Maintenance of Warfarin Anticoagulation for Patients Undergoing Vitreoretinal Surgery

Pouya N. Dayani, MD; M. Gilbert Grand, MD

Objective: To evaluate the risk of hemorrhagic complications associated with vitreoretinal surgery in patients whose warfarin sodium therapy was continued throughout the surgical period.

Methods: A review of 1737 records of patients undergoing pars plana vitrectomy was conducted. Inclusion criteria included patients receiving warfarin therapy whose international normalized ratios (INRs) were elevated above normal values on the day of surgery. Intraoperative and postoperative hemorrhagic complications were documented.

Results: Fifty-four patients underwent 57 vitreoretinal surgical procedures with warfarin therapy and were divided into groups as follows: group S with INRs of 1.20 to 1.49, values considered subtherapeutic; group B with INRs of 1.50 to 1.99, values considered borderline therapeutic; group T with INRs of 2.00 to 2.49, values considered therapeutic; and group HT with INRs of 2.50 or greater, values considered highly therapeutic. No patients experienced anesthesia-related or intraoperative hemorrhagic complications. Two (7.7%) of 26 eyes in group S and 2 (16.7%) of 12 eyes in group HT experienced postoperative hemorrhages. All of the patients with vitreous hemorrhages had spontaneous clearing without additional treatment.

Conclusions: Many patients may safely undergo vitreoretinal surgery while maintaining therapeutic levels of warfarin anticoagulation. We experienced no intraoperative hemorrhagic complications; the 4 postoperative complications resolved spontaneously without persistent visual sequelae or the need for supplemental surgery.

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Warfarin sodium (Coumadin; Bristol-Myers Squibb Co, New York, NY) anticoagulation is generally used for the management of potentially life-threatening diseases. Experience regarding the safety of vitreoretinal procedures in patients in whom warfarin anticoagulation has been maintained is limited. Maintenance of anticoagulation during surgery for such patients may be associated with an increased risk of intraoperative or postoperative hemorrhage. However, discontinuation may subject patients to the risk of systemic complications such as embolic disease or cerebrovascular accident. Therefore, decisions regarding maintenance, modification, or perioperative discontinuation of anticoagulation therapy pose a significant dilemma for the ophthalmic surgeon. The purpose of this study is to provide further information regarding the results of vitreoretinal surgery in patients in whom warfarin therapy was continued throughout the surgical period.

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as scleral buckling), and the method of anesthesia (subdivided into general anesthesia or local infiltration with monitored anesthesia care [MAC]). Preoperative and postoperative nonstandardized Snellen visual acuities were determined. The INR at the time of surgery was collected and PT and partial thromboplastin time (PTT) were recorded when available. Intraoperative hemorrhages were reported by the surgeon and recorded in the operative note. Postoperative hemorrhagic complications were defined as bleeding that was detected on the first postoperative day or within 1 month following the operation.

## RESULTS

The retrospective record review detected 54 patients who underwent 57 vitreoretinal surgical procedures while receiving warfarin anticoagulation therapy. These patients’ records were subdivided into 4 groups based on their INRs obtained on the day of surgery. Group S included patients whose INRs ranged from 1.20 to 1.49, values that were considered subtherapeutic. Group B included patients whose INRs ranged from 1.50 to 1.99, values that were considered borderline therapeutic. Group T included patients whose INRs ranged from 2.00 to 2.49, values that were considered therapeutic. Group HT included patients whose INRs were 2.50 or greater, values that were considered highly therapeutic.

### GROUP S

Twenty-four patients undergoing 26 vitreoretinal procedures had a mean INR of 1.30 (range, 1.20–1.49). Patients in this group had a mean PT of 16.0 seconds (range, 15.0–17.5 seconds). One patient had an abnormal PTT equal to 38.8 seconds (the normal PTT is 35.0 seconds). Patients receiving other concomitant medications associated with prolonged bleeding included 2 patients receiving aspirin and 2 receiving Plavix. The group included 15 men and 9 women with a mean age of 72 years (range, 51–93 years) (Table 1).

