

Clinical progress note: Noncardiac complications in adults with congenital heart disease

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INTRODUCTION

Heart disease is the most common congenital defect, affecting 1% of all births in the United States. Due to improvements in outcomes with cardiac surgery, life expectancy has markedly improved over the past four decades with over 90% of congenital heart disease (CHD) patients reaching adulthood.¹ This has resulted in an epidemiological shift, with a generation of patients at risk for the development of cardiac and noncardiac complications² leading to chronic multisystem disease in adulthood. With these comorbid issues, CHD patients consistently require more prolonged, costly, and complicated hospital stays for noncardiac diagnoses with higher associated health care resource utilization.³ This clinical progress note offers an overview of the noncardiac complications of adults with CHD and considerations for the hospitalist provider in managing this unique patient population.

Though CHD embodies a complex and heterogeneous group of cardiac disorders, we will review common noncardiac complications associated with three main categories of disease: two-ventricle physiology, unrepaired cyanotic CHD and Eisenmenger syndrome (ES), and single-ventricle (Fontan) physiology.

TWO-VENTRICLE PHYSIOLOGY

The majority of adults with CHD have repaired, unrepaired, or palliated lesions with two-ventricle physiology. The most frequently seen congenital heart lesions include bicuspid aortic valve, ventricular

septal defect (VSD), atrial septal defect (ASD), atrioventricular septal defect (AVSD), tetralogy of Fallot (TOF), coarctation of the aorta (CoA), D-transposition of the great arteries (D-TGA) and valvular stenotic and regurgitant lesions. Management strategies for extra-cardiac complications for adult CHD with repaired two-ventricle physiology are similar to the general population, with a few special considerations.

Abnormal pulmonary function is common, with spirometry revealing a restrictive lung disease pattern in 44% of adults with CHD compared to 9% prevalence in the general adult population and up to 76% of patients with TOF.⁴ Additionally, recurrent pneumonia, pulmonary hemorrhage, and pulmonary emboli are more common in this population, with pneumonia being one of the leading causes of death.⁵

Risk of infectious disease is increased in adults with CHD compared to the general population, not only due to their structural heart lesions, but also underlying immune dysfunction and associated genetic conditions, such as heterotaxy syndrome or DiGeorge Syndrome.² Endocarditis risk is elevated in repaired and unrepaired CHD and secondary antibiotic prophylaxis is important with extra-cardiac bacteremia-inducing procedures (Figure 1).⁶

Renal dysfunction is common in adults with all forms of CHD, with one study demonstrating up to 50% of young adults having impaired renal function.⁷ In adults with mild renal disease, there is a two-fold increase in 6-year mortality; those with moderate to severe renal dysfunction demonstrate a five-fold increase.⁷

Hypertension is frequently seen in the adult CHD population, with nearly 60% of patients with CoA developing hypertension,⁸

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SBE prophylaxis IS indicated	SBE prophylaxis is NOT indicated
History of infective endocarditis	Bicuspid aortic valve
Prosthetic cardiac valves	Mitral valve prolapse with regurgitation
Unrepaired CYANOTIC heart disease, including palliative shunts and conduits	Valve repair without prosthetic material
Completely repaired heart defect with prosthetic material, device, or stent, for 6 months following the procedure	Acquired valve disease
Repaired CHD with residual defects adjacent to a prosthetic patch or device	Simple atrial septal defect
Cardiac transplant recipients who develop valvulopathy	More than six months from ASD closure or VSD closure, provided there is no residual shunt

FIGURE 1 Conditions for which SBE prophylaxis is and is not indicated. Adapted from Wilson et al.⁶ ASD, atrial septal defect; CHD, congenital heart disease; SBE, subacute bacterial endocarditis; VSD, ventricular septal defect.

regardless of repair or recurrent coarctation. Studies have also suggested a five-fold higher prevalence of intracranial aneurysms in patients with CoA compared to the general population.¹ Blood pressure guidelines are similar to those for the general population.

Patients with L-transposition of the great arteries (L-TGA) and older patients with D-TGA who underwent atrial switch palliation (Mustard procedure) demonstrate two-ventricle physiology, but with a systemic right ventricle. Management of noncardiac complications is similar to non-CHD patients.

