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The Impact of Uninterrupted Warfarin on Hand and Wrist Surgery

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Abstract

Purpose—To determine the impact of uninterrupted use of warfarin on hand and wrist surgery.

Methods—This single-center, prospective cohort trial enrolled adult patients undergoing hand and wrist surgery. Between May 2009 and August 2014, 47 surgical patients on uninterrupted warfarin (50 procedures) were enrolled and matched as a group by age and procedure type to 48 surgical patients (50 procedures) who were not prescribed warfarin. Complications, defined as bleeding, infection, or wound dehiscence requiring reoperation, were recorded for each group. Surgical outcome measures comprised objective findings impacted by surgical site bleeding (i.e., ecchymosis extent, hematoma presence, 2-point discrimination) and standardized patient-rated assessments (QuickDASH, visual analog scales: pain and swelling). Data were collected preoperatively and at 2 and 4 weeks postoperatively. Statistical analyses contrasted complications and outcomes data between the patient groups.

Results—One procedure (2%, 95% CI:0–11%) in a patient taking warfarin was complicated by hematoma requiring reoperation secondary to an elevated postoperative International Normalized Ratio=5.4. There were no complications among controls (0%, 95%CI:0–7%). At 2 weeks postoperatively, patients on warfarin more frequently had hematomas (28% vs 10%) and demonstrated greater extent of ecchymosis from the surgical incision (50mm vs 19mm). At 4 weeks, no differences in hematoma presence or extent of ecchymosis existed between the groups. The incidence of transiently elevated 2-point discrimination was not different between the groups (10% warfarin, 6% controls). Visual analog scores for pain and swelling were not significantly different between the groups at any time. Differences in QuickDASH scores between the groups never exceeded a minimal clinically important difference.

Conclusions—Uninterrupted use of warfarin in patients undergoing surgery of the hand and wrist was associated with an infrequent risk of bleeding complication requiring reoperation.

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Increased rates of hematoma and ecchymosis in patients taking warfarin normalized by 4 weeks postoperatively.

Level of Evidence—II Therapeutic

Keywords

anticoagulation; hand; surgery; warfarin; wrist

INTRODUCTION

Warfarin is one of the most common anticoagulant medications used in North America, with over 23 million prescriptions annually.¹ Highly effective in the prevention of thromboembolic events, warfarin indirectly inhibits the activation of vitamin K dependent factors through blockade of the enzyme vitamin K epoxide reductase.² Vitamin K dependent factor inhibition reduces both clot formation (thrombosis) and migration (embolization).² In patients with nonvalvular atrial fibrillation, the rate of thromboembolism averages 4.5% per year but can be as high as 12% in patients with a previous history of cerebral embolism.^{3–6} Anticoagulation therapy not only reduces the risk of stroke by 66% but also decreases the severity and improves the functional outcome should a stroke occur.^{3,7} Mechanical heart valves impart a thromboembolism risk averaging 8% each year. This risk is reduced by 75% with oral anticoagulation.⁸ In patients with an acute episode of venous thromboembolism, anticoagulation therapy reduces the risk of reoccurrence by approximately 80%.⁸

Approximately 10% of patients receiving daily warfarin therapy will require an invasive surgical procedure each year.⁹ Preparation for a surgical procedure is the most common reason for temporary interruption of anticoagulant medication.¹⁰ Safe continuation of anticoagulation therapy has been documented in patients undergoing dermatologic surgery, endoscopic gastrointestinal surgery, and ophthalmologic surgery.^{11–13} Anticoagulation therapy is frequently discontinued for major abdominal surgery and large joint surgery.² It is unclear exactly where hand and wrist surgery falls along the spectrum in terms of bleeding risk when performed while continuing anticoagulant medication. The temporary perioperative interruption of anticoagulant medications poses a substantial risk by increasing the risk of a thromboembolic event both during the period of cessation and potentially beyond.^{10,14,15} In addition, the unintentional prolonged discontinuation of warfarin therapy is twice as likely in patients in whom the medication was stopped during the perioperative period.¹⁶ Therefore, the risks of therapy continuation must be weighed against the risks of discontinuation.