The underlying systemic causes requiring warfarin anticoagulation included atrial fibrillation (14 patients), cardiac valve surgery (3 patients), deep vein thrombosis

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<tr>
<th>Age, y</th>
<th>INR</th>
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<th>Ocular Diagnosis</th>
<th>Surgical Procedure</th>
<th>Postoperative Complications</th>
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Abbreviations: AMD, age-related macular degeneration; CABG, coronary artery bypass graft; CRVO, central retinal vein occlusion; DVT, deep vein thrombosis; ERM, epiretinal membrane; FNA, fine-needle aspiration; INR, international normalized ratio; MH, macular hole; MP, membrane peeling; PDR, proliferative diabetic retinopathy; PE, pulmonary embolism; PPV, pars plana vitrectomy; PTT, partial thromboplastin time; RD, retinal detachment; SB, scleral buckling; SO, silicone oil; SOR, silicone oil removal; SPA, subretinal tissue plasminogen activator; TRD, fractional retinal detachment; VH, vitreous hemorrhage.

*Group S includes patients with INRs of 1.20 to 1.49, indicating subtherapeutic levels of anticoagulation.
†The values of PTT are expressed as seconds.
‡Recurrent VH on postoperative day 1 cleared spontaneously per the local physician.
§Dense VH at postoperative week 2 cleared spontaneously. Recurrent VH at postoperative week 7 cleared to a visual acuity of 20/80.

Values that were considered borderline therapeutic. Group T included patients whose INRs ranged from 2.00 to 2.49, values that were considered therapeutic. Group HT included patients whose INRs were 2.50 or greater, values that were considered highly therapeutic.

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gical procedures included fine-needle aspiration biopsy and a combination of fine-needle aspiration biopsy and vitrectomy. One eye underwent a procedure, and 1 underwent administration of subretinal tissue plasminogen activator. One eye had vitrectomy associated with membrane peeling, 1 had an additional scleral buckling procedure, and 1 underwent administration of subretinal tissue plasminogen activator. One eye underwent a combination of fine-needle aspiration biopsy and vitrectomy. Five procedures were managed using general anesthesia and 21 using local infiltration of anesthesia with MAC. A standard 3-port 20-gauge pars plana vitrectomy was used for 24 eyes whereas 25-gauge vitrectomy was used for 1 eye. Preoperative visual acuity ranged from 20/40 to hand motion, and postoperative visual acuity ranged from 20/25 to hand motion. Preoperative and postoperative distribution of visual acuities is shown in Figure 1.

There were no intraoperative or anesthetic complications. Postoperatively, 1 patient had a recurrent vitreous hemorrhage on the first postoperative day. Follow-up by his local physician indicated spontaneous clearing of the hemorrhage. This patient’s INR was 1.28 at the time of surgery for an extramacular subretinal hematoma with overlying vitreous hemorrhage. The surgical procedures included fine-needle aspiration biopsy as well as vitrectomy. A second patient with an INR of 1.41 had a recurrent vitreous hemorrhage 2 weeks following surgery for proliferative diabetic retinopathy with vitreous hemorrhage. The surgical procedure was vitrectomy with membrane peeling, peripheral cryopexy, and endolaser. The hemorrhage spontaneously cleared; however, at 7 weeks postoperatively, this patient experienced a second vitreous hemorrhage that also spontaneously cleared (Table 1).

GROUP B

Eleven patients undergoing 12 vitreoretinal procedures had a mean INR of 1.70 (range, 1.50-1.99). Patients in this group had a mean PT of 19.9 seconds (range, 17.7-21.9 seconds).

Four patients also had an abnormal PTT, with values ranging from 35.6 to 46.8 seconds (the normal PTT is 35.0 seconds). Concomitant medications included aspirin in 1 patient and Plavix in 1. The group included 9 men and 2 women with a mean age of 73 years (range, 41-85 years) (Table 2).

