I. PURPOSE

To provide clinical guidance for the safe clinical management of patients with Ventricular Assist Device (VAD) placement and on anticoagulation/antiplatelet therapies.

II. INDICATIONS

The policy applies to advanced heart failure patients who are awaiting or status-post VAD or TAH placement.

III. EXAMINATION

Physical Examination General appearance, vital signs, weight, VAD parameters, signs of bleeding or thrombosis

IV. ANTIMOAGULANT/ANTIPLATELET THERAPY GUIDELINES

1. Preoperative:
   a. Laboratory data:
      CBC, PTT, INR
      TEG (plain cup only if not on heparin; plain & heparinase cup if on heparin)
      LFTs & LDH
      Plasma hemoglobin
      PFA-ADP & -EPI
      Von Willebrand factor studies with multimer evaluation
      P2Y12 reactivity if recently on inhibiting agent (e.g. Clopidogrel, Prasugrel, Ticagrelor)
   
   b. Goals
      Platelet count >150,000;
      Hemoglobin >11 g/dL;
      INR ≤1.1;
      TEG: R-time <7.5 min, angle ≥60, MA >50;
      PFA: ADP ≤110, EPI ≤150.
   
   c. Interventions:
      - Discontinue antiplatelets (except ASA or Omega-3) at least 5 days preoperatively.
      - Discontinue Warfarin at least 3 days preoperatively.
      - Discontinue Direct Thrombin Inhibitors (DTIs) at least 12 hours preoperatively.
      - Contact surgeon for preferred approach to elevated INR.
      - Consider FFP for elevated TEG R-time or low TEG angle with normal R.
-Consider DDAVP for prolonged PFAs.
-Consider platelet transfusion for low MA or low platelet count.
-Follow CSICU protocol for diagnosis/work-up of HIT.
-For confirmed HIT, use Argatroban per UMMC protocol.
-Check iron studies and begin repletion if deficient. Consider Erythropoietin if hemoglobin < 11 g/dl.

For all patients, administer Pentoxifylline (Trental) 400 mg prior to surgery (typically the evening before if an AM case).

If patient is awaiting elective VAD, start standing Trental at 400mg TID.

If patient is not on a statin, start Atorvastatin 40 mg daily.

2. **Immediately Post-VAD/Correction of Bleeding:**

   a. Laboratory data:
      - CBC, PTT, INR on arrival
      - Plain & heparinase TEG on arrival.
      - Plasma hemoglobin on arrival & every 8hrs x 24 hrs if temporary device or initial value >40mg/dl
      - PFA-ADP & -EPI on arrival

   b. Goals
      Plain cup R-time 5-10;
      Heparinase R-time < 1.5x plain R-time
      Angle (alpha) 55-70;
      MA 50-70;
      Lyse-30 < 7.5%.

   c. Interventions:
      Start Trental at 200mg TID for anti-inflammatory and hemolysis prophylaxis.
      For TEG correction:
      For plain R >10 and > 1.5x heparinase R, give protamine.
      For plain R >10 and < 1.5x heparinase R, give 1 FFP for R 11-15; 2 FFP for R 15-20; 4 FFP for R > 20.
      If R-time is in goal range: consider cryoprecipitate for angle < 55; consider DDAVP for MA 40-50; consider platelet transfusion for MA < 40.
      For R-time > 5 with lyse-30 > 7.5%, give amicar (10g load, then 1g/hr x 5 hrs).
      In patients with severe bleeding:
      Consider empirically transfusing 1 FFP for at least every 2 units pRBC.
      If bleeding is uncontrollable, factor VIIa may be given at implanting surgeon’s discretion.
      Factor VIIa doses ≥30 mcg/kg are contraindicated as they have been associated with a higher risk of thromboembolism in VAD patients.
Stable Postoperative Phase:

a. Laboratory Data

PTT every 6 hours starting with initiation of heparin until therapeutic x2, then daily while on heparin.

PTT every 6 hours starting with initiation of DTIs until therapeutic x2, then daily while on DTIs.

Anti-Xa LWMH if suspect over- or under-anticoagulation with Enoxaparin or Fondaparinux. See hospital guidelines for timing of assay (differs by agent).

PT/INR daily while titrating Coumadin; twice weekly once stable, therapeutic INR x2.

PFA-100 ADP & epinephrine (EPI) daily starting once platelet count >100,000. Two-three times weekly once no longer titrating antiplatelet agents.