This prospective cohort study was performed to assess the impact of the perioperative continuation of warfarin in patients undergoing surgery of the hand and/or wrist. Our working hypothesis was that complications would remain rare despite the use of warfarin considering prior trials demonstrating minimal complications after hand surgery without interrupting antiplatelet medications and 3 published investigations (2 retrospective) reporting safe continuation of perioperative warfarin for hand surgery.^{17–20}

MATERIALS AND METHODS

This prospective cohort study was approved by our institutional review board. From May 2009 through August 2014, all adult patients (>18 years) who underwent surgery of the hand or wrist by 1 of 5 hand-fellowship trained orthopedic surgeons at a single tertiary center were eligible for enrollment. Prospectively identified comparative groups were defined according to use of warfarin. Inclusion in the warfarin cohort required patient-reported consistent use of the anticoagulant medication warfarin with or without additional antiplatelet therapy. Patients reporting no intake of anticoagulant or antiplatelet medication were enrolled as controls. Control patients were undergoing hand and wrist surgery by the same surgeons during the study period. They were a non-consecutive sample due to competition with other ongoing investigations. As a group, the control patients were identical to the patients taking warfarin except without a need for anticoagulation. Written informed consent was obtained for all patients during preoperative office visits. Criteria for exclusion from both anticoagulant and control groups included a lack of English proficiency, inconsistent use of anticoagulant medication, perioperative discontinuation of an anticoagulant medication, surgery proximal to the distal radius metaphysis, and pregnancy. Patients considered to have inconsistent use of anticoagulant medications included anyone who reported taking warfarin less frequently than prescribed or missing doses at least weekly. Infrequently, patients mistakenly discontinued anticoagulant medication perioperatively, and they were excluded from the study. Patients taking daily warfarin were required to have an International Normalized Ratio (INR) <3.5 at the time of surgical indication when study enrollment was performed. Our IRB approval did not include reversing patients with INR values >3.5 at presentation. Although the situation did not arise, we would have also excluded any patient after enrollment if they had an INR >3.5 on the day of surgery. We did not study surgical procedures in the forearm or elbow because of a perceived increased risk of bleeding complications in surgeries that require dissection through muscle. Our group has routinely required discontinuation of anti-thrombotic medications due to this perceived risk during forearm or elbow surgery. The use of non-steroidal anti-inflammatory medication was not considered in patient classification or study eligibility due to widespread use universally unrelated to anti-thrombotic effects and difficulty by patients in accurately reporting dosage consumed.

Fifty procedures were performed on 47 patients taking warfarin during the perioperative period. (Table 1) The warfarin cohort comprised 25 men and 22 women with an average age of 67 years (range, 43–92). Thirty patients took isolated warfarin therapy while 17 were prescribed warfarin combined with aspirin. The average preoperative INR in patients treated with warfarin was 2.3 (SD ± 0.96). Indications for warfarin therapy included coronary artery disease (5), atrial fibrillation (21), mechanical heart valve, (5) and deep vein thrombosis (16). The control cohort comprised 48 patients (50 procedures), 17 men and 31 women with an average age of 63 years (range, 44–86), was used for comparison. This control cohort was selected from a population of 82 enrolled controls. Controls were matched to anticoagulated patients based on patient age and procedure type (bone versus soft tissue). As controls were more often younger patients, the selection of the final set of controls used the

oldest available patients to match the group of patients taking warfarin according to the percentage of bony procedures.