The underlying systemic causes requiring warfarin anticoagulation included atrial fibrillation (4 patients), cardiac valve surgery (1 patient), DVT with pulmonary embolism (2 patients), aortic aneurysms and coronary artery bypass surgery (1 patient), unspecified arrhythmia (1 patient), and unknown (2 patients). The preoperative vitreoretinal diagnoses included vitreous hemorrhage (1 patient), retinal detachment (6 patients), epiretinal membrane (2 patients), chronic vitritis (1 patient), tractional retinal detachment (1 patient), and retained silicone oil (1 patient). Eleven eyes underwent pars plana vitrectomy procedures; 4 eyes were associated with membrane peeling, 2 with scleral buckling, and 2 with pars plana lensectomy. One patient underwent vitrectomy for silicone oil removal. General anesthesia was used in 4 patients and local infiltration anesthesia with MAC in 8. The surgical techniques involved standard 3-port 20-gauge pars plana vitrectomy in 11 procedures and 25-gauge vitrectomy in 1 procedure.

Preoperative visual acuity ranged from 20/40 to hand motions, and postoperative visual acuity ranged from 20/40 to counting fingers. The distribution of preoperative and postoperative visual acuities is shown in Figure 1.

There were no anesthetic complications. No patients in this group developed intraoperative or postoperative hemorrhagic complications.

GROUP T

Seven patients undergoing a total of 7 vitreoretinal procedures had a mean INR of 2.10 (range, 2.00-2.49). The mean PT was 24.0 seconds (range, 22.8-26.0 seconds). One patient had an abnormal PTT of 46.1 seconds (the normal PTT is 35.0 seconds). Concomitant medications included aspirin in 1 patient, celecoxib (Celebrex; Pfizer, Inc, New York) in 2, and rofecoxib (Vioxx; Merck and Co, Inc, Whitehouse Station, NJ) in 1. The group comprised 5 men and 2 women with a mean age of 38 years and a median age of 68 years (range, 8-72 years) (Table 3).
The underlying systemic causes requiring warfarin anticoagulation included atrial fibrillation (2 patients), DVT (1 patient), heart transplantation with a prosthetic valve (1 patient), and unknown (2 patients). The preoperative vitreoretinal diagnoses included retinal detachment (6 patients) and retained silicone oil (1 patient). The surgical procedure was pars plana vitrectomy in 6 patients, with associated membrane peeling in 5, scleral buckling in 4, and lensectomy in 1. One patient underwent silicone oil removal by means of pars plana vitrectomy. The surgical technique involved standard 3-port 20-gauge vitrectomy in all of the patients. General anesthesia was used in 3 patients and local infiltrative anesthesia with MAC in 4. Preoperative visual acuity ranged from 20/25 to counting fingers, and postoperative visual acuity ranged from 20/20 to no light perception. The distribution of preoperative and postoperative acuities is shown in Figure 2.

There were no anesthetic complications. No patients in this group developed intraoperative or postoperative hemorrhages.

<table>
<thead>
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<th>Age, y</th>
<th>INR</th>
<th>Abnormal PTT or Other Medication†</th>
<th>Reason for Warfarin Therapy</th>
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Abbreviations: CABG, coronary artery bypass graft; DVT, deep vein thrombosis; ERM, epiretinal membrane; INR, international normalized ratio; MP, membrane peeling; PE, pulmonary embolism; PPL, pars plana lensectomy; PPV, pars plana vitrectomy; PTT, partial thromboplastin time; PVD, posterior vitreous detachment; RD, retinal detachment; SB, scleral buckling; SO, silicone oil; SOR, silicone oil removal; TRD, tractional retinal detachment; VH, vitreous hemorrhage.

* Group B includes patients with INRs of 1.50 to 1.99, indicating borderline therapeutic levels of anticoagulation.

† The values of PTT are expressed as seconds.

Table 3. Characteristics of Group T*

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<th>Age, y</th>
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Abbreviations: DVT, deep vein thrombosis; INR, international normalized ratio; MP, membrane peeling; PPL, pars plana lensectomy; PPV, pars plana vitrectomy; PTT, partial thromboplastin time; RD, retinal detachment; SB, scleral buckling; SO, silicone oil; SOR, silicone oil removal.