UNREPAIRED CYANOTIC CHD AND ES

Cyanosis is seen in several congenital cardiac conditions, most commonly with unrepaired cyanotic disease and ES. Unrepaired cyanotic heart disease represents a unique subset of patients where surgical repair or palliation was not offered, leaving the patient in a persistent cyanotic state since birth, such as TOF, pulmonary atresia, and certain variants of tricuspid atresia. On the contrary, ES is a unique form of PAH that develops due to a systemic-to-pulmonary artery shunt, with shunt reversal over time. The key stages in the progression to ES are illustrated in Figure 2.⁹ Several unrepaired cardiac lesions are associated with ES, including VSD, ASD, AVSD, partial anomalous pulmonary venous return, and patent ductus arteriosus, as well as complex lesions such as conotruncal defects and D-TGA. Regardless of anatomy, the presence of a persistent intracardiac shunt can lead to PAH and subsequent ES. The following review of multisystem complications is seen in patients with both unrepaired cyanotic disease and ES. Although these represent unique physiologies, we will discuss them together as the resultant noncardiac complications show significant overlap.

There is an increased prevalence of chronic pulmonary emboli and hemoptysis. Intrapulmonary hemorrhage can be severe and life-threatening. Small airway compression and airway trapping are often seen and misdiagnosed as obstructive pulmonary diseases with poor response to traditional therapies.

Cyanotic patients develop secondary erythrocytosis. Despite erythrocytosis, phlebotomy should be avoided and only performed in the setting of hyperviscosity syndrome, with volume replacement being

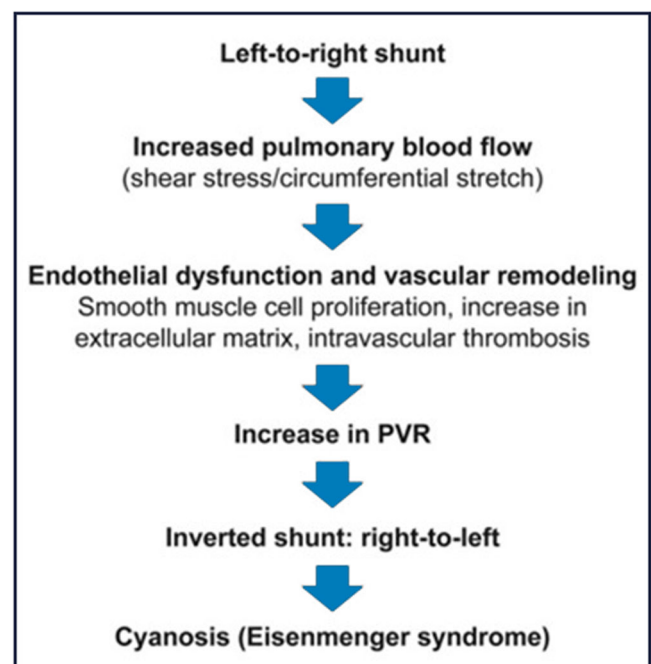


FIGURE 2 Key stages in the development of Eisenmenger syndrome. Reprinted from *Journal of the American College of Cardiology* 53(9):733-740, 2009, M Beghetti and N Galiè, Eisenmenger syndrome a clinical perspective in a new therapeutic era of pulmonary arterial hypertension, Copyright 2009, with permission from Elsevier. PVR, pulmonary venous return.

the preferred treatment.¹⁰ Symptoms of anemia develop at a “normal” hematocrit. Thus, hemoglobin and hematocrit should be interpreted relative to patient’s baseline. ACC/AHA 2018 guidelines suggest iron infusion therapy when transferrin saturation falls below 20%.¹ Increased red cell turnover often results in pigmented gallstone formation.

Baseline cyanosis predisposes patients to coagulopathy, with an increased risk of both bleeding and thrombosis.¹¹ Although the prevalence of pulmonary artery thrombosis is up to 20%, the use of anticoagulation is controversial given bleeding risks.¹² Benefits may outweigh risks in specific cases and expert consultation is advised. Deep vein thrombosis or thrombus formation in the setting of atrial

arrhythmias or transvenous pacing wires increases the risk of paradoxical embolus and stroke.¹² Hemoptysis and menorrhagia are common. Suppression of menorrhagia is beneficial, however, estrogen-containing contraceptives should be avoided. Pregnancy is contraindicated due to high maternal mortality.

Subacute bacterial endocarditis prophylaxis is indicated in all patients with the unrepaired cyanotic disease (Figure 1)⁶ and endocarditis should be of high clinical suspicion with any concerning symptoms. There is an increased risk for brain abscesses due to shunting and should be considered for patients with stroke-like symptoms.¹

Cyanotic kidney disease manifests as hyperuricemia and proteinuria.⁷ Routine monitoring of uric acid levels, electrolytes, and renal function are recommended. Nephrotoxic agents should be avoided and prehydration for contrast studies should be considered. Serum uric acid levels rise in proportion to the degree of hypoxemia, often leading to gout.

Sudden afterload reduction with anesthesia should be avoided as a drop in systemic arterial pressure can increase right-to-left shunting. Dehydration can also precipitate this. Given the presence of a right-to-left shunt, extra measures should be taken to avoid air emboli, including air filters on all intravenous lines. Patients should also avoid extended time at altitude.