During this study, we continued our division's standard practice that existed prior to this study by instructing patients to continue all anti-thrombotic medications without perioperative discontinuation for wrist and hand surgery. Tourniquets were used during all surgeries. The timing of deflation (i.e., deflation prior to or following skin closure and dressing application) was determined by the treating surgeon and was not affected by patient study participation and/or use of anticoagulation. The tourniquet was deflated prior to skin closure for hemostasis in 16/50 procedures in patients taking warfarin and in 14/50 procedures in those not taking warfarin. Only local anesthetics without epinephrine were injected at the surgical sites.

Data Collection

Study data were collected at the preoperative visit (baseline) and at 2 and 4 weeks postoperatively. Identical data were recorded for the entire cohort. All study-related physical examination measurements and patient-rated outcome measures were collected by a certified hand therapist who was blinded to the patients' anticoagulant status (warfarin vs control) to minimize bias.

Complications were recorded for each cohort. A complication was defined as a hematoma or surgical site bleeding, surgical site infection, or wound dehiscence requiring reoperation. These complications were chosen as they could be reasonably attributed to greater surgical site bleeding. We quantified only those complications requiring reoperation as these were felt to represent clinically relevant wound complications imparting a substantial morbidity to the patient. We monitored patients for clinically apparent thromboembolic events during the first 4 weeks after surgery.

Physical examination measures included preoperative and postoperative static 2-point sensibility on the fingertips. This was measured based on the rationale that postoperative swelling or hematoma could produce quantifiable nerve dysfunction. Relevant change in 2-point discrimination was defined as an increase in 2mm from preoperative value to the first postoperative visit. The presence of a visible hematoma (present/absent) and greatest extent of continuous ecchymosis from the surgical incision (mm) were measured at the 2 and 4-week postoperative visit.

All patient-rated measures were self-administered in paper form. The Quick Disability of the Arm, Shoulder, and Hand (QuickDASH) was completed both pre- and postoperatively. The QuickDASH was administered to determine if any differential hematoma incidence or ecchymosis extent was associated with a change in patient-rated disability. At each postoperative visit, patients also completed visual analog scales (VAS) for hand pain and swelling where a value of 0 represented no pain or swelling and a value of 10 represented extreme pain or swelling.

Statistical Analysis

The incidence of complications was determined for each cohort of patients (warfarin and control). Ninety-five percent confidence intervals were calculated to quantify the precision of the estimated complication incidence.

Descriptive statistics were produced to characterize the warfarin and control cohort demographic data. All outcome data were contrasted between warfarin and control patients. The unpaired 2 sided Student t-test contrasted continuous variables, and categorical variables were assessed by the Fisher exact test. Missing data were excluded. Significance was set at $P < 0.05$. We did not correct for multiple statistical testing, which increases the risk of type 1 error, as our goal was to detect and present any indication of increased risk associated with operating on patients taking warfarin.

An *a priori* sample size estimation was performed. We set $\alpha = 0.05$ and $\beta = 0.2$ before considering our outcomes of interest. We calculated the number of procedures to determine incidence of complications with reasonable precision (95% CI $\pm 5\%$), to detect a minimally important QuickDASH difference between groups of 14 (SD ± 14) (17 procedures per group needed) and 2 point differences on VAS scales (SD ± 2.5) (26 procedures per group needed).^{21,22} Based on the calculation that would require the most patients, we determined that we needed 46 procedures within each group assuming the incidence of complications to be low.

Qualitative subgroup analyses were performed without significance testing due to insufficient statistical power.

RESULTS

There were no complications (hematoma, infection, or wound dehiscence) requiring reoperation in the control cohort (95% CI 0–7%). In patients taking daily warfarin, there was one (2%: 95% CI 0–11%) wound complication requiring reoperation. That patient developed a hematoma and acute carpal tunnel syndrome 4 days following a proximal row carpectomy performed for a chronic lunate dislocation. Preoperatively his INR level was 2.1. The patient presented on the 4th postoperative day with increasing pain, swelling, and paresthesias in the median distribution. Repeat INR at that time was 5.4. The patient underwent partial reversal of his anticoagulation and emergent hematoma evacuation and carpal tunnel release. The patient experienced no long-term sequela and had normal 2-point discrimination (< 5 mm) at his 4-week postoperative visit. Surgeons prescribed antibiotics for potential postoperative infections in 3/50 procedures in patients taking warfarin (1 wound erythema, 1 serous drainage, 1 pin site erythema at 4 weeks) and in 2/50 procedures in controls (1 wound erythema, 1 wound induration). Each of these presumed infections was treated without culture and resolved with oral antibiotics.

