7. CARDIAC COMPLICATIONS

Principles

- To identify cardiac complications in patients with sickle cell disease (SCD), including left ventricular dysfunction and myocardial ischemia.
- To appropriately monitor and manage cardiac complications.

Recommendations

Left-ventricular Dysfunction

- All asymptomatic adult patients should have a baseline echocardiogram performed.
- Consider baseline echocardiogram in asymptomatic children starting at age 10.
- Any new signs or symptoms of cardiac dysfunction should be investigated with echocardiogram.
- If echocardiogram demonstrates high right-ventricular systolic pressure (RVSP) or pulmonary artery systolic pressure (PASP), right-heart catheterization should be considered to assess for pulmonary hypertension (*see Part II, section 6 on Pulmonary Hypertension and Chronic Pulmonary Disease for more detailed recommendations*).
- Patients who have evidence of left-ventricular dysfunction should be evaluated by a cardiologist.
- Newer load-independent methods such as strain imaging should be considered.

Myocardial Ischemia

- Clinical evaluation in patients presenting with acute chest pain should include screening for possible myocardial ischemia.
- ST changes on ECG or other markers of myocardial ischemia (e.g., cardiac troponin) should prompt cardiologist involvement.
- Echocardiography or MUGA scan can be used to evaluate for fixed focal-wall motion abnormalities.
- Stress-perfusion cardiac MRI or Thallium-201 SPECT scanning at rest and with exercise may be performed to evaluate for fixed and reversible perfusion defects.
- Serial noninvasive studies may be useful to ascertain whether focal abnormalities or perfusion defects are reversible or permanent.
- Optimal management of myocardial ischemia in SCD requires further study, as the underlying pathophysiology appears to differ from typical coronary artery disease.

a. Pulmonary Hypertension and Right-ventricular Dysfunction

Patients with SCD are at increased risk of pulmonary hypertension and right-ventricular hypertrophy (RVH). In children and young adults, a small series study of 32 children found RVH in 25% of subjects, and resting pulmonary hypertension in 16% as estimated by the tricuspid regurgitant jet velocity (TRV).[1] Pulmonary hypertension may be over-diagnosed by echocardiography, and, therefore, direct measurement of pulmonary arterial pressure by right heart catheterization is the gold standard for diagnosis.[2]

See Part II, section 6 on Pulmonary Hypertension and Chronic Pulmonary Disease for in-depth discussion of pulmonary hypertension.

b. Cardiac Iron Overload

Patients requiring chronic transfusion are at increased risk of iron overload. SCD patients on chronic transfusions have lower rates of cardiac iron overload than similarly transfused patients with thalassemia major. Longer duration of chronic transfusion and poor adherence to prescribed chelation therapy are associated with a higher risk of cardiac iron overload in SCD patients.[3]

See Part II, section 14 on Iron Overload for in-depth discussion of cardiac iron overload.

c. Left Ventricular Dysfunction

Chronic anemia in SCD often leads to left ventricular (LV) dilatation, which may progress to eccentric LV hypertrophy with increasing age, and can result in LV diastolic dysfunction. Subclinical cardiac dysfunction may be evident on routine echocardiography screening, but clinical heart failure from LV dysfunction is a late and uncommon occurrence.[4]

The largest study in adolescents and adults was a prospective, multicenter, observational study evaluating 191 stable outpatients over 13 years of age.[5] Compared with normal controls, patients had increased left and right ventricular dimensions, increased left-atrial dimensions, and increased interventricular septal thickness. Diastolic dysfunction was present in 18% of patients, and was an independent risk factor for mortality. Dilated left-chamber dimensions were associated with low hemoglobin level and increased age.[6] Despite these changes, contractility generally remained normal.

Pediatric studies demonstrate LV hypertrophy, LV dilatation and LV diastolic dysfunction compared with controls but normal LV systolic function.[7] Increase in left-ventricular size is inversely proportional to hemoglobin.[8] Using different methods of measurement, contractility is variably reported as normal[9] or reduced.[8,10] Newer echocardiographic methods provide a less load-dependent measure of cardiac function, and offer potential early identification of dysfunction. Using strain imaging, peak longitudinal strain was reduced in patients with normal left-ventricular ejection fraction (LVEF) during a sickle cell crisis[11] and RV longitudinal systolic strain was reduced in children with SCD with normal LV systolic function.[12] Further study of these methods is required to ascertain their role in screening, diagnosis, prognosis, and management of cardiac disease in patients with SCD.

d. Myocardial Ischemia

In patients with SCD and chest pain, myocardial ischemia should be considered in the differential diagnosis. In a group of adult patients prospectively evaluated for chest pain during painful crisis, significant ST-T wave changes were present upon electrocardiogram (ECG) in half of patients (10 of 20). When other noninvasive evaluations were performed, 6 of these patients had focal-wall motion abnormalities on multigated acquisition (MUGA) scan, and/or perfusion defects with thallium-201 scans, suggesting myocardial ischemia. The study was not able to determine whether these defects were permanent or reversible.[13]

Evidence of myocardial infarction has been found in a small proportion of adult SCD patients at autopsy. In a study of 72 patients with SCD autopsied between 1955 and 1982, 10% (7 of 72) showed evidence of myocardial infarction, although no gross obstructive or artherosclerotic lesions were identified in the coronary arteries. During life, 6 of the 7 patients had chest pain clinically.[14] Mechanisms contributing to ischemia in SCD may include microthrombi in the arteriolar circulation, anemia, coronary vasospasm, and vaso-occlusion due to red blood cell sickling. Endothelial dysfunction and increased arterial stiffness in the larger vessels also contribute to the vasculopathy, and have a global effect on cardiovascular function in SCD.[15]

Stress-perfusion cardiac MRI may be superior to radionuclide techniques for the detection of myocardial ischemia. A small study in asymptomatic SCD found reduced perfusion reserve and diffuse fibrosis using MRI techniques.[16]

In a few small studies in children, thallium-201 single-photon emission computerized tomography (SPECT) scanning has shown myocardial perfusion abnormalities in a proportion of asymptomatic[17,18] and symptomatic patients with SCD.[19] In one small case series, myocardial perfusion improved after six months of hydroxyurea treatment.[19] Rates, clinical importance, optimal diagnostic strategy, and management of myocardial ischemia in children with SCD all require further study.

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