* Group T includes patients with INRs of 2.00 to 2.49, indicating therapeutic levels of anticoagulation.

† The values of PTT are expressed as seconds.

The underlying systemic causes requiring warfarin anticoagulation included atrial fibrillation (2 patients), DVT (1 patient), heart transplantation with a prosthetic valve (1 patient), cardiac valve surgery (1 patient), and unknown (2 patients). The preoperative vitreoretinal diagnoses included retinal detachment (6 patients) and retained silicone oil (1 patient). The surgical procedure was pars plana vitrectomy in 6 patients, with associated membrane peeling in 5, scleral buckling in 4, and lensectomy in 1. One patient underwent silicone oil removal by means of pars plana vitrectomy. The surgical technique involved standard 3-port 20-gauge vitrectomy in all of the patients. General anesthesia was used in 3 patients and local infiltrative anesthesia with MAC in 4. Preoperative visual acuity ranged from 20/25 to counting fingers, and postoperative visual acuity ranged from 20/20 to no light perception. The distribution of preoperative and postoperative acuities is shown in Figure 2.

There were no anesthetic complications. No patients in this group developed intraoperative or postoperative hemorrhages.

**GROUP HT**

Twelve patients undergoing 12 vitreoretinal procedures had a mean INR of 2.80 (range, 2.50-3.60). Patients in this group had a mean PT of 29.4 seconds (range, 26.3-36.4 seconds). Six patients had an associated abnormal PTT, with values ranging from 40.2 to 73.4 seconds. Concomitant medications included aspirin in 1 patient and Celebrex in 1. The group included 10 men and 2 women with a mean age of 67 years (range, 42-79 years) (Table 4).

The underlying systemic causes requiring anticoagulation were atrial fibrillation (5 patients), DVT with pul- monary embolism (3 patients), valve replacement surgery (3 patients), and an unspecified arrhythmia (1 patient). The preoperative vitreoretinal diagnoses included retinal detachment in 5 patients (1 of whom had an associated vitreous hemorrhage) and vitreous hemorrhage without retinal detachment in 4 patients (3 of whom had proliferative diabetic retinopathy). One patient with proliferative diabetic retinopathy had iris neovascularization with secondary glaucoma and hy-
phema. Other diagnoses included epiretinal membrane (1 patient), retained lens fragments (1 patient), and macular edema (1 patient). The surgical procedure was pars plana vitrectomy in all 12 patients, with associated membrane peeling in 3, removal of lens fragments in 1, anterior chamber washout in 1, and scleral buckling in 1. The surgical technique was standard 3-port 20-gauge pars plana vitrectomy in 11 patients and 25-gauge vitrectomy in 1. General anesthesia was used in 1 patient, and 11 patients underwent local infiltrative anesthesia with MAC.

Preoperative visual acuity ranged from 20/20 to light perception, and postoperative visual acuity ranged from 20/25 to counting fingers. The distribution of preoperative and postoperative visual acuities is shown in Figure 2.

In this group, there were no anesthetic complications. No patients experienced intraoperative hemorrhagic complications. Postoperatively, 2 patients (16.7%) were noted to have an intraocular hemorrhage. One patient with an INR of 2.68 and a normal PTT underwent surgery for proliferative retinopathy with vitreous hemorrhage. This patient had hemorrhage in the inferior vitreous cavity at 1 week postoperatively, and it spontaneously resolved without therapy over the ensuing 2 months. A second patient with an INR of 2.69 underwent surgery for proliferative diabetic retinopathy with iris neovascularization, hyphema, and vitreous hemorrhage. This patient had vitreous hemorrhage and hyphema postoperatively. It was unclear whether this hemorrhage represented residual or recurrent bleeding. A nasal choroidal detachment was also noted on the first postoperative day; however, it was not determined whether the detachment was hemorrhagic or serous. The hyphema, vitreous hemorrhage, and choroidal detachment resolved spontaneously without additional treatment.

