

Anticoagulation Protocol

This protocol is developed to provide guidance for the use of anticoagulation following renal transplantation. It is understood that the principles outlined below should be the starting point for the use of anticoagulation but that the patient's clinical course may dictate deviations from the protocols outlined below.

Risk and rationale

Prevention of renal vein or renal artery thrombosis, and to a lesser extent, venous thromboembolism, constitutes the major rationale for consideration of perioperative anticoagulation. At the same time, the risk of hemorrhage after a vascular procedure such as renal transplant must be considered. It should also be considered that there are no randomized controlled trials in transplantation to guide therapy, therefore this approach and these protocols are based on single center retrospective studies and extrapolation of RCTs from other clinical situations. This policy initially divides renal transplant candidates into three groups according to their putative risk for postoperative vascular thrombosis and puts forward an anticoagulation protocol for each group. An important aspect of this risk stratification is a history of a significant thrombotic event. We have defined this as follows:

Significant thrombotic events definition

It is recognized that not all thrombotic events are the same in their severity, potential disability or in the implications that they carry for underlying risk of subsequent thrombotic events. The determination is ultimately up to the clinician but the following guidelines should be considered.

- A single episode of a DVT with an inciting condition, since adequately treated and the inciting condition removed (eg, a DVT after a central line, over a year ago) and without a biochemically defined thrombophilia should not be considered a significant thrombotic event
- Vascular access thromboses, without a biochemically defined thrombophilia and where anticoagulation was not considered or implemented should not be considered a significant thrombotic event.
- A patient on chronic anticoagulation for a previous thrombotic event where the workup was not adequate or where adequate records cannot be obtained to determine causality should be considered to have had a significant thrombotic event.
- If a determination of whether an event should be considered a significant thrombotic event, it is probably better to err on the side of caution and consider it significant.

Risk groups are stratified as follows:

Low Risk

- No known biochemical thrombophilia
- No history of significant thrombotic events
- Patients on warfarin for atrial fibrillation only without any history of thrombotic events

Moderate Risk

- Biochemical thrombophilias without previous history of any thrombotic events

- Previous significant thrombotic event but without an accompanying biochemical thrombophilia, not on chronic anticoagulation.
- Intraoperative vascular anastomotic problems of minimal or moderate severity (eg. Arterial anastomosis needed to be redone because of poor perfusion or transient occlusion with causative factor removed)
- IVC filter in place due to DVT/PE for causes subsequently successfully treated (eg, DVT after trauma, prophylactic filter placed).
- Patients on warfarin for multiple vascular access thromboses without biochemical thrombophilia.
- Surgical anatomical considerations otherwise not stated above.
- Prior use of birth control pills within 30 days of surgery

High Risk

- Current biochemical thrombophilia with previous history of any thrombotic event
- History of unexplained significant thrombotic events in the absence of biochemical thrombophilia
- Severe intraoperative or postoperative vascular problems (eg after return to OR for thrombosis, or multiple re-dos of artery with questionable perfusion)
- Prosthetic cardiac valve on anticoagulation (certain patients with prosthetic aortic valves and preserved EF may be downgraded to moderate risk after consultation with cardiology)
- Surgical, medical or anatomic consideration otherwise not stated above (for example, high titer APAb should be considered high risk and not moderate risk even without a history of thrombotic events)

Biochemical Workup

Current antithrombotic workup includes: history and physical, review of past thrombotic events and antiphospholipid antibodies, lupus anticoagulant, Factor V Leiden, $\beta 2$ glycoprotein levels, and prothrombin gene mutation.

Perioperative Protocols

Low Risk Patients

- Perioperative anticoagulation should be limited to recommended venous thromboembolism prophylaxis per patients VTE risk category

Moderate Risk Patients

- Recommended VTE prophylaxis per patient's VTE risk category
- Intraoperative heparinization (5000U) before clamping

- Maryland protocol heparin postoperatively (300 U/hr day 1, 400 U/hr day 2, no PTT goal), to start between 2 and 4 hours postoperatively to continue for 48-72 hours
- Antiplatelet therapy (clopidogrel 75mg daily) for 4 weeks postoperatively starting 24-72 hours postoperatively. Loading dose at discretion of the team

High Risk Patients

- If chronically anticoagulated, reverse warfarin (please refer to Chest: Guidelines, Chest 2012 Feb; 141(2 Suppl): e 326S-e350S
 - 133:299-339S), place on heparin gtt, discontinue 4 hours previous to incision. INR goal of <2.5 before going to OR.
- Intraoperative heparinization before clamping (5000 units)
- Continue heparin gtt through OR (if problems with perioperative hemostasis, may discontinue heparin gtt, restart with Maryland dose heparin in PACU, then gradually increase to therapeutic PTT as hemostasis allows)
- No bolus vascular heparin gtt protocol to be used.
- Transition to warfarin. INR target to be determined by underlying condition.
- Duration of warfarin therapy may be determined by underlying condition but should in all cases be a minimum of 4 weeks.

Patients requiring long term anticoagulation.

For transplant patients requiring long term anticoagulation, we recommend using either a Vitamin K Antagonist (VKA) such as warfarin or a DOAC. The DOAC of choice is apixaban based on cumulative data from current randomized controlled trials. The following conditions will be observed:

- Conversion from parenteral anticoagulation to oral VKAs will be accomplished in hospital
- Apixaban will be used when the eGFR is consistently above ml/min/1.73m²
- We will wait one month from transplant to achieve stable eGFR before converting a patient previously using a VKA to apixaban

The above protocols are recognized to be a starting point for therapy. The risk of perioperative thrombosis is greatest in the first two weeks and is negligible after 4 weeks. As the risk changes over time, there are likely many scenarios where the anticoagulation protocol may need to be adjusted for conditions that arise a week or two postoperatively (e.g., a moderate risk patient for an intraoperative issue who needs a biopsy at three weeks would likely be best served by early discontinuation of anticoagulation). The operating surgeon will make the ultimate decision as to initiating the protocol.

DOAC use Pretransplant

For transplant candidates on DOAC therapy, MTP requires they be converted to a VKA prior to transplantation. Rationale: there are no recommended reversal agents for us prior to surgery. Thus DOAC therapy poses unacceptable risk of bleeding complications. The timing of conversion will be decided by the transplant team.

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