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Pectus Excavatum: Not Just a Cosmetic Concern



Dawn Jaroszewski, MD, MBA

Pectus deformities are the most common malformation of the chest wall, occurring in approximately one of every 150-1000 births with a 3:1 male predominance. It is more common in the Caucasian race. Pectus excavatum (PEX), where the chest caves inward, occurs approximately five to six times more often than pectus carinatum (outward projection, Figure 1).

The exact cause of PEX is not known, but the primary theory centers around unbalanced overgrowth in the costochondral regions. One study showed that asymmetric PEX patients had shorter ribs on the more severely depressed side of the deformity. Up to 43% of PEX patients have a family history of the disease. It is thought to be a disease of multifactorial inheritance, and the exact genes implicated are unknown. PEX can be associated with scoliosis and connective tissue disorders such as Marfan syndrome , Ehlers-Danlos syndrome, and Noonan's syndrome.

"PEX is of particular concern. In addition to cosmetic considerations, it may result in cardiac compression and cardiopulmonary impairment," says Dawn Jaroszewski, MD, cardiothoracic surgeon at Mayo Clinic in Arizona. "Although some patients are born with pectus, most notice development and significant progression of the deformity during rapid adolescent growth. This may be accompanied by onset or worsening of symptoms." Sternal depression usually involves the lower sternum, with depression of the 4th through 7th costal cartilages. Varying degrees of rotation and asymmetry may be seen.



Figure 1. Example of pectus carinatum deformity.

Symptoms

Symptoms may include disproportional dyspnea on exertion, loss of endurance, exertional and non-exertional chest pain, progressive fatigue, palpitations and tachycardia, exercise-induced wheezing, frequent respiratory tract infections, and syncope/presyncope. Chest wall restriction and decreased thoracic volume are believed to play a role. Cardiac compression may reduce stroke volume. The psychosocial issues associ-

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ated with altered body image can be significant, especially in adolescents and young adults. The importance of "cosmetic concerns" to affected individuals and their families should not be underestimated by providers.

Evaluation

Evaluation needs to be individually tailored to the patient's symptoms. Noncontrast CT of the chest should be done to three-dimensionally assess extent of the bony and cartilaginous deformity. MRI reduces radiation exposure but bone detail is better visualized by CT scan. The *Haller index of severity* should be calculated by measuring the inner width of the chest at the lowest level of the PEX defect, and dividing it by the anterior-posterior distance (between the posterior surface of the sternum and the anterior surface of the spine) again at the lowest level of the defect. The mean calculated index in non-affected individuals is 2.52; an index ≥ 3.25 is considered severe.

Arrhythmias can be documented by electrocardiographic monitoring. Transthoracic or transesophageal echocardiography may be useful in assessing the degree of right atrial and right ventricular compression, and can also document the presence of mitral valve prolapse. Evaluation of the aorta and aortic root should be performed in individuals with suspected or confirmed Marfan syndrome or other connective tissue syndromes. Pre- and post-operative echocardiographic imaging has shown a significant improvement in patients' right ventricular output and flow with surgical repair and correction of cardiac compression (Figure 2).

Static pulmonary function tests are less sensitive in demonstrating compromised pulmonary function than dynamic testing, but may show reduced forced vital capacity and maximal ventilatory volumes.

Cardiopulmonary exercise testing (CPET) is an important tool for assessing the severity and effect of PEX on a patient. CPET can be used to quantify the degree to which PEX affects a patient's ability to move and utilize oxygen. Cardiac limitation due to the defect can be demonstrated by an abnormally low peak max anaerobic VO2 during exercise testing. In studying PEX patients during exercise, patients were unable to reach the stroke volumes of control subjects at any intensity of exercise. Because of this, cardiac output is decreased, which leads to a limitation in peak exercise capacity. Exercise ability and peak VO2 have been shown in some studies to be statistically improved after repair of PEX.

Surgical Repair?

Most patients should be considered for surgical repair if they demonstrate any two of the criteria listed in the table. "Ideally, patients are referred for evaluation during adolescence," says Dr. Jaroszewski. "Repair during the teens allows the patient to complete growth and reduces the chance of recurrence." Correction is readily accomplished in these individuals. Repair in younger children with severe symptoms can be considered. Adult repair, although more difficult, can be performed with good results.

