ANTICOAGULATION AND ANTIPLATELET RECOMMENDATIONS FOR MCS PATIENTS

Purpose: Combined anti-coagulation with anti-platelet therapy is provided to prevent thromboembolism, which is a risk associated with mechanical circulatory support devices. Simultaneously, the adverse risk of bleeding should be minimized.

Considerations: Following discharge, anticoagulation will be managed by the UWMC Anticoagulation Clinic. Exceptions include patients in Skilled Nursing Facilities and patients who request transfer to local and/or remote anticoagulation clinics. Nevertheless, we encourage patients to obtain anticoagulation management through the UWMC ACC. There are reports describing increased platelet aggregation and endothelial activation in the setting of infection, particularly bacteremia, resulting in increased risk of stroke. In this setting, antiplatelet therapy may need to be intensified.

** Please note that we strongly recommend venous draws only for INR, as point-of-care machines can yield variability in results.
** Further, we strongly advise against holding warfarin in the setting of over-anticoagulation, in the absence of major bleeding.
** We strongly recommend that a single tablet strength of warfarin (1mg, 2mg or 5mg tablets), be dispensed in order to maximize dosing flexibility.

I. HEARTMATE II, HEARTMATE 3 and HEARTWARE Ventricular Assist Devices (VADs)

A. Post-Operative Heparin

1. Intra-operative anticoagulation will be reversed prior to leaving the operating room after implantation of VAD.

2. Start IV heparin infusion at 500 units/hour POD 0 at midnight if CT output <50ml/hr, if hemodynamically stable and if hematocrit is stable not requiring blood transfusion.

3. Advance heparin infusion at 0600 POD 1 to MCS Heparin Protocol if above parameters met.

4. If unable to start at midnight POD 0, start heparin 500 units/hr at 0600 POD 1 if CT output <100 ml/hour. Advance to MCS Heparin Protocol at 1700 POD 1 if CT output remains <100 ml/hour.
5. Monitor paired anti-Xa and PTT values for all heparin infusions, per **MCS Heparin Protocol**

B. **Post-Operative Aspirin**

1. Give aspirin 324mg chewable (81mg x4 tablets) on POD 0 per tube or PO if platelet count is above 100, if patient is hemodynamically stable and hematocrit stable not requiring blood transfusion. Continue aspirin dosing daily thereafter.
2. If unable to start aspirin POD 0 due to the above criteria, start aspirin POD 1.

C. **Post-Operative Warfarin**

1. **Standard risk**
   a) For standard risk patients, target INR 2.5 (goal range 2.0-3.0) in the absence of a separate indication for anticoagulation.

2. **High risk**
   - High risk patients include those with separate indications for anticoagulation and include the following, with INR targets as follows:
     - A-Fib or history of recurrent DVT/PE: Target INR 2.5 (Goal range 2.0-3.0)
     - Mechanical mitral valve: Target INR 3 (Goal range 2.5-3.5)
     - Recurrent venous/arterial thrombosis despite adequate anticoagulation: Higher INR goal (discuss with MCS team)
     - History of major bleeding: These patients will have customized goals, but often will be in the 1.8-2.5 range with target INR 2. In some cases anticoagulation may be stopped or modified per MCS attending discretion only.

3. **Major bleeding**
   a) For patients with major bleeding history during therapeutic anticoagulation, a modified INR goal, specific for each case, will be determined by the MCS team.
   b) Administration of FFP, vitamin K and other factors will be addressed on a case-by-case basis. Routine reversal of high INR values, in the absence of significant clinical hemorrhage, is not indicated unless INR is greater than 7. An attending provider should be contacted prior to reversal.
D. Long Term Antithrombotic Therapy: In general patients will be maintained on:

1. **Warfarin** with goal INR as outlined above:
   - During the implant stay, the patient’s warfarin dose will be increased by 20% at the time of discharge.
   - Management by UWMC ACC is required if available.
   - Patients should be instructed to test INR at hospital-based laboratories and to complete blood draw by 8AM.
   - INR testing using venous blood draw is required; finger stick testing is not the standard of care.
   - A minimum of once-weekly INR testing/ACC visits during the first 3 months s/p LVAD implantation should be expected by the patient.
   - 2mg tablets are recommended for greater dosing flexibility.

2. **Chewable ASA** 324mg (81 mg x 4) administered orally once daily in most cases.

3. For patients with **confirmed aspirin allergy or suspected pump thrombosis**:
   - Change from aspirin to clopidogrel (Plavix) 75mg PO for destination therapy patients or for status 7 bridge-to-transplant patients.
   - If a destination therapy patient is switched to transplant candidate status, or if a bridge-to-transplant patient is re-activated, antiplatelet therapy should be switched from clopidogrel (Plavix) to aspirin prior to transplant listing.

