

Management of Warfarin Therapy Perioperatively

Betty Anne Johnson, MD, PhD

Introduction

Warfarin therapy is used to treat a wide variety of thromboembolic disorders and currently is used by more than one million persons. The risks versus benefits of stopping anticoagulation therapy in the preoperative period will be discussed in this chapter and guidance given to the management of these patients perioperatively. Since there are few randomized, prospective trials to guide these management decisions, many of these recommendations will be given in terms of “general consensus” with references provided.

General Considerations

The most common thromboembolic disorders treated by warfarin therapy include atrial fibrillation, the presence of a mechanical heart valve, venous thromboembolism and hypercoagulable states. If anticoagulant therapy is interrupted to allow these patients to undergo surgery, the risk of thromboembolism increases variably depending upon the underlying disorder, the type of surgery and the acuteness of the episode of venous thromboembolism. On the other hand, patients who undergo surgery while on anticoagulation may experience excessive bleeding at a rate of about 3%.¹

Risk of Bleeding by Procedure

After stopping warfarin therapy, the international normalized ratio (INR) will drop to 1.5 within four days in nearly all patients.² Most types of major surgery, including surgery in which a body cavity is entered, can be safely performed with an INR \leq 1.5.¹⁻⁶ For neurosurgery, however, most neurosurgeons recommend that the INR be normal prior to surgery.¹

Table 1 shows some minimally invasive surgeries that may be performed safely while patients remain anticoagulated.³

Anticoagulation and Procedures:

The following precautions should be followed in administering anesthesia to the anticoagulated patient⁷:

1. Oral or intravenous anesthesia is preferred to intramuscular or subcutaneous routes.
2. It is safer to insert a central venous catheter through the brachial vein in the antecubital

fossa than through the internal jugular or subclavian vein.

3. Laryngoscopy and tracheal intubation should ideally be atraumatic.

4. Nasogastric tubes should be avoided because of the high incidence of epistaxis.

To avoid bleeding and neurologic complications when a spinal or epidural catheter is inserted or removed in an anticoagulated patient, the following recommendations should be followed:

1. Anticoagulation should be completely reversed before epidural or spinal catheter placement or removal. Waiting at least 3 hours after discontinuing standard heparin (15 hours in the case of low-molecular weight heparin (LMWH)) should assure full reversal.
2. Standard heparin or LMWH may be restarted 2 hours after catheter placement or removal. If bleeding occurs during insertion or withdrawal of the catheter, re-anticoagulation should be further delayed.

Risk of Thrombosis After Stopping Anti-coagulation:

Risk of thrombosis after stopping anticoagulation varies depending upon the pro-thrombotic effect of surgeries, possible rebound hypercoagulability after stopping warfarin, and the nature of the underlying thromboembolic disorder. Although stopping warfarin may increase certain clotting factors⁸, there has been no clinical evidence that this increases thrombotic complications.⁹

Table 2 shows thrombosis risks (high versus low) related to various thromboembolic disorders.

After resuming warfarin therapy, it takes about three days for the INR to reach 2.0.¹⁰ If warfarin is withheld for four days prior to surgery and restarted as soon as possible after surgery, the patient should have a subtherapeutic INR for about two days before and two days after surgery.¹

For the patient with the conditions shown in Table 3, the estimated risk of thrombotic events during the perioperative period can be calculated from the annualized risk of thrombotic events if not anticoagulated.³

Table 1: Minimally Invasive Surgery and Bleeding Risk in Anticoagulated Patients

Surgery Type	Can patient safely remain anti-coagulated?	Comment
Ophthalmic including cataract extraction, trabeculectomy, vitreoretinal surgery	Yes	Complex lid, lacrimal or orbital surgery may increase bleeding risk.
Dental procedures including hygiene, simple extractions, restorations, endodontics, prosthetics	Yes	Multiple tooth extractions or more extensive surgeries should be performed at an INR \leq 1.5. Tranexamic acid mouth washes may decrease excessive bleeding if it occurs.
TURPs (transurethral resection of the prostate)	Controversial	If the patient remains anti-coagulated, some urologists believe that TURPs should be performed using laser techniques only.
Endoscopy with or without biopsy	Controversial	Most gastroenterologists stop anti-coagulation before upper or lower endoscopy.
Dermatologic procedures	Probably	More study needed
Podiatric procedures including nail avulsions, phenol matrixectomies	Probably	More study needed

Table 2: Thrombosis Risk Perioperatively³

<u>High</u>	<u>Low</u>
Mitral mechanical valves	Newer (second-generation) aortic mechanical valve
Older (first-generation) aortic, mechanical valves (Ball, Bjork-Shiley, Lillehei-Kaster)	Atrial fibrillation without multiple risk factors for stroke
Atrial fibrillation plus a history of stroke or multiple risk factors for stroke	Deep venous thrombosis treated for > 1 month
Deep venous thrombosis diagnosed within the last month	
Hypercoagulable state plus recent thrombosis or history of life-threatening thrombosis	