Figure 2. Preoperative and postoperative visual acuity (VA) results following vitreoretinal surgery in patients receiving warfarin therapy with highly therapeutic and therapeutic levels of anticoagulation. CF indicates counting fingers; HM, hand motion; NLP, no light perception.

Warfarin is an anticoagulant typically used in patients with atrial fibrillation, venous thromboembolism, mechanical or diseased heart valves, cardioembolic cerebroischemic events, and acute myocardial infarction. When planning elective surgery, the surgeon must consider the alternatives of maintenance, ie, modification or discontinuation of anticoagulation. It is of singular importance to evaluate the rationale for which the patient is receiving anticoagulation therapy. Patients at low risk of thromboembolic disease include those with a history of DVT after 3 months without high-risk factors, non-valvular atrial fibrillation, or cardiomyopathy without atrial fibrillation. Those at high risk for thromboembolic disease are patients with hypercoagulable states, mechanical valves, DVT with high-risk factors or of recent history, or atrial fibrillation with high-risk factors such as a history of prior thromboembolic episodes, heart failure, left ventricular dysfunction, mitral stenosis, thyroid disease, or age greater than 75 years with a history of diabetes or hypertension.12

There is no current consensus regarding the management of patients undergoing elective surgery while receiving long-term anticoagulation therapy. The primary concern associated with the discontinuation of anticoagulation prior to surgery is the increased risk of thromboembolism and cerebrovascular accident. There is also concern regarding life-threatening rebound hypercoagulability following the abrupt cessation of anticoagulation.53 These concerns need to be weighed against the potential for hemorrhagic complications that may occur during or following surgery.

Maintenance of anticoagulation has been shown to be safe in elective, nonocular surgical procedures including cholecystectomy,9 gastric resection,8 and dental extractions.78

Kallio et al9 studied the risk of hemorrhagic complications related to ocular anesthesia. In a series of 1383 patients undergoing intraocular surgery, 76 patients were receiving warfarin. This study showed no predisposition to hemorrhage associated with either retrobulbar or peribulbar anesthesia.

Current articles concerning the risk of hemorrhagic ocular complications with ophthalmic surgery in patients receiving anticoagulation therapy have mixed results. Some studies10-13 have found an increased risk of bleeding whereas others8,14-25 have not. Most articles9,14,25 suggest that warfarin therapy may be safe in patients undergoing cataract or oculoplastic surgery. In a review of 19 283 cataract procedures, Katz et al18 identified 752 patients receiving warfarin therapy. In this study, there were no ocular hemorrhages among those receiving warfarin, whether treatment was discontinued within 4 days of surgery or not. In a series of 41 patients receiving anticoagulation therapy and undergoing a range of 50 ophthalmic procedures, McCormack et al19 found no significant hemorrhagic complications associated with anesthesia or surgery. Gainey et al10 also reviewed the outcomes of 50 patients receiving warfarin therapy and undergoing ocular surgery. There was no significant
difference in hemorrhagic complications observed among patients in whom warfarin therapy was continued and those in whom it was discontinued. In a review of patients undergoing cataract surgery, Jonas et al25 found that 21 patients receiving systemic anticoagulation with warfarin sodium (Coumadin) had no increased risk of intraoperative or postoperative hemorrhage.

The existing literature regarding the safety of vitreoretinal procedures in patients in whom aspirin therapy or warfarin anticoagulation is maintained is limited. Flaxel and Blach26 described 3 patients treated with aspirin who had INRs ranging from 1.28 to 1.41 were associated with postoperative hemorrhage but required no additional surgery. There were 19 patients with INRs of 2.00 or greater who underwent 19 vitreoretinal procedures. In this group, there were no intraoperative hemorrhagic complications. Two patients (10.5%) with INRs of 2.68 and 2.69 experienced postoperative hemorrhagic complications. The complications in both patients resolved spontaneously, requiring no additional surgery. It is noteworthy that among the 4 patients with postoperative hemorrhagic complications, 1 had an elevated PTT of 55.3 seconds and another was receiving concurrent aspirin therapy.

