Perioperative Management of Anticoagulation
by Steven L. Cohn, MD, FACP
Director, Medical Consultation Service, Kings County Hospital Center, Clinical Professor of Medicine, SUNY Downstate, Brooklyn, NY

Slide 1: Perioperative Management of Anticoagulation
Learning Objectives

After taking part in this activity, participants should be able to:

- Understand risks of bleeding and thromboembolism in patients taking anticoagulants

- Discuss options for perioperative management of anticoagulation

- Review ACCP recommendations regarding bridging therapy
In order to decide how to manage the patient's anticoagulation before surgery, you need to take into account the balance between the risk of bleeding and the risk for thromboembolism. As far as bleeding risk is concerned, you need to go over the patient's anticoagulation regime—what they are on, how long they have been on it, are they stable; the type of surgery, in terms of the bleeding risk for the operation that is planned; and the patient's comorbid conditions or risk factors for bleeding. On the other hand, the risk for thromboembolism depends on why the patient is on anticoagulation in the first place. Did they have a venous thromboembolism (VTE)—a deep vein thrombosis (DVT) or a pulmonary embolism (PE)? Did they have an arterial embolism? Or did they have a mechanical prosthetic heart valve?
If we look at the risk for thromboembolism, that means if a patient does not take anticoagulation before surgery, it depends on why the patient was on anticoagulation as I just mentioned. If they had a VTE, and it has been less than one month since the time they had it, there is 40% chance of recurrence or approximately 1% chance per day if they had had less than one month of treatment. Once you get that month of treatment into the patient, the risk then decreases, so with the second and third month, it’s about 10%, and after three months of treatment, the risk is about 5%, and it tends to stabilize around there. There is a risk reduction with anticoagulation of approximately 80%.

If the patient is on anticoagulation because of an arterial embolism and is at the highest risk in the first month after the clot, it’s about 15% or about 0.5% per day. And if the patient has atrial fibrillation, it depends on the patient’s risks factors or the CHADS\textsubscript{2} score, and the risk can vary between 1% and 12% per year. Again, with anticoagulation, there is a risk reduction of about 66%.

If a patient has a prosthetic heart valve, it depends on what type they have. The mechanical mitral valve has approximately twice the risk of an aortic valve, and the risk varies between 8% and 22% per year without anticoagulation, and this is reduced by about 75%.

Ansell J. *Chest.* 2004;126:204S-233S.
If we look at the other side—what's the risk of bleeding if we continue anticoagulation?—you need to find out what the patient’s anticoagulation regimen is, what drug or drugs are they on, what's the intensity of therapy in terms of the INR, what's the duration that they have been on the drug, and have they been stable as far as INR is concerned. You also need to take into account the type of surgery—are they scheduled for a major procedure [or] prolonged surgery? Is there something where there is indirect access to a bleeding site where the patient may be at more risk for bleeding? What's the patient's age, because the elderly are more at risk than a younger patient? What are the patient’s associated comorbidities and risk factors, and what other drugs are they on that affect hemostasis? Are they also on heparin besides warfarin, for example? Are they taking antiplatelet agents, aspirin, or clopidogrel, in addition to the warfarin? All these things add up and have to be taken into account as far as the risk for bleeding. And the estimate for major postoperative bleeding, if you continue anticoagulation, is approximately 3%.
Now, if we look at the consequences of thrombosis and bleeding, what happens if the patient gets a clot or what happens if the patient develops perioperative bleeding? If they have a recurrent venous thromboembolism, approximately 6% of these will be fatal, and a few percent will result in serious disability. If it's an arterial clot, 20% may be fatal, and 40% may cause serious disability. On the other hand, with major postoperative bleeding, only about 3% will be fatal but up to half of these patients will require a reoperation or return to the operating room, and 1% may be left with serious disability. So, this is something the surgeons are definitely concerned about.
What options do we have for perioperative anticoagulation? Well, the first is that we can continue the patient on warfarin and operate with full anticoagulation on board, and a lot of times the surgeons do not want to let us do that.

The second alternative is to discontinue warfarin and do not give anything as far as anticoagulants are concerned or just use subcutaneous heparin prophylaxis perioperatively, and then resume the warfarin as soon as possible postoperatively.