During this study, no patient taking warfarin sustained a postoperative thromboembolic event.

Table 2 presents the comparative outcome data for the warfarin and control cohorts. The presence of hematoma and extent of ecchymosis were increased in patients taking warfarin at 2 weeks (OR 3.5 for hematoma presence, 95% CI 1.05–13.45). By 4 weeks postoperatively, these differences resolved. The QuickDASH scores were not different at baseline or at 2 weeks postoperatively between groups. Control patients demonstrated statistically superior QuickDASH scores at 4 weeks although the difference failed to exceed a clinically relevant difference. Patient ratings of pain and swelling were similar for each patient group at both 2 and 4 weeks postoperatively.

Table 3 presents the subgroup data of patients taking warfarin (N = 32) compared to patients taking combined warfarin and aspirin (N = 18). Table 4 details the outcomes of warfarin patients undergoing soft tissue procedures (N = 38) compared to bony procedures (N = 12). For each of these subgroup analyses, the incidence of hematoma formation were within 10%. Differences in QuickDASH scores only exceeded the minimal clinically important difference (14 points) at 2 weeks when patients following bony procedures reported more disability than those having undergone soft tissue surgery.²¹ Both VAS scores were within 2 points at all times.²¹

One patient on warfarin was excluded from the study but deserves mention. She presented with a displaced distal radius fracture while chronically taking warfarin following a cerebral vascular accident. Her INR at presentation was 6.1, which caused exclusion. Guided by her internist, she was partially reversed to an INR of 2.3 before fracture fixation and carpal tunnel release. On postoperative day 8 her INR increased to 3.9 and she developed a hematoma in the distal forearm and experienced elevated 2-point discrimination. She was not taken back to the operating room and healed the fracture but only partially recovered the lost sensibility after 6 months.

DISCUSSION

We found that the perioperative continuation of warfarin is reasonable in patients undergoing surgery of the hand and/or wrist. The increased incidence of hematoma formation and extent of ecchymosis associated with warfarin use at 2 weeks postoperatively resolved by 4 weeks. Anticoagulated patients reported no clinically relevant difference in pain, swelling, or upper extremity disability compared to controls.²¹

Our finding of infrequent postoperative bleeding complications attributable to warfarin use is consistent with prior retrospective studies. Smit et al. reported no complications following open carpal tunnel release (n=9) and fasciotomy for Dupuytren contractures (n=13) in patients taking warfarin.¹⁸ A second series reported 2 hematomas that resolved with nonoperative treatment after 55 procedures (soft tissue and bony) in 39 patients on warfarin.¹⁷ In one prospective cohort, 57 operations (49 soft tissue, 8 bony) were completed without interruption of warfarin (INR<3.0).²⁰ Of these 57 procedures, 5 had qualitative excessive bruising postoperatively, and one wound became infected. Excessive intra-operative bleeding and postoperative hematomas were not encountered. We believe our data substantiate published findings and expand on available evidence by providing real time

quantitative data collection (objective and patient-rated measures) with assessment against a comparative group of control patients.