The two most common approaches to repair include various modifications of the open, or Ravitch, approach, and the minimally invasive, or Nuss, approach. The open repair as described by Ravitch in 1949 involves resecting a minimal amount of cartilage, and then placing a metal strut to support the sternum for six to 12 months. The procedure and its variations yield excellent results with low morbidity, and it is ideal for individuals with a combination excavatum and carinatum defect, severe asymmetry, or extensive defects of the upper ribs and cartilage.

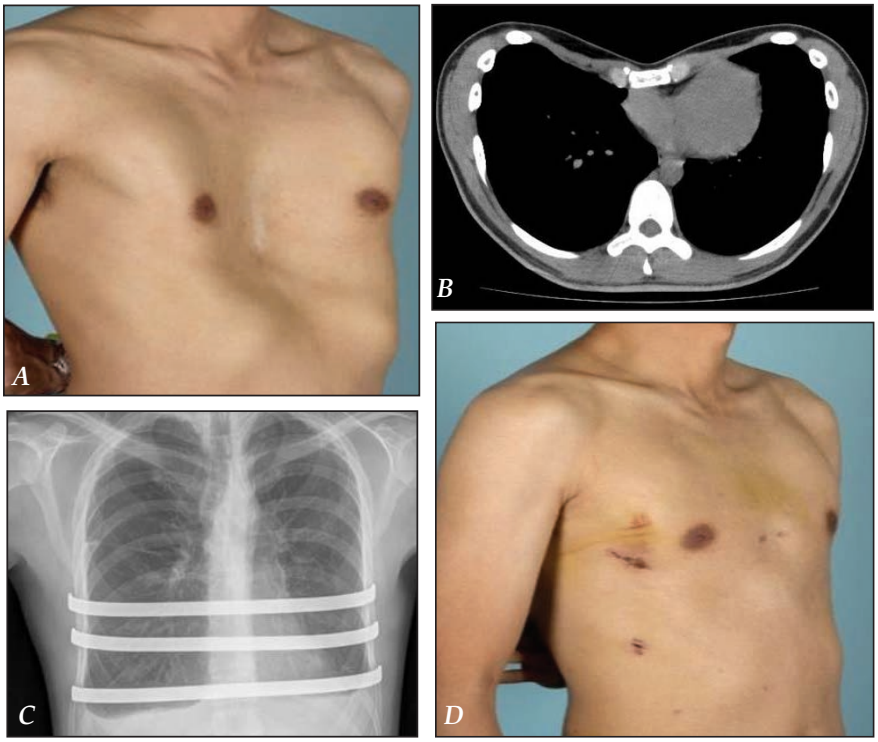


Figure 2. Severe PEX in a 38-year-old male with Haller index of severity of 4.05. A) Chest wall before minimally invasive repair. B) CT scan of chest demonstrating compression of the right ventricle by the deformity. C) Chest x-ray after placement of 3 support bars. D) Chest wall after repair.

Table: Criteria for Surgical Referral

- Severe deformity as noted by Haller Index > 3.25
- Evidence for cardiopulmonary disability
  - Decreased peak anaerobic VO2
  - Restrictive pulmonary disease
  - Right-sided cardiac compression seen by echocardiogram or thoracic imaging
  - Shift of heart into left thorax
- Symptoms of severe defect
- Severe body image disturbance

The minimally invasive approach was first described by Nuss and colleagues in 1998. This procedure involves the placement of a substernal concave bar behind the sternum, which is then flipped into a convex position to elevate the sternum. This bar is left in place for two to three years while the sternum, associated cartilage, and ribs remodel. Advantages include smaller skin incisions, and avoidance of cartilage and bone resection. Cosmetic results are good to excellent in > 85% of patients. Higher rates of complications and more post-operative pain have been reported in some series. Overall, both approaches yield excellent results.

Silicone implants have also been used for cosmetic correction, but the underlying deformity is not corrected. This option is probably best reserved for adults with mild, non-compromising defects.

The progressive cardiopulmonary consequences of untreated PEX are now well recognized. Operative correction by experienced surgeons in high-volume centers is very successful. "Early referral and evaluation is critical to obtaining optimal results," says Dr. Jaroszewski.