And the third option is to discontinue warfarin preoperatively and give what we call bridging therapy, using either intravenous unfractionated heparin or low-molecular-weight heparin perioperatively while the INR is subtherapeutic, and then resuming warfarin as soon as possible postoperatively and possibly using a bridge again until the patient is therapeutic, using unfractionated heparin or low-molecular-weight heparin in the interim.
A classification for risk of surgical bleeding was developed. It's the Johns Hopkins classification that you see here, and there are five categories based on the invasiveness of the surgery and the expected blood loss. And you can see that for categories one and two there is minimal or minimal-to-moderate blood loss, less than 500 cc, and you can see some of the examples of these procedures including biopsies, like a breast biopsy, arthroscopic surgery, hernia repair, or laparoscopic cholecystectomy. As you move into the categories three, four, and five, there is moderate-to-significant blood loss going upward of 500 cc to as much as 1,500 cc in category five. So, these are procedures such as a thyroidectomy, joint replacement, a Whipple procedure, and intracranial and open-heart surgery.
What procedures can we do without stopping warfarin? Now, this is what the recommendations are, although a lot of surgeons will not necessarily agree with these.
The first is, as far as dental procedures are concerned, restorations, endodontics, prosthetics, simple tooth extractions, cleaning, and periodontal therapy do not need the patient to stop the warfarin.
As far as GI procedures, we can do EGD and colonoscopy, certainly without a biopsy or polypectomy, and you can do ERCP without a sphincterotomy. Again, if a patient is going for a screen colonoscopy, for example, a lot of gastroenterologists do not want to continue the warfarin because if they find something, they feel that they have to do a second procedure; they won't biopsy the patient or remove a polyp at that time.
As far as ophthalmologic surgery, cataract extractions are associated with minimal blood loss and certainly can be done without stopping warfarin, but you may need to find the ophthalmologist who is willing to do that because a number of them are not. Trabeculectomy is another procedure that you can do.
As far as dermatology procedures, most surgery and simple excisions can be done on full-dose anticoagulation. For orthopedic procedures, you can do joint aspirations and soft-tissue injections without stopping anticoagulation, and you can perform electroconvulsive therapy as well.
What happens if the patient shows up in the emergency room or in the hospital and needs urgent or emergent surgery and is on anticoagulation at a therapeutic level?

The first thing you can do is immediate reversal of anticoagulation using either fresh-frozen plasma, primarily, or you can give intravenous vitamin K. It's probably the only time you might give IV vitamin K, although it does not work that fast. And the last option, which we tend not to do—it's expensive and it actually causes clots—is use of recombinant activated factor VII or NovoSeven. This is a drug that is very expensive and is really used for life-threatening bleeding rather than for the most part to reverse anticoagulation. So, this is if a patient really needs to go to the OR quickly, and you do not really have any time to reverse it.

More commonly we will see patients who need to go to surgery within 24 to 96 hours or so—so-called “semi-urgent surgery.” They do not have to go now, but they have to go maybe tomorrow or the day after. In these cases, we can give oral vitamin K at low doses, usually 1 milligram to 2 milligrams, and the reason we do not use higher doses is that we want to prevent resistance to postoperative anticoagulation. So, if you gave 5 milligrams to 10 milligrams, it's going to make it that much more difficult for the patient to get restarted on anticoagulation and get to a therapeutic INR.
In which cases would we use perioperative bridging? In other words, when is a patient at such a high risk of getting a clot that we want to minimize the time that they are off anticoagulation or do not have a therapeutic INR?

Patients who are considered to be at high risk for developing a clot where bridging is advised include three groups:

The first is patients with a mechanical heart valve in the mitral position (an older aortic valve as opposed to the newer ones), or a patient who has a mechanical heart valve who has also had a stroke or a TIA in the past six months.

The second group is patients with atrial fibrillation who have had a recent stroke or TIA within three months; atrial fibrillation with rheumatic valvular disease or a mechanical valve; and atrial fibrillation patients who have multiple risk factors with a CHADS\textsubscript{2} score of five or six. The CHADS\textsubscript{2} score represents the “C” as congestive heart failure, the “H” is hypertension, and “A” is age greater than 75, “D” is diabetes, and “S” is a stroke, and you get two points for that.

The third high-risk group is patients who have had a venous or arterial embolism—who had a recent clot, as far as a VTE is concerned—within three months; or patients who have had history of a VTE and have so-called “severe thrombophilia.” This includes patients with protein C or protein S deficiency, antiphospholipid syndrome, or a homozygous factor V Leiden. These are the high-risk patients where bridging is advised.
The next group of patients is felt to be at moderate risk, and the recommendation here is to use bridging on a case-by-case basis. Patients in this category include those with a bileaflet aortic valve plus one of the factors here: atrial fibrillation, prior stroke or TIA, hypertension, diabetes, heart failure, or age over 75. So, it's basically bileaflet aortic valve plus the CHADS₂ score or atrial fibrillation.