TEG: Daily while titrating anticoagulation and antiplatelets. Decrease to two-three times weekly once on stable anticoagulation and antiplatelet therapy.

LDH & plasma Hgb: Every 8hrs x24hrs for temporary devices, daily for permanent devices.

Continue daily through POD14. For any device, if plasma Hgb >40 mg/dL, send confirmatory value within 12 hrs and increase frequency to every 8 hours. After POD14, check twice weekly.

vWF with multimer evaluation: At occurrence of any GI bleed or severe epistaxis, at discharge or 90d postop (whichever comes first) and every 3 months postop afterward.

b. Goals

Plasma Hgb < 10 mg/dL
TEG MA 50-70
PFA-ADP 160-250
PFA-EPI >225
PTT: 45-55 in permanent devices; 45-55 for 24 hours then 60-80 in temporary devices, hybrid BiVADs, or patients with an additional indication for anticoagulation Titrate heparin per Cardiac Surgery nomograms.

If plain TEG R-time is consistently > 15 in permanent devices or >20 in temporary devices, consider decreasing heparin until within range.

INR (once on warfarin): 2.0-2.5 for Heartmate II; 2.5-3.0 for other devices

c. Interventions:

i) Anti-inflammatory/anti-hemolysis prophylaxis
In absence of GI intolerance (dyspepsia/nausea/vomiting), increase Trental to 400mg TID.

Trental should not be held or discontinued for bleeding.

Tolerance is increased by administering tablet instead of oral suspension, giving with food, separating from Dipyridamole by at least 2 hours.

Resume or add statin once liver function tests have normalized, and up-titrate as tolerated.

**ii) Systemic anticoagulation:**

Initiate once postoperative bleeding has resolved (total mediastinal chest tube output \(\leq 30\) ml/hr for 4 consecutive hours; and no other sources of ongoing bleeding noted).

In absence of HIT, start heparin & titrate to goals specified above per Cardiac Surgery nomograms.

Follow CSICU protocol for diagnosis/work-up of HIT. For confirmed HIT, use Argatroban per UMMC protocol.

For patients in whom the goal is prevention or avoidance of HIT, use Bivalirudin at starting dose \(\leq 0.04\) mg/kg/hr; further down-titrate for renal failure using dose-adjustment chart below:

<table>
<thead>
<tr>
<th>Renal Function (GFR ml/min)</th>
<th>Clearance (ml/min/kg)</th>
<th>Half-life (minutes)</th>
<th>% Reduction in infusion dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&gt;90)</td>
<td>3.4</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Mild Impairment (60-80)</td>
<td>3.4</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (30-59)</td>
<td>2.7</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Renal Function (GFR ml/min)</td>
<td>Clearance (ml/min/kg)</td>
<td>Half-life (minutes)</td>
<td>% Reduction in infusion dose</td>
</tr>
<tr>
<td>Severe (10-29)</td>
<td>2.8</td>
<td>57</td>
<td>20</td>
</tr>
<tr>
<td>Dialysis Dependent (off dialysis)</td>
<td>1</td>
<td>310</td>
<td>80</td>
</tr>
</tbody>
</table>

- Goal PTT 60-80 for temporary devices or in patients (with an additional indication for anticoagulation)
- Goal PTT 45-55 for permanent devices.
- Maintain continuous anticoagulation until INR >2 for two consecutive days.

**iii) Platelet inhibition:**

Start dipyridamole (Persantine) at 50mg TID once platelet count \(\geq 50,000\) and TEG MA \(\geq 50\).

Increase for two consecutive PFA-ADP <160 with MA >50; or, Two consecutive MA >70 with PFA-ADP <250 and R-time >5. Maximum dose 450mg TID.

Decrease in 25-50 mg TID increments for two consecutive PFA-ADP >250 with MA <70; or,
Two consecutive MA <50 with PFA-ADP >160. Minimum dose 25mg TID.

In patients with ischemic disease or otherwise high-risk for stroke, add ASA 81mg on postop day 1.

In patients on minimum-dose Persantine:

If PFA-ADP >250 x2 and MA <70; or, If MA <50 x2 and PFA-ADP >160: Discontinue Persantine and start Omega-3 at 1g TID.

Once platelet count is consistently >100,000 and patient is on stable dose of Persantine 100mg TID.

If MA >50 and PFA-ADP <250; or, PFA-EPI <225: Start omega-3 at 1g TID

In patients on max-dose Persantine and on omega-3 1g TID:

If PFA-ADP <160 x2 and MA >50; or, If PFA-EPI <225 x2 and MA >50; or, If MA >70 x2 with R-time >5 and PFA-ADP <250: Add enteric-coated ASA 81mg or increase ASA in ischemic/high-CVA-risk patients.