RECOGNITION

Professor Jane Somerville, MD was the speaker at the first annual Carole A. Warnes Lectureship, held October 17, 2016 at the Foundation House in Rochester, Minnesota. Dr. Somerville (left), who pioneered the field of adult congenital heart disease, is pictured with Dr. Warnes (right).



Thom W. Rooke, MD, cardiologist specializing in vascular medicine at Mayo Clinic in Rochester, Minnesota, has received the 2016 ATLAS award from Vascular Interventional Advances, a not-for-profit organization dedicated to advancing the field of vascular medicine and intervention through education and research. The ATLAS (A Teacher, Leader, And Scholar) award is presented annually to individuals who have distinguished themselves as scholars and leaders in their respective vascular fields.



Lawrence J. Sinak, MD, cardiologist at Mayo Clinic in Rochester, has received the Mayo Clinic 2016 Laureate Award for Cardiovascular Diseases. This award is presented annually to an individual who has provided outstanding service to the Department of Cardiovascular Diseases and its mission of promoting patient care, research, and education.



Bernard J. Gersh, MD, cardiologist at Mayo Clinic in Rochester, is one of two recipients of the 2016 Gold Medal awarded by the European Society of Cardiology. This award is presented annually to cardiologists for exceptional contributions to the field, and with the hope that the recognition will be an inspiration to future generations of physicians. Dr. Gersh (right) is pictured with his fellow awardee, Professor Alain Cribier, MD of Rouen, France (left). The award was presented at the annual meeting of the society in Rome, Italy.



Life after Fontan Palliation



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Overview

The Fontan operation involves routing of systemic venous return directly into pulmonary circulation bypassing the subpulmonary ventricle. This is an effective palliation in patients with complex congenital heart disease involving single ventricle physiology. The unoperated single ventricle physiology is characterized by intracardiac mixing of oxygenated and deoxygenated blood, creating two primary hemodynamic problems: cyanosis and ventricular volume overload. The Fontan operation separates systemic venous return (deoxygenated blood) from pulmonary venous return (oxygenated blood).

The Fontan operation has undergone several modifications since its original description in 1971 (Figure). The most recent modification is the extra-cardiac Fontan, which involves routing of systemic venous blood to the pulmonary circulation using an extracardiac conduit.

The 20-year survival of the initial cohort of patients who underwent Fontan operation in the 1970s and 1980s was less than 50%. Survivors commonly have Fontan-related morbidities such as arrhythmias, chronic liver disease, protein-losing enteropathy, thromboembolic complications, heart failure, ventricular and valvular dysfunction, renal failure, and plastic bronchitis. "Although the later modifications of the Fontan operation have resulted in improved survival and reduced morbidity, the adult congenital cardiologist still provides care for the older and sicker Fontan cohort with their myriad of comorbidities," according to Alexander C. Egbe, MBBS, MPH, cardiologist at Mayo Clinic in Rochester. "There are limited data to guide management of these patients, making patient care very challenging."

As the adult Fontan population and the complexity of their comorbidities continue to increase, there is an enormous demand on the health care providers caring for these patients. Mayo Clinic has developed a dedicated, multidisciplinary group staffed by a team of congenital cardiologists, cardiovascular surgeons, electrophysiologists, cardiac radiologists, and hepatologists. The purpose is to provide streamlined, individualized and comprehensive care for patients with the different Fontan-associated complications, to develop best practice protocols for the different morbidities, to update treatment protocols as new evidence-