4. For patients with **major or recurrent bleeding**, consider (a) decreasing ASA to 81 mg daily and/or (b) decreasing INR target goal.

E. Management of sub-therapeutic anticoagulation

1. Prior to initiating bridge therapy, confirm INR test results:
   - Repeat INR using a venous sample if original sample was obtained inadvertently by point-of-care finger stick testing.
   - Repeat INR at UWMC if original sample was obtained at an outside lab.
2. Bridge Therapy Options:

a) **Outpatient bridging with enoxaparin (Lovenox)** – consider in the following situations:

- Patient is greater than 60 days post-implant
- Patient does not have active bleeding
- Patient does not have a history of major bleeding or thrombosis
- Patient has estimated CrCl > 30 ml/min
- Patient’s total body weight is < 140kg
- If a patient remains sub-therapeutic on warfarin for > 5 days, inpatient bridging with IV heparin will be necessary
- In patients with CrCl 30-60 ml/min exposed to enoxaparin, an anti-factor Xa trough can be considered to guide frequency of dosing; measuring peak anti-factor Xa levels is not recommended
- Dosing recommendations enoxaparin (Lovenox):
  - CrCl > 30 ml/min: enoxaparin 0.5mg/kg SQ q12h
  - CrCl < 30 ml/min: admit for IV heparin

b) **Hospital admission for IV heparin** – used in the following situations:

- Patient is less than 60 days post-implant
- Suspected pump thrombosis or history of pump thrombosis.
  NOTE: for patients with a history of pump thrombosis, a single dose of enoxaparin 0.5mg/kg SQ should be administered by the patient while en route to the hospital for admission, unless otherwise contraindicated.
- History of thromboembolic or hemorrhagic stroke
- When enoxaparin is contraindicated due to impaired renal function or excessive total body weight
- History of major and/or recurrent bleeding (GI, epistaxis, etc.)
- History of HIT (fondaparinux may be considered, but has traditionally not been utilized in our program)
## c) Process for patient management prior to admission for IV heparin

<table>
<thead>
<tr>
<th>Blood draw</th>
<th>Patient Location</th>
<th>Process</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UWMC</strong></td>
<td>At UWMC</td>
<td><strong>ACC pharmacist</strong>&lt;br&gt;• contact VAD coordinator to report subtx INR.&lt;br&gt;• enter note in EPIC &lt;br&gt;<strong>VAD coordinator</strong>&lt;br&gt;• arrange hospital admission&lt;br&gt;• enter note in EPIC&lt;br&gt;• send electronic message to MCSAdmit and contact admitting physician</td>
</tr>
<tr>
<td><strong>UWMC</strong></td>
<td>has left UWMC and can arrive at UWMC in 1-2 hrs</td>
<td><strong>ACC pharmacist</strong>&lt;br&gt;• contact VAD coordinator to report subtx INR.&lt;br&gt;• enter note in EPIC to document conversation&lt;br&gt;<strong>VAD coordinator</strong>&lt;br&gt;• contact patient to return to UWMC for admission&lt;br&gt;• arrange hospital admission&lt;br&gt;• enter note in EPIC&lt;br&gt;• send electronic message to MCSAdmit and contact admitting physician</td>
</tr>
<tr>
<td><strong>UWMC</strong></td>
<td>has left UWMC and cannot arrive at UWMC until &gt; 2 hrs</td>
<td><strong>ACC pharmacist</strong>&lt;br&gt;• contact VAD coordinator to report subtx INR.&lt;br&gt;• <strong>recommend loading dose of warfarin</strong>&lt;br&gt;• enter note in EPIC to document conversation&lt;br&gt;<strong>VAD coordinator</strong>&lt;br&gt;• contact patient to return to UWMC for repeat INR testing, <strong>to take loading dose of warfarin</strong>, and for possible admission&lt;br&gt;• arrange hospital admission if repeat INR is subtx&lt;br&gt;• enter note in EPIC&lt;br&gt;• send electronic message to MCSAdmit and contact admitting physician&lt;br&gt;• contact ACC pharmacist if repeat INR is therapeutic; ACC will contact patient to arrange further dosing and followup</td>
</tr>
<tr>
<td><strong>External lab</strong></td>
<td>Can arrive at UWMC in 1-2 hrs</td>
<td><strong>ACC pharmacist</strong>&lt;br&gt;• contact VAD coordinator to report subtx INR.&lt;br&gt;• enter note in EPIC to document conversation&lt;br&gt;<strong>VAD coordinator</strong>&lt;br&gt;• contact patient to return to UWMC for repeat INR testing and possible admission&lt;br&gt;• arrange hospital admission if repeat INR is subtx&lt;br&gt;• enter note in EPIC&lt;br&gt;• send electronic message to MCSAdmit and contact admitting physician&lt;br&gt;• contact ACC pharmacist if repeat INR is therapeutic; ACC will contact patient to arrange further dosing and followup</td>
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</tr>
</tbody>
</table>
d) if inpatient admission is delayed > 2 hrs, patient should be sent to the UWMC ED for initiation of IV heparin