The second group in moderate risk is patients with atrial fibrillation who have a CHADS₂ score of three to four. And the third group is patients who have had a venous thromboembolism 3 to 12 months before; or patients who have had a recurrent VTE; patients with a VTE who have non-severe thrombophilia (not the things I mentioned before); and patients who have had a VTE who also have active cancer, so they are at risk for recurrence.
The third group is patients who are considered to be at low risk for developing a thromboembolism, and, in these cases, bridging is not recommended. The patients in this group include those with a bileaflet aortic valve replacement who don't have atrial fibrillation or other risk factors for a stroke; patients with atrial fibrillation with a low CHADS\textsubscript{2} score—zero to two—and they didn't have a stroke as part of that CHADS\textsubscript{2} score; or patients who have had a single VTE more than 12 months before who have no other risk factors. So bridging is not recommended for any of these low-risk patients.
If you plan to use bridging therapy, what's the protocol and how do you go about using it? The first thing is that before the procedure, you need to discuss the plan with the surgeon and anesthesiologist so that everybody knows what the plan is and they are in agreement with it. Then you find out what the patient's INR is and if it's in the usual target range between two and three, the recommendation is now to stop warfarin at least five days before surgery. It used to be four days, but it's now five days or four doses. However, if patients have a high INR, the recommendation is to stop the warfarin six days before, but typically we stop at five days before. You can check the INR the day before surgery, and if it's still elevated, some people will recommend giving a small dose of vitamin K, 1 milligram to 2 milligrams by mouth. After you have stopped the warfarin for five days, or you plan to stop it five days before, when do you start your bridging therapy with low-molecular-weight heparin or unfractionated heparin? And the recommendation is to start therapeutic dose anticoagulation with one of the heparins 36 hours after the last warfarin dose. They prefer low-molecular-weight heparin over IV unfractionated heparin for cost-effective reasons. The patient can stay out of the hospital, and it doesn't cost as much as being hospitalized. You need to check the PTT if the patient is on IV unfractionated heparin. You do not need to monitor anything if the patient is on low-molecular-weight heparin.

Now, when it comes down to when to stop the dose before surgery, for the low-molecular-weight heparin, the last dose is given 24 hours before surgery. So, if a patient is going for surgery tomorrow, I will stop it the morning before, which is now. If the patient is on IV unfractionated heparin, the recommendation is to stop it at least four hours before surgery. I usually tend to stop it six hours and sometimes as much as eight hours before.

You should also check the INR on the morning of surgery just to be sure that it's not in the therapeutic range, and most people like it to be less than 1.5.

As far as what you can use for bridging therapy, the low-molecular-weight heparins that have been used are enoxaparin 1 milligram per kilogram twice a day, most commonly, or dalteparin 100 to 120 units per kilogram every 12 hours.
Now that the patient has had surgery, do you continue the bridging protocol after the procedure has been done? The first thing is that you need to consider the bleeding risk of the surgery. For minor procedures, they feel that you can restart the low-molecular-weight heparin or IV unfractionated heparin 24 hours postoperatively, but again that is assuming adequate hemostasis in patients who are not at high risk for bleeding, and this is something that should be discussed with the surgeon.

On the other hand, if you feel the patient had major surgery or high-bleeding risk surgery, then the recommendation is to delay restarting therapeutic dose anticoagulation for at least 48 to 72 hours. That's one option. You can use a prophylactic dose for the first one to three days, rather than a full dose, or avoid using postoperative anticoagulation with heparin completely. You should restart the patient’s warfarin 12 to 24 hours post-op. Typically, it’s done on the evening they have the surgery, assuming again that adequate hemostasis exists. And then you need to start checking the INR the day after that, and you should be checking platelet counts every three days if the patient is on unfractionated heparin; less so if they are on low-molecular-weight heparin. And you will discontinue your low-molecular-weight heparin or IV unfractionated heparin once the INR is greater than or equal to two for 24 hours.
So, to summarize the important points for perioperative anticoagulation, you need to assess and balance the risks of bleeding if you continue anticoagulation or developing thromboembolism if you discontinue anticoagulation before surgery. Next, it's important that you discuss in advance with the surgeon and anesthesiologist your plan for management. You can continue anticoagulation for low-risk surgery because the risk of bleeding with the procedure is less than the risk of getting a clot if you discontinue it. You can stop anticoagulation for low-risk patients, meaning patients who are unlikely to develop a clot but more likely to bleed. You can use bridging therapy for patients at high-risk for developing clots, and you should individualize the plan for those patients felt to be at moderate risk. So, hopefully, by using these recommendations from the American College of Chest Physicians, you will feel more comfortable the next time you have to manage your patient on anticoagulation when they go for a surgical procedure.