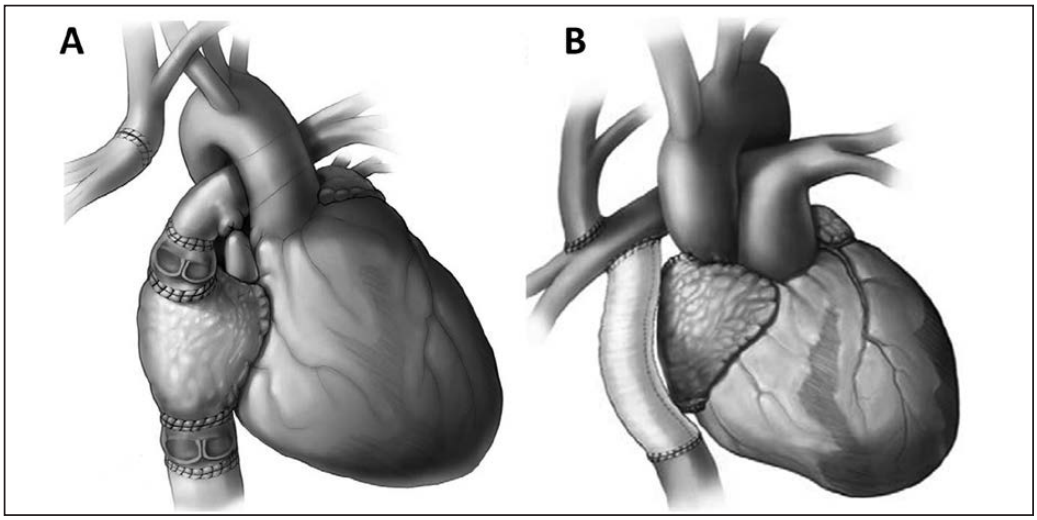


Figure. Schematics of Fontan palliation: (A) The original Fontan procedure, which entailed anastomosis of the distal end of right pulmonary artery to superior vena cava; anastomosis of right atrial appendage to proximal end of right pulmonary artery by means of an aortic valve homograft; closure of atrial septal defect; insertion of a pulmonary valve homograft into inferior vena cava; and ligation of main pulmonary artery. (B) Extracardiac conduit Fontan involving anastomosis of a vascular graft between the IVC and the pulmonary artery which allows more uniform flow with less turbulence.

based data emerges, to integrate laboratory-based and clinical research, and to become a model for other congenital heart disease centers.

Fontan Research

The Adult Congenital Heart Disease group at Mayo Clinic recently embarked on a focused Fontan research program in an effort to narrow the knowledge gaps and improve patient care in this population. This research focuses on management of atrial arrhythmias, thromboembolic complications and the role of cardiopulmonary exercise testing.

Atrial Arrhythmia Management

About two-thirds of adult Fontan patients have a history of atrial arrhythmias. Atrial arrhythmias are poorly tolerated in these patients because of reduced preload and a dependence on atrial systole to achieve adequate ventricular filling. The use of direct current cardioversion for treatment of hemodynamically stable atrial arrhythmias in Fontan patients is often viewed with skepticism because of concerns about thromboembolic complications, and the risk of provoking ventricular arrhythmia and hemodynamic instability.

A review of 152 Fontan patients at Mayo Clinic who underwent direct current cardioversion for treatment of atrial arrhythmias showed that cardioversion was successful in 73% of the patients, and the success rate was higher in the patients who received class I or III antiarrhythmic drugs prior to cardioversion. More importantly, there were no cases of thromboembolic complications related to cardioversion, likely due to meticulous anticoagulation and the liberal use of transesophageal echocardiography to screen for intracardiac thrombus even in the patients with documented therapeutic anticoagulation. Based on this study, the Mayo Clinic practice is shifting towards a more aggressive approach to restore sinus rhythm in all Fontan patients, including anticoagulation for all patients and antiarrhythmic drug therapy prior to direct current cardioversion when clinically feasible.

In spite of the success with direct current cardioversion as described above, arrhythmia recurrence rate was 53% within 36 months. Antiarrhythmic drug therapy has been the first line treatment for chronic arrhythmia management in this population, and a common practice is to keep switching to a different class of antiarrhythmic drug whenever patients experience arrhythmia recurrence. Invasive arrhythmia therapies such as catheter ablation and Fontan conversion surgery have been reserved for those patients who have failed multiple antiarrhythmic drug treatment.

Dr. Egbe and his colleagues reviewed 264 Fontan patients seen at the Mayo Clinic, comparing recurrence rates of atrial arrhythmias in individuals who received medical therapy, catheter ablation, or Fontan conversion surgery. "Our data showed that medical therapy alone was associated with unacceptably high arrhythmia recurrence rate of 93% within 5 years, in contrast to 59% and 41% for catheter ablation and Fontan conversion surgery respectively," says Dr. Egbe. "Furthermore, catheter ablation had an acute procedural success rate of 94% with minimal complication rate in our practice. Based on the data, our practice is shifting towards early referral for catheter ablation as this is associated with better outcomes."