UNIVENTRICULAR PHYSIOLOGY

Multiple congenital cardiac defects can lead to univentricular palliation, the most common being hypoplastic left heart syndrome, tricuspid atresia, unbalanced AVSD, double outlet right ventricle, and double inlet left ventricle. Regardless of the congenital cardiac diagnosis, the final univentricular palliative surgery is similar. The resultant "Fontan physiology" involves a single systemic ventricle pumping to the aorta, while systemic venous return occurs passively to the pulmonary vascular bed via superior vena cava and inferior vena cava anastomosis to the pulmonary arteries. Consequently, the cardiac output becomes sensitive to changes in pulmonary vascular resistance and preload conditions. There are many cardiac and noncardiac complications to consider in patients with Fontan physiology. For this review, we will focus on the most common and more severe complications.

In addition to restrictive lung disease from multiple sternotomies, there is chronic endothelial dysfunction from passive pulmonary blood flow through the pulmonary vasculature.¹³ This may lead to increased pulmonary vascular resistance, thereby increasing central venous pressure and decreasing cardiac output.

Not all Fontan patients have cyanosis, however, if they have a fenestration or collateral venous connections, they will have a right-to-left shunt. Knowledge of a patient's baseline hemoglobin is key to management. Except in late-stage failing Fontan circulation, a saturation <85% is considered abnormal and should prompt cardiac and pulmonary workup. Chronic cyanosis can lead to compensatory polycythemia, with comorbid hyperviscosity as well as iron

deficiency.² Although there are no transfusion threshold criteria for Fontan patients, symptomatic anemia is frequently seen, particularly if the hemoglobin level is greater than 4.0 g/dl below the baseline.

Pulmonary embolism is particularly problematic for Fontan physiology, as it directly increases pulmonary vascular resistance and impairs cardiac output.¹⁴ Fontan patients are at increased risk of venous thrombosis due to elevated central venous pressures leading to diffuse venous endothelial dysfunction. It is essential that any CT angiogram evaluating for pulmonary embolism be protocolled appropriately due to abnormal blood flow mechanics in the pulmonary arteries. An improperly protocolled CT angiogram can lead to both false-positive and false-negative scans.

A rare complication of the Fontan physiology is plastic bronchitis (PB), whereby abnormal lymphatic channels in the pulmonary vascular bed lead to thick, plastic-like bronchiolar cast formation.¹ These casts present initially as small airway obstruction but can lead to subsequent large airway obstruction. PB should be considered in the differential of a Fontan patient presenting with pneumonia-like symptoms or complaining of a change in sputum production.

A well-described complication of Fontan physiology is protein-losing enteropathy (PLE). PLE develops as a result of abnormal lymphatic drainage in the intestines due to high venous pressures.¹⁵ This results in chronic diarrhea characterized by massive protein loss and electrolyte disturbances. Lymphopenia, hypogammaglobulinemia, coagulopathy, and bone loss often develop. Fluid management can be challenging due to large volume loss with low oncotic pressure leading to third-spacing. Aggressive fluid and electrolyte management is essential, and there is a substantial risk of morbidity and mortality once PLE develops.

Fontan patients are particularly susceptible to acute kidney injury and chronic kidney disease due to abnormal hemodynamics as well as chronic cyanosis.⁶ This can be exacerbated by the need for iodinated contrast agents and nephrotoxic medications. The estimated glomerular filtration rate can appear normal, while the directly measured renal function is abnormal in up to 50% of patients. Electrolyte management can be challenging, particularly in the setting of PLE. Consultation with a congenital cardiologist is strongly encouraged when managing PLE or PB.

Fontan physiology leads to a unique form of congestive hepatopathy and cirrhosis termed Fontan-associated liver disease. It can include manifestations of ascites, esophageal varices, spontaneous bacterial peritonitis, hepatic encephalopathy, and jaundice.² Coagulopathy due to thrombocytopenia or synthetic dysfunction is common. Additionally, there is an increased risk of hepatocellular carcinoma compared to other etiologies of cirrhosis.¹⁶ Any patient who underwent cardiac surgery prior to 1992 may have been exposed to hepatitis C virus either due to cardiopulmonary bypass or blood transfusions.¹

SUMMARY

Patients with adult CHD encompass a wide-ranging and diverse set of complex physiologies. Noncardiac complications are frequently seen and a cause for frequent and prolonged hospitalizations. It is

imperative for all inpatient providers caring for this unique population to have a basic understanding of these noncardiac complications. Consultation with Adult Congenital Cardiology experts is strongly recommended for assistance in the management of all hospitalized patients with adult CHD and congenital cardiac anesthesia should be involved in discussions of procedural sedation and anesthesia.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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