# 6. Thromboembolic Disease

## Principles

- Patients with thalassemia have a hypercoagulable state.
- Patients with thalassemia should have individualized risk assessments to determine whether a thrombosis risk reduction strategy should be employed.

## Recommendation

- Patients should have an individualized risk assessment for thrombosis. Known risk factors for thrombosis include: splenectomy, age >35, NTDT, transfusion naivety, elevated platelet count, elevated nRBC count, pulmonary hypertension, pregnancy, as well as conventional cardiovascular risk factors.
- Patients who develop thrombosis should be treated according to national standards of practice.
- There is no evidence to support routine thromboprophylaxis in all patients.
- Consider low dose aspirin as primary prophylaxis in splenctomized patients with high platelet counts.
- Consider VTE prophylaxis for 2-4 weeks post splenectomy.

## Background

Beta thalassemia is characterized by a hypercoagulable state and an increased risk of thrombosis. The mechanisms contributing include platelet activation, alteration of red cell membranes, adhesion molecules on endothelial cells, and of the hemostatic factors. The risk is significantly higher in NTDT than TDT. There is also an increased risk of arterial thromboses, namely cerebral infarcts. VTE risk is reduced by regular blood transfusions, and increased by splenectomy. (13 Similar risk factors are associated with ECHO-defined pulmonary hypertension.

Thrombotic complications in thalassemia patient are well known, however, there is still a paucity of robust clinical evidence to derive evidence-based recommendations[435]. Overall the rates of thrombotic complications are higher in NTDT than in TDT. In a pediatric study the thrombosis rate was 4% for TDT and 9.6% for TDT[436]. In the OPTIMAL CARE study, a large study of over 8000 patients, thrombosis occurred 4.38 times more frequently in NTDT patients compared to TDT patients[435]. This study found that age >20, splenectomy, family history of thrombosis, and prior thrombosis were risk for thrombotic complications in TDT patients. Further patients on aspirin had lower rates of recurrent thrombosis. The majority of thrombotic complications in NTDT patients are venous, including deep vein thrombosis, pulmonary embolism, and portal vein thrombosis[437], while a history of transfusions and a hemoglobin > 90 g/L were protective against thrombosis.

There are higher rates of cerebral vascular events in TDT and NTDT patients, with overt stroke in one study reported at 28% of NTDT and 9% of TDT patients[436]. Recent data demonstrate high rates of silent infarcts on MRI are evident on a large percentage of NTDT patients. The risk factors associated with stroke in NTDT are still unclear.

## Intervention

- Splenectomy significantly increases the risk of thrombosis, and careful risk to benefit analysis should be done prior to recommending splenectomy[435].
- Post splenectomy patients with elevated platelet counts should be considered for primary thrombosis prophylaxis with low dose aspirin.
- Patients should have an individualized risk assessment of thrombosis.
    - High risk factors for thrombosis include: NTDT, high number of circulating nRBCs, age >35, a

ferritin > 1000 mcg/L, pulmonary hypertension and splenectomy[435]

- Protective risk factors against thrombosis include: chronic transfusion therapy, maintaining a Hb > 90 g/L

- Transfusion therapy should be considered in NTDT patients that develop thrombosis, or in patients at high risk for developing thrombosis.
- Patients with TDT and NTDT should be considered at high risk for thrombosis when hospitalized or undergoing surgery, and should have appropriate thromboprophylaxis[437].
- Pregnant and post-partum patients with TDT and NTDT are at higher risk of thrombosis espically splectonomized patients, and should be given appropriate thromboprophylaxis.
- There is no role for inherited thrombophilia screening in thalassemia patients.
- For patients with indwelling central venous catheters the risk of catheter associated thrombosis is low, and there is no evidence to support routine thromboprophylaxis[440].
- For adults with thalassemia classical cardiovascular risk factors (atrial fibrillation, hypertension, diabetes, hyperlipidemia) should be routinely screened for and treated according to national guidelines[439].
- Patients who develop VTE or ATE should be treated according to the current standards of practice[437].
- There is currently insufficient evidence to support the use of hydroxyurea or chelation for the prevention of thrombosis.