Thromboembolic Prophylaxis and Treatment

There is an increased risk of thromboembolic complications in patients with Fontan palliation, especially in those with concomitant atrial arrhythmias. Anticoagulation in this population is very challenging because of an increased risk of bleeding due to hepatic dysfunction and because procoagulant and anticoagulant factor abnormalities are prevalent in these patients. Dr. Egbe and colleagues studied 278 adult Fontan patients with atrial arrhythmias and estimated a thromboembolic complication rate of 6.5 per 100 patient-years. Anticoagulation with warfarin resulted in a risk reduction by 2.5 events per 100 patient-years compared to aspirin, without an increase in bleeding risk.

The clinical presentation and management of confirmed thromboembolism in Fontan patients is quite different from that of patients with biventricular circulation. Even a small pulmonary embolus can cause important hemodynamic derangement because of the absence of a subpulmonary ventricle. As a result, several published case series have shown a bias for surgical intervention such as thrombectomy or Fontan conversion in these patients. Out of 98 patients who received a trial of anticoagulation for confirmed thrombotic and embolic complications in our series, none of the patients required acute surgical intervention, and 20% of them (mostly with right atrial thrombus and pulmonary embolus) had complete thrombus resolution.

Exercise Testing

The reduced survival of the initial cohort of patients who underwent Fontan operation is, to a large extent, due to the hemodynamic pitfalls of the old style (atriopulmonary) Fontan. In a bid to improve survival and quality of life, Fontan conversion operation (conversion of atriopulmonary Fontan to extracardiac Fontan) has emerged as a rescue strategy for patients with failing Fontan physiology. Unfortunately this operation is associated with perioperative mortality of up to 10% in some series. Appropriate selection of patients who are likely to benefit from this operation is critical because of the associated perioperative mortality risk.

Cardiopulmonary exercise test (CPET) results

in a study of 75 patients who underwent Fontan conversion in the Mayo Clinic practice showed that preoperative peak oxygen consumption was a robust prognostic tool both for predicting perioperative mortality and for identifying patients most likely to experience improved quality of life (exercise capacity and New York Heart Association functional class) after Fontan conversion.

The average age of the adult Fontan cohort at Mayo Clinic is 30-35 years. These patients are in their prime and want to know their expected longevity and risk of cardiovascular adverse events. Unfortunately, no clinical, echocardiographic or demographic parameters have been shown to be prognostic in the Fontan population; however, a review of 145 Fontan patients who underwent serial CPET at Mayo Clinic over 10 years showed that serial peak oxygen consumption was a good predictor of future cardiovascular adverse event (deaths, cardiac surgery and transcatheter interventions). A decline in peak oxygen consumption by ≥3 percentage points peryear was associated with a 2.8-fold risk of cardiovascular adverse events within five years.

The Future of Fontan Research

Chronic liver disease is the second most common comorbidity in the Fontan population, affecting one-third of all adult Fontan patients. A combined heart and liver transplant is currently the only treatment option for this disease. Mayo Clinic is currently enrolling Fontan patients in a pilot study to assess the efficacy of phosphodiesterase-5 inhibitor for the treatment of Fontan associated liver disease (Role of Sildenafil in Fontan Associated Liver Disease [SiFALD]). This is the first study exploring alternative therapy for liver disease in this patient population, and it is hoped that the data will illuminate the clinical landscape of liver disease in this population.

Important Fontan studies have emerged from Mayo Clinic in the past two decades, mostly focused on outcomes after Fontan operation. However, the heterogeneity of the Fontan population makes it difficult to study certain rare Fontan complications even in a tertiary center such as the Mayo Clinic. Doctors are pursuing multicenter collaborations with other congenital heart disease centers of excellence, providing a more in-depth understanding of this disease.

Finally, a laboratory- and animal-based Fontan research program has been initiated, with the primary goals including creating a chronic animal model of Fontan physiology and investigating the role of mechanical assistance for patients with failing Fontan physiology.

"Fontan research at Mayo Clinic has evolved over time: the past was good, the present is better and the future is bright," says Dr. Egbe. For additional information please contact Dr. Egbe at 507-284-2520 or egbe.alexander@mayo.edu.

