TEN QUESTIONS/ALLIED PROFESSIONALS

# Anticoagulation practice in cardiac electrophysiology


## Julie B. Shea, MS, RNCS

*From Cardiac Arrhythmia Service, Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts.*


**1. What is the most common indication for anticoagulation in electrophysiology?**

*Answer:* Atrial fibrillation (AF) is the most common arrhythmia affecting more than two million individuals in the United States annually. It is an important independent risk factor for stroke. Anticoagulation with warfarin is common practice in patients with paroxysmal, persistent, and permanent AF to help minimize stroke risk. Numerous clinical trials have consistently demonstrated the superiority of adjusted-dose warfarin compared with aspirin or placebo in reducing stroke risk in the AF patient population.[1–8] Patients with lone AF (without structural heart disease) do not necessarily require anticoagulation.

Additional indications for anticoagulation in the electrophysiology (EP) patient population include the following:

- Atrial flutter (same risk factors as for AF)
- After extensive ablation in the left atrium or ventricle
- Upper-extremity deep vein thrombosis (DVT) following device implantation

**2. What are the different types of anticoagulation methods used?**

*Answer:* The most common form of anticoagulation is adjusted-dose warfarin. However, the following anticoagulants also can be used:

- Antiplatelet agents: aspirin (acetylsalicylic acid [ASA]), clopidogrel
- Low-molecular-weight heparin (LMWH)
- Unfractionated heparin (UFH)

**3. What are the key patient education issues?**

*Answer:* Patient education is an integral component of anticoagulation management, which is necessary to maximize compliance and minimize potential complications. Specific topic areas to be covered should include the following:

- Purpose of the medication
- Dosing guidelines
- International normalized ratio (INR) monitoring
- Food and medication interactions
- Reportable signs and symptoms
- Medical alert bracelet

**4. What are the follow-up considerations?**

*Answer:* Careful monitoring of the INR is essential to maintain a therapeutic blood level and prevent potentially catastrophic bleeding or clotting complications. For patients with AF, the typical target INR is 2–3 to prevent thrombus while minimizing the risk of hemorrhage. Dedicated anticoagulation clinics should be used routinely in the management of patients undergoing chronic warfarin therapy.

**5. How should anticoagulation be managed preprocedurally?**

*Answer:* The half-life of warfarin typically is 7 days. The effective half-life ranges between 20 and 60 hours, with a duration of action between 2 and 5 days; therefore, warfarin should be discontinued at least 3 to 4 days prior to the planned procedure to allow time for normalization of the INR. For patients requiring continuous anticoagulation, such as those with a prior history of stroke and/or patients with artificial heart valves, bridging with LMWH typically is used (Figure 1). Administration of subcutaneous LMWH has been established as a feasible method of bridging patients who require uninterrupted anticoagulant therapy, but it has not been systematically evaluated by randomized clinical trials.[9] When considering a patient for thromboprophylaxis with LMWH, several factors should be taken into consideration[10]:

- Type of procedure
- Timeline for the procedure
- Thromboembolic risk
- Hemorrhagic risk
- Weight (obesity)
- Renal function and baseline platelet count (dosage adjustment needed for elevated creatinine)
- Instruction on performing self injections
- Detailed and patient-specific bridging schedule that outlines
  - A. When to stop oral anticoagulation
  - B. When to start and stop LMWH
    1. 12 hours prior to percutaneous procedures
    2. 24 hours prior to device implantation
  - C. Timing of postprocedure INRs
  - D. Contact phone numbers for follow-up care

Low-risk patients with AF who do not require bridging are individuals with lone AF, age less than 65 years, and no


**Address reprint requests and correspondence:** Ms. Julie B. Shea, Cardiac Arrhythmia Service, Cardiovascular Division, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115.

E-mail address: jshea@partners.org.



