (0.96–1.08)	0.63
Hemoglobin A1c	0.90 (0.58–1.41)	0.65
Creatinine	0.73 (0.30–1.77)	0.48
Charlson Comorbidity Index	1.89 (1.13–3.16)	0.02*

*Significant at $p \leq 0.05$ level

March 1, 2021, 16 patients were deceased, and the survival of the other subjects was verified by an MVAHCS encounter documented within the preceding 6 months. Among the deceased patients, the mean length of remaining life after the procedure was 4 (median 3, range 0–11) years. Among the 23 living patients, the mean time since the procedure was 5 (median 5, range 1–14) years.

There was no difference in survival between patients with NVG secondary to DR compared to other etiologies (Fig. 2, $p = 0.32$), although patients with NVG caused by DR had their first procedure at a younger age ($p = 0.04$). The mean (range) age at first operation was 66.6 (52–84) years for patients with NVG caused by DR and 73.6 (47–88) years for patients with NVG caused by other etiologies.

Cox regression analysis of preoperative clinical parameters shows higher Charlson Comorbidity Index (CCI) values (hazard ratio = 1.89, $p = 0.02$) and higher logMAR preoperative best-corrected visual acuity (BCVA), which corresponds to poorer vision, of the NVG-affected eye (hazard ratio = 3.44, $p = 0.05$) in subjects with reduced survival in the 5-year postoperative period, although BCVA of the NVG-affected eye only just met criteria for significance (Table 2). The other preoperative clinical parameters assessed–preoperative BCVA of the better-seeing eye, maximum IOP, hemoglobin A1c, and creatinine–were not associated with survival during the 5-year follow-up period after the NVG procedure.

We also compared the effectiveness of IOP reduction between tube shunt and cyclodestructive procedure. Twenty-five eyes that underwent tube shunt placement and nine eyes that underwent cyclodestruction (8 of CPC and 1 of cyclocryoablation) had both preoperative IOP and 6 months postoperative IOP measurements recorded, so these eyes were included in the analysis. There was no significant difference in age at operation between the patients who had tube shunt vs cyclodestruction ($p = 0.12$), but postoperative IOP was lower in those with tube shunt implantation. Six months after the procedure, the mean percentage IOP reduction from maximum IOP before the procedure was 71% in eyes with tube shunt and 48% in eyes with cyclodestruction ($p = 0.08$); furthermore, the mean absolute value of 6 months postoperative IOP was 14 mm Hg for tube shunt and 27 mm Hg for cyclodestruction ($p = 0.03$).

Discussion

At 5-year postoperative follow-up, patients with NVG at the MVAHCS who underwent tube shunt or cyclodestructive procedures had reduced survival compared to age- and gender-matched controls, but the 5-year survival rate was greater than 50%. The leading two causes of our patients' NVG were DR and central retinal vein occlusion, which is consistent with existing literature,[1,2] and both DR and retinal vein occlusion are known risk factors for death from cardiovascular diseases.[10,11] The majority of the patients have cardiovascular diseases and/or diabetes mellitus. Although we did not identify a difference in survival, the patients with NVG secondary to DR had their procedure at a younger age compared to those with NVG secondary to other etiologies.

Our findings suggest that CCI and preoperative BCVA of the NVG-affected eye may help predict patient survival after glaucoma procedures for NVG. Prior NVG survival studies have not evaluated CCI, but since CCI is designed to predict 10-year survival, it is not surprising that CCI is associated with 5-year survival in the present study. We recommend that ophthalmologists consult with the patients' primary care physician, especially in patients with high CCI, to maximize the survival of patients with NVG.

The association between better BCVA of the affected eye at presentation and improved survival in our study concurs with the 2004 study of NVG patients in New Zealand undergoing Molteno

implantation surgery[5] but contrasts with a 2019 study of diabetic patients with NVG that specifically evaluated mortality from cardiovascular events where poor visual acuity of the affected eye was not associated with mortality.[12] Also, although we found an association between BCVA of the NVG-affected eye and survival, we did not find an association between BCVA of the better-seeing eye and survival. Prior studies evaluating survival and visual impairment often focus on the relationship between mortality risk and BCVA of the better-seeing eye,[13] but the results from our study and the New Zealand NVG study[5] suggest that it may be useful to expand these analyses to include BCVA in the affected eye, depending on the underlying ocular pathology.

Key differences between our study and the 2004 New Zealand NVG study[5] include timing of procedures, types of procedures, and patient demographics. Procedures in our study occurred between January 2002 and December 2019, compared to October 1977 to March 2001. Our study included patients undergoing cyclodestructive procedures and glaucoma drainage devices, whereas the New Zealand study evaluated only those with Molteno implants. In addition to nationality (United States vs New Zealand), there were other demographic differences between the studies. The United States (US) veteran population is predominantly male and tends to have a poorer health status and more medical conditions than the general US population.[14] Furthermore, the US veterans have barriers in access to glaucoma surgery, including lack of transportation, scheduling challenges, and delayed referral.[15]

Both CPC and tube implantation surgery are used in the treatment of NVG. Since more than half of our subjects lived at least 5 years after their glaucoma procedure, it is ideal to choose an effective and durable procedure. Our limited data indicate that tube shunt implantation may be more effective than cyclodestruction 6 months after surgery in our study population, but the study was not designed to evaluate the merits of one compared to the other. Prior studies do not reach a consensus on whether tube shunt is associated with more vision-threatening complications[12] or more effective in maintaining or improving visual acuity than CPC, but both Ahmed tube and CPC were shown to have similar and successful IOP control in NVG up to 24–40 months,[12,16,17] indicating that either may be a reasonable option for IOP control. With modern techniques of CPC and tube implantation, and the survival data at hand, the choice of the procedure should be based on logistics, the difficulty of aftercare, and social situation, rather than a presumed mortality risk of the disease.

The limitations of this study include the retrospective study design, small sample size, and predominantly male gender in the study population. Some patients' procedures were performed very close to the time of the study, resulting in a short follow-up period. Also, since our data were collected over nearly 20 years, medical management of systemic diseases has changed during the study course, resulting in systemic disease treatment heterogeneity. Still, the reasonable postoperative survival in the veteran population, which tends to be less healthy than the nonveteran population,[14] provides justification for surgical intervention if needed for long-term IOP control in NVG. Our data give one confidence to go forward with realistic expectations in recommending the best ophthalmologic surgical treatment to improve patients' quality of life by improving or sustaining vision, relieving pain, and/or reducing medication burden.

Conclusion

Patients with NVG have reduced survival compared to the age and sex-matched general population, but our study population showed improved survival following the glaucoma procedure compared to previous NVG studies. Preoperative BCVA of the affected eye and CCI were predictive of postprocedure survival. Ophthalmologists may consider survival and the factors predictive of survival in preoperative discussions, informed consent, and planning of glaucoma procedures. It is helpful to use a multidisciplinary approach to patients with NVG that addresses underlying systemic diseases to optimize care.

Clinical Significance

Our findings provide an updated perspective on survival in the setting of neovascular glaucoma. Knowledge about patient survival and the factors predictive of survival can help ophthalmologists provide patient-centered and holistic care.

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