Table 3: Risk of Thrombotic Events During Lapses in Anticoagulation

Condition	Risk of Thrombotic Event/Yr	Risk of Thrombotic Event/Day	Risk of Thrombotic Event in the Perioperative Period (4-6 days)
Atrial fibrillation	1-20%*	0.003%-0.05%	0.012%-0.3%
Mechanical prosthetic heart valves	8-22%	0.02%-0.06%	0.08%-0.36%
Venous Thromboembolic Disease			
1 st month		1%	4-6%**
2 nd -3 rd month		0.2%	0.8-1.2%
> 3rd month		0.04%	0.16-0.24%
Hypercoagulable states [^]	Unknown+	Unknown+	Unknown+

*Varies with the number of co-existent risk factors for thromboembolism

****Because of the high risk of recurrent venous thromboembolism within the first month, all elective surgeries should be avoided in the first month after venous thromboembolism.**

[^]Includes factor V Leiden mutation, prothrombin gene mutation, anticardiolipin antibody, protein C deficiency, protein S deficiency or antithrombin III deficiency

+May have increased risk for thromboembolism while briefly off anticoagulants if there has been a recent thrombotic event, recurrent thrombosis or a life-threatening thrombotic complication.

Summary Recommendations³:

1. For patients undergoing minimally invasive procedures (see Table 1) with low bleeding risk:

- a. If the INR is at the low end of the therapeutic range (ie: 2.0), the surgery can be safely performed.
- b. If the INR is at the high end (e.g.3.0), hold warfarin for 1-2 days and then restart the evening after the procedure.
- c. Delay the restart if bleeding complications occur during the procedure.

2. For patients with a low thrombosis risk undergoing procedures (see Table 2) with a high bleeding risk:

- a. Stop warfarin 4-5 days prior to the procedure.
- b. Check the INR on the morning of the procedure.
- c. If the INR > 1.5, delay the procedure by 1-2 days and reassess the INR prior to surgery.
- d. If the surgery must be performed urgently, consider fresh frozen plasma. You may also give 0.5 to 1.0 mg vitamin K orally or subcutaneously. (Avoid higher doses of vitamin K or resistance to re-anticoagulation may occur.)
- e. Restart warfarin after the procedure.
- f. If the patient was being anticoagulated for DVT and is at bed rest postoperatively, heparin as well as warfarin should be started after the procedure when the surgeon judges the bleeding risk to be acceptable. Heparin should be continued until the INR is 2.0 or the patient is ambulatory.

3. For patients with a high thrombosis risk (see Table 2) undergoing procedures with a high bleeding risk:

- a. Avoid elective surgery within the first month of a venous thromboembolic event.
- b. Stop warfarin 4-5 days prior to surgery.

- c. When the INR is subtherapeutic, begin IV heparin (requires hospitalization and partial thromboplastin time 6 hours after heparin injection should be approximately 2x control) or adjusted dose subcutaneous heparin (dose heparin every 12 hours)
- d. Discontinue IV heparin 2 hrs prior to procedure; discontinue adjusted dose subcutaneous heparin 12 hours prior to procedure.
- e. Restart heparin plus warfarin after surgery when the bleeding risk is judged to be acceptable by the surgeon. Discontinue heparin when the INR is therapeutic.

It is important to remember that the absolute risk of thromboembolism associated with a few days of perioperative subtherapeutic anticoagulation is generally very low, while the risk of bleeding associated with postoperative intravenous heparin is often relatively high.¹

4. The role of low molecular weight heparin (LMWH):

The US Food and Drug Administration has approved the use of LMWH for prevention of deep vein thrombosis. LMWH can probably be used safely using the following guidelines¹¹:

1. Give enoxaparin (dosing range = 30 mg every 12 hours to 1 mg/kg every 12 hours).
2. Stop enoxaparin at least 12 hours before the procedure.
3. Restart enoxaparin and warfarin after the procedure when the surgeon judges the risk of bleeding to be acceptable.

You should however be aware that Aventis Pharmaceuticals has sent a warning letter (March 1,2002) to prescribers advising that the use of LOVENOX is NOT recommended for thromboprophylaxis in patients with prosthetic heart valves. Cases of prosthetic heart valve thrombosis have been reported in patients with prosthetic valves who have received enoxaparin for thromboprophylaxis. Some of these cases were pregnant women in whom thrombosis led to maternal deaths and fetal deaths. Furthermore, congenital anomalies have occurred in infants born to women who received enoxaparin during pregnancy. A cause and

effect relationship has not been established nor has the incidence been shown to be higher than in the general population.

References

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