In patients who continue to are refractory to max-dose Persantine and 1G TID omega-3 or who are intolerant of max doses of either or both, titrate ASA in 81mg increments to a maximum dose of 325mg for PFA-EPI <225 x2 with MA >50.

Clopidogrel (Plavix) 75mg may be considered for patients on max-dose Persantine, ASA, and Omega-3, or who are intolerant of max doses of any of those agents, or who are severely hypercoagulable (MA > 75 despite R-time >5 and PFA-ADP <160) x 2 days.

Permission should be obtained from the attending surgeon before starting Plavix. Discontinue upon listing status 1A for transplant.

Clopidogrel may also be substituted for Dipyridamole to decrease medication regimen complexity in destination therapy patients.

Check baseline P2Y12 activity before starting drug.

Taper off Dipyridamole while following PFA-ADP and TEG-MA.

After 5-7 days on therapy, check P2Y12 reactivity.

In patients with high reactivity (≥240), consider Prasugrel or resume Dipyridamole.

When down-titrating antiplatelet agents for elevated PFAs, low MAs, low platelets, etc., decrease or discontinue clopidogrel first.

In ischemic or high CVA risk patients, taper Dipyridamole, then ASA. In non-ischemics/low CVA risk, ASA first, then Dipyridamole; Omega-3 should be the last agent decreased or stopped.
4. **Special Situations**

   a. **Late Post-Operative Bleeding**

      In general, follow guidelines in 2c) above for correction of TEG to normal. If severe bleeding (>2 units PRBC/24hrs), consider DDAVP if PFA-ADP >160 or PFA-EPI >225.

      If continued bleeding despite DDAVP, consider recombinant vWF (Humate-P) if PFAs remain elevated.

      If MA <50 with ongoing severe bleeding, consider platelet transfusion.

      In patients with GI bleeding, there is anecdotal evidence that high-dose erythropoietin (300-500U/kg/day) for 3-5 days may also be effective. Intravenous administration may also be more effective than subcutaneous. ASA may also be preferentially stopped before other agents if evidence of upper GI bleeding.

   b. **Severe sepsis (Requiring ICU Admission)**

      Discontinue warfarin and initiate continuous intravenous anticoagulation as specified in 3c)ii) above; consider PTT goal 60-80 regardless of device. Consider correcting elevated INR or TEG R-time with FFP once systemic anticoagulation is in place.

      Consider increasing Trental dose to 800-1200 mg TID.

      Consider adding or uptitrating omega-3.

   c. **Hemolysis without evidence of device thrombosis**

      Consider continuous IV fluids.

      Consider CVVH with filtration for large molecules.

      Consider increasing Trental to 800-1200 mg TID.

   d. **Hemolysis with evidence of device thrombosis**

      In addition to the steps outlined in 4c) above, consider systemic anticoagulation with Bivalirudin, (PTT goal 70-100).

      Consider adding continuous Anti-Gp2b3a inhibition if VAD parameters or hemolysis markers do not trend downward within 24 hours on high-dose Bivalirudin.

      If the patient is refractory to the above after > 24 hrs or the VAD is malfunctioning (e.g. frequent pump stoppages): consult attending surgeon for emergent pump replacement.

5. **Outpatient VAD Anticoagulation**

   a. VAD patients will have weekly and prn INR at discharge until in goal x 2: then will have at least biweekly INR.

   b. All out-patient INR’s will be tracked in EPIC on the VAD A/C flowsheet.

   c. Patient will be bridged with lovenox 1mg/kg bid for INR <2.

   d. If INR remains <1.8 for 2 INR checks (3-5 days apart) in a row (while on lovenox); will consider admission for IV heparin and Coumadin titration.
e. **Re-admitted patients**, without concern for thrombosis, will be discharged on lovenox once trending up and INR /+1.8.

f. Patient’s readmitted for concern of pump thrombosis will **not** be discharged on lovenox and will remain on IV heparin or bivalirudin until INR >2.0 x2.

g. Patients with “Alere” monitors will have yearly accuracy validation against UMMS lab

V. **DOCUMENTATION**

The patient’s clinical team shall document in the patient’s electronic medical record as the patient’s clinical condition necessitates including but not limited to any change in the clinical status of the patient and/or changes in the plan of care.

VI. **REFERENCES**