Perioperative warfarin use is associated with some risk of increased surgical site bleeding that must be weighed against the risk of systemic thromboembolic event if discontinued. An analysis of 2197 ischemic strokes revealed that 5% occurred within 60 days of stopping an anti-thrombotic medication, and in 54% of these cases the medication was warfarin.²³ In a multicenter prospective trial involving 1683 episodes of temporary interruption in warfarin treatment for surgery, the 30-day stroke/systemic embolism/myocardial infarction/death rate of 0.7%, compared to an overall stroke rate in the study population of 2.2% per year.^{10,14,15}

Not only are the protective benefits lost with warfarin therapy cessation, but a transient rebound hypercoagulable state may occur.²⁴ This rebound effect, combined with the prothrombotic post-surgical state, may increase an individual's risk of thromboembolism even beyond that observed in the uncoagulated at-risk individual. Although our series includes a limited number of surgical procedures, no thromboembolic complications occurred.

In this study, there was one bleeding complication in an enrolled patient taking warfarin. The patient required emergent revision surgery postoperative day 4 after proximal row carpectomy when his INR had increased to 5.4. This patient had used warfarin for 6 months preoperatively. We could not determine a reason why his INR increased, but he may have had less time to establish a stable medication dose than many of our patients on chronic warfarin. As was done for this patient, we recommend repeat examination when any postoperative patient taking warfarin experiences a sudden increase in pain or swelling. A second complication occurred in a patient who was not enrolled (presentation INR>3.5) also occurred in the setting of elevated postoperative INR values. Her case is illustrative of the risk encountered in patients with fluctuating INR values. In the 6 months prior to surgery, she had 3 INR values >3.5 (range 1.1–4.8). Although she was monitoring her INR daily after surgery, her levels continued to fluctuate, and we believe that resulted in her surgical site complication. These complications highlight the importance of vigilant monitoring and careful INR control in patients taking warfarin.

There are several limitations to our study. Despite similarity between the warfarin and control patients with regard to age and type of procedure performed (bony versus soft tissues), this was not a randomized control trial, and unrecognized inequalities between the groups may have impacted the results. The management of the tourniquet was not standardized. A tourniquet was used for all procedures, but the decision to deflate the tourniquet prior to closure or following application of the dressing varied between surgeons. The inherent risk of bleeding varies with the type of surgical procedure performed. Seventy-six percent of procedures performed in the warfarin cohort and 78% of the procedures in controls were isolated to soft tissues. While procedure type did not impact outcome in this study, the results are limited by a relative underrepresentation of bony procedures, which affects the ability to generalize our data to all hand and wrist surgery. Our results do not generalize to all anti-thrombotic medications. The effect of warfarin is reversible, which increases our comfort with perioperative use. Some anti-thrombotic medications are not

reversible, which imparts additional surgical risk that prevents us from attempting surgery without their discontinuation.

Despite the limitations, this study provides clinically relevant data. Surgeons managing perioperative anticoagulants must balance the risk of bleeding with the risk of thromboembolism. According to our data, surgery of the hand and wrist, including both soft tissue and bone procedures, can be performed in patients who are taking warfarin with a preoperative INR < 3.5 with unlikely chance of bleeding complication requiring reoperation. However, warfarin requires monitoring as its anticoagulant effect may be potentiated by multiple factors including illness and changes in diet. Therefore, we recommend caution when continuing perioperative warfarin in patients who have not demonstrated stable INR values or who have recently started warfarin therapy.

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Table 1

Surgical procedures performed in control patients and patients taking warfarin.

	Warfarin Patients	Control Patients
<u>Soft tissue</u>	Total Procedures: 50	Total Procedures: 50
Open carpal tunnel release	27	21
Trigger finger release	2	8
Excision of mass or ganglion	5	0
Tendon transfer, repair, or tenosynovectomy	4	3
First dorsal compartment release	0	3
Wrist arthroscopy with TFCC debridement	0	1
Other	0	3
Total	38	39
<u>Bone Involvement</u>		
Open reduction and internal fixation distal radius fracture	3	3
Wrist arthrodesis	0	3
Total wrist arthroplasty	0	1
Proximal row carpectomy	1	0
Scapholunate ligament repair with radial styloidectomy	2	0
Thumb CMC arthrodesis or interpositional arthroplasty with trapezium excision	1	3
Open reduction and internal fixation or fusion of carpal bone or phalanx	2	1
Amputation (digit)	2	0
Excision osteophyte (digit)	1	0
Total	12	11

Table 2

Outcome data according to patient group.