1547-5271/$ -see front matter



doi:10.1016/j.hrthm.2005.11.015

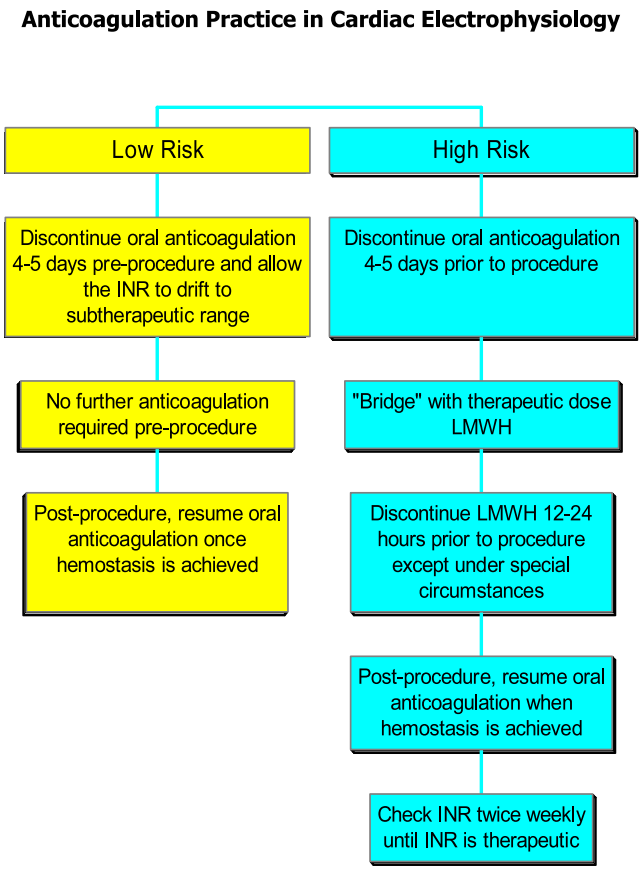


**Figure 1** Brigham and Women's Hospital Anticoagulation Service Critical Pathway for Bridging with LMWH. Piazza et al, Crit Pathways in Cardiolog 2003;2:96-103.

risk factors for stroke, such as a history of hypertension, reduced left ventricular systolic function, diabetes mellitus, or history of thromboembolism or stroke.[10] In these situations, the incidence of embolic stroke in the absence of anticoagulation is less than ~5% per year. In addition, patients with bioprosthetic valves who are not anticoagulated do not require bridging.[10] High-risk patients with any identifiable risk factor for stroke should be bridged with either LMWH or UFH, depending on the patient's clinical situation. Intravenous UFH should be discontinued at least 5 hours prior to the scheduled procedure, whereas the last dose of subcutaneous LMWH should be given 12 to 24 hours prior to the procedure, particularly in patients with impaired renal function.

Recommendations for discontinuation of antiplatelet therapy are similar to those for cardiac surgery. Aspirin can generally be continued safely, but platelet aggregation inhibitors (clopidogrel) should be discontinued, when permissible, for at least 5 days and preferably 7 days prior to the procedure.

**6. How should anticoagulation be used postprocedurally?**

*Answer:* In most instances, anticoagulation can be resumed the evening of the procedure. For patients who have received an implantable device, delaying initiation of anticoagulation with warfarin for 2 to 3 days, when permissible, should be considered to allow for stabilization of the device pocket. Special attention should be paid to those patients requiring UFH, such as those with a mechanical heart valve, to prevent hematoma formation at the site. The measured effect of UFH on the activated partial thromboplastin time (aPTT) is important to patient outcome, and the predominant variable mediating the effect of a given dose of UFH is weight; therefore, it is important to administer the initial dosage of UFH as a weight-adjusted bolus. A 60 to 70 U/kg bolus followed by a maintenance infusion of 12 U/kg/hr (with a maximum 4,000-U bolus and 1,000 U/hr initial infusion for patients weighing more than 70 kg) is recommended. The partial thromboplastin time (PTT) should be monitored closely, targeting a value of 60 to 80 seconds. In addition, a pressure dressing can be applied to the site for 24 hours to reduce the incidence of hematoma. LMWH is generally avoided after device implantation. Either form of heparin is administered along with warfarin until the INR is in the appropriate target range.

## Management of upper-extremity DVT following device implantation

Upper-extremity DVT after device implantation occurs as a consequence of the presence of device hardware within the venous system that results in a reduction or cessation of blood flow. This condition typically manifests clinically as swelling in the upper or entire arm on the side ipsilateral with the device, pain/discomfort, and, later, a superficial venous pattern on the chest. The diagnosis is generally made by patient symptomatology, upper-extremity venous ultrasound, or upper-extremity venogram (typically this diagnostic method is performed during concomitant thrombolysis and/or suction thrombectomy).

Management of upper-extremity DVT involves anticoagulation with warfarin and LMWH (dosed until INR is therapeutic). Patients should be instructed to keep the affected limb elevated as much as possible. A graduated compressed sleeve can be prescribed to reduce limb swelling and discomfort. Pain management should be considered based on the patient's level of discomfort. In some instances, depending on the severity of DVT and the patient's perceived level of discomfort related to arm swelling, a percutaneous interventional procedure (local thrombolysis, suction thrombectomy, venoplasty) can be performed.

**7. What is the common anticoagulation practice after catheter ablation?**

*Answer:* This depends on the type of ablation procedure. At this time, no clinical data on anticoagulation practices after VT ablation are available.