3. **Bridge therapy decision tree**: follow the table below

<table>
<thead>
<tr>
<th>GOAL INR</th>
<th>TIME SINCE LVAD PLACEMENT</th>
<th>INCIDENT INR (Venous sample)</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target: 2.5 Goal: 2-3</td>
<td>&lt; 60 days</td>
<td>&lt; 2.0</td>
<td>Admit for IV heparin bridge. Discharge when INR &gt; 2.2</td>
</tr>
<tr>
<td></td>
<td>&gt; 60 days</td>
<td>&lt;2.0</td>
<td>Bridge with enoxaparin if not contraindicated, or admit for heparin. *If not admitted reload warfarin x1-2 days. Repeat INR in 1-2 days. If admitted, discharge when INR &gt; 2.2</td>
</tr>
<tr>
<td>Target: 3 Goal:2.5-3.5</td>
<td>&lt; 60 days</td>
<td>&lt;2.5</td>
<td>Admit for IV heparin bridge. Discharge when INR &gt; 2.7</td>
</tr>
<tr>
<td></td>
<td>&gt; 60 days</td>
<td>&lt;2.5</td>
<td>Bridge with enoxaparin if not contraindicated, or admit for heparin. *If not admitted reload warfarin x1-2 days. Repeat INR in 1-2 days. If admitted, discharge when INR &gt; 2.7</td>
</tr>
<tr>
<td>Target: 2 Goal: 1.8-2.5</td>
<td>&lt; 60 days</td>
<td>&lt;1.8</td>
<td>Admit for IV heparin bridge. Discharge when INR &gt; 2.0</td>
</tr>
<tr>
<td></td>
<td>&gt; 60 days</td>
<td>&lt;1.8</td>
<td>Bridge with enoxaparin if not contraindicated, or admit for heparin. *If not admitted reload warfarin x1-2 days. Repeat INR in 1-2 days. If admitted, discharge when INR &gt; 2.0</td>
</tr>
</tbody>
</table>

**F. Management of Supra-therapeutic anticoagulation**

<table>
<thead>
<tr>
<th>INR</th>
<th>CLINICAL SYMPTOMS</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5.0</td>
<td>No sign of bleeding, hemodynamically stable</td>
<td>Manage on an outpatient basis. Avoid holding doses of warfarin</td>
</tr>
<tr>
<td>5.0 or greater</td>
<td>No sign of bleeding, hemodynamically stable</td>
<td>Admit to hospital for observation; do not reverse INR. Avoid holding doses of warfarin</td>
</tr>
<tr>
<td>7.0 or greater</td>
<td>Admit regardless of clinical symptoms</td>
<td>Admit to hospital; contact attending for guidance for reversal</td>
</tr>
<tr>
<td>For all INR levels</td>
<td>If patient is bleeding and hemodynamically unstable</td>
<td>Admit to hospital; contact attending for guidance for reversal</td>
</tr>
</tbody>
</table>
II. SYNCARDIA TAH-T (TOTAL ARTIFICIAL HEART)

A. **Peri-operative management**

   - Intra-operative anticoagulation will be reversed prior to leaving the operating room after implantation of TAH device.
   - Once post-operative bleeding is minimal (i.e. CT output is less than 50 cc/hr), initiate heparin per **MCS Heparin Protocol**.
   - Patients are maintained on heparin until their INR is therapeutic for long-term management (as below). (Can consider using heparin until serum pre-albumin level is > 20 and the serum albumin level is > 2.8 based on recommendations from SynCardia. The goal is to remain on heparin until end organ function has stabilized. This may require ~ 30 days in many cases.)

B. **Long Term Care** — Once end organ function has stabilized and the patient is preparing for long term maintenance therapy or home therapy:

   - Warfarin is administered to achieve target INR 3.0 (goal range 2.5-3.5)
   - Once INR > 2.5, consider discontinuing heparin
   - Chewable ASA 324mg PO (81 mg x 4) once daily

IV. CENTRIMAG

A. **Anticoagulation**

   - Once post-operative bleeding concerns have abated, usually after 6-12 hours, and CT output has decreased to < 50 cc per hour, initiate heparin, following **MCS Heparin Protocol**
   - Flow should be maintained at greater than 4Lpm to minimize the risk of clot formation.

B. **Antiplatelet**

   - aspirin 325mg orally once daily

V. IMPELLA

   - Start heparin [or bivalirudin] in purge solution immediately
   - If the patient has no evidence of bleeding, initiate heparin per **MCS Heparin Protocol**, in addition to the heparin purge solution