	Warfarin (n=50)	Controls (n=50)	P value
Age ($\pm$ SD)	67 $\pm$ 14	63 $\pm$ 8	0.08
% Bony procedures	22%	22%	1.00
Increased 2PD*	10%	6%	0.46
Hematoma (%)			
2 Weeks	28%	10%	0.04
4 Weeks	0%	4%	0.50
Ecchymosis (mm)			
2 Weeks	51 $\pm$ 98	19 $\pm$ 41	0.04
4 Weeks	2 $\pm$ 8	4 $\pm$ 20	0.58
QuickDASH			
Preoperative	43 $\pm$ 25	41 $\pm$ 23	0.69
2 Week	49 $\pm$ 24	45 $\pm$ 21	0.34
4 Week	41 $\pm$ 23	28 $\pm$ 20	0.01
VAS Pain			
2 Week	2.7 $\pm$ 2.6	2.7 $\pm$ 2.3	0.95
4 Week	2.9 $\pm$ 2.6	2.9 $\pm$ 2.6	0.41
VAS Swelling			
2 Week	3.4 $\pm$ 2.9	2.9 $\pm$ 2.6	0.38
4 Week	2.9 $\pm$ 2.6	2.5 $\pm$ 2.3	0.43

*
2PD: 2-point discrimination

Table 3

Outcome data for patients on isolated warfarin versus combined warfarin and aspirin.

	Warfarin (n=32)	Warfarin + Aspirin (n=18)
Age ($\pm$ SD)	64 $\pm$ 14	73 $\pm$ 11
% bony procedures	9 (28%)	2 (11%)
Increased 2PD	2 (6%)	3 (17%)
Hematoma (%)		
2 Weeks	8 (26%)	5 (28%)
4 Weeks	0	0
Ecchymosis (mm)		
2 Weeks	30 $\pm$ 54	25 $\pm$ 37
4 Weeks	3 $\pm$ 11	1 $\pm$ 3
QuickDASH		
Preoperative	47 $\pm$ 26	37 $\pm$ 24
2 Week	52 $\pm$ 22	44 $\pm$ 27
4 Week	40 $\pm$ 23	40 $\pm$ 25
VAS Pain		
2 Week	3.0 $\pm$ 2.8	2.6 $\pm$ 2.4
4 Week	3.2 $\pm$ 2.7	2.3 $\pm$ 2.2
VAS Swelling		
2 Week	3.8 $\pm$ 2.5	2.1 $\pm$ 2.9
4 Week	2.9 $\pm$ 2.9	1.9 $\pm$ 1.8

Table 4

Outcome data according to procedure type for patients taking warfarin.

	Soft Tissue (n=39)	Bony (n=11)
Age ($\pm$ SD)	71 $\pm$ 11	55 $\pm$ 15
Increased 2PD	5 (13%)	0
Hematoma (%)		
2 Weeks	10 (26%)	4 (36%)
4 Weeks	0	0
Ecchymosis (mm)		
2 Weeks	28 $\pm$ 38	41 $\pm$ 84
4 Weeks	0	0
QuickDASH		
Preoperative	40 $\pm$ 25	56 $\pm$ 23
2 Week	46 $\pm$ 24	62 $\pm$ 21
4 Week	37 $\pm$ 23	49 $\pm$ 25
VAS Pain		
2 Week	2.8 $\pm$ 2.8	3.2 $\pm$ 2.1
4 Week	3.0 $\pm$ 3.0	3.3 $\pm$ 2.1
VAS Swelling		
2 Week	3.0 $\pm$ 3.0	4.5 $\pm$ 1.7
4 Week	2.9 $\pm$ 2.8	2.9 $\pm$ 3.1