RECOGNITION

Each year, residents in the Mayo Clinic Internal Medicine Residency Program recognize faculty who have provided exceptional educational experiences throughout the training year. Members of the Department of Cardiovascular Diseases so honored in 2016 were top row, from left: Nandan S. Anavekar, MD, Mackram F. Eleid, MD, Robert D. McBane, MD, and bottom row, from left: Hector I. Michelena, MD, Vuyisile T. Nkomo, MD, MPH, and Peter C. Spittell, MD.



Heart Failure Research at Mayo Clinic in Florida

Cardiologists at Mayo Clinic in Florida are participating in two important clinical trials sponsored by the National Institutes of Health evaluating management of heart failure:

Genomic Analysis of Enhanced Response to Heart Failure Therapy in African Americans. (GRAHF Study).

It has been previously reported that the presence of a functional polymorphism of guanine nucleotide binding protein beta polypeptide 3 subunit (GNB3) influences the therapeutic efficacy of fixed dose combination isosorbide dinitrate/hydralazine (FDC I/H) in African American patients with heart failure reduced ejection fraction (HFrEF) when compared to similar white cohorts. The study will evaluate African American patients who have a history of symptomatic HFrEF (LVEF ≤ 35%, NYHA II, II, or IV) for at least six months and who have been on standard heart failure therapy that includes either ACE inhibitors or both angiotensin II receptor blocker and beta-blocker for at least 3 months. These patients will be treated with FDC I/H for two years. The study involves no placebo or control arm and has two specific aims:

a) Compare the impact of FDC I/H treatment in individuals with the GNB3 TT genotype to those with GNB3 C genotypes.

b) Evaluate LV function after six months of therapy with FDC I/H and compare the impact of therapy on reverse remodeling (increased LVEF and decreased LVEDD) by GNB3 genotype.

Participants will be required to provide a blood specimen for genetic analysis, and will be followed by phone and with a visit every three months. The impact of FDC I/H on clinical outcomes (survival, heart failure hospitalizations, and change in quality of life) will be compared by GNB3 genotype subset. It is hypothesized that patients with the GNB3 TT genotype will demonstrate enhanced therapeutic benefit from FDC I/H. This study will shed light on the influence of global genomic ancestry as a determinant of drug response. For more information about participating in this study, please contact principal investigator Steven Ung, MD at 904-953-7279.

Telemonitoring and Patient-Centric Health Coaching Strategy (Tele-HC Study)

This study is a randomized investigation of the effectiveness of an integrated telemonitoring and patient-centric health coaching strategy in adult patients recently hospitalized with acute decompensated heart failure (ADHF) compared to standard care. Chronic HF is characterized by suboptimal self-care behaviors, frequent hospitalizations, and a national 23% readmission rate at 30 days. The drivers of readmission are multifactorial and it is often attributed to fragmented transitions from the hospital to the home or skilled facility due to a lack of communication and care coordination. Behavioral factors including poor self-care combined with scarcity of economic resources, insufficient social support, and lifestyle choices also contribute to rehospitalization. This study was initiated with the primary objective of testing an integrated telemonitoring and patient-centric health coaching system to reduce hospital readmissions in HF patients. The study entails physiologic monitoring using a remote wireless monitoring BodyGuardian device; patient education; health coaching; self-care with medication adherence; and communication. The primary end point is occurrence of all-cause hospital readmissions or death within 60 days of randomization. A designated medical team will focus on disease management including symptom recognition, adherence to treatment strategies, care coordination, medication matters, and problem solving. Medication management includes initial medication reconciliation and the organization of resources to obtain medications for patients who have socioeconomic challenges. The medical team will also be responsible for onboarding subjects, managing socioeconomic challenges, and providing a nutrition and wellness assessment and goal setting. This study will evaluate whether a comprehensive transitional care model that links providers, patients with chronic diseases, and health coaches will help patients navigate the health care matrix following an acute hospitalization and reduce hospital readmissions. For information about participating in this trial, please contact study investigators Mohamad H. Yamani, MD or Charles J. Bruce, MD, or study coordinator Satya Dhandapani, at 904-953-3421. Dr. Bruce and Mayo Clinic have a financial interest related to this research. This research has been reviewed by the Mayo Clinic Conflict of Interest Review Board and is being conducted in compliance with Mayo Clinic Conflict of Interest policies.

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