- *AV nodal ablation:* Lifelong anticoagulation with warfarin because the atria remain in fibrillation
- *AF ablation:* Pulmonary vein isolation*
  A. Aspirin 325 mg the morning of the procedure, then 81 mg/day

B. LMWH 1/mg/kg 6 hours after sheath removal, then 0.5 mg/kg bid until INR is therapeutic
C. Resume warfarin the evening of the procedure and maintain for a minimum of 3 months (unless AF recurs, then anticoagulation should be continued indefinitely)

- *Ventricular tachycardia ablation**

| | |
|---|---|
| Good left ventricular function | Poor left ventricular function |
| Small area of ablation (ablation limited to the right ventricle)† | Extensive left ventricular ablation (radiofrequency lines >3 cm) |
| ASA 325 mg/day for 6 weeks† | UFH started 6 hours post procedure |
| | Resume warfarin |
| | LMWH 0.5 mg/kg bid until INR is therapeutic |
| | ASA 81 mg/day |

*Brigham and Women's Hospital protocol (unpublished data)
†Use of ASA is common practice in most centers, but data regarding efficacy are limited

**8. When are there exceptions to anticoagulation?**

*Answer:* Thromboprophylaxis should be avoided in patients who have experienced a prior untoward effect from warfarin use, such as those with gastrointestinal bleeding or hemorrhagic stroke. Heparin is contraindicated in patients with a history of heparin-induced thrombocytopenia (HIT). The risks and benefits of anticoagulation use must be considered for each patient.

**9. How does warfarin interact with commonly used antiarrhythmic medications?**

*Answer:* Warfarin interacts with numerous medications due to both pharmacodynamic and pharmacokinetic effects (Table 1). Warfarin is completely absorbed after oral administration and is metabolized by hepatic microsomal enzymes (cytochrome P450). Drugs can interact with warfarin by means of pharmacodynamic effects (impaired hemostasis, reduced clotting factor synthesis, antagonistic effects [vitamin K]) and/or by heredity resistance.[11] The pharmacokinetic mechanisms for drug interactions are related to enzyme induction, enzyme inhibition, and/or reduced plasma protein binding. Some drugs may interact by more than one mechanism.[11] Elderly patients may exhibit a greater than expected response; therefore, dosage adjustments should be considered in this age group.[11,12]

**10. Are there alternatives to anticoagulation with warfarin?**

*Answer:* Alternative methods of anticoagulation for thromboprophylaxis in patients with AF are under clinical investigation.

- Direct thrombin inhibitors

To date, no superior method of thromboprophylaxis for stroke reduction, compared with warfarin therapy, has been demonstrated.

**Table I** Drug interactions with warfarin

| Medication | Increased INR | Decreased INR | No Listed Interaction |
|---|---|---|---|
| Amiodarone | √√ | | |
| Sotalol | | | √ |
| Dofetillide | | | √ |
| Procainamide | | | √ |
| Propafenone | √ | | |
| Digoxin | | | √ |
| Verapamil | | | √ |
| Metoprolol | | | √ |
| Atenolol | | | √ |

Amiodarone significantly reduces warfarin metabolism and therefore the dosage of warfarin should be adjusted accordingly (reduce initiation dose by 25%). Patients who develop hyperthyroidism secondary to amiodarone may have an additional increased anticoagulant effect.[13]

## References


1. Petersen P, Boysen G. Godtfredsen J, Anderson ED, Anderson B. Placebo-controlled, randomized trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. Lancet 1989;1:175–179.
2. Gullov AL, Koefoed BG, Petersen P, Pedersen TS, Anderson ED, Godtfredsen J, et al. Fixed mini-dose warfarin and aspirin alone and in combination vs. adjusted dose warfarin for stroke prevention in atrial fibrillation: Second Copenhagen Atrial Fibrillation, Aspirin and Anticoagulation Study. Arch Intern Med 1998;158:1513–1521.
3. Stroke Prevention in Atrial Fibrillation Study. Final results. Circulation 1991;84:527–539.
4. Warfarin versus aspirin for prevention of thromboembolism in atrial fibrillation: Stroke Prevention in Atrial Fibrillation II Study. Lancet 1994;343:687–691.
5. Adjusted-dose warfarin versus low intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial. Lancet 1996;348:633–638.
6. The effect of low-dose warfarin on the risk for stroke in patients with non-rheumatic atrial fibrillation. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators. N Engl J Med 1990;323:1505–1511.
7. Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C. Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. J Am Coll Cardiol 1991;18:349–355.
8. Secondary prevention in non-rheumatic atrial fibrillation after transient ischemic attack or minor stroke. EAFT (European Atrial Fibrillation Trial) Study Group. Lancet 1993;342:1255–1262.
9. Kovacs MJ, Kearon C, Rodger M, Anderson DR, Turpie AG, Bates SM, Desjardins L, Douketis J, Kahn SR, Solymoss S, Wells PS. Single-arm study of bridging therapy with low-molecular-weight heparin for patients at risk of arterial embolism who require temporary interruption of warfarin. Circulation 2004;110:1658–1663.
10. Piazza G, Goldhaber SZ. Periprocedural management of the anticoagulated patient: critical pathways for bridging therapy. Crit Pathways Cardiol 2003;2:96–103.
11. http://coumadin.com. Last accessed October 19, 2005.
12. Marine JE, Goldhaber SZ. Controversies surrounding long-term anticoagulation of very elderly patients in atrial fibrillation. Chest 1998;113:1115–1118.
13. Micromedix. http://www.thomsonhc.com/hcs/librarian. Last accessed October 19, 2005.