Our surgical technique for these patients was identical to that used in patients who did not receive anticoagulation therapy. Meticulous bipolar diathermy was used to control bleeding during the initial exposure of the globe and during isolation of muscles in those patients undergoing scleral buckling in addition to vitrectomy. Scleral buckling procedures, especially those involving encirclement, require considerably more dissection with the potential for greater intraoperative bleeding. In the series by McDonald,27 1 patient developed subretinal hemorrhage in the course of scleral buckling. Dissection of retinal fibrovascular proliferation was accompanied by intracocular diathermy. It is possible that the postoperative hemorrhages seen in our patients were related to bleeding from sclerotomies or incisions into fibrovascular proliferative stalks. However, no such bleeding occurred intraoperatively.

Subretinal hemorrhage is a known complication of external drainage during scleral buckling procedures. In the series by McDonald,27 1 patient developed subretinal hem-
orrhagic complications.

Clooxygenase 2 therapy developed new postoperative hem-

platelet function. No patients in our series receiving cy-
tive nonsteroidal anti-inflammatory drugs may lead to

gery was performed while maintaining warfarin

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selection bias. Our study did not randomize patients

had therapeutic levels of warfarin anticoagulation. The

date of vitreoretinal surgical procedures in patients who

To our knowledge, this is the single largest study to
date of vitreoretinal surgical procedures in patients who

had therapeutic levels of warfarin anticoagulation. This

risk is increased by multiple mechanisms, including in-
terference with platelet function through inhibition of
cyclooxygenase 1. The use of cyclooxygenase 2–selective
nonsteroidal anti-inflammatory drugs may lead to fewer
complications, as these agents do not interfere with

platelet function. No patients in our series receiving cy-
clooxygenase 2 therapy developed new postoperative hem-

orrhagic complications.

CONCLUSIONS

To our knowledge, this is the single largest study to
date of vitreoretinal surgical procedures in patients who

had therapeutic levels of warfarin anticoagulation. The

study is limited in that it was conducted in a retrospec-
tive fashion, the sample size was small, and there was

no control group. Studies such as this may suffer from

selection bias. Our study did not randomize patients

into groups for whom warfarin therapy was continued

vs those for whom it was discontinued. This article is

the result of an observational study to determine the

risk of hemorrhage in a group of patients for whom sur-

gery was performed while maintaining warfarin

therapy. Additionally, we were unable to collect data

regarding whether the patients ingested herbal supple-
ments known to have an anticoagulation effect or to

potentiate the effects of warfarin anticoagulation. However, it would seem logical that the concomitant
use of such supplements would increase rather than
decrease the risk of intraoperative or postoperative
hemorrhage and would be unlikely to skew results
toward fewer hemorrhagic complications.

Our findings suggest that many patients may safely
undergo vitreoretinal surgery while maintaining ther-
apeutic levels of warfarin anticoagulation. In our series,

no patient had an intraoperative hemorrhagic complica-
tion. Four eyes (7.0%) experienced postoperative hem-

orrhages that resolved spontaneously without persistent visual sequelae or the need for supplemental surgery.

The ultimate visual results for our patients were quite
favorable (Figure 1 and Figure 2). Based on these find-
ings, when caring for patients in whom the systemic

risks of cessation of anticoagulation therapy may be sub-

stantial, ophthalmic surgeons may wish to consider

undertaking vitreoretinal procedures while maintaining
anticoagulation therapy. Anesthetic and surgical tech-
niques may need to be modified or adjusted to avoid

maneuvers thought to increase the risk of hemorrhage.

The decision to withhold, modify, or continue anti-
cogulation should be individualized, taking into consider-

ation the patient’s medical history, systemic findings,

and the specific surgical procedure required for manage-
ment of the underlying vitreoretinal abnormality. Con-

sulation with the physician responsible for monitoring

the patient’s anticoagulation is prudent. Finally, such

patients must be fully informed of the risks involved

with either maintenance or discontinuation of antico-

